IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE, *et al.*, *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION, *et al.*, *Defendants*.	Case No. 1:26-cv-12638-WGY **ORAL ARGUMENT REQUESTED**

PLAINTIFFS' MOTION FOR PRELIMINARY RELIEF UNDER 5 U.S.C. § 705 AND PRELIMINARY INJUNCTION

Pursuant to 5 U.S.C. § 705 and Federal Rule of Civil Procedure 65(a), and Local Rule 7.1, Plaintiffs hereby respectfully move for preliminary relief under 5 U.S.C. § 705 and a preliminary injunction prohibiting Defendants from implementing, enforcing, effectuating, or giving effect to certain agency policies, including those set forth in the FY 2026 HRSA General Terms and Conditions, issued on March 11, 2026, and in Notices of Funding Opportunity ("NOFOs") relating to the Ryan White HIV/AIDS Program, created under the Ryan White Comprehensive AIDS Resources Emergency Act, codified as amended at 42 U.S.C. §§ 300ff–11 to 300ff–140, which prohibit Ryan White funding recipients from acknowledging, affirming, and/or respecting the identities of transgender patients or from providing gender-affirming medical care under the Ryan White Program, and that incorporate or implement Executive Order 14168, "Defending Women From Gender Ideology Extremism and Restoring Biological Truth to the Federal Government."

In support of this request for preliminary relief under 5 U.S.C. § 705 and a preliminary injunction, Plaintiffs rely on the memorandum of law, declarations, and other evidence filed in support of this motion. Plaintiffs respectfully request that the Court grant preliminary relief under

5 U.S.C. § 705 and enter a preliminary injunction in the form set forth in the proposed order attached to this motion.

REQUEST FOR ORAL ARGUMENT

Pursuant to Local Rule 7.1(d), Plaintiffs respectfully suggest that oral argument may assist the Court in considering this motion for preliminary relief under 5 U.S.C. § 705 and a preliminary injunction.

Dated: June 10, 2026

Respectfully submitted,

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Rule 7.1 Certificate of Compliance

I certify that, on June 10, 2026, counsel for Plaintiffs provided notice of this motion, seeking to ascertain defendants' position as to the relief requested herein, to the following attorneys at the U.S. Department of Justice by electronic mail:

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As of the time of filing, the aforementioned counsel at the U.S. Department of Justice acknowledged receipt of the request but were unable to provide Defendants' position by June 10, 2026.

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CERTIFICATE OF SERVICE

I certify that, on June 10, 2026, counsel for Plaintiffs provided a copy of the forgoing motion and any attachments thereto to the following attorneys at the U.S. Department of Justice by electronic mail:

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE; et al., *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION; et al., *Defendants*.	Case No. 1:26-cv-12638-WGY

[PROPOSED] ORDER GRANTING PLAINTIFFS' MOTION FOR PRELIMINARY RELIEF UNDER 5 U.S.C. § 705 AND PRELIMINARY INJUNCTION

Pursuant to 5 U.S.C. § 705 and Federal Rule of Civil Procedure 65(a), Plaintiffs have moved this Court for preliminary relief under 5 U.S.C. § 705 and a preliminary injunction prohibiting Defendants from implementing, enforcing, effectuating, or giving effect to certain agency policies, including those set forth in the FY 2026 HRSA General Terms and Conditions, issued on March 11, 2026, and in Notices of Funding Opportunity ("NOFOs") relating to the Ryan White HIV/AIDS Program, which prohibit Ryan White funding recipients from acknowledging, affirming, and/or respecting the identities of transgender patients or from providing gender-affirming medical care under the Ryan White Program, and that incorporate or implement Executive Order 14168, "Defending Women From Gender Ideology Extremism and Restoring Biological Truth to the Federal Government."

The Court may issue a preliminary injunction when a plaintiff establishes that: "(1) it is likely to succeed on the merits; (2) it is likely to suffer irreparable harm in the absence of preliminary relief; (3) the balance of equities tips in its favor; and (4) an injunction is in the public

interest." *New Jersey v. Trump*, 131 F.4th 27, 33 (1st Cir. 2025) (citation modified). The Court may also stay final agency action to prevent irreparable injury pursuant to 5 U.S.C. § 705 under the same standard. *California v. Kennedy*, 802 F. Supp. 3d 273, 281 (D. Mass. 2025). The Court finds that Plaintiffs have carried their burden to satisfy each of those factors and that immediate relief is appropriate.

Having considered all relevant submissions, evidence, declarations, briefing, and arguments of counsel, and good cause appearing therefore, the Court **GRANTS** Plaintiffs' Motion for Preliminary Relief under 5 U.S.C. § 705 and Preliminary Injunction and **ORDERS THAT**:

1. Pursuant 5 U.S.C. § 705, the provisions of the FY 2026 HRSA General Terms and Conditions, issued on March 11, 2026, and the Notices of Funding Opportunity ("NOFOs") relating to the Ryan White HIV/AIDS Program, including the NOFOs for the Ryan White Program's Part B Supplemental, Part C, and Part F issued in June 2026, which prohibit Ryan White funding recipients from acknowledging, affirming, and/or respecting the identities of transgender patients or from providing gender-affirming medical care under the Ryan White Program are hereby temporarily stayed, postponed, and set aside during the pendency of this litigation. These provisions (hereafter the "Challenged Conditions") include the following:

    a. With regards to the FY 2026 HRSA General Terms and Conditions, the following terms and conditions are hereby temporarily stayed, postponed, and set aside:

        i. The requirement that funding recipients "apply[] sex-based definitions grounded in biological reality";

        ii. The requirement that funding recipients "ensure that all activities funded" under the program be "implemented in a manner consistent with HRSA's mission and strategic priorities," such that they (a) must comply with the

"HRSA priority to recognize that a person's sex as either male or female is unchangeable and determined by objective biology, and to ensure its programs accurately reflect science, including the biological reality of sex"; (b) may not affirm transgender people's identities or provide gender-affirming medical care, which HRSA has deemed "social or medical experimentation" that is part of "radical ideological agendas and policies"; or (c) must certify that they are "compliant with Title IX of the Education Amendments of 1972, as amended, 20 U.S.C. §§ 1681 et seq., including the requirements set forth in Presidential Executive Order 14168 titled Defending Women From Gender Ideology Extremism and Restoring Biological Truth to the Federal Government," and "will remain compliant for the duration of the Agreement" and that these are "material terms of the Agreement"; and

iii. any provision of the Health Resources and Services Administration's General Terms and Conditions, including any version incorporated into or enforced through the Ryan White HIV/AIDS Program NOFOs challenged in this action, or through any future Ryan White HIV/AIDS Program NOFO, award, continuation award, renewal, supplement, or other grant process that is materially similar to the challenged terms and would prohibit Ryan White Program funding recipients from acknowledging, affirming, and/or respecting the identities of transgender patients or from providing gender-affirming medical care under the Ryan White Program.

b. With regards to the Ryan White Program NOFOs issued in June 2026, or thereafter, the following terms and conditions are hereby temporarily stayed, postponed, and set aside:

   i. The requirement that Ryan White Program funding recipients must ensure that "[a]ll activities proposed in [an] application and budget narrative must align with applicable law, including but not limited to statutes, executive orders, federal regulations and applicable judicial holdings," such that it requires alignment and compliance with Executive Order 14168;

   ii. The requirement that funding awards "shall not be used to fund, promote, encourage, subsidize, or facilitate . . . denial by the recipient of the sex binary in humans, or the belief that sex is a chosen or mutable characteristic";

   iii. The requirement that Ryan White Program funding recipients comply with any of the Challenged Conditions in the FY 2026 HRSA General Terms and Conditions, as set forth above; and

   iv. any provision in a current or future Ryan White HIV/AIDS Program NOFO, or in any future notice of award, continuation award, renewal, supplement, or other grant process that is materially similar to the challenged terms herein and would prohibit Ryan White Program funding recipients from acknowledging, affirming, and/or respecting the identities of transgender patients or from providing gender-affirming medical care under the Ryan White Program.

2. Pursuant to Federal Rule of Civil Procedure 65, Defendants, including their employees, agents, servants, attorneys, successors and any person or entity in active concert or participation with them, are ENJOINED from implementing, enforcing, effectuating, or giving effect to the Challenged Conditions—or any materially similar policy that prohibits Ryan White funding recipients from acknowledging, affirming, and/or respecting the identities of transgender patients or from providing gender-affirming medical care under the Ryan White Program—against Provider Plaintiffs and Associational Plaintiffs' Members.

3. It is further ORDERED that the security requirement is hereby waived because Defendants will not suffer any costs from the preliminary injunction and imposing a security requirement would pose a hardship for Plaintiffs. *See* Fed. R. Civ. P. 65(c).

4. Nothing in this Order shall prohibit Defendants from administering the Ryan White HIV/AIDS Program in a manner otherwise consistent with federal law and this Order.

IT IS SO ORDERED.

Dated: _____, 2026

_____
United States District Judge

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE; *et al.*, *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION; *et al.*, *Defendants*.	Case No. 1:26-cv-12638-WGY

MEMORANDUM OF LAW IN SUPPORT OF PLAINTIFFS' MOTION FOR PRELIMINARY RELIEF UNDER 5 U.S.C. § 705 AND PRELIMINARY INJUNCTION

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INTRODUCTION

Effectively addressing the HIV/AIDS epidemic requires affirming, culturally competent healthcare tailored to the health needs of LGBTQ people living with HIV, including transgender people living with HIV. Yet, seeking to turn back the clock to the early days of the HIV/AIDS epidemic, the current administration is deliberately attacking the ability of transgender patients living with HIV who rely on the Ryan White HIV/AIDS Program ("the Ryan White Program") to access needed healthcare. The government thus threatens not only the health and wellbeing of transgender people living with HIV, but also our Nation's ability to finally end the HIV/AIDS epidemic.

As part of the administration's campaign to repudiate the existence of transgender people and single them out for discrimination and opprobrium, Defendants have adopted a policy to prohibit healthcare providers participating in the Ryan White Program from acknowledging, affirming, or respecting their transgender patients' identities, including by prohibiting the provision of gender-affirming medical care as treatment for gender dysphoria. This policy, which effectuates one of the President's executive orders targeting transgender people, is set forth in guidance documents, the Health Resources and Services Administration's ("HRSA") general terms and conditions, and notices of funding opportunity relating to the Ryan White Program (hereafter the "Challenged Conditions," further defined in Plaintiffs' Complaint (at ¶¶ 164–187) and at Background § C, *infra*).

Providers who do not abide by these conditions risk losing access to the critical funding that allows them to care for *all* people living with HIV that rely on the Ryan White Program, which supports over half of all Americans living with HIV. Congress specifically intended Ryan White funding to support comprehensive healthcare for the most vulnerable populations. But when providers are compelled to disavow their transgender patients' existence and deny them necessary

medical care, the trust between the patients and their doctors will be broken and transgender patients will stop showing up for HIV care, risking their lives and public health generally. It is no understatement to say that, because of the Challenged Conditions, people will die.

The Challenged Conditions are not just harmful; they are illegal. They violate the Administrative Procedure Act ("APA"), the Affordable Care Act ("ACA"), the Fifth Amendment, and the First Amendment. Accordingly, and because the Challenged Conditions will cause immediate and grave harm to Plaintiffs, as well as threaten to damage the Ryan White Program's remarkable public health success, Plaintiffs and their patients, respectfully request that this Court temporarily set aside or enjoin the Challenged Conditions pending resolution of this case, just as other courts have done with regard to similar policies and executive action. The status quo will protect not only the lives, health, and wellbeing of the transgender people living with HIV who rely on the Ryan White Program for their healthcare, but also our Nation's HIV care infrastructure.

BACKGROUND

Provider Plaintiffs and Associational Plaintiffs' members are healthcare providers who offer comprehensive HIV care and primary care, including gender-affirming medical care, to their transgender patients living with HIV, through the Ryan White Program.[1] They, along with their transgender patients living with HIV who rely on the Ryan White Program for their healthcare needs, will suffer irreparable harm should the Challenged Conditions go into effect.[2]

A. HIV/AIDS Disproportionately Affects Transgender People.

Transgender people—particularly transgender women—bear a profoundly disproportionate burden of the country's HIV epidemic. Notwithstanding progress to end the

[1] Brody Decl. ¶ 20; Fox Decl. ¶¶ 31–34; Collins-Ogle Decl. ¶¶ 20–23; Doe Decl. ¶¶ 22–27; Roe Decl. ¶ 20; Packett Decl. ¶ 23; Weddle Decl. ¶ 10; Zuniga Decl. ¶ 13.
[2] Brody Decl. ¶¶ 5, 17; Fox Decl. ¶¶ 42–45; Collins-Ogle Decl. ¶¶ 5, 15–16; Roe Decl. ¶ 7; Doe Decl. ¶¶ 8, 14; Packett Decl. ¶¶ 5–6; Weddle Decl. ¶¶ 5–6, 17–18; Zuniga Decl. ¶¶ 5–6.

epidemic, HIV continues to be a major public health concern among sexual and gender minority populations.[3] The risk of acquiring HIV among transgender and other gender-minority individuals is thirteen times that of the cisgender population.[4] According to the Centers for Disease Control and Prevention ("CDC"), transgender people make up 2% of new HIV diagnoses in recent year-to-year data despite comprising only about 1% of the United States population aged 13 and older. *Id.* The CDC further estimates that approximately 14% of transgender women in the United States are living with HIV, with prevalence rates reaching 44% among Black transgender women and 26% among Hispanic/Latina transgender women.[5] This disproportionate impact is driven by structural barriers like stigma, discrimination, poverty, homelessness, and lack of access to culturally competent and gender-affirming healthcare, all of which significantly impair access to HIV prevention and treatment services.[6]

B. Providing Gender-Affirming Medical Care Through the Ryan White Program Furthers the Program's Purpose, as Set by Congress.

Congress created the Ryan White Program as a comprehensive, integrated system of HIV care. The goal of the Program is to offer a safety net for people living with HIV by providing outpatient HIV care, treatment, and support services to those without health insurance or who experience gaps in coverage.[7] Following its initial adoption and implementation, the Ryan White Program was expanded by Congress to address the unmet care and treatment needs of people living with HIV by focusing funding on primary healthcare and support services to enhance access to and retention in care and adherence to daily treatment.[8]

Because HIV is a complex, chronic condition that disproportionately affects medically and

[3] Zuniga Decl. ¶ 19.
[4] Zuniga Decl. ¶ 20.
[5] Abrigo Decl., Ex. A
[6] Zuniga Decl. ¶¶ 24–25; *see also* Zuniga Decl., Ex. D at 1–2.
[7] Weddle Decl. ¶ 16. Packett Decl. ¶ 25.; Collins-Ogle Decl. ¶ 5.
[8] Weddle Decl. ¶ 17.

socially vulnerable populations, Congress structured the Ryan White Program to address the full spectrum of health and supportive service needs of people living with HIV.[9] It does so to prevent new HIV infections, improve health outcomes for people living with HIV, reduce the health disparities affecting people living with HIV, and achieve integrated and coordinated efforts that address the HIV/AIDS epidemic. *Id.* Over half of all people diagnosed with HIV are served through the Ryan White Program, and many would not have access to necessary healthcare services and treatment without the program.[10]

The Ryan White statute repeatedly references coordinated "systems of care," continuity of care, retention in care, and outpatient primary healthcare for people living with HIV. *See* 42 U.S.C. §§ 300ff–11, 300ff–12(b)(4), 300ff–21, 300ff–23(a), (c), 300ff–51, 300ff–71. Consistent with that structure, as HRSA explains, the various parts of the Ryan White Program "give [Ryan White] recipients flexibility to address HIV care needs."[11] The statute authorizes broad categories of outpatient and ambulatory health services, mental health treatment, substance use treatment, medical case management, transportation, outreach, and adherence support services. *See* 42 U.S.C. §§ 300ff–14(c)–(d), 300ff–22(b)–(c), 300ff–51(c)–(d), 300ff–71(b).

Under the Ryan White statute, local planning councils and state consortia are charged with assessing local epidemiological data; identifying unmet service needs among affected subpopulations and historically underserved communities; establishing funding priorities based on the priorities of the communities with HIV for whom the services are intended; and designing coordinated systems of care pursuant to the statute's broad purpose, as set by Congress. *See* 42 U.S.C. §§ 300ff–12(b)(1), (b)(4)(B)(ii), (d); 300ff–23(a), (c); 300ff–27(b)(7)(B).

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[9] Packett Decl. ¶ 25.
[10] Weddle Decl. ¶ 15.
[11] Health Res. & Servs. Admin., U.S. Dep't of Health & Hum. Servs., *Ryan White HIV/AIDS Program: Legislation* (Dec. 2024), https://tinyurl.com/4m3hkcfe [https://perma.cc/D7DK-PZSL].; *see also* Packett Decl. ¶ 27.

Providing affirming healthcare (i.e., care that is mindful and respectful of a transgender patient's identity) and medical treatment for gender dysphoria (i.e., "gender-affirming medical care"), such as gender-affirming hormone therapy, through the Ryan White Program furthers the Program's central goals of retention in care, treatment adherence, and long-term viral suppression for people living with HIV.[12] Patients living with HIV are more likely to remain engaged in treatment when they receive integrated and affirming care addressing their broader healthcare needs.[13] Ryan White-funded providers have long incorporated gender-affirming medical care into integrated HIV treatment models designed to improve adherence and retention in care.[14] Ryan White planning councils, planning bodies, and consortia across the country likewise recognize transgender people as a priority population disproportionately affected by HIV and have prioritized strategies that fund and emphasize gender-affirming care to improve engagement in HIV treatment and health outcomes. *See* Compl. ¶¶ 116–125 (collecting guidance).

C. The Challenged Conditions Prevent Healthcare Providers from Acknowledging their Transgender Patients and Providing Gender-Affirming Medical Care.

This case challenges conditions imposed on recipients of Ryan White funding through Defendants' implementation of Executive Order 14168, *Defending Women From Gender Ideology Extremism and Restoring Biological Truth to the Federal Government*, 90 Fed. Reg. 8650 (Jan. 20, 2025) ("Gender Order"), which directs that federal funding not be used to promote "gender ideology," including through the FY 2026 HRSA General Terms and Conditions ("Updated FY2026 General Terms"), issued on March 11, 2026, and the Ryan White Program Notices of Funding Opportunity ("NOFOs") issued or projected to be issued in June 2026.[15]

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[12] Brody Decl. ¶¶ 5, 17; Fox Decl. ¶¶ 5, 16–18; Collins-Ogle Decl. ¶ 5; Roe Decl. ¶ 7.
[13] Brody Decl. ¶¶ 13–15; Fox Decl. ¶¶ 16–18; Collins-Ogle Decl. ¶¶ 5–16.
[14] Brody Decl. ¶¶ 5, 12–17; Fox Decl. ¶¶ 5, 11, 16–18; Collins-Ogle Decl. ¶¶ 5, 10, 14–15; Weddle Decl. ¶¶ 10, 12, 17; Zuniga Decl. ¶¶ 13–14.
[15] Abrigo Decl., Ex. B (HRSA GTC), Ex. I (Part B Suppl. NOFO), Ex. J (Part C NOFO), Ex. K (Part F NOFO).

The Updated FY2026 General Terms require Ryan White funding recipients to "apply[] sex-based definitions grounded in biological reality" and incorporate HRSA's "strategic priorities," which specify that, "[i]t is a HRSA priority to recognize that a person's sex as either male or female is unchangeable and determined by objective biology, and to ensure its programs accurately reflect science, including the biological reality of sex."[16] The NOFOs incorporate the Updated FY2026 General Terms and further implement them in various ways, such as by prohibiting the use of Ryan White funds for "sex-trait modification procedures" or "to fund, promote, encourage, subsidize, or facilitate . . . denial by the recipient of the sex binary in humans, or the belief that sex is a chosen or mutable characteristic."[17]

The Updated FY2026 General Terms and the NOFOs implement the Gender Order. The Gender Order commands federal agencies to reject recognition of transgender identities and implement policies based on sex assigned at birth, including by denying gender-affirming medical care for transgender people.[18]

Together, the Updated FY2026 General Terms, any similar terms in the NOFOs, and any other actions implementing the Gender Order with regard to the Ryan White Program constitute the "Challenged Conditions" in this case. *See* Compl. ¶¶ 164-187; *see also id.* ¶¶ 156-157.

The Challenged Conditions apply or will apply across Ryan White funding streams, including Parts A, B, C, D, and F, incorporated through HRSA grant conditions and various Notices of Award. Compl. ¶¶164-187. In concert, the Challenged Conditions impose restrictions on Ryan White-funded providers providing integrated HIV care to transgender patients, including hormone therapy and other affirming care delivered as part of outpatient primary healthcare. Compl. ¶¶ 90–

[16] Abrigo Decl., Ex. B (HRSA GTC) and Ex. C (HRSA Priorities).
[17] Abrigo Decl., Ex. D (ADAP NOFO), Ex. I (Part B Suppl. NOFO), Ex. J (Part C NOFO), Ex. K (Part F NOFO).
[18] Abrigo Decl. Ex. E.

103, 164–187. Compliance with the Challenged Conditions would require providers to either (1) refrain from acknowledging, affirming, or respecting the identities of transgender people and from using federal funds to provide medically indicated gender-affirming medical care to transgender patients living with HIV or (2) risk losing critical Ryan White funding necessary to operate their HIV programs and to care for their patients living with HIV, including transgender people.[19]

D. The Challenged Conditions Are Part of a Broader Systematic Campaign Against Transgender People.

The Challenged Conditions do not arise in isolation. They are part of a broader government-wide effort to erase recognition of transgender people and restrict access to gender-affirming medical care. *See generally* Compl. ¶¶ 130–163. They are "part of a constellation of close-in-time executive actions directed at transgender Americans that contained powerfully demeaning language." *Orr v. Trump*, 778 F.Supp.3d 394, 417 (D. Mass. 2025) (documenting actions), *appeal dismissed as moot and injunction vacated on other grounds,* No. 25-1579 (1st Cir. June 5, 2026); *see also Endocrine Soc'y v. Fed. Trade Comm'n*, No. CV 26-512 (JEB), 2026 WL 1257289, at *2 (D.D.C. May 7, 2026); *Talbott v. United States*, 775 F.Supp.3d 283, 330-32 (D.D.C. 2025), *aff'd in part*, *vacated in part, remanded,* No. 25-5087, 2026 WL 1532205 (D.C. Cir. 2026).

E. The Challenged Conditions Will Cause Harm to Plaintiffs and Their Patients.

The Challenged Conditions are particularly harmful in the context of the HIV epidemic because transgender people, especially transgender women of color, experience disproportionately high rates of HIV and significant barriers to healthcare. *See* Background Section A, *supra*.[20] The Challenged Conditions undermine longstanding public health efforts designed to improve engagement in HIV care for populations disproportionately affected by HIV and threaten to

[19] Brody Decl. ¶¶ 5, 17; Fox Decl. ¶¶ 5, 16–18; Collins-Ogle Decl. ¶¶ 5, 15–16; Roe Decl. ¶ 7; Doe Decl. ¶¶ 8, 14, 19; Packett Decl. ¶¶ 5–6; Weddle Decl. ¶¶ 5–6, 17–18; Zuniga Decl. ¶¶ 5–6; Compl. ¶¶ 188–202; Abrigo Decl. Ex. L.
[20] Weddle Decl. ¶ 6; Zuniga Decl. ¶ 6; Brody Decl. ¶¶ 11, 17; Roe Decl. ¶¶ 7, 13.

destabilize integrated HIV treatment systems developed over decades through the Ryan White Program.[21]

The Challenged Conditions thus threaten immediate and concrete harm to Provider Plaintiffs, Associational Plaintiffs' members, and their patients. Ryan White-funded HIV programs are structured around integrated models of care that depend on providers being able to offer affirming, comprehensive, and continuous treatment to transgender patients living with HIV.[22]

Transgender patients living with HIV already face substantial barriers to healthcare engagement, including stigma, discrimination, unstable housing, mental health conditions, and distrust of medical systems.[23] Integrated gender-affirming medical care and care that respects patients' identities promotes trust, retention in care, medication adherence, and long-term viral suppression.[24]

The Challenged Conditions directly threaten those treatment relationships. Being able to acknowledge and respect the identities of transgender patients who rely on the Ryan White Program for their HIV care and other health needs, and to provide them with gender-affirming medical care when indicated through Ryan White funds, is "critical to maintaining patient trust, adherence to antiretroviral therapy, retention in care, and sustained viral suppression." Collins-Ogle Decl. ¶ 5. "Research . . . consistently shows that when transgender people feel supported and affirmed in their identity by health care providers, they are more likely to access HIV testing, engage with pre-exposure prophylaxis, adhere to ART [antiretroviral therapy], and achieve viral suppression." Zuniga Decl. ¶ 35. If Ryan White-participating clinics and providers are prohibited

[21] Weddle Decl. ¶¶ 6, 15–18; Packett Decl. ¶¶ 5–6, 10–13; Zuniga Decl. ¶¶ 6, 12–14; Collins-Ogle Decl. ¶¶ 5, 12–15; Compl. ¶¶ 81–125, 126–129, 143–163.
[22] Brody Decl. ¶¶ 13–17; Fox Decl. ¶¶ 5, 10–11; Collins-Ogle Decl. ¶¶ 14–16; Doe Decl. ¶¶ 13, 22.
[23] Compl. ¶¶ 54–57, 99–103; Brody Decl. ¶¶ 5, 11, 17; Packett Decl. ¶ 32; Zuniga Decl. ¶ 38.
[24] Brody Decl. ¶ 5; Fox Decl. ¶¶ 16–18; Collins-Ogle Decl. ¶¶ 15–16.

from acknowledging and respecting the identities of their transgender patients or lose their ability to provide gender-affirming medical care, patients will be less "open and honest with their healthcare providers about symptoms, behaviors, and healthcare needs," which will lead to "misdiagnosis, missed diagnosis, not being offered preventative health services like screenings, and other adverse health outcomes." Fox Decl. ¶ 40. Causing "transgender patients to lose trust in their healthcare providers and [] clinic[s] in general," in turn, "lead[s] to a lack of engagement in healthcare and avoidance of dealing with acute or chronic illness." Brody Decl. ¶ 17.[25] This can result in "missed medications," "treatment interruptions," "loss of viral suppression," and "significant deterioration in mental health, including increased depression and suicidality," *Id.* as well as resistance to medications that were previously effective, limiting treatment options.[26] Transgender patients who disengage from care may develop preventable complications of their HIV infection and other conditions, "which are significantly more difficult to treat once they have progressed." Brody Decl. ¶ 37.

These harms are especially acute in medically underserved communities, including rural and non-Medicaid expansion jurisdictions where Ryan White-funded HIV clinics often serve as the only viable source of competent HIV care and gender-affirming medical care for transgender patients living with HIV,[27] as well as for homeless patients who "often have lasting consequences because re-engagement is extremely challenging." Brody Decl. ¶ 53.

The Challenged Conditions also harm Plaintiffs and their members by disrupting integrated HIV care programs and interfering with their ability to deliver evidence-based HIV treatment

[25] Fox Dec. ¶ 40; Doe Decl. ¶ 44; *see also* Packett Decl. ¶ 31; Brody Decl. ¶ 26; Roe Decl. ¶ 36.
[26] Packett Decl. ¶¶ 32, 42; Zuniga Decl. ¶ 38; Weddle Decl. ¶ 53; Doe Decl. ¶¶ 43–45; Roe Decl. ¶¶ 35–37; Brody Decl. ¶ 5.
[27] Collins-Ogle Decl. ¶¶ 11–12; Roe Decl. ¶¶ 7, 9, 11.

consistent with accepted medical standards.[28]

Absent preliminary relief, Plaintiffs and their patients are likely to suffer irreparable harm, including disruption of treatment relationships, loss of medically necessary care, reduced retention in HIV treatment, worsening health outcomes, and increased risk of HIV transmission.[29]

LEGAL STANDARD

A party seeking a preliminary injunction must show: "(1) it is likely to succeed on the merits; (2) it is likely to suffer irreparable harm in the absence of preliminary relief; (3) the balance of equities tips in its favor; and (4) an injunction is in the public interest." *New Jersey v. Trump*, 131 F.4th 27, 33 (1st Cir. 2025) (citation modified). The final two factors merge where the government is the opposing party. *See Nken v. Holder*, 556 U.S. 418, 435 (2009). The APA independently authorizes a reviewing court to stay final "agency action" to "prevent irreparable injury." 5 U.S.C. § 705. The standard for granting a § 705 stay is the same as that for obtaining a preliminary injunction. *See California v. Kennedy*, 802 F.Supp.3d 273, 281 (D. Mass. 2025).

ARGUMENT

I. Plaintiffs Have Standing.

"To have standing, a plaintiff must present an injury that is concrete, particularized, and actual or imminent; fairly traceable to the defendant's challenged behavior; and likely to be redressed by a favorable ruling." *Dep't of Com. v. New York*, 588 U.S. 752, 766 (2019) (citation modified). Each Provider Plaintiff and Associational Plaintiff satisfies this standard.

A. Provider Plaintiffs Have Standing.

Provider Plaintiffs have standing under the APA because they are regulated parties adversely affected by agency action and their interests are "within the zone of interests to be

[28] Packett Decl. ¶¶ 5–6, 11–13; Weddle Decl. ¶¶ 5–6, 11–13; Zuniga Decl. ¶¶ 5–6, 11–14, 31.
[29] Brody Decl. ¶¶ 5, 17; Fox Decl. ¶ 20; Collins-Ogle Decl. ¶¶ 15–16; Roe Decl. ¶ 7.

protected or regulated by the statute." *See Food & Drug Admin. v. R.J. Reynolds Vapor Co.*, 606 U.S. 226, 232–33 (2025). Plaintiffs are Ryan White-funded HIV providers directly regulated by the Challenged Conditions and are precisely the entities Congress intended to operate the comprehensive systems of HIV care established under the Ryan White Program.

As a direct result of Defendants' conduct, Provider Plaintiffs face immediate and concrete injuries to their medical practices, professional obligations, and Ryan White-funded HIV programs. The Challenged Conditions force providers to choose between continuing to provide affirming healthcare and gender-affirming medical care to transgender patients living with HIV and risk losing critical Ryan White funding or ending their provision of respectful, medically appropriate care to their transgender patients in violation of accepted standards of medicine and thereby disrupting longstanding treatment relationships.[30]

Provider Plaintiffs also have third-party standing to assert the rights of their transgender patients living with HIV. Courts have consistently recognized that healthcare providers may assert the constitutional and statutory rights of their transgender patients where challenged government action interferes with the provision of medical care. *See*, *e.g.*, *Am. Ass'n of Physicians for Hum. Rts., Inc. v. Nat'l Institutes of Health*, 795 F.Supp.3d 678, 693–94 (D. Md. 2025) ("*GLMA*"); *San Francisco A.I.D.S. Found. v. Trump*, 786 F.Supp.3d 1184, 1212–13 (N.D. Cal. 2025) ("*SFAF*"); *Washington v. Trump*, 768 F.Supp.3d 1239, 1258 (W.D. Wash. 2025); *Whitman-Walker Clinic, Inc. v. U.S. Dep't of Health & Hum. Servs.*, 485 F.Supp.3d 1, 34–36 (D.D.C. 2020); *City & Cnty. of S.F. v. Azar*, 411 F.Supp.3d 1001, 1011 (N.D. Cal. 2019).

B. Associational Plaintiffs Have Standing.

Associational Plaintiffs satisfy the requirements for associational standing because: "(a)

[30] Doe Decl. ¶¶ 51–52; Brody Decl. ¶ 39; Fox Decl. ¶¶ 44–45.

[their] members would otherwise have standing to sue in their own right; (b) the interests [they] seek[] to protect are germane to the organization[s'] purpose[s]; and (c) neither the claim asserted nor the relief requested requires the participation of individual members in the lawsuit." *See Hunt v. Wash. State Apple Advert. Comm'n*, 432 U.S. 333, 343 (1977); *see also Students for Fair Admissions, Inc. v. President & Fellows of Harvard Coll.*, 600 U.S. 181, 199–201 (2023).

First, Associational Plaintiffs each have members who independently possess standing for the same reasons Provider Plaintiffs have standing.[31]

Second, the interests Associational Plaintiffs seek to protect are germane to their organizational missions: The Academy exists to support HIV practitioners and promote accessible, quality HIV care, including through education, credentialing, and advocacy relating to integrated HIV treatment; HIVMA advances access to healthcare services for people living with HIV and supports a robust and culturally competent HIV workforce; and IAPAC's mission is to expand access to and improve the quality of HIV prevention, care, treatment, and support services for people living with HIV worldwide.[32] Ensuring that their members can continue to provide evidence-based care for transgender patients living with HIV falls squarely within those missions.

Third, neither Plaintiffs' claims nor the requested relief requires participation of individual members. *See United Food & Com. Workers Union Loc. 751 v. Brown Grp*., Inc., 517 U.S. 544, 546 (1996) ("individual participation is not normally necessary when an association seeks prospective or injunctive relief for its members") (citation omitted). Plaintiffs challenge the legality of Defendants' nationwide funding conditions under the APA, Section 1557 of the Affordable Care Act, and the Constitution. They seek declaratory and injunctive relief prohibiting

[31] Packett Decl. ¶¶ 5–6, 11–13; Weddle Decl. ¶¶ 5–6, 10, 15–18; Zuniga Decl. ¶¶ 5–6, 12–14; Brody Decl. ¶¶ 16–20; Fox Decl. ¶¶ 31–34; Collins-Ogle Decl. ¶¶ 20–25; Roe Decl. ¶¶ 20–21; Doe Decl. ¶¶ 22–28.
[32] Packett Decl. ¶¶ 7–13; Weddle Decl. ¶¶ 7–13; Zuniga Decl. ¶¶ 7–11.

their enforcement. Because the claims turn on the lawfulness of Defendants' policies, not member-specific factual determinations, any relief would benefit all affected members and their patients alike and does not require their individual participation. *See Warth v. Seldin*, 422 U.S. 490, 515 (1975).

Furthermore, Associational Plaintiffs have derivative standing to assert claims on behalf of the transgender patients of its provider members. *See Pa. Psychiatric Soc'y v. Green Spring Health Servs., Inc.*, 280 F.3d 278, 293 (3d Cir. 2002) ("If on remand the Pennsylvania Psychiatric Society warrants associational standing to represent its members, we conclude it also may have derivative authority to raise the claims of its members' patients.").

II. Plaintiffs Are Likely to Succeed on the Merits.

A. The Challenged Conditions are Final Agency Actions for Purposes of the APA.

The APA authorizes judicial review of "final agency action." 5 U.S.C. § 704. An agency action is final when it "mark[s] the consummation of the agency's decisionmaking process" and determines "rights or obligations . . . from which legal consequences will flow." *Bennett v. Spear*, 520 U.S. 154, 177–78 (1997) (citation modified).

The Challenged Conditions, including the Updated FY2026 General Terms and the Part B Supplemental, Part C, and Part F NOFOs, are final agency action under the APA. Assessing a previous version of the HRSA General Terms and Conditions at issue here, another court in this Circuit held that "[t]he insertion of the Challenged Conditions into prospective and current grant agreements" constitutes final agency action. *Rhode Island Coal. Against Domestic Violence v. Kennedy*, 812 F.Supp.3d 180, 191 (D.R.I. 2025) ("*R.I. Coalition*") (finding prior version of HRSA's general terms as well as NOFOs to be final agency action), *appeal dismissed sub nom. Rhode Island Coal. Against Domestic Violence v. United States Dep't of Hous. & Urb. Dev.*, No. 25-2229, 2026 WL 926474 (1st Cir. Jan. 5, 2026).

"As numerous other courts have likewise explained, the decision to attach the conditions [to NOFOs] can be final even if the final decision to award the funds and issue the NOFOs is still pending." *Illinois v. Fed. Emergency Mgmt. Agency*, 801 F.Supp.3d 75, 89 (D.R.I. 2025) (holding that final agency action had occurred where "the challenged conditions remain applicable to all FY 2025 grants"); *see also Freedom Network USA v. Trump*, Civ. Act. No. 25 C 12419, 2026 WL 800392, at *19 (N.D. Il. Mar. 23, 2026) (conditions attached to NOFOs "demonstrated the consummation of [defendant's] decision-making process regarding its priorities and considerations in evaluating grant applications" and they "require[] an immediate and significant change in the plaintiffs' conduct of their affairs with serious penalties attached to noncompliance.").

Accordingly, the Challenged Conditions—funding requirements that compel grantee conduct "in no uncertain terms"—constitute final agency action. *See Freedom Network USA*, 2026 WL 800392, at *19.[33]

B. The Challenged Conditions Violate the APA Because They Are Arbitrary and Capricious.

The APA directs reviewing courts to "hold unlawful and set aside agency action[s]" that are arbitrary or capricious. 5 U.S.C. § 706(2)(A). Agency action is arbitrary and capricious when it "relie[s] on factors which Congress has not intended it to consider, entirely fail[s] to consider an important aspect of the problem, offer[s] an explanation for its decision that runs counter to the evidence before the agency, or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise." *Motor Vehicle Ass'n v. State Farm Mut. Auto. Ins.*, 463 U.S. 29, 43 (1983). Agency action is also arbitrary and capricious when the agency has failed to "consider[] the factors relevant to" its decision "that will best serve the purposes" of the statute it

[33] In addition, as numerous courts have found, the agency action here—the implementation of grant terms and conditions—is not committed to exclusive agency discretion. *See R.I Coalition*, 812 F.Supp.3d at 192-93. Accordingly, the Challenged Conditions are subject to judicial review under the APA.

is applying. *Am. Paper Inst., Inc. v. Am. Elec. Power Serv. Corp.*, 461 U.S. 402, 413 (1983); *see also River Street Donuts, LLC v. Napolitano*, 558 F.3d 111, 117 (1st Cir. 2009) (same).

In addition, when agency action deviates from past policy or practice, the agency must provide a "more detailed justification than what would suffice for a new policy created on a blank slate." *FCC v. Fox Television Stations, Inc.*, 556 U.S. 502, 515 (2009). And when the prior policy "has engendered serious reliance interests," *id.*, the agency must "assess [those] reliance interests, determine whether they were significant, and weigh any such interest against competing policy concerns," *Dep't of Homeland Sec. v. Regents of the Univ. of Cal.*, 591 U.S. 1, 33 (2020).

The Challenged Conditions are arbitrary and capricious for multiple reasons, any one of which is sufficient to render them unlawful. Plaintiffs are therefore likely to succeed on Count I.

1. The Challenged Conditions Are Contrary to the Purpose and Structure of the Ryan White Program.

The Challenged Conditions contravene the purpose and structure of the Ryan White Program. Congress set forth several clear purposes that Defendants were required to consider in structuring the Ryan White Program. *First*, Congress directed that the Program provide comprehensive care for *all* individuals living with HIV, and particularly "those communities and populations that have been historically most underserved, as well as those that are experiencing rapid increases in HIV infection and AIDS case counts." S. Rep. No. 106-294, 12 (2000); *see also*, 42 U.S.C. § 300ff–12(b) (requiring local planning councils to determine the needs of the local population living with HIV and establish priorities paying "particular attention to" the needs of "disproportionately affected and historically underserved groups"); 42 U.S.C. § 300ff–52(a)(2) (directing that funding recipients "shall serve underserved populations"). *Second*, Congress directed Ryan White funds to be used to "improve the quality of life for those infected or affected" by the HIV epidemic by strengthening care retention rates, increasing viral suppression, and

bettering overall health outcomes. H. Rep. 109-695, 2 (2006). *Third*, Congress "recognize[d] and affirm[ed]" that the HIV epidemic is "best addressed through a local process" spearheaded by decisionmakers familiar with "shifting trends in the local epidemic, disparities in healthcare access and outcomes, and the need for capacity developing with the HIV health care infrastructures." S. Rep. No. 106-294, 13; *see also* 42 U.S.C. § 300ff–12(b) (requiring the creation of local planning councils); § 300ff–23(a), (c) (establishing consortia and directing them to demonstrate a record of service to subpopulations that reflect local incidence of HIV, based on identified needs of those communities).

The Challenged Conditions flout those congressional mandates. *First*, instead of supporting historically underserved groups, such as transgender people, the Challenged Conditions require Plaintiffs to discriminate against transgender patients by refusing to acknowledge, respect, or affirm their identities in any respect, even if unconnected to the provision of gender-affirming medical care, and prohibit Plaintiffs from providing gender-affirming medical care.[34] As the statute contemplated, "Ryan White-funded clinics open the door for treatment for transgender patients who often do not access routine healthcare because clinicians can address patients' comprehensive health needs, including gender-affirming medical care, when administering HIV care." Zuniga Decl. ¶ 35.[35] But the Challenged Conditions would discourage many prospective patients from accessing and retaining HIV-related care altogether.[36]

Second, the Challenged Conditions would harm the health, wellbeing, and quality of life for individuals infected or affected by HIV by reducing care retention rates, decreasing viral suppression, and worsening overall health outcomes population-wide, which will "create[] an

[34] S*ee* Weddle Decl. ¶ 22; Zuniga Decl. ¶¶ 19–26, 34.
[35] *See also* Collins-Ogle Decl. ¶¶ 20, 23, 36; Fox Decl. ¶ 29; Roe Decl. ¶ 19–21.
[36] *See* Collins-Ogle Decl. ¶¶ 28–30, 41–45; Fox Decl. ¶ 30; Roe Decl. ¶ 24–31; Zuniga Decl. ¶ 38; *cf.* Weddle Decl. ¶ 49 (noting the likely economic impact of the Challenged Conditions)

exponential problem that compromises public health." Weddle Decl. ¶¶ 54–55.[37] By dissuading transgender patients from accessing and retaining HIV-related care, the Challenged Conditions are likely to "increas[e] the risk of transmitting HIV . . . [to] the community-at-large" across demographic groups. Weddle Decl. ¶ 53.[38] This will diminish overall patient- and community-health outcomes across the country well-beyond the community of individuals living with HIV who are transgender.[39]

Third, the Challenged Conditions ignore Congress's determination that local entities, specifically, the State Consortia and local planning councils—not Defendants—are best equipped to analyze shifting trends in local HIV epidemics, to address disparities in healthcare access and outcomes in local communities, and to build effective local HIV health-care infrastructure. *See* Background Section B, *supra*. Instead, Defendants seek to impose a global rule that prohibits respectful and affirming care for an entire population without considering local conditions or priorities.

2. The Agency's Change in Policy Ignores the Evidence Before Defendants and Ignores Important Reliance Interests.

The Challenged Conditions fail to acknowledge—let alone justify—Defendants' departure from their prior policies supporting respecting transgender patients' identities and the use of Ryan White funding for gender-affirming medical care. Those prior policies were based on the scientific consensus that gender-affirming medical care is beneficial and medically necessary for people with gender dysphoria and enhances treatment adherence. Further, those prior policies "engendered serious reliance interests," *Fox Television*, 556 U.S. at 515, that Defendants also failed to adequately assess, *see Regents of the Univ. of Cal.*, 591 U.S. at 33.

[37] *See* Collins-Ogle Decl. ¶¶ 30, 35, 41–48; Packett Decl. ¶ 42; Zuniga Decl. ¶ 38; Weddle Decl. ¶ 53.
[38] *See also* Collins-Ogle Decl. ¶ 64; Weddle Decl. ¶ 42; Zuniga Decl. ¶ 38.
[39] *See* Collins-Ogle Decl. ¶¶ 41–48; Zuniga Decl. ¶ 38.

As Defendants themselves acknowledged in 2021: "Providing gender-affirming medical care is an important strategy to effectively address the health and medical needs of transgender people with HIV." Weddle Decl., Ex. J. Defendants explained that healthcare providers could use Ryan White funds to help transgender patients receive a variety of forms of gender-affirming medical care including by "purchas[ing] and maintain[ing] private health insurance, Medicaid, and Medicare coverage" that can support the health needs of transgender people with HIV; providing mental health services for individuals suffering from gender dysphoria and social and emotional stress stemming from anti-transgender discrimination, stigma, and rejection; and providing housing, case management, and substance use disorder treatment services for transgender individuals. *Id.* at 2.

Similarly, 2024 guidance published by HHS previously affirmed, *inter alia*, that "[a]dherence to [gender-affirming] hormone therapy correlates with adherence to ART," that "integrating HIV care with gender care facilitates treatment and is associated with higher rates of viral suppression," that "care integration makes it easier to discuss concerns about drug–drug interactions between HIV treatment and gender-affirming medications," that "HIV care services should be provided within a gender-affirmative care model to reduce potential barriers to ART [antiretroviral therapy] adherence and to maximize the likelihood of achieving sustained viral suppression," and that "[i]ntegrating hormone therapy with HIV services is the recommended practice." Weddle Decl., Ex. F at I-102–03. Not only did HHS delete the chapter "Transgender People with HIV" from the 2025 version of the guidelines, without any explanation, but the Challenged Conditions completely ignore this guidance.[40]

The Challenged Conditions abandon this guidance and now prohibit the very forms of care

[40] Weddle Decl. ¶ 32; *see also* Weddle Decl., Ex. G (2025 version of HHS guidelines); Compl. ¶ 158.

that Defendants previously encouraged, without any acknowledgement of the change, much less the "more detailed justification" that such an about-face requires. *See Fox Television*, 556 U.S. at 515.

In reversing course now, Defendants ignore the strong scientific consensus that gender-affirming medical care is evidence-based and, for many transgender patients living with HIV, necessary to achieve long-term positive health outcomes for the patient and for the broader community.[41] That consensus is shared by nearly every major medical association.[42] What is more, Defendants ignore that access to gender-affirming medical care is crucial to encouraging continued participation in comprehensive healthcare, including HIV treatment, which in turn helps maintain viral suppression and control the spread of HIV infections in the larger population.[43]

Defendants have also altogether failed to "assess whether there were reliance interests" in their prior policy, "determine whether they were significant, and weigh any such interest against competing policy concerns." *Regents of the Univ. of Cal.*, 591 U.S. at 33. In a recent case, a court preliminarily enjoined similar funding conditions that barred the promotion of "gender ideology." *R.I. Coalition*, 812 F.Supp.3d at 199. That court found a likelihood of success on the merits that the conditions were arbitrary and capricious in part because "it is impossible for this Court to find that the Defendants considered the harmful impact their decision would have on . . . the vulnerable populations they serve." *Id*. at 193 (quotation omitted).

Plaintiffs have used Ryan White funds to structure entire care models that improve

[41] *See* Weddle Decl. ¶¶ 40–41, 53.
[42] *See* Abrigo Decl., Ex. F (collecting statements from, *inter alia*, the American Medical Association, American Academy of Pediatrics, American College of Physicians, American Psychiatric Association, American Psychological Association, Endocrine Society, World Health Organization, and World Professional Association for Transgender Health); *see also* Abrigo Decl., Ex. G. *See also Grimm v. Gloucester Cnty. Sch. Bd.*, 972 F.3d 586, 595 (4th Cir. 2020), *as amended* (Aug. 28, 2020); *Edmo v. Corizon, Inc.*, 935 F.3d 757, 769 (9th Cir. 2019).
[43] *See* Zuniga Decl. ¶ 34; Packett ¶ 17; Weddle Decl., Ex. F (2024 HHS guidelines) at I-102–03.

retention rates and viral suppression among transgender individuals living with HIV.[44] Plaintiffs and their members have made significant investments in staffing and facilities to provide holistic care to people living with HIV—interweaving gender-affirming medical care as a part of treatment plans that include other necessary medical treatment, family support, case management, medical transportation, access to specialists, and hospice care.[45]

The Challenged Conditions will disrupt that infrastructure by forcing providers to forgo crucial government support for current staff and programs unless they are willing to abandon their commitments to offer comprehensive and effective care to *all* their patients.[46] Such abandonment of care would shatter patients' trust, which in turn would undermine their reliance interests, jeopardize their health and wellbeing, and damage the Ryan White Program's public health goal of controlling the spread of HIV.[47] The Updated FY2026 General Terms worsen that impact by barring Plaintiffs from communicating with transgender patients living with HIV using the pronouns and other language that aligns with their identities, even when providing medical services not banned by the Challenged Conditions. *See* Updated FY2026 General Terms § 5(b) (requiring "sex-based definitions grounded in biological reality"). This would make it impossible for Plaintiffs—often the only providers to whom transgender individuals have access—to provide any care at all.[48]

* * *

All told, the Challenged Conditions are not the products of reasoned decision-making

[44] *See* Collins-Ogle Decl. ¶¶ 17, 21–22; Doe Decl. ¶ 23; Brody Decl. ¶ 20.
[45] *See* Brody Decl. ¶¶ 11–12; Doe Decl. ¶ 23.
[46] *See* Doe Decl. ¶¶ 22, 31–41; Packett Decl. ¶ 35.
[47] *See* Roe Decl. ¶¶ 14–16, 27–28; Plackett Decl. ¶ 31.
[48] *See* Fox Decl. ¶ 39 ("If we cannot continue to . . . use a patient's name, gender identity, and pronouns, it is likely that our transgender patients would stop coming and would drop off from all care, including HIV care."); Roe Decl. ¶ 25 ("[B]eing able to acknowledge and affirm my transgender patients' identities[] is essential to building trust with [them]. . . . That trust directly affects whether my patients remain in care.").

proceeding from a rational assessment of data, evidence, potential impact, or reliance interests. Defendants can offer no coherent explanation of how the Challenged Conditions serve Congress's purposes in providing Ryan White funding. Nor have they attempted to justify singling out one type of recipient (transgender people) and one form of medical treatment from all other types of core medical services (both HIV-specific and non-HIV-specific) funded by Ryan White. This lack of explanation renders the Challenged Conditions arbitrary and capricious. *See Massachusetts v. Nat'l Institutes of Health*, 770 F.Supp.3d 277, 305 (D. Mass. 2025) ("*Massachusetts v. NIH*") ("[A]gencies must provide reasons that both exhibit sufficient consideration of the relevant factors and pertinent aspects of the problem and demonstrate a rational connection between the facts and choice that was made."), *judgment entered,* No. 1:25-CV-10338, 2025 WL 1063760 (D. Mass. Apr. 4, 2025), and *aff'd*, 164 F.4th 1 (1st Cir. 2026).

Instead, the Challenged Conditions self-evidently reflect "unjustifiable bias." *Level the Playing Field v. FEC*, 961 F.3d 462, 464 (D.C. Cir. 2020). The Challenged Conditions thus appear to be yet another attempt from the current Administration to target and stigmatize the transgender community—all while ignoring the considered judgments of Congress and the state and regional councils and consortia that Congress empowered to formulate treatment priorities.

C. The Challenged Conditions Violate the APA Because They Are Not in Accordance with Law.

The APA directs reviewing courts to "hold unlawful and set aside agency action[s]" that are "not in accordance with law." 5 U.S.C. § 706(2)(A). "An agency action that violates a statute is not in accordance with law within the meaning of the APA." *Ctr. for Biological Diversity v. Zeldin*, 171 F.4th 356, 376 (D.C. Cir. 2026) (citation modified). Plaintiffs are likely to succeed on Count II because the Challenged Conditions contravene the plain text of both the Ryan White statute and the Affordable Care Act.

1. The Challenged Conditions Are Contrary to the Ryan White Program's Enabling Statute.

The Challenged Conditions disregard both the foundational principles and the statutory scheme codified in the Ryan White statute. The Ryan White statute mandates that funding be provided to establish a system of comprehensive care that "improve[s] the quality, availability[,] and organization of health care services for individuals and families with HIV/AIDS." 42 U.S.C. § 300ff-21 (Part B); *see also id.* § 300ff-11(a) (Part A); *id*. § 300ff-29a (Part B Supp.); *id*. § 300ff-51 (Part C); *id*. § 300ff-71 (Part D). The Ryan White statute further requires that funding be used to provide "core medical services" and "support services" for persons living with HIV, to improve access to and retention of HIV-related care, increase viral suppression, and improve overall health outcomes. *See* 42 U.S.C. § 300ff-14(c)–(d) (Part A); *id.* § 300ff-22(a) (Part B); *id.* § 300ff-29a (Part B Supp.); *id.* § 300ff-51(b) (Part C); *id.* § 300ff-71 (Part D). The statute defines "core medical services" to encompass "outpatient and ambulatory health services," "including services regarding the co-occurring conditions of the individual" for an individual living with HIV/AIDS. 42 U.S.C. §§ 300ff-14(c), 300ff-22(b) (identical), 300ff-51(c) (identical).

Core medical services can include gender-affirming medical care. "The term 'outpatient care' means care and treatment of a disability, and preventive health services, furnished to an individual other than hospital care or nursing home care." 38 U.S.C. § 1803.[49] And according to the Ryan White Statute, "[t]he term 'co-occurring conditions' means one or more adverse health conditions in an individual with HIV/AIDS, without regard to whether the individual has AIDS

[49] This is consistent with the ordinary meaning of the term. *See*, *e.g.*, *Outpatient Services*, Health Library, New York-Presbyterian Hospital, (May 1, 2025) https://tinyurl.com/z3vhrdxy [https://perma.cc/9V9C-TYFS] ("Outpatient services are medical procedures, surgeries, therapies, classes, or tests that are done in a qualified medical center without the need for an overnight stay.").

and without regard to whether the conditions arise from HIV." 42 U.S.C. § 300ff-88(2).[50] And gender dysphoria is a serious medical condition "that is characterized by debilitating distress and anxiety resulting from the incongruence between an individual's gender identity and birth-assigned sex." *Grimm*, 972 F.3d at 594–95. Gender-affirming medical care, more specifically, gender-affirming hormone therapy, falls squarely within these ordinary definitions.

Accordingly, Plaintiffs use Ryan White funding to maintain integrated care models that provide holistic care and "core medical services" to patients living with HIV, which includes not only HIV specialty care but also, *inter alia*, sexual healthcare, counseling, mental-health support, medication monitoring, and, when appropriate, gender-affirming medical care for the co-occurring condition of gender dysphoria.[51]

By forcing Plaintiffs to exclude gender-affirming medical care from these models, the Challenged Conditions "directly undermine" their efforts to provide *comprehensive* care and core medical services to patients living with HIV.[52] The Challenged Conditions will thus "fragment care, exclude necessary services for" transgender HIV patients, and "create gaps that [Plaintiffs'] [i]ntegrated [p]lans are specifically designed to prevent." Doe Decl. ¶ 48. This violates the Ryan White statute.

2. The Challenged Conditions Violate Section 1554 of the ACA.

Section 1554 of the ACA prohibits HHS from promulgating any regulation that, *inter alia*, "creates any unreasonable barriers to the ability of individuals to obtain appropriate medical care," "impedes timely access to health care services," "interferes with communications regarding a full

[50] A co-occurring condition, also known as a comorbid condition, refers to a condition "existing simultaneously with and usually independently of another medical condition." *Comorbid*, *Merriam-Webster.com Dictionary*, Merriam-Webster, https://tinyurl.com/33c2ajee (accessed June 9, 2026).
[51] *See* Doe Decl. ¶ 21; Collins-Ogle Decl. ¶ 22; Fox Decl. ¶¶ 15–17; Zuniga Decl. ¶ 34.
[52] Packett Decl. ¶ 46; Doe Decl. ¶ 32; Weddle Decl. ¶ 46; *see also* Zuniga Decl. ¶ 40 ("The restriction would also undermine our members' ability to treat their patients by erasing data on transgender people living with or at risk of HIV.").

range of treatment options between the patient and the provider," "restricts the ability of health care providers to provide full disclosure of all relevant information to patients making health care decisions," "violates . . . the ethical standards of health care professionals," or "limits the availability of health care treatment for the full duration of a patient's medical needs." 42 U.S.C. § 18114. The Challenged Conditions offend Section 1554 in numerous ways.

First, the Challenged Conditions create unreasonable barriers to the ability of transgender patients living with HIV to obtain appropriate HIV medical care as well as gender-affirming medical care for their gender dysphoria and impede timely access to such care. At its essence, this case is "about placing limits on the ability to act" of providers participating in the Ryan White Program. *See Mayor of Baltimore v. Azar*, 973 F.3d 258, 288 (4th Cir. 2020). Pursuant to the Challenged Conditions, healthcare providers participating in the Ryan White Program must "abstain" from respecting their transgender patients' identities while providing HIV-related care and from providing gender-affirming medical care. *See Whitman-Walker.*, 485 F.Supp.3d at 53. In doing so, the Challenged Conditions "make[] it harder" for transgender patients living with HIV to access HIV care and gender-affirming medical care, thereby imposing an "unreasonable barrier" to medical care. *Planned Parenthood of Maryland, Inc. v. Azar*, No. 20-cv-00361-CCB, 2020 WL 3893241, at *9 (D. Md. July 10, 2020). In other words, they impose a "substantive barrier" to the ability of transgender patients living with HIV to obtain "appropriate medical care." *Whitman-Walker*, 485 F.Supp.3d at 53 (quoting *California ex rel. Becerra v. Azar*, 950 F.3d 1067, 1094–95 (9th Cir. 2020) (en banc)).

The Challenged Conditions erect myriad barriers to appropriate care. As to HIV care, the Challenged Conditions would prohibit HIV care providers from providing integrated health services that comprehensively attend to the primary healthcare needs of patients and have been

shown to have positive impacts with regards to HIV treatment.[53] For example, this would prevent providers from addressing interactions between medications provided as part of HIV treatment and those provided as part of gender dysphoria treatment.[54] In addition, by prohibiting the acknowledgement and affirmation of transgender patients' identities and the provision of medically indicated gender-affirming medical care, the Challenged Conditions will cause transgender patients living with HIV who rely on Ryan White funding to disengage from HIV care.[55] This in turn will cause reduced antiretroviral therapy adherence and lower levels of viral suppression.[56] But as HHS's own guidelines regarding HIV care acknowledge, "HIV care services should be provided within a gender-affirmative care model to reduce potential barriers to ART [antiretroviral therapy] adherence and to maximize the likelihood of achieving sustained viral suppression." Weddle Decl., Ex. F at I-103. And the Ryan White Program is often the only means by which transgender patients may obtain gender-affirming medical care, so the Challenged Conditions would effectively cut off access to such care.[57] The Challenged Conditions thus "amount to direct government interference with health care by requiring providers or patients to perform or abstain from certain conduct." *See Whitman-Walker*, 485 F.Supp.3d at 53 (quoting *California ex rel. Becerra*, 950 F.3d at 1094) (citation modified).

Second, the Challenged Conditions interfere with communications between HIV care providers and their transgender patients living with HIV regarding the full range of treatment options and information they need to make informed and clinically appropriate healthcare decisions. Acknowledging a transgender patient's identity and gender incongruence would, in

[53] Weddle Decl. ¶ 30.
[54] Weddle Decl. ¶¶ 33, 34; Fox Decl. ¶ 20.
[55] Brody Decl. ¶¶ 26–27, 33–35; Fox Decl. ¶¶ 41, 41, 43; Collins-Ogle Decl. ¶ 33; Doe Decl. ¶ 45; *cf.* Doe Decl. ¶¶ 34-40 (providing patient example).
[56] Packett Decl. ¶ 42; Zuniga Decl. ¶ 38; Brody Decl. ¶ 55; Fox Decl. ¶ 43; Roe Decl. ¶¶ 32–34; Collins-Ogle Decl. ¶ 39.
[57] Zuniga Decl. ¶ 39; Collins-Ogle Decl. ¶¶ 40–42; Roe Decl. ¶¶ 38–40; Doe Decl. ¶ 59.

Defendants' view, "promote gender ideology" and "promote, encourage, . . . or facilitate . . . denial by the recipient of the sex binary in humans, or the belief that sex is a chosen or mutable characteristic." *E.g.*, Abrigo Decl. Ex. E (Gender Order), Ex. I (Part B Suppl. NOFO). HIV care providers, therefore, will be prohibited from discussing concerns about drug interactions between HIV treatment and gender-affirming hormone therapy, patient priorities regarding care, treatment options regarding gender dysphoria, and other issues related to a patient's particularized needs and circumstances.[58] As such, the Challenged Conditions "quite clearly 'interfere[] with communications' about medical options between a patient and her provider" and "require[] health care providers to hide the ball from their patients." *Mayor of Baltimore*, 973 F.3d at 288 (quoting 42 U.S.C. § 18114(3)).

Third, the Challenged Conditions require healthcare providers to violate the ethical standards of their professions by denying medical care they consider necessary and essential for the care of their patients and forcing them to discriminate against their patients. *See Mayor of Baltimore*, 973 F.3d at 288.[59]

In short, the Challenged Conditions are unlawful because they are contrary to the plain text and structure of the Ryan White statute and are contrary to Section 1554.

D. The Challenged Conditions Violate the APA Because They Are in Excess of Statutory Authority and Violate the Separation of Powers.

The APA directs reviewing courts to "hold unlawful and set aside agency action" that is "in excess of statutory jurisdiction, authority, or limitations, or short of statutory right," 5 U.S.C. § 706(2)(C), or "contrary to constitutional right, power, privilege, or immunity," *id.* § 706(2)(B). To determine whether an agency has exceeded its authority, "the court looks to the scope of the

[58] Weddle Decl., Ex. F at I-102–03; Zuniga Decl. ¶¶ 38, 41; Brody Decl. ¶ 42; Fox Decl. ¶¶ 27, 29; Doe Decl. ¶ 56.
[59] *See also* Packett Decl. ¶ 36; Weddle Decl. ¶¶ 46–48; Brody Decl. ¶¶ 39–41; Fox Decl.¶ 45; Collins-Ogle Decl. ¶¶ 47–51.

agency's statutory authority and discretion and determines whether the agency's statutory authority encompasses the action taken." *Nat'l Educ. Ass'n v. U.S. Dep't of Educ.*, 779 F.Supp.3d 149, 197 (D.N.H. 2025) (citation modified). "Phrased simply, the question is 'whether the agency has gone beyond what Congress has permitted it to do.'" *Id.* (quoting *City of Arlington v. FCC*, 569 U.S. 290, 298 (2013)).

Here, nothing in the Ryan White statute authorizes Defendants to impose the Challenged Conditions on recipients of Ryan White funds. Absent such Congressional authorization, the Constitution bars Defendants from exercising that power unilaterally.

First, the Challenged Conditions violate the Appropriations Clause of the Constitution. "The Appropriations Clause . . . gives Congress exclusive power over federal spending." *Nat'l Council of Nonprofits v. Off. of Mgmt. & Budget*, 763 F.Supp.3d 36, 55 (D.D.C. Feb. 3, 2025) (citation modified); *see also Biden v. Nebraska*, 600 U.S. 477, 505 (2023). Indeed, the Clause "was intended as a restriction upon the disbursing authority of the Executive [Branch]." *Cincinnati Soap Co. v. United States*, 301 U.S. 308, 321 (1937).

Consistent with those principles, Congress, not Defendants, "may impose appropriate conditions on the use of federal property or privileges," including federal grants. *Massachusetts v. United States*, 435 U.S. 444, 461 (1978). And when Congress intends to place conditions on federal funds, "it has proved capable of saying so explicitly." *Pennhurst State Sch. & Hosp. v. Halderman*, 451 U.S. 1, 17–18 (1981); *see*, *e.g.*, 42 U.S.C. § 300ff-1 (proscribing use of Ryan White funds to provide "individuals with hypodermic needles or syringes so that such individuals may use illegal drugs"); Further Consolidated Appropriations Act, Pub. L. No. 118-47, § 526 (2024) (grant conditions regarding provision of sterile needles); *id.* § 202 (grant condition regarding salary caps). But the Executive Branch "does not have the power to place conditions on federal funds" that run

counter to the will of Congress. *Cnty. of Santa Clara v. Trump*, 250 F.Supp.3d 497, 531 (N.D. Cal. 2017); *cf. Fed. Elec. Comm'n v. Cruz*, 596 U.S. 289, 301 (2022) (An agency "'literally has no power to act'—including under its regulations—unless and until Congress authorizes it to do so by statute." (quoting *La. Pub. Serv. Comm'n v. FCC*, 476 U.S. 355, 374 (1986)).

The Ryan White Program is no exception to these rules. Congress did not condition the issuance of Ryan White grants on whether the recipient promotes "gender ideology," denies the "sex binary" in humans, expresses the belief that sex is a "chosen or mutable characteristic," or provides gender-affirming medical care. To the contrary: Congress explicitly directed the Executive Branch to *refrain* from taking actions that burden access to and communications regarding appropriate healthcare, or that discriminate based on sex. *See* 42 U.S.C. §§ 18114(1)–(5), 18116. And it expressly structured the Ryan White Program so that entities and individuals like Plaintiffs would be able to provide care to *all* individuals living with HIV, especially historically underserved communities "experiencing rapid increases" in HIV case counts, like the transgender population. S. Rep. No. 106-294, at 12 (2000).

Here, the Challenged Conditions "run[] headlong into the Ryan White Program's statutory mandate" to provide for the provision of outpatient services for the co-occurring conditions of patients living with HIV. *SFAF*, 786 F.Supp.3d at 1230. What's more, the Challenged Conditions "contravene the antidiscrimination requirements within the ACA." *Id.* at 1231; *see* Section II.E, *infra*. In so doing, the Challenged Conditions unconstitutionally intrude upon the Congressional prerogative to control the public fisc. *See California v. Trump*, 786 F.Supp.3d 359, 388–89 (D. Mass. 2025) (holding that Election Assistance Commission acted outside statutory authority in attempting to "impose an extra-statutory condition on the disbursement" of Congressionally approved funding); *New York v. Trump*, 764 F.Supp.3d 46, 51 (D.R.I. 2025); *City of Chicago v.*

Noem, No. 25 C 12765, 2025 WL 3251222, at *7 (N.D. Ill. Nov. 21, 2025).

Second, the Challenged Conditions also contravene Articles I and II of the Constitution. Article I requires that every bill pass both the House of Representatives and the Senate before it is presented to the President. U.S. Const. art. I, § 7, cl. 2. These procedural "steps" are non-negotiable: They were designed to "erect enduring checks on each Branch and to protect the people from the improvident exercise of power by mandating certain prescribed steps." *INS v. Chadha*, 462 U.S. 919, 957 (1983). And Article II requires the Executive Branch to "take Care that the Laws be faithfully executed[.]" U.S. Const. art. II, § 3. This means that the Executive Branch has an "'affirmative[]'" duty to execute duly enacted law, *PFLAG, Inc. v. Trump*, 769 F.Supp.3d 405, 432 (D. Md. 2025), irrespective of what "policy reasons" it might have "for wanting to spend less than the full amount appropriated by Congress for a particular project or program," *In re Aiken Cnty.*, 725 F.3d 255, 261 n.1 (D.C. Cir. 2013) (Kavanaugh, J.).

Neither Article I nor Article II authorizes Defendants to effectively amend the Ryan White statute by issuing the Challenged Conditions. Instead of abiding by the "single, finely wrought and exhaustively considered procedure" for adding substantive grant conditions to Ryan White, *Chadha*, 462 U.S. at 951, Defendants have attempted to "impose by brute force [such] conditions" through the grant application process, *City of Providence v. Barr*, 954 F.3d 23, 30, 34 (1st Cir. 2020) (holding DOJ imposed unlawful conditions on grantees of the Byrne JAG Grant Program when it attempted to "superimpose its policy views on [the recipients'] law enforcement efforts"). That brute force approach defies Articles I and II. *See New York*, 764 F.Supp.3d at 51 (stating that should the Executive "believe[] that appropriations are inconsistent with the President's priorities—it must ask Congress, not act unilaterally.").

Plaintiffs are likely to succeed in showing that the Challenged Conditions are "in excess of

statutory . . . authority," and are "contrary to constitutional right, power, privilege, or immunity" because they violate the separation of powers. 5 U.S.C. § 706(2)(B)–(C). Plaintiffs are therefore likely to succeed on Counts III and IV.

E. The Challenged Conditions Unlawfully Discriminate Based on Transgender Status and Sex.

The Challenged Conditions impermissibly discriminate based on transgender status and sex, in violation of the ACA and the Fifth Amendment, such that Plaintiffs are likely to prevail on Counts II, IV, V, and VI. Effectively, the Challenged Conditions seek to prohibit transgender people from accessing federally funded healthcare if it is provided in a way that respects their identities. However, the federal government cannot engage in discrimination, either directly or by forcing grantees to engage in discrimination, that is directly prohibited by federal law or the Constitution.

Section 1557 of the ACA provides that an individual shall not, on the basis of, *inter alia*, any ground prohibited by Title IX of the Education Amendments of 1972, "be excluded from participation in, be denied the benefits of, or be subjected to discrimination under, any health program or activity, any part of which is receiving Federal financial assistance." 42 U.S.C. § 18116(a). To succeed on a Section 1557 claim asserting discrimination on the basis of sex, a plaintiff must show: (1) the defendant is a health program or activity, any part of which is receiving Federal financial assistance; (2) the plaintiff was excluded from participation in, denied the benefits of, or subjected to discrimination on the basis of sex; and (3) the plaintiff's claim is enforceable under Title IX. *See* 42 U.S.C. § 18116(a).

Plaintiffs easily meet this standard. *First*, Defendants HHS and HRSA are covered entities that fall within the scope of Section 1557. *See* 45 C.F.R. § 92.4 (defining "covered entity" to include "The Department;" defining "Department" to mean "U.S. Department of Health and Human Services;" and defining "health program or activity" to include projects that "[p]rovide or

administer health-related services" or "[p]rovide clinical, pharmaceutical, or medical care").

Second, Plaintiffs allege that they and their patients will be excluded from participation in, denied the benefits of, and subjected to discrimination under the Ryan White program. As a condition of receiving Ryan White funding, the Challenged Conditions require that grantees stop respecting their transgender patients' identities and stop providing gender-affirming medical care. However, as Plaintiffs have asserted, providing integrated care is the norm and developing a relationship of trust is crucial both to engaging and maintaining patients in HIV care and to treating their conditions effectively.[60] The Challenged Conditions put Plaintiffs in an untenable position: They and their members can either continue to acknowledge their transgender patients' identities and provide necessary gender-affirming medical care but be excluded from the Ryan White Program, or they can stop providing affirming care and exclude their transgender patients.

Third, discrimination based on transgender status constitutes discrimination on the basis of sex in violation of Title IX. In *Bostock v. Clayton County*, the Supreme Court held that "it is impossible to discriminate against a person for being . . . transgender without discriminating against that individual based on sex." 590 U.S. 644, 660 (2020). While the First Circuit has not directly addressed the applicability of *Bostock* to Title IX claims, the First Circuit generally interprets Title IX's protections consistently with Title VII. *See*, *e.g.*, *Ing v. Tufts Univ.*, 81 F.4th 77, 82 (1st Cir. 2023) ("[T]he standards governing claims arising under Title VII and Title IX are the same."). And numerous courts of appeal, as well as district courts in the First Circuit, have applied *Bostock* to Title IX claims. *See*, *e.g.*, *Grimm*, 972 F.3d at 616-17; *Doe v. Snyder*, 28 F.4th 103, 114 (9th Cir. 2022); *Tirrell v. Edelblut*, 748 F.Supp.3d 19, 42-43 (D.N.H. 2024); *Carlan v. Fenway Cmty. Health Ctr., Inc.*, No. CV 23-12361-MJJ, 2025 WL 1000478, at *5 (D. Mass. Mar.

[60] *E.g.*, Fox Decl. ¶¶ 5, 17–19, 40; Brody Decl. ¶¶ 23–24, 35.

28, 2025), *appeal pending*, No. 25-1315 (1st Cir.).

Other courts have preliminarily enjoined policies with virtually identical language to the Challenged Conditions or involving the Gender Order, which the Challenged Conditions implement, because they facially discriminated on the basis of transgender status and therefore sex. *See*, *e.g.*, *GLMA*, 795 F.Supp.3d at 695; *SFAF*, 786 F.Supp.3d at 1231; *PFLAG*, 769 F.Supp.3d at 444. In finding that the Gender Order's prohibition on using grant money to "promote gender ideology" and its statement that "[i]t is the policy of the United States to recognize two sexes, male and female. These sexes are not changeable" discriminated based on sex, likely violating Section 1557 (and the Fifth Amendment), one court stated: "The Court cannot fathom discrimination more direct than the plain pronouncement of a policy resting on the premise that the group to which the policy is directed does not exist." *PFLAG*, 769 F.Supp.3d at 443–44. The same is true here.

For similar reasons, the Challenged Conditions violate the Equal Protection Component of the Fifth Amendment because they discriminate based on sex and transgender status and because they are motivated by animus towards an unpopular minority. Classifications based on sex or gender are subject to intermediate scrutiny and must be "substantially related to achieving an important governmental objective." *Massachusetts v. U.S. Dep't of Health & Hum. Servs.* (*Massachusetts v. HHS*), 682 F.3d 1, 9 (1st Cir. 2012). The burden of justification "is demanding and it rests entirely on the State." *Tirrell*, 748 F.Supp.3d at 30 (quoting *United States v. Virginia*, 518 U.S. 515, 533 (1996)). The government's justification for the policy "must be genuine, not hypothesized or invented *post hoc* in response to litigation." *Virginia*, 518 U.S. at 533.

Classifications based on transgender status are classifications based on sex and so warrant intermediate scrutiny. *See*, *e.g.*, *Doe v. Horne*, 115 F.4th 1083, 1107 (9th Cir. 2024); *Grimm*, 972 F.3d at 608-09; *Tirrell*, 748 F.Supp.3d at 33–36; *Doe v. Austin*, 755 F.Supp.3d 51, 68-69 (D. Me.

2024); *Bos. All. of Gay, Lesbian, Bisexual & Transgender Youth v. United States Dep't of Health & Hum. Servs.*, 557 F.Supp.3d 224, 244 (D. Mass. 2021) (citing *Bostock*, 590 U.S. at 669). Further, discrimination based on the failure of transgender people to conform to sex stereotypes is sex discrimination and subject to heightened scrutiny. *See*, *e.g.*, *Tirrell*, 748 F.Supp.3d at 37–38; *Evancho v. Pine-Richland Sch. Dist.*, 237 F.Supp.3d 267, 285–86, 296–97 (W.D. Pa. 2017).[61]

By prohibiting Plaintiffs from acknowledging, affirming, and respecting transgender patients' identities or providing outpatient services to transgender patients (and only transgender patients) for a co-occurring condition, the Challenged Conditions classify based on transgender status and therefore sex, and are thus subject to heightened scrutiny. However, there is no important governmental interest that is served by and could justify excluding Plaintiffs and their patients from the Ryan White Program. The wholesale exclusion of healthcare that supports transgender people conflicts with Congress's directive to support minority populations under the Ryan White Statute, and with HRSA's past practice of funding these services, and does not constitute an important state interest. *See GLMA*, 795 F.Supp.3d at 697–98.

Finally, even if the Challenged Conditions were not subject to heightened scrutiny based on transgender status and sex, under First Circuit precedent, the Court must apply a more searching review than ordinary rational basis scrutiny for policies targeting groups that have "long been the subject of discrimination." *Massachusetts v. HHS*, 682 F.3d at 11. As other courts have acknowledged, "transgender people have been the subject of a long history of discrimination that continues to this day." *F.V.*, 286 F.Supp.3d at 1145. In fact, just the disclosure of a person's transgender status may "expose[] transgender individuals to a substantial risk of stigma,

[61] Courts have also held that classifications based on transgender status independently warrant heightened scrutiny, which warrants applying heightened scrutiny here. *See*, *e.g.*, *Grimm*, 972 F.3d at 608; *Karnoski v. Trump*, 926 F.3d 1180, 1200-01 (9th Cir. 2019); *Talbott*, 775 F.Supp.3d at 319–22; *F.V. v. Barron*, 286 F.Supp.3d 1131, 1144–45 (D. Idaho 2018); *Evancho*, 237 F.Supp.3d at 288; *Adkins v. City of New York*, 143 F.Supp.3d 134, 140 (S.D.N.Y. 2015).

discrimination, intimidation, violence, and danger." *Arroyo González v. Rosselló Nevares*, 305 F.Supp.3d 327, 333 (D.P.R. 2018).

The Supreme Court has recognized that "a bare . . . desire to harm a politically unpopular group cannot constitute a *legitimate* governmental interest." *Romer v. Evans*, 517 U.S. 620, 634-35 (1996) (quoting *U.S. Dep't of Agric. v. Moreno*, 413 U.S. 528, 534 (1973)) (emphasis in original). Yet, this is exactly what is occurring here. The Challenged Conditions are just one piece of the Administration's sustained campaign against transgender people. *See* Background Section D, *supra*; *see also Orr*, 778 F.Supp.3d at 417–18 (discussing the Gender Order among the Administration's other executive actions that "are built on a foundation of irrational prejudice" toward transgender Americans and finding that "such targeting of a politically unpopular group" violates equal protection). So, "[i]n addition to facially discriminating based on transgender status," the Challenged Conditions "purposefully discriminate based on transgender status." *SFAF*, 786 F.Supp.3d at 1216. This purposeful targeting violates *Romer* regardless of what level of scrutiny would otherwise apply.

For all these reasons, Plaintiffs are likely to succeed on their claims that the Challenged Conditions violate Section 1557 of the ACA and the Constitution's guarantee of Equal Protection.

F. The Challenged Conditions Violate the Right to Free Speech.

The First Amendment prohibits the government from abridging the freedom of speech. *See Reed v. Town of Gilbert*, 576 U.S. 155, 163 (2015); U.S. Const. amend. I. Ordinarily, "the government may not regulate speech based on its substantive content or the message it conveys." *Rosenberger v. Rector & Visitors of Univ. Va.*, 515 U.S. 819, 828 (1995). In the context of federal funding, the government may attach certain conditions to eligibility for that funding, *Agency for Int'l Dev. v. All. for Open Soc'y Int'l, Inc.*, 570 U.S. 205, 213–15 (2013) ("*AID*"); however, there are limitations on the types of conditions that the government may attach to federal funds without

violating the First Amendment. Funding conditions "can result in an unconstitutional burden on First Amendment rights" if the conditions "seek to leverage funding to regulate speech outside the contours of the program itself," *AID*, 570 U.S. at 214–15, or if the conditions seek to achieve a censorious purpose and suppress a recipient's dangerous ideas independent of any objective of the federally funded program, *Nat'l Endowment for the Arts v. Finley*, 524 U.S. 569, 587 (1998).

The Challenged Conditions express a disparaging and unscientific view of gender identity, repudiate the existence of transgender people, deem their identities to be false, order their exclusion from government recognition and protection, and seek to coerce others to do the same by threatening termination of federal funding and other penalties. This violates the First Amendment in two distinct ways.

First, the Challenged Conditions create a funding condition that does not further the objectives of the Ryan White Program and thus place an unconstitutional burden on the First Amendment rights of Provider Plaintiffs and Associational Plaintiffs' members. While the government is permitted to impose conditions on funding that are "relevant to the objectives of the program" itself, placing such conditions is impermissible where, as here, "the Government has placed a condition on the *recipient* of the subsidy rather than on a particular program or service." *AID*, 570 U.S. at 214, 218–19 (quoting *Rust v. Sullivan*, 500 U.S. 173, 197 (1991)) (emphasis in original). Indeed, the Ryan White statute, which establishes a program to provide HIV care, has "no programmatic message" that allows the government to regulate speech concerning *gender* as "deemed necessary" for the Ryan White Program's "legitimate objectives." *Legal Servs. Corp. v. Velazquez*, 531 U.S. 533, 548 (2001). Rather, the Challenged Conditions seek to coerce and penalize federal funding recipients, including Provider Plaintiffs and Associational Plaintiffs' members, whose speech, trainings, research, and services acknowledge the existence of

transgender people and advocate for their equality and respect. *Cf. Thakur v. Trump*, No. 25-4249, 2026 WL 1466303, at *7-11 (9th Cir. May 26, 2026) (per curiam) (applying same First Amendment analysis to hold that policies implementing executive orders, including the Gender Order, that require the termination of funding for research that is DEI-related constitute unlawful viewpoint discrimination).

Second, "even in the provision of subsidies, the government may not 'ai[m] at the suppression of dangerous ideas.'" *Nat'l Endowment for the Arts*, 524 U.S. at 587 (quoting *Regan v. Taxation with Representation of Wash.*, 461 U.S. 540, 550 (1983)). Through the Challenged Conditions, the government unlawfully violates the First Amendment by administering subsidy programs with a censorious purpose. *See Student Gov't Ass'n v. Bd. of Tr. of Univ. of Massachusetts*, 868 F.2d 473, 479 (1st Cir. 1989) (acknowledging such government conditions on subsidies or benefits based on viewpoint may violate both free speech and equal protection rights); *see also Koala v. Khosla*, 931 F.3d 887, 898 (9th Cir. 2019) (recognizing the Supreme Court's continued cautionary admonition that First Amendment will not tolerate the administration of subsidy programs with a censorious purpose).

The Challenged Conditions are designed and intended to silence, defund, and otherwise penalize Plaintiffs for acknowledging that transgender people exist and providing them with healthcare services under the Ryan White Program in a manner that affirms who they are. As another court stated in preliminarily enjoining grant terms and conditions that incorporated the Gender Order: "The categorial and expansive nature of the Challenged Conditions telegraph that the Defendants will deny federal funding to a whole class of programs based on viewpoint alone. It cannot be mistaken that in this case federal funding is being employed as a carrot to impose a "disproportionate burden calculated to drive 'certain ideas or viewpoints from the marketplace.'"

R.I. Coalition, 812 F.Supp.3d at 195 (quoting *Nat'l Endowment for the Arts*, 524 U.S. at 587). Provider Plaintiffs and Associational Plaintiffs' members, as well as the transgender patients they serve under the Ryan White Program, suffer irreparable harm as a direct result of the unlawful imposition of the Challenged Conditions. Accordingly, Plaintiffs are likely to succeed on their First Amendment claims (Counts IV and VII).

III. Provider Plaintiffs, Associational Plaintiffs' Members, and Their Transgender Patients Will Suffer Irreparable Harm Absent a Preliminary Injunction.

It is well-established that acts that "diminish[] access to high-quality health care" cause irreparable harm. *PFLAG*, 769 F.Supp.3d at 449; *see also Planned Parenthood S. Atl. v. Baker*, 941 F.3d 687, 707 (4th Cir. 2019); *GLMA*, 795 F.Supp.3d at 699; *SFAF*, 786 F.Supp.3d at 1233 ("Without an injunction against those provisions, Plaintiffs' patients and clients will suffer irreparable harm in being deprived [of] vital healthcare services."). As such, courts within this district have held that "threats to patients' lives represent[] a dire risk of a quintessentially irreparable nature." *Massachusetts v. NIH*, 770 F.Supp.3d at 320. Unless enjoined, Defendants' actions will cause Plaintiffs and their transgender patients to suffer irreparable harm, including threats to patients' lives, loss of healthcare, loss of provider trust, harm to careers and income, loss of human capital and talent, psychological distress, and the deprivation of constitutional rights. *See* Background Section E, *supra*.

Transgender patients are less likely to remain engaged in HIV care if providers cannot acknowledge their identities or provide medically indicated gender-affirming care as part of integrated care programs.[62] Disruptions in care risk missed appointments, reduced medication adherence, viral rebound, drug resistance, and increased HIV transmission.[63]

[62] Brody Decl. ¶ 17; Fox Decl. ¶¶ 30, 41.
[63] Brody Decl. ¶¶ 5, 17; Collins-Ogle Decl. ¶¶ 5, 15–16; Fox Decl. ¶ 42–43; Doe Decl. ¶ 45; Packett Decl. ¶ 42; Weddle Decl. ¶ 53; Zuniga Decl. ¶ 38.

Moreover, given the nature of the Ryan White Program, the program is often the only means by which patients may be able to access healthcare services, so the restrictions created by the Challenged Conditions would result in the loss of access to healthcare for many transgender patients living with HIV.[64]

Beyond these quintessentially irreparable harms to patients, the Challenged Conditions will cause irreparable harm to Plaintiff healthcare providers by threatening their ability to comply and follow established medical standards of care, their ethical duties and responsibilities, and state and federal anti-discrimination laws.[65] *Cf. Oregon v. Kennedy*, No. 6:25-CV-02409-MTK, 2026 WL 1048354, at *19 n.3 (D. Or. Apr. 18, 2026) ("A policy categorically superseding professionally recognized standards of care as to gender-affirming care causes irreparable harm to Plaintiffs' interests and obligations under state law to ensure access to gender-affirming care[.]"). Further, the First Circuit has acknowledged that the nonpecuniary effects from a loss of federal funding may constitute irreparable harm warranting a preliminary injunction. *New York v. Trump*, 171 F.4th 1, 24 (1st Cir. 2026) (discussing "possible layoffs, reductions in service, and closures of childcare programs; and significant impediments to the delivery of basic health care services to vulnerable populations") (citation modified).[66]

In addition, even temporary deprivation of individual constitutional rights in and of itself constitutes irreparable injury supporting preliminary injunctive relief. *See*, *e.g.*, *Talbott v. United States*, No. 25-5087, 2026 WL 1532205, at *18 (D.C. Cir. June 1, 2026) (equal protection); *Sindicato Puertorriqueño de Trabajadores v. Fortuño*, 699 F.3d 1, 15 (1st Cir. 2012) (free speech);

[64] Zuniga Decl. ¶ 39; Doe Decl. ¶ 59; Roe Decl. ¶¶ 39–40; Collins-Ogle Decl. ¶¶ 60–63.
[65] Packett Decl. ¶ 36; Weddle Decl. ¶ 47; Doe Decl. ¶ 54; Roe Decl. ¶ 41; Brody Decl. ¶ 40; Fox Decl. ¶ 45.
[66] Packett Decl. ¶ 35; *see also* Zuniga Decl. ¶ 29 (discussing operational disruptions from prior Trump Administration actions, including "closure of programs, reduction in ability to provide services, and adjustment of staffing, including staff layoffs.").

Free the Nipple-Fort Collins v. City of Fort Collins, 916 F.3d 792, 806 (10th Cir. 2019) (equal protection); *SFAF*, 786 F.Supp.3d at 1232–33 (free speech and equal protection).

Finally, even if the showing of harm were not so clear-cut—although it is here—where, as here, "the likelihood of success on the merits is great, a movant can show somewhat less in the way of irreparable harm and still garner preliminary injunctive relief." *E.E.O.C. v. Astra U.S.A., Inc.*, 94 F.3d 738, 743 (1st Cir. 1996).

IV. The Remaining Factors Favor Preliminary Relief.

The balance of equities and the public interest merge when the government is the party opposing the preliminary injunction, *Nken*, 556 U.S. at 435, and also strongly favor relief here.

"There is a substantial public interest in having governmental agencies abide by the federal laws that govern their existence and operations." *New York v. McMahon*, 784 F.Supp.3d 311, 372 (D. Mass. 2025) (quotation omitted). Where, as here, Plaintiffs have "demonstrated a high likelihood of success" on the merits, that "is a strong indicator that a preliminary injunction would serve the public interest." *Id.* (citation modified).

There is also "a strong public interest in health and safety." *Massachusetts v. NIH*, 770 F.Supp.3d at 326. Besides the adverse effects on the health of the transgender patients who depend on the Ryan White Program, the Challenged Conditions "will increase the viral load population-wide and increase transmission rates" because of diminished HIV care adherence. Fox Decl. ¶ 43.[67] The impact of the Challenged Conditions in destabilizing the country's HIV service system "will necessarily cause long-term public health crises." Packett Dec. ¶ 42. In addition, the Challenged Conditions are likely to create an increased financial and workforce burden on the

[67] *See also* Brody Decl. ¶ 49; Zuniga Decl. ¶ 38; Doe Decl. ¶ 45.

healthcare system.[68]

By contrast, Defendants will suffer no harm if the Court grants Plaintiffs a preliminary injunction. "There is generally no public interest in the perpetuation of unlawful agency action." *League of Women Voters of United States v. Newby*, 838 F.3d 1, 12 (D.C. Cir. 2016). Defendants have not articulated any public health goals consistent with Congress's mandate that would be frustrated by preliminarily enjoining the Challenged Conditions. Because an injunction would merely delay implementation of Defendants' likely illegal actions and would protect Plaintiffs' proven treatment models and further public health and safety, the balance of the equities and the public interest strongly weigh in favor of Plaintiffs' requested relief.

V. The Court Should Require No Bond.

The Court should exercise its discretion to forgo a bond because Defendants will not suffer any harm from the absence of one. *See Pineda v. Skinner Servs., Inc.*, 22 F.4th 47, 57 (1st Cir. 2021) (courts have substantial discretion to dictate terms of injunction bonds). A bond is additionally inappropriate because "[t]he First Circuit has recognized an exception to the bond requirement in suits to enforce important federal rights or public interests, as is precisely the case here." *McMahon*, 784 F.Supp.3d at 373 (internal citation omitted).

CONCLUSION

For the foregoing reasons, the Court should grant Plaintiffs' motion preliminary relief under 5 U.S.C. § 705 and for a preliminary injunction and enter the attached proposed order.

[68] *See*, *e.g.*, Weddle Decl. ¶ 56 (noting the Challenged Conditions will contribute to "undue workforce strain and attrition"); *id.* at ¶ 54 (stating that the Challenged Conditions will cause exponential costs as each new infection requires lifetime treatment ranging from $500,000 to $1.2 million per person); Brody Decl. ¶ 38 (noting overall health costs increase as patients turn to emergency care settings); Fox Decl. ¶ 38 (noting that if clinicians no longer provided HIV care and gender-affirming medical care together, a "generation of providers" will lose knowledge and experience, degrading the HIV specialty profession); Doe Decl. ¶ 54 (describing likelihood that a colleague will leave her job if the restriction goes into effect).

Dated this 10th day of June 2026.

Respectfully submitted,

/s/ Omar Gonzalez-Pagan

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CERTIFICATE OF SERVICE

I certify that, on June 10, 2026, counsel for Plaintiffs provided a copy of the forgoing motion and any attachments thereto to the following attorneys at the U.S. Department of Justice by electronic mail:

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IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE; HIV MEDICINE ASSOCIATION, a division of the INFECTIOUS DISEASES SOCIETY OF AMERICA; INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE; JENNIFER K. BRODY, MD; and CHRISTOPHER B. FOX, NP, *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION; THOMAS J. ENGELS, in his official capacity as the Administrator of the Health Resources and Services Administration; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., in his official capacity as Secretary of the U.S. Department of Health and Human Services, *Defendants*.	Case No.

DECLARATION OF BRUCE J. PACKETT II, EXECUTIVE DIRECTOR OF THE AMERICAN ACADEMY OF HIV MEDICINE

I, Bruce J. Packett II, hereby state as follows:

1. I am over 18 years of age, of sound mind, and in all respects competent to testify.

2. I have personal knowledge of the facts set forth in this declaration and would testify competently to those facts if called to do so.

3. I am the Executive Director of The American Academy of HIV Medicine ("The Academy"), which is an organizational plaintiff in this case bringing claims on behalf of its members and the transgender patients of its members.

4. I first joined the Academy in 2005, as part of its policy staff, and then served as the Director of Educational Programming and Deputy Executive Director. Since 2019, I have served as the Academy's Executive Director. For the last 21 years, as part of the Academy's staff, I have been engaged in HIV advocacy on behalf of medical providers, including support to the Academy's member; clinical education and curriculum development relating to HIV care; nonprofit business management and development; board management; publication of the Academy's textbook, Fundamentals of HIV Medicine; and oversight and execution of government grants, donor relationships, and partnerships at the Academy.

5. I submit this declaration in support of Plaintiffs' Motion for Preliminary Relief under 5 U.S.C. § 705 and for a Preliminary Injunction, which seeks to prevent Defendants from giving effect to certain conditions relating to transgender people and gender-affirming medical care set forth in Ryan White HIV/AIDS Program ("Ryan White Program" or "RWHAP") Notices of Funding Opportunity issued or forecasted to be issued in 2026 and the 2026 Updated HRSA General Terms and Conditions, issued on March 11, 2026 (collectively, "Challenged Conditions").

6. In this declaration, I explain that HIV providers are under significant stress due to mass retirements, health disparities, and funding challenges amid already high rates of medical provider burnout. I then describe how the Ryan White Program is vital for Academy members' ability to provide comprehensive HIV care, including gender-affirming medical care, and that the effect of a gender-affirming medical care restriction under Ryan White will cause disruptions of operations and patients' HIV care and force Academy members to act against their ethical obligations as medical providers. I conclude by explaining that these problems together will result in future long-term public health crises.

I. Background on the Academy

7. The Academy is a 501(c)(3) nonprofit membership organization and one of the nation's largest independent HIV provider organizations, supporting the HIV practitioners and promoting accessible, quality care for all Americans living with HIV disease.

8. The Academy's membership of HIV practitioners and credentialed providers, which together amount to over 5,000 HIV care providers, give direct care to the majority of HIV patients in the United States.

9. The Academy's mission is to ensure that healthcare professionals have the resources needed to provide prevention, treatment, and care for those with or at risk for HIV and related conditions to achieve optimal health. The Academy works to create an empowered, skilled, and robust healthcare workforce able to intervene at all levels of prevention, care, and treatment for those at risk for or living with HIV. Through a focus on overall wellness, we aim to see a reduction in HIV transmission, an increased quality of life for those living with HIV, and ultimately, an end to the HIV/AIDS epidemic.

10. The Academy was founded in 1999 when there was no specialization for HIV care and no sub-specialty for HIV medicine in medical schools. The Academy created HIV-focused professional certifications in 2001, which are the first and only credentials offered to physicians, nurse practitioners, physician assistants, and pharmacists specializing in advanced-level HIV care. HIV specialty recognition is important because it signals competency to patients, but more broadly, it prepares medical professionals to provide the highest quality of care. The complex nature of HIV care includes evolving clinical guidelines based on best available evidence, complex co-infections and co-morbidities, and a deep understanding of the social drivers of HIV and the cultural competencies that are needed to address the full picture of medical care.

11. The Academy leverages the unique perspective and powerful collective voice of HIV health care providers to address policy issues impacting HIV care practice, patients with and at risk for HIV, sexual health and HIV prevention, and care access and delivery. As an organization and through strategic partnerships, we advocate for Ending the Epidemic initiatives, with a clear emphasis on underserved populations, such as transgender people with HIV, geographic disparities, and elimination of structural and intersectional stigma around those with and at risk for HIV.

12. The Academy's educational and professional development programs help HIV care providers remain current with HIV's rapidly evolving treatment and prevention landscape. The Academy's programs and curricula expand beyond just HIV disease to include clinical issues of primary care and wellness, Hepatitis C ("HCV") and other common co-conditions, overall sexual health, mental health, substance use disorder, and common conditions of an aging population.

13. The Academy's credentialing programs promote standards of care as an independent verification of a provider's knowledge of HIV and HCV care, professional ethics, and overall sexual health competencies. It is nationally recognized for training and certifying medical professionals, known as HIV Specialists™, HIV Experts™, and HIV Pharmacists™, guaranteeing the healthcare professionals' ability to provide robust HIV care.

14. The Academy's credentialing program is so well respected that some Ryan White Planning Councils, the Ryan White-mandated groups that make recommendations regarding the allocation of funding under the Ryan White Program, request that providers be credentialed through the Academy. Similarly, certain specialty pharmacies also require their pharmacists to be Academy credentialed. Several states codify the Academy's credentialing under the state-recognized definition of HIV specialty care, including California, Maryland, and New York.

15. The Academy's training materials provide a complete overview of HIV care, including gender-affirming medical care for transgender patients. In support of this training, the Academy publishes a comprehensive and authoritative reference on the clinical care of HIV/AIDS. Created by over 50 expert clinicians, *Fundamentals of HIV Medicine* is a clinical textbook on HIV care, which includes the latest science, research, and guidelines for care. *Fundamentals of HIV Medicine* highlights the various needs of transgender patients with HIV, providing discussions on evaluations, health maintenance, health disparities, HIV care and prevention for special populations, and gender-affirming medical care.

16. Many of the Academy's members provide medical care to their HIV patients through the Ryan White Program, including through funding under all its parts, as well as any supplementary funding. For their transgender HIV patients, this often includes hormone therapy as treatment for their gender dysphoria (also known as "gender-affirming hormone therapy" or "gender-affirming medical care").

17. Recognizing how integral gender-affirming medical care is to ensure access and adherence to HIV care for transgender patients with HIV, the Academy issued a statement titled "The American Academy of HIV Medicine Statement on Transgender Care and Gender-Diverse Care," in September 2023. The Academy's statement observed, in part, as follows:

> [P]roviding health care for the whole person, including gender-affirming care, is an integral part of status-neutral care delivery and the federal Ending the HIV Epidemic initiative. We will not achieve the goal of ending the HIV epidemic without providing comprehensive medical care for transgender and gender-diverse (TGD) individuals. The Academy's mission is to ensure health care professionals have the resources needed to provide prevention, treatment, and care for those with or at risk for HIV and related conditions to achieve optimal health. In upholding our mission, we support gender-affirming care for TGD individuals, because barriers to comprehensive gender-affirming care exacerbate existing health inequities and prevent TGD individuals from accessing HIV prevention and treatment services that may be appropriate for them.

A copy of the Academy's statement is attached as **Exhibit A.**

18. In addition, the Academy has created a "Transgender Health Resource Center" within its website (https://aahivm.org/transgender-health-resource-center), where it provides resources to its members and other HIV care providers, including webinars regarding the care of transgender patients with HIV and links to practice guidelines relating to HIV care and gender-affirming medical care.

II. Current Stress on HIV Providers

19. Since its inception, the Academy has specifically focused on the needs of the HIV provider workforce.

20. With significant effort and sustained funding, the world of HIV care has dramatically transformed for the better. While HIV care was scaled up to handle the increased demand, over the last decade, the supply of HIV specialists waned as many early experts retired from the field. By 2018, nearly one-third of the Academy's providers were considering retirement. Then the COVID-19 pandemic hit. This put significant stress on every aspect of medical care, especially for the HIV providers who had to help their immunocompromised patients survive a new deadly disease. Today, many Academy members are overwhelmed trying to navigate growing health disparities and funding challenges. Burnout of healthcare providers remains a problem in the medical field, as rates remain worryingly high. Moreover, most medical professionals work for large organizations, which restrict their autonomy. Physician burnout worsens the quality of patient care, increases the risk of medical errors, and decreases patient satisfaction. It also leads to medical professionals leaving the workforce, increasing the workload for those who stay.

21. The number of HIV specialists in the United States is also steadily decreasing as the need for HIV care and prevention is expected to increase. In my experience, a significant number of current HIV clinicians plan to leave the field within the next five years. Reasons for

leaving included burnout, retirement, administrative burdens, and inadequate support. Academy members report increased funding and staffing as the top priorities needed to improve HIV services in the face of burnout and an approaching wave of retirements.

III. Ryan White Funding and Gender-Affirming Medical Care

22. When HIV providers say they are worried about funding, they are primarily worried about Ryan White funding. Approximately 37% of Academy members and credentialed providers rely in part on the Ryan White funding to provide HIV care. This funding is essential to support HIV care, as it more often than not involves caring for patients who are uninsured, underinsured, or marginalized. Indeed, as a whole, HIV-infected patients are appropriately classified as a medically underserved and vulnerable population. Even those members who do not receive Ryan White Program grants are increasingly concerned about Ryan White Program funding cuts negatively impacting other parts of the fragile health coverage system.

23. Academy members rely on each part of the Ryan White Program to provide care for their patients. For example, the Ryan White Program can pay for part or all of the salaries for doctors and nurses to provide gender-affirming medical care, for therapists who serve transgender patients, and for administrative staff support.

24. Because so much of HIV care in the United States, including that provided by Academy members, is affected and funded by the Ryan White Program, as executive director of the Academy, I am aware of the contours of the program and how it affects the Academy's members.

25. The Ryan White Program is a care model designed to provide comprehensive healthcare for people with HIV. The Ryan White Program has four main goals: 1) preventing new HIV infections, 2) improving health outcomes for people with HIV, 3) reducing health disparities

and health inequities for people with HIV, and 4) achieving integrated and coordinated efforts that address the HIV epidemic. Because Ryan White funding reaches so far and wide, it serves most people diagnosed with HIV in the United States. By addressing the full spectrum of needs for people living with HIV, Ryan White has been extraordinarily successful.

26. The Ryan White Program is broken up into different parts based on the type of grant recipient or the purpose of the grant. Part A formula grants are directed at local governments (cities and county governments), and Part B formula grants are directed at States and territories. HIV care providers and organizations receive Part A and Part B funding as passthrough funding from local, state, and territorial entities. Funding is provided to states and territories (Part B), cities and counties (Part A), and directly to providers, community-based organizations (CBOs), and other institutions (Parts C, D, and F) in the form of grants. Funding recipients under Parts A, B, and C must provide comprehensive primary health care to eligible HIV patients.

27. In recognition of the varying nature of the HIV epidemic, Ryan White funding recipients are typically given broad discretion to design key aspects of their programs, including service priorities.

28. Academy members rely on all parts of Ryan White funding to provide care for their HIV patients.

29. Gender-affirming medical care is primary healthcare—or in Ryan White terminology, "a core medical service"—and an essential part of HIV care. As the Academy's Chief Medical Officer noted in a recent Clinical Research Update from the Academy in reference to a study by Reisner, et al. published in March 2025[1], "Gender affirming hormone therapy can be

[1] Sari L. Reisner et al., *HIV Seropositivity and Viral Non-suppression in Transgender, Non-binary, and Gender-diverse People in Primary Care Receiving Gender-affirming Hormone Therapy in the USA Between 2013 and 2019 (LEGACY): An Observational, Longitudinal, Cohort Study*, 12 THE LANCET HIV e283 (2025).

effectively integrated within primary care settings, and results of this unique longitudinal study help affirm the role and necessity of gender-affirming hormone therapy (and low barrier access to such services) on key HIV outcomes, namely HIV seropositivity and viral non-suppression." Copies of the Academy's Clinical Research Update and the Reisner et al. study are attached hereto as **Exhibits B** and **C**.

30. Of the Academy members who rely on Ryan White program funding, 40% of them report providing gender-affirming medical care, although the actual number is likely even higher. Gender-affirming medical care is necessary for Academy members to effectively treat transgender people living with HIV. In fact, Academy members report that transgender patients receiving gender-affirming medical care from Ryan White providers have high rates of maintaining consistent HIV treatment.

31. The Academy knows that Ryan White funding is vital for patients' health. Without it, many Ryan White Program patients would have no access to HIV care because they are generally low-income, uninsured, or underinsured, making them reliant on the program as a payer of last resort for high-cost medicine and support services. The program serves as a critical safety net for the patients of the Academy's members that fills gaps in coverage not met by Medicaid, Medicare, or private insurance, particularly in states that have not expanded Medicaid.

32. Ryan White funding is particularly important for the transgender patients of Academy members and credentialed providers. These providers use Ryan White funds to facilitate both HIV care and gender-affirming medical care, which is crucial for retaining transgender patients in HIV care. Integration of gender-affirming medical care with HIV care improves viral suppression and retention in treatment by building trust and reducing the stigma that often deters transgender people from seeking medical treatment. Additionally, we know that many clinics

funded by Ryan White specialize in transgender health, which helps to overcome historic medical mistrust and discrimination that act as barriers to HIV care. Trust in a provider is one of the most vital components of successful HIV care. If Ryan White clinics and providers specializing in medical care for transgender patients are prohibited from acknowledging and respecting the identities of their transgender patients, as required by the HRSA terms, or lose their ability to provide gender-affirming medical care, transgender patients will lose trust in their providers, and providers will lose patients.

33. Other medical funding sources are unable to cover the loss caused by a restriction on providing gender-affirming medical care under Ryan White and the restriction on acknowledging and respecting transgender patients' identities. Medicaid coverage for gender-affirming medical care is restricted in many states, Medicare cannot, by its nature, cover all transgender patients, and most Ryan White patients do not have private insurance. Without the Ryan White Program, most transgender patients have nowhere else to go. Indeed, in rural settings and in some states, Academy members report that many patients have lost access to gender-affirming medical care through Medicaid, and in some cases, clinical care for gender-affirming medical care has stopped entirely. Based on survey research by the Emergency HIV Clinic Response Task Force, of which the Academy is a member, we know that already 18% of HIV medical professionals report disruptions in their ability to provide gender-affirming medical care. A copy of the Emergency HIV Clinic Response Task Force's report, titled *HIV Response in U.S. Experiencing Renewed Strain* and published in 2026, is attached hereto as **Exhibit D.**

IV. The Impact of the Challenged Conditions on Academy Members and Their Patients

34. The effects of a gender-affirming medical care restriction under Ryan White and the conditioning of funding on not acknowledging and respecting transgender patients' identities

would immediately impact patient care. Academy members would be forced to disrespect their patients and to stop providing essential medical care, that as the Academy's own statement acknowledges is often lifesaving, and I expect that patients would stop showing up.

35. This restriction will cause both immediate and long-term operational disruptions. Compliance with the Challenged Conditions would require clinics and providers to unnecessarily dismantle integrated models of care. This drain on resources would result in needless operational burdens, such as service reductions, hiring freezes, layoffs of support staff, delayed procurements, program closures, and general loss of income for medical practices.

36. A gender-affirming medical care restriction will also force Academy members to act against their ethical obligations as medical providers. Gender-affirming medical care is evidence-based care that can be medically necessary for transgender patients who experience gender dysphoria. And it is, in many cases, lifesaving. Compliance with the prohibition on the use of Ryan White funding for gender-affirming medical care makes providers unnecessarily deviate from standards of care and their own professional judgement. The restriction, as well as the conditioning of funding on not acknowledging and respecting transgender patients' identities, will result in Academy members and credentialed providers being compelled to make an impossible choice: protect either the Ryan White funding that enables them to care for all their HIV patients or fulfill their duty of care to their transgender patients with HIV and risk losing essential funding. These restrictions cause providers to feel disillusioned and stressed by their inability to provide the care that they are sworn to provide and want to provide. As a result, Academy members will lose their credibility as scientific and medical authorities, and the trust between patients and providers could be permanently eroded.

37. In the absence of public health leadership that is guided by evidence and our goal to end the HIV epidemic, it is falling on the Academy to monitor the strains on providers and patients so we can address the challenges in real time. To better understand the impact on providers today, the Academy and the Emergency HIV Clinical Response Task Force surveyed our members about the ongoing challenges they face in providing competent HIV care. The Academy's provider-members believe that restrictions, such as the upcoming Ryan White restriction on providing gender-affirming medical care, will cause massive operational changes, including workflow changes, service disruptions, staffing adjustments, hiring freezes, delayed procurements, staff layoffs, and program closures. They report that HIV clinical and supportive service disruptions have already affected one population more than any other, and that is their transgender patients with HIV. When asked about the most urgent needs to safeguard the continuity of HIV services, providers said they were particularly concerned about the funding landscape, with a specific emphasis on Ryan White funding. The restriction on the use of Ryan White funding for gender-affirming medical care, as well as the conditioning of funding on not acknowledging and respecting transgender patients' identities, would devastate a population that is already teetering on the line of falling out of care.

38. Academy members are already trying to alter how they secure and deliver resources to provide their transgender patients with HIV with the gender-affirming medical care that they need in response to these federal restrictions. And while many have begun seeking alternative funding streams to maintain their patients currently in care, no source of funding is sufficient to replace the funding provided by the Ryan White Program. Nor can any alternative source of funding cure the harms caused by the HRSA Terms' conditioning of funding on recipients not acknowledging and respecting transgender patients' identities.

39. Given the environment created by the current administration's actions relating to transgender people and gender-affirming medical care, some of the Academy's members are scared to talk about gender-affirming medical care and fear publicly disclosing the fact they offer this essential care to their transgender patients due to safety and security concerns, as well as concerns of retaliation, including loss of funding.

40. Academy members and credentialed providers have shared how incredibly concerned they are with the changing HIV prevention and care environment. Our members are experiencing compounding emotional fatigue from witnessing the harm their patients have endured because of this administration's misguided healthcare policies, alongside their own challenges in navigating a discriminatory environment. Many of these same providers experienced the early days of the epidemic, and they know how many lives will be unnecessarily lost without immediate action. Not long ago, we were close to ending the HIV epidemic in this country. Now, we appear to be moving backwards.

41. The unnecessary stress caused by the Challenged Conditions restricting the use of Ryan White funding will exacerbate the problems facing an already strained system and result in worse health outcomes for patients. In my opinion, current clinicians will leave the field or retire earlier, and the small pool of new medical professionals interested in HIV specialization will be discouraged from joining the field. The remaining providers will navigate their already challenging jobs with workforce shortages and accelerated burnout. The lack of providers will create a gap in care for all people living with HIV and increase the operational burden of clinics, causing the destabilization of the United States' HIV care.

42. The destabilization of HIV services will necessarily cause long-term public health crises in the future. Once patients fall out of care, community viral load and HIV transmissions

increase. Limiting these disruptions is vital to safeguarding lives and decades of progress in the United States' HIV response. If the Ryan White gender-affirming medical care restriction and the conditioning of funding on not acknowledging and respecting transgender patients' identities are allowed to go into effect and be incorporated into the Ryan White funding streams, the effects will be devastating and the fight against HIV will be lost for decades.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: June 8, 2026

Bruce J. Packett II
Executive Director, The Academy

EXHIBIT A

21 Sep The American Academy of HIV Medicine Statement on Transgender Care and Gender-Diverse Care

Posted at 17:20h in Press Releases by Adrianne Wyatt • 0 Comments • 0 Likes • Share

Transgender care, gender-diverse care, and gender-affirming care is life-saving health care. As an organization whose members are comprised of health care providers and clinicians, the Academy unequivocally supports transgender care, gender-diverse care, and gender-affirming care as well as the professionals who provide it. We uphold the sanctity of the patient-provider relationship and the individual decisions regarding the provision of health care that the patient and their provider make together.

Additionally, providing health care for the whole person, including gender-affirming care, is an integral part of status-neutral care delivery and the federal Ending the HIV Epidemic initiative. We will not achieve the goal of ending the HIV epidemic without providing comprehensive medical care for transgender and gender-diverse (TGD) individuals. The Academy's mission is to ensure health care professionals have the resources needed to provide prevention, treatment, and care for those with or at risk for HIV and related conditions to achieve optimal health. In upholding our mission, we support gender-affirming care for TGD individuals, because barriers to comprehensive gender-affirming care exacerbate existing health inequities and prevent TGD individuals from accessing HIV prevention and treatment services that may be appropriate for them.

EXHIBIT B

CLINICAL RESEARCH UPDATE

by Carolyn Chu, MD, MSc, AAHIVS, AAHIVM Chief Medical Offi

April 8, 2025

FEATURED LITERATURE:

Reisner SL, Pletta DR, Mayer KH, et al. HIV seropositivity and viral non-suppression in transgender, non-binary, c gender-affirming hormone therapy in the USA between 2013 and 2019 (LEGACY): an observational, longitudinal, c 3018(25)00004-9. doi:10.1016/S2352-3018(25)00004-9.

This analysis describes key HIV-related outcomes from the LEGACY study, which followed a diverse cohort of trans qualified health centers in the northeast US. Investigators assessed whether gender affirming hormone therapy (G seropositivity and viral non-suppression in the past 12 months. GAHT was delivered per established standards, ar medical provider determination. De-identified health record data were extracted across seven years of follow-up. and 6.9% in 2019, and viral non-suppression decreased: 22.4% of participants with HIV in 2013 were not suppresse analyses, participants with a current GAHT prescription had significantly lower risk of HIV seropositivity: factors ass group; being a transgender woman or non-binary assigned male at birth; identifying as a racially or ethnically minc Among participants with HIV, people with current GAHT prescription had significantly lower risk of viral non-suppr groups; being a transgender woman; and living at 100–199% FPL and 200–299% FPL (vs. 0–99% FPL).

Author's Commentary:

Gender affirming hormone therapy can be effectively integrated within primary care settings, and results of this unique l gender-affirming hormone therapy (and low barrier access to such services) on key HIV outcomes, namely HIV seropositi importance of engagement in care to increase screening and identify new HIV infections among trans people, and enhan

View archived Clinical Research Update entries here.

EXHIBIT C

HIV seropositivity and viral non-suppression in transgender, non-binary, and gender-diverse people in primary care receiving gender-affirming hormone therapy in the USA between 2013 and 2019 (LEGACY): an observational, longitudinal, cohort study

Sari L Reisner, David R Pletta, Kenneth H Mayer, Madeline B Deutsch, Tonia Poteat, Jennifer Potter, Andrea L Wirtz, Alexander Harris, Juwan Campbell, Alex S Keuroghlian, Jaclyn M W Hughto, Alex Gonzalez, Asa E Radix

Summary

Background Gender-affirming hormone therapy is medically necessary for many transgender, non-binary, and gender-diverse (trans) individuals and might improve HIV clinical outcomes for trans people. This study evaluated gender-affirming hormone therapy delivered in primary care as an intervention to improve HIV outcomes for trans adults in the USA.

Methods LEGACY is a longitudinal cohort of trans adult participants receiving primary care at two US federally qualified health centres: Fenway Health (Boston, MA, USA) and Callen-Lorde Community Health Center (New York, NY, USA). Eligibility criteria were age at least 18 years, gender identity differing from assigned sex at birth, past 12-month medical visit, and signed consent with no research exclusion documented in electronic health record data. Eligible participants contributed electronic health data from 2013 to 2019. The exposure was gender-affirming hormone therapy prescription. Clinical outcomes were HIV seropositivity (all participants) and viral non-suppression (participants with HIV; ≥200 copies per mL) in the past 12 months. Log-Poisson generalised estimating equations assessed the longitudinal association of gender-affirming hormone therapy prescription (puberty blockers, anti-androgens, oestrogens, progesterone, and testosterone) with outcomes, adjusting for individual-level confounders.

Findings Among the 8109 trans participants in 2019, median age was 29 years (IQR 24–37). 2960 (36·5%) were transgender women, 2541 (31·3%) were transgender men, 1507 (18·6%) were non-binary, and 1101 (13·6%) were another trans identity. 4446 (54·8%) were White, 1323 (16·3%) were Black or African American, 498 (6·1%) were multiracial, and 1663 (20·5%) were Hispanic or Latinx. 2736 (33·7%) of 8109 participants were publicly insured and 451 (5·6%) participants were uninsured. In 2013, 2549 (85·5%) of 2983 participants were prescribed gender-affirming hormone therapy, 272 (9·1%) of 2983 participants were HIV seropositive, and 61 (22·4%) of 272 participants were not virally suppressed. In 2019, 7252 (89·4%) of 8109 participants were prescribed gender-affirming hormone therapy, 560 (6·9%) of 8109 participants were HIV seropositive, and 88 (15·7%) of 560 participants were not virally suppressed. Gender-affirming hormone therapy prescription was associated with reduced rates of HIV seropositivity (adjusted risk ratio [RR] 0·63, 95% CI 0·56–0·70) and viral non-suppression (adjusted RR 0·56, 95% CI 0·45–0·69) across follow-up.

Interpretation Gender-affirming care is important for optimising HIV outcomes among trans people. Our results underscore the vital role of gender-affirming models of care and access to gender-affirming hormone therapy for trans people.

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See Comment page e244

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Introduction

In the USA, transgender, non-binary, and gender-diverse (trans) people who have a gender identity that differs from the sex assigned to them at birth are highly burdened by HIV and have suboptimal HIV clinical outcomes, including high viral non-suppression rates.[1,2] Trans people, particularly transgender women and Black transgender people, were a prioritised population in the National HIV/AIDS Strategy (NHAS) for 2022–25.[3] For example, NHAS 2022–25 had a goal of increasing viral suppression among transgender women from the baseline of 80·5% to 95·0%.[3] According to Health Resources and Services Administration Ryan White HIV/AIDS Program data from 2021, viral suppression in transgender people was 84·8%, well below the national goal.[4] Gender-affirming hormone therapy is medically

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Research in context

Evidence before this study

In the USA, transgender, non-binary, and other gender-diverse (trans) people were prioritised in the National HIV/AIDS Strategy. Gender-affirming hormone therapy is medically necessary for many trans people and might improve HIV outcomes.
We searched PubMed and Google Scholar using Medical Subject Headings and keyword terms for US-based publications reporting gender-affirming hormone therapy, HIV, and viral non-suppression between Jan 1, 2014, and July 31, 2024, for articles published in English. The HIV burden in trans people was high, with suboptimal viral non-suppression rates. For example, a meta-analysis of 22 US studies from 2006 to 2021 on HIV outcomes in trans people by Becasen and colleagues found the weighted mean proportion of transgender women currently virally suppressed was 59·3% (95% CI 49·5–68·4), well below national targets. Our search identified only two studies of transgender men and none of non-binary people. Few investigations assessed gender-affirming hormone therapy alongside viral non-suppression, with existing studies restricted to transgender women and having mixed findings. Most studies were cross-sectional and had small sample sizes with short follow-up periods, which might, in part, account for the inconsistent results. There is a need for additional longitudinal research and larger sample sizes to address these limitations.

Added value of this study

Our study included a large and diverse cohort of transgender, non-binary, and gender-diverse primary care participants drawn from federally qualified health centres in the USA, laboratory-confirmed outcomes from electronic health record data, and unprecedented longitudinal data on gender-affirming hormone therapy and HIV outcomes. We evaluated gender-affirming hormone therapy delivered in primary care as an intervention to improve HIV outcomes for trans adults. Compared with trans participants not prescribed gender-affirming hormone therapy, those prescribed gender-affirming hormone therapy had a lower risk of past-year HIV seropositivity and, among those with HIV, a lower risk of viral non-suppression during the 7 years of follow-up. Our consideration of gender identity, gender-affirming hormone therapy, and HIV outcomes is important, given that US HIV surveillance efforts do not routinely collect these data.
Our findings contribute to the evidence base for the health-promoting role of gender-affirming hormone therapy, showing that gender-affirming hormone therapy is associated with reduced HIV morbidity longitudinally for trans people, and underscore the vital role of gender-affirming models of care and access to gender-affirming hormone therapy for trans people. Our results could inform gender-affirming interventions to mitigate HIV inequities for trans people, including those incorporating gender-affirming hormone therapy.

Implications of all the available evidence

Integrating gender-affirming hormone therapy with HIV testing and care delivery is recommended for trans people. Gender-affirming care is important for optimising HIV outcomes among trans people.

necessary for many trans people and is known to improve many health outcomes.[5] However, few studies have assessed the association between gender-affirming hormone therapy and HIV acquisition in trans individuals. Furthermore, studies evaluating the association of gender-affirming hormone therapy with viral load suppression have had mixed findings.[6–9] Notably, most previous research has been cross-sectional,[9,10] and most existing longitudinal studies have small sample sizes[11] or short follow-up periods (or both),[8] which might, in part, account for the inconsistent results. Studies with larger sample sizes of trans people living with HIV have not assessed gender-affirming hormone therapy.[6] There is a need for additional longitudinal research to address these limitations and to examine differences by gender identity among trans people, including disaggregating for trans men and non-binary individuals, given the dearth of research about these groups.[1]

In this study, we sought to evaluate gender-affirming hormone therapy delivered in primary care as an intervention to improve HIV outcomes for trans adults. We assessed whether gender-affirming hormone therapy was associated with reduced rates of HIV seropositivity and viral non-suppression in the past 12 months for 7 years of follow-up in a cohort of adult trans individuals in primary care who were diverse in age, race, ethnicity, and gender identity. We hypothesised that gender-affirming hormone therapy would reduce HIV seropositivity and viral non-suppression incidence. We use trans as a collective term throughout this paper to refer to transgender, non-binary, and gender-diverse populations but do not intend to exclude or minoritise populations contained within this phrasing, and we acknowledge those who use other terms.

This manuscript was accepted before Executive Orders were issued by US President Trump related to gender ideology and diversity, equity, and inclusion in the USA, which have made some of the materials referenced in this Article inaccessible. The references were available upon acceptance of the manuscript.

Methods

Study design and participants

LEGACY is a longitudinal cohort of trans adult participants receiving primary care at two US federally qualified health centres: Fenway Health (Boston, MA, USA) and Callen-Lorde Community Health Center (New York, NY, USA).[12] Both federally qualified health centres specialise in provision of gender-affirming health care, including delivery of gender-affirming hormone

therapy using an informed consent protocol.[5] 8109 LEGACY participants were followed up from 2013 to 2019. In this period, gender-affirming hormone therapy was delivered as part of primary care according to the same established standards by both federally qualified health centres.[5] Qualitative research with trans people informed cohort implementation,[13] and a community advisory board oversaw the study. The detailed LEGACY protocol has been published elsewhere.[12]

Participants were considered eligible for LEGACY if they had a gender identity different to their assigned sex at birth (verified using a two-step method to cross-categorise sex and gender identity self-reported on participant registration or ICD-10 code of F64·0–9); were aged at least 18 years; were a primary care patient with at least one medical visit in the past 12 months; and had a signed informed consent form on file and no research exclusion indicated in their patient chart. All study procedures were approved by the Fenway Health institutional review board (FWA00000145).

Procedures

Eligible trans participants contributed to the LEGACY research database. De-identified electronic health record data were extracted (eg, laboratory testing data and provider-documented diagnoses) and harmonised across sites. We compared 12-month HIV seropositivity (for all participants) and viral non-suppression (for participants with HIV) in groups who did and did not receive gender-affirming hormone therapy across the 7 years of follow-up. Within a given year, trans participants' electronic health records contained information related to their HIV serostatus, viral load (for those with HIV), gender-affirming hormone therapy prescription, sociodemographic characteristics, substance use, mental health, and other sexual health indicators.

Outcomes

Two binary outcomes were operationalised. Outcome 1 was HIV-positive serostatus (for all participants). Participants were considered to be living with HIV if they tested positive for HIV, or a clinician added an indicator for HIV-positive serostatus to the participant's electronic health record. HIV testing was done for participants who had clinical indications, as determined by their medical provider. Outcome 2 was viral non-suppression (for participants with HIV). Based on standards from the US Centers for Disease Control and Prevention (CDC),[14] HIV viral non-suppression was defined as having a viral load of 200 copies per mL of blood or greater. Individuals could not count toward both outcomes in one year, as each outcome was operationalised according to the calendar year.

The exposure variable of gender-affirming hormone therapy was coded as a binary variable of being prescribed gender-affirming hormone therapy (yes *vs* no) in electronic health record data. This variable was operationalised using the date of first gender-affirming hormone therapy prescription and the date of last gender-affirming hormone therapy prescription in each year of observation in the cohort. A participant was dichotomously coded as either having a gender-affirming hormone therapy prescription within the year versus having no gender-affirming hormone therapy prescription within the year. Hormone variable prescription types were pubertal blockers (eg, leuprolide), antiandrogens (eg, spironolactone), oestrogens (eg, estradiol), progesterone (eg, micronised progesterone), and testosterone (eg, testosterone cypionate).

Sociodemographics included age, continuously and grouped in years (18–24, 25–30, 31–40, 41–50, or ≥51). Gender identity was operationalised by cross-tabulating participants' self-reported gender identity and sex assigned at birth and coding as transgender woman, transgender man, non-binary assigned male at birth, non-binary assigned female at birth, or transgender, not specified. Racial identity was documented in the electronic health record as American Indian or Alaskan Native, Asian, Black or African American, multiracial, Native Hawaiian or Pacific Islander, White, or other race. Hispanic or Latinx ethnicity was indicated dichotomously (yes *vs* no). Type of medical insurance included private insurance, public insurance, and no insurance. The Ryan White HIV/AIDS program was counted as public health insurance in this analysis. A participant's individual income percentage of the federal poverty level was coded categorically as 0–99%, 100–199%, 200–299%, or 300% or more.[15] Study site was coded as Boston or New York City.

Alcohol use disorder was determined based on diagnosis per the Diagnostic and Statistical Manual of Mental Disorders (F10.10–21)[16] using documented ICD-10 coding, as captured in the electronic health record. Psychological distress was measured using the validated self-reported Patient Health Questionnaire 9-item (PHQ-9)[17] as part of routine care. A score of 10 or more was considered clinically elevated (hereafter, PHQ depression) consistent with validated cutoffs (88% sensitivity and 88% specificity for major depression).[17] When only a narrative, non-integer appraisal of a participant's PHQ-9 score was provided in the electronic health record, an a-priori decision was made by the investigative team that a rating of moderate depression, moderately severe depression, or severe depression was indicative of depression, whereas a rating of mild depression or no depression was not. Sexual health measures included whether a participant tested positive for anogenital gonorrhoea or chlamydia. A positive anogenital sexually transmitted infection diagnosis was defined as having had a positive urethral, cervical, or rectal test within the past year for either chlamydia or gonorrhoea (yes *vs* no). Pre-exposure prophylaxis (PrEP) for HIV prevention was defined as having a PrEP prescription within the past year (yes *vs* no). Years in the cohort (2013–19) was operationalised as a continuous variable of years retained in care, ranging from 1 to 7.

	2013			2019		
	Total (n=2983)	GAHT prescription (n=2549)	No GAHT prescription (n=434)	Total (n=8109)	GAHT prescription (n=7252)	No GAHT prescription (n=857)
Study site						
Fenway Health	1079 (36·2%)	907 (35·6%)	172 (39·6%)	3610 (44·5%)	3046 (42·0%)	564 (65·8%)
Callen-Lorde	1904 (63·8%)	1642 (64·4%)	262 (60·4%)	4499 (55·5%)	4206 (58·0%)	293 (34·2%)
Age, years						
Median (IQR)	30 (24–40)	31 (25–40)	27 (23–36)	29 (24–37)	29 (24–37)	28 (23–34)
18–24	785 (26·3%)	632 (24·8%)	153 (35·3%)	2167 (26·7%)	1870 (25·8%)	297 (34·7%)
25–30	751 (25·2%)	639 (25·1%)	112 (25·8%)	2470 (30·5%)	2222 (30·6%)	248 (28·9%)
31–40	727 (24·4%)	637 (25·0%)	90 (20·7%)	1984 (24·5%)	1797 (24·8%)	187 (21·8%)
41–50	420 (14·1%)	372 (14·6%)	48 (11·1%)	776 (9·6%)	721 (9·9%)	55 (6·4%)
≥51	294 (9·9%)	263 (10·3%)	31 (7·1%)	710 (8·8%)	640 (8·8%)	70 (8·2%)
Missing	6 (0·2%)	6 (0·2%)	0	2 (0·0%)	2 (0·0%)	0
Gender identity						
Transgender man	764 (25·6%)	646 (25·3%)	118 (27·2%)	2541 (31·3%)	2370 (32·7%)	171 (20·0%)
Transgender woman	1086 (36·4%)	975 (38·3%)	111 (25·6%)	2960 (36·5%)	2776 (38·3%)	184 (21·5%)
Non-binary assigned female at birth	143 (4·8%)	74 (2·9%)	69 (15·9%)	1006 (12·4%)	702 (9·7%)	304 (35·5%)
Non-binary assigned male at birth	61 (2·0%)	44 (1·7%)	17 (3·9%)	501 (6·2%)	384 (5·3%)	117 (13·7%)
Transgender, not specified	929 (31·1%)	810 (31·8%)	119 (27·4%)	1101 (13·6%)	1020 (14·1%)	81 (9·5%)
Racial identity						
American Indian or Alaskan Native	22 (0·7%)	19 (0·7%)	3 (0·7%)	79 (1·0%)	71 (1·0%)	8 (0·9%)
Another racial identity	11 (0·4%)	10 (0·4%)	1 (0·2%)	57 (0·7%)	47 (0·6%)	10 (1·2%)
Asian	131 (4·4%)	118 (4·6%)	13 (3·0%)	387 (4·8%)	348 (4·8%)	39 (4·6%)
Black or African American	464 (15·6%)	399 (15·7%)	65 (15·0%)	1323 (16·3%)	1236 (17·0%)	87 (10·2%)
Multiracial	177 (5·9%)	148 (5·8%)	29 (6·7%)	498 (6·1%)	430 (5·9%)	68 (7·9%)
Native Hawaiian or Pacific Islander	47 (1·6%)	40 (1·6%)	7 (1·6%)	90 (1·1%)	85 (1·2%)	5 (0·6%)
White	1557 (52·2%)	1310 (51·4%)	247 (56·9%)	4446 (54·8%)	3914 (54·0%)	532 (62·1%)
Missing	574 (19·2%)	505 (19·8%)	69 (15·9%)	1229 (15·2%)	1121 (15·5%)	108 (12·6%)
Hispanic or Latinx ethnicity						
Yes	704 (23·6%)	619 (24·3%)	85 (19·6%)	1663 (20·5%)	1539 (21·2%)	124 (14·5%)
No	2279 (76·4%)	1930 (75·7%)	349 (80·4%)	6446 (79·5%)	5713 (78·8%)	733 (85·5%)
Insurance type						
Private	1320 (44·3%)	1129 (44·3%)	191 (44·0%)	4085 (50·4%)	3582 (49·4%)	503 (58·7%)
Public	1140 (38·2%)	963 (37·8%)	177 (40·8%)	2736 (33·7%)	2490 (34·3%)	246 (28·7%)
Uninsured	108 (3·6%)	92 (3·6%)	16 (3·7%)	451 (5·6%)	398 (5·5%)	53 (6·2%)
Missing	415 (13·9%)	365 (14·3%)	50 (11·5%)	837 (10·3%)	782 (10·8%)	55 (6·4%)
Percentage of the federal poverty level						
0–99	1431 (48·0%)	1223 (48·0%)	208 (47·9%)	3370 (41·6%)	3070 (42·3%)	300 (35·0%)
100–199	435 (14·6%)	373 (14·6%)	62 (14·3%)	950 (11·7%)	850 (11·7%)	100 (11·7%)
200–299	235 (7·9%)	197 (7·7%)	38 (8·8%)	651 (8·0%)	576 (7·9%)	75 (8·8%)
≥300	461 (15·5%)	397 (15·6%)	64 (14·7%)	1186 (14·6%)	1041 (14·4%)	145 (16·9%)
Missing	421 (14·1%)	359 (14·1%)	62 (14·3%)	1952 (24·1%)	1715 (23·6%)	237 (27·7%)
Alcohol use disorder						
Yes	39 (1·3%)	35 (1·4%)	4 (0·9%)	210 (2·6%)	187 (2·6%)	23 (2·7%)
No	2944 (98·7%)	2514 (98·6%)	430 (99·1%)	7899 (97·4%)	7065 (97·4%)	834 (97·3%)
PHQ-9 depression						
Yes	96 (3·2%)	78 (3·1%)	18 (4·1%)	886 (10·9%)	747 (10·3%)	139 (16·2%)
No	2887 (96·8%)	2471 (96·9%)	416 (95·9%)	7223 (89·1%)	6505 (89·7%)	718 (83·8%)
PrEP prescription						
Yes	4 (0·1%)	3 (0·1%)	1 (0·2%)	233 (2·9%)	196 (2·7%)	37 (4·3%)
No	2979 (99·9%)	2546 (99·9%)	433 (99·8%)	7876 (97·1%)	7056 (97·3%)	820 (95·7%)

(Table 1 continues on next page)

	2013			2019		
	Total (n=2983)	GAHT prescription (n=2549)	No GAHT prescription (n=434)	Total (n=8109)	GAHT prescription (n=7252)	No GAHT prescription (n=857)
(Continued from previous page)						
Anogenital STI diagnosis						
Yes	95 (3·2%)	79 (3·1%)	16 (3·7%)	340 (4·2%)	309 (4·3%)	31 (3·6%)
No	2888 (96·8%)	2470 (96·9%)	418 (96·3%)	7769 (95·8%)	6943 (95·7%)	826 (96·4%)
HIV serostatus						
HIV-positive	272 (9·1%)	229 (9·0%)	43 (9·9%)	560 (6·9%)	512 (7·1%)	48 (5·6%)
HIV-negative	2711 (90·9%)	2320 (91·0%)	391 (90·1%)	7549 (93·1%)	6740 (92·9%)	809 (94·4%)
HIV viral suppression						
Not virally suppressed (≥200 copies per mL)	61 (2·0%)	46 (1·8%)	15 (3·5%)	88 (1·1%)	78 (1·1%)	10 (1·2%)
Virally suppressed (<200 copies per mL)	185 (6·2%)	162 (6·4%)	23 (5·3%)	430 (5·3%)	396 (5·5%)	34 (4·0%)
Missing viral load	26 (0·9%)	21 (0·8%)	5 (1·2%)	42 (0·5%)	38 (0·5%)	4 (0·5%)
Not applicable, not living with HIV	2711 (90·9%)	2320 (91·0%)	391 (90·1%)	7549 (93·1%)	6740 (92·9%)	809 (94·4%)
Years retained in care 2013–19, median (IQR)	6 (4–6)	6 (4–6)	6 (4–6)	3 (1–5)	3 (1–6)	1 (0–3)

Data are n (%), unless otherwise indicated. GAHT=gender-affirming hormone therapy. PHQ-9=Patient Health Questionnaire 9-item. PrEP=pre-exposure prophylaxis. STI=sexually transmitted infection.

Table 1: **Characteristics of transgender, non-binary, and gender-diverse individuals in primary care in 2013 and 2019**

Statistical analysis

The study was powered (80% power, α=0·05) to detect a statistically significant association between gender-affirming hormone therapy and viral non-suppression (see published study protocol for sample size calculation).[12] Data analyses were done using R (version 4.3.1) and RStudio (version 2023.06.1). Descriptive statistics were generated for the full sample in 2019 and variable missingness was assessed descriptively. Missingness ranged from 0·0% for age to 24·1% for federal poverty level percentage. Test statistics and p values comparing trans participants with and without HIV were generated by χ^2 tests of independence with Monte Carlo-simulated p values (2000 replicates; categorical) and Wilcoxon rank sum tests with continuity corrections (continuous). A second longitudinal dataset was generated, restricted to participants with HIV. Analyses imputed 100 datasets for both the full cohort dataset and the restricted to participants living with HIV dataset, using multiple imputation with chained equations via the mice package in R (appendix p 1).[18] Cumulative HIV seropositivity and viral non-suppression rates were graphically visualised by race and ethnicity, and stratified by gender identity.

Bivariate and multivariable log-Poisson generalised estimating equation models with cluster-robust SEs were fitted with an exchangeable working correlation structure to the imputed datasets to produce risk ratios (RRs), adjusted RRs, and 95% CIs for a participant's risk of having HIV-positive serostatus (outcome 1, all participants) and being virally non-suppressed (outcome 2, participants with HIV) over time. For outcome 1, PrEP prescription was not included in the model as there were no new HIV cases among PrEP users. For stability in model estimands, non-binary assigned male at birth and non-binary assigned female at birth categories were combined for the viral non-suppression outcome due to small sample sizes. Generalised estimating equation models estimated the marginal or population-averaged effect of concurrent gender-affirming hormone therapy on HIV seropositivity or viral non-suppression, using robust SEs and adjusting for repeated measures. All variables were incorporated into a multivariable model for each outcome. p<0·05 was considered to indicate a statistically significant difference.

Interpretations of associations incorporated epidemiological guidance to reduce reliance solely on p values and consider the magnitude and direction of associations and 95% CIs, in addition to p values, when making inferences.

The effect of unmeasured confounders was evaluated in sensitivity analyses by estimating the E-value and corresponding 95% confidence limits.[19] The E-value is a measure of the minimum strength of the association that an unmeasured confounder (or set of confounders) would need to have, with both the exposure and the outcome, to fully explain the exposure–outcome association on the RR.[19]

See Online for appendix

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Among the 8109 trans participants in 2019, the median age was 29 years (IQR 24–37). Participants were diverse in gender identity with 2960 (36·5%) being transgender women, 2541 (31·3%) transgender men, 1507 (18·6%) non-binary, and 1101 (13·6%) another trans identity

(table 1). Participants were mostly White (4446 [54·8%]), followed by Black or African American (1323 [16·3%]), multiracial (498 [6·1%]), and Hispanic or Latinx (1663 [20·5%]). 1837 (22·6%) participants were living at 200% of the federal poverty level or greater; 2736 (33·7%) were publicly insured and 451 (5·6%) were uninsured. 210 (2·6%) had an alcohol use disorder diagnosis; 886 (10·9%) screened positive for depression via the PHQ-9. 340 (4·2%) had anogenital gonorrhoea or chlamydia diagnoses in the past 12 months. 3·1% of participants without HIV had a current PrEP prescription.

Most participants had a gender-affirming hormone therapy prescription (85·5% in 2013 and 89·4% in 2019; table 1). Rates of HIV seropositivity were 9·1% in 2013 and 6·9% in 2019, and viral non-suppression decreased across the 7 years of follow-up (61 [22·4%] of 272 participants with HIV in 2013 and 88 [15·7%] of 560 participants with HIV in 2019). In 2019, on average, participants with HIV were older than participants without HIV (median age 37 years [IQR 30–37] *vs* 28 years [24–36]; p<0·0001).

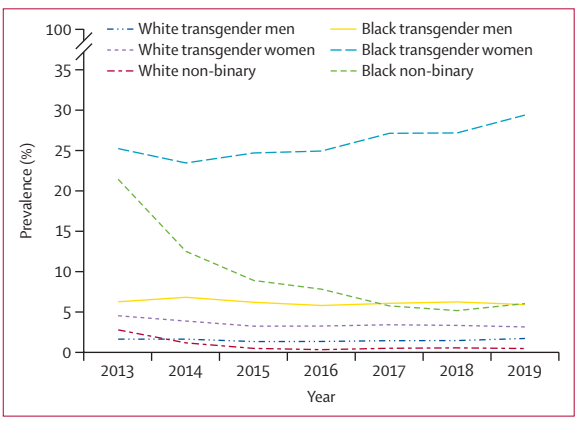


Figure 1: **HIV seropositivity rates among transgender, non-binary, and gender-diverse participants by race and year, stratified by gender identity (2013–19)**

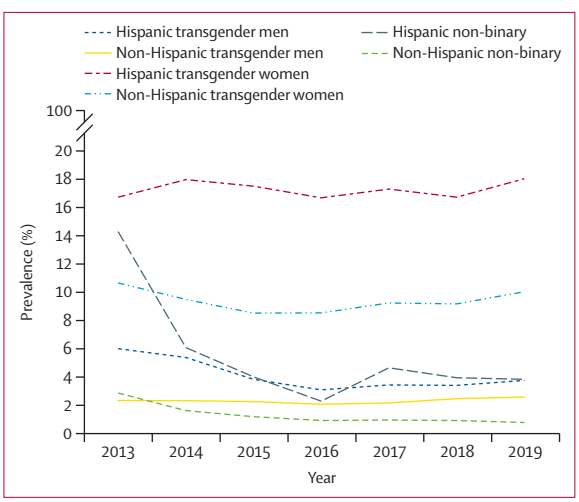


Figure 2: **HIV seropositivity rates among transgender, non-binary, and gender-diverse participants by ethnicity and year, stratified by gender identity (2013–19)**

Cumulative HIV seroprevalence rates stratified by gender identity are displayed by race (figure 1; appendix p 2) and ethnicity (figure 2; appendix p 3). In 2019, in terms of racial identity, the highest HIV seropositivity rates were in Black (164 [29·4%] of 558 participants), other race (19 [18·6%] of 102 participants), and multiracial (35 [17·8%] of 197 participants) transgender women, followed by other race (two [9·5%] of 21 participants) and Black (seven [6·0%] of 116 participants) non-binary participants. In terms of ethnicity, the highest HIV seropositivity rates were among Hispanic (129 [18·0%] of 716 participants) and non-Hispanic (225 [10·0%] of 2244 participants) transgender women, followed by Hispanic non-binary (six [3·8%] of 157 participants) and Hispanic transgender men (19 [3·7%] of 508 participants). HIV prevalence in transgender men ranged from one (0·8%) of 131 participants (multiracial transgender men) to 25 (5·9%) of 424 partcipants (Black transgender men). HIV seropositivity appeared stable for most subpopulations during follow-up, but increased for some groups (eg, Black transgender women; figure 1. In 2019, by racial identity, the highest rates of viral non-suppression were in Black non-binary participants (two [28·6%] of seven participants) and multiracial (ten [28·6%] of 35 participants), other race (four [21·1%] of 19 participants), and Black (33 [20·1%] of 164 participants) transgender women. In terms of ethnicity, in 2019, the highest rates of HIV viral non-suppression were among non-Hispanic transgender women (40 [17·8%] of 225 participants), followed by Hispanic non-binary participants (one [16·7%] of six participants) and Hispanic transgender men (three [15·8%] of 19 participants).

In a multivariable model, participants with a current gender-affirming hormone therapy prescription (adjusted RR 0·63, 95% CI 0·56–0·70) had a significantly lower risk of HIV seropositivity compared with participants without a gender-affirming hormone therapy prescription during follow-up (table 2). The E-value calculated was 2·55 (95% confidence limit 2·21–2·97) for the covariate-adjusted association between gender-affirming hormone therapy prescription and risk for HIV-positive serostatus.

In this model, factors associated with significantly higher risk of HIV positivity were as follows: being in an older age group compared with those aged 18–24 years; being a transgender woman or non-binary assigned male at birth compared with a transgender man; identifying as a racially or ethnically minoritised group compared with identifying as White; having public insurance and no insurance compared with having private insurance; having a positive anogenital gonorrhoea or chlamydia sexually transmitted infection diagnosis; and greater number of years in care (table 2). Variables associated with a significantly lower risk of living with HIV were being non-binary assigned female at birth compared with a transgender man and living at 100–199% of the federal poverty level or 300% or higher of the federal

poverty level compared with 0–99% of the federal poverty level.

In the multivariable model, participants with a gender-affirming hormone therapy prescription had significantly lower risk of viral non-suppression compared with those not on hormones during follow-up (adjusted RR 0·56, 95% CI 0·45–0·69, table 3). The E-value was 2·97 (95% confidence limit 2·26–3·87) for the covariate-adjusted association between gender-affirming hormone therapy prescription and viral non-suppression risk.

Factors associated with a significantly decreased risk of viral non-suppression were as follows: being in older age groups compared with the 18–24 years group; being a transgender woman compared with a transgender man; living at 100–199% of the federal poverty level and 200–299% of the federal poverty level versus 0–99% of the federal poverty level; and a greater number of years in care. Latinx participants living with HIV had a lower risk of viral non-suppression compared with White individuals (adjusted RR 0·84, 95% CI 0·69–1·01, table 3).

Discussion

This longitudinal study of trans participants receiving primary care at federally qualified health centres found that gender-affirming hormone therapy prescribed through informed consent protocols was associated with reduced rates of HIV seropositivity and viral non-suppression over time. The mechanisms by which gender-affirming hormone therapy affects HIV serostatus and viral suppression outcomes for trans participants in this study remain unclear. Gender-affirming hormone therapy is prospectively associated with reduced mental health distress and improved quality of life;[20] these effects might, in turn, facilitate improved health behaviours, such as condom use or antiretroviral medication adherence. Gender-affirming hormone therapy-related care might also increase trust with providers, thereby reducing barriers to discussing concerns about sexual health or adherence difficulties. Years retained in care predicted increased risk for HIV seropositivity and decreased risk for viral non-suppression, highlighting engagement in care as key to identifying new HIV infections and enhancing viral suppression. Future research is necessary to understand the pathways through which gender-affirming hormone therapy is associated with HIV clinical outcomes in this study.

Although overall HIV seropositivity declined across follow-up, rates increased among some subpopulations. We observed higher HIV seropositivity across several sociodemographic characteristics, mirroring national HIV epidemic statistics.[21–23] Ethnically and racially minoritised groups had a significantly increased risk for HIV seropositivity across the years we observed. Our findings highlight the urgent need for efforts to address the unique HIV prevention and care needs of trans participants of colour, mirroring national trends in cisgender populations. Transgender women and non-binary assigned male at

	Bivariate models		Multivariable model	
	RR (95% CI)	p value	Adjusted RR (95% CI)	p value
Exposure				
Gender-affirming hormone therapy prescription				
Yes	1·16 (1·04–1·30)	0·0079	0·63 (0·56–0·70)	<0·0001
No	1 (ref)	..	1 (ref)	..
Covariates and confounders				
Study site				
Fenway Health	0·20 (0·18–0·23)	<0·0001	0·53 (0·47–0·59)	<0·0001
Callen-Lorde	1 (ref)	..	1 (ref)	..
Age group, years				
18–24	1 (ref)	..	1 (ref)	..
25–30	2·70 (2·33–3·14)	<0·0001	2·59 (2·23–3·00)	<0·0001
31–40	4·97 (4·31–5·74)	<0·0001	4·57 (3·96–5·26)	<0·0001
41–50	8·09 (6·99–9·38)	<0·0001	6·79 (5·85–7·87)	<0·0001
≥51	6·32 (5·41–7·38)	<0·0001	6·29 (5·36–7·38)	<0·0001
Gender identity				
Transgender man	1 (ref)	..	1 (ref)	..
Transgender woman	4·77 (4·24–5·35)	<0·0001	2·34 (2·10–2·62)	<0·0001
Non-binary assigned female at birth	0·23 (0·15, 0·36)	<0·0001	0·35 (0·23–0·55)	<0·0001
Non-binary assigned male at birth	1·82 (1·45–2·27)	<0·0001	2·00 (1·63–2·46)	<0·0001
Racial identity				
Asian	1·97 (1·60–2·43)	<0·0001	1·45 (1·17–1·78)	0·0006
Black or African American	6·71 (6·09–7·41)	<0·0001	3·24 (2·91–3·60)	<0·0001
Multiracial	2·43 (2·07–2·86)	<0·0001	1·76 (1·51–2·05)	<0·0001
Another race	5·85 (5·03–6·79)	<0·0001	2·30 (1·96–2·70)	<0·0001
White	1 (ref)	..	1 (ref)	..
Hispanic or Latinx ethnicity				
Yes	2·33 (2·18–2·50)	<0·0001	1·39 (1·29–1·50)	<0·0001
No	1 (ref)	..	1 (ref)	..
Insurance type				
Private	1 (ref)	..	1 (ref)	..
Public	9·09 (8·12–10·16)	<0·0001	3·52 (3·06–4·04)	<0·0001
Uninsured	1·59 (1·18–2·13)	0·0021	1·68 (1·25–2·26)	0·0005
Percentage of the federal poverty level				
0–99	1 (ref)	..	1 (ref)	..
100–199	0·46 (0·41–0·53)	<0·0001	0·69 (0·61–0·78)	<0·0001
200–299	0·36 (0·31–0·43)	<0·0001	0·87 (0·74–1·02)	0·080
≥300	0·22 (0·19–0·25)	<0·0001	0·72 (0·60–0·85)	0·0001
Alcohol use disorder				
Yes	1·11 (0·87–1·41)	0·39	1·13 (0·91–1·41)	0·26
No	1 (ref)	..	1 (ref)	..
PHQ-9 depression				
Yes	0·49 (0·42–0·58)	<0·0001	1·02 (0·87–1·20)	0·80
No	1 (ref)	..	1 (ref)	..
Anogenital sexually transmitted infection diagnosis				
Yes	4·70 (4·32–5·12)	<0·0001	2·34 (2·13–2·57)	<0·0001
No	1 (ref)	..	1 (ref)	..
Years retained in care	1·30 (1·27–1·33)	<0·0001	1·03 (1·00–1·05)	0·016

PHQ-9=Patient Health Questionnaire 9-item. RR=risk ratio.

Table 2: **Bivariate and multivariable longitudinal log-Poisson generalised estimating equation models for HIV seropositivity in transgender, non-binary, and gender-diverse primary care participants (40 692 observations)**

	Bivariate model		Multivariable model	
	RR (95% CI)	p value	Adjusted RR (95% CI)	p value
Exposure				
Gender-affirming hormone therapy prescription				
Yes	0·63 (0·52–0·76)	<0·0001	0·56 (0·45–0·69)	<0·0001
No	1 (ref)	..	1 (ref)	..
Covariates and confounders				
Study site				
Fenway Health	0·66 (0·50–0·87)	0·0034	0·73 (0·53–0·99)	0·040
Callen-Lorde	1 (ref)	..	1 (ref)	..
Age, years				
18–24	1 (ref)	..	1 (ref)	..
25–30	0·79 (0·64–0·98)	0·030	0·88 (0·70–1·09)	0·25
31–40	0·49 (0·40–0·61)	<0·0001	0·58 (0·46–0·73)	<0·0001
41–50	0·28 (0·21–0·37)	<0·0001	0·34 (0·25–0·46)	<0·0001
≥51	0·17 (0·11–0·26)	<0·0001	0·22 (0·14–0·34)	<0·0001
Gender identity				
Transgender man	1 (ref)	..	1 (ref)	..
Transgender woman	1·29 (0·97–1·73)	0·085	1·48 (1·05–2·08)	0·025
Non-binary*	0·79 (0·36–1·73)	0·55	0·92 (0·41–2·04)	0·83
Racial identity				
Asian	1·50 (0·97–2·34)	0·071	1·17 (0·75–1·82)	0·48
Black or African American	1·75 (1·38–2·23)	<0·0001	1·12 (0·86–1·48)	0·40
Multiracial	1·98 (1·41–2·76)	0·0001	1·35 (0·95–1·91)	0·094
Other race	1·18 (0·79–1·76)	0·42	1·00 (0·67–1·49)	0·10
White	1 (ref)	..	1 (ref)	..
Hispanic or Latinx ethnicity				
Yes	0·88 (0·75–1·03)	0·11	0·84 (0·69–1·01)	0·059
No	1 (ref)	..	1 (ref)	..
Insurance type				
Private	1 (ref)	..	1 (ref)	..
Public	1·44 (1·08–1·91)	0·012	1·01 (0·76–1·35)	0·94
Uninsured	1·81 (0·90–3·65)	0·095	1·07 (0·53–2·15)	0·86
Percentage of the federal poverty level				
0–99	1 (ref)	..	1 (ref)	..
100–199	0·65 (0·46–0·91)	0·014	0·69 (0·49–0·97)	0·033
200–299	0·46 (0·25–0·84)	0·012	0·44 (0·24–0·80)	0·0080
≥300	0·70 (0·48–1·02)	0·065	0·82 (0·55–1·21)	0·31
Alcohol use disorder				
Yes	0·73 (0·38–1·40)	0·34	1·01 (0·54–1·91)	0·9665
No	1 (ref)	..	1 (ref)	..
PHQ-9 depression				
Yes	0·86 (0·58–1·28)	0·46	0·98 (0·66–1·45)	0·91
No	1 (ref)	..	1 (ref)	..
Anogenital sexually transmitted infection diagnosis				
Yes	1·52 (1·27–1·81)	<0·0001	1·07 (0·89–1·28)	0·46
No	1 (ref)	..	1 (ref)	..
Years retained in care	0·90 (0·86–0·93)	<0·0001	0·94 (0·90–0·99)	0·012

RR=risk ratio. PHQ-9=Patient Health Questionnaire 9-item. *Non-binary and transgender not specified, including participants assigned female at birth and assigned male at birth.

***Table 3*: Bivariate and multivariable longitudinal log-Poisson generalised estimating equation models for viral non-suppression in transgender, non-binary, and gender-diverse primary care participants living with HIV (≥200 copies per mL; 2955 observations)**

birth participants had the highest HIV rates, yet HIV seropositivity and viral non-suppression rates were also higher for transgender men and non-binary assigned female at birth participants than national HIV surveillance data. Consistent with previous research on socioeconomic marginalisation,[24] having public insurance or no insurance compared with private insurance and living in poverty significantly predicted HIV seropositivity. Furthermore, corroborating synergistic effects of HIV and sexually transmitted infections,[25] trans participants with a positive anogenital bacterial sexually transmitted infection diagnosis had an increased risk of HIV seropositivity over follow-up. The risk of HIV seropositivity was significantly increased in older age groups, highlighting the need for early HIV prevention. This finding contrasts with national HIV epidemiological surveillance data, wherein HIV infection rates are highest in those aged 18–24 years, and might be due to the large number of non-binary assigned female at birth participants aged 18–24 years not living with HIV in our cohort. Relatedly, the risk of viral non-suppression was lower for the 31–40 years, 41–50 years, and 50 years and older age groups compared with the 18–24 years group, underscoring the need for supportive interventions to enhance viral suppression in the youngest age group. Latinx participants living with HIV had a lower risk of viral non-suppression compared with White individuals, a finding with clinical relevance that highlights the potential heterogeneity in HIV seropositivity and viral non-suppression outcomes and the need to consider the unique needs of different racial and ethnic groups in health care. Our findings highlight the need for continued interventions in clinical settings to address HIV inequities.

Combination interventions that pair gender-affirming hormone therapy with other services, such as PrEP for HIV prevention and HIV care, might hold promise. The low uptake of PrEP observed in our study highlights the need for focused efforts to increase PrEP uptake for this population. Interventions are needed to address HIV inequities by race, ethnicity, gender identity, socioeconomic status, and age, including those culturally tailored to reach specific trans populations bearing disproportionate HIV burden. Examples of focused HIV-related efforts are Entre Nosotras, a peer-led PrEP project for trans Latina women,[26] and Project LifeSkills, a HIV status-neutral HIV prevention intervention for young transgender women.[27] Incorporating gender-affirming hormone therapy alongside these interventions represents an important future strategy. For example, HIV Prevention Trials 091 is currently testing the co-location of gender-affirming hormone therapy and PrEP delivery for transgender women across five sites (four in the USA and one in Brazil) to increase PrEP uptake and adherence. Additional interventional research to identify and test integrated strategies is warranted.

This study has several limitations. The federally qualified health centres in our study are specialised in providing gender-affirming hormone therapy through

an informed consent model, minimising gatekeeping and barriers to access. The association of gender-affirming hormone therapy with HIV outcomes might be confounded by the gender-affirming context in which clinical care occurred (eg, trained providers and affirming name or pronoun use policies). Second, participants were drawn from urban settings in the northeast USA, which might reduce generalisability to trans people in other regions. Furthermore, 33·7% of our participant population was publicly insured, higher than the national estimate of 23% found in a large community survey of more than 27 000 trans adults;[28] 5·6% of participants were uninsured, which is lower than the estimated 8% in a US representative study.[29] Future research examining the association between gender-affirming hormone therapy and HIV outcomes in samples with more publicly and uninsured individuals is recommended. Third, participants self-selected into gender-affirming hormone therapy treatment. Fourth, this study cannot rule out the possibility that participants received PrEP from other clinics or providers. Fifth, unmeasured confounding might be an issue, since some variables known to be associated with HIV outcomes (eg, housing instability) were not measured. However, the sensitivity analyses using E-values provide a sense of the magnitude of association that potential unmeasured confounders would need to fully explain the observed exposure–outcome associations, and the small E-value confidence intervals indicate that unmeasured confounding is unlikely. Sixth, the duration of hormone use or gender-affirming surgery was not assessed. A previous study of trans people in New York found gender-affirming surgery was associated with sustained viral suppression,[30] and a study of Black and Latina transgender women in Washington, DC and Baltimore found that the desire and unmet need for gender-affirming surgery was associated with increased odds of HIV treatment interruptions.[10] Thus, future research considering both gender-affirming hormone therapy duration and gender-affirming surgery is recommended. Additionally, the current study was 80% powered on the viral non-suppression outcome, but not on HIV seropositivity; additional research investigations of gender-affirming hormone therapy and HIV seropositivity are therefore needed. Finally, given that US HIV surveillance efforts do not have data about gender-affirming hormone therapy, we discuss adjusted parameter estimates for covariates and confounders to contextualise known HIV disparities (eg, by race and ethnicity) alongside gender-affirming hormone therapy, yet caution should be taken interpreting these estimates.[31]

Limitations notwithstanding, our study has strengths, including its primary care cohort (ie, not restricted to individuals presenting at gender clinics) and diversity in terms of HIV serostatus, gender identity, race, and ethnicity. The longitudinal design examined gender-affirming hormone therapy and HIV clinical outcome associations across 7 years of follow-up in real-world clinical settings. Data were reported for non-binary participants, a group for whom scarce HIV data exist. This research was informed by the priorities of trans people.[13] Our consideration of gender identity and gender-affirming hormone therapy in the context of HIV acquisition and viral suppression is novel, given that many HIV surveillance efforts do not routinely collect this trans-specific information.

In conclusion, in this federally qualified health centre-based study of a large sample of trans people in primary care, being prescribed gender-affirming hormone therapy was longitudinally associated with reduced rates of HIV seropositivity and viral non-suppression. Our findings contribute to the evidence base for the health-promoting role of gender-affirming hormone therapy, showing that gender-affirming hormone therapy is a medically necessary treatment that reduces HIV morbidity and improves HIV outcomes longitudinally for trans people. Our study found low rates of PrEP uptake in the cohort, representing another future intervention target to reduce HIV rates. Our results underscore the vital role of gender-affirming models of care and access to gender-affirming hormone therapy for trans people. Gender-affirming hormone therapy services were supported by the Health and Human Resources Administration and Ryan White HIV/AIDS Programs.[32] Integrated gender-affirming hormone therapy and HIV care is safe[33] and recommended for trans people.

Contributors

SLR wrote the first draft of the manuscript, was responsible for the decision to submit the manuscript for publication, and secured funding for the study. DRP conducted statistical analyses with support from SLR. All authors had full access to all the data in the study. SLR, DRP, and JC had verified the data. SLR, KHM, MBD, and AER co-designed the study. All authors critically reviewed, provided scientific input to the manuscript, and agreed with the decision to submit the manuscript.

Declaration of interests

SLR, JP, and ASK receive royalties from McGraw Hill for co-editing the textbook *Transgender and Gender Diverse Health Care: The Fenway Guide*. ASK reports royalties as editor of the American Psychiatric Association textbook *Gender-Affirming Psychiatric Care*. ALW receives separate research funding to her institute from ViiV Healthcare. All other authors declare no competing interests.

Data sharing

Data from this study are not publicly available for use. For data requests, please email the corresponding author. Data requests will be considered from investigators with funding support, after approval of a concept proposal by all study investigators, and with a signed data access agreement.

Acknowledgments

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EXHIBIT D

AMERICAN ACADEMY OF HIV MEDICINE

ANAC Association of Nurses in AIDS Care

GLMA Health Professionals Advancing LGBTQ+ Equality

hivma hiv medicine association

IAPAC INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE

HIV Response in U.S. EXPERIENCING RENEWED STRAIN

Emergency HIV Clinical Response Task Force
April 2026

KEY TAKEWAYS

- HIV service disruptions are occurring, especially for vulnerable populations. These disruptions affect clinical care, prevention and supportive services, and workforce capacity.
- Structural and social determinants of health – particularly unemployment, housing instability, food insecurity, and insurance loss – are emerging as drivers of disruption.
- Clinics are making operational adjustments to their services and staffing that may further limit access to HIV prevention, treatment, and care services.
- Vulnerable populations are falling out of care, notably transgender people, migrants and undocumented individuals, and people experiencing homelessness.
- Continuing to monitor service disruptions will be important as state AIDS Drug Assistance Programs (ADAPs) contract and the Medicaid expansion cuts take effect.

BACKGROUND

Despite decades of progress in HIV prevention and treatment, the HIV response in the United States is experiencing renewed strain. Funding uncertainty, workforce attrition, policy shifts, and rising social and economic precarity are reshaping the delivery of HIV services at the clinic and community levels. In response to reports of HIV clinical and supportive service disruptions, five U.S.-based professional medical and nursing associations – the American Academy of HIV Medicine, Association of Nurses in AIDS Care, Gay and Lesbian Medical Association, HIV Medicine Association, and International Association of Providers of AIDS Care – launched the Emergency HIV Clinical Response Task Force (Task Force) in June 2025.

The Task Force fielded an online Emergency HIV Clinical Response Survey in July 2025 to quantify the scope, nature, and equity dimensions of these disruptions as experienced by frontline HIV service providers across the U.S. A follow-up survey was fielded in November through December 2025 to map additional dimensions related to HIV service disruptions, including structural and social determinants of health, as well as operational austerity measures in the face of federal funding cuts.

METHODOLOGY

Between November 6, 2025, and December 11, 2025, a follow-up online Emergency HIV Clinical Response Survey was distributed to HIV service providers nationwide through the five members of the Emergency HIV Clinical Response Task Force. Analyses are based on 383 clinical provider respondents who completed the survey across 47 states and Puerto Rico. Respondents included physicians, nurses, pharmacists, case managers, social workers, and community-based providers working across academic medical centers, Federally Qualified Health Centers (FQHCs), hospitals, private practices, and outreach settings. Questions were intended to capture the breadth of disruptions and impacts experienced from July to October 2025.

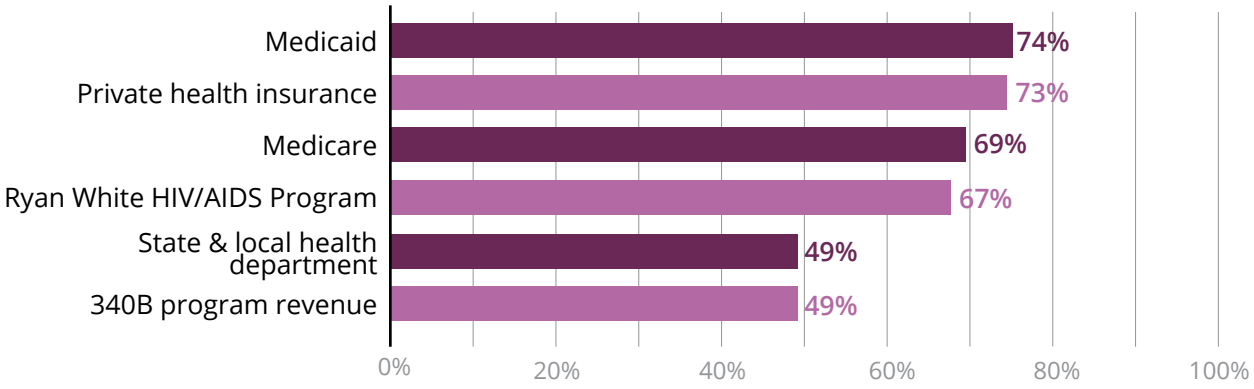
RESPONDENT AND SITE PROFILES

The perspectives captured reflect a cross-section of the HIV workforce and a diversity of clinical settings that deliver HIV care:

- Clinical roles dominated the sample, with physicians (30%), nurse practitioners (23%), and registered nurses (14%) comprising two-thirds of respondents.
- Over 65% of responses came from hospital-based clinics (33%) and community health centers and FQHCs (32%), underscoring impacts within core HIV care infrastructure.
- The South accounted for more than one-third of responses (36%), with responses from three other regions: Northeast (24%), West (23%), and Midwest (18%).

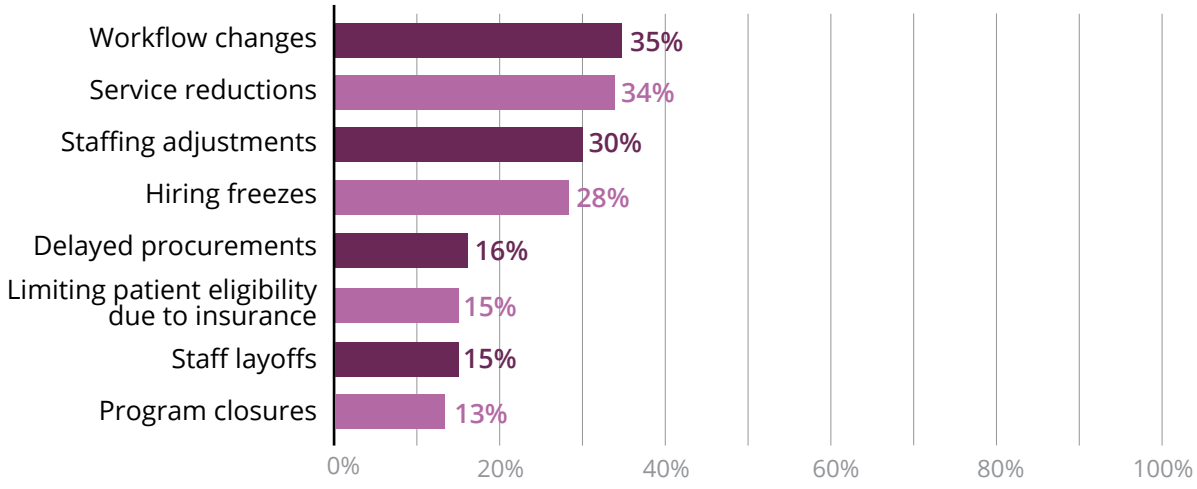
SOURCES OF FUNDING

Respondents reported a combination of funding sources for their clinical settings, including:



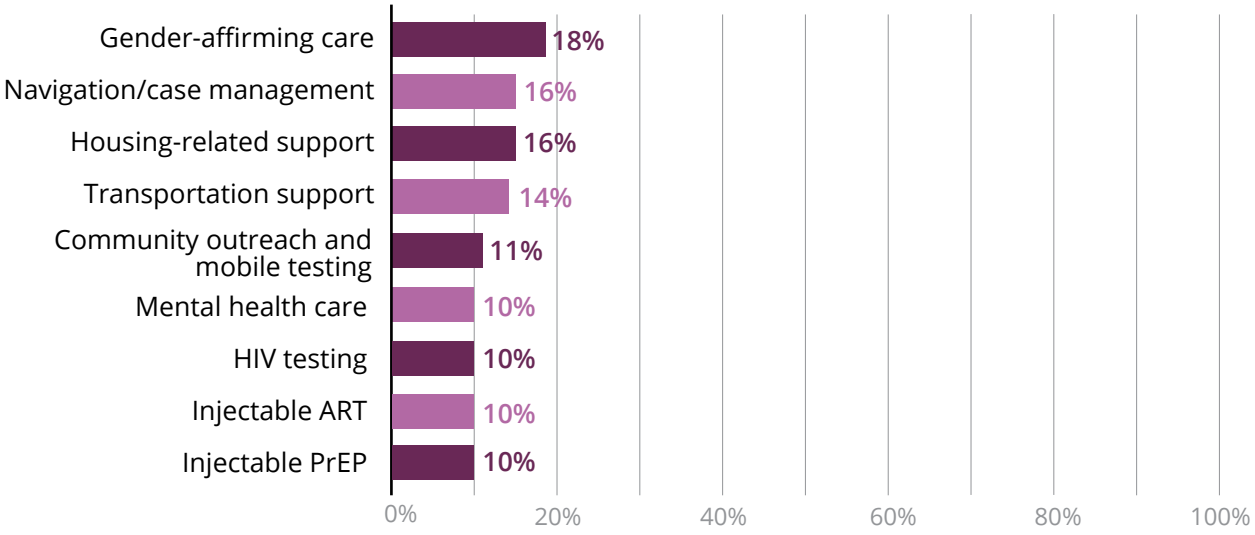
OPERATIONAL DISRUPTIONS

Sixty-eight percent of respondents reported one or more operational changes in their clinical settings due to changes in federal or state policies or funding cuts, including:



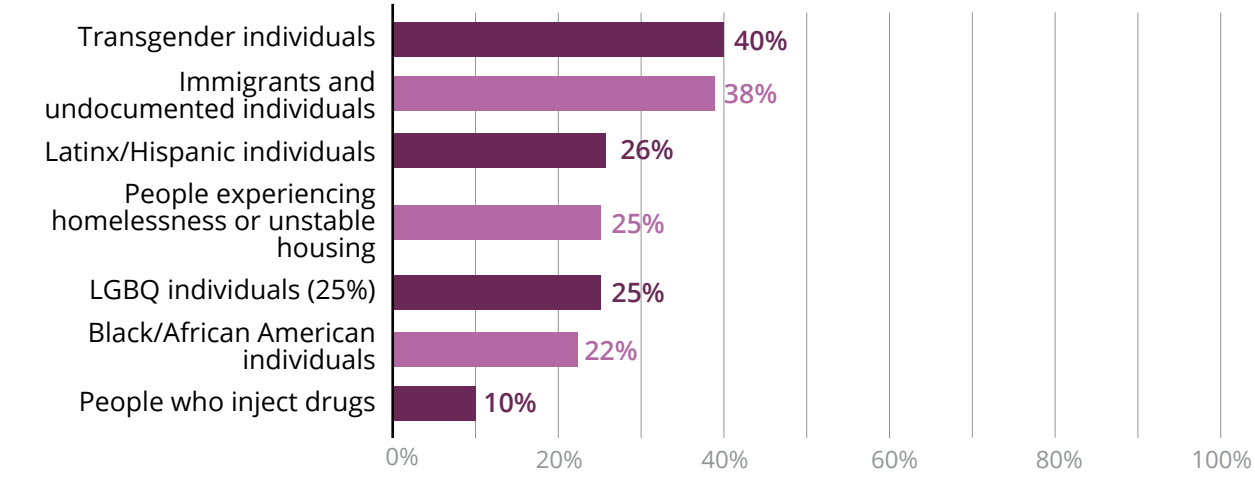
HIV AND OTHER HEALTH SERVICE DISRUPTIONS

Sixty-one percent of respondents reported at least one HIV service disruption in their clinical setting. Reported service disruptions spanned the HIV care continuum and beyond:



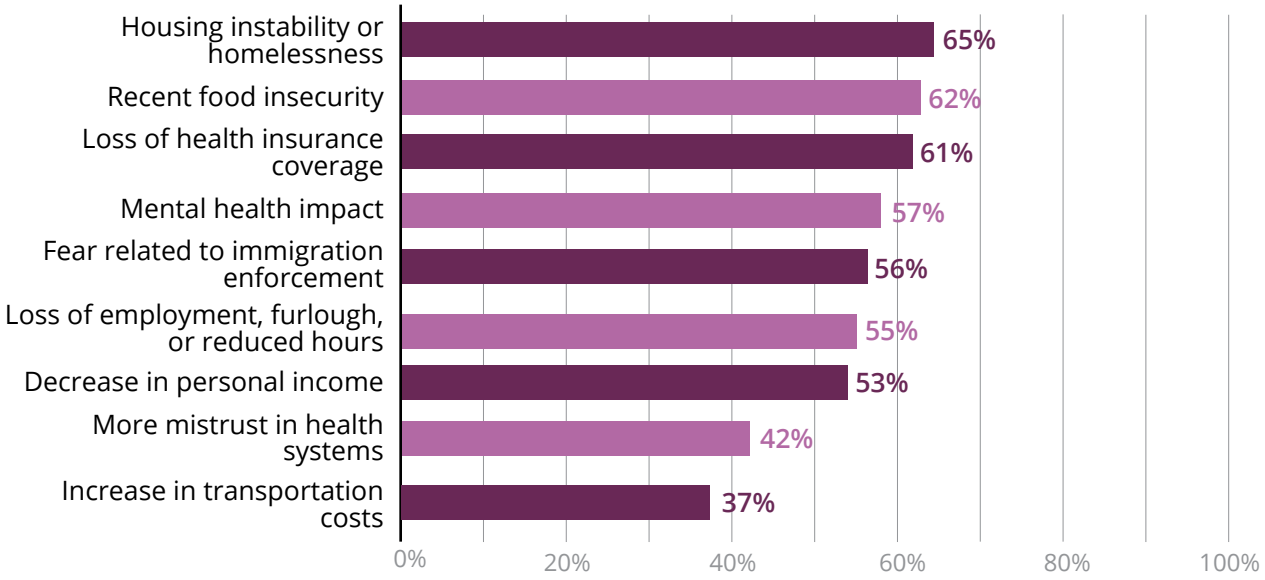
EQUITY IMPACTS: POPULATIONS MOST AFFECTED

Of the 69% of respondents who reported at least one population-level service disruption, the following key populations were cited as most affected:



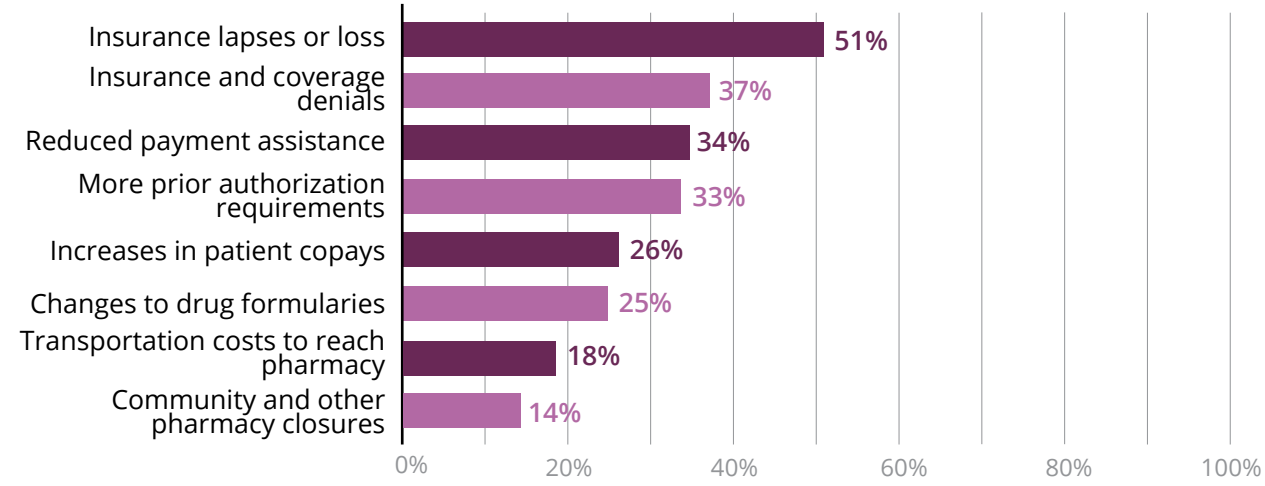
PATIENT-REPORTED BARRIERS TO ENGAGEMENT IN CARE

Among the 92% of respondents who reported hearing from patients about specific barriers to remaining engaged in care, the following were the most cited:

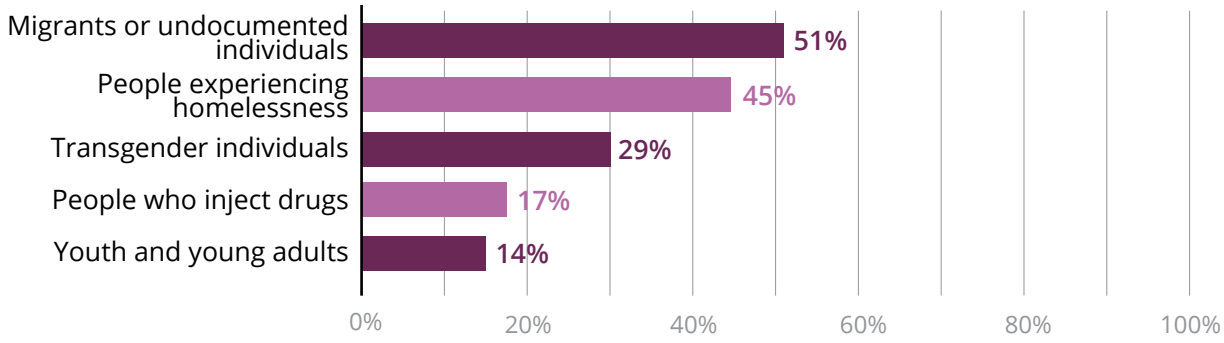


MEDICATION ACCESS AND LOSS TO FOLLOW-UP

Of the 69% of respondents who reported their patients spoke with them about medication access, the following factors were most associated with medication access barriers:



Although 14% of respondents reported no significant population-specific effects on retention in HIV care, of the 86% of respondents who did report effects the following key populations were cited as the most affected:



INSIGHTS FROM OPEN-ENDED QUESTIONS

Forty-six percent of respondents provided additional insights through an open-ended survey question about the most urgent resources needed to safeguard continuity of HIV services:

- Funding concerns dominate the landscape, mentioned by 37% of respondents, with specific emphasis on Ryan White HIV/AIDS Program (20%) and 340B Drug Pricing Program (4%) sustainability.
- Health insurance coverage was reported as critical, with 27% of respondents citing Affordable Care Act/insurance concerns and 13% specifically mentioning Medicaid enrollment challenges.
- Social determinants of health, including housing (17%), transportation (13%), and food security (7%), were recognized as essential to maintaining HIV care continuity.

Forty-two percent of respondents answered a second open-ended question seeking insights into declines in clinic attendance by undocumented or migrant individuals observed in the respondents' clinical settings, with 83% of this subset of respondents citing fear of immigration enforcement and deportation as the primary contributing factor.

One survey response detailed a patient death directly attributed to this fear:

"Due to a fear of being detained by ICE, a patient with relapsed Hodgkin's lymphoma delayed care and then it became an emergency which resulted in his death."

CONCLUSION

The outcomes of the second Emergency HIV Clinical Response Survey document a clear warning signal that the Trump administration-led policy and funding actions taken over the last year are destabilizing the delivery of HIV services in the U.S.

Continued monitoring is critical in addition to locally-driven, novel, and nimble interventions to prevent disruptions in HIV testing, prevention, care, and treatment with a focus on key populations most affected by federal policy and budget shocks.

Addressing these disruptions is imperative to safeguarding lives and decades of progress in the U.S. HIV response.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE; HIV MEDICINE ASSOCIATION, a division of the INFECTIOUS DISEASES SOCIETY OF AMERICA; INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE; JENNIFER K. BRODY, MD; and CHRISTOPHER B. FOX, NP, *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION; THOMAS J. ENGELS, in his official capacity as the Administrator of the Health Resources and Services Administration; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., in his official capacity as Secretary of the U.S. Department of Health and Human Services, *Defendants*.	Case No.

DECLARATION OF ANDREA WEDDLE, EXECUTIVE DIRECTOR OF THE HIV MEDICINE ASSOCIATION

I, Andrea Weddle, hereby declare and state as follows:

1. I am over 18 years of age, of sound mind, and in all respects competent to testify.

2. I have personal knowledge of the facts set forth in this declaration and would testify competently to those facts if called to do so.

3. I am the Executive Director of the HIV Medicine Association ("HIVMA"), which is an organizational component of the Infectious Diseases Society of America ("IDSA"), a 501(c)6

nonprofit organization. IDSA is bringing claims in this case on behalf of HIVMA's members and the transgender patients of its members.

4. I have been the executive director at HIVMA for 18 years and with the association since its inception 25 years ago. In my role, I oversee the strategy development for HIVMA. This includes the policy and programmatic agendas and activities that support our members to provide high-quality care to their patients, advance public health, and conduct HIV research. My work is informed by a postgraduate social work degree from the University of California, Berkeley, and expertise developed over the last two and a half decades on healthcare access and financing, with a focus on people with HIV and other complex, chronic conditions.

5. I submit this declaration in support of Plaintiffs' Motion for Preliminary Relief under 5 U.S.C. § 705 and for a Preliminary Injunction, which seeks to prevent Defendants from giving effect to certain conditions relating to transgender people and gender-affirming medical care set forth in Ryan White HIV/AIDS Program ("Ryan White Program" or "RWHAP") Notices of Funding Opportunity issued or forecasted to be issued in 2026 and the 2026 Updated HRSA General Terms and Conditions, issued on March 11, 2026 (collectively, "the Challenged Conditions").

6. In this declaration, I explain how the Ryan White Program protects public health by providing the majority of people diagnosed with HIV in the United States with comprehensive healthcare. I further describe how transgender people are disproportionately impacted by HIV, and that providing gender-affirming medical care under the Ryan White Program is an important strategy to administer effective HIV care to transgender people with HIV. By restricting their care, the Challenged Conditions are contrary to medical evidence and will likely result in a rise of HIV

transmissions. I conclude by explaining how the Challenged Conditions will cause significant patient and provider harm as well as negative economic impacts.

I. Background on HIVMA

7. IDSA established HIVMA in 2001.

8. HIVMA is a community of nearly 6,000 healthcare professionals who advance a comprehensive and humane response to the HIV pandemic, informed by science and social justice. HIVMA works to increase access to healthcare services and coverage for people with HIV and populations heavily impacted by HIV and to foster a robust, diverse, and culturally competent HIV workforce.

9. A majority of HIVMA members report patient care as their primary professional activity, and most manage the care of patients with HIV.

10. Many HIVMA members provide medical care to their HIV patients through the Ryan White Program, including through funding under Ryan White Parts A, B, C, D, F, and any supplementary funding under these parts. For their transgender HIV patients, this can include hormone therapy as treatment for their gender dysphoria (also known as "gender-affirming hormone therapy" or "gender-affirming medical care").

11. HIVMA develops national guidelines for HIV care, creates practice tools for HIV health care professionals, develops HIV continuing education programs, advocates for federal HIV policy, and leads the field towards ending the HIV epidemic.

12. For example, HIVMA has published *Primary Care Guidance for Providers Who Care for Persons with Human Immunodeficiency Virus*, last updated in 2024, and relied on by HIV medical providers since 2009. A copy of the Guidance is attached hereto as **Exhibit A**. The Guidance, which is published in the peer-reviewed journal *Clinical Infectious Diseases*, includes

a whole section on "Considerations for Transgender and Gender-Diverse Adults" that addresses the importance of gender-affirming hormone therapy as part of the primary care for transgender patients living with HIV. In addition, HIVMA has published a Gender-Affirming Care Resource Brief for its members.

13. HIVMA also created and has sponsored the Ryan White Medical Providers Coalition for twenty years. The Ryan White Medical Providers Coalition is a voice for Ryan White clinicians from across the nation who deliver quality HIV care to their patients using funding from the Ryan White Program. The coalition first convened in 2006 as a call to action led by physicians, advanced practice providers, and other healthcare professionals who work in Ryan White-funded clinics. The coalition evolved with the support of HIVMA and today is a respected and leading voice in federal advocacy related to Ryan White HIV/AIDS Program funding and policies.

II. Ryan White and HIV Care

14. Because so much of HIV care in the United States is affected and funded by the Ryan White Program, as executive director of HIVMA, I am aware of the contours of the program and how it affects HIVMA's members.

15. The Ryan White Program serves the majority of people diagnosed with HIV in the United States. In 1990, Congress passed the Ryan White legislation in response to the HIV/AIDS epidemic. Since then, healthcare providers, including current HIVMA members, have relied on Ryan White funding to serve their patients living with HIV, including transgender patients. Over half of all people diagnosed with HIV are served through the Ryan White Program, and many would not have access to necessary healthcare services and treatment without the program. Many HIVMA provider members would also not be able to meet the healthcare needs of their patients with HIV without Ryan White funding.

16. The goal of the Ryan White Program is to provide a safety net for people living with HIV by providing outpatient HIV care, treatment, and support services to those without health insurance, filling in gaps in coverage, and assisting with costs for those with insurance limitations. Funding is distributed to states/territories, cities, and clinics and community-based organizations in the form of grants.

17. Following its initial adoption and implementation, the Ryan White Program was expanded by Congress to address the unmet care and treatment needs of people living with HIV by focusing Ryan White funding on primary healthcare and support services important to enhancing access to and retention in care and adherence to daily treatment. This update to the Ryan White Program prioritized funding for core medical services, including services for co-occurring conditions for patients with HIV, as well as support services.

18. Medical advances in antiretroviral therapy ("ART") have made it possible for people living with HIV to have a lifespan that approaches that of people without HIV, without progressing to AIDS or transmitting HIV to others. Because of those advances, our members can now focus on maintaining health throughout the lifespan. Maintaining all aspects of HIV patient health is a necessary component of successful and effective HIV care and treatment. The Ryan White Program care model has proven to be highly successful at treating a complex patient population. As a result, demand for Ryan White services has steadily increased without an increase in resources, placing great strain on the HIV workforce and their ability to provide care.

19. As HIVMA's primary care guidance for people with HIV explains, to receive optimal medical care and achieve desired outcomes, persons with HIV must be consistently engaged in care and able to access uninterrupted treatment. Providing primary care for people with HIV is complex and involves management of multiple co-morbidities and the associated

challenges of polypharmacy—the concurrent use of multiple medications—while also attending to HIV-specific health concerns. HIV providers, such as our members, must address issues specific to preventive health, including cancer screening, reducing the risk of cardiovascular disease, providing recommended vaccinations, and promoting sexual health. Additionally, providers must address issues for specific populations, like those with childbearing potential, adolescents, and transgender people.

20. Creating a patient-centered care environment without stigma and discrimination, like that supported by the Ryan White Program, is essential for effectively treating people with HIV and sustaining care engagement, as evidenced by the higher viral suppression rates for Ryan White clients compared to the national average. To end the HIV epidemic by dramatically reducing HIV transmissions, barriers to care must be decreased at every level—societal, health system, clinic, and individual. Many populations with an increased likelihood of acquiring HIV disproportionately experience barriers to accessing care and treatment, including income inequality, unstable housing, food insecurity, joblessness, and poor access to transportation. These barriers emerge from a social framework replete with discrimination against those whose race, ethnicity, sexual orientation, or gender identity is in the minority. Increasingly, HIV care must acknowledge and address these issues in all affected populations to end the HIV epidemic. Ensuring that clinical settings are free of stigma and discrimination is a first and essential step.

III. Transgender Patients with HIV

21. Public health data show that between 55-78% of transgender people rely on public health coverage, such as Medicaid and Medicare.[1] And medical literature documents that

[1] Centers for Disease Control and Prevention. Individual-level Social Determinants of Health and Quality of Life Among Persons with Diagnosed HIV Infection—Medical Monitoring Project, United States, 2022 Data Cycle (June 2022–May 2023). HIV Surveillance Special Report 38, 45 tbl.3a. https://stacks.cdc.gov/view/cdc/168909. Published November 2024. (attached as **Exhibit B**).

transgender adults are more likely to be uninsured than their cisgender counterparts.[2] In addition, some states have prohibited state Medicaid funding for gender-affirming medical care. Given this landscape, Ryan White funding is essential to supplement the public health coverage of transgender people with HIV. Thus, for many transgender people with HIV, the Ryan White Program is the only way they can access the gender-affirming medical care that is medically indicated.

22. Of the more than half a million people served by the Ryan White Program, 2.1%, over 11,000, are transgender.[3]

23. It is well-understood that the HIV epidemic has disproportionately affected certain populations. Gay and bisexual men, other men who have sex with men, and transgender persons, particularly Black and Latina transgender women, are overrepresented among people living with HIV and represent the largest proportion of new HIV diagnoses every year in the United States.[4] As documented in HIVMA's primary care guidance for HIV patients, estimates show a pooled HIV prevalence of 19.9% among transgender women, with 66-fold higher odds of HIV prevalence than the general population, and an estimated HIV prevalence of 2.56% among transgender men.

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[2] Downing, J., Lawley, K. A., & McDowell, A. (2022). Prevalence of Private and Public Health Insurance Among Transgender and Gender Diverse Adults. *Medical care*, *60*(4), 311–315. https://tinyurl.com/yc6xsfa5 [https://doi.org/10.1097/MLR.0000000000001693].

[3] Health Resources and Services Administration. Ryan White HIV/AIDS Program Annual Data Report 2022: Ryan White HIV/AIDS Program Services Report (Dec. 2023) (attached as **Exhibit C**).

[4] Centers for Disease Control and Prevention, Fast Facts: HIV and Gay and Bisexual Men (Oct. 7, 2024), https://tinyurl.com/5ad5vw4e [https://perma.cc/29WA-RZZD]; Centers for Disease Control and Prevention, Fast Facts: HIV and Transgender People (Mar. 28, 2024), https://tinyurl.com/55vmp6bz [https://perma.cc/HW73-GHW8]; Herbst, J.H., Jacobs, E.D., Finlayson, T.J. *et al.* Estimating HIV Prevalence and Risk Behaviors of Transgender Persons in the United States: A Systematic Review. *AIDS Behav.* 12, 1–17 (2008). https://tinyurl.com/3r94djsr [https://doi.org/10.1007/s10461-007-9299-3].

In 2022, transgender people accounted to 2% of all HIV cases.[5] That is more than three times the proportion of transgender people in the United States (0.6%).[6]

24. Studies have found that access to gender-affirming hormone therapy is associated with reduced rates of HIV acquisition among transgender patients and, in transgender people with HIV, higher rates of viral suppression.[7]

25. Because of the presence of these health disparities and how they affect HIV care, HIVMA and its members need to be aware of the health needs and barriers affecting the populations most impacted by HIV.

26. Indeed, HIVMA's primary care guidance for HIV patients documents that stigma and discrimination are serious issues that threaten the quality of care for transgender persons, noting that "Nearly half of transgender persons face family rejection, 40% report a history of attempted suicide, 29% live in poverty, 30% have experienced homelessness, 33% have experienced discrimination within the healthcare system, and 23% avoid the healthcare system due to fear of discrimination."

27. The above is consistent with the medical literature, which documents that a significant number of transgender people experience negative interactions with their healthcare providers or avoid the healthcare system due to fear of being mistreated because they are transgender. For example, misinformation about transgender people and gender-affirming care is undermining trust in healthcare institutions, delaying or preventing them from accessing healthcare

[5] Centers for Disease Control and Prevention, Fast Facts: HIV in the United States (Apr. 22, 2024), https://tinyurl.com/3zactezx [https://perma.cc/LCE9-W2E5].
[6] Herman, J.L., Flores, A.R., O'Neill, K.K. (2022). How Many Adults and Youth Identify as Transgender in the United States? The Williams Institute, UCLA School of Law.
[7] Sari L. Reisner et al., *HIV seropositivity and viral non-suppression in transgender, non-binary, and gender-diverse people in primary care receiving gender-affirming hormone therapy in the USA between 2013 and 2019 (LEGACY): an observational, longitudinal, cohort study*,12 The Lancet HIVe283-e292 (2025).

services and contributing to the spread of diseases.[8] Based on literature cited in HIVMA's primary care guidance, this discrimination plays a dominant role in understanding why transgender women have 66-fold higher odds of HIV prevalence than the general population.[9] In an environment of misinformation and medical discrimination, providers play an important role in confronting misinformation while providing evidence-based care.

28. The U.S. Department of Health and Human Services, through the HHS Panel on Antiretroviral Guidelines for Adults and Adolescents, a working group of the NIH Office of AIDS Research Advisory Council, publishes and regularly updates the "Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV." Prior to 2025, including the September 2024 version, these guidelines contained a section titled "Transgender People with HIV."[10]

29. According to the 2024 HHS guidelines, of which HIVMA and its members keep regularly apprised, "Because transgender and nonbinary people bear a disproportionate burden of HIV, it is important for HIV care providers to be knowledgeable about the specific HIV care needs of these individuals." **Ex. F** at I-100.

30. The guidelines stated that:

> Individuals are more likely to engage in HIV care when gender affirmation needs are met. A national study of transgender people with HIV found that participants who work with HIV care providers who affirm their gender (e.g., providers who use their chosen name and pronoun) were more likely to be virologically suppressed. **Adherence to hormone therapy correlates with adherence to ART**.
>
> …

[8] Ciszek et al., *Health Communication in an Era of Disinformation: Perceived Source Credibility Among Transgender and Gender Diverse Individuals*, 29 Journal of Health Communication 432–439 (2024) (attached as **Exhibit D**).
[9] Sarah E. Stutterheim et al., *The worldwide burden of HIV in transgender individuals: an updated systematic review and meta-analysis*, 16 PLoS One e0260063 (2021) (attached as **Exhibit E**).
[10] U.S. Department of Health and Human Services, Panel on Antiretroviral Guidelines for Adults and Adolescents, Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV (updated September 12, 2024) (attached hereto as **Exhibit F**).

> According to research with transgender youth and adults, **integrating HIV care with gender care facilitates treatment and is associated with higher rates of viral suppression**. In addition to minimizing the number of provider visits and potentially stressful clinical interactions, **care integration makes it easier to discuss concerns about drug–drug interactions between HIV treatment and gender-affirming medications**.
>
> …
>
> **HIV care services should be provided within a gender-affirmative care model to reduce potential barriers to ART adherence and to maximize the likelihood of achieving sustained viral suppression** … Clinicians should also ask people with HIV about their gender identity, chosen names, and pronouns, using developmentally appropriate language.
>
> …
>
> **Integrating hormone therapy with HIV services is the recommended practice; this requires HIV providers to become knowledgeable about hormone therapy and other aspects of gender-affirming services**.

Ex. F at I-102 – I-103 (emphases added).

31. The guidelines further documented,

> In 2022, the Ryan White HIV/AIDS Program (RWHAP) provided services for 11,085 transgender people, representing 2.8% of RWHAP clients. Of these transgender clients, 2.3% were transgender women, 0.3% transgender men, and 0.2% with another gender identity (e.g., nonbinary). Among RWHAP participants, retention in care (73.5%) and viral suppression (86.4%) for transgender adults and adolescents were lower than the national averages (77.5% and 89.6%, respectively).

Ex. F at I-101.

32. Unfortunately, the current administration eliminated the section on "Transgender People with HIV" and virtually every other mention of transgender people in the September 25, 2025 version of the guidelines.[11]

33. Nonetheless, as documented in HIVMA's guidance and the medical literature, in addition to reducing stigma and discrimination in order to facilitate patient empowerment, care

[11] U.S. Department of Health and Human Services, Panel on Antiretroviral Guidelines for Adults and Adolescents, Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV (updated September 25, 2025) (attached hereto as **Exhibit G**).

engagement, and viral suppression, it is crucial for HIV providers to monitor their patients' gender-affirming care for polypharmacy management. When pharmacokinetic interactions between medications are anticipated, providers should monitor clinical effects and adjust hormone doses as needed. It is important to provide patients with accurate information on drug–drug interactions between their ART and hormone therapy, including the lack of deleterious effects on hormone therapy, and to make dose adjustments as appropriate.

34. Our members use research, like that referenced in HIVMA's primary care guidance, to inform their care and educate their patients.[12] Such research shows how various HIV medications may decrease or increase hormone levels. Moreover, lack of communication around drug–drug interaction concerns may contribute to fear of drug–drug interactions and poor adherence to one therapy or the other. For these reasons, it is considered best practice for HIV care providers to also ensure their patients can obtain gender-affirming medical care when medically indicated.

35. In furtherance of the Ryan White Program's purpose and our shared goal to end the HIV epidemic, and based on the evidence as documented in the scientific and medical literature, HIVMA's primary care guidance included four primary recommendations for the care of transgender people with HIV. First, transgender people with HIV should have access to care that is gender-affirming, nondiscriminatory, non-stigmatizing, and culturally sensitive. Second, intake forms, medical records, and other documentation should include gender identity options in addition to sex assigned at birth, providers should address patients using their chosen name and

[12] *See*, *e.g.*, Lauren R. Cirrincione et al., *Drug interactions with gender-affirming hormone therapy: focus on antiretrovirals and direct acting antivirals*, 16 Expert Opin Drug Metab Toxicol 565–82 (2020) (attached as **Exhibit H**); Braun et al., *Transgender women living with HIV frequently take antiretroviral therapy and/or hormone therapy differently than prescribed due to drug-drug interaction concerns*, 4 LGBT Health 371–5 (2017) (attached as **Exhibit I**).

pronouns, and educational materials should reflect the experiences of transgender people. Third, transgender people should be offered medically necessary gender-affirming interventions in accordance with national guidelines. And fourth, HIV care providers should be familiar with gender-affirming hormone treatment and necessary clinical and laboratory monitoring, or work in concert with a provider or endocrinologist experienced in transgender care.

IV. Gender-Affirming Medical Care under the Ryan White Program

36. Given the above and Congress's instruction that the Ryan White Program shall be used to cover "outpatient and ambulatory health services" "including services regarding the co-occurring conditions" of HIV patients, HIVMA members who care for transgender patients with HIV have provided gender-affirming hormone therapy to these patients as part of their efforts to address the comprehensive healthcare needs of their patients.

37. As such, a Dear Colleague Letter issued by the Health Resources and Services Administration ("HRSA") issued on December 16, 2021, recognized that "RWHAP funds may be used to support gender affirming care across various HRSA RWHAP core medical and support service categories." A copy of the Dear Colleague Letter is attached hereto as **Exhibit J**. According to the Dear Colleague Letter, "Providing gender-affirming care is an important strategy to effectively address the health and medical needs of transgender people with HIV."

38. What is more, since 2010, HRSA, as the administrator of the Ryan White Program, has published a strategic plan to end the HIV epidemic. In 2024, HRSA introduced Ryan White Program 2030: Engaging People with HIV in Care to End the HIV Epidemic, which it updated on January 21, 2026. A copy of the 2024 Ryan White Program 2030 Briefer is attached hereto as **Exhibit K**, and a copy of the 2026 Ryan White Program 2030 Briefer is attached hereto as **Exhibit L**. This strategic plan recommends building off the lifesaving successes of the Ryan White

Program by "sustain[ing] high-quality care and treatment for people currently receiving services through the RWHAP while expanding efforts to identify and engage individuals with HIV who are undiagnosed or out-of-care." From 2010 to 2024, the Ryan White program successfully increased HIV viral suppression from 69.5% to 91.4%. Nationally, the average viral suppression rate is just 67%. Achieving viral suppression keeps people with HIV healthy and prevents HIV transmissions by stopping the sexual transmission of HIV, which also reduces long-term healthcare costs. The plan reiterates that Ryan White grantees, such as HIVMA's members, "play a critical role in advancing the goals of RWP 2030," "are responsible for employing sound planning and decision-making processes to determine which HIV-related services are prioritized," and "must continue to base service priorities and resource allocation decisions on the size, demographics, and needs of people with or affected by HIV." This plan concludes by reminding the HIV provider community to leverage the infrastructure and expertise of the Ryan White Program, along with its innovations and high-impact activities, to reach people with HIV who are out of care, "ensuring that no one is left behind in our efforts to end the HIV epidemic."

39. The Challenged Conditions seem to be at odds with the goals of the Ryan White Program 2030 plan. This plan recommends HIV providers advocate for and provide the best course of HIV care, while at the same time explicitly recommending that transgender patients' identities be disrespected and that their healthcare needs related to gender dysphoria, when such a co-occurring condition exists, be "left behind." This, in turn, has caused confusion and concern among HIVMA's members.

40. Leaving transgender patients behind by requiring that their identities be unacknowledged or disrespected and prohibiting the use of Ryan White funding for gender-affirming medical care is a turn of events that has led to deep concerns among HIVMA members.

Prohibiting the use of Ryan White funding for gender-affirming medical care is counter to the medical evidence and will cause harm to transgender people with HIV, likely leading to individuals falling out of care and, therefore, likely resulting in a rise in HIV transmissions. HIVMA has been educating HIV providers to provide person-centered, comprehensive, evidence-based care since it was established in 2001. And after the HRSA Dear Colleague letter was issued in 2021, there was an intentional push from the federal government and within the HIV care community to encourage Ryan White providers, to the degree they were not already doing so, to affirm their transgender patients and provide them with gender-affirming hormone therapy if medically indicated.

41. Understanding how the provision of gender-affirming medical care increases HIV care adherence and leads to viral suppression for transgender patients with HIV has been a central tenet of our HIVMA members providing effective HIV care to transgender patients, and is necessary to achieve our nation's goal to end the epidemic. Indeed, the entire national HIV care structure came to recognize that providing transgender patients with this necessary and helpful care ensures that such patients stay in HIV care. And that it is therefore necessary to achieve our goal to end the HIV epidemic.

42. Given this understanding, no one anticipated a future policy prohibiting the use of Ryan White funding for the necessary care of transgender patients with HIV. That is, until the Challenged Conditions and HRSA's actions under the current administration.

V. The Impact of the Challenged Conditions on HIVMA Members and their Patients

43. Given the current administration's stance towards transgender people and gender-affirming medical care, the Challenged Conditions, as well as the recent attacks on gender-affirming medical care, HIVMA has sought to better understand the funding challenges our

members face because of any restrictions on gender-affirming medical care, including the Challenged Conditions.

44. Concerns about restrictions on gender-affirming medical care services for people with HIV and the impact those restrictions would have on patient care are routinely raised in regular engagements with HIVMA members during open forums and Board, committee, and working group meetings, in addition to surveys. These concerns have also been a focus of discussion at HIVMA/Ryan White Medical Providers Coalition annual luncheons, which cumulatively have been attended by hundreds of providers. In response to the concerns raised, HIVMA created a gender-affirming care resource guide to support members.

45. Among HIVMA members, there is a lot of uncertainty and confusion around the Challenged Conditions and fears that some institutions may preemptively restrict gender-affirming care to protect Ryan White Program funding. Our members are also concerned that the Challenged Conditions will impact all their medical interactions with transgender patients, as the Challenged Conditions seem to suggest.

46. The Challenged Conditions place our members in an untenable position. If they choose to comply with the Challenged Conditions, they endanger the health and wellbeing of their transgender patients with HIV. If they follow their duty to their patients by providing their transgender patients with HIV the best care and the care they need, they risk losing essential federal funding for all their HIV patients, the vast majority of which is unrelated to gender-affirming care, and endanger the health and wellbeing of other HIV patients.

47. Our members also face difficult questions about navigating non-discrimination mandates when the use of Ryan White funds, which sometimes is the only source of funding for medical care, prohibits the provision of gender-affirming medical care. Or when, as the General

Terms and Conditions intimate, members must not acknowledge or respect their transgender patients' identities. By requiring our members to disrespect transgender patients and to deny them evidence-based care, it also puts them out of compliance with state and federal non-discrimination laws. Our members use Ryan White funding to provide comprehensive primary care services, addressing the full spectrum of co-occurring medical conditions for their non-transgender patients with HIV. But they cannot use Ryan White funding to provide their transgender patients with HIV with the same comprehensive primary care services, despite the fact that such care is often essential to maintaining engagement in HIV treatment and longitudinal care.

48. Beyond the unethical demands, HIVMA members are unsure how to navigate administrative and logistical challenges. HIVMA members have long relied on the Ryan White Program as an essential, stable, and comprehensive funding source that supports HIV medications as well as medically necessary healthcare that patients with HIV may need, like primary care and care for co-occurring conditions. This includes gender-affirming medical care for the transgender people living with HIV who need it. HIVMA members have structured integrated care programs on the understanding that Ryan White funds can, and are intended, to deliver such comprehensive primary care. This reliance is based on the structure and purpose of the Ryan White Program, as well as how the program has operated in the past.

49. The Ryan White Program often funds a clinic or a provider's salary, not just the individual care or medication that a patient needs. Even if alternative funding were available, which for many HIVMA members it is not, it remains unclear how providers could meaningfully separate or untangle Ryan White-funded services from the provision of medically necessary care for their transgender patients. Indeed, some Ryan White clinics have expressed concern that the restrictions could jeopardize their operations altogether.

50. The abrupt restrictions on care created by the Challenged Conditions would upend the settled expectations of HIV care providers participating in the Ryan White Program and those of their transgender patients; force providers to dismantle established care models, withdraw needed services from the transgender patients who depend on them; require them to discriminate against their transgender patients, which would cause these patients to fall out of care; and jeopardize both individual health outcomes and broader public health goals.

51. Our members fear that the Challenged Conditions will lead the HIV community to lose even more of its already depleted healthcare workforce, as they are morally depleted by being forced to deny evidence-based services to their patients.

52. If Ryan White healthcare providers are prohibited from providing gender-affirming care or required to discriminate against their transgender patients by refusing to acknowledge and respect their identities, the public health consequences would be serious and significant.

53. As noted, research shows that adherence to HIV care is negatively affected by stigma and discrimination. Transgender patients who are unable to receive gender-affirming medical care or receive care that is affirming and respectful of their identities lose trust in their providers, experience mental health declines, struggle to stay in stable housing, risk losing their jobs, and suffer from greater food insecurity. Ryan White funding addresses these issues because taking care of the whole person is *necessary* to prevent people from falling out of care. Falling out of care can lead to loss of viral suppression, leading to an increase in HIV transmission, and the development of viral resistance to medication, which then requires more intensive therapies. It also puts patients at risk of opportunistic infections that can be life-threatening and require intensive healthcare resource utilization, including inpatient hospitalizations. When people with HIV lose access to HIV treatment, the virus rebounds, impairing the immune system, potentially causing

irreparable harm depending on the length of the treatment disruption and other factors, and increasing the risk of transmitting HIV, leading to not only consequences for the individual, but the community-at-large.

54. Besides the human devastation, there is an economic cost. Lifetime HIV treatment costs for an individual range from $500,000 to $1.2 million. The more people with HIV, the more it costs to treat them and stop the spread. Denying access to services necessary to effectively treat HIV for transgender patients creates an exponential problem that compromises public health.

55. Before the COVID-19 pandemic, epidemiologists and public health experts warned about the system failures they were witnessing. HIVMA and its members fear that HIV care may be reaching a similar crisis point if the Challenged Conditions are allowed to take effect.

56. As the Executive Director of HIVMA, I see that the prohibition of Ryan White funding for gender-affirming medical care and the requirement that Ryan White healthcare providers refrain from respecting the identities of their transgender patients as a condition for funding are contributing to the funding uncertainty, undue workforce strain and attrition, policy shifts, and rising social and economic instability that predate system failure. HIVMA, along with the American Academy of HIV Medicine, Association of Nurses in AIDS Care, GLMA—Health Professionals Advancing LGBTQ+ Equality, and the International Association of Providers of AIDS Care, has joined together in the Emergency HIV Clinical Response Task Force to respond to these threats. The goal of this task force is to monitor and better understand how threats and restrictions on federal funding are impacting HIV care. Based on the 2025 surveys, gender-affirming medical care is the service area most at risk of disruption. By monitoring these threats, HIVMA can advocate for policies that respond to the needs of our members and their patients.

57. HIVMA members cannot achieve the goal of advancing a comprehensive and humane response to the HIV epidemic without addressing the needs of transgender people living with HIV.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: June 9, 2026

Andrea Weddle

Andrea Weddle
Executive Director, HIVMA

Weddle Declaration
Exhibit A

Clinical Infectious Diseases

IDSA GUIDELINES

IDSA Infectious Diseases Society of America hivma hiv medicine association OXFORD

Primary Care Guidance for Providers Who Care for Persons With Human Immunodeficiency Virus: 2024 Update by the HIV Medicine Association of the Infectious Diseases Society of America

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Advances in antiretroviral therapy (ART) have made it possible for persons with human immunodeficiency virus (HIV) to have a lifespan that approaches that of people without HIV without progressing to AIDS or transmitting HIV to sexual partners or infants. There is, therefore, increasing emphasis on maintaining health throughout the lifespan. To receive optimal medical care and achieve desired outcomes, persons with HIV must be consistently engaged in care and able to access uninterrupted treatment, including ART. Comprehensive, evidence-based HIV primary care guidance is, therefore, more important than ever. Creating a patient-centered, stigma-free care environment is essential for care engagement. Barriers to care must be decreased at the societal, health system, clinic, and individual levels. As the population ages and noncommunicable diseases arise, providing comprehensive healthcare for persons with HIV becomes increasingly complex, including management of multiple comorbidities and the associated challenges of polypharmacy while also attending to HIV-specific health concerns. Clinicians must address issues specific to preventive health, including cancer screening, providing recommended vaccinations, and promoting sexual health, including sexually transmitted infection diagnosis, treatment, and prevention. Clinicians also must address issues for specific populations, including persons of childbearing potential during preconception and pregnancy, children, adolescents, and transgender and gender-diverse individuals. This guidance from an expert panel of the HIV Medicine Association of the Infectious Diseases Society of America updates the previous 2020 HIV Primary Care Guidance.

Keywords. HIV; primary care; immunizations; comorbidities; STIs.

Continuous access to antiretroviral therapy (ART) and engagement in a patient-centered, stigma-free, high-quality care environment are essential to assist people with human immunodeficiency virus (HIV) to achieve their health goals, improve their quality and length of life, and eliminate HIV transmission to sexual partners and infants through viral suppression. As effective ART has become simpler over time, HIV care and the care environment have become increasingly complex, and updated HIV primary care guidance is needed. As people with HIV live longer, clinicians must attend to preventing and managing comorbidities and coinfections that often occur earlier and more frequently in people with HIV than in people without HIV. This becomes increasingly important as individuals age. Likewise, screening for and addressing substance use and mental health conditions throughout the lifespan is essential to effective HIV care. At the same time, a strained HIV workforce struggles to provide care to an ever-increasing population of people with HIV and to do so with diminishing resources. Many people with HIV, including those at increased likelihood of acquiring HIV, disproportionately experience barriers to accessing care and treatment, including income inequality, unstable housing, food insecurity, joblessness, and poor access to transportation.

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These barriers are embedded in a social framework interwoven with racism, sexism, and discrimination against those whose race, ethnicity, sexual orientation, or gender identity is in the minority. Increasingly, HIV care must acknowledge and address these issues to end the HIV epidemic in all populations. Ensuring that clinical settings are free of stigma and discrimination is a first and essential step. Unfortunately, the United States is still far below its goals for ending the epidemic. The most recent available data show that among all people estimated to be living with HIV (diagnosed or undiagnosed), only 57% had suppressed virus, with lower levels among Black, Hispanic/Latino, and Indigenous populations; people who inject drugs; and heterosexual cisgender men. Only 47% of all people with HIV met the definition for care retention, with even lower rates in many populations [1]. Such disparities highlight the fact that HIV care, as well as HIV prevention, must be person-centered, inclusive of attention to social determinants of health, and based on equity.

While this Guidance primarily addresses care for people with HIV, a patient-centered and individualized approach to HIV prevention and care is required to end the HIV epidemic. Substantial health disparities that are driven by societal inequities continue to be seen among those with new HIV diagnoses. Although pre-exposure prophylaxis (PrEP) is a highly effective tool for HIV prevention, its implementation is not yet equity-based or centered in the populations who would most benefit [2–4]. Some HIV care providers also provide PrEP, but expansion of both HIV testing and PrEP access is needed using novel service-delivery approaches that are beyond the traditional clinic visit to improve access. Similarly, the ongoing sexually transmitted infection (STI) epidemic disproportionately affects people with and vulnerable to HIV. STI screening, treatment, and prevention should be included in a syndemic approach to HIV prevention and care.

All of these factors contribute to the need for evolving HIV care recommendations in order to meet new and intensified challenges. This version of the Primary Care Guidance for Providers Who Care for Persons With Human Immunodeficiency Virus contains an expanded section devoted to patient-centered optimization of HIV care, including use of tools such as multidisciplinary care teams, telehealth, and street medicine. The Guidance has new sections devoted to immunizations, cancer screening, and STIs, including a focus on mpox (formerly monkeypox) and STI prevention using doxycycline postexposure prophylaxis (doxyPEP). An updated discussion of metabolic diseases addresses statin use in people with HIV as well as approaches to comorbidity screening and management. A section on children with HIV has been added, along with updated sections on care for adolescents, persons of childbearing potential, and transgender and gender-diverse populations, and on coronavirus disease 2019 (COVID-19) and people with HIV.

METHODS

Panel Composition

Participants on the panel are HIV Medicine Association (HIVMA) members who are experts in the care of persons with HIV and who volunteered to participate. Two co-chairs (M. A. H. and M. A. T.) with experience in developing guidelines led the expert panel.

Literature Review, Analysis, and Consensus Development of Evidence-based Recommendations

The expert panel, with the assistance from a consultant experienced in medical literature reviews, conducted a literature review to identify new contributions to the field from the date of the last guideline publication in 2020 to December 2023, except when noted in the literature cited. In particular, changes to key guidelines and recommendations and late-breaking data deemed to be practice-changing were included up to the time of manuscript submission. Panel members responsible for each section evaluated the evidence and developed recommendations accordingly. The entire panel reviewed all recommendations, and decisions on the final recommendations were made by consensus based on the evidence. The full panel participated in reviewing and editing the final document. A medical writer contributed to copy editing and formatting prior to submission.

Disclosure and Management of Potential Conflicts of Interest

All panel members complied with the Infectious Diseases Society of America (IDSA) policy on conflicts of interest, which requires disclosure of any financial or other interest that might be construed as constituting an actual, potential, or apparent conflict. Panel members were provided with IDSA's conflict of interest disclosure statement and asked to identify ties to companies that develop products that might be affected by promulgation of the guidance or any other potential conflicts. Information for panel members and spouses was requested regarding employment, consultancies, stock ownership, honoraria, research funding, expert testimony, and membership on company advisory committees. Disclosure of new conflicts of interest was solicited at the beginning of each panel meeting. The panel made decisions on a case-by-case basis as to whether an individual's role should be limited as a result of a conflict or potential conflict. No limiting conflicts were identified.

RECOMMENDATIONS FOR THE PRIMARY CARE OF PERSONS WITH HIV

The following recommendations are based on evidence available to the panel at the time of publication. Many of the recommendations refer to other guidelines and recommendations, including, but not limited to, those from the Department of Health and Human Services (HHS), Centers for Disease

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Control and Prevention (CDC), and the CDC Advisory Committee on Immunization Practices (ACIP), with the recognition that these sources evolve over time and that no single primary care guidance publication can fully anticipate these changes. In general, recommendations from the most current versions of guidelines and ACIP recommendations should be followed.

SECTION 1: OPTIMIZING CARE ENGAGEMENT, MEDICATION ADHERENCE, AND VIRAL SUPPRESSION

Recommendations

- All persons with HIV should be provided timely access to routine and urgent medical care via a patient-centered approach, beginning with Rapid ART at entry, if feasible.
- Longitudinal low-barrier models, such as extended or nontraditional business hours, walk-in acute or primary care, telehealth, and alternate care venues, including street medicine, should be incorporated as feasible.
- HIV care sites should provide linguistically and culturally appropriate care.
- HIV care sites should maximize diversity of the workforce to represent the patient population served in terms of gender identity, sexual orientation, race, ethnicity, primary language, and meaningful representation of persons with HIV.
- HIV care sites should implement programs that incorporate evidence-based and evidence-informed interventions shown to improve HIV care engagement and viral suppression, including providing gender-affirming and trauma-informed care, addressing structural and social determinants of health, and integrating mental health and substance use treatment with harm reduction and cultural humility at the core.
- HIV care sites should use a multidisciplinary team model but identify a primary clinician with experience and expertise in HIV for each patient and support the development of trusting long-term patient–clinician relationships.
- Because HIV-related stigma and misinformation remain highly prevalent within healthcare systems, HIV care site employees and clinicians should advocate for patients' rights throughout the healthcare system to ensure that people with HIV are appropriately considered for medical and surgical procedures.
- Surgical and dental decisions for people with HIV should be based on shared decision-making among the HIV specialist, surgeon, and patient while weighing all relevant factors and should not depend on the CD4 cell count or HIV RNA level alone.
- People with HIV should be considered as both solid organ recipients (regardless of donor HIV status) and solid organ donors to people with HIV.

Evidence Summary

Initiating ART on the day of or within 7 days of diagnosis is considered Rapid ART [5]. Rapid ART is a pillar of Ending the HIV Epidemic: A Plan for America and the National HIV/AIDS Strategy, while also being endorsed in each of the major clinical HIV treatment guidelines [6–9]. ART should be offered unless a clinical concern exists that warrants delaying ART initiation, such as cryptococcal or tuberculous meningitis, or if the patient expresses a desire to delay therapy. Structural, systemic, or programmatic barriers that would impede Rapid ART should be removed [10]. Elimination of barriers to the initial linkage to care leads to shorter times to viral suppression. Delay from diagnosis to the initial appointment for HIV care has been shown to be a predictor of failure to engage in care, which Rapid ART mitigates [11]. Persons engaged in Rapid ART programs may need enhanced support to achieve continuous care engagement and viral suppression [12].

The long-term effectiveness of ART is dependent on durable suppression of viral replication. Clinicians should emphasize that viral suppression not only improves the patient's health but prevents HIV transmission to others [13]. "Undetectable = Untransmittable" (U = U) messaging is welcomed and encouraged by communities with HIV and should be part of routine messaging in the clinic to mitigate stigma and encourage ART adherence. Pursuit of viral suppression should ensure that those individuals whose virus is not suppressed do not feel further stigmatized. Conversations should be conducted in a nonjudgmental fashion and should seek reasons and potential solutions for the adherence challenges that result in viremia. Stigma mitigation is important to optimizing adherence and viral suppression as stigma is a significant driver of care disengagement and adherence challenges [14].

Wherever persons with HIV are cared for, people-first language (such as "people with HIV" instead of "HIV-infected people") and gender-affirming language should be used, and appropriate pronouns and names should be used in electronic health records and when addressing patients directly [15]. Knowledge dissemination is critical to combating stigma in healthcare settings, while many myths about HIV remain [16, 17]. Clinicians should disseminate knowledge regarding scientific advances, including that HIV is a chronic illness in the setting of effective ART; that risk of transmission in healthcare settings is <1% with no reports of healthcare transmission in the modern ART and post-exposure prophylaxis (PEP) era; and that surgical and dental decisions should be based on shared decision-making among the HIV specialist, surgeon, and patient while weighing all relevant clinical factors. Decisions related to surgical and dental procedures should not depend on the CD4 cell count or HIV RNA level alone [18, 19]. Furthermore, people with HIV can be considered as both recipients and donors in solid organ transplantation, and HIV alone should not be an exclusionary factor [20–23]. People with HIV can receive

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organs from all donors, while people with HIV can only donate organs to other people with HIV. The HIV Organ Policy Equity Act, enacted in 2013, reversed a federal ban on use of organs from people with HIV in recipients with HIV and set standards for research and clinical care in solid organ transplantation among people with HIV. It is important for clinicians to consider referrals for transplantation; updated lists of approved transplantation centers for people with HIV are accessible through the Health Resources and Services Administration Organ Transplantation and Procurement Network webpage [24].

The primary reason for treatment failure, particularly among patients on their first ART regimen, is suboptimal adherence to care or treatment regimens [25, 26]. Medication adherence is essential to achieving and maintaining viral suppression with modern ART, although 100% adherence may not always be necessary for optimal viral suppression outcomes [27]. Discussions and education around adherence to ART should use an empathetic lens with the goal of identifying barriers to adhering to regular medication use and brainstorming feasible solutions. Counseling about the importance of medication adherence should be provided carefully and thoughtfully so as not to perpetuate (or lead to) a sense of self-guilt or anxiety about missed doses. Further, inconsistent adherence may be linked to other important health outcomes, for example, cardiovascular disease and increased mortality, even in the setting of viral suppression [28].

There are many drivers of poor treatment adherence including inconsistent access to medications (including inability to afford medications, limited pharmacy hours, requirements to pick up prescription refills monthly); structural and societal-level barriers (including inadequate transportation; health system barriers to engagement; food or housing insecurity; stigma and discrimination based on HIV status, race, ethnicity, gender identity, sexual orientation, disability, or immigration status); clinic-level barriers (including stigmatizing/discriminatory language or practice by office staff or clinicians, restrictive hours, inaccessible location, lack of a mutually trusting and respectful, collaborative patient–clinician relationship); and patient-level barriers (mental health and substance use issues, pill fear, pill fatigue) [29–34]. Additionally, periods of transition (eg, postpartum, relocation, employment/insurance changes, incarceration) may lead to disengagement in care. Some populations may warrant dedicated programs and support to assist with care reengagement [35]. All of these factors must be considered when designing systems to improve care engagement.

Adherence to care means not only medication adherence but also medical visit attendance and continual engagement in care [36]. Low adherence to visits and poor engagement in care have been found to predict approximately 50% higher mortality among persons with HIV [37]. Thus, it is critically important that HIV care providers and clinics have evidence-based and evidence-informed strategies to effectively engage and assist patients in staying in care [38]. Interventions that improve care engagement or viral suppression generally achieve 1 of 3 things: care coordination through a multidisciplinary team of providers (both physical and behavioral health) and social supports, provision of an essential need such as housing or food assistance, or creation of an environment that elicits and acknowledges patients' goals, motivations, and care needs. Specific considerations may include physical location, clinic environment, and the individual's biopsychosocial situation. Inherent in each of these is a strengths-based approach that leverages a patient's strengths as a part of the solutions [39]. While many interventions have demonstrated some impact on care engagement and adherence to medication, none have a very large effect size [38]. Barriers to care are heterogeneous; therefore, programs to overcome these barriers will need to be similarly heterogeneous. Differentiated service delivery, whereby the location, intensity, frequency of the service, and who delivers that service are tailored to individual needs, is a model that factors in heterogeneous needs at a large scale [40].

Components that could provide a foundation for individual care engagement include social engagement programs, reminders around the clinic about the importance of attending appointments, patient navigation (including enhanced personal contacts), financial incentives, nutrition assistance, and mobile health platforms that leverage mobile devices to better engage patients [41–46]. Intake assessments and ongoing assessments of barriers to care should include social and economic factors such as stigma, violence, social support, food insecurity, unstable housing, and transportation challenges. Lack of adequate food or safe housing can impact the ability to remain adherent to a treatment regimen and even be associated with increased risk of death [47]. Early assessment by a qualified social worker or case manager is essential, and ongoing access to effective case management teams is necessary to overcome barriers to care [48].

At times, how and where care is delivered needs to shift entirely. Accordingly, there are several promising new care models that can help advance access and thus improve health outcomes. Telehealth is a technological innovation that was widely implemented during the COVID-19 public health emergency that allows clinicians to interface with patients via synchronous audio or video to overcome barriers and improve continuity of care [49]. Telehealth consultations can be leveraged to bring HIV care to a primary care clinic or resource-limited and rural settings or to address the shortage of HIV clinicians via peer mentoring [50–54]. The Centers for Medicare & Medicaid Services guidance issued in June 2023 requires audio-video technology for most nonbehavioral telehealth consultations and permits audio-only for mental health encounters [55]. A systematic review showed improved physician-defined outcomes with videoconferencing as opposed to audio-only.

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However, because patient outcomes were comparable between videoconference and audio-only, lack of videoconferencing capability should not be a barrier to telehealth encounters [56]. The benefits of a telehealthcare model include enhanced access to a multidisciplinary care team, on-demand care, and flexibility [57]. Despite these benefits, telehealth has the potential to introduce privacy and confidentiality concerns and potentially worsen disparities via the digital divide [58–60]. Telehealth also operates under ambiguous state-by-state piecemeal regulations that change in a dynamic environment. Laboratory and vaccination coordination are additional challenges. Telehealth can, however, bring evidence-based care to resource-limited populations such as incarcerated individuals and people who inject drugs. The Drug Enforcement Agency and Substance Abuse and Mental Health Services Administration rules have approved telehealth as an acceptable modality for medications for opioid use disorder and other co-occurring mental health disorders [61–63]. Further, telehealth provides an opportunity to optimize HIV care through low-barrier models such as harm reduction, an approach to healthcare that is guided by the philosophy of "meeting people where they are," both mentally and physically, and treating them with dignity and respect [64]. Syringe services programs and potential alternative care venues are the cornerstone of harm reduction, aimed at mitigating the harms associated with injection drug use [65]. Another low-barrier model is street medicine, a rapidly evolving form of harm reduction that sets the traditional healthcare system aside and enables providers to physically meet people from vulnerable communities (including persons who are unhoused) at sites accessible to them, such as walk-in clinics and other alternative care venues [66–71]. The incorporation of these innovative modalities into the practice of HIV medicine offers an opportunity to optimize care engagement in diverse and need-to-reach communities.

The quality of the patient–provider relationship is often cited as one of the most important factors in care engagement. Having a provider with whom the patient feels comfortable and can communicate effectively and honestly is key to developing this type of relationship [32, 72, 73]. The multidisciplinary care model for care coordination often helps patients remain in care, identifies unmet care needs, and improves adherence to medications [74–76]. Having an HIV team that includes a case manager, social worker, or staff with similar responsibilities and skills has been shown to enhance adherence to care and engagement [39]. Other team members may include physicians, HIV clinical pharmacists, nurses, nurse practitioners, physician assistants, mental health professionals, peers, health educators, patient navigators, and nutritionists. Culturally and linguistically competent care is critical to successful care engagement. Stigma mitigation is facilitated by diversifying the workforce to represent the patient population served in terms of gender identity, sexual orientation, race, ethnicity, and primary language and by ensuring meaningful representation of persons with HIV. A broad range of components, from having staff of the same race, culture, or lifestyle to having art and reading material in the clinic that reflects the culture of the local community, may be useful in facilitating this goal [77]. Tailored programs that facilitate care engagement are an essential component of effectively caring for persons with HIV. Ensuring the meaningful involvement of people with HIV in program design and implementation is critical to shaping clinical programs that prioritize access and care engagement.

Ongoing monitoring of care engagement and viral suppression is one element in a comprehensive package of quality and performance measures that can enhance care outcomes for persons with HIV. A national expert panel with participants from HIVMA and IDSA has developed HIV quality-of-care performance metrics [78]. These metrics are endorsed by the National Quality Forum and the CMS and have been adopted by many care organizations. Importantly, mortality decreases when performance measures are met [79].

SECTION 2: INITIAL EVALUATION AND IMMEDIATE FOLLOW-UP FOR PERSONS WITH HIV

Recommendations

- A comprehensive present and past medical history that includes HIV-related information, medication/social/family history (Tables 1 and 2), review of systems, and physical examination (Table 3) should be obtained for all patients upon initiation of care, ideally at the first visit or, if not feasible, as soon as possible after the first visit. In particular, in settings of Rapid ART initiation, clinicians may initially truncate parts of the comprehensive history and physical and provide a more targeted exam but with close follow-up to complete the essential and more comprehensive assessment.
- As many patients will not be able to recall details of prior treatments and laboratory results, medical records should be requested and reviewed, and the current medical record should be updated accordingly. Baseline laboratory assessments should be obtained at the initial visit (Table 4).

Evidence Summary

History of the Present Illness and HIV-Related and Other Medical and Surgical Histories

Table 1 outlines pertinent elements of the history of present illness (the reason that the patient presents to the clinic) and HIV-related information that should be obtained at the initial assessment. Table 2 outlines pertinent elements of current and past medical conditions, as well as other pertinent history to be addressed at the initial visit. Because of the high incidence of coinfections and comorbidities in people with HIV, special

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Table 1. Initial Assessment: History of the Present Illness and Human Immunodeficiency Virus–Specific History

History of the present illness
• Questions should focus on establishing rapport, putting the patient at ease, and determining the patient's primary reason for the visit, if not simply to establish the patient in HIV care
• Assess the patient's level of knowledge about HIV treatment and prevention, evaluate educational needs, and determine what ancillary and social support might be necessary (ideally in collaboration with effective case management)
• If not previously treated with ART, assess the patient's readiness to begin ART immediately, including on the day of the first visit if feasible
• If previously but not currently on ART, assess the patient's readiness to reinitiate ART immediately, including on the day of the first visit if feasible and if adequate information is available to choose an appropriate regimen
• Assess the need for assistance with social services such as housing, transportation, and food access, and involve support staff early if appropriate
HIV-specific history
• Approximate date of HIV diagnosis
• Approximate date of HIV acquisition and likely cause for HIV acquisition (including sexual trauma if appropriate), which can sometimes be determined on the basis of prior negative test results, occurrence of symptoms suggestive of acute retroviral infection, or timing of activities that may have resulted in exposure
• Prior HIV care
• Nadir CD4 cell count and highest viral load
• Current and past exposure to antiretroviral drugs
o Use of pre- or postexposure prophylaxis (including medications and date of last use)
o Use of antiretrovirals for prevention of perinatal transmission
o Prior antiretroviral treatment
• Drug regimens taken and HIV RNA level while on those regimens
• Duration of therapy
• Reasons for changing regimens (eg, virologic failure, tolerability, simplification) and adherence challenges
• Past medical record review (request records if not available)
o Results of all prior resistance testing
• Prior HIV-associated conditions
o Opportunistic infections and/or malignancies according to the Centers for Disease Control and Prevention stage 3 definition
o Other HIV-related conditions (eg, thrush)
History for people who currently inject drugs
• Current drug-use practices
• Source of needles and needle-sharing practices
• Access to naloxone

Abbreviations: ART, antiretroviral therapy; HIV, human immunodeficiency virus.

attention should be paid to this aspect of the history as well as any risk factors that may contribute to the development of comorbidities.

Family Medical History

A family medical history has become more important now that persons with HIV are living longer and are at increased risk for age- and sex-specific conditions in addition to HIV- and treatment-related complications. Clinicians should ask about any family history of conditions that might predispose the patient to malignancies, neurologic diseases, osteoporosis, and atherosclerotic disease and whether there is a family history of early coronary artery disease.

Social History

Clinicians should ask how the patient is adjusting to the diagnosis of HIV, who they have informed of their HIV status, and what support they receive from family and friends. If needed, patients should be offered assistance with the disclosure process. Work and educational histories should be discussed, including whether these have been affected by the diagnosis of HIV. Assessment of access to housing, food, transportation, and other primary social needs is essential. Other pertinent information includes insurance issues, financial status, relationship and family status, and plans for having children.

It is critical to obtain a sexual history in an open, nonjudgmental manner by using a sexual health framework and asking about the 5 "P's": past and current partners, practices, protection from STIs (including past PrEP use), past history of STIs, and pregnancy intention. Although targeted toward the general population, the CDC publishes an excellent step-by-step guide to taking a sexual history [80]. Important considerations for counseling and education are discussed in Section I of that document (Optimizing Care). Very few states require healthcare providers to notify sex partners of patients, but clinicians should be aware of laws in their own jurisdiction and advocate for repeal of laws that criminalize HIV status [81]. All clinicians should familiarize themselves with basic discussions about gender identity, including communication about appropriate pronouns, and fundamentals of care for transgender and gender-diverse individuals. See Section 11 for additional discussion of gender-affirming care.

As part of the initial evaluation and at periodic intervals thereafter, clinicians should assess for the presence of depression, anxiety, post-traumatic stress disorder (PTSD), and sexual or physical abuse, including domestic violence, using direct questions or validated screening tools (Patient Health Questionnaire-9 [PHQ-9] and Generalized Anxiety Disorder 2-item [GAD-2]) [82, 83]. Persons with HIV have high rates of adult sexual and physical abuse and childhood sexual abuse. A history of current and past psychoactive drug use, including

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Table 2. Other Medical and Surgical History

Comorbidities

Current or past chronic medical conditions that might affect the choice of therapy or response to therapy

- Prior and present gastrointestinal disease
- Liver disease including viral hepatitis A, B, and C; past treatment for hepatitis B and/or C
- Cardiovascular disease and risk factors, including hyperlipidemia, hypertension, diabetes mellitus, and smoking
- Osteopenia or osteoporosis
- Kidney disease
- History of receipt of blood products, organ transplant, or tattoos

Other past medical conditions that may have implications for persons with HIV

- Chickenpox or shingles, measles
- *Mycobacterium tuberculosis* illness, exposure, treatment; prior testing or treatment for latent tuberculosis
- STIs including syphilis, chlamydia, gonorrhea, herpes simplex, trichomoniasis, chancroid, HPV
- Abnormal anal cytology; past anorectal disease including warts, fissures

Gynecologic and obstetric history

- Past pregnancies and plans for future pregnancy, history of artificial insemination by an unidentified donor
- Birth control practices
- Last cervical Pap test, abnormal Pap test ever, colposcopy, loop electrosurgical excision procedure, biopsy (cone/knife)
- Menstrual history
- Other gynecologic conditions including pelvic inflammatory disease

Mental health history, current and past

- Previous or current psychotherapy and medication treatment
- Anxiety disorders, bipolar disorder, depression, violent behavior
- Suicidal, homicidal ideation; history of hospitalization due to mental health issues
- History of trauma, including sexual and physical abuse, intimate partner and other violence; post-traumatic stress disorder (with appreciation for the sensitive nature of these inquiries and the emotional responses they may elicit)
- History of substance use and treatments for substance use (if any, note which substances used)

Current or past use of psychoactive substances

- Tobacco including e-cigarettes; years of use and estimate of cumulative exposure
- Cannabis and cannabinoids (including vaping)
- Vaping (regardless of substance)
- Alcohol use: quantify daily/weekly/monthly use
- Stimulants, including methamphetamine, cocaine, crack cocaine
- Opioids
- Other nonprescription drugs
- Misuse or overuse of prescription drugs
- Other substances primarily used with sex (amyl nitrate [poppers], erectile dysfunction drugs)
- Past injection drug use (regardless of substance used); history of needle sharing; hospitalizations related to injection drug use

Past hospitalizations, surgical procedures, transfusions, or blood product receipt, especially during 1975–1985 or outside the United States and Canada

Immunization status (obtain from past medical records if possible)

- Childhood vaccination including for measles, mumps, rubella, rotavirus
- Coronavirus disease 2019
- Hepatitis A and B
- HPV
- Influenza
- Meningococcus
- Mpox
- Pneumococcus: with type of vaccine
- Varicella zoster
- Tetanus/diphtheria or tetanus/diphtheria/acellular pertussis
- Respiratory syncytial virus
- Travel vaccinations

Travel and residential history pertinent to endemic infectious diseases that may be reactivated, including histoplasmosis (Ohio and Mississippi River valleys), coccidioidomycosis (southwestern deserts), or tuberculosis

Pediatric medical history

- Maternal HIV, obstetric, and birth history
- Exposure to antiretroviral drugs perinatally
- Growth and development milestones
- Childhood vaccination history
- Caregiver environment and support
- Education history

Family medical history

- Diabetes
- Early heart disease: myocardial infarction in a first-degree relative before age 55 years in male relatives and before age 65 years in female relatives
- Hypertension

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Table 2. Continued

• Hyperlipidemia • Cancer • Any other significant medical condition
Social history
• Race and ethnicity • Gender identity and sexual orientation; pronouns • Patient birthplace, residence, and travel history • Employment history • Incarceration history • Education history • Financial support • Children: ages, plans for having children in the future, HIV status of children • Pets • Diet and exercise • Sexual history: nonjudgmental inquiry about types of activity including partners (number, gender, whether met online) and practices (genital, anal, oral; use of drugs with partners; exchange of sex to meet needs such as money, housing, drugs; assessment of satisfaction with sexual performance); STI prevention including use of barrier protection such as condoms or dental dams, frequency of barrier use, and prior HIV preexposure prophylaxis or doxycycline postexposure prophylaxis use; past STIs and treatment (including mpox); sexual trauma, violence, and abuse also should be explored, recognizing the sensitivity of these issues • Marital/relationship status o Partner(s) health and HIV status o Partner(s) access to healthcare, including HIV testing (if appropriate) o Disclosure of HIV status to partner(s) • Social support and participation in support groups • Disclosure history: friends, family, work colleagues • Access to stable housing, food, transportation • For minors, review legal guardianship and consent/assent
Medications
• Current medications, including over-the-counter medications, supplements • Use of complementary or alternative therapy or treatment
Allergies and intolerance
• Dates and types of reactions, including hypersensitivity reactions to antiretroviral therapy
Healthcare maintenance and preventative health screenings (as appropriate) Dates of last:
• Cervical or anal Pap (and results, if known) • Mammogram • Bone density • Colonoscopy and/or anoscopy (and results, if known) • Abnormal aortic aneurysm screening • Dental visit • Dilated eye exam • Lung cancer screening (if applicable and results, if known)

Abbreviations: HIV, human immunodeficiency virus; HPV, human papillomavirus; STI, sexually transmitted infection.

alcohol and tobacco, and injection drug use should be taken. See Section 3 for more on screening and treatment for mental health and substance use issues.

Allergies and Medications

A discussion of allergies and intolerances should include questions about hypersensitivity reactions to antibiotics and ART. Clinicians should ask about all current medications, including dietary or herbal supplements, some of which have been shown to interact with ART. All prior ART regimens, including years of use, prior side effects, and reasons for switching, should be recorded. It is also important to assess prior adherence to medications and document viral loads while on each regimen.

Review of Systems

The review of systems should be comprehensive and include questioning about common HIV-related symptoms (see Table 3). Patients should be questioned about how their current weight compares with their past weights, and a dietary assessment should be performed. Given the high incidence of comorbidities in people with HIV, eliciting a history of comorbidities and their risk factors is essential. Depression, anxiety, and PTSD are common among people with HIV, especially cisgender women and lesbian, gay, bisexual, transgender, queer plus (LGBTQ+) populations, and the review of systems should include questions that focus on changes in mood, libido, sleeping patterns, appetite, concentration, and memory.

Physical Examination

A complete physical examination should be performed at the initial encounter or as soon afterward as possible. In addition to recording all vital signs (including height and weight), persons aged >50 years should be assessed for frailty. For all patients, the overall body habitus should be assessed, looking

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Table 3. Initial Assessment—Review of Systems and Physical Examination

Review of Systems	Physical Examination
A complete review of systems with special attention to the areas listed below: • Unexplained weight loss or gain, night sweats, fever, changes in body habitus • Skin: skin discoloration, rash, ulcers, or lesions • Lymph nodes: localized or generalized enlargement of lymph nodes • Eyes: vision change or loss • Mouth: gum disease, ulcers, oral lesions or pain, dental health and dentition for children • Cardiopulmonary: chest pain, palpitations, wheezing, dyspnea, orthopnea • Gastrointestinal: odynophagia, dysphagia, diarrhea, nausea, pain • Endocrinology: symptoms of hyperglycemia, thyroid disease, hypogonadism • Neurologic and psychiatric: persistent and severe headaches, memory loss, loss of concentration, depression, apathy, anxiety, mania, mood swings, lower-extremity paresthesias, pain or numbness, paralysis or weakness, cognitive difficulties, dizziness, seizures, sleep disorders • Genitourinary: dysuria, urethral or vaginal discharge or lesions, hematuria • Orthopedic: hip pain, joint pain, fractures, diagnosis of or risk factors for osteopenia/osteoporosis • Anorectal: anal discharge, rectal bleeding, rectal itching, pain or fullness in anal area • Developmental milestones: for infants and young children, assess for motor or speech delays • Growth delay and failure to thrive for infants and children	A complete physical examination should be performed, with special attention to the following areas: • Vital signs: including height and weight • General: including body habitus, evidence of obesity, wasting, lipodystrophy, assessment of frailty, ambulatory ability • Skin: seborrheic dermatitis, ecchymoses, purpura, petechiae, Kaposi sarcoma, herpes simplex or zoster, psoriasis, molluscum contagiosum, onychomycosis, folliculitis, condylomata, cutaneous fungal infections, acanthosis • Lymph nodes: generalized or localized lymphadenopathy • Eye: retinal exudates or cotton wool spots, hemorrhages, pallor, icterus • Oropharynx: oral hairy leukoplakia, candidiasis (thrush, palatal erythema, angular cheilitis), aphthous ulcers, gingivitis, periodontal disease, Kaposi sarcoma, tonsillar or parotid gland enlargement • Cardiovascular: heart exam, peripheral pulses, presence/absence of edema or bruits • Chest: lung exam • Breast: nodules, nipple discharge • Abdomen: hepatomegaly, splenomegaly, masses, tenderness • Genitourinary: ulcers, warts, chancres, rashes; gynecologic exam including bimanual exam, discharge (if male: testicular exam; evaluation for hernia) • Anorectal: ulcers, warts, fissures, internal or external hemorrhoids, masses, Kaposi sarcoma; prostate exam when appropriate • Neuropsychiatric: depression; mania; anxiety; signs of personality disorder; difficulties in concentration, attention, and memory; signs of dementia; speech problems; gait abnormalities; focal deficits (motor or sensory); lower-extremity vibratory sensation; deep tendon reflexes

for evidence of wasting, obesity, or, particularly in patients who have received older ART regimens, evidence of drug-related lipohypertrophy (including dorsocervical fat pad, gynecomastia, or visceral abdominal fat accumulation) and/or lipoatrophy (including loss of subcutaneous fat in the face, extremities, or buttocks). All adult patients with CD4 count <50 cells/μL, as well as infants and young children with profound immunodeficiency, should be referred to an ophthalmologist for a dilated funduscopic examination. Though persistent generalized lymphadenopathy is common among untreated persons with HIV, it does not correlate with prognosis or disease progression. However, focal or rapidly progressive lymphadenopathy may require further evaluation, including biopsy. Additionally, if lymphadenopathy does not quickly resolve with initiation of ART, diagnostic studies should be pursued. Neurology and/or neuropsychology referral for assessment of neurocognitive disorders, dementia, and focal neuropathies may be indicated [84, 85]. Cervical motion and uterine or adnexal tenderness on bimanual pelvic examination suggest pelvic inflammatory disease and should prompt STI testing. An anorectal examination is important to evaluate for anal warts, other STIs, and anal cancer, with age-appropriate screening for prostate abnormalities if assigned male at birth.

Baseline Laboratory Evaluation

A number of initial laboratory studies are indicated for persons who present with a new HIV diagnosis or for persons who reengage in care (see Table 4). Other tests may be indicated depending on the age and sex of the patient and/or symptoms. When rapid initiation of ART is possible, it is important to obtain baseline laboratory tests, including HIV RNA level, CD4 cell count, resistance testing, and viral hepatitis serology, and to assess for safety and general medical condition; however, ART initiation need not be delayed until results are received. The absence of results for HIV RNA level, HIV genotype, and hepatitis B surface antigen (HBsAg) will influence the choice of antiretrovirals (ARVs) for rapid initiation. If results of HIV screening are not available for review, an HIV diagnosis should be confirmed, preferably using a fourth-generation antigen/antibody test with rapid turnaround time.

Recommendations

HIV-Specific Tests for All Persons With HIV

- Patients who have no documentation of their HIV status or who were tested anonymously should have an HIV antigen/antibody screening test performed upon initiation of care. When HIV RNA is obtained, in addition to antigen/antibody for HIV screening, an isolated positive HIV RNA should be verified by repeat testing if HIV antibody is negative, especially in the setting of prior use of long-acting cabotegravir as PrEP.
- A CD4 cell count with percentage should be obtained upon initiation of care.
- Measurement of the CD8 cell count and the ratio of CD4 to CD8 cells is not considered necessary, as the results are not used in clinical decision-making.

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Table 4. Recommended Initial Laboratory Screening and Other Studies in Persons With Human Immunodeficiency Virus

Test	Comment(s)
HIV-specific tests for all persons with HIV	In infants and children aged <18 years with perinatal HIV exposure, maternal antibodies can persist up to 24 months; therefore, HIV RNA nucleic acid tests are considered diagnostic; infants, children, and adolescents with HIV and history of initiating early ART may have negative antigen/antibody test
• HIV antigen/antibody testing	If written evidence of diagnosis not available or if viral load low or undetectable (an isolated positive HIV RNA with negative HIV antibody should be verified by repeat testing, especially in the setting of prior CAB-LA exposure as PrEP)
• CD4 cell count and percentage	CD4 cell count and percentage access are necessary to assess for immunosuppression and support decisions on OI prophylaxis and vaccinations
• Plasma HIV RNA polymerase chain reaction (HIV viral load)	Establish baseline and monitor viral suppression
• HIV resistance testing	• Baseline genotype for protease inhibitor, nonnucleoside reverse transcriptase inhibitor, nucleoside/nucleotide reverse transcriptase inhibitor, mutations for persons who have never initiated therapy or who are reengaging in care and not on therapy or with inconsistent access to therapy; INSTI genotype is recommended if clinical concern for transmitted INSTI resistance and/or acquired INSTI resistance, as in the setting of prior CAB-LA (as PrEP) exposure
HIV-related tests in selected patients	
• Coreceptor tropism assay	If use of C-C motif chemokine receptor 5 antagonist is being considered
• Human leukocyte antigen (HLA) B*5701	If use of abacavir is being considered
Other laboratory tests	
• Complete blood cell count with differential	Assess for anemia, neutropenia, thrombocytopenia
• Alanine aminotransferase, aspartate aminotransferase, total bilirubin, alkaline phosphatase	Assess for evidence of liver damage, hepatitis, or systemic infection (eg, elevated alkaline phosphatase with some OIs)
• Total protein and albumin	High total protein common with untreated HIV infection due to increased immunoglobulin fraction secondary to B-cell hyperplasia; low albumin may indicate nutritional deficiency or nephrotic syndrome
• Electrolytes, blood urea nitrogen, creatinine	Assess kidney function; use creatinine to calculate estimated glomerular filtration rate
• Lipid profile and blood glucose; hemoglobin A1c	Fasting not needed for initial lipid and glucose assessment; if abnormal, repeat fasting (hemoglobin A1c should be measured prior to ART initiation but is not used for diagnosis of diabetes in those on ART)
• Urinalysis	Assess for evidence of proteinuria, hematuria
Screening for coinfections	
• Gonorrhea, chlamydia	Nucleic acid amplification test (NAAT) with sites based on exposure history (eg, urine, vaginal, rectal, oropharyngeal; 3-site testing preferred for all patients)
• Trichomoniasis	In all persons who have vaginal sex
• Syphilis	Using local protocol (either rapid plasma reagin or treponemal-specific antibody tests)
• Latent *Mycobacterium tuberculosis*	Tuberculin skin test or IGRA; IGRA preferred if history of Bacillus Calmette-Guérin vaccination
• Varicella virus	Anti-varicella IgG if no known history of chickenpox or shingles
• Viral hepatitis A, B, C	Measure HBsAg, HBsAb, HBcAb, HCV Ab, HAV IgG antibody. If HBsAg-positive or HBcAb-positive, order HBV DNA level. If HCVAb-positive, known past HCV, or considering acute HCV, order HCV RNA level. HCV genotype should be collected unless a pan-genotypic treatment regimen will be used. Screen for hepatocellular carcinoma for all adult patients with cirrhosis and noncirrhotic patients with chronic HBV for an extended period
• Measles titer	Adequate evidence of immunity includes being born in the United States before 1957, written documentation of adequate vaccination, or serologic evidence of immunity [104]. Persons born in the 1960s may have been vaccinated with a vaccine other than MMR and may have waning immunity. Patients may opt to receive a booster MMR vaccine rather than check serology
• Cryptococcal antigen	Indicated for patients with CD4 count <100 cells/μL or symptoms consistent with infection
• Toxoplasma antibody	Indicated for patients with CD4 count <200 cells/μL or symptoms consistent with infection
Tests that may be performed under certain circumstances	
• Chest radiography	For patients with evidence of latent *Mycobacterium tuberculosis* infection; consider in patients with underlying lung disease for use as comparison in evaluation of future respiratory illness
• Cytology: cervical and/or anal Pap test	Cervical; anal if indicated. Abnormal results require follow-up with colposcopy or high-resolution anoscopy, respectively
• Glucose-6-phosphate dehydrogenase	Screen for deficiency in persons, especially those assigned male at birth, who are of African, Mediterranean, or Asian descent before prescribing oxidant drugs such as dapsone and primaquine in those with glucose-6-phosphate dehydrogenase deficiency. Sulfonamides should be used with caution without prior screening
• Pregnancy test in persons of childbearing potential	Pregnancy status is required to inform choice of ART and discussions about conception in persons of childbearing potential

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Table 4. Continued

Test	Comment(s)
• Serum testosterone level	In cisgender males with fatigue, weight loss, loss of libido, erectile dysfunction, or depression or who have evidence of reduced bone mineral density. Morning free testosterone is preferred. See Section 7 for management of hypogonadism
Tests that are not recommended for general screening purposes	
• HSV IgG, CMV IgG, biomarkers of inflammation	In asymptomatic persons, routine testing for all persons is not recommended for HSV, CMV. Biomarkers of inflammation are not recommended. CMV IgG may be considered if blood transfusion is contemplated in a person at low risk for CMV exposure. A negative CMV IgG may support use of CMV-free blood products

Abbreviations: ART, antiretroviral therapy; CAB-LA, long-acting cabotegravir, CMV, cytomegalovirus; HAV, hepatitis A virus; HBV, hepatitis B virus; HBcAb, hepatitis B core antibody; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HSV, herpes simplex virus; IgG, immunoglobulin G; IGRA, interferon-γ release assay; INSTI, integrase strand transfer inhibitor; MMR, measles, mumps, rubella; OI, opportunistic infection; PrEP, preexposure prophylaxis.

- A quantitative HIV RNA level (HIV viral load) should be obtained upon initiation of care.
- Patients should be assessed for transmitted drug resistance with a genotype assay for protease and reverse transcriptase mutations upon initiation of care.
- If baseline integrase strand transfer inhibitor [INSTI] resistance is suspected (eg. transmitted mutations) or if HIV was acquired after receipt of long-acting cabotegravir for PrEP, regardless of the time since drug discontinuation due to the long half-life of injectable drug, genotypic testing for integrase resistance should be obtained.
- Resistance testing should be obtained for patients who reengage in care and who are currently not on ART or who have not had consistent ART access, recognizing that the absence of resistance mutations does not guarantee the absence of resistance when no selective pressure is present.
- Resistance testing, including for integrase mutations if appropriate, is indicated for patients who are experiencing virologic failure to guide modification of ART and should be performed while the patient is on the failing ART regimen or within 4 weeks of discontinuing the ART regimen.

Evidence Summary

Clinicians should be familiar with the current CDC HIV testing algorithms and interpretation of results based on the algorithms and assays used [86]. Confirming an HIV diagnosis is especially important in patients who are asymptomatic and have a normal CD4 cell count and an undetectable or very low viral load. In addition, patients may present to care with misinformation regarding previous test results. Delayed seroconversion may occur in persons who acquire HIV while taking oral PrEP or, especially, after exposure to cabotegravir as PrEP. If HIV infection is suspected within 3 months of taking oral PrEP or within 12 months following exposure to injectable long-acting cabotegravir (CAB-LA), HIV antibody testing and an HIV RNA level should be obtained. A positive HIV RNA result in the absence of a positive antibody should be verified by repeat testing because of the high rate of false-positive HIV RNA results reported in HIV Prevention Trials Network (HPTN) 083, especially if the last dose of CAB-LA was less than 6 months prior to screening [87, 88]. As new data emerge, CDC guidelines should be consulted for recommendations on screening for HIV in the setting of PrEP use [89].

The initial CD4 cell count is used to stage HIV infection, establish the risk of specific HIV-associated complications, and determine the need for prophylaxis against opportunistic infections (OIs). It is important that the clinician and patient be aware of the substantial variation in CD4 cell counts, especially during acute illness. Because CD4 cell counts may be affected by a variety of medications and intercurrent illnesses, caution should be taken when interpreting CD4 cell counts in these situations. Although the absolute CD4 cell count is the measure that is most often used in clinical practice, the CD4 cell percentage can also be used to assess immune function and is somewhat less variable than the absolute count. Total CD4 counts of 200 and 500 cells/μL generally correspond to CD4 cell percentages of 14% and 29%, respectively. In children aged <5 years, there is more variability in the absolute CD4 cell count; therefore, CD4 percentage is generally preferred for monitoring immune status [86, 90, 91].

The initial HIV RNA level defines the patient's baseline so that response to therapy can be measured. Clinicians should be aware of changes in the type of HIV RNA assay used, the associated variability, and differences in interpretation of results between assays. Thresholds for lower limits of detection for the most commonly used assays range from 20 to 50 copies/mL. Viral load should be measured during the initial evaluation of the untreated patient when establishing care or when a patient reengages in care. Viral suppression is defined as a viral load that is persistently below the level of quantification of the assay; however, the threshold for prevention of HIV sexual transmission is considered to be <200 copies/mL [7].

Drug-resistant HIV can be transmitted from one person to another. The purpose of baseline genotypic resistance testing is to assess for resistance (transmitted or acquired) that would

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influence ART selection. Baseline genotypic resistance testing for protease and reverse transcriptase mutations should be performed for all persons beginning treatment [7]. Resources are available and frequently updated to assist clinicians in the interpretation of drug-resistance mutations [92, 93]. Because transmission of integrase mutations is currently uncommon, baseline integrase genotyping is recommended only when transmission of integrase resistance is suspected, such as when HIV is suspected to have been acquired from an individual known to have been taking a regimen that contains an integrase inhibitor [94]. All persons who acquired HIV after using cabotegravir for HIV PrEP should have integrase resistance testing performed due to the long half-life of this drug and the risk of selecting integrase resistance when fully inhibitory drug levels are no longer present. These individuals should not receive INSTI therapy until an integrase genotype test is performed and sensitivity is demonstrated [7]. Lack of genotypic testing limits the regimens that may be prescribed, including 2-drug regimens such as dolutegravir/lamivudine fixed-dose combination, and other combinations in which resistance to one drug would result in functional monotherapy [7]. In persons who reengage in care and who have been off therapy for 4 or more weeks, resistance mutations may be absent due to lack of selective pressure rather than absence of resistance, and results should be interpreted with this in mind.

Patients who are taking a failing ARV regimen (HIV RNA level >200 copies/mL) should undergo resistance testing to guide interventions and improve viral control. In those with HIV RNA levels between 201 and 500 copies/mL, testing may not be successful but should be considered.

HIV-Related Tests in Select Patients

Recommendations

- Co-receptor tropism testing should be performed if the use of a chemokine receptor 5 (CCR5) antagonist is being considered.
- Human leucocyte antigen (HLA) B*5701 testing should be performed before initiation of abacavir therapy.
- Patients who are positive for the HLA B*5701 haplotype are at high risk for abacavir hypersensitivity reaction and should never be treated with abacavir (this should be noted appropriately in the medical record).

Evidence Summary

Co-receptor tropism testing is needed to determine which patients are appropriate candidates for initiation or continuation of a CCR5 antagonist [7]. CCR5 antagonists are not effective for patients with X4 or dual/mixed-tropic (D/M) virus. The use of a CCR5 antagonist under these circumstances could increase the risk of virologic failure and the development of resistance to the other drugs in the regimen. Tropism screening may fail to detect X4 or D/M virus if it is present at very low levels, and patients may experience treatment failure with CCR5 antagonists because of the presence of pre-existing X4 or D/M virus not detected by the tropism assay. Patients who exhibit virologic failure while taking a CCR5 antagonist may also be considered for tropism testing. Routine tropism testing is not recommended prior to initiation of regimens that do not contain a CCR5 antagonist. Repeat tropism testing is recommended when considering the use of a CCR5 antagonist as part of the ART regimen, even if previously done in the past, unless the previous tropism was X4 or D/M. Tropism may shift from R5 to X4 or D/M during the course of infection, especially with more advanced immunodeficiency (CD4 count <100 cells/μL). A proviral DNA tropism assay can be used in patients with undetectable HIV RNA when considering the use of a CCR5 antagonist in a new regimen [7].

Screening for the HLA B*5701 haplotype is essential in patients being considered for abacavir therapy in order to identify those who are at high risk for the abacavir hypersensitivity reaction [7]. A negative test result does not rule out the possibility of a hypersensitivity reaction but indicates that it is extremely unlikely. Patients who have negative test results should still be counseled about a hypersensitivity reaction before being treated with abacavir [7].

Laboratory Tests to Assess Safety and General Health

Recommendations

- A complete blood count with differential white blood cell count and chemistry panel with electrolytes, glucose, creatinine, calculated creatinine clearance (or estimated glomerular filtration rate [eGFR]), blood urea nitrogen, total protein, albumin, total bilirubin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and urinalysis should be obtained upon initiation of care.
- Because many ARV drugs, the HIV infection, and host factors are associated with abnormal cholesterol and triglyceride levels, a lipid profile should be obtained upon initiation of care and repeated fasting, if appropriate.

Evidence Summary

Anemia, leukopenia, and thrombocytopenia are common among persons with untreated HIV. The complete blood count is also used to calculate the absolute CD4 cell count. A chemistry panel (including electrolytes, glucose, creatinine, eGFR, blood urea nitrogen, total protein, albumin, total bilirubin, AST, and ALT) is an important tool to assess renal and hepatic function and to look for evidence of pre-existing liver injury or hepatitis.

Kidney function is abnormal in up to 30% of persons with untreated HIV, and HIV-associated nephropathy is a relatively

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common cause of end-stage renal disease, especially in Black persons with HIV, although both rates and mortality have declined with more effective ART [95, 96]. A calculated creatinine clearance or eGFR should be obtained to further assess baseline renal function. The eGFR assists in prescribing ARV agents and other commonly used medications that require renal dosing. Clinicians should be aware that some medications such as cobicistat, dolutegravir, bictegravir (BIC), and trimethoprim may affect creatinine secretion and elevate serum creatinine without affecting renal function [97]. A screening urinalysis for proteinuria should be considered at initiation of care and annually thereafter, especially in patients who are at increased risk for developing kidney disease (including those with CD4 counts <200 cells/μL or HIV RNA >4000 copies/mL and those with diabetes mellitus, hypertension, or hepatitis C virus [HCV] coinfection) [7]. Patients with proteinuria of grade ≥1 by dipstick analysis or reduced kidney function can be referred to a nephrologist for consultation and should undergo additional studies, including quantification of proteinuria, renal ultrasound, and possible renal biopsy. As discussed in Section 7, screening for glucose intolerance and diabetes mellitus is recommended because of the increased prevalence in this population. Among adults and children with HIV, fasting blood studies are more problematic because of feeding schedules in children and work schedules in adults, and clinicians should obtain fasting levels when nonfasting levels are abnormal [7]. The lipid profile is important because of high rates of cardiovascular disease in this population and the importance of managing risk factors. Additionally, several ARVs affect lipid levels or have drug interactions with statins (see Section 7).

Screening for Coinfections

Recommendations

- Upon initiation of care, persons with HIV without a history of tuberculosis or a prior positive tuberculosis screening test should be screened for *Mycobacterium tuberculosis* infection using either a tuberculin skin test (TST) or an interferon-gamma release assay (IGRA). Those with positive test results should be treated for latent *M. tuberculosis* infection after active tuberculosis has been excluded.
- Persons with HIV who have close contact with persons with infectious tuberculosis should be treated for latent *M. tuberculosis* infection regardless of their TST or IGRA results, age, or prior courses of tuberculosis treatment; active tuberculosis should be excluded first.
- Persons with HIV should be screened for evidence of hepatitis B virus (HBV) infection upon initiation of care by detection of HBsAg, hepatitis B surface antibody (HBsAb), and antibody to hepatitis B total core antigen (anti-HBc or HBcAb). If HBsAg is positive, HBV viral load should be ordered.
- Persons with HIV should be screened for evidence of immunity to hepatitis A virus (HAV) with HAV immunoglobulin G (IgG).
- Persons with HIV should be screened for HCV antibody upon initiation of care. If positive, HCV RNA should be ordered to assess for active HCV infection. Curative therapy should be offered to all who are diagnosed with active HCV. HCV RNA testing is indicated ≥12 weeks post-completion of anti-HCV treatment to check for successful and sustained treatment. HCV RNA should be used for screening if HCV infection within the last 6 months is suspected or there is a history of prior HCV infection that has cleared due to spontaneous resolution or curative treatment. HCV RNA testing should be considered in persons with advanced immunosuppression (CD4 cell count <200 cells/μL).
- Infants born to persons with HBV and/or HCV should be tested for HBV and HCV transmission.
- Persons who are not immune to HAV and HBV should be immunized according to current national guidelines.
- All persons with HIV born in 1957 or after should be tested for immunity to measles, mumps, and rubella (MMR) by measuring antibodies.
- MMR vaccine should be given to protect against measles, mumps, and rubella if persons were born in 1957 or after and have not received this vaccine or do not have immunity to these infections.
- Serologic screening for varicella zoster virus (VZV) may be considered for persons who have not had chickenpox or shingles and who have not been previously vaccinated (see Section 4).
- Screening for toxoplasma IgG is recommended for asymptomatic persons with CD4 count <200 cells/μL and for those with symptoms suggestive of toxoplasmosis.
- Testing for serum cryptococcal antigen is indicated in persons with CD4 count <100 cells/μL and in symptomatic patients but is not routinely recommended in asymptomatic persons if CD4 count is ≥100 cells/μL.
- Screening for syphilis, chlamydia, gonorrhea, and, for persons having vaginal sex, trichomonas should be performed at entry to care (Please refer to Section 6).

Evidence Summary

All persons with HIV should be tested for *M. tuberculosis* infection using TST or IGRA upon initiation of care [7, 98, 99]. A TST or IGRA should be performed any time there is concern about a recent exposure. For those with CD4 count ≤200 cells/μL, testing should be repeated after the CD4 count increases to >200 cells/μL following initiation of ART. For a person with HIV, induration of >5 mm by TST is considered a positive result and should prompt chest radiography and other evaluation, as warranted, to rule out active tuberculosis [100]. Annual testing should be considered for those who have

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negative results by TST or IGRA but are at ongoing risk for exposure [7, 101]. Routine cutaneous anergy testing is not recommended because of lack of standardization of reagents and poor predictive value and because prophylaxis provided to anergic persons has been shown to prevent few cases of tuberculosis [102]. The QuantiFERON-TB Gold in-tube test (Cellestis Limited) and the T-SPOT TB test (Oxford Immunotech) are approved by the US Food and Drug Administration (FDA) as aids for detecting latent *M. tuberculosis* infection.

A large meta-analysis suggests that IGRAs perform similarly to TSTs when identifying persons with HIV with latent tuberculosis infection [103]. However, prior vaccination with Bacillus Calmette-Guérin (BCG) vaccine may result in a positive TST result, whereas there is less cross-reactivity with the IGRA. IGRAs that are reported as indeterminant should be repeated, as follow-up testing may be negative. The CDC states that use of an IGRA is preferred over the TST in patients with a history of BCG vaccination and in patients with a low likelihood of returning to have their skin test read. Advanced immunosuppression may be associated with false-negative results in all types of immunologically based tests used for detection of *M. tuberculosis* infection. The routine use of the IGRA in children, especially those aged <5 years, is currently not recommended due to limited data and some evidence of lower sensitivity.

Screening for and prevention of HAV, HBV, and HCV are critical in the management of people with HIV. Those who have HBV and/or HCV coinfection should be managed according to the most current published guidelines [98, 104–106]. Hepatitis A vaccination is especially important for persons with unstable housing, for persons who inject drugs (PWID), and for those with chronic liver disease due to recent outbreaks in certain communities [107]. Prevaccination screening for HAV infection is cost-effective when there is a seroprevalence of >30% in the patient population [108]. Because of worse outcomes for persons with HIV and HBV coinfection, persons with HIV who also have HBV should be adequately treated for HBV [7]. Because many persons with HIV may be treated with tenofovir-based ART that also suppresses HBV, stopping tenofovir-based ART may result in a flare of HBV, especially when changing ART to a 2-drug regimen that does not contain tenofovir. Persons with HBV are at higher risk for hepatocellular carcinoma (HCC) even in the absence of cirrhosis. Screening for HCC in persons with HBV should be conducted according to the American Association for the Study of Liver Diseases guidelines [104]. Persons not immune to HAV and HBV should be immunized according to applicable guidelines (see Section 4).

Persons with HIV should be screened for HCV antibody upon initiation of care. If positive, HCV RNA should be ordered to assess for active HCV infection. HCV RNA should be used in persons with a negative HCV antibody if infection within the last 6 months is expected and in persons with a history of prior HCV infection that has cleared due to spontaneous resolution or curative treatment. HCV RNA should be considered in persons with advanced immunosuppression (CD4 count <200 cells/μL), especially in persons who are HCV-seronegative with a history of injection drug use or with unexplained increased serum transaminases because approximately 2%–4% of persons with HIV–HCV coinfection have false-negative HCV antibody results; this occurs primarily among those with advanced immunosuppression [98]. According to multiple studies, the rate of mother-to-infant HCV transmission is up to 3-fold higher among women with HIV, and pregnant people with HIV should be tested for HCV with each pregnancy [106, 109]. Infants can be tested for HCV RNA after age 2 months or for HCV antibody after age 18 months [110]. All persons diagnosed with chronic HCV should be offered curative treatment. Eradication of HCV reduces, but does not eliminate, the risk of HCC in persons with cirrhosis; therefore, ongoing HCC screening in this group is warranted. Screening for HCC is recommended in all patients with cirrhosis due to hepatitis B or C or other nonviral etiologies (including alcohol use and fatty liver disease) [111].

Acceptable evidence of immunity against measles includes at least 1 of the following: written documentation of adequate vaccination, laboratory evidence of immunity, laboratory confirmation of measles, or birth in the United States before 1957 [112, 113]. It is advisable to determine anti-varicella IgG levels for patients who are unable to verify a history of chickenpox or shingles [114, 115]. STI screening should be obtained as part of the initial assessment. See Section 6.

In spite of a high prevalence of toxoplasma IgG in the population, toxoplasma encephalitis occurs among those with advanced immune deficiency. Screening for toxoplasma IgG, therefore, is indicated for asymptomatic persons with CD4 count <200 cells/μL and for those with a clinical presentation suggestive of toxoplasmosis. Testing for serum cryptococcal antigen is indicated in persons with CD4 count <200 cells/μL or in symptomatic individuals [98].

Tests That May Be Performed Under Certain Circumstances

Recommendations

- A baseline chest radiograph should be obtained in all persons with HIV who have a positive tuberculosis screening test result in order to rule out active tuberculosis. It may also be useful in other patients who are likely to have pre-existing lung abnormalities, including those who smoke or have a history of injecting drugs.
- Before starting therapy with oxidant drugs such as dapsone and primaquine, screening for glucose-6-phosphate dehydrogenase (G6PD) deficiency is recommended, particularly

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for individuals assigned male at birth of African, Mediterranean, or Asian descent. Sulfonamides should be used with caution without prior screening.
- Persons of childbearing potential should have a pregnancy test upon initiation of care or reengagement in care.
- In general, routine testosterone testing is not recommended among cisgender males with HIV. However, morning serum testosterone levels are recommended in adult cisgender men with decreased libido, erectile dysfunction, reduced bone mineral density (BMD) or low trauma fractures, hot flashes, or sweats.
- Obtaining testosterone levels in cisgender women at baseline in non-research settings is not recommended.

Evidence Summary

In general, all persons with HIV do not require a baseline chest X ray. However, persons with HIV are susceptible to a variety of pulmonary complications. A radiograph obtained at baseline in these individuals, as well as in persons with a history of pulmonary disease or smoking, may be useful for comparison in the evaluation of future respiratory complaints. Because people who inject drugs are especially likely to have radiographic abnormalities that may be mistaken for infiltrates, careful clinical history and physical assessment are warranted to guide subsequent medical decision-making. For discussion of cancer screening in persons who smoke, see Section 5. G6PD deficiency is a genetic condition that may result in hemolysis after exposure to oxidant drugs. Persons assigned male at birth and individuals of African, Mediterranean, and Asian descent have higher likelihood of these genetic variants. Dapsone and primaquine are often used to treat persons with HIV and can lead to hemolysis in the presence of G6PD deficiency. Sulfonamides should be used with caution without prior screening [116, 117].

The pregnancy status of all persons of childbearing potential should be assessed at the initial visit. In addition, the intent to have children, intent or ability to use consistent birth control, and timing of potential conception should be discussed. Although preliminary data suggested that neural tube defects were associated with dolutegravir use during conception, updated data showed no statistical significance, and dolutegravir is now a recommended drug for treatment during conception as well as pregnancy [118, 119]. The HHS perinatal guidelines provide ART recommendations for pregnant individuals [120]. The HHS ART guidelines provide recommendations for individuals who are planning to conceive and those unable to use reliable contraception [7] (see Sections 8 and 9).

Cisgender men with HIV, especially those with advanced disease, are at risk for hypogonadism. Interpretation of testosterone values must be made in clinical context, as all currently available assays (including measures of total, free, and bioavailable testosterone) are associated with technical issues that may result in significant variability. Testing should be performed on a specimen obtained in the morning (ideally before 10 AM) and confirmed with repeat testing if the result is below the lower limit of normal. Recommendations differ regarding the optimal assay to use for initial testing in the setting of HIV. Testosterone circulates primarily bound to plasma proteins (including sex hormone–binding globulin and albumin). If total testosterone is used for initial testing, a determination of sex hormone–binding globulin and/or free testosterone is strongly recommended when alterations of binding proteins are suspected (including patients with cirrhosis and hepatitis, hyper- or hypothyroidism, or nephrotic syndrome). Free testosterone may be determined by equilibrium dialysis (most reliable but most expensive) or using the free online testosterone calculator developed by the Hormonology Department, University Hospital of Ghent, Belgium [121]. So-called direct free testosterone (analogue) assays are unreliable and should not be used. If a diagnosis of hypogonadism is established, measurement of luteinizing hormone and follicle-stimulating hormone is recommended to determine whether the source of dysfunction is primary (testicular) or central (pituitary or hypothalamic) in origin. Hypogonadism should be treated by clinicians who are familiar with monitoring patients on androgen replacement therapy (see Section 4). For recommendations pertaining to age-appropriate cancer screening, see Section 5.

Tests Not Recommended for General Screening Purposes

Recommendations

- Routine testing for herpes simplex virus (HSV) IgG, cytomegalovirus (CMV) IgG, and biomarkers of inflammation is not recommended.

Evidence Summary

Routine screening for HSV is not recommended [122]. Routine screening for CMV IgG is not generally useful because CMV seroprevalence is extremely high and generally not actionable [98]. Testing for CMV IgG may be considered, however, if blood transfusion is contemplated in a person at low risk for CMV exposure. The identification of seronegativity would prompt the use of CMV-negative or leukocyte-reduced blood products when transfusions are needed, thus reducing the risk of iatrogenic infection. There are no data supporting the use of inflammatory biomarkers for risk assessment of comorbidities [123].

SECTION 3: ROUTINE HEALTHCARE MAINTENANCE CONSIDERATIONS FOR PEOPLE WITH HIV

Effective HIV primary care requires regular health maintenance, including HIV-related lab monitoring, mental health and substance use screenings, oral health examination, and patient education and counseling. Health assessments that are

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recommended for the general population (age- and gender-guided) as well as those specific for people with HIV should be reviewed and addressed at least annually with patients with HIV, whether performed at 1 or more visits (Table 5).

HIV-Specific Monitoring Following the Initial Assessment

Recommendations

- After initiation of ART, HIV RNA should be rechecked after 2–4 weeks but no later than 8 weeks and then every 4–8 weeks until suppression is achieved. Afterward, viral load should be monitored every 3–4 months to confirm maintenance of suppression below the limit of assay detection. This interval may be prolonged to every 6 months for patients whose viral load has been suppressed for more than 1 year and whose clinical and immunologic status is stable. Viral load should be monitored more frequently after reinitiating or changing ART, preferably within 2–4 weeks, with repeat testing every 4–8 weeks until viral load becomes undetectable. More frequent testing may be considered in other clinical scenarios, such as pregnancy and/or breastfeeding.
- If HIV RNA results are above the limit of assay detection but <200 copies/mL, referred to as "blips," assessing and addressing medication adherence, tolerability, and drug–drug interactions are warranted with an earlier repeat of HIV RNA testing.
- CD4 cell count should be monitored to determine the need for prophylaxis against OIs and to aid in generating appropriate differential diagnoses. CD4 cell counts should generally be monitored every 3–6 months for the first 2 years or if the virus is not suppressed. After 2 years, for patients on suppressive ART regimens with CD4 counts of 300–500 cells/μL, CD4 cell count can be monitored every 12 months unless there are changes in the patient's clinical or virologic status. If the CD4 count rises above 500 cells/μL, CD4 monitoring is optional.
- Repeat HIV genotypic resistance testing for mutations in the reverse transcriptase and protease genes, including in the integrase genes, when there is history of INSTI use, should be performed if virologic failure occurs and when clinically indicated. If ART initiation has been delayed, repeat genotype testing prior to ART initiation should be considered.

Evidence Summary

Frequency of HIV RNA monitoring depends on the response to therapy and duration and consistency of viral suppression. Once ART has been initiated, HIV RNA is monitored to confirm response to therapy and attainment and maintenance of viral suppression. After HIV RNA becomes undetectable, monitoring is approximately quarterly but can be every 6 months for persons with at least 1 year of continuous suppression and stable clinical and immune status [7]. More frequent testing may be warranted during pregnancy and/or breastfeeding, and the HHS Perinatal Antiretroviral Guidelines should be followed [120].

After virologic suppression has been achieved, if a viral load blip (isolated increase in HIV RNA above the limit of assay detection but <200 copies/mL that is followed by spontaneous suppression) or persistent low-level viremia with HIV RNA <200 copies/mL occurs, medication adherence should be assessed, and any identified barriers should be addressed. Medication tolerability should be reviewed, and side effects should be managed. Potential drug–drug interactions, including with over-the-counter medications and supplements, should also be reviewed. Earlier HIV RNA testing, for example, after 2–4 weeks, to ensure that no virologic failure (2 consecutive HIV RNA levels >200 copies/mL) has occurred is recommended [6]. If low-level viremia occurs, HIV viral load should be checked at least every 3 months to ensure that virologic failure has not occurred. As discussed in Section 1, assessing adherence regularly, ideally through a multidisciplinary team approach, is essential for identifying and addressing barriers, with a goal of preventing loss of virologic suppression and promoting improved adherence after such loss. Once ART is initiated and sustained virologic suppression is achieved, CD4 cell count can be monitored less frequently. Once the virus is suppressed for at least 2 years and CD4 cell count rises above the level associated with risk for opportunistic diseases, monitoring can occur annually or not at all if the CD4 count is >500 cells/μL [7].

The recommended frequency of HIV RNA and CD4 monitoring is not the only determinant of how frequently patients should be seen for overall healthcare needs. Patients with concurrent medical conditions may need to be seen more frequently, as well as patients who need ancillary services, such as treatment adherence counseling, mental health and substance use treatment services, STI screening, HIV education, case management services, or harm-reduction counseling.

If virologic failure occurs, genotypic resistance testing for mutations in reverse transcriptase, protease, and integrase (if indicated) genes should be performed to guide the choice of the next treatment regimen. If ART initiation has been substantially delayed, repeat resistance testing may be considered prior to initiating ART [7].

Other Lab Monitoring

Recommendations

- Complete blood count should be monitored every 12 months or when clinically indicated.
- A chemistry panel including glucose, creatinine, eGFR, electrolytes, AST/ALT, and total bilirubin should be done 1–2 months after ART initiation or change. Otherwise, it should be done every 6 months and when clinically indicated. If the

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Table 5. Routine Health Care Maintenance for People With Human Immunodeficiency Virus After Initial Assessment

Type of Intervention	Intervention	Recommendation	Comments
-specific monitoring	HIV RNA	Assess every 4–8 weeks after initiation of ART until undetectable and then every 3–4 months. In patients with consistent viral suppression and stable CD4 cell count for more than 1 year, measure every 6 months. If viral blip occurs (HIV RNA detectable but <200 copies/mL), assess adherence and barriers and repeat after 2–4 weeks.	
	CD4 cell count	Assess every 3–6 months for the first 2 years after starting ART or if viremia is present or if CD4 <300 cells/μL. If CD4 300–500 cells/μL and HIV RNA suppressed for 2 years, measure every 12 months. If CD4 >500 cells/μL and HIV RNA suppressed for 2 years, measurement is optional.	
	HIV genotype	Repeat if virologic failure occurs and when clinically indicated. Genotypic testing should include mutations in protease PR/reverse transcriptase genes as well as integrase genes when there is a history of integrase strand transfer inhibitor use, including use of cabotegravir PrEP.	
	Human leucocyte antigen B*5701 testing	No need to repeat this test if done in past. A negative test result is required prior to use of abacavir.	
	Tropism testing	Should be done prior to use of CCR5 antagonist regardless if tropism was done in past. If result is ever X4 or dual-mixed, no need to repeat again as CCR5 antagonist can never be used.	
Other labs	Complete blood count	Perform once a year or when clinically indicated.	
	Chemistry panel	Perform 1–2 months after antiretroviral start or change. Then, every 6 months and when clinically indicated. If not on ART, every 6–12 months.	Including creatinine, estimated glomerular filtration rate, electrolytes, and aspartate aminotransferase/ alanine aminotransferase/total bilirubin.
	Urinalysis	Perform annually if at risk of kidney disease and when clinically indicated. Perform before and during use of tenofovir disoproxil fumarate/tenofovir alafenamide.	
	Pregnancy test	Perform in persons of childbearing potential prior to ART start or change and when clinically indicated.	
Screening for mental health and substance use issues	Depression screening	Perform using a validated tool such as Patient Health Questionnaire (PHQ)-2 or -9 at least annually if resources available and when clinically appropriate.	
	Anxiety screening	Perform using a validated tool such as General Anxiety Disorder -2 or -7 in patients aged <65 years at least annually, if resources available and when clinically indicated.	
	Tobacco use screening	Perform for every adolescent and adult at every visit and offer smoking cessation options if current smokers.	
	Substance and alcohol use screening	Perform using validated tools such as alcohol use disorders identification test and drug abuse screening test at least annually when clinically indicated. Refer to treatment if substance or alcohol use disorder is diagnosed.	

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Table 5. Continued

Type of Intervention	Intervention	Recommendation	Comments
Screening for and monitoring of metabolic disorders	Blood pressure screening	Perform at every visit.	
	Weight measurement	Perform at every visit.	
	Screening for hyperlipidemia	Lipid profile: perform every 5 years if normal; more frequently if abnormal or other cardiovascular risk factors present (every 6–12 months); if abnormal, repeat fasting.	Follow atherosclerotic cardiovascular disease risk calculator. Consider testing 1–3 months after starting or changing ART. See Section 7 for further discussion.
	Screening for diabetes mellitus and glucose intolerance	Serum glucose: perform annually; if abnormal, obtain fasting glucose. Hemoglobin A1C should be obtained prior to initiation of ART, if possible. In persons with diabetes, repeat at least every 6 months (more frequently if clinically indicated). Urine microalbumin or urine protein/creatinine ratio: in patients with diabetes, repeat at least every 6 months (more frequently if clinically indicated).	Consider testing 1–3 months after starting or changing antiretroviral medications. Hemoglobin A1c is not used to diagnose diabetes in persons on ART. It may be used for screening and monitoring. Consider threshold cutoff of 5.8%. See Section 7 for further discussion.
	Screening for bone mineral density	Baseline bone densitometry by dual-energy X-ray absorptiometry should be performed in all postmenopausal women and men aged ≥50 years.	See Section 7 for further discussion.
Screening for infectious diseases	Syphilis screening	Perform at least annually in asymptomatic persons; repeat every 3–6 months in asymptomatic persons if risk of acquisition is high, regardless of doxyPEP use.	Acquisition risk depends on sexual activities, use of barrier protection, and local prevalence.
	Gonorrhea and chlamydia screening	Perform at least annually in asymptomatic persons; can repeat every 3–6 months in asymptomatic persons if risk of acquisition is high, regardless of doxyPEP use.	Screening by NAAT at all sites of sexual contact (rectal, oropharyngeal, vaginal, urine/urethral) is recommended for all sexually active persons with HIV. Acquisition risk depends on sexual activities, use of barrier protection, and local prevalence.
	Trichomoniasis screening	Perform annually for persons having vaginal sex.	Screen using NAAT testing.
	Hepatitis A, B, and C screening	Hepatitis C: in sexually active cisgender men and transgender women who have sex with cisgender men and people who inject drugs, screen annually. Hepatitis B: repeat HBV serology (HBsAg, HBsAb, and HBcAb total) in persons without known HBV infection or immunity prior to switching to ART without tenofovir and when clinically indicated, including prior to HCV treatment with direct-acting antivirals.	In those with new abnormal liver function tests, check for acute HAV, HBV, and HCV. Use HCV RNA and HBV DNA testing when clinically appropriate, including for HCV screening in persons with past HCV or those suspected of recent infection within the past 6 months.
	Tuberculosis screening	Perform annually in patients at risk for tuberculosis.	Perform either tuberculin skin test or interferon-γ release assay.
Screening for and prevention of cancer	Smoking	Screen at every visit and for smokers, advise about benefits of cessation and offer pharmacotherapy and referral to behavioral interventions.	Provide resources per local guidelines, including classes, agents that facilitate smoking cessation.
	Low-dose chest computed tomography scan	Those aged between ages 50 and 80 years who have ≥20 pack-years of smoking and are current or former smokers should have an annual low-dose computed tomography scan of the lungs.	
	Prostate cancer screening	Digital rectal exam: considered primary evaluation before PSA screening; consider for patients aged 55–69 years. PSA screening: Age 50–69 years: discuss risks and potential benefits with patient. Age ≥70 years: PSA screening is not recommended.	The impact of HIV on prostate cancer risk is not yet known. African Americans and people with a relative with prostate cancer have a higher burden of prostate cancer. Clinicians should follow US Preventative Services Task Force or American Cancer Society guidelines and consider patient wishes.

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Table 5. Continued

Type of Intervention	Intervention	Recommendation	Comments
	Colon cancer screening	Perform for those aged 45–75 years if average risk (including personal and family history). Age 76–85 years: individualize screening based on overall health and prior screening. Consider screening earlier if first-degree relatives diagnosed with colon cancer prior to age 50 years.	Screening tests include: stool-based screening (guaiac fecal occult blood test, FIT, FIT-DNA) every year (or up to 3 years for FIT-DNA) or colonoscopy every 10 years if normal, or more frequently if polyps are identified.
	Breast cancer screening	Age 50–75 years: mammography performed at least every 2 years.	Age 40–49 years: inform of the potential risks and benefits of screening and offer screening every 2 years.
	Cervical cancer screening	Age <21 years: Pap test within 1 year of sexual activity, no later than age 21 years. Age 21–29 years: Pap test at diagnosis of HIV, repeat yearly × 3, then if all normal, Pap test every 3 years. Age <30 years: no HPV testing unless abnormalities are found on Pap test. Age ≥30 years: Pap test only, same as age 21–29 years. Or Pap test with HPV testing, if both negative, then Pap test with HPV every 3 years.	Abnormal Pap test and/or HPV follow-up similar to general population. Note: In general, continue screening past age 65 years.
	Anal cancer screening	Digital anorectal exam: perform at least annually if asymptomatic. Anal Pap: screen transgender women and men aged >35 years who have sex with men and all other people with HIV aged >45 years, with anal Pap smears if there is access to or ability to refer for high-resolution anoscopy and treatment.	Abnormal anal Pap tests should prompt referral for high-resolution anoscopy.
	Hepatocellular carcinoma screening	Perform alpha-fetoprotein and liver ultrasound every 6 months.	For patients with cirrhosis from any cause or chronic hepatitis B, as well as fibrosis levels F3 or F4 among patients with hepatitis C.
Other healthcare maintenance	Reproductive desires	All persons with HIV regardless of sexual orientation and gender identity should be asked about their reproductive desires. Persons of childbearing potential should be routinely asked about their plans and desires regarding pregnancy.	ART, hormone therapy, and other treatments may affect pregnancy and pregnancy plans.
	Oral health examination	All persons with HIV should have oral health examinations biannually.	
	Patient education	Tailor education at every visit to patient's current needs. Regularly address with all patients the importance of medication adherence and viral suppression for personal health and preventing sexual transmission (undetectable equals untransmittable) and provide information on sexual health and harm-reduction practices including PrEP, PEP, safer injection practices, syringe services programs, and naloxone.	Brief counseling and tailored interventions should be offered to patients who may benefit from them to reduce risk. Refer patients to programs that offer interventions not accessible locally, such as medication for opioid use disorder, mental health services, sexually transmitted infection testing, viral hepatitis treatment, PrEP, PEP.

Abbreviations: ART, antiretroviral therapy; CCR5, C-C motif chemokine receptor 5; doxyPEP, doxycycline postexposure prophylaxis; FIT, fecal immunochemical test; HAV, hepatitis A virus; HBcAb, hepatitis B core antibody; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HPV, human papillomavirus; NAAT, nucleic acid amplification test; PEP, postexposure prophylaxis; PrEP, preexposure prophylaxis; PSA, prostate-specific antigen.

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patient is not on ART, a chemistry panel should be done every 6–12 months.
- Urinalysis should be monitored annually for those at risk for kidney disease and when clinically indicated. Urinalysis should be monitored before and during treatment with tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF).
- Tuberculosis screening should be performed annually for persons at risk for infection. Repeat testing is recommended in patients with advanced HIV disease who initially had negative TST or IGRA results but subsequently experienced an increase in CD4 cell count to >200 cells/μL on ART and who may thus have developed sufficient immune competence to mount a positive reaction.
- HCV screening with HCV antibody should be repeated every 12 months for persons at increased likelihood of exposure or when clinically indicated. Screening with HCV RNA rather than HCV antibody is indicated for persons with suspected HCV infection within the past 6 months and previous HCV infection that has cleared due to spontaneous resolution or curative treatment. Screening with HCV RNA instead of HCV antibody should be considered for persons with severe immunodeficiency (CD4 count <200 cells/μL).
- Consider repeating hepatitis B serology, including HBsAb, HBsAg, and HBcAb, in persons not infected with or immune to HBV who are switching to an ART regimen that does not contain tenofovir and when clinically indicated, including before starting HCV treatment with direct-acting antiviral (DAA) medication.
- Pregnancy testing in people with HIV of childbearing potential should be performed prior to ART initiation or modification and when clinically indicated.
- Screening for sexually transmitted infections should be performed periodically, as discussed in Section 6.

Evidence Summary

Complete blood count and chemistry panels should be monitored regularly to assess medication toxicity and to monitor potential for existing comorbid conditions (eg, chronic kidney disease, hepatitis). Monitoring frequency depends on the presence of underlying medical conditions and the need to monitor for ART toxicities, depending on the regimens chosen [6, 7, 124]. Persons with co-occurring diabetes, hypertension, HCV, nephrotoxic medication such as tenofovir, genetic predisposition, or advanced HIV disease are at increased likelihood of kidney disease and should be monitored for renal function at least every 6 months, and urinalysis should be performed at least annually. Urinalysis should be monitored before and during treatment with tenofovir-containing compounds [6, 7, 124].

Annual tuberculosis screening should be considered for those who have negative results for latent tuberculosis but are at ongoing risk for exposure, such as through incarceration, congregate settings, homelessness, and travel to countries with high tuberculosis incidence [98, 101]. A TST or IGRA should be performed any time there is concern of a recent exposure or after a CD4 count increase to >200 cells/μL following initiation of ART. Routine cutaneous anergy testing is not recommended.

HCV screening should be repeated at least annually in persons who are at increased likelihood of exposure, such as persons who inject drugs, cisgender men who have sex with cisgender men, and transgender women [98, 125–128]. HCV RNA testing is indicated for screening when HCV infection within the past 6 months is suspected and in people who had previous HCV infection that cleared spontaneously or through treatment. HCV RNA testing should be considered when a person has severe immunodeficiency with CD4 count <200 cells/μL, especially if the person has a history of injection drug use or an ALT level above the upper limits of normal [7, 129]. Repeating HCV RNA after confirmed curative therapy (undetectable HCV RNA at least 12 weeks post-completion of treatment) is not necessary unless there is a clinical indication, such as evidence of unexplained liver injury or ongoing exposure [106].

Persons who have negative hepatitis B serology should be vaccinated (see Section 4). Persons who test positive for HBV infection (with the presence of HBsAg or HBV DNA) should have TDF or TAF and emtricitabine (FTC) or lamuvidine (3TC) included in the ART regimen. People who test positive only with HBcAb may have resolved HBV infection with loss of HBsAb, and HBV DNA testing can be performed to confirm. If the HBV DNA test is negative, the person should then be vaccinated. HBV reactivation can occur in patients during and after treatment with HCV DAA medication, and repeat hepatitis B screening (including with HBV DNA testing if indicated) should be considered in patients not infected with or immune to HBV, especially those with isolated HBcAb, prior to treatment with HCV DAAs [7, 130–132].

A pregnancy test should be performed in persons of childbearing potential prior to initiating or modifying ART. Clinicians should discuss the benefits of ART with the patient as well as regimens that are recommended during pregnancy and their potential toxicities. Shared decision-making with the patient should occur regarding the choice of ART for initiation, continuation, or modification.

Screening and Treatment for Mental Health and Substance Use Issues

Recommendations

- Screening for depression using a validated screening tool should be conducted on every adult patient at least once, with screening frequency based on risk. Annual screening is reasonable, given the elevated risk of depression in people with HIV.

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- Screening for anxiety using a validated screening tool should be conducted on every adult patient aged <65 years, with screening frequency based on risk. Annual screening is reasonable, given the elevated risk of anxiety in people with HIV.
- Screening for tobacco use should be conducted for every person with HIV at every visit. Current smokers should be advised of the benefits of quitting and offered options to assist with smoking cessation, including pharmacotherapy and connection to behavioral interventions.
- Screening for unhealthy alcohol use and substance use using validated screening tools should be conducted on every adult patient at least once, with screening frequency based on need. Annual screening is reasonable given the elevated risk of unhealthy alcohol and substance use in people with HIV. Individuals diagnosed with an alcohol or substance use disorder should be offered treatment, including pharmacotherapy (such as methadone or buprenorphine for opiate use disorder) and connection to behavioral health interventions.
- Individuals who inject drugs should be counseled on safer injection and substance use practices to prevent viral hepatitis and other infectious diseases and injection-related conditions such as endocarditis, osteomyelitis, cellulitis, and abscesses. They should be educated on PrEP and PEP for injection partners and provided information on syringe services programs, where available.
- All individuals with substance misuse or use disorders should be provided with life-saving medications such as naloxone for overdose prevention.

Evidence Summary

People with HIV have high rates of depression; anxiety; and tobacco, alcohol, and substance use disorders. After initial screening, optimal screening intervals for mental health and substance use disorders are not known. Repeat screening on a regular basis, such as annually, is reasonable because of the high prevalence of these conditions among people with HIV [133–136]. Screening for depression and anxiety should include the use of validated screening tools such as Patient Health Questionnaire-2 (PHQ-2), PHQ-9, and GAD-2 [82, 83, 137, 138]. People with HIV should be screened for drug and alcohol use with validated screening tools such as the Alcohol Use Disorders Identification Test and the Drug Abuse Screening Test [134, 136, 139]. Self-reported substance use screening tools can be incorporated into electronic health records [140]. Patients who are found to have alcohol or substance misuse or use disorders should be offered or referred for pharmacotherapy, such as buprenorphine or methadone for opioid use disorder and naltrexone for alcohol or opioid use disorder, and/or behavioral health treatment provided within a harm-reduction model of care. Education on safer injecting practices and drug use, syringe services programs, and overdose prevention provides people with choices on how to minimize health risks such as injection-related infections and where to access services if and when they are ready. Naloxone should be provided for overdose prevention. Co-location of substance use treatment with HIV care is ideal [141]. Brief interventions that include use of motivational interviewing can be provided by trained healthcare personnel [142].

Tobacco use is a major cause of decreased life expectancy and poor health outcomes, including cardiovascular disease and lung cancer, in people with HIV [143–146]. People with HIV should be asked about tobacco use at every visit [147–149]. This can be accomplished when taking the patient's vital signs. People who smoke tobacco should be counseled on the benefits of quitting, offered pharmacotherapy, especially varenicline, and connected to behavioral health interventions [150, 151]. See Section 5 for cancer screening in smokers.

Other Health Maintenance Considerations

Recommendations

- All persons with HIV, regardless of sexual orientation and gender identity, should be asked about their pregnancy intentions. Persons of childbearing potential should be routinely asked about their pregnancy intentions, especially prior to treatments that may affect the ability to have children or the outcome of pregnancy.
- Patient education should be tailored at every visit based on the patient's current needs. In particular, the clinician should evaluate the need for education on the following:
  - The importance of medication adherence in achieving viral load suppression to maximize personal health and eliminate HIV transmission to sexual partners (U = U);
  - Optimizing sexual health of the patient and their sexual partners by informing patients about PrEP, PEP, barrier methods, and other strategies for HIV and STI prevention; and
  - Safer use of recreational drugs and their potential side effects and known drug interactions.
- All persons with HIV should have regular oral health examinations at least every 6–12 months.

Evidence Summary

It is important to discuss pregnancy intention and family planning with every patient, especially prior to prescribing medication or treatments that may affect pregnancy or fertility, such as ART or hormone therapy for gender-affirming care. Education should include U = U and the ability to become pregnant without risk of HIV transmission, as well as available options for preserving sperm/ova for future family planning prior to certain treatments. Every patient should also be informed of the possibility of becoming or getting their partner pregnant; if

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desired, options for birth control should be reviewed and offered (see Section 8).

Barriers to adherence and care engagement should be repeatedly assessed. Clinicians should engage in effective patient education in a respectful and nonjudgmental manner for maintenance of physical, emotional, spiritual, and sexual health. Providing information on medication adherence, sexual health, and recreational drug use is critical for engaging and retaining patients in care (see Section 1).

People with HIV have frequent oral health complications, especially if the CD4 cell count is low [152]. Any identified oral health complication should be addressed immediately. In addition, every patient should have regular oral health exams. Given the risks for oral complications, a biannual oral health examination for people with HIV is reasonable.

SECTION 4: IMMUNIZATIONS FOR PERSONS WITH HIV

Vaccinations are routinely provided as part of primary care visits, and HIV primary care providers play a unique and trusted role in providing counseling and guidance on recommended immunization strategies. However, due to the time required for counseling, it is advisable to use standing orders and delegate routine vaccinations, which do not require shared decision-making, to other members of the healthcare team, such as qualified nursing or pharmacy staff. Shared decision-making is a collaborative process often used when there is uncertainty regarding the benefits of a specific treatment for a particular population [153, 154]. The healthcare provider shares clear and understandable information about a health condition, explains the necessary decisions and available options, and allows the patient to express their preferences and values. Together, the patient and provider discuss the pros and cons, including risks, which results in a collaborative decision that respects the patient's autonomy. Studies have shown that when shared decision-making is not required, computerized standing orders are more effective than computerized reminders, especially for offering influenza and pneumococcal vaccinations [153, 155]. Vaccination receipt is increasingly regarded as a measure of healthcare quality, and all members of the healthcare team can collectively contribute to achieving these quality metrics. Current immunization recommendations are included in Table 6. However, recommendations change frequently, and HHS OI guidelines and ACIP recommendations should be checked frequently [98, 110, 156].

Pneumococcus, Influenza, Meningococcus, Tetanus-Diphtheria-Pertussis

Recommendation

- Vaccination against infection with pneumococcus, influenza, meningococcus, and tetanus-diphtheria-pertussis should be offered to all people with HIV.

Evidence Summary

Evidence of increased invasive disease due to 7 serotypes not covered in the pneumococcal conjugate vaccine (PCV) 13 (Prevnar13) and the approval of new vaccines with broader coverage have led to revised recommendations for pneumococcal vaccination. The use of PCV20 (Prevnar 20; Vaxneuvance) alone or a combination with PCV15 plus 23-valent pneumococcal polysaccharide vaccine (PPSV23; Pneumovax23) given at least 8 weeks later is now recommended for all individuals aged ≥65 years and for those aged between 19 and 64 years with underlying conditions (such as HIV) who are unvaccinated or whose vaccination status is unknown (see Figure 1). Although there are no clinical outcome data for people with HIV, no additional PPSV23 doses are needed when PCV20 is used, making this a simple and preferred regimen [157, 158]. For those who have received both PCV13 and PPSV23 and are aged <65 years, 1 dose of PCV20 can be administered at least 5 years after the last dose of PPSV23 to complete the series or a second dose of PPSV23 can be administered at least 5 years after the prior dose, with a third and final dose administered at age 65 years or later but at least 5 years after the last PPSV23 dose. For persons aged at least 65 years at the time of a PPSV23 dose, no additional doses are needed. Those who have received only PPSV23 can be given PCV20 with no additional vaccinations or they can be given PCV15 followed by PPSV23 after 8 weeks. Those who have received only PCV13 can be given PCV20 at least 1 year later to complete the series or be given PPSV23 at least 8 weeks later with subsequent PPSV23 doses to complete the series. When there is no access to PCV15, PPSV23, or PCV20, patients should receive whatever is available to receive protection. For those who are aged <65 years and have received PCV20 or PCV15 with PPSV23 at least 8 weeks later, no additional pneumococcal vaccine is needed at age 65. Shared decision-making is recommended when considering PCV20 for adults aged ≥65 years who completed their series with other vaccines. If the decision to administer is made, it should be administered at least 5 years after the last PPSV23 dose. PCV21 (Capvaxive) has also been approved by the FDA and could be substituted for PCV20 in adults for whom a dose of PCV20 is currently recommended [159]. At the time of publication of this guidance, no specific data are available for PCV21 in people with HIV.

All people with HIV should receive an annual influenza vaccination, but they should not receive live vaccination via nasal spray (LAIV4 Flumist). Patients aged >65 years should receive 1 of 3 high-dose, adjuvanted, or recombinant influenza vaccines: HD-IIV4 (Fluzone), aIIV4 (Fluad), or RIV4 (Flublok) [160, 161]. Recommendations for tetanus toxoid, reduced diphtheria toxoid, and reduced acellular pertussis (Tdap; Adacel, Boostrix) are the same as for the general population. Pregnant individuals should receive Tdap during each pregnancy between 26 and 37 weeks' gestation [162]. Adults with

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Table 6. Immunizations for People With Human Immunodeficiency Virus

Vaccination	Dose	Revaccination	Comment
Influenza, standard dose: IIV4 (Afluria, Fluarix, FluLaval, Fluzone), ccIV4 (Flucelvax), aIIV4 (Fluad), RIV4 (Flublok); high dose: HD-IIV4 (Fluzone)	1	Yearly	Age >65 years high dose (HD-IIV4, aIIV4, RIV4). LAIV4 (FluMist) is contraindicated for people with HIV; for people with egg allergy, use IIV or RIV.
Tetanus, diphtheria, and acellular pertussis: TdaP (Adacel, Boostrix); tetanus, diphtheria (Tenivac, Tdvax);	1	10 years	Td can be given every 10 years; give TdaP with each pregnancy, give Td if contaminated wound and none received in 5 years.
Meningococcus (MenACWY-TT vaccine; MenQuadfi or Menveo)	2 doses, 2 months apart	5 years	MenACWY-TT: every 5 years after primary series. MenACWY-D is no longer available. Vaccination against meningococcus B not routinely recommended for all individuals. Two MenB vaccines are available, MenB-4C (Bexsero) and MenB-FhBp (Trumenba). A pentavalent meningococcal is available from serogroups ACWY and B (Penvrava) if both vaccines are indicated.
Measles, mumps, rubella	2 doses, 1 month apart	…	CD4 >200 cells/μL and no immunity; if pregnant and not immune, administer after delivery if CD4 >200 cells/μL.
Hepatitis A (Havrix, Vaqta)	2 doses, 6 months apart	…	Check for evidence of immunity post-vaccination, 1–2 months post-vaccination series complete.
Hepatitis B	…	Nonresponders to primary series: repeat full primary series of recombinant, adjuvanted vaccine 0, 1 months (can give third dose at 6 months if HBsAb not seroprotective). Alternatives for revaccination due to nonresponse: double dose recombinant vaccines (Engerix-B, Recombivax HB) at 0, 1, 6 months.	Vaccinate those who do *not* have chronic hepatitis B virus. Check for evidence of immunity postvaccination (HBsAb titer >10 mIU/mL).
• Hepatitis B–naive to vaccination, primary series: recombinant, adjuvanted vaccine (HepB- CpG, Heplisav-B)	2 doses, 0, 1 month	…	Primary series: HepB-CpG (Heplisav-B): after 2 doses, check antibody levels at 1–2 months (and if not immune [titer is not >10 mIU/mL] may consider third dose).
• Alternatives to HepB-CpG: recombinant vaccine double dose (Engerix-B, Recombivax-HB)	3 doses, 0, 1, and 6 months (double dose)	…	Alternatives to HepB-CpG: Engerix-B (20 μg; double dose = 40 μg); Recombivax HB (10 μg; double dose = 20 mcg); check HBsAb titer 1–2 months after complete series.
• Alternatives to HepB-CpG and needing hepatitis A vaccination: combined hepatitis A and recombinant hepatitis B vaccine (Twinrix)	0, 1, and 6 months	…	…
Human papillomavirus (Gardisil)	3 doses (0, 1–2, 6 months)	…	Recombinant 9-valent can be offered to people with HIV up to age 45 years with shared decision-making; vaccination should not be given during pregnancy.
Mpox (Jynneos)	2 doses, 4 weeks apart (subcutaneous or intradermal)	…	Jynneos live nonreplicating vaccinia vaccine requires both doses for maximal immunity (subcutaneous preferred); ACAM 2000 vaccine contraindicated with HIV.
RSV (Arexvy, Abrysvo)	1 dose	…	Those aged ≥75 years should receive a dose; those aged 60–74 years with likelihood of severe RSV should receive a dose (2 different vaccines available); limited data in people with HIV.
VZV (Varivax)	2 doses, 3 months apart		Contraindicated if CD4 <200 cells/μL.
Recombinant zoster vaccine (Shingrix for prevention of recurrence)	2 doses, 0, 2–6 months apart		Can be given to those aged ≥18 years to prevent recurrence of herpes zoster (if prior VZV).
Severe acute respiratory syndrome coronavirus 2 (COVID-19); primary series in persons who are moderately to severely immunocompromised	Because of the changing nature of COVID-19 vaccine policy, see the Centers for Disease Control and Prevention COVID-19 vaccine recommendations for details (https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html)		
• Unvaccinated	3 doses (mRNA; Pfizer-BioNTech or Moderna); 2 doses Novavax	…	Pfizer-BioNTech: second dose 3 weeks from first dose, third dose 4 weeks from second dose. Moderna: each dose 4 weeks apart; Novavax: 3 weeks apart.

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Table 6. Continued

Vaccination	Dose	Revaccination	Comment
• Received 1 dose prior mRNA	2 doses		Moderna: each dose at least 4 weeks apart. Pfizer-BioNTech: 3 weeks from last dose; 4 weeks from first and second updated.
• Received 2 doses prior mRNA	1 dose	…	Moderna or Pfizer-BioNTech at least 4 weeks after last dose.
• Received 1 or more Novavax or Janssen	1 dose	…	Moderna, Pfizer-BioNTech, or Novavax: at least 8 weeks after last dose.
Vaccination following primary series completion: Please check ACIP recommendations for updates			
• Received complete series not including 2023–2024 vaccine	1 dose 2023–2024 vaccine	…	…
• Received complete series including 2023–2024 vaccine	Age ≥65 years: 1 additional dose 2023–2024 vaccine; age 19–64 years: may give 1 additional 2023–2024 vaccine based on risk		
• Subsequent revaccination	Please check ACIP recommendations.		
Pneumococcus (please see Figure 1 for illustration)			
• PCV20 (Prevnar20) • PCV21 (Capvaxive may be substituted for PCV20)	1 dose	No further doses of PCV20 or PCV21 are needed after first dose. At any time, if PCV20 or PCV21 is substituted for PPSV23, the pneumococcal vaccination series is complete. …	• If no pneumococcal vaccine given or unknown, 1 dose of PCV20 completes pneumococcal vaccination (preferred due to simplicity). PCV21 could be substituted for PCV20 in adults in whom a dose of PCV20 is currently recommended. • If previous PPSV23 or PCV13 alone, can give 1 dose of PCV20 at least 1 year later to complete the series. • If previous PCV13 and PPSV23 received before age 65 years, may give 1 dose PCV20 at least 5 years later to complete series. • If previous PCV13 and 1 dose of PPSV23 received at age ≥65 years, no further vaccine needed, but may receive 1 dose PCV20 at least 5 years later with shared decision-making.
• PCV15 (Vaxneuvance)	1 dose	Give PPSV23 8 weeks after PCV15 to complete the series.	• If no pneumonia vaccine given or unknown, may give 1 dose, followed by PPSV23 8 weeks later (alternative). • If previous PPSV23 alone, give 1 dose PCV15 at least 1 year later to complete series. • If previous PCV13 alone, no PCV15 needed; give PPSV23 at least 8 weeks later or PCV20 at least 1 year later.
• PPSV23 (Pneumovax23)	Do not give as initial vaccine	If only received PPSV23, give PCV20 or PCV15 at least 1 year later to complete series.	If received PCV13 and PPSV23: • If received PPSV23 at age <65 years, may give third and final PPSV23 dose at least 5 years after second PPSV23 dose; OR may receive 1 dose PCV20 at least 5 years after last PPSV23. • If received PPSV23 at age ≥65 years, no further PPSV23 needed (may receive 1 dose of PCV20 with shared decision-making).
Travel Vaccines			
• Vibrio cholera (CVD103-HGR; Vaxchora)	1 dose, oral	…	CVD103-HgR live attenuated; give 10 days prior to exposure; lasts for 3 months; do not give if CD4 <200 cells/μL.
• Polio (Ipol)	3 doses (0, 1–2, 6–12 months)	…	IM, inactivated vaccine for those at high risk for exposure to poliovirus.
• Typhoid (Thyphim Vi)	1 dose	…	Thyphim Vi polysaccharide vaccine (IM), administer 1 week prior to exposure; note: do not give oral vaccine; avoid in pregnancy.

Abbreviations: ACIP, Advisory Committee on Immunization Practices; COVID-19, coronavirus disease 2019; CpG, cytidine monophosphate guanosine; HBsAb, hepatitis B surface antibody; HIV, human immunodeficiency virus; IM, intramuscular; mRNA, messenger ribonucleic acid; PCV. pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine; RSV, respiratory syncytial virus; VZV, varicella zoster virus.

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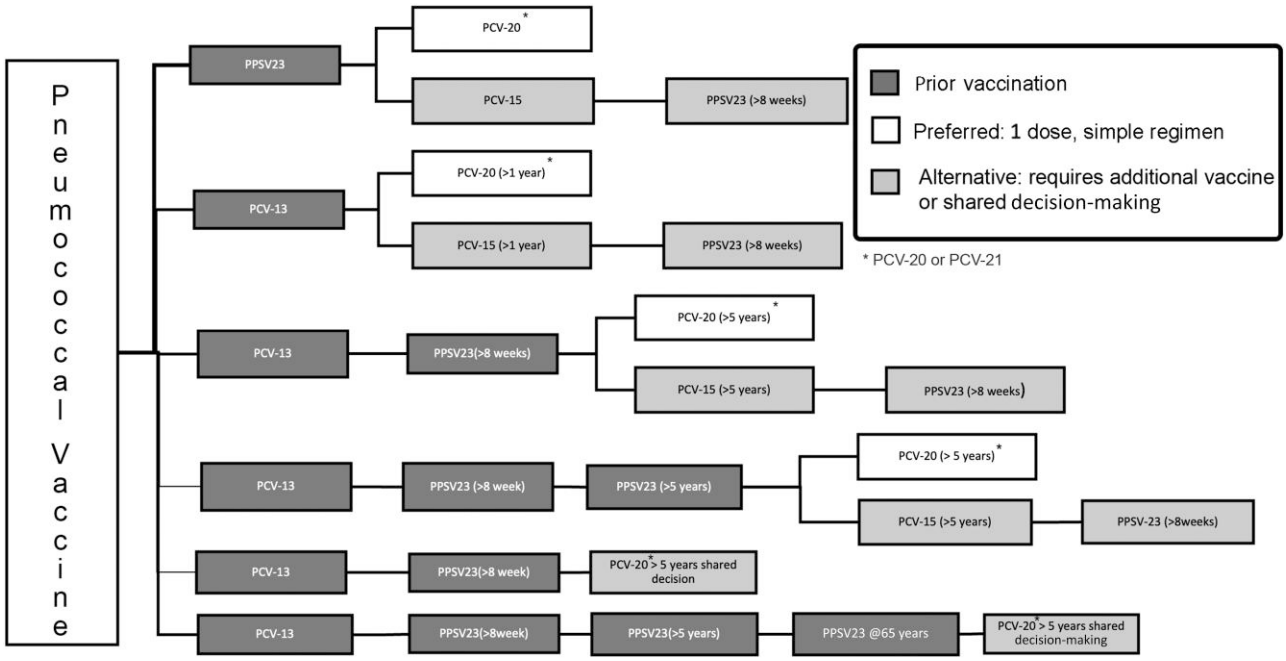


Figure 1. Vaccinations to prevent pneumococcus infection. Abbreviations: PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine.

HIV should receive a 2-dose quadrivalent meningococcal conjugate vaccine primary series of serogroup A, C, W, and Y (Menveo, MenQuadfi) at least 2 months apart if not previously vaccinated. After the primary series, revaccination should occur every 5 years. Serogroup B meningococcal vaccine (Bexsero, Trumenba) is not routinely recommended but may be given to persons aged 16–23 years and under certain circumstances [163]. Although there are no specific data for people with HIV, a new pentavalent meningococcal vaccine that contains antigens from serogroups ACWY and B (Penbraya) may be given when both vaccines are indicated at the same time [156].

HAV and HBV

Recommendations

- Vaccination for HAV is recommended for all nonimmune individuals with HIV, especially those with indications for hepatitis A vaccine (including PWID, those unstably housed, those with current or prior incarceration, gay and bisexual men or transgender persons with chronic liver disease, travelers to countries with high endemicity, and persons who have hepatitis B and/or C).
- HAV IgG antibody testing should be repeated 1–2 months or at the next scheduled visit after the second vaccine to assess for immunogenicity. A repeat vaccine series is recommended in those who remain seronegative.
- Individuals susceptible to infection should be vaccinated against HBV.
  - The adjuvant recombinant vaccine (HepB-CpG; Heplisav-B) 2 doses at 0, 1 month is preferred.
  - Alternative regimens can be used if HepB-CpG is not available, including double doses of the recombinant hepatitis B vaccines Engerix-B 40 µg (two 20-µg doses) or Recombivax-HB 20 µg (two 10-µg doses) or standard doses of the combined hepatitis A and recombinant hepatitis B vaccine (Twinrix) given at 0, 1, and 6 months.
- HBsAb levels should be checked 1–2 months after completion of the primary immunization series. If HBsAb is <10 mIU/mL, revaccination with a full vaccine series is necessary. Three doses of HepB-CpG may be considered.
- Vaccination should be recommended for nonimmune sexual partners of persons who are positive for HBsAg.
- Persons who are negative for HBsAg and HBsAb but positive for HBcAb should receive vaccination.

Evidence Summary

Responses to both HAV and HBV vaccines are reduced in patients with a CD4 count <200 cells/µL and those with quantifiable HIV RNA levels. An interim analysis of AIDS Clinical Trial Group (ACTG) study A5379 of adjuvanted recombinant HepB-CpG (Heplisav-B) given at 0, 1, and 6 months to unvaccinated people with HIV who had viral suppression and a median CD4 count of 625 cells/µL (range, 149–1562) showed that 100% developed seroprotective titers of HBsAb >10 mIU/mL

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at 28 weeks (4 weeks after a 3-dose vaccine series). At 24 weeks (after 2 doses and prior to the third dose), 98.5% had seroprotective titers. In addition, at 28 weeks (4 weeks after the third dose), 83.8% had titers >1000 mIU/mL [164]. These data are promising, but durability of such high titers is unknown and will be assessed in the ongoing A5379 study [164]. In a person with a high CD4 cell count, a 2-dose HepB-CpG series is seroprotective, but the high titers achieved after a third dose in persons with high CD4 cell counts and suppressed virus, as well as improved responses after a third dose in persons without HIV but who had chronic kidney disease, suggest that those with low CD4 cell counts might achieve a more robust response with 3 doses. Until additional data are available, if a titer >10 mIU/mL is not achieved, consider the patient to be a nonresponder, and a full revaccination series is recommended [98].

Vaccines that can be used if HepB-CpG is not available include 2 recombinant hepatitis B vaccines (Engerix-B or Recombivax-HB) using a double dose at 0, 1, and 6 months or combined hepatitis A and hepatitis B recombinant vaccine at 0, 1, and 6 months. PreHevbrio® is a third recombinant vaccine for which insufficient data exist for people with HIV. Patients who fail to respond to an initial series can be revaccinated with a full series of double-dose Engerix-B or Recombivax-HB (at 0, 1, and 6 months) or a complete 2-dose series of HepB-CpG. Initial data from ACTG 5379 look promising for 2 or 3 doses of HepB-CpG for people with HIV who did not achieve seroprotection from an initial vaccination series. In these individuals, either 2 or 3 doses of HepB-CpG was superior to 3 single-strength doses of Engerix-B, with seroprotective responses of 93.1%, 99.4%, and 80.6%, respectively [165]. Although few people with low CD4 counts were included in the study, these preliminary data suggest that 3 doses of HepB-CpG might be an effective strategy for revaccination in these individuals. A 2-dose strategy is likely to achieve seroprotection for many, and checking HBsAb levels 2 months after the second dose can inform if a third dose should be given at 6 months, as both strategies were superior to 3-dose single-strength recombinant vaccine. However, ACTG 5379 is ongoing, and the durability of seroprotection is still unknown. No safety data on HepB-CpG are available in pregnancy; therefore, HepB-CpG should be avoided in this population. For those initially vaccinated when the CD4 count was <200 cells/μL, an improved response may be observed after virologic suppression on ART and a CD4 count >200 cells/μL are achieved. One dose of vaccine should be administered to patients who have a positive anti-HBc with a negative HBsAg and HBsAb. If the HBsAb titer is not >100 mIU/mL, a full series should be administered [166]. Prior to administration of any HBV vaccine, it is necessary to confirm that the patient does not have chronic HBV.

Those who have been incompletely vaccinated should receive 1 dose of hepatitis B vaccine following exposure to HBV. Those who have not been vaccinated should receive hepatitis B immune globulin (IG) within 24 hours to 7 days for percutaneous exposure to HBV and up to 14 days for sexual exposure to HBV. All infants born to HBsAg-positive persons should receive hepatitis B IG and hepatitis B immunization, preferably in the first 12 hours of life. Routine vaccination for HAV and HBV is recommended for all infants [120, 167]. Serologic testing for viral hepatitis should be repeated if suspected exposure occurs or if there are newly elevated transaminase levels.

MMR, Papillomavirus, and VZV

Recommendations

- MMR vaccine should be administered to people with CD4 count ≥200 cells/μL to protect against measles, mumps, and rubella if they were born in the United States in 1957 or after and have not received this vaccine or do not have immunity to these infections.
- Persons aged between 9 and 26 years should be vaccinated against human papillomavirus (HPV), and those aged 27–45 years who are unvaccinated or inadequately vaccinated should be offered the vaccination series, if appropriate, through shared decision-making.
- Persons who are susceptible to VZV (those who have not been vaccinated, have no history of varicella or herpes zoster, or are seronegative for VZV) should receive PEP with varicella zoster IG as soon as possible (but within 10 days) after exposure to a person with varicella or shingles.
- Varicella primary vaccination should be considered in VZV-seronegative persons aged >8 years with CD4 count >200 cells/μL and in children with HIV aged 1–8 years with CD4 cell percentages >15%. Primary varicella vaccination is contraindicated for persons with CD4 count <200 cells/μL.
- Recombinant zoster vaccine (RZV), 2-dose series, should be given to those aged ≥18 years to prevent reactivation. Response may be better if suppressed on ART and the CD4 count is >200 cells/μL.

Evidence Summary

In 2019, there were 1274 individual cases of measles in 31 states, the highest number reported in the United States since 1992 [168]. The majority of cases occurred in individuals who had not received measles vaccination. The MMR vaccine is administered in a 2-dose series with at least 1 month between doses. MMR should not be given if CD4 is <200 cells/μL. Acceptable evidence of immunity against measles includes written documentation of adequate vaccination, laboratory evidence of immunity, laboratory confirmation of measles, or birth in the United States before 1957 [113].

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A preventive 9-valent HPV vaccine (9vHPV; Gardisil) is routinely recommended in a 3-dose schedule for all persons with HIV aged 9–26 years. Catch-up vaccination can be offered to those aged 27–45 years based on shared decision-making [156, 169]. The vaccine is safe and highly effective in preventing infection with the HPV subtypes associated with genital warts and those responsible for approximately 70% of cervical cancers and most anal cancers. Evidence shows a vaccine-associated decrease in the prevalence of HPV infections, anogenital lesions, and precancerous cervical neoplasia [169]. Studies show the safety of HPV vaccine in women, men, and children [170]; however, the efficacy data for people with HIV are limited, with mixed results [171–174]. Furthermore, little is known about the efficacy of HPV vaccination in older age groups. One study reported that when HPV vaccination was given to those with HIV at an older age but <45 years anal dysplasia was reduced [175]. The vaccine is not expected to impact the development of cancer in those who already harbor oncogenic subtypes. All persons with HIV should receive 3, rather than 2, doses of vaccine, regardless of age [176].

Varicella vaccination (Varivax) should be considered (2 doses of single-antigen varicella vaccine, not measles/mumps/rubella/varicella, administered 3 months apart) for adults and adolescents with HIV with a CD4 count >200 cells/μL on suppressive ART who do not have prior evidence of immunity to varicella (including documented prior infection) [177, 178]. Children should also receive the vaccine if aged >8 years and with a CD4 cell percentage ≥15%. Persons without evidence of immunity who have no history of varicella or shingles and no history of vaccination against VZV and who are at risk of developing severe disease or complications should receive varicella zoster IG within 10 days after exposure to persons with varicella or shingles [110, 177, 178]. Varicella zoster IG is not indicated for persons who received 2 doses of varicella vaccine and became immunocompromised later in life [110, 177]. RZV (Shingrix) should be administered to adults aged ≥18 years using 2 doses 2–6 months apart for the prevention of herpes zoster [98]. Those whose virus is suppressed on ART with CD4 count >200 cells/μL may respond better, but the vaccine can be safely given regardless of CD4 cell count. Those who have not had varicella exposure (either infection or vaccination) should not be offered this vaccine. Data indicate that 99% of those born prior to 1980 have had varicella, even if they do not recall receiving the vaccination [179]. Studies in HIV have found the vaccine to be safe and immunogenic after 2 doses.

COVID-19, Mpox, and Respiratory Syncytial Virus

Recommendations

- All people with HIV should receive updated COVID-19 vaccines as recommended by the CDC. Due to rapid changes in recommendations, the CDC guidance should be checked for the most current information.
- The following should be counseled about transmission of mpox and offered vaccination with the live-nonreplicating modified vaccinia Ankara-Bavarian Nordic (MVA-BN) vaccine. The full 2-dose series is required for optimum protection.
  - Persons without mpox lesions who have known or suspected exposure to someone with mpox or with a sex partner in the past 2 weeks who was diagnosed with mpox;
  - Cisgender men who have sex with cisgender men or transgender, nonbinary, or gender-diverse persons who, in the last 6 months, have had a new diagnosis of an STI or more than 1 sexual partner;
  - Persons who, in the last 6 months, have had sex at a commercial sex venue or sex related to a large commercial event or in a geographic area where mpox transmission is occurring;
  - Persons who have a sex partner with any of the above risks or persons who anticipate experiencing any of the above scenarios.
- Persons aged ≥75 years should receive 1 dose of a respiratory syncytial virus (RSV) vaccine. Those aged 60–74 years who are at increased likelihood of severe RSV should receive 1 dose of an RSV vaccine.

Evidence Summary

Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has had a dramatic impact in reducing severe illness, hospitalization, and mortality. People with HIV are at increased likelihood of reinfection with SARS-CoV-2 [180] and for post-COVID-19 conditions (PCCs, formerly postacute symptoms of COVID-19 or PASC); vaccination protects against development of PCCs [181]. Those who are previously unvaccinated or who received a monovalent COVID-19 vaccine in the past should receive an updated COVID-19 vaccine at least 2 months after the last dose [182]. Note that these recommendations continue to change, and all clinicians should check the CDC website for the most current information [183].

The CDC recommends vaccination against mpox for cisgender gay, bisexual, and other men who have sex with cisgender men and those who are transgender, gender-diverse, or nonbinary and who, in the past 6 months, have had a new diagnosis of at least 1 STI or more than 1 sex partner. Additionally, persons who, in the last 6 months, have had sex at a commercial sex venue or sex in association with a large public event or in a geographic area where mpox transmission is occurring should be offered vaccination. Vaccination is recommended for sexual partners of persons described above and persons who anticipate experiencing any of the above [156]. A live nonreplicating vaccinia virus vaccine for smallpox and mpox (MVA-BN; Jynneos) is safe to administer to those with

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immunocompromising conditions, including HIV, although the immune response may be diminished in this population, particularly those with low CD4 cell counts or unsuppressed virus. There are insufficient data during pregnancy and breastfeeding. The peak antibody response is achieved 2 weeks after the second dose [184]. Data from an electronic record review suggest that the Jynneos vaccine was effective in preventing mpox disease [185]. It is crucial that both doses are received for optimal immunity. Those who are unvaccinated and have had exposure should receive the complete series with the first dose within 4–14 days of exposure [98]. The duration of protection remains uncertain, but there is evidence that suggests that severity of disease is reduced in individuals who develop mpox after vaccination, including those with HIV [186–188]. The live attenuated ACAM 2000 smallpox vaccine should not be given to people with HIV (see Section 6).

RSV is a highly contagious virus that can cause severe lower respiratory infections in young children and older adults. Recently, the FDA approved 2 vaccines for those aged ≥60 years, based on risk for severe RSV disease. The RSVPreF3 is a single-dose adjuvanted recombinant prefusion F protein (preF) vaccine, and the RSVPreF is a single-dose recombinant stabilized preF vaccine (Arexvy, Abrysvo). In clinical trials, the efficacy of preventing RSV-associated lower respiratory infection varied from 77% to 81% [189]. Of 38 177 participants who received the vaccines, 6 cases of inflammatory neurologic events after RSV vaccination occurred [189]. Persons aged 60–74 years who have heart or lung disease or weakened immune systems, who are frail, or who live in a group setting are at increased likelihood of severe RSV and should receive 1 dose of an RSV vaccine. Persons aged ≥75 years should receive 1 dose of an RSV vaccine. Data regarding RSV vaccine in people with HIV are limited. Risks and benefits should be assessed based on shared decision-making [190].

Travel Vaccination

Recommendation

- Individuals who travel should be advised to follow CDC guidelines, with particular attention to CD4 cell count, based on their travel activities and destinations.

Evidence Summary

Cholera is a toxin-mediated bacterial infection that results from ingestion of contaminated food or water, leading to severe watery diarrhea. Cholera is likely to occur in areas with inadequate sanitation. CVD103-HgR (Vaxchora) is a single-dose live attenuated oral cholera vaccine recommended for travel to high-risk areas in which *Vibrio cholera* transmission can occur. The duration of protection is approximately 3 months, and vaccine efficacy may be lower in people with HIV. CVD103-HgR should be given at least 10 days prior to potential exposure among those aged 18–64 years [191]. Before 2022, poliovirus cases had not been seen in the United States for more than 30 years, and only a limited number of cases had been reported in Afghanistan and Pakistan. In 2022, there was a 23% increase globally in polio cases caused by circulating vaccine-derived poliovirus and decreased polio vaccination rates, including a paralytic case in New York City, accompanied by local wastewater surveillance for poliovirus [192]. The risk of acquiring vaccine-derived polio is low and can be mitigated by vaccination. Those who may have high-risk exposure can receive a 3-dose vaccine (Ipol) if CD4 is >200 cells/μL and if the benefits outweigh the risks [193]. Typhoid fever can cause life-threatening illness due to *Salmonella* Typhi. Individuals who travel to high-incidence areas should consider vaccination to reduce the risk for typhoid fever. Typhoid vaccine Thyphim Vi covers *Salmonella enterica* serotype paratype A, B, and C. The intramuscular vaccine should be administered 1 week prior to travel. People with HIV should avoid the live-attenuated oral vaccine (Vivotif) [194].

SECTION 5: SCREENING FOR AND PREVENTING CANCER

Because of an increased likelihood of both first and second primary cancers among people with HIV, enhanced cancer prevention, screening, and treatment efforts are needed for people with HIV both before and after an initial cancer diagnosis. It is recommended that clinicians who are treating patients with cancer inquire and screen for HIV if serostatus is not established [195, 196]. Clinicians treating HIV should regularly inquire about cancer risks and ensure recommended screenings [195]. Although persons with HIV have increased rates of certain cancers, recommendations for screening (prostate, breast, colon, lung) are not different from those for the general population, and providers should follow US Preventive Services Task Force (USPSTF) and American Cancer Society guidelines. However, AIDS-defining cancers and non–AIDS-defining cancers, especially virally based cancers, occur more frequently in people with HIV and merit increased attention [197–199]. Higher CD4 count (≥350 cells/μL) and maximal viral suppression are associated with lower 5-year mortality among patients with HIV and any cancer diagnosis [200]. While most cancers are not diagnosed at younger ages in people with HIV, lung cancer, anal cancer, and myelomas may occur at younger ages among people with HIV compared with those without HIV. People with HIV are at greater risk for oral/pharyngeal and kidney cancers [198, 201]. Viral suppression is especially associated with lower risk of virally associated and non–AIDS-defining cancers among those on ART [201]. As such, as with most comorbidities, viral suppression is urged for people with HIV who have cancer. Because people with HIV have

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higher mortality rates after they develop cancer, increased observation, vigilance, and screening are required [202].

Recommendations

Prevention

- All patients should be asked about tobacco use at every healthcare encounter, and those who smoke should be strongly encouraged to stop smoking and offered smoking cessation assistance, including pharmacotherapy and behavioral interventions.
- Because alcohol increases risk of certain cancers, moderation in alcohol consumption should be recommended.
- Vaccinations against HPV and HBV are essential to reduce the risk of cervical, anal, head, and neck cancers and hepatocellular carcinoma.

Screening and Detection

- Providers should be vigilant for cancer, especially human oncogenic viral-based cancers, associated with Epstein-Barr virus (EBV), HPV, HCV, and HBV, even if no specific screening is recommended.
- Screening for prostate, breast, lung, and colon cancer should be conducted according to USPSTF and American Cancer Society guidelines for the general population.
- Biennial mammogram screening is recommended for persons aged 40–74 years, per USPSTF guidelines.
- A digital anal rectal exam should be performed annually, whether or not high-resolution anoscopy (HRA) is available.
- Transgender women, cisgender men aged >35 years who have sex with cisgender men, and all other people with HIV aged >45 years should be screened with an anal Papanicolaou (Pap) test if there is access to or ability to refer for HRA (preferred) and treatment. The IDSA recommends HPV testing with cytology only and not just HPV testing alone.
  - For low-grade squamous intraepithelial lesions or worse, the patient should be referred for HRA and HPV testing if aged <45 years. Patients aged at least 45 years should be referred for HRA and HPV testing.
  - All high-grade squamous intraepithelial lesions (HSILs) should be treated, ideally with hyfrecation, and monitored routinely among people with HIV and aged >35 years.
  - All patients with anal cancers should be referred to surgical oncology for treatment.
- Persons with HIV aged between 21 and 29 years should have a cervical Pap test annually. If the results of 3 consecutive cervical Pap tests are normal, follow-up Pap screening should be in 3 years.
  - Abnormal Pap test results require either follow-up colposcopy by a qualified practitioner or repeat Pap test in 6–12 months.
  - For persons aged ≥30 years, cervical Pap tests should be done annually. If the results of 3 consecutive Pap tests without an HPV test are normal, a follow-up Pap should be performed in 3 years. If the Pap test is done with HPV testing and both the cytology and HPV testing are negative, follow-up cervical cancer screening can be done in 3 years after a single Pap smear.
  - Unlike for people without HIV, there is no age limit for Pap screening.
  - If HPV testing reveals HPV16 or HPV16/18, referral for colposcopy is recommended.
- Providers should follow USPSTF screening recommendations for prostate cancer.
  - Shared decision-making for prostate-specific antigen (PSA) testing is recommended for patients aged 50–69 years with at least a 10-year life expectancy.
  - PSA-based prostate cancer screening should be considered for persons of Black or African descent, people with prostates aged 45–49 years with at least a 10-year life expectancy, and persons who have at least 1 first-degree relative with prostate cancer.
- Screening for hepatocellular carcinoma every 6 months by ultrasound with or without alpha-fetoprotein is recommended for those with cirrhosis from any cause, those with chronic hepatitis B, and those with a history of chronic hepatitis C (treated or untreated) and stage F3 or F4 fibrosis.

Special Populations

- After vaginoplasty, patients should be reminded that screening for conditions related to remaining organs, such as prostate cancer, is still necessary.
- Cancer screening for transgender and gender-diverse persons should be conducted based on guidelines for the organs and tissues present in the individual.
- Among transgender people with prostates, PSA is unreliable for those on androgen blockers and those who have undergone orchiectomy. For those with a neovagina, a neovaginal and rectal exam should be used to examine the prostate.

Evidence Summary

Acquired immunodeficiency, as encountered among people with HIV, is associated with an increased risk for cancer [203]. As such, interventions that may prevent cancer are essential to HIV care. Healthcare systems should maintain a record of patients' current smoking status. All clinicians should advise patients to stop smoking and document this message at least yearly in the health record. Pharmacotherapy such as varenicline should be offered, as well as referrals for behavioral

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interventions to assist with smoking cessation [146, 150, 204]. The CMS, American Cancer Society, and USPSTF recommend that adults aged between 50 and 80 years with a ≥ 20 pack-year smoking history and who currently smoke or have quit within the past 15 years receive screening noncontrast low-dose computed tomography (LDCT) scan of the chest to detect lung cancer [205]. Persons with HIV may receive the same mortality benefit from LDCT screening as those not living with HIV if the CD4 count is >500 cells/μL and the patient is ART-adherent [206].

Heavy alcohol use can negatively impact most cancer treatments and may put people at greater risk for esophageal, stomach, and liver cancers [207]. As such, reduced alcohol use is advised. Further, vaccination against HBV and HPV is also strongly recommended to prevent liver cancer and HPV-associated cancers, including anal, cervical, and head and neck cancers. Although persons with HIV have increased rates of certain cancers, recommendations for screening (prostate, breast, colon, lung) are not different from those for the general population. Because people with HIV are at increased risk of both primary and additional cancers, screening for cancer is needed, and enhanced secondary cancer prevention is essential [196].

While screening for most cancers in adults with HIV is not different from that of the general population, including breast cancer screening, providers who treat adults with HIV should have high suspicion for cancers, even if no regular screening is recommended. Providers should be especially vigilant for human oncogenic virally based cancers, including cancers that are due to EBV, HPV, HBV, and HCV [203]. Higher CD4 count (≥350 cells/μL) and maximal viral suppression are associated with lower 5-year mortality among patients with HIV and any cancer diagnosis. Maximal viral suppression should be encouraged, especially if people with HIV and cancer are undergoing chemotherapy or radiation therapy [200]. Genital, oral, cervical, and anal warts should be treated to prevent development of cancer [208].

Screening for hepatocellular carcinoma every 6 months by ultrasound with or without alpha-fetoprotein is recommended for those with cirrhosis from any cause [209]. This recommendation applies to people with HIV and chronic HBV and those with treated or untreated HCV and fibrosis stage F3 or F4. Breast cancer is the second leading cause of cancer-related deaths in women in the United States after lung cancer [210]. It does not appear to be increased in prevalence among people with HIV, although unusual clinical presentations and rapid progression have been reported, suggesting that breast cancer may behave more aggressively in this setting (bilateral disease, poorly differentiated carcinoma, and early metastasis) [210]. At present, screening mammography in persons with HIV should follow USPSTF and American Cancer Society guidelines for the general population, which are not always concordant [211, 212].

Anal cancer incidence (as well as oral cancers that are of HPV origin) is greatly elevated among people with HIV, especially among cisgender men who have sex with cisgender men, older people with HIV, people with CD4 count <200 cells/μL, and African Americans [208, 213]. There are national screening guidelines for the use of anal Pap tests in healthcare maintenance, especially among people with HIV [214]. For all people with HIV who have a prostate, a digital rectal exam is recommended to detect masses, blood, or prostate size and smoothness. Data published in 2022 demonstrate the benefit of anal cancer screening and treatment among cisgender men with HIV aged >35 years who have sex with cisgender men and all other people with HIV aged >45 years if there is access to or ability to refer to HRA (preferred) and treatment. If an anal Pap test or HRA is done, all HSILs should be treated, preferably using hyfrecation, and monitored regularly for clearance or recurrence. The exact timing of follow-up monitoring is still undetermined [215, 216]. Additional data are needed to determine whether persons with a history of receptive anal intercourse and all persons with genital warts should have periodic anal Pap tests if access to appropriate referral for follow-up, including HRA, is available [217]. If anal cancer is diagnosed, referral should be made to oncology or surgical oncology for appropriate treatment [208]. Data are needed to generate recommendations for anal cancer screening and prevention in cisgender women.

Prostate cancer screening that follows USPSTF guidelines is generally recommended. There is increasing evidence, however, that prostate cancers among people with prostates aged 50–69 years who have a 10-year life expectancy should have shared decision-making about PSA testing. Among Black adults with a prostate, the lower age limit for PSA screening is 45 years. PSA screening is not recommended at this time for adults with a prostate aged ≥70 years [218–220].

For persons aged between 21 and 29 years, cervical cancer screening should be performed within 1 year of sexual debut but not later than age 21 years or at the diagnosis of HIV. If the initial Pap test is negative, some experts recommend that a repeat Pap test be performed within 6–12 months. If the results of 3 consecutive Pap tests are normal, a follow-up Pap test should be performed at 3 years. The use of HPV co-testing in this age group is not recommended. For persons aged >30 years, cervical cancer screening should commence at diagnosis and be continued throughout a patient's lifetime and not stopped at age 65 years as recommended for the general population. In this age group, Pap testing can be done with cytology alone or with the addition of HPV co-testing. Some experts recommend that a repeat Pap test be done 6 months after the initial Pap test. If the results of 3 consecutive Pap tests are normal, a follow-up Pap test should be done in 3 years. If testing is done with Pap and HPV co-testing and if the results of both tests are normal, the next screening can occur in 3 years [221, 222].

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Special considerations are needed for transgender adults with HIV in regard to cancer. While likely multifactorial, transgender persons have a greater risk of being diagnosed with cancer later than the general population, lower odds of receiving appropriate oncologic treatment, and worse odds of survival than other people with cancer. Thus, greater vigilance is needed for transgender individuals at risk of cancer [223]. Further, even after vaginoplasty, there needs to be lifelong follow-up for prostate cancer and other cancers found among people born with male sex organs that are not removed. It also should be noted that among transgender individuals with prostates, PSA testing may be unreliable if they are taking androgen blockers or are status post-orchiectomy. For those with a neovagina, a neovaginal exam of the prostate should be performed [224].

SECTION 6: STI SCREENING, TREATMENT, AND PREVENTION

In 2022, the United States experienced extremely high rates of chlamydia, gonorrhea, and syphilis, with continuing and striking disparities by race/ethnicity, gender, sexual orientation, age, and geography. People with HIV accounted for 36.4% of cases of primary and secondary syphilis among gay and bisexual men [225]. Trichomonas is common among persons who have vaginal sex, although most cases are asymptomatic. Beginning in 2022, global outbreaks of mpox disproportionately affected people with HIV and have been particularly frequent and more severe among those with advanced immune suppression [226]. Evidence is evolving to support prevention of some STIs using doxyPEP, although the risk of antimicrobial resistance is an ongoing concern. It is essential that STI screening, treatment, and prevention efforts be centered on equity-based strategies.

Screening and Treatment for STIs

Chlamydia, Gonorrhea, Syphilis, and Trichomonas

Recommendations

- Services for STI (including mpox) screening, treatment, and prevention should be convenient and affordable, delivered in a stigma-free environment, and made accessible to populations with the highest prevalence of infection using equity-based strategies.
- All patients should be screened for gonorrhea, chlamydia, and syphilis upon entry into care. Persons who have receptive vaginal sex should be screened for trichomonas using the vaginal or cervical nucleic acid amplification test (NAAT). Screening for gonorrhea and chlamydia should be by NAAT at all sites of sexual contact (oral, anal, urethral/urine, vaginal/neovaginal). Done correctly, self-collected NAAT swabs may be used to enhance acceptability.
- In asymptomatic sexually active persons, screening for gonorrhea, chlamydia, and syphilis should be repeated at least annually. Persons who have receptive vaginal sex should be screened for trichomonas at least annually.
- In persons with multiple or anonymous sex partners, screening should be conducted every 3–6 months depending on sexual activities, presence of recent STIs in the patient or their partner(s), and local community STI prevalence. Those found to have gonorrhea, chlamydia, syphilis, or trichomonas on initial screening should be treated and rescreened in 3 months because of high reinfection rates.
- For those diagnosed with pharyngeal gonorrhea, a test of cure should be performed at 7–14 days with an NAAT or culture, although testing at 7 days is associated with a higher rate of false-positive results. If an NAAT obtained for test of cure is positive, a culture should be obtained, and positive cultures should undergo antimicrobial susceptibility testing.
- For gonorrhea that is unresponsive to treatment, regardless of site, culture should be obtained, and positive cultures should undergo antimicrobial susceptibility testing.
- All persons with syphilis should be screened for ocular and otic involvement as well as neurologic symptoms and signs. However, a lumbar puncture is not indicated in individuals with isolated ocular or otic symptoms. A lumbar puncture should be performed in those with neurologic findings.
- Retreatment after treatment failure should be implemented according to CDC STI guidelines. Following a diagnosis of syphilis, nontreponemal titers should be followed and a lumbar puncture performed if titers increase by 4-fold (sustained by at least 2 weeks) without evidence of reinfection after treatment. Cerebrospinal fluid (CSF) examination and retreatment may be considered if titers do not decrease 4-fold by 24 months.
- Pregnant individuals should be screened for chlamydia, gonorrhea, and syphilis at the first prenatal visit, 28 weeks, and also, for syphilis, at delivery. Screening for trichomonas should be offered at the first prenatal visit. Screening should be more frequent depending on past STI incidence in the patient or partner(s) and community STI prevalence. Partners of pregnant persons with STIs should be offered screening and treatment.
- Because of increasing antibiotic resistance, especially with gonorrhea, CDC STI treatment guidelines should be consulted frequently, and treatment should follow these recommendations.
- In cisgender women, trichomonas should be treated using metronidazole 500 mg twice daily for 7 days, while a single 2-g dose may be used in cisgender men.

Evidence Summary

Between 2018 and 2022, gonorrhea diagnoses increased by 11% overall but were lower than in 2021, with 40% occurring among

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gay, bisexual, and other cisgender men who have sex with men. Syphilis diagnoses increased a striking 78.9%; this includes 3755 cases of congenital syphilis, a 183% increase since 2018. Cases of chlamydia were level compared with 2018 but at a high incidence of 1 649 716 cases. Chlamydia, gonorrhea, and syphilis continued to disproportionately affect racial and ethnic minorities, with 31% of these cases occurring in non-Hispanic African Americans and half of diagnosed STIs occurring among persons aged 15–24 years [225].

Screening

Nucleic acid amplification testing is the most sensitive screening method for chlamydia and gonorrhea and should be obtained from all sites of sexual exposure. For persons with a vagina/neovagina, swabs from that area are more sensitive than urine, while urine is acceptable for persons with a penis. Self-collected vaginal/neovaginal and anal swabs are as sensitive as those collected by care providers and may be more acceptable and adaptable to at-home testing. The COVID-19 pandemic accelerated interest in home-testing for STIs, sometimes paired with telemedicine or online ordering of test kits, particularly for gonorrhea and chlamydia [227]. In a pilot study in Washington, DC, in which self-tests for HIV, chlamydia, and gonorrhea were sent to users by mail, positivity rates for chlamydia and gonorrhea (especially in extragenital areas) were high in returned samples [228]. Clinicians should be familiar with CDC's updated laboratory testing guidelines for syphilis [229]. Diagnosis of syphilis generally relies on serologic testing that consists of a nontreponemal test (with positives expressed in titers) and a treponemal test. However, self-testing has relied on treponemal antibody testing, which may be falsely negative in early infection or positive long after an initial infection has been treated. Clinicians should be familiar with considerations regarding point-of-care testing for syphilis from the National Syphilis and Congenital Syphilis Syndemic Federal Task Force [230]. The development of nontreponemal tests suitable for self-testing remains a research gap of high interest.

All persons with syphilis should be screened for ocular and otic syphilis and for neurologic signs and symptoms. Persons with syphilis and ocular or otic symptoms should receive treatment immediately to preserve vision and hearing. However, a lumbar puncture is not required unless neurologic signs or symptoms are present. A lumbar puncture is indicated in those with neurologic findings and those whose nontreponemal titer has increased 4-fold (sustained for more than 2 weeks) without evidence of reinfection. Persons whose nontreponemal titers have not decreased 4-fold by 24 months should be examined clinically; a CSF examination and retreatment may be considered. CDC STI guidelines should be consulted when treatment fails [213]. Pregnant persons are at high risk for STIs and should be screened for gonorrhea, chlamydia, syphilis, and trichomonas at the first prenatal visit, 28 weeks, and also at delivery for syphilis [120, 225]. Congenital syphilis is preventable and can be eliminated by diligent screening and treatment during pregnancy, including at delivery. Note that treponemal antibody tests (such as fluorescent treponemal antibody absorption (FTA-ABS) or microhemagglutination assay for *Treponema pallidum* (MHA-TP)) often remain positive for life despite effective treatment [231].

Trichomoniasis is the most common STI among those who have vaginal sex, with disproportionately high rates among Blacks and cisgender women with HIV [231]. It is associated with increased HIV shedding in those without viral suppression, with pelvic inflammatory disease, and with adverse pregnancy outcomes. Screening should be conducted using an NAAT or an FDA-approved rapid test and repeated in 3 months for those who test positive, as reinfection rates are high. During pregnancy, screening should occur at the first prenatal visit and during the third trimester, at minimum, with treatment delivered as needed.

Treatment

Antibiotic resistance is of high concern, especially for gonorrhea, although most strains have remained sensitive to ceftriaxone to date. In 2020, CDC recommended gonorrhea treatment with a single dose of intramuscular ceftriaxone 500 mg (or 1000 mg for those who weigh ≥150 kg) without concurrent azithromycin [232]. Test of cure with an NAAT or culture is recommended for pharyngeal gonorrhea at 7–14 days after treatment, although testing at 7 days is associated with a higher rate of false-positive results. Culture should be obtained for all gonorrhea treatment failures so that antimicrobial susceptibility testing can be performed [231]. The preferred treatment for early, secondary, latent, and late-latent syphilis continues to be benzathine penicillin G. However, doxycycline can be used for 14–28 days, depending on the stage of the disease in the event of true penicillin allergy or penicillin shortage. If neurosyphilis is present or the patient is pregnant, intravenous aqueous crystalline penicillin G should be used, even if desensitization is required. The high price of commercially obtained benzathine penicillin and intermittent shortages of this drug are barriers to ending the syphilis epidemic, particularly among pregnant women for whom no other viable regimens are recommended. In cisgender women with HIV, treatment of trichomonas using metronidazole 500 mg twice daily for 7 days was more effective than a single 2-g dose of metronidazole; cisgender men can be treated using the single-dose regimen [231]. In most cases, chlamydia is treated with doxycycline 100 mg twice daily for 7 days. However, rectal chlamydia associated with inguinal lymphadenopathy or symptoms of proctocolitis (such as bloody discharge, tenesmus, ulcers) raises suspicion of lymphogranuloma venereum (LGV). Although LGV and non-LGV chlamydia can be distinguished by molecular testing, LGV is usually diagnosed clinically and treated with 21 days of doxycycline 100 mg twice daily. Close monitoring of and referral

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to the CDC STI treatment guidelines are essential, as susceptibilities and recommendations change over time [231].

Mycoplasma Genitalium

Recommendations

- Persons with recurrent urethritis or cervicitis should be screened with an NAAT for *Mycoplasma genitalium* (Mgen). Screening should be considered for those with pelvic inflammatory disease.
- Screening for Mgen in asymptomatic persons or screening of extragenital sites is not recommended.

Evidence Summary

Mgen is a cause of nongonococcal/nonchlamydial penile urethritis and can cause persistent or recurrent urethritis. It has been associated with cervicitis, endometritis, and pelvic inflammatory disease in cross-sectional studies. Case-control and cross-sectional studies suggest that urogenital Mgen is more common among people with HIV and may be associated with HIV shedding among people not taking ART [231]. Resistance to azithromycin is widespread, and fluoroquinolone resistance is increasing. Multidrug resistance to azithromycin, fluoroquinolones, and doxycycline has been identified [233]. Resistance testing for refractory or recurrent infections should be performed where available, but molecular tests are not yet widely available outside of research settings. There are insufficient data on clinical outcomes associated with asymptomatic Mgen, and antibiotic use in this setting could increase the prevalence of resistant organisms. Therefore, screening of asymptomatic persons for Mgen is not recommended. The efficacy of doxyPEP for prevention of symptomatic Mgen is an area of active investigation, as is the risk of Mgen resistance in this setting [234].

Mpox

Screening and Treatment

Recommendations

- Persons exposed to mpox through sexual activity or close contact should be advised to monitor for symptoms for 21 days, consider vaccination if asymptomatic and within 14 days of exposure, and seek medical care immediately if symptoms develop.
- Persons with cutaneous, oropharyngeal, or anorectal lesions suspected to be due to mpox should receive polymerase chain reaction (PCR) testing of lesions for orthopoxvirus (mpox) and should isolate as recommended in the CDC guidelines.
- Persons with suspected mpox should be offered screening for HIV (if not known to have HIV) and STIs, especially chlamydia, gonorrhea, and syphilis.
- ART initiation should not be delayed when HIV is diagnosed concurrent with mpox, and therapy should be adjusted as soon as possible for those on ART with virologic failure in the setting of mpox.
- Treatment with tecovirimat should be offered to people with HIV whose virus is not suppressed or whose CD4 count is <350 cells/μL, those who are pregnant, and those who have other immunocompromising conditions; severe disease; oropharyngeal, anorectal, genital lesions; bacterial superinfection, especially requiring debridement; or other conditions that put them at high risk of poor outcomes, as designated by the CDC.

Evidence Summary

Compared with previous mpox outbreaks, the global outbreak that began in 2022 occurred predominantly among cisgender men and transgender women who have sex with cisgender men and has been associated with more mucosal and anorectal disease and delayed prodromal symptoms compared with previous outbreaks in endemic countries. A global systematic review of 52 studies that included 6345 persons with mpox found that 40% of persons also had HIV [235]. A global series of mpox among 382 people with HIV and CD4 count <350 cells/μL found high prevalence of serious outcomes, including necrotizing skin lesions, lung involvement, secondary infections, and sepsis, particularly in those with CD4 count <100 cells/μL. In the group as a whole, 28% were hospitalized and 7% died. Among those who died, all had CD4 count <200 cells/μL, and mortality was especially high (57%) among 21 persons who developed mpox immune-related inflammatory syndrome (IRIS) after initiation or reinitiation of ART. In this series, only 16% received tecovirimat (TPOXX) [226]. Initiation of ART, however, should not be delayed because of concern about IRIS, as viral suppression can be lifesaving in this population. As of March 2023, the CDC reported that 94% of deaths associated with mpox in the United States were among people with HIV. In those with CD4 count data available, 96% of deaths were among people with CD4 counts <50 cells/μL. Among those with treatment data available, only 9.1% were receiving ART prior to their mpox diagnosis. Of all mpox deaths, 90% occurred among Black men [236]. An equity-based approach to mpox screening, treatment, and prevention is essential, prioritizing people with HIV, especially those with low CD4 counts or uncontrolled virus and racial and ethnic groups that bear a disproportionate burden of severe mpox.

PCR testing of mpox lesions is associated with the highest diagnostic yield [237], although virus can often be recovered from the anorectal and oropharyngeal regions. Other STIs often occur concurrently with mpox, and STI (and HIV if status is unknown) screening is imperative in persons who present with suspicion of mpox. People with suspected or confirmed mpox who are at risk of serious outcomes should receive TPOXX under an expanded access investigational new drug submission administered by the CDC [238]. This includes people with unsuppressed virus or CD4 count <350 cells/μL; other immunocompromising conditions; severe disease;

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oropharyngeal, anorectal, or genital lesions; or bacterial superinfection, especially requiring debridement. People without severe disease may consider enrolling remotely in the Study of Tecovirimat for Human Mpox Virus (STOMP) trial, a National Institutes of Health–sponsored study to determine the effectiveness of TPOXX [239].

Although the 2022 mpox outbreak peaked in the summer of 2022 and was curtailed by vaccination, education, and behavior change among persons at highest likelihood of acquisition, clusters of resurgence continued to occur in 2023 and increased in early 2024 [188, 240]. A health alert from the CDC in December 2023 notified health professionals of the human-to-human transmission of clade I mpox within the Democratic Republic of Congo (DRC), with concern for international spread. Mpox infections in the United States have been with the clade II virus, while clade I is associated with increased transmissibility and more severe outcomes than with clade II. Clinicians should be aware of the possibility of clade I infection in persons returning from the DRC and other affected nations who develop symptoms within 21 days of travel. Both Jynneos vaccination and TPOXX treatment are thought to be effective against the clade I virus [241]. Vaccination efforts are of ongoing importance, including ensuring that both doses of vaccine are received. As of November 2023, only 61% of people who received an initial MVA-BN smallpox vaccine (Jynneos) received the full series [242]. A global case series of 37 persons with mpox reinfection or mpox that occurred after adequate vaccination found that cases were mild, with few lesions and little mucosal involvement, no deaths, and only 1 hospitalization in spite of only 2 individuals receiving TPOXX [187]. Therefore, while a 2-dose vaccination series may not prevent infection, it likely will prevent severe disease (see Section 4: Immunizations).

Prevention of STIs

Recommendations

- Individuals with recurrent STIs and ongoing sexual activities that place them at high likelihood of STI acquisition should receive tailored HIV and STI prevention messages that are appropriate to the individual's sexual health goals. If available, persons with recurrent STIs may benefit from counseling or more structured programs that offer interventions to reduce acquisition.
- Clinicians should discuss the potential benefits and harms of doxyPEP with individuals who may benefit from it. DoxyPEP should be discussed with and offered to cisgender gay, bisexual, and other men who have sex with cisgender men; transgender women; and people with HIV who have had syphilis, chlamydia, or gonorrhea in the last 12 months or who anticipate engaging in sexual activities associated with the increased likelihood of acquiring an STI. The dose of doxycycline is 200 mg as a single dose (maximum 200 mg in 24 hours), ideally taken as soon as possible after sex but no later than 72 hours afterward.
- At present, data are inadequate to support the efficacy of doxyPEP in cisgender women, cisgender heterosexual men, transgender men, and gender-diverse persons assigned female at birth. Shared decision-making should be used in these populations.
- Persons who actively use doxyPEP should be screened for syphilis, chlamydia, and gonorrhea at 3- to 6-month intervals, depending on sexual practices.

Evidence Summary

Persons with frequent recurrent STIs may benefit from counseling and other structured interventions to decrease STI acquisition. Condoms can be effective in decreasing STI acquisition and should be offered. Some individuals with recurrent STIs may benefit from prevention of bacterial STIs using doxyPEP, defined as a single dose of doxycycline 200 mg taken as soon as possible after sex but no later than 72 hours afterward. The maximum dose of doxycycline is 200 mg within 24 hours.

Preliminary data that support the activity of doxycycline in preventing chlamydia and syphilis came from a substudy of the French National Agency for Reserch on AIDS (ANRS) Ipergay trial of intermittent HIV PrEP, in which participants took doxycycline 200 mg within 72 hours of sexual exposure. Doxycycline use was associated with a 70% decrease in chlamydia and syphilis but no decrease in gonorrhea [234]. Two randomized trials subsequently demonstrated the efficacy of doxyPEP in preventing chlamydia, gonorrhea, and syphilis among cisgender gay and bisexual men and transgender women. The DoxyPEP trial, a randomized, open-label trial in Seattle, Washington, and San Francisco, California, included 630 cisgender gay and bisexual men and transgender women. In May 2022, the study was stopped by its data and safety monitoring board after a planned interim analysis showed statistically significant reductions in syphilis (relative risk [RR], 0.23; 95% confidence interval [CI], .04–1.29), chlamydia (RR, 0.26; 95% CI, .12–.57), and gonorrhea (RR, 0.43; 95% CI, .26–.71) and no safety concerns, including among people with HIV [243]. In the PrEP cohort, the RRs were 0.45 (95% CI, .32–.65) for gonorrhea, 0.12 (95% CI, .05–.25) for chlamydia, and 0.13 (95% CI, .03–.59) for syphilis. In the cohort of people with HIV, the RRs were 0.43 (95% CI, .26–.71) for gonorrhea, 0.26 (95% CI, .12–.57) for chlamydia, and 0.23 (95% CI, .04–1.29) for syphilis [244]. The limited antimicrobial resistance data from this study are inconclusive, although 6 of 20 incident gonorrhea isolates in the doxycycline arm displayed tetracycline resistance [245]. ANRS 174 (DOXYVAC) was a French randomized, open-label, factorial-design trial that evaluated doxyPEP and meningococcal B vaccine (4CMenB) in gay and bisexual men on PrEP. The study was stopped by its data

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and safety monitoring board after an unplanned interim analysis found statistically significant reductions in first cases of syphilis, chlamydia, gonorrhea, and Mgen in those on doxyPEP compared with no doxyPEP [246]. Although the interim analysis suggested that 4CMenB vaccination was protective against gonorrhea, this finding was not confirmed after missing study data were included. The final analysis confirmed statistically significant preventative effects of doxyPEP against first episodes of chlamydia (adjusted hazard ratio [aHR], 0.14; 95% CI, .09–.23; $P < .0001$), syphilis (aHR, 0.21; 95% CI, .11–.41; $P < .001$), and gonorrhea (aHR, 0.67; 95% CI, .52–.87; $P = .003$), although the effect against gonorrhea was modest and less than in the interim analysis. The effect of 4CMenB vaccination on incident gonorrhea was not statistically significant. Consistent with local epidemiology, tetracycline resistance was seen in all available gonorrhea samples from baseline and follow-up, and high-level tetracycline resistance (minimum inhibitory concentration > 8 mg/L) was more common in incident samples from the doxyPEP arm than the control arm (36% vs 13%; $P < .043$). No chlamydia resistance was detected, and there was no statistically significant difference between the arms in detection of pharyngeal methicillin-resistant *Staphylococcus aureus* or rectal extended-spectrum β-lactamase–producing *Escherichia coli* [247]. A randomized, open-label trial compared doxyPEP to standard of care among 449 nonpregnant cisgender Kenyan women aged 18–30 years who were taking HIV PrEP. The study (dPEP Kenya) showed no difference between the doxyPEP arm and the standard-of-care arm in the incidence of chlamydia or gonorrhea. In a subset of participants in the doxyPEP arm, doxycycline was present in only 29% of hair samples. Low uptake of the intervention limited the ability to understand the true efficacy of doxycycline for bacterial STI prevention in cisgender women under more ideal adherence conditions. In addition, high-level tetracycline resistance, previously described in Kenya, was seen in 100% of gonorrhea samples identified at baseline and at study visits in both study arms [248]. DoxyPEP, therefore, is recommended for cisgender gay, bisexual, and other men who have sex with cisgender men and for transgender women who have a history of at least 1 diagnosis of syphilis, chlamydia, or gonorrhea within the last 12 months or who anticipate sexual activities associated with increased likelihood of STI acquisition. No recommendations can be made at this time for the use of doxyPEP in cisgender women, cisgender heterosexual men, transgender men, and other gender-diverse persons; additional research is needed. Use of doxyPEP in these populations should be based on shared decision-making.

The main concern for doxyPEP implementation is the risk of antimicrobial resistance, particularly for gonorrhea, but also for the microbiome, including common organisms such as *Staphylococcus*. Additional data are needed to fully assess the public health impact of doxyPEP. Until more data are available, it will be important to judiciously target its use. Modeling based on a cohort at Fenway Clinic (Boston, Massachusetts) found that targeting doxyPEP to cisgender gay and bisexual men, transgender women, and nonbinary persons assigned male at birth who had been diagnosed with a bacterial STI within the last 12 months or with repeated STIs was the most efficient use of doxyPEP. Providing doxyPEP to all PrEP users or people with HIV prevented more STIs but was less efficient and exposed more people to doxycycline (higher number needed to treat to prevent 1 STI) [249]. As data evolve, the CDC recommendations for use of doxyPEP will be updated [250]. People who receive doxyPEP should continue to receive routine screening for asymptomatic STIs and ongoing evaluation of the need for continuing doxyPEP.

SECTION 7: METABOLIC AND OTHER NONCOMMUNICABLE COMORBIDITIES ASSOCIATED WITH HIV, ANTIRETROVIRAL THERAPY, AND AGING

Now that approximately 50% of the global population of people with HIV is aged >50 years, concern has heightened about increased rates of common comorbidities associated with age [251, 252], including long-term cardiovascular morbidity, especially in those with traditional risk factors such as dyslipidemia, glucose intolerance or diabetes mellitus, hypertension, and smoking. The benefits of ART used in accordance with published guidelines outweigh the risks of cardiovascular disease and other comorbidities associated with long-term exposure [253]. Multiple guidelines are available to assist providers in the identification and management of lipid abnormalities, diabetes mellitus, excess weight, liver steatosis, and other comorbidities [254–258]. People with HIV also are at higher risk for weight gain, loss of BMD, hypogonadism, frailty, and neurocognitive disorders.

Recommendations

- Fasting (optimal) or random lipid levels should be obtained prior to and within 1–3 months after starting ART. Abnormal random lipid levels should be repeated when fasting. Patients with abnormal lipid levels should be managed according to the National Lipid Association Part 2 and 2018 Multispecialty Blood Cholesterol Guidelines. All patients should be assessed for 10-year atherosclerotic cardiovascular disease (ASCVD) risk. Those at high risk should be further evaluated and managed according to established guidelines that recognize HIV risk-enhancing factors.
- Statin therapy is recommended for primary prevention of cardiovascular disease in people with HIV aged 40–75 years, regardless of lipid levels and ASCVD risk. The recommendation is strongest for those with a 10-year ASCVD risk of 5% or higher. For people with HIV aged <40 years, evidence is

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insufficient to recommend for or against statin therapy for primary prevention of cardiovascular disease. Decisions in this age group should be individualized, taking into consideration risk-enhancing factors for the general population and for people with HIV.
  - High-intensity statins (atorvastatin 40–80 mg daily or rosuvastatin 20–40 mg daily) are recommended for persons with a 10-year ASCVD risk above 20%.
  - At least moderate-intensity statins (specifically, pitavastatin 4 mg daily, atorvastatin 20 mg daily, and rosuvastatin 10 mg daily) are recommended for persons with HIV and at lower risk.
- Prior to starting ART, random or fasting blood glucose and hemoglobin A1c (HbA1c) should be obtained. If random glucose is abnormal, fasting glucose should be obtained. After initiation of ART, HbA1C is insensitive and may significantly underestimate the risk of diabetes. However, an HbA1C that is >6.5% remains a reliable criterion for diagnosis of diabetes in people with HIV. If HbA1C is <6.5%, fasting plasma glucose is the best screening test for people with HIV receiving ART. Those with a diagnosis of diabetes mellitus should have their HbA1c level monitored at least every 6 months, with an HbA1c goal of <7% in accordance with the American Diabetes Association (ADA) guidelines.
- Weight should be obtained at every visit. In addition, waist circumference (an indirect marker of visceral fat) should be measured annually. Monitoring and counseling on diet, exercise, and alcohol intake should start at the time of ART initiation and be done at every visit.
- Current data do not support switching an ART regimen solely because of weight gain.
- If liver transaminases are increased, workup for nonalcoholic fatty liver disease (NAFLD) should include ultrasound, magnetic resonance imaging (MRI), or CT scan. Presence of steatosis should lead to a fibrosis workup that includes FIB-4, Fibroscan, or MRI elastography, although biopsy remains the standard. Weight reduction is the cornerstone of treatment of NAFLD. Persons with nonalcoholic steatohepatitis (NASH) or fibrosis should be referred to a hepatologist.
- Baseline bone densitometry (DXA) screening for osteoporosis should be performed in post-menopausal cisgender women and men aged ≥50 years. Screening for transgender people should follow national recommendations based on their individualized risk for osteoporosis.
- Testosterone replacement therapy for cisgender men should be prescribed with caution and only in those with symptomatic hypogonadism, given the long-term side effects. See Section 11 for discussion of hormone therapy for transgender men.
- Annual screening for frailty should be considered in people with HIV aged >50 years; the frailty phenotype screen is the most commonly used tool.

Evidence Summary

Lipid Abnormalities and Cardiovascular Risk

HIV infection is associated with dyslipidemia. In the absence of ART, HIV infection results in lower total cholesterol, high-density lipoprotein (HDL-C), and low-density lipoprotein (LDL-C) levels. Initiation of ART, specifically with boosted protease inhibitors (PIs), increases LDL-C and improves HDL-C, but the latter does not normalize to pre-HIV levels [259]. Among nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs), TDF has been associated with lipid-lowering effect [260]; however, TDF is less commonly used currently due to its effect on kidney function and bone mineral density. Other NRTIs, such as TAF and abacavir, appear to have a similar and minimal effect on lipids [261].

HIV is a recognized independent atherosclerotic cardiovascular disease (ASCVD) risk enhancer in the 2018 American College of Cardiology/American Heart Association (ACC/AHA) multispecialty cholesterol management guidelines [255]. At this time, there are no validated cardiovascular risk assessment tools for use in people with HIV, and the default is to use the pooled cohort equations from the 2013 ACC/AHA guidelines and to adjust for the presence of HIV risk enhancers, understanding the limitations of such [255]. The frequency of follow-up testing and response to therapy should be based on the current National Lipid Association Recommendations for Patient-Centered Management of Dyslipidemia: Part 2 and the 2018 Multispecialty Blood Cholesterol guidelines [255, 262]. All patients should be assessed for ASCVD risk. Those with elevated risk should be further evaluated and managed according to established guidelines.

Statin drugs are known to exert a multifactorial effect to prevent cardiovascular disease in the general population. The randomized controlled the Stopping Atherosclerosis and Treating Unhealthy Bone With Rosuvastatin in HIV (SATURN)-HIV trial showed that in individuals with HIV and virologic suppression, LDL-C <130 mg/dL, and evidence of heightened inflammation, rosuvastatin decreased carotid intima-media thickness, improved kidney function, and attenuated systemic and vascular inflammation, including decreasing T-cell and monocyte activation [263–267], but worsened insulin resistance [268]. Recently, the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) study, a multinational placebo-controlled study that enrolled 7769 participants with HIV aged 40–75 years who had low to intermediate ASCVD risk, found that pitavastatin 4 mg daily reduced the risk of major cardiovascular events by 36%, including for those with LDL-C levels below current guideline thresholds for statin initiation [269, 270]. Overall, the protective effect was seen across demographics, CD4 cell count ranges, and viral load levels. REPRIEVE is a practice-changing study, and statin use is now recommended in people with HIV aged ≥40 years, assuming no known allergy to statins or other contraindications,

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Table 7. Effect of Protease Inhibitors and Nonnucleoside Reverse Transcriptase Inhibitors on Statins

Statin	Protease Inhibitors	Nonnucleoside Reverse Transcriptase Inhibitor
Atorvastatin	Use lowest atorvastatin starting dose and titrate, monitor for safety, as risk for myopathy/rhabdomyolysis can be increased with some protease inhibitors Do not coadminister with atazanavir/cobicistat Maximum dose of atorvastatin is 20 mg with darunavir/cobicistat or darunavir + ritonavir	Acceptable with appropriate dosing and monitoring Efavirenz and etravirine decrease atorvastatin's AUC No data for nevirapine; may need higher atorvastatin starting dose Doravirine does not affect levels of atorvastatin
Fluvastatin	Use lowest fluvastatin starting dose and titrate, monitor for safety, as risk for myopathy/rhabdomyolysis can be increased with some protease inhibitors	Acceptable with appropriate dosing and monitoring Etravirine may increase fluvastatin's AUC May need lower fluvastatin starting dose with etravirine No data on doravirine
Lovastatin	Contraindicated (greatly increases lovastatin's AUC)	Acceptable with appropriate dosing and monitoring Decrease in simvastatin AUC, so may need higher lovastatin starting dose No data on doravirine
Pitavastatin	Acceptable with appropriate dosing and monitoring No significant change in pitavastatin's AUC with lopinavir/ritonavir Pitavastatin's mean AUC decreased 26% with darunavir	No data for NNRTIs
Pravastatin	Acceptable with appropriate dosing and monitoring, except with darunavir Decrease in pravastatin's AUC, except with darunavir, which increases pravastatin's AUC by 81%	Acceptable with appropriate dosing and monitoring Efavirenz decreases pravastatin's AUC, but no change with etravirine No data for nevirapine, rilpivirine, doravirine May need higher pravastatin starting dose with efavirenz
Rosuvastatin	Use lowest rosuvastatin starting dose and titrate, monitor for safety, as risk for myopathy/rhabdomyolysis can be increased with some protease inhibitors Maximum dose of rosuvastatin is 10 mg with atazanavir, atazanavir/cobicistat, or atazanavir + ritonavir and 20 mg with darunavir/cobicistat Lopinavir/ritonavir and tipranavir + ritonavir increases rosuvastatin's AUC No dose adjustments with cobicistat; cobicistat increases Cmax 89% and AUC by 38%	Acceptable with appropriate dosing and monitoring No data on doravirine
Simvastatin	Contraindicated (greatly increase simvastatin's AUC)	Acceptable with appropriate dosing and monitoring Efavirenz and etravirine decrease simvastatin's AUC No data for nevirapine, doravirine May need higher simvastatin starting dose

Abbreviations: AUC, area under the curve; NNRTI, nonnucleoside reverse transcriptase inhibitor.

regardless of CVD risk or lipid levels. The strength of the benefit rises as the ACC/AHA pooled cohort equation score predicting 10-year risk of ASCVD events increases, with the number needed to treat to prevent a major event within 5 years decreasing from 130 and above for those with scores below 5% to 53 or lower for scores of 5% and above. Therefore, the recommendation for statin use is stronger for those with a 10-year ASCVD risk of 5% and higher. For those with lower scores, the benefit is still present but less pronounced. To decide on statin use in this population, additional risk factors, as described for the general population as well as risk-enhancing factors for people with HIV, should be considered. High-intensity statin therapy is recommended for those with risk greater than 20%, as for the general population, while at least moderate-intensity statin therapy is now recommended for those with lower risk. Additionally, statins may be considered in people with HIV who are younger than the REPRIEVE population (aged <40 years) with additional risk factors, including those with neonatal or pediatric acquired infection who are now adults with long-standing HIV, a population not included in the risk calculators. It is important to note that a slightly higher risk of diabetes was seen in REPRIEVE with pitavastatin than placebo (6.0% vs 4.7%, respectively), although at this time, it is unclear whether participants who developed incident diabetes in the study had pre-diabetes or were at high risk of diabetes at the time of enrollment in REPRIEVE. Treatment-limiting or grade 3 or higher muscle symptoms were seen in 2.3% of the pitavastatin group and 1.5% of the placebo group. Based on data from REPRIEVE, recommendations regarding statin therapy in people with HIV have been published by the HHS Adult and Adolescent Antiretroviral Guidelines Panel and a multisociety team that includes the ACC, AHA, and HIVMA [271].

Despite the fact that pitavastatin was used in REPRIEVE, it is likely that this preventive effect is generalizable across statins and that other statins can be used. High-intensity statins include atorvastatin 40–80 mg and rosuvastatin 20–40 mg, while moderate-intensity statins include pitavastatin 4 mg, atorvastatin 10–20 mg, and rosuvastatin 10 mg (all taken daily). Caution should be used, however, when prescribing statins with PIs (especially ritonavir), cobicistat, and some nonnucleoside reverse transcriptase inhibitors (NNRTIs) due to

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potentially serious drug–drug interactions (Table 7). Most PIs and cobicistat inhibit the metabolism of statins, thereby increasing the potential for statin toxicity, with the strongest interactions seen with simvastatin and lovastatin, which are contraindicated with ritonavir or cobicistat. However, pitavastatin and pravastatin are metabolized by glucuronidation, thereby having little effect when coadministered with a boosted PI or cobicistat. However, pravastatin may adversely interact with darunavir, and dose modification may be needed. In addition, atorvastatin and rosuvastatin may be used in patients who take a boosted PI or boosted elvitegravir but should be initiated at low doses and titrated carefully according to tolerability and effect. Efavirenz induces statin metabolism, resulting in lowering of statin levels. Nevirapine, etravirine, and rilpivirine have not been extensively studied. Doravirine does not affect levels of atorvastatin [272]. Cobicistat is expected to have interactions that are similar to those for ritonavir with statins; however, these interactions have not been fully studied. There may be other pathways that affect drug metabolism and lead to unexpected interactions, and it is advisable to refer to the package insert of the ARV or drug–drug interaction tables from the HHS ART guidelines before prescribing lipid-lowering agents.

Glucose Metabolism and Diabetes

Among people with HIV, HbA1c is insensitive, although highly specific for diagnosing diabetes. As such, HbA1c is no longer the preferred method for diagnosing diabetes among persons with HIV [273–276]. The ADA established the diagnostic criteria of diabetes mellitus as a fasting plasma glucose level of ≥126 mg/dL (7.0 mmol/L), a 2-hour plasma glucose level of ≥200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test conducted with a standard loading dose of 75 g, or an HbA1c ≥ 6.5% [273]. However, recognizing the potential underestimation of the risk of diabetes by using HbA1C in HIV, the National Health and Nutrition Examination Survey and others endorse an HbA1C cutoff of ≥5.8% to improve the sensitivity for diagnosis in the population with HIV [274]. Although data are lacking on the effects of integrase inhibitors on HbA1c, some studies, but not all, suggest that NNRTIs, PIs, and the NRTIs zidovudine and abacavir may affect HbA1c and result in misleading results [274, 275, 277]. The ADA 2019 Standards recommend against the use of HbA1c to diagnose diabetes in persons with HIV on ART and states that in cases of HbA1c and fasting glucose discordance, the abnormal laboratory test should be repeated, and the diagnosis of diabetes should be made only if repeat testing is again above the diagnostic cut point [273].

Random or fasting serum glucose and HbA1c should be obtained prior to starting ART. If random blood glucose is abnormal, fasting blood glucose should be obtained. After initiation of ART, only plasma glucose criteria should be used to diagnose diabetes. A random glucose >200 mg/dL should prompt further testing with a fasting blood glucose. Therefore, either a random or fasting glucose should be obtained at entry to care and annually thereafter for screening of diabetes. Patients with diabetes mellitus should have their HbA1c level monitored at least every 6 months, with a HbA1c goal of <7% in accordance with the ADA guidelines. Though controversial, the American College of Physicians recommends less stringent control, with an aim to achieve an HbA1c between 7% and 8% [278]. Given the potential for over- or underestimation of HbA1c in patients on ART, it is prudent to assess the correlation of blood glucose levels with HbA1c values on an individual basis in order to determine the appropriate HbA1c target.

Lifestyle interventions such as weight loss, increased physical activity, and dietary modification remain the cornerstone of diabetes prevention and management. However, if treatment is needed, insulin-sensitizing agents are preferred. Patients should be managed according to the ADA guidelines [273, 279]. No data suggest that switching ARVs is beneficial in patients with impaired glucose tolerance associated with HIV infection itself or traditional risk factors.

Weight and Fat Gain

Weight gain is a well-recognized consequence of ART initiation and is more common in non-White and female individuals [280]. Some regimens, namely integrase inhibitors and TAF, have been associated with larger gains in weight. However, it is presently unclear whether the regimens used as comparators suppress weight gain with ART initiation. For instance, TDF use has been associated with weight suppression in PrEP studies and in HIV treatment initiation studies. Also, when TDF is switched to TAF, an increase in weight of about 1 kg on average is seen in the initial 6–12 months after switch [281, 282]. Similarly, the ADVANCE study showed that efavirenz (EFV) led to smaller gains in weight when compared with dolutegravir, both given with TAF/FTC [283]. A substudy that assessed the genetic mutations that control EFV metabolism revealed that only slow metabolizers (high EFV blood level) had blunted weight gain, whereas fast metabolizers gained an amount of weight that was similar compared with those on dolutegravir [284]. These data suggest that the weight-suppressive effect of EFV may not be desirable and may signal toxic effects. TDF has been associated with mitochondrial dysfunction in subcutaneous adipose tissue, signaling the potential for adipose dysfunction with TDF [285]. As such, the weight-suppressive effect of TDF should not necessarily be viewed as desirable.

The weight gain seen with ART is concerning for patients and providers as studies have linked it to a higher incidence of diabetes [286] and hypertension [287]. There is also evidence of ectopic fat depositions in people with HIV, for example, in the liver and pericardium, which may be detrimental. The HIV provider who is treating a patient with large gains in weight after ART may contemplate switching ART. It is important to know that switches have not been successful at reversing

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weight gain [288, 289], including switches off of INSTIs, unless the switch is from INSTI to EFV. However, the EFV-linked weight suppressive effect is likely a toxic effect and should not be seen as desirable. A randomized, placebo-controlled switch study in virologically [290] suppressed individuals on BIC/TAF/FTC showed similar weight gain at 48 weeks after switching to islatravir/doravirine compared with continuing on BIC/TAF/FTC [291]. Discontinuation of TAF did not improve weight in the TANGO study, questioning the independent effect of TAF on weight [289]. The TAF-to-TDF switch effect, for the purpose of suppressing weight gain, is modest at best, could lead to adipose tissue dysfunction and mitochondrial toxicity, and thus is not recommended as a strategy to decrease weight [292]. The benefit of the modest effect on weight of TAF-to-TDF switch also needs to be weighed against the bone and renal toxicities of TDF. Switch studies from daily oral BIC/FTC/TAF to injectable cabotegravir/rilpivirine given every 2 months did not lead to a significant change in weight compared with continuation of the oral regimen, further evidence that TAF is not likely a culprit in weight gain [293]. Glucagon-like peptide (GLP)-1 receptor agonists for obesity should be reserved for select situations while awaiting results of ongoing trials among people with HIV.

All patients on ART should be routinely counseled on lifestyle modifications, including alcohol reduction/cessation, increased physical activity, healthier diet with reduction in saturated fat and added sugars, and increase in dietary fiber. Patients with large gains in weight may benefit from some of the new agents recommended for obesity in the general population, such as GLP-1 receptor agonists. Although there are few data on their use in people with HIV, a randomized controlled trial in people with lipohypertrophy (abdominal obesity) showed excellent safety and efficacy with decrease in weight and visceral and trunk fat [294].

Liver Steatosis

More data show that NAFLD is common in HIV, with prevalence ranging from 20% to 63%, even in people with HIV without HCV. Liver steatosis is linked to obesity and happens at lower body mass index (BMI) in the HIV population. NAFLD represents the most common cause of increased transaminases in people with HIV without excess alcohol or infectious hepatitis. NAFLD has been associated with older toxic ART such as didanosine or stavudine but not clearly with newer regimens. NAFLD can progress to NASH, liver cirrhosis, fibrosis, and ultimately cancer. NAFLD is also an independent risk factor for cardiovascular disease, diabetes mellitus, and all-cause mortality [295, 296]. Although NAFLD is known to be associated with obesity, HIV-associated NAFLD occurs at lower BMI than in the general population. Diagnosis of NAFLD may involve histology (liver biopsy) or imaging (ultrasound, CT scan, or MRI). Once NAFLD is identified, further workup should be performed to assess for fibrosis. Although biopsy remains the standard, newer modalities, including Fibroscan and MRI elastography, are increasingly used. In addition, clinicians have used soluble markers to estimate fibrosis, such as FIB-4, with low FIB-4 (<1.3) conferring a low likelihood of advanced fibrosis. Lifestyle modification and weight reduction are the cornerstone of treatment. Pharmacotherapy should be reserved for individuals with NASH, particularly for those with significant fibrosis ≥ F2 or individuals with less severe disease but at high risk of faster disease progression, such as persons with diabetes. Promising investigational therapies for HIV-associated NAFLD include tesamorelin [297] and GLP-1 receptor agonists [298].

Bone Metabolism

Baseline bone densitometry by DEXA should be performed in all post-menopausal cisgender women and men aged ≥50 years, based on expert opinion with limited supporting evidence [299–304]. If DEXA scan reveals osteopenia or osteoporosis, a workup for secondary causes of osteopenia should be performed. The most common secondary causes of osteopenia are vitamin D deficiency, hypogonadism, excess alcohol (>3 drinks/day), smoking, and hyperthyroidism or hyperparathyroidism. The initiation of any ART regimen leads to a decrease in BMD of 2%–6%, and the decrease is more prominent in the first 24–48 weeks of ART. Among all ART, TDF has been shown to lead to a 1%–2% larger decrease in BMD when compared with any other non-TDF regimen, including TAF [305, 306]. When TDF is combined with ritonavir-boosted PI, bone loss is even more accentuated than when combined with unboosted integrase inhibitors [307, 308]. If the DEXA demonstrates osteoporosis or there is a history of fragility fracture, intervention with vitamin D, calcium, and a bisphosphonate or other medical therapy may be warranted. Bisphosphonates appear to be safe and effective in improving BMD [309] and in blunting the initial drop in BMD after ART initiation [310]. It is important to exclude osteomalacia prior to initiating a bisphosphonate, as this could lead to increased fragility and fracture. Common reasons for osteomalacia in this population are tenofovir-induced renal phosphate wasting and vitamin D deficiency, which have been reported in 40%–80% of people with HIV. The spectrum and severity of metabolic complications associated with vitamin D deficiency among adults with HIV remain to be better characterized. Patients with vitamin D deficiency and osteopenia by DEXA should be treated with vitamin D and calcium without bisphosphonates until the vitamin D deficiency has resolved. A follow-up DEXA should be repeated 1 year later to monitor the response to therapy. It is now clear that switching off of TDF to another NRTI or to an NRTI-sparing regimen is effective at increasing BMD and should be considered [311, 312].

Routine screening for vitamin D deficiency in patients with normal or unavailable DEXA is not recommended, given the

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lack of data among people with HIV. The USPSTF concludes that the evidence on screening for vitamin D deficiency in asymptomatic adults to improve health outcomes is insufficient [313]. However, patients should be counseled about the health benefits of regular exercise, with resistance exercise being especially important to bone building, normal dietary calcium, and vitamin D intake and the harmful risks of cigarette smoking and excessive alcohol consumption.

In people with HIV, avascular necrosis (AVN) was reported to be associated with exposure to tenofovir for longer than 1 year in one study [314]. Other more common causes of AVN include moderate to high alcohol consumption, hyperlipidemia, and corticosteroid use [314, 315]. Routine radiographic monitoring for AVN in asymptomatic persons is not recommended. However, for patients who present with persistent hip pain who have normal standard radiologic studies, MRI is the preferred method of diagnosis, and both sides should be imaged regardless of whether pain is bilateral or not. Most patients with symptomatic AVN will ultimately require surgical intervention, including hip replacement [315, 316].

Hypogonadism

The prevalence of hypogonadism among cisgender men with HIV has been reported to be high prior to the introduction of ART. However, screening for hypogonadism is recommended only for men who have symptoms [317, 318]. In 2014, the FDA released safety alerts that warned of potential increased cardiac risk associated with testosterone replacement products [319–321]. Subsequently, a large systematic review and meta-analysis failed to demonstrate an increased risk of cardiac events in the general population; however, caution remains [322]. Although the Endocrine Society Guidelines [323] recommend short-term testosterone replacement therapy (TRT) for cisgender men with HIV and low testosterone, many patients have remained on TRT long term. It is unclear whether those who were diagnosed with hypogonadism at the time of their HIV diagnosis need to remain on TRT after immune recovery on ART. Since the FDA advisory, the overall percentage of cisgender men who use TRT has declined, but less so among those with HIV [324, 325]. As the population of men with HIV ages, clinicians should balance the benefits against the harms of continuing TRT that may no longer be indicated. TRT may result in testicular atrophy and permanent inability to produce the natural hormone. Men may experience "withdrawal" when TRT is stopped, given the steroidal effects of testosterone as well. Therefore, initial TRT should be prescribed with caution and only in cisgender men with symptomatic hypogonadism, given the long-term side effects.

Neurocognitive Impairment

Neurocognitive impairment is more common in older people with HIV than those not living with HIV [326]. HIV-associated neurocognitive disorder (HAND) encompasses multiple neurocognitive effects of HIV and associated inflammation on the central nervous system, resulting in deficits that range from asymptomatic neurocognitive impairment to dementia [327]. While there are no specific treatments for HAND at this time, clinicians should be aware that some persons with HIV may experience neurocognitive decline that is out of proportion to their age and should provide an appropriate workup when such symptoms present.

Frailty

People with HIV are disproportionately affected by frailty and at a younger age than those without HIV [328]. Prevalence of frailty and prefrailty in people with HIV aged >50 years is about 11% and 47%, respectively [329]. Frailty is a strong predictor of both mortality and incident comorbidity in people with HIV, independent of other risk factors [330]. Annual screening for frailty should be considered in people with HIV aged >50 years. The most commonly used screening tools include the frailty phenotype [331] and the frailty index [332], with the former being simpler and more commonly recommended, although it requires a dynamometer. HIV virologic suppression decreases the risk of frailty [333]. The most effective interventions to prevent and treat frailty are increasing physical activity and structured exercise [334]. Nutritional optimization is effective and increases the efficacy of an exercise intervention [334]. Diagnosing and treating concomitant depression is also paramount. There are no data yet to recommend pharmacologic interventions for HIV frailty.

SECTION 8: SPECIAL CONSIDERATIONS FOR INDIVIDUALS OF CHILDBEARING POTENTIAL AND FOR PREVENTION OF PERINATAL HIV TRANSMISSION

People with HIV who are of childbearing potential are living long, healthy lives, and the need for routine gynecological care has increased. They have the same reproductive health needs and concerns as those not living with HIV. As part of the initial assessment, a comprehensive gynecologic and obstetrical history should be obtained that consists of menstrual history, sexual practices, hormonal therapy history and current use, male or female condom use and consistency of use, previous STIs and other genital tract infections, prior abnormal Pap test results including subsequent evaluation and treatment, pregnancy history, history of gynecologic conditions (including uterine fibroids, endometriosis, and infertility) or surgery (including gender reassignment surgery), and current gynecologic symptoms (including abnormal vaginal discharge, abnormal vaginal bleeding, amenorrhea, and pelvic pain). Recommendations for care during menopause do not differ from those for persons not diagnosed with HIV.

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Contraception and Prepregnancy Care

Recommendation

- All persons with HIV who are of childbearing potential should be asked about their plans and desires regarding pregnancy upon initiation of care and routinely thereafter. Clinicians should ensure that informed decisions are made about contraception to prevent unintended pregnancy and offer counseling if pregnancy is desired. Counseling should include considerations for the choices of ART and infant feeding methods.

Evidence Summary

Any encounter with a nonpregnant patient with reproductive potential is an opportunity to counsel about wellness and healthy habits that may improve reproductive and obstetrical outcomes if the patient decides to reproduce [335]. An in-depth discussion about childbearing is indicated if the patient expresses the desire for future pregnancy, is not trying to conceive but is not using appropriate contraception, or expresses uncertainty about reproductive plans. Regardless of the patient's sex, the goal is to ensure that informed decisions are made about contraception with prevention of an unintended pregnancy and to offer counseling if pregnancy is desired. Patients should explicitly be asked to communicate with their provider if their plans change, when they are ready to consider pregnancy, or when they have questions related to reproduction and parenthood. In persons who are at risk for pregnancy (trying to conceive or not using effective and consistent contraception), providers should carefully review all medications, including over-the-counter medications, and avoid drugs with potential reproductive toxicity. The time of greatest risk to the fetus is early in pregnancy, often before the pregnancy has been recognized. Ideally, a prenatal vitamin with folic acid should be prescribed prior to conception. Choice of ART for use during pregnancy and breast/chest feeding is discussed in detail in HHS perinatal guidelines [120].

Individuals who do not wish to become pregnant should be counseled on effective contraception. Combined estrogen–progestin hormonal contraceptives (birth control pill, transdermal patch, and vaginal ring) are one option; however, they may have interactions with several ARVs, resulting in decreased effectiveness or increased risk of adverse effects. Contraceptive implants, injectable contraception (depot medroxyprogesterone acetate), and intrauterine devices are other available options. Spermicides have been associated with an increased risk of HIV acquisition and are not recommended for use with partners who are not diagnosed with HIV [336].

Providers should be prepared to discuss conception among serodifferent couples. The partner with HIV should always be started/continued on ART and achieve/maintain sustained HIV RNA suppression to below the limits of detection prior to beginning efforts to conceive. With durable viral suppression, there is effectively no risk of sexual transmission. For couples that are using condoms and wish to limit their episodes of condomless sex, a discussion about sex during the time of peak fertility is appropriate. Prepregnancy administration of ARV PrEP for the partner not diagnosed with HIV offers an additional means to reduce the risk of sexual transmission [336].

Prevention of Perinatal Transmission

Recommendations

- To prevent perinatal transmission, all pregnant and breast-/chest-feeding persons with HIV should be treated with ART, regardless of their immunologic or virologic status. Therapy should be initiated as early as possible, preferably prior to conception.
- Infants exposed to HIV in utero should be managed according to HHS perinatal guidelines.

Evidence Summary

Perinatal transmission of HIV is preventable if pregnant persons are screened for HIV and, if diagnosed with HIV, receive immediate ART according to HHS perinatal guidelines [120, 337]. If HIV status is unknown, pregnant people should be tested for HIV at the first antenatal visit and again in the third trimester if there is ongoing risk of exposure to HIV. In those who start ART before conception and maintain viral load suppression <50 copies/mL, there is essentially zero risk of perinatal transmission [120, 337].

If an individual in labor presents for delivery without having antenatal HIV testing, an expedited HIV test (preferably fourth-generation HIV antigen/antibody testing) should be performed. If the test is positive, intravenous zidovudine should be initiated immediately without waiting for confirmatory tests [120]. Persons who are pregnant and who have an HIV viral load that is unknown or >1000 copies/mL at or near delivery (within 4 weeks), independent of antepartum ART, should be counseled regarding the potential benefit of cesarean delivery. If the patient consents, a scheduled cesarean delivery at 38 weeks' gestation should be offered to reduce the risk of perinatal transmission [120]. All newborns who were exposed perinatally to HIV should receive postpartum ARV drugs to reduce the risk of perinatal transmission of HIV. Post-exposure prophylaxis in the neonate should be initiated ideally within 6 hours [120]. A newborn's ARV regimen should be determined by maternal HIV transmission risk factors according to the perinatal guidelines. Providers with questions about ARV management of perinatal HIV exposure should consult an expert in pediatric HIV infection or the Perinatal HIV/AIDS National Clinician Consultation Center hotline [338].

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Infant Feeding

Recommendations

- In the United States, persons with HIV should receive evidence-based, patient-centered counseling to support shared decision-making about infant feeding.
- Individuals with HIV who are on ART with a sustained undetectable viral load and who choose to breast/chest feed should be supported in their decision.
- Engaging Child Protective Services is not an appropriate response to the choice of infant feeding for individuals with HIV.

Evidence Summary

Counseling about infant feeding should begin prior to conception or as early as possible in pregnancy and should be repeated throughout pregnancy and again after delivery [120]. Choosing a method of feeding for a baby is one of the most important decisions a new parent makes. The decision can be compounded by mixed messages from providers who are uncomfortable talking about infant feeding for people with HIV. With current ART, rates of HIV transmission through breast/chest feeding are low but not zero. Currently, there is no consensus on a universal approach, and diverse strategies are used for HIV RNA monitoring for the breast-/chest-feeding parents, infant HIV testing, and ARV prophylaxis [120, 339]. Individuals with HIV who choose to formula feed should be supported in this decision. Providers should ask about potential barriers to formula feeding and explore ways to address them. Replacement feeding with formula or banked pasteurized donor human milk is recommended to eliminate the risk of HIV transmission through breast/chest feeding when people with HIV are not on ART and/or do not have a suppressed viral load during pregnancy (at a minimum throughout the third trimester), as well as at delivery. Engaging Child Protective Services or similar agencies is not an appropriate response to the infant feeding choices of an individual with HIV.

SECTION 9: SPECIAL CONSIDERATIONS FOR CHILDREN

Recommendations

- A plasma HIV NAAT (HIV RNA or HIV DNA) is equally recommended to diagnose HIV in infants and children aged <18 months with perinatal and post-natal HIV exposure.
- In infants with perinatal and post-natal HIV exposure, the results of a plasma HIV NAAT can be affected by maternal ART or by ARV drugs administered to the infant as prophylaxis or presumptive HIV therapy.
- For children aged 18 to ≤24 months with nonperinatal HIV exposure and for all children aged >24 months, HIV antibody or HIV antigen/antibody tests are recommended for diagnostic testing.
- Infants and children diagnosed with HIV should be started on ART immediately or within days of diagnosis. The urgency of Rapid ART initiation is especially critical for children aged <1 year who carry the highest risk of rapid disease progression and mortality.
- In children with disseminated *Mycobacterium avium* complex disease, *M. tuberculosis* disease, and cryptococcal meningitis, ART initiation may be delayed by 2–8 weeks with treatment for the OI prioritized. Appropriate timing of ART initiation in these cases should be discussed with a pediatric HIV specialist.
- If a child with HIV has not initiated ART, healthcare providers should closely monitor the virologic, immunologic, and clinical status at least every 3–4 months while continuing to educate and work with the family to overcome barriers to treatment.
- Absolute CD4 cell count (or CD4 percentage in children aged <5 years) and HIV RNA levels should be evaluated at the time of diagnosis and should be monitored at least every 3–4 months in infants and children. Close follow-up also allows for timely weight-based ART dose adjustment in infants and young children.
- Childhood vaccinations should be administered according to ACIP schedules for infants and children with HIV.
- Infants and children with HIV should be managed by a specialist with knowledge of the unique therapeutic, pharmacologic, behavioral, psychosocial, and developmental issues associated with pediatric HIV infection.

Evidence Summary

Most pediatric HIV infections are caused by perinatal transmission of the virus from the mother during pregnancy, delivery, or breastfeeding. The racial and ethnic disparities in the HIV epidemic among adults in the United States are, therefore, mirrored in pediatric populations. The rate of acquisition of HIV infection among infants has decreased significantly in the United States, primarily because of effective measures to prevent mother-to-child transmission of HIV. Between 2010 and 2019, annual perinatal HIV diagnosis rates declined from 1.9 to 0.9 per 100 000 live births, and perinatal HIV transmission rates declined from 1.6% to 0.9%. National elimination goals for diagnosis and transmission rate of perinatal HIV were first achieved in 2019. However, perinatal transmission of HIV still occurs, and racial and ethnic disparities persist, requiring ongoing public health investment and efforts [340]. Other routes of HIV transmission in children include feeding blood-tinged premasticated food, contact of nonintact skin with blood-containing body fluid, transfusion of contaminated blood products, and sexual abuse. These scenarios should prompt testing of the child for HIV infection. HIV testing should also

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be conducted among all children in foster care and those who were adopted domestically (if unknown exposure or at risk for acquiring HIV) and internationally (since perinatal HIV screening is variable in global settings) [341]. Children with HIV are frequently born outside the United States, including adopted children and members of immigrant families. These children may have non-B subtypes of HIV, incomplete medical and treatment histories, and an increased risk of tuberculosis and other infections.

Neonates and infants (including breastfed infants) who are exposed to HIV perinatally or postpartum should be managed according to HHS perinatal and pediatric guidelines [91]. Plasma HIV RNA and HIV DNA NAATs are equally recommended for diagnosis of HIV in infants aged <18 months. However, both tests can be affected by maternal ART through transplacental transfer of ARV drugs from the mother to the fetus or by ARV drugs administered to the infant as prophylaxis or presumptive HIV therapy. Qualitative whole blood HIV proviral DNA PCR assays to detect cell-associated virus are less affected by ARV drugs [120]. For children aged 18 to ≤24 months with nonperinatal HIV exposure and for all children aged >24 months, HIV antibody or HIV antigen/antibody tests are used for diagnostic testing. For suspected acute HIV infection, an additional HIV NAAT may be necessary to diagnose HIV infection.

All infants and children diagnosed with HIV should be started on ART as soon after diagnosis as possible (immediately or within days) using regimens based on pediatric HHS guidelines [91]. Multiple studies have reported that early ART initiation in infants and children preserves immune function and is associated with improved growth and neurodevelopmental outcomes [342–344]. In infants with perinatally acquired infection, early ART initiation may limit the formation of the viral reservoir and control of viral replication before HIV can evolve into diverse and potentially more pathogenic and/or resistant quasi-species, preserve immune function, prevent clinical disease progression, and improve neurodevelopmental outcomes. Early initiation of suppressive ART in infants aged <6 months results in a considerable proportion of infants with HIV who fail to produce their own HIV-specific antibodies. These infants are HIV-seronegative when tested; however, viral reservoirs remain, and viral rebound occurs if ART is stopped [342–344]. It is, therefore, important to educate the caregiver on the importance of continuing consistent ART without treatment interruptions.

Genotypic resistance testing should be performed at the time of diagnosis; however, ART can be initiated before results are available. All infants should receive *Pneumocystis jirovecii* prophylaxis in the first year of life, irrespective of CD4 cell count or percentage [110]. In general, infants with untreated perinatally acquired HIV have higher viral loads than adults, and there are age-specific differences in CD4 cell counts, with infants having higher normal absolute lymphocyte counts than adults. In young children (aged <5 years), CD4 percentages are less variable than absolute counts [345]. Infants and children with undiagnosed HIV are likely to present with unexplained fevers, hepatosplenomegaly, generalized lymphadenopathy, parotitis, persistent oral and diaper candidiasis, recurrent invasive bacterial infections, recurrent diarrhea, failure to thrive, central nervous system diseases, and delays in growth and development [346].

While initiating and managing pediatric ART, it is essential to understand that achieving consistent adherence in children is often challenging. Intensive adherence counseling and follow-up during the first few weeks to months after ART initiation is recommended to support the child and caregiver, including detailed instructions on the administration of ARV drugs and caregiver treatment literacy [91]. After initiation of ART or after a change in ARV regimen, children should be followed up in 1–2 weeks to assess effectiveness, tolerability, and adverse events and to evaluate and support medication adherence. Head circumference should be measured in children aged <3 years and plotted against standard growth curves. Furthermore, developmental assessment is important in infants and children. Laboratory testing for toxicity and viral load response is recommended at 2–4 weeks after treatment initiation or change in ARV regimen. Clinicians and multidisciplinary teams should schedule frequent clinical in-person and/or telemedicine visits to monitor patients closely during the first few months after initiating a new ART regimen. For infants, more frequent clinical visits are required to ensure that growth and development are on schedule, that appropriate adjustments of dosage are made, and that the infant is tolerating ART. CD4 cell count can be monitored less frequently (every 6–12 months) in children who are adherent to therapy, who have sustained virologic suppression and CD4 cell count values that are well above the threshold for OI risk, and who have stable clinical status [91]. Viral load measurement every 3–4 months is recommended to monitor ART adherence.

Caregivers, families, and children with HIV face a wide array of socioeconomic, educational, legal, immigration, and structural challenges that affect adherence and retention in care and require ongoing case management support to achieve and sustain positive HIV disease, health, and developmental outcomes. Disclosure of HIV status to children with perinatally acquired HIV is an emotionally and socially complex process that requires caregiver and child support. Studies suggest that disclosure of perinatal HIV status can increase self-esteem and adherence to ART and improve access to psychosocial support [347–350].

All recommended childhood immunizations should be administered to infants exposed to HIV. If HIV infection is confirmed, immunologic status (CD4 cell count or percentage) should be assessed, and guidelines for the immunizations of

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the child with HIV should be followed [156, 346]. Children with HIV should be immunized with all age-appropriate inactivated vaccines. Inactivated influenza vaccine should be administered annually according to the most current recommendations. In general, the administration of live vaccines, such as MMR and varicella, is guided by the CD4 cell count or percentage. Rotavirus vaccine, however, should be administered to infants with HIV or exposed to HIV irrespective of CD4 cell count or percentage [346].

In the era of ART, there has been a substantial decrease in frequency of OIs and malignancies in children [346]. Prevention and treatment of OIs in children should be managed according to the HHS pediatric OI guidelines [110]. Leiomyosarcomas and non-Hodgkin B-cell lymphomas of the Burkitt type (including those in the central nervous system) occur more frequently in children with HIV than in immunocompetent children. Kaposi sarcoma, caused by human herpesvirus 8, is rare in children in the United States but has been documented in children with HIV who have emigrated from sub-Saharan African countries.

SECTION 10: SPECIAL CONSIDERATIONS FOR ADOLESCENTS

Recommendations

- Adolescents with HIV require an individual and developmentally guided approach to therapy and care, ideally through an HIV specialist and team with expertise in this population.
- Adolescents with HIV should be counseled about preventative measures, including smoking cessation, alcohol and other substance use prevention, gender, and sexual health, including safer sex practices, to prevent development of comorbidities.
- Screening for early detection and management of comorbidities should be considered for adolescents with HIV.
- Vaccinations should be administered according to ACIP schedules for children with HIV, including ensuring catch-up vaccinations, if applicable, and administration of vaccines that prevent comorbidities, if applicable.
- Adolescents with HIV should have a coordinated, deliberate transition to adult care, with an emphasis on supporting their capacity for self-care including, but not limited to, retention, adherence to care, medical literacy, and engagement in mental health and substance use treatment.

Evidence Summary

The care of adolescents with HIV, whether perinatally or nonperinatally acquired, presents many challenges [347, 348, 351]. The median age of the US cohort of children who acquired HIV early in life, primarily via perinatal transmission, is now mid to late teens, and many have reached adulthood [352, 353] with varying degrees of health. Youth with HIV, in addition to the biological and psychosocial changes that normally occur in adolescence, often cope with stigma, disclosure, loss of family members, and negotiation of sexual activity. In many studies, rates of cognitive, psychiatric, and behavioral problems are higher in those with perinatally acquired infection [354, 355]. As a result of these challenges, many youths with perinatally acquired infection have poorer adherence to ART and may experience decreased engagement in care compared to with other populations [347]. Disclosure for this population is complicated as it includes becoming aware of one's own diagnosis and the subsequent self-disclosure of one's diagnosis to others (eg, sexual partners). While disclosure of diagnosis by the caregiver to the child or adolescent can be overwhelming to caregivers, it should occur by late childhood and prior to adolescence, as it has been correlated with better adjustment to illness, lower rates of depression, and improved adherence with care and ART [91, 348, 351]. Support should be provided for both types of disclosure. Screening for and addressing mental health challenges and concerns is an important part of caring for this population.

Puberty may affect drug metabolism, underscoring the importance of adolescent-specific studies. Decisions regarding dosing should take into consideration sexual maturity, with those with a sexual maturity rating ≥4 being dosed according to adult treatment guidelines. This is becoming less relevant because weight-based dosing is becoming the standard of care. Special attention should be paid to attaining and maintaining viral suppression, along with risk reduction counseling, STI and pregnancy prevention, and secondary HIV prevention in early or later adolescence [356, 357].

Long-term treatment, which may result in treatment fatigue, viral resistance due to suboptimal adherence or good adherence to suboptimal regimens, or potential end-organ toxicity, therefore, requires monitoring [358]. Early-acquired HIV, particularly in the setting of suboptimal viral suppression, can result in chronic immune activation and inflammation, which leads to noncommunicable disease comorbidities (eg, metabolic syndrome, dyslipidemia, chronic kidney disease, obesity, bone disease, atherosclerotic vascular disease, and cardiopulmonary abnormalities) [352, 358–361]. This risk is compounded by modifiable risk factors, particularly smoking/vaping and poor diet, which often begin during adolescence. Caring for youths with early-acquired HIV necessitates a life course approach with counseling regarding modifiable risk factors; prevention, including smoking cessation, dietary modification, and vaccination against preventable conditions; and screening for and early management of comorbidities [362, 363].

Youth who acquired HIV through sexual activity or injection drug use, in addition to the biological and psychosocial changes that normally occur in adolescence, have issues that are similar to those for adults, including high rates of substance use; STIs;

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mental health comorbidities such as depression, anxiety, and PTSD [352]; and social determinants that may present barriers to care [7]. Sexual and gender identity and sexual behaviors should be discussed in a nonjudgmental manner in order to understand sexual risk and diminish stigma [364]. Multidisciplinary teams that simultaneously address biological and psychosocial issues are critical in optimizing outcomes, including early initiation of therapy and adherence support to maximize immune recovery and health and minimize transmission risk [365, 366]. ART should be prescribed according to established adult and adolescent treatment guidelines [7] (see also Section 1: Optimizing Care).

The transition of adolescents from pediatric to adult care usually occurs between the ages of 18 and 25 years and is impacted by variable factors, from patient preference to availability of providers and system/clinic rules. Youths are at high risk of falling out of care and experiencing poor clinical outcomes during this transition period [367, 368]. The transition of care from pediatric or adolescent providers to adult providers should be a deliberate, comprehensive, and coordinated multidisciplinary youth-friendly process that involves the healthcare team and the patient [369–371]. Care must be given to synergistically attend to the diverse needs of the adolescent that extend beyond medical care, including employment, independent living, and intimate relationships. Over time, youths must learn to negotiate the healthcare system and assume increasing responsibility for their healthcare. There are several resources on best practices for transitioning youths with HIV to adult care [7, 372–375].

SECTION 11: CONSIDERATIONS FOR TRANSGENDER AND GENDER-DIVERSE ADULTS

Recommendations

- Transgender and gender-diverse persons with HIV should have access to care that is gender-affirming, nondiscriminatory, nonstigmatizing, and culturally sensitive.
- Intake forms, medical records, and other documentation should include gender identity options in addition to sex assigned at birth, chosen name and pronouns, and legal name.
- Transgender persons should be offered medically necessary gender-affirming interventions in accordance with national guidelines.
- HIV care providers should be familiar with gender-affirming hormone treatment and necessary clinical and laboratory monitoring or provide referral to a clinician or endocrinologist experienced in transgender care.

Evidence Summary

Transgender people identify with a gender that differs from their sex assigned at birth. Recent data estimate that approximately 1.3 million adults in the United States identify as transgender or gender diverse [376]. It is important to use the appropriate terminology when talking with and about transgender persons. Many terms are used and often are confused with each other or used incorrectly (Table 8). Gender dysphoria refers to the discomfort that some transgender people may experience due to the discrepancy between their gender identity and sex assigned at birth. Some individuals opt for medical interventions, such as the use of gender-affirming hormones and surgeries, to align their physical characteristics with their gender identity.

Table 8. Terminology Associated With Gender Identity and Hormonal Therapy

Gender identity: An individual's sense of being male, female, nonbinary, agender, etc.
Transgender, trans, nonbinary, gender diverse: Adjectives used to refer to persons whose gender identity does not align with their sex recorded at birth (the latter primarily based on visible physical anatomy)
Nonbinary: An adjective used to refer to persons whose gender identity is outside the gender binary, that is, do not identify exclusively as a man or a woman; some nonbinary persons may not identify with any gender (agender)
Cisgender: An adjective used to refer to people whose gender identity corresponds to the sex they were assigned at birth
Gender expression: How a person communicates their gender through appearance, dress, name, pronouns, mannerisms, and speech
Gender-affirming hormone treatment and surgeries: Broad categories of medical interventions that transgender persons might consider to align their appearance and their gender identity
Gender affirmation: An overall process of alignment of physical characteristics and/or gender expression with gender identity
Gender dysphoria: Discomfort felt by some persons due to lack of alignment between gender identity and the sex recorded at birth; not all transgender persons have dysphoria, but many US insurance companies require this diagnosis for payment for gender-affirming medical and surgical interventions
Feminizing hormone therapy: The use of estrogens and often androgen blockers with the objective of inducing changes in physical characteristics to better match patient gender identity
Masculinizing hormone therapy: The use of testosterone with the objective of inducing changes in physical characteristics to better match patient gender identity
Sex assigned at birth: Refers to a person's status as male, female, or intersex based on physical characteristics at birth

Stigma and discrimination are serious issues that threaten the quality of care for transgender and gender-diverse persons, regardless of HIV status. Nearly half of transgender persons face family rejection, 40% report a history of attempted suicide, 29% live in poverty, 30% have experienced homelessness, 33% have experienced discrimination within the healthcare system, and 23% avoid the healthcare system due to fear of discrimination [377]. Global estimates show a pooled HIV prevalence of 19.9% (95% CI, 14.7%–25.1%) among transgender women, with 66-fold higher odds of HIV prevalence than the general population [378]. Data among transgender men are limited, but estimated HIV prevalence is 2.56% (95% CI, .0%–5.9%) [378]. Given the disproportionate impact of HIV on transgender individuals and the psychosocial barriers they face, health systems and healthcare providers should strive to create more

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welcoming, affirming, and trauma-informed clinical environments. Clinic intake and registration forms should allow selection of gender identity in addition to assigned sex at birth [379]. Patients should be addressed using their chosen name (when different from legal name) and pronouns. Additionally, educational and health promotional materials designed for transgender individuals create a better sense of inclusion. Staff should undergo training on gender diversity and delivery of culturally competent and sensitive care. This comprehensive approach by all staff may facilitate patient empowerment, care engagement, and viral suppression [380, 381].

Gender-affirming hormone therapy (GAHT) is safe when provided under medical supervision. This care is often provided by primary care providers and HIV specialists who have received training, including informally, through mentorship or continuing medical education [224]. HIV care providers should be familiar with gender-affirming hormone treatment and necessary clinical and laboratory monitoring or provide referral to a medical provider or endocrinologist experienced in transgender care. Persons should be offered GAHT in accordance with established clinical practice guidelines, such as those published by the Endocrine Society [382] and the World Professional Association for Transgender Health [224]. Before initiating gender-affirming medical therapy for adult patients, the clinician should ascertain that the patient's gender identity is persistent and that they have the capacity to consent to treatment. The clinician should review expectations in terms of the timeline for changes and types of changes associated with hormone therapy, as well as a balanced risk assessment of those therapies. Prior to initiating hormone therapy or undergoing gonadectomy, clinicians should discuss parenthood goals, the impact of these interventions on fertility, and available options for sperm or oocyte preservation [224]. Some payers may require an assessment and referral letter from a mental health professional prior to gender-affirming medical interventions.

Feminizing hormone regimens typically use estrogen and antiandrogen medications, such as spironolactone. In 3–6 months, patients may start to experience breast growth, decreased muscle mass, softer skin, redistribution of body fat, and fewer spontaneous erections [224]. Transgender individuals who receive estrogen therapy may be at increased risk of hypertriglyceridemia, venous thromboembolism (VTE), and cardiovascular disease. Transdermal estrogen formulations may pose lower risk of thrombosis and are preferred for those aged >45 years, with a history of VTE, or with known risk factors for cardiovascular disease [224]. Oral conjugated estrogen formulations and ethinyl estradiol are not recommended due to an increased risk of thromboembolic events [224]. Smoking cessation should be encouraged. Clinical evaluations with laboratory monitoring of serum estradiol and testosterone should occur every 3 months for the first year and once to twice per year thereafter, with potassium monitoring at the same intervals for those on spironolactone. Target levels for individuals receiving feminizing GAHT are serum total testosterone <50 ng/dL and serum estradiol approximately 100–200 pg/mL [224].

For masculinizing hormone therapy, testosterone remains the mainstay treatment. Results, including cessation of menses, deepening of voice, increased muscle mass, and facial hair, typically start within 3–6 months [224]. Androgen therapy may result in erythrocytosis, increases in LDL cholesterol, and increases in serum creatinine [224, 383]. After initiating testosterone therapy, hemoglobin/hematocrit and serum testosterone should be measured every 3 months for the first year and 1–2 times per year thereafter. The serum total testosterone level should be maintained in the normal physiologic cisgender male range of 400 to 700 ng/dL [224].

Several ARV regimens, including NRTIs, unboosted INSTIs, rilpivirine, and doravirine, are not anticipated to impact GAHT and require no additional monitoring [384, 385]. Estradiol levels may be decreased by the NNRTIs efavirenz, etravirine, and nevirapine. Ritonavir-boosted PIs may increase or decrease estradiol levels, while cobicistat-boosted PIs may increase estradiol [386]. Testosterone levels are increased by boosted PIs and elvitegravir/cobicistat and decreased by efavirenz, etravirine, and nevirapine [386]. When pharmacokinetic interactions are anticipated, clinicians should monitor clinical effects as well as serum hormone concentrations and adjust hormone doses as needed. It is important to provide patients with accurate information on drug–drug interactions between their ART and hormone therapy, including the lack of deleterious effects on hormone therapy, and to make dose adjustments as appropriate. Lack of communication around this concern may contribute to fear of drug–drug interactions and poor adherence to one therapy or the other [387].

SECTION 12: COVID-19 AND HIV

People with HIV have been impacted by SARS-CoV-2 infection (COVID-19) since the early days of the pandemic. Early on, the presumption was that people with HIV would fare poorly due to damaged immune systems, but that has not necessarily proven to be the case. This section discusses the interaction of COVID-19 and HIV only. IDSA has excellent living guidelines for COVID-19 management and treatment for the general population [388]. The best protections against COVID-19 for people with HIV are up-to-date vaccinations and good health hygiene and safety. It is important for providers to remember that HIV care should not be disrupted simply due to COVID-19. In fact, aiming for viral suppression and maximization of CD4 count is recommended to prevent more severe COVID-19 infections [389, 390]. Early in the pandemic, and even 1 year after general quarantines ended, access to HIV care was limited, and many people with HIV had disruptions in HIV

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care, including refills of ART, disease monitoring, provider visits, and laboratory testing [390, 391]. Providers who care for people who are more severely immunocompromised (CD4 <200 cells/μL) should ensure that their office is safe for people with HIV. The CDC guidelines should be consulted for the latest healthcare facility guidelines[392].

Recommendations

- CD4 count and viral suppression should be maximized to lower risk for COVID.
- Weight loss should be encouraged because obesity is a significant risk factor for severe COVID-19 infection.
- Pulmonary comorbidities should be treated to maximize protection against severe COVID-19 infection.
- It is important to ensure that patients with more advanced HIV are fully vaccinated, including vaccines targeted to newer SARS-CoV-2 variants, and to use mRNA vaccines when possible (see Section 4).
- There is no evidence that people with HIV and COVID-19 require a change to their ART simply due to presence of COVID-19 coinfection.
- HIV is not a contraindication to COVID-19 vaccination, and COVID-19 vaccination does not impact HIV viremia.
- Treatment recommendations for COVID-19 in people with HIV are the same as for people without HIV, and treatment recommendations do not change by HIV viral load or CD4 cell count.
- Treatment of COVID-19 is not changed by HIV infection, and ART is not changed due to treatment for COVID-19.
- Dexamethasone and other corticosteroids should not be used in the outpatient setting when caring for people with HIV who have COVID-19 in the absence of other indications.
- It is important to be cognizant of significant drug–drug interactions with ritonavir-boosted nirmatrelvir and all medications and supplements. Antiretroviral therapy does not require dose adjustments in this setting.
- Previously disproven COVID-19 treatment should not be used for people with HIV, including ivermectin and sotrovimab in the outpatient setting.
- Because people with HIV may be at increased risk of PCCs, ask about PCC-related symptoms among people with HIV who are post-30 days from COVID-19 diagnosis.

Evidence Summary

People with HIV are at increased risk of acquiring SARS-CoV-2 infection and possibly of becoming reinfected with SARS-CoV-2, with risk inversely proportional to CD4 cell count, especially if CD4 count is <200 cells/μL [180, 393–395]. In multiple studies, it was found that a CD4 count <200 cells/μL was associated with increased mortality, while CD4 <350 cells/μL was associated with an increased risk of hospitalization [393, 396]. People with HIV should be on ART and aim for CD4 count >200 cells/μL but ideally >350 cells/μL. This is especially important for decreasing the risk of hospitalization or more severe COVID-19 infection [393]. Additional evidence suggests that all persons (regardless of HIV status) would benefit from weight loss, as obesity is associated with more severe COVID-19 infection [397]. Data also suggest that a higher risk for more severe COVID-19 is associated with cirrhosis, alcoholic hepatitis, chronic kidney disease, diabetes mellitus, and smoking [395]. Further, chronic pulmonary disease, specifically bronchiectasis, chronic obstructive pulmonary disease, interstitial lung disease, pulmonary embolism, and pulmonary hypertension, have been associated with more severe COVID-19 infection, including greatly increased risk of hospitalization and death. All of these conditions should be maximally optimized prior to infection (including stopping smoking) to lower the risk of severe infection.

Early data (from 2020) showed an association between decreased access to testing among non-Latino Blacks and Latinos and late diagnoses with more severe COVID-19 infections [398]. While testing access improved during the pandemic and the public health emergency has ended, access to testing may remain key for certain subpopulations. Vaccination against COVID-19, including all recommended boosters, is key for COVID-19 prevention and lowering risk for severe COVID-19 infections in people with HIV (see Section 4). Consistent evidence indicates that people with HIV with CD4 count >200 cells/μL have robust immune response (approximating that of people without HIV infection), but mRNA vaccines perform superiorly to other vaccines [396, 399, 400]. Further, HIV is not a contraindication to COVID-19 vaccination, regardless of CD4 count or degree of HIV viral suppression, and COVID-19 vaccination does not impact HIV viremia [181, 401]. Even with effective vaccination, there is still some evidence that people with HIV are at increased risk for breakthrough infection; however, the need for hospitalization or risk of death is not increased relative to people without HIV [399, 402].

Controversy persists on the role of ARV agents in preventing COVID-19 infection or mitigating the severity of infection in people with HIV. Observational evidence from several studies has suggested that tenofovir may be associated with lower risk of severe COVID-19; however, no confirmatory data from randomized trials exist [403]. Similarly, evidence for PIs and prevention of COVID-19 remains inconclusive [404]. There is no evidence to suggest that people with HIV and COVID-19 require a change to their ART simply because of the COVID-19 infection. No change is required to ART while on anti–COVID-19 treatment, including remdesivir or ritonavir-boosted nirmatrelvir. Close monitoring for potential increased risk of side effects is recommended. However, dexamethasone and other corticosteroids used as anti–COVID-19

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treatment should be avoided in the outpatient setting because side effects may increase due to drug–drug interactions [405].

As discussed in Section 4, PCCs are an ever-increasing phenomenon following SARS-CoV-2 infection. The exact incidence is unclear, and treatment is mainly symptomatic. There is some evidence that people with HIV may be at increased risk for PCCs, especially if not virally suppressed or with a lower CD4 count [406–408]. As such, providers should ask about PCC-related symptoms among people with HIV who are 30 days post–COVID-19 diagnosis. No treatment modifications for ART or comorbidities are indicated in the presence of PCCs.

Notes

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Disclaimer. This guidance cannot account for individual variation among patients and is not intended to supplant clinician judgment with respect to particular patients or special clinical situations. The HIVMA and the IDSA consider adherence to this guidance to be voluntary, with the ultimate determination regarding its application to be made based on individual patient circumstances.

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Weddle Declaration
Exhibit B

Number 38

HIV SURVEILLANCE REPORT

SPECIAL REPORT



Individual-level Social Determinants of Health and Quality of Life Among Persons With Diagnosed HIV Infection

Medical Monitoring Project, United States, 2022 Data Cycle (June 2022–May 2023)

Centers for Disease Control and Prevention
National Center for HIV, Viral Hepatitis, STD, and TB Prevention

This HIV Surveillance Special Report is published by the Behavioral and Clinical Surveillance Branch of the Division of HIV Prevention, National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, Georgia.

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MMP project areas—https://www.cdc.gov/hiv-data/mmp/index.html#cdc_survey_profile_surveys_used-project-areas

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Commentary

Social determinants of health (SDOH) are the "conditions in the places where people live, learn, work, and play that affect a wide range of health and quality-of-life risks and outcomes" [1]. Addressing social determinants of health among people with HIV (PWH) is a national priority highlighted in the White House's National HIV/AIDS Strategy (NHAS), as it is essential for reducing disparities in health outcomes and achieving health equity among people with HIV [2, 3], particularly among priority groups, including: gay, bisexual, and other men who have sex with men (MSM) (in particular, Black, Latino, and American Indian/Alaska Native men); Black women; transgender women; youths aged 13–24 years; and people who inject drugs. Further, NHAS added several indicators in 2022 based on community input to monitor quality of life (QoL) among PWH that are related to SDOH, including aspects of physical health (i.e., self-reported health status), mental or emotional health (i.e., unmet needs for mental health services), and structural or subsistence factors (i.e., unemployment, hunger/food insecurity, and unstable housing or homelessness) [4].

The Centers for Disease Control and Prevention (CDC) Medical Monitoring Project (MMP) is the only source of nationally representative data on individual-level SDOH and QoL among adults with diagnosed HIV in the United States, including among priority populations highlighted in NHAS. Estimates are also representative for each of MMP's reporting project areas, including: California (including the separately funded jurisdictions of Los Angeles County and San Francisco), Delaware, Florida, Georgia, Illinois (including the separately funded jurisdiction of Chicago), Indiana, Michigan, Mississippi, New Jersey, New York (including the separately funded jurisdiction of New York City), North Carolina, Oregon, Pennsylvania (including the separately funded jurisdiction of Philadelphia), Puerto Rico, Texas (including the separately funded jurisdiction of Houston), Virginia, and Washington state. Data from MMP are critical for achieving the goals of NHAS [4] and the Ending the HIV Epidemic in the U.S. (EHE) initiative [5], which seek to reduce new HIV infections in the United States by 90% by 2030 and prioritize reducing HIV-related disparities and health inequities and improving PWH's health and well-being. Continuing to monitor SDOH and QoL among PWH is an essential step towards meeting national goals to end the HIV epidemic and ensuring good health and well-being among PWH in the United States.

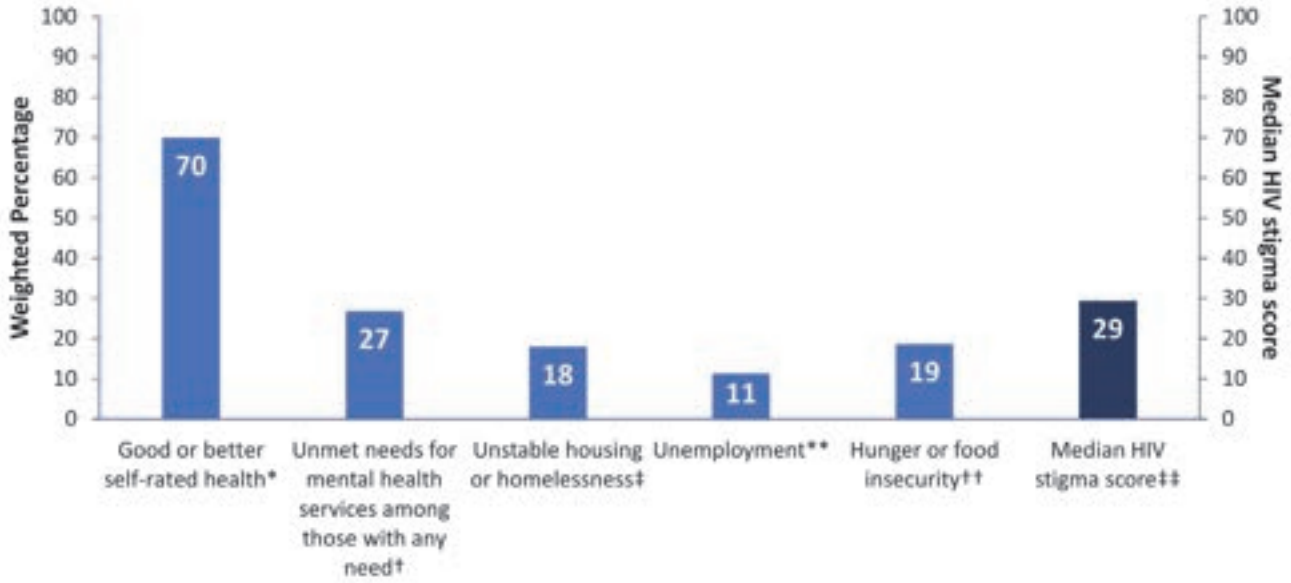
This report presents unweighted frequencies and weighted prevalence estimates with 95% confidence intervals (CIs) for all characteristics represented by categorical variables. Continuous variables are represented using median values and 95% CIs. The period referenced for estimates is the 12 months before the respondents' interviews unless otherwise noted. Statistical software (SAS, version 9.4) was used for analysis of weighted data. For categorical variables, data are not reported for estimates derived from a denominator size <30 or for estimates with a coefficient of variation ≥0.30. For continuous variables, estimates based on a denominator sample size <30 were suppressed. In both the tables and the narrative, estimates with an absolute confidence interval width ≥30, estimates with an absolute confidence interval width between 5 and 30 and a relative confidence interval width ≥130%, and estimates of 0% or 100% are marked with an asterisk (*) and should be interpreted with caution. Estimates are rounded to the nearest whole number in the commentary and figures, and to the nearest tenth in the tables; comparisons between groups in the commentary are based on estimates presented in the tables. Estimates from the 2020–2022 cycles presented in this report may have been affected by the COVID-19 pandemic. Estimates for persons identifying as American Indian/Alaska Native or Native Hawaiian/other Pacific Islander were suppressed for all measures due to small numbers. Many estimates for Asian persons were also unreliable and were suppressed. Additional information on MMP is available at https://www.cdc.gov/hiv-data/mmp/index.html.

HIGHLIGHTS OF ANALYSES

Individual-level SDOH and QOL

MMP reports information on QoL indicators and HIV stigma to monitor progress towards meeting national HIV prevention and treatment goals highlighted in NHAS. During 2022, 70% of persons with HIV had good or better self-rated health (2025 NHAS goal: 95%), and 27% had an unmet need for services from a mental health professional among those with any need (2025 NHAS goal: 12%) (Figure 1; Table 1). Overall, 18% experienced unstable housing or homelessness during the past 12 months (2025 NHAS goal: 11%), 11% were unemployed (2025 NHAS goal: 7%), and 19% experienced hunger or food insecurity during the past 12 months (2025 NHAS goal: 11%). During 2022, the median HIV stigma score based on a scale that ranged from 0 (no stigma) to 100 (high stigma) was 29 among PWH (2025 NHAS goal: 16).

Figure 1. National HIV/AIDS Strategy indicators among adults with diagnosed HIV—Medical Monitoring Project, United States, 2022



* "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

† "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

‡ "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

** Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

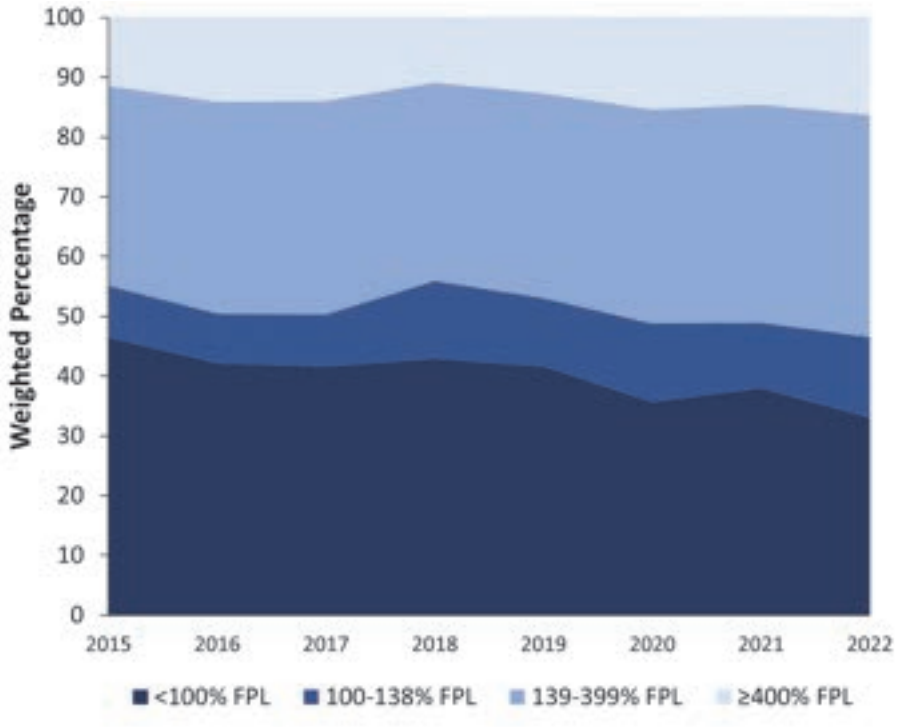
†† "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

‡‡ "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico.

MMP also collects information on other individual-level SDOH related to economic stability, education, health-related factors, and social and community context. During 2022, 84% of PWH were living in a household with an income <400% of the federal poverty level (FPL); 33% were living in a household with an income <100% of the FPL, 14% in a household with an income between 100%–138% of the FPL, and 37% in

a household with an income between 139%–399% (Figure 2; Table 1). The percentage of PWH living in a household with an income <100% of the FPL was lowest in 2022 (33%) and highest in 2015 (46%).

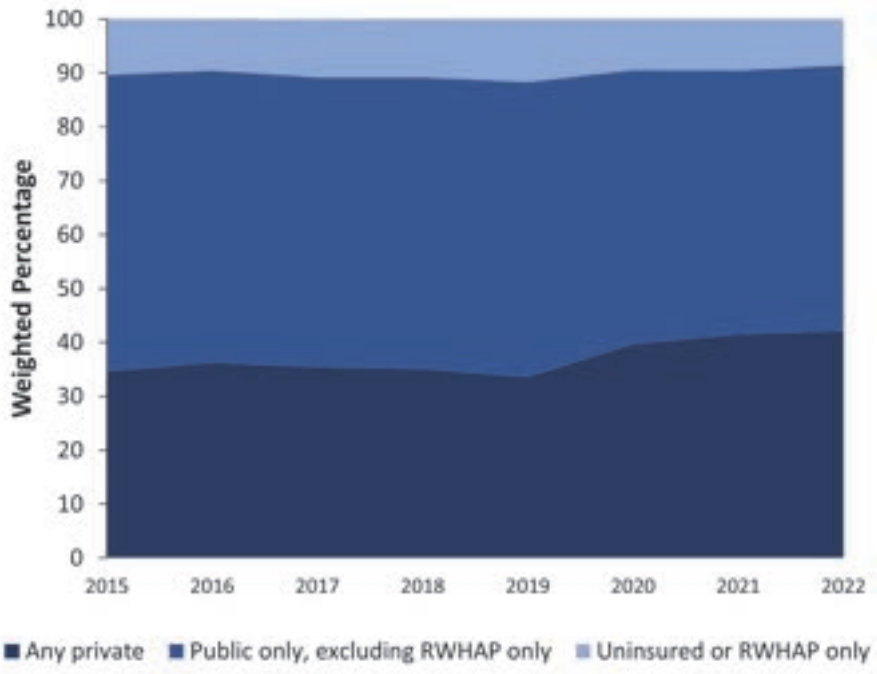
Figure 2. Household poverty level of adults with diagnosed HIV—Medical Monitoring Project, United States, 2015–2022



Note. Poverty guidelines as defined by HHS. Respondents were asked about their household income from all sources during the calendar year prior to the interview date. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

During the past 12 months, 42% had any private insurance coverage, 49% had public insurance or coverage only (excluding those who had Ryan White HIV/AIDS Program [RWHAP] assistance only), and 9% were uninsured or received RWHAP assistance only (Figure 3; Table 1). The percentage of PWH who had any private insurance was lowest during 2019 (34%) and highest during 2022 (42%). In addition, 47% received any RWHAP assistance during the past 12 months (Table 1).

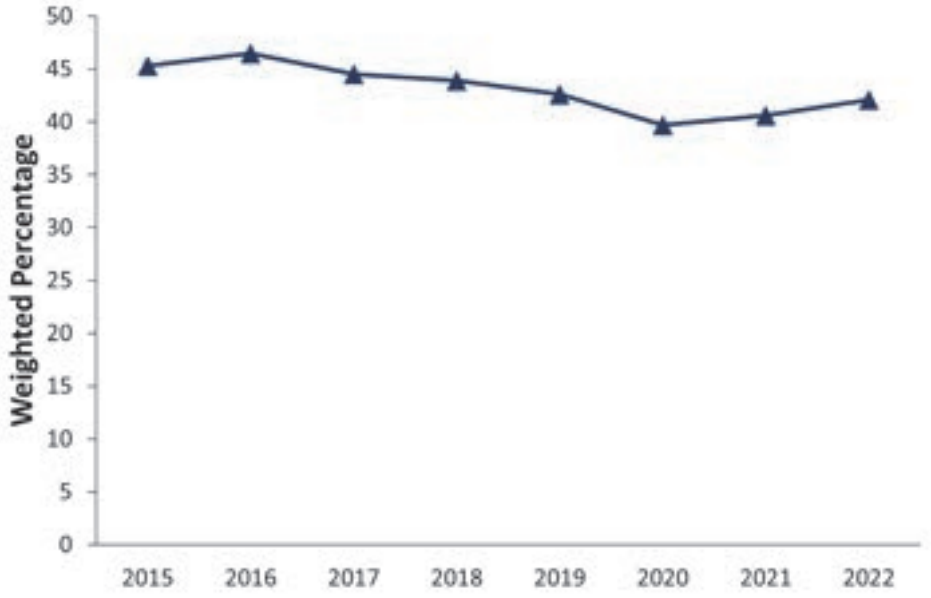
Figure 3. Health insurance or coverage among adults with diagnosed HIV—Medical Monitoring Project, United States, 2015–2022



Abbreviation: RWHAP, Ryan White HIV/AIDS Program.

During 2022, 42% of PWH reported a physical, mental, or emotional disability; the percentage of PWH with one or more disabilities was lowest during 2020 (40%) and highest during 2016 (47%).

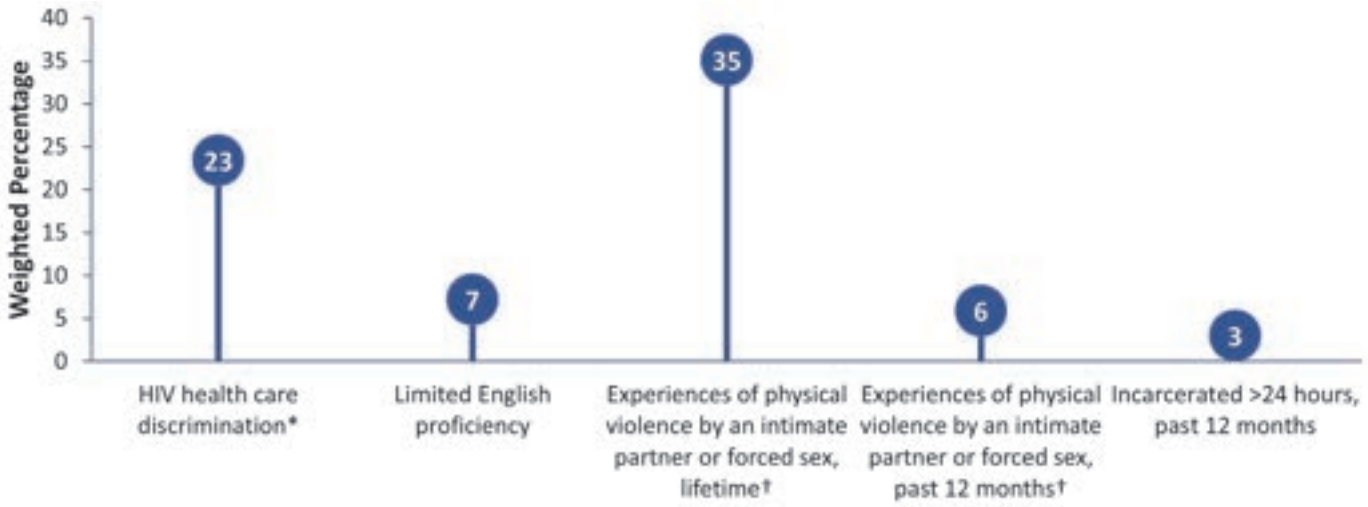
Figure 4. Disability among adults with diagnosed HIV—Medical Monitoring Project, United States, 2015–2022



Note. Disabilities are self-reported and include physical, mental, and emotional disabilities.

During 2022, 23% of PWH experienced any HIV health care discrimination during the past 12 months, and 7% reported speaking English "less than well" (Figure 5; Table 1). Overall, 35% had experiences of physical violence by an intimate partner or forced sex during their lifetime, and 6% had these experiences during the past 12 months. Three percent of PWH reported being incarcerated during the past 12 months.

Figure 5. HIV health care discrimination, limited English proficiency, experiences with physical violence by an intimate partner or forced sex, and incarceration among adults with diagnosed HIV—Medical Monitoring Project, United States, 2022



* HIV health care discrimination among those who received HIV care during the past 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced this never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

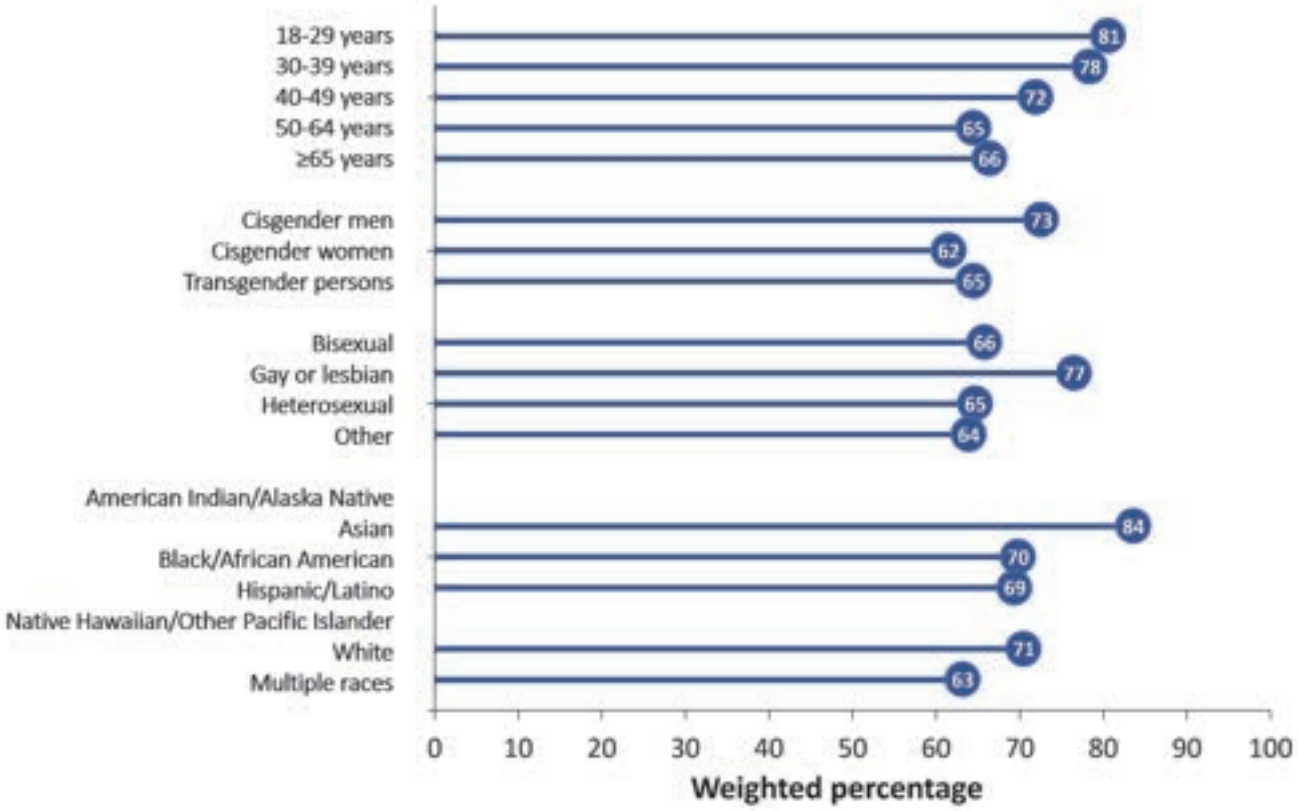
† Physical violence by an intimate partner was defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex was defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

NHAS Indicators and Other Individual-level SDOH by Demographic Characteristics

Estimates of all NHAS indicators and other individual-level SDOH are reported by demographic characteristics. Absolute and relative disparities (using prevalence differences and prevalence ratios, respectively) were used to quantify differences in indicators and other SDOH by demographic characteristics, which are reported in Tables 2–5.

Good or better self-rated health varied by age, current gender identity, sexual orientation, and race/ethnicity (Tables 2–5, Figure 6). When stratified by age, good or better self-rated health was highest among persons aged 18–29 years (81%) and lowest among persons aged 50–64 years (65%). When stratified by current gender identity, good or better self-rated health was highest among cisgender men (73%) and lowest among cisgender women (62%). When stratified by sexual orientation, good or better self-rated health was highest among persons who identified as gay or lesbian (77%) and lowest among persons who identified as another sexual orientation (i.e., not bisexual, gay or lesbian, or heterosexual; 64%). When stratified by race/ethnicity, good or better self-rated health was highest among persons who identified as Asian (84%) and lowest among persons who identified as multiple races (63%).

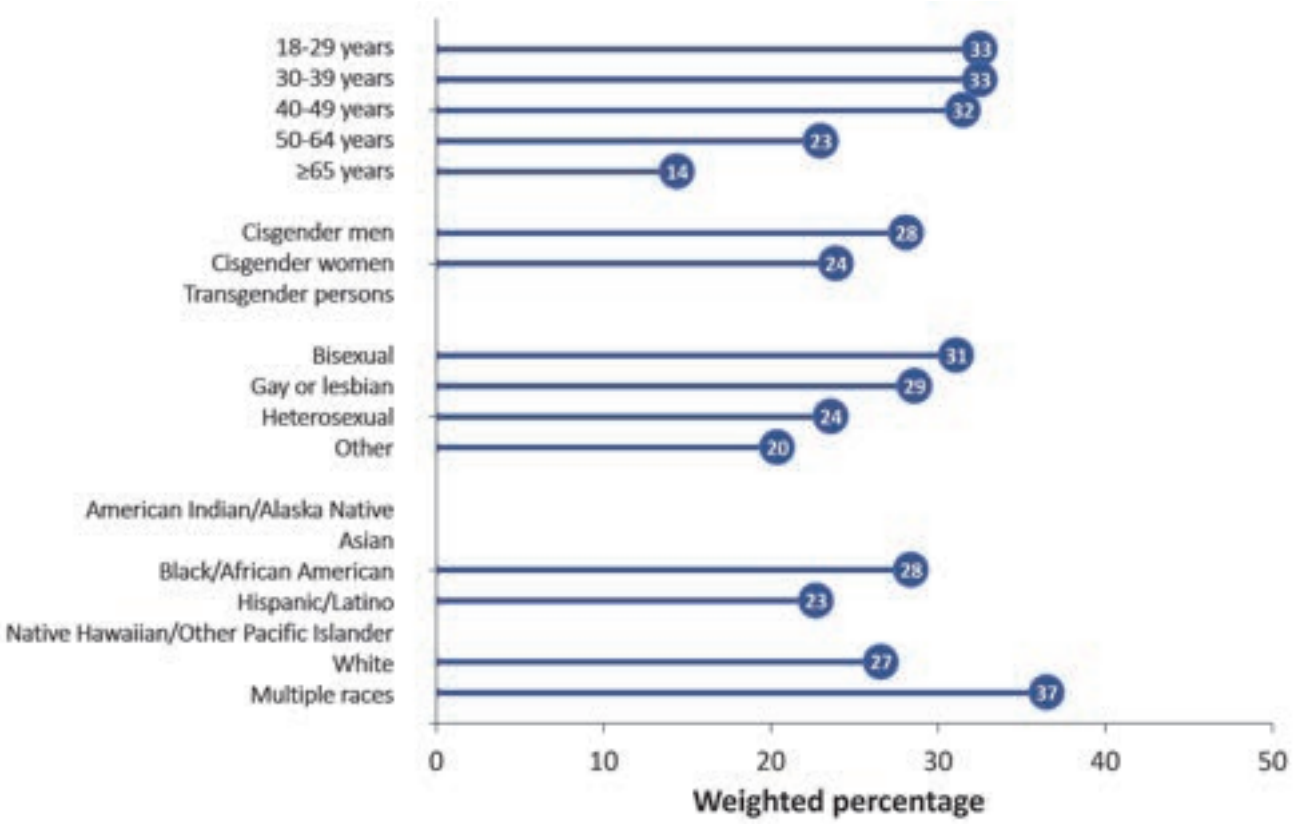
Figure 6. Good or better self-rated health among adults with diagnosed HIV, by age, gender, sexual orientation, and race/ethnicity—Medical Monitoring Project, United States, 2022



Note. "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size <30. Persons were classified as cisgender if sex at birth and gender reported by the person were the same. Persons were classified as transgender if sex at birth and gender reported by the person were different, or if the person chose "transgender" in response to the question about self-identified gender. Hispanics or Latinos can be of any race. Persons are classified in only 1 race/ethnicity category.

Unmet needs for services from a mental health professional among those who needed them varied by age, current gender identity, sexual orientation, and race/ethnicity (Tables 2–5, Figure 7). When stratified by age, unmet needs for mental health services among those who needed them were highest among persons aged 18–29 years and 30–39 years (both 33%) and lowest among persons aged ≥65 years (14%). When stratified by current gender identity, unmet needs for mental health services among those who needed them were highest among cisgender men (28%) and lowest among cisgender women (24%). When stratified by sexual orientation, unmet needs for mental health services among those who needed them were highest among persons who identified as bisexual (31%) and lowest among persons who identified as another sexual orientation (i.e., not bisexual, gay or lesbian, or heterosexual; 20%). When stratified by race/ethnicity, unmet needs for mental health services among those who needed them were highest among persons who identified as multiple races (37%) and lowest among persons who identified as Hispanic/Latino (23%).

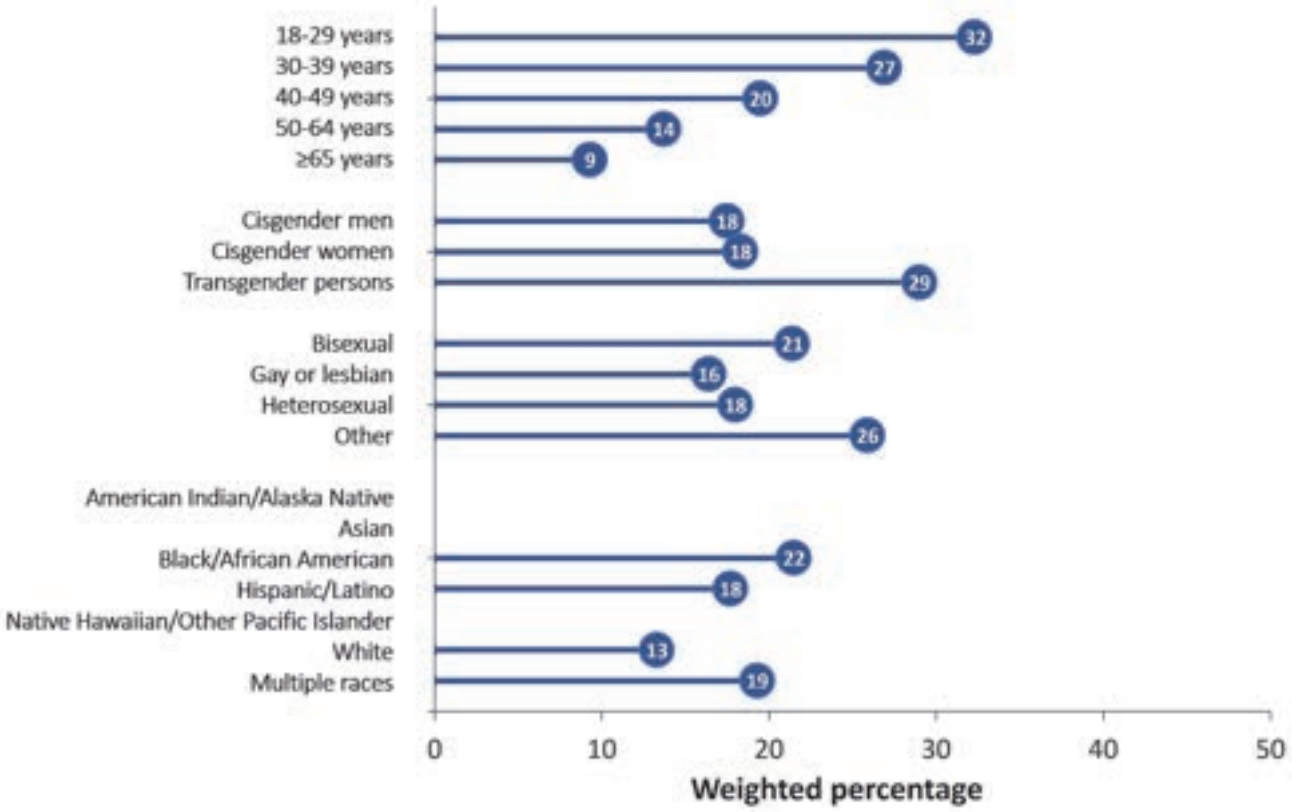
Figure 7. Unmet needs for services from a mental health professional among adults with diagnosed HIV with a need for services, by age, gender, sexual orientation, and race/ethnicity—Medical Monitoring Project, United States, 2022



Note. "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size <30. Persons were classified as cisgender if sex at birth and gender reported by the person were the same. Persons were classified as transgender if sex at birth and gender reported by the person were different, or if the person chose "transgender" in response to the question about self-identified gender. Hispanics or Latinos can be of any race. Persons are classified in only 1 race/ethnicity category.

Unstable housing or homelessness varied by age, current gender identity, sexual orientation, and race/ethnicity (Tables 2–5, Figure 8). When stratified by age, unstable housing or homelessness was highest among persons aged 18–29 years (32%) and lowest among persons aged ≥65 years (9%). When stratified by current gender identity, unstable housing or homelessness was highest among transgender persons (29%) and lowest among cisgender men (18%). When stratified by sexual orientation, unstable housing or homelessness was highest among persons who identified as another sexual orientation (i.e., not bisexual, gay or lesbian, or heterosexual; 26%) and lowest among persons who identified as gay or lesbian (16%). When stratified by race/ethnicity, unstable housing or homelessness was highest among persons who identified as Black/African American (22%) and lowest among persons who identified as White (13%).

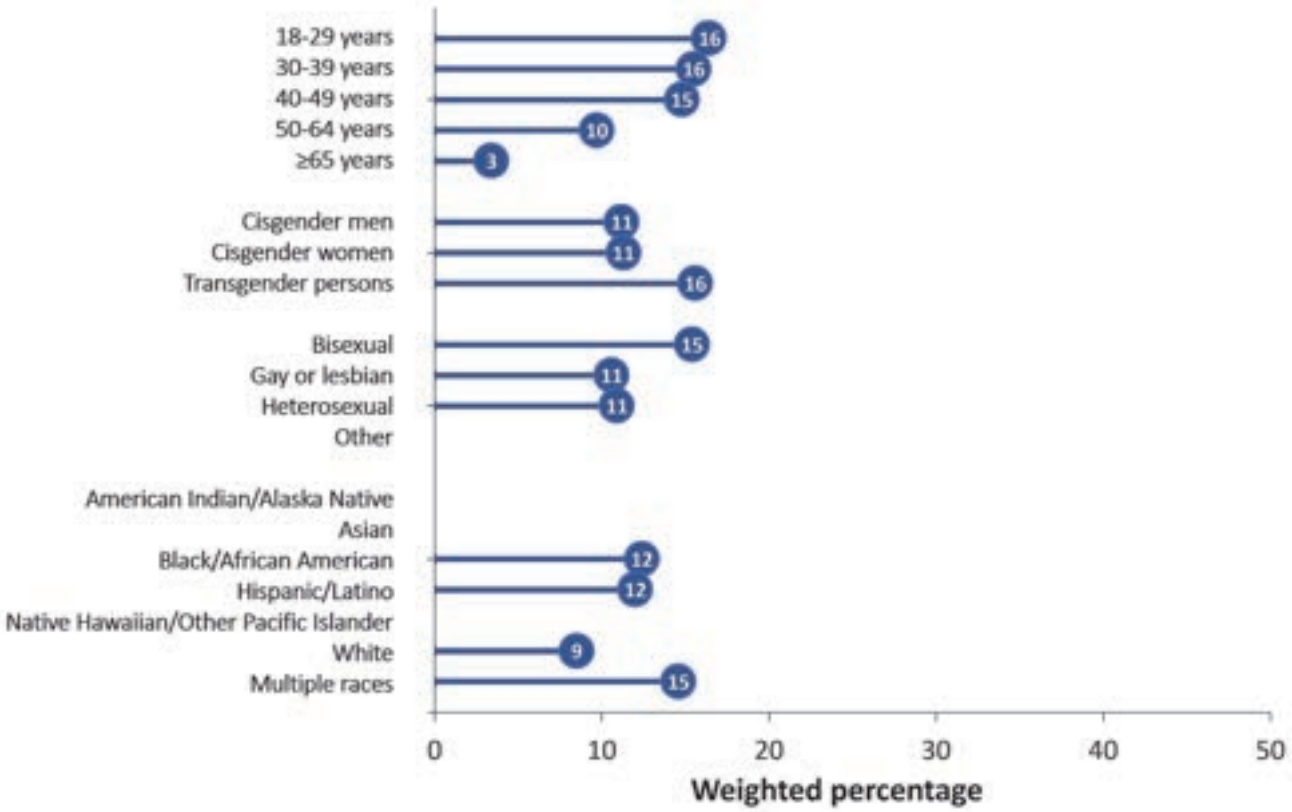
Figure 8. Unstable housing or homelessness among adults with diagnosed HIV, by age, gender, sexual orientation, and race/ethnicity—Medical Monitoring Project, United States, 2022



Note. "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size <30. Persons were classified as cisgender if sex at birth and gender reported by the person were the same. Persons were classified as transgender if sex at birth and gender reported by the person were different, or if the person chose "transgender" in response to the question about self-identified gender. Hispanics or Latinos can be of any race. Persons are classified in only 1 race/ethnicity category.

Unemployment varied by age, current gender identity, sexual orientation, and race/ethnicity (Tables 2–5, Figure 9). When stratified by age, unemployment was highest among persons aged 18–29 years (16%) and lowest among persons aged ≥65 years (3%). When stratified by current gender identity, unemployment was highest among transgender persons (16%) and lowest among cisgender men (11%). When stratified by sexual orientation, unemployment was highest among persons who identified as bisexual (15%) and lowest among persons who identified as gay or lesbian (11%). When stratified by race/ethnicity, unemployment was highest among persons who identified as multiple races (15%) and lowest among persons who identified as White (9%).

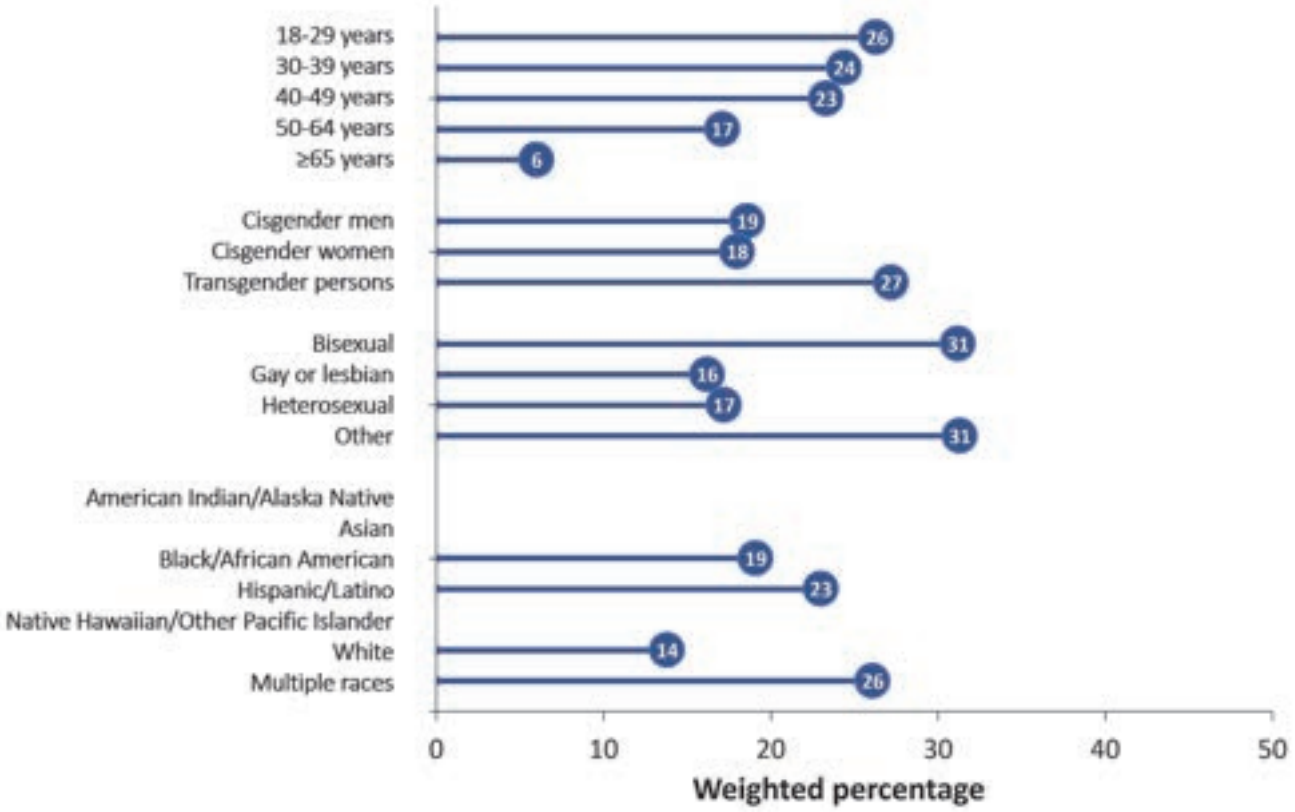
Figure 9. Unemployment among adults with diagnosed HIV, by age, gender, sexual orientation, and race/ethnicity—Medical Monitoring Project, United States, 2022



Note. Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size <30. Persons were classified as cisgender if sex at birth and gender reported by the person were the same. Persons were classified as transgender if sex at birth and gender reported by the person were different, or if the person chose "transgender" in response to the question about self-identified gender. Hispanics or Latinos can be of any race. Persons are classified in only 1 race/ethnicity category.

Hunger or food insecurity varied by age, current gender identity, sexual orientation, and race/ethnicity (Tables 2–5, Figure 10). When stratified by age, hunger or food insecurity was highest among persons aged 18–29 years (26%) and lowest among persons aged ≥65 years (6%). When stratified by current gender identity, hunger or food insecurity was highest among transgender persons (27%) and lowest among cisgender women (18%). When stratified by sexual orientation, hunger or food insecurity was highest among persons identifying as another sexual orientation (i.e., not bisexual, gay or lesbian, or heterosexual; 31%) and lowest among persons who identified as gay or lesbian (16%). When stratified by race/ethnicity, hunger or food insecurity was highest among persons who identified as multiple races (26%) and lowest among persons who identified as White (14%).

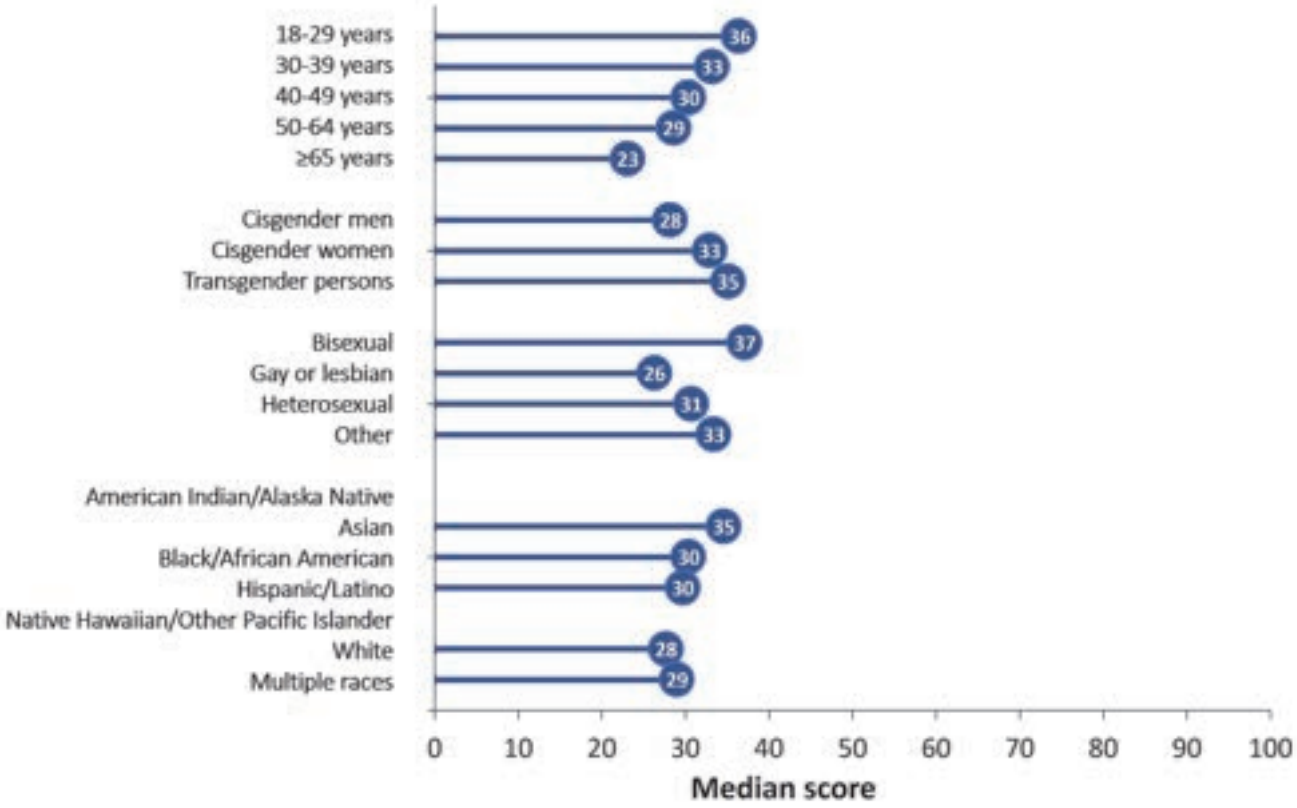
Figure 10. Hunger or food insecurity among adults with diagnosed HIV, by age, gender, sexual orientation, and race/ethnicity—Medical Monitoring Project, United States, 2022



Note. "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size <30. Persons were classified as cisgender if sex at birth and gender reported by the person were the same. Persons were classified as transgender if sex at birth and gender reported by the person were different, or if the person chose "transgender" in response to the question about self-identified gender. Hispanics or Latinos can be of any race. Persons are classified in only 1 race/ethnicity category.

Median HIV stigma scores varied by age, current gender identity, sexual orientation, and race/ethnicity (Tables 2–5, Figure 11). When stratified by age, the median HIV stigma score was highest among persons aged 18–29 years (36) and lowest among persons aged ≥65 years (23). When stratified by current gender identity, the median HIV stigma score was highest among transgender persons (35) and lowest among cisgender men (28). When stratified by sexual orientation, the median HIV stigma score was highest among persons who identified as bisexual (37) and lowest among persons who identified as gay or lesbian (26). When stratified by race/ethnicity, the median HIV stigma score was highest among persons who identified as Asian (35) and lowest among persons who identified as White (28).

Figure 11. Median HIV stigma scores among adults with diagnosed HIV, by age, gender, sexual orientation, and race/ethnicity—Medical Monitoring Project, United States, 2022



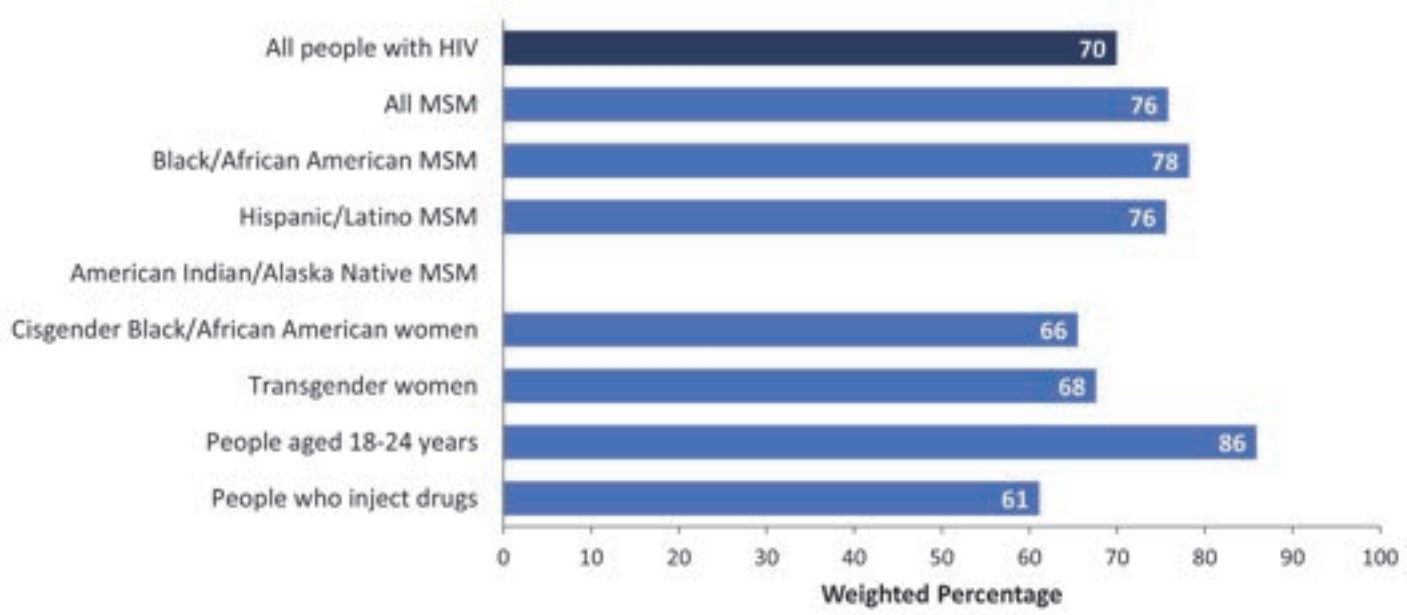
Note. "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. Estimates were suppressed if they were based on a denominator sample size <30. Persons were classified as cisgender if sex at birth and gender reported by the person were the same. Persons were classified as transgender if sex at birth and gender reported by the person were different, or if the person chose "transgender" in response to the question about self-identified gender. Hispanics or Latinos can be of any race. Persons are classified in only 1 race/ethnicity category.

Stratifications of other SDOH by age, current gender identity, sexual orientation, and race/ethnicity are reported in Tables 2–5.

NHAS Indicators and Other SDOH by NHAS Priority Populations

Table 6 shows that patterns in NHAS indicators and SDOH differed for each NHAS priority population during the 2022 MMP cycle (Table 6, Figures 12–17). For instance, good or better self-rated health was highest among persons aged 18–24 years (86%) and lowest among persons who inject drugs (61%). Unmet needs for services from a mental health professional among persons who needed services were highest among persons who inject drugs (37%) and lowest among cisgender Black or African American women (19%). Unstable housing or homelessness was highest among persons who inject drugs (51%) and lowest among MSM (17%). Unemployment was highest among persons who inject drugs (26%) and lowest among MSM (11%). Hunger or food insecurity was highest among persons who inject drugs (44%) and lowest among cisgender Black or African American women (14%). Median HIV stigma score was highest among persons aged 18–24 years (37) and lowest among Black or African American MSM (27).

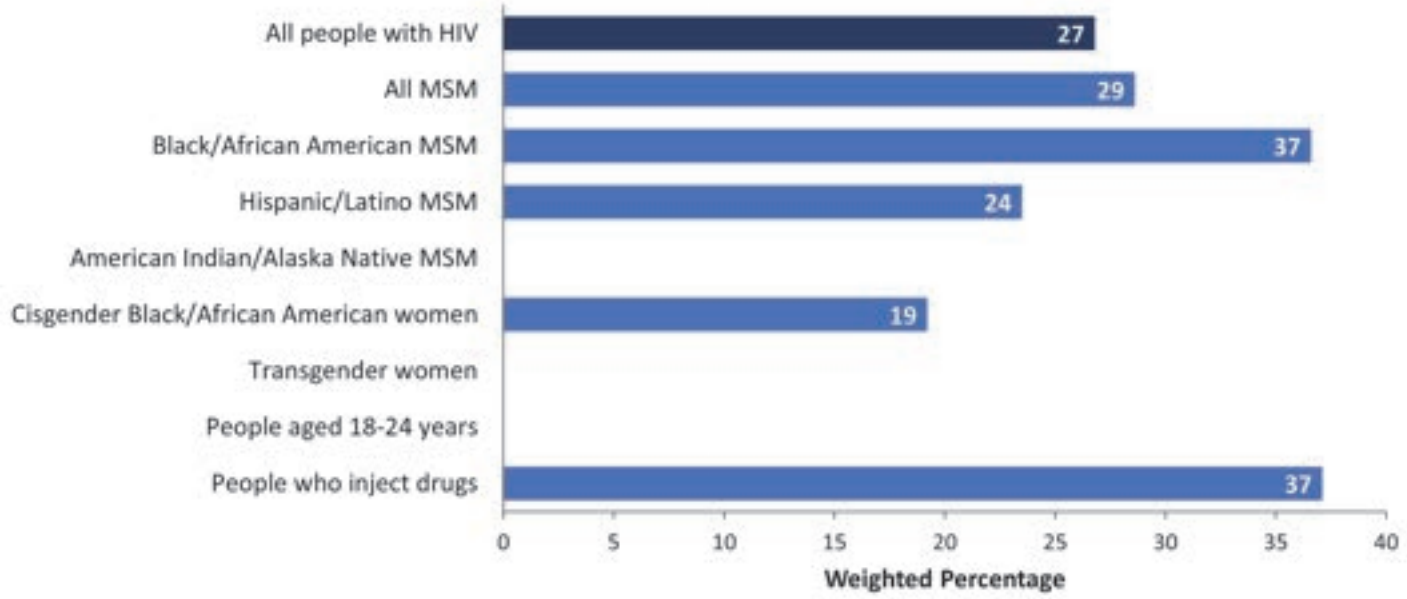
Figure 12. Good or better self-rated health among adults with diagnosed HIV, by NHAS priority population—Medical Monitoring Project, United States, 2022



Abbreviations: NHAS, National HIV/AIDS Strategy; MSM, cisgender men who have sex with cisgender men.

Note. "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size < 30.

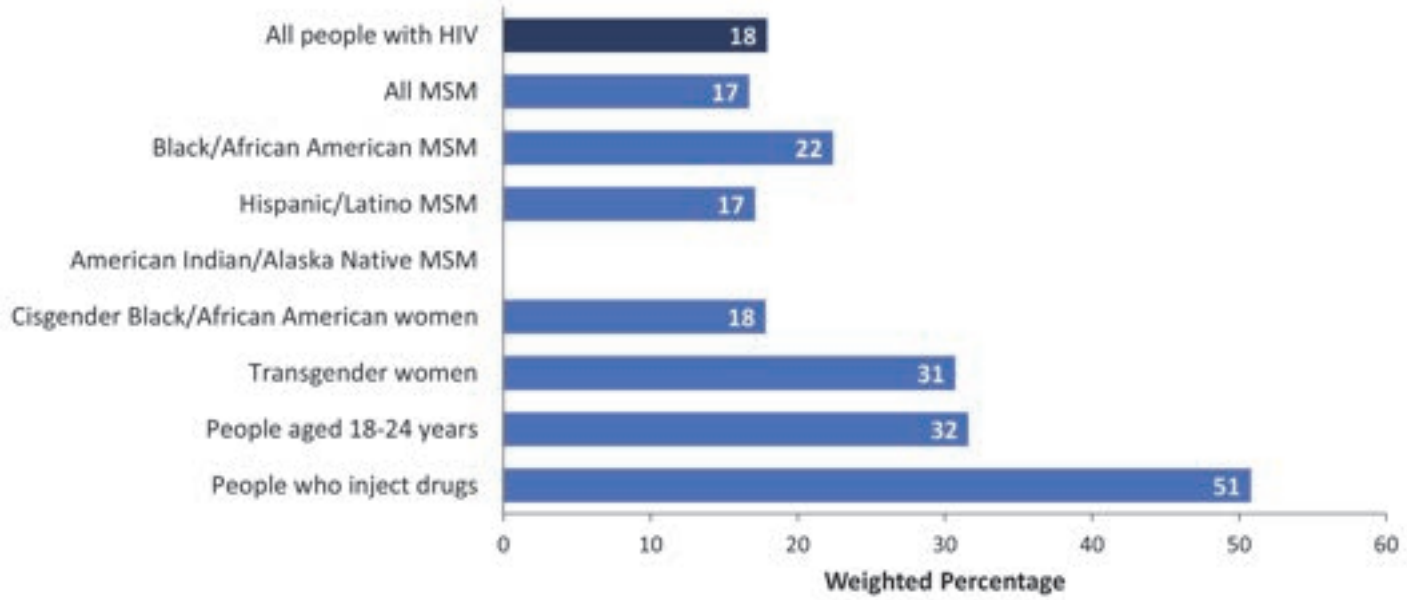
Figure 13. Unmet needs for services from a mental health professional among adults with diagnosed HIV who needed services, by NHAS priority population—Medical Monitoring Project, United States, 2022



Abbreviations: NHAS, National HIV/AIDS Strategy; MSM, cisgender men who have sex with cisgender men.

Note. "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size < 30.

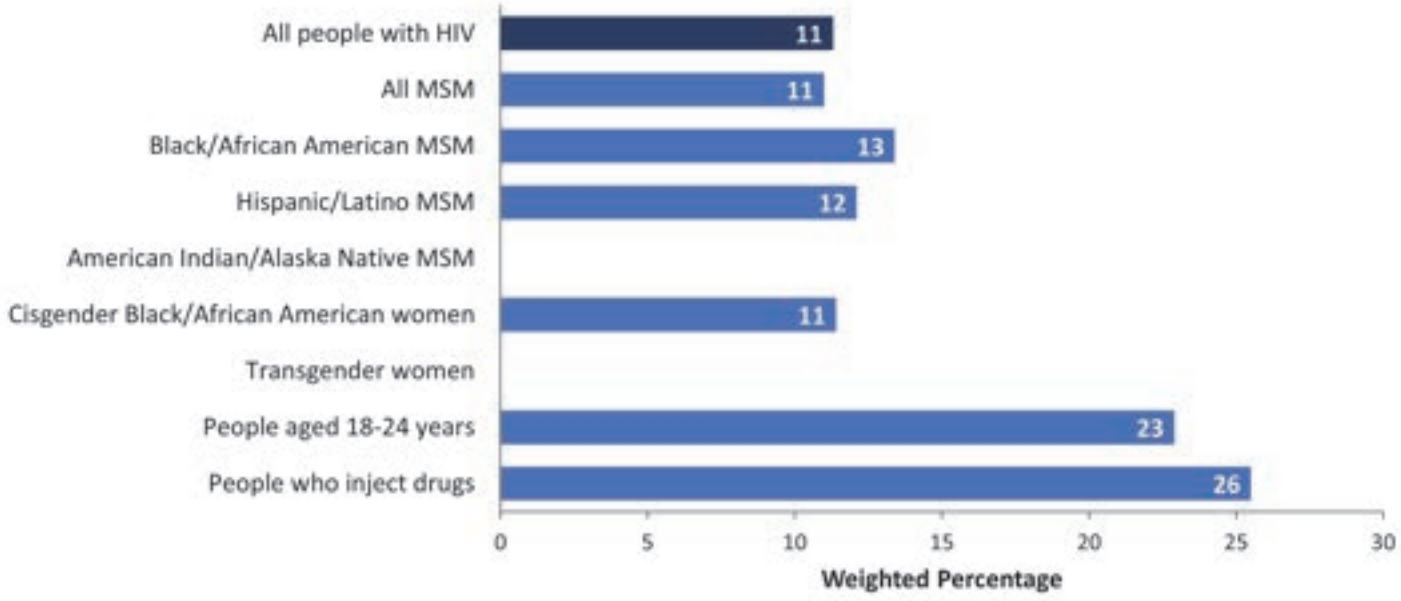
Figure 14. Unstable housing or homelessness among adults with diagnosed HIV, by NHAS priority population—Medical Monitoring Project, United States, 2022



Abbreviations: NHAS, National HIV/AIDS Strategy; MSM, cisgender men who have sex with cisgender men.

Note. "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size < 30.

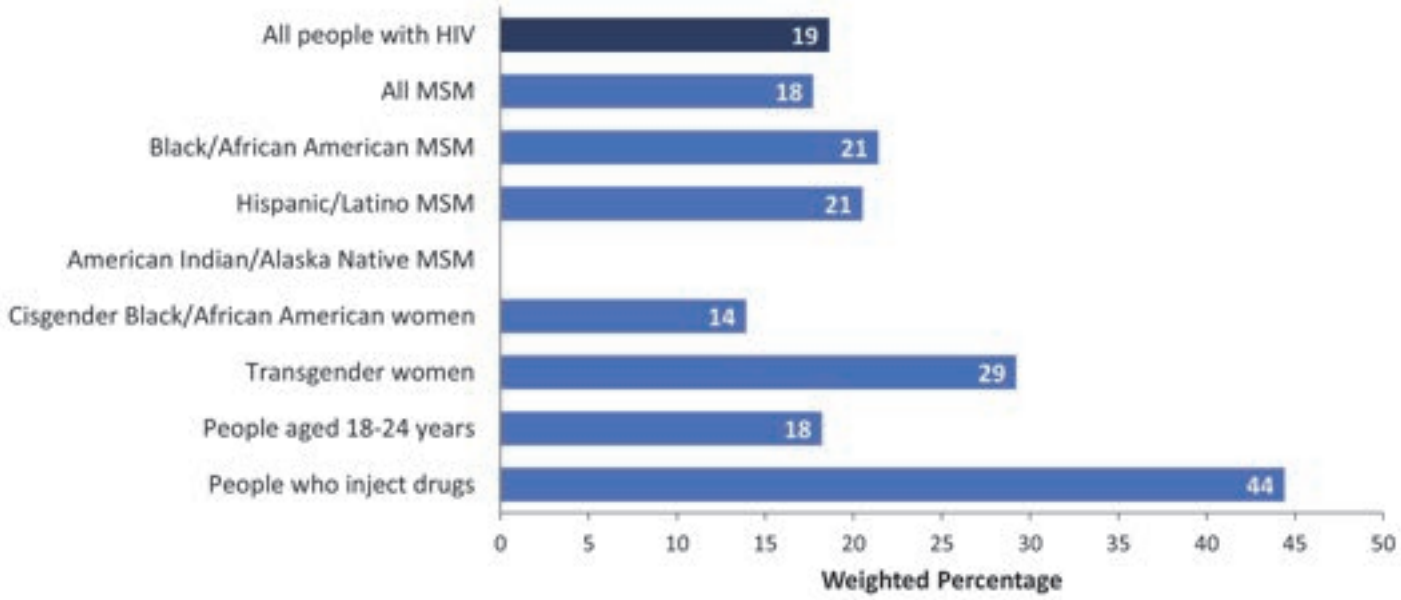
Figure 15. Unemployment among adults with diagnosed HIV, by NHAS priority population—Medical Monitoring Project, United States, 2022



Abbreviations: NHAS, National HIV/AIDS Strategy; MSM, cisgender men who have sex with cisgender men.

Note. Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size < 30.

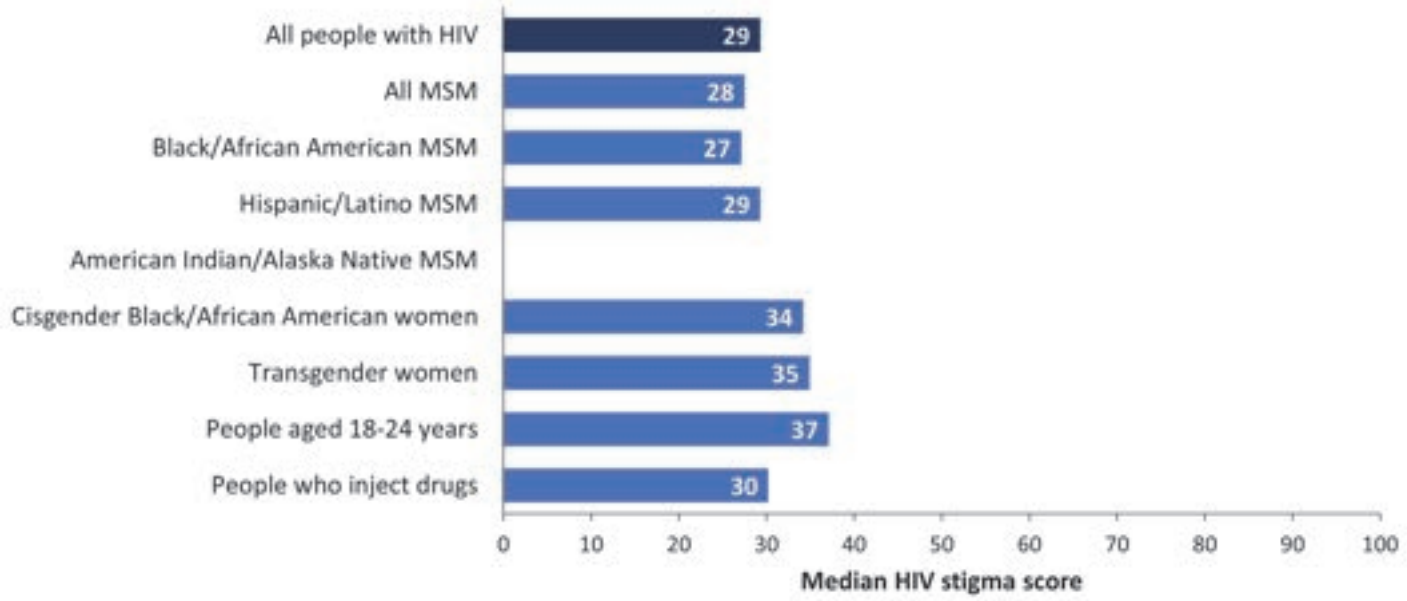
Figure 16. Hunger or food insecurity among adults with diagnosed HIV, by NHAS priority population—Medical Monitoring Project, United States, 2022



Abbreviations: NHAS, National HIV/AIDS Strategy; MSM, cisgender men who have sex with cisgender men.

Note. "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size < 30.

Figure 17. Median HIV stigma scores among adults with diagnosed HIV, by NHAS priority population—Medical Monitoring Project, United States, 2022



Abbreviations: NHAS, National HIV/AIDS Strategy; MSM, cisgender men who have sex with cisgender men.

Note. "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. Estimates were suppressed if they were based on a denominator sample size <30.

Estimates for other SDOH for each NHAS priority population are presented in Table 6.

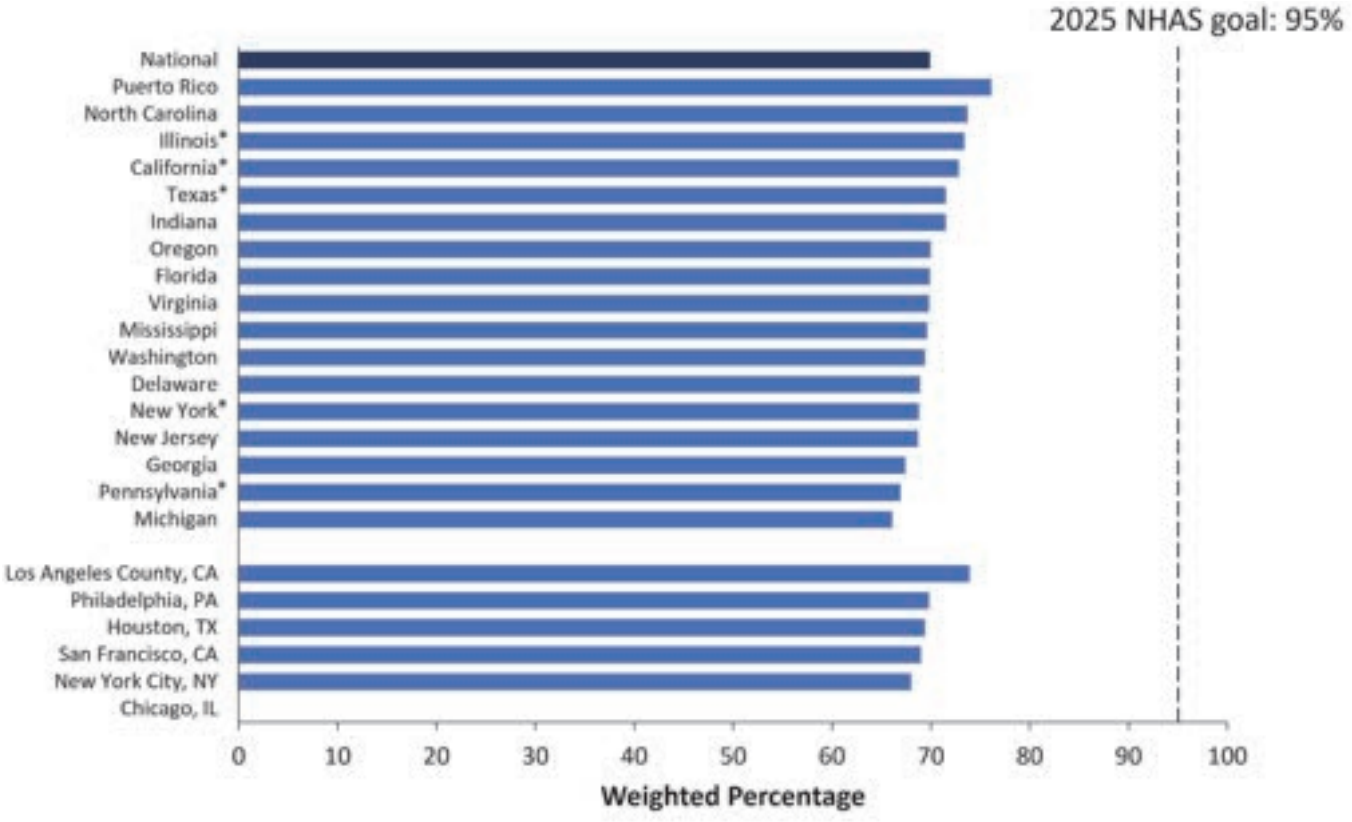
NHAS Indicators by Individual SDOH

During the 2022 MMP cycle, NHAS indicators related to QoL and HIV stigma varied by other SDOH related to economic stability, education, health-related factors, neighborhood and built environment, and social and community context (Table 7).

NHAS Indicators by MMP Jurisdictions

NHAS indicators related to QoL and HIV stigma varied by jurisdiction. During the 2022 MMP cycle, the percentage of persons with good or better self-rated health ranged from 66% in Michigan to 76% in Puerto Rico (Table 8; Figure 18). The percentage of persons with unmet needs for services from a mental health professional during the past 12 months among those who needed them ranged from 16% in Los Angeles County to 37%* in Mississippi (Table 8; Figure 19). The percentage of persons who experienced unstable housing or homelessness during the past 12 months ranged from 8% in Puerto Rico to 25% in Florida (Table 8; Figure 20). Unemployment ranged from 8% in Oregon to 19% in New York City (Table 8; Figure 21). Hunger or food insecurity ranged from 12% in Puerto Rico to 24% in Texas (Table 8; Figure 22). Median HIV stigma scores ranged from 24 in San Francisco to 34 in Michigan (Table 8; Figure 23).

Figure 18. Good or better self-rated health among adults with diagnosed HIV, by jurisdiction—Medical Monitoring Project, United States, 2022

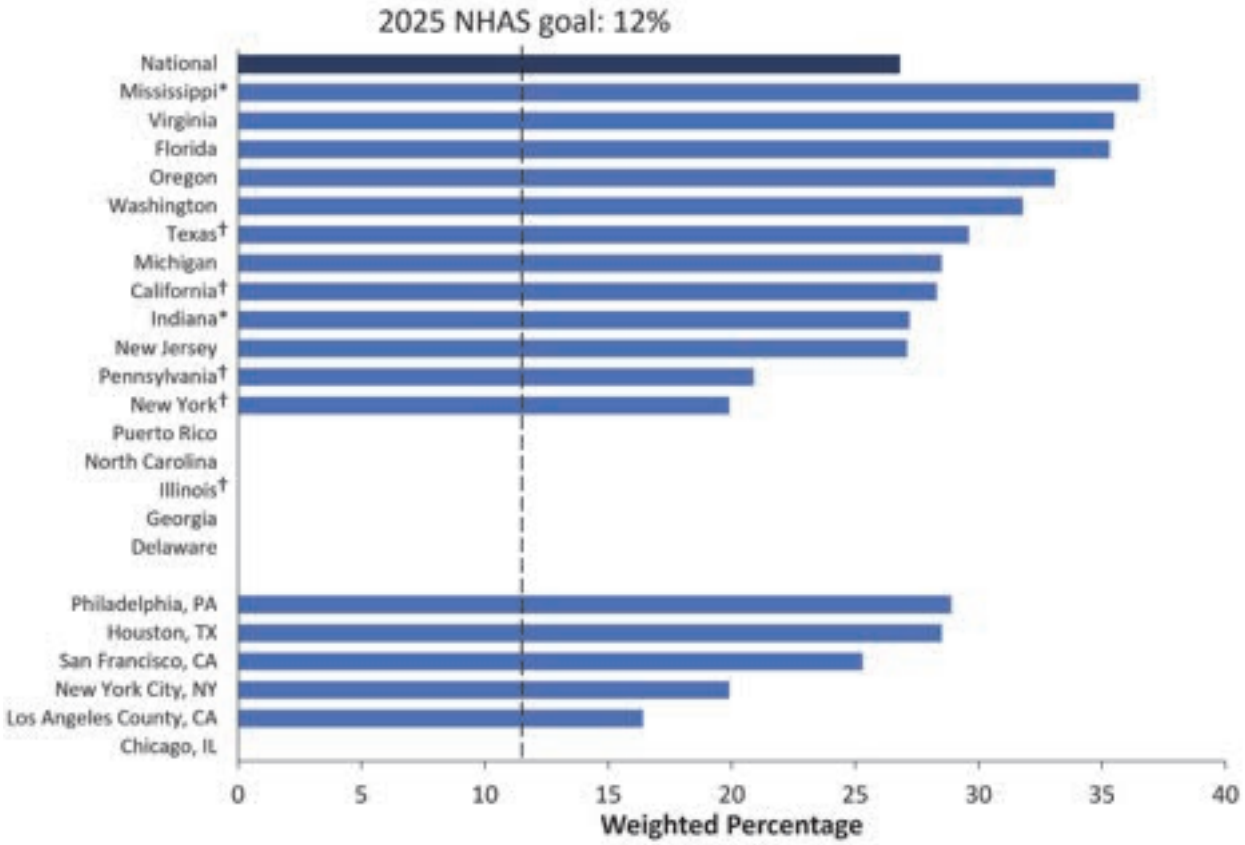


Abbreviations: NHAS, National HIV/AIDS Strategy; MMP, Medical Monitoring Project.

Note. "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size <30.

* Includes separately funded jurisdictions within each state.

Figure 19. Unmet needs for services from a mental health professional among adults with diagnosed HIV who needed services, by jurisdiction—Medical Monitoring Project, United States, 2022

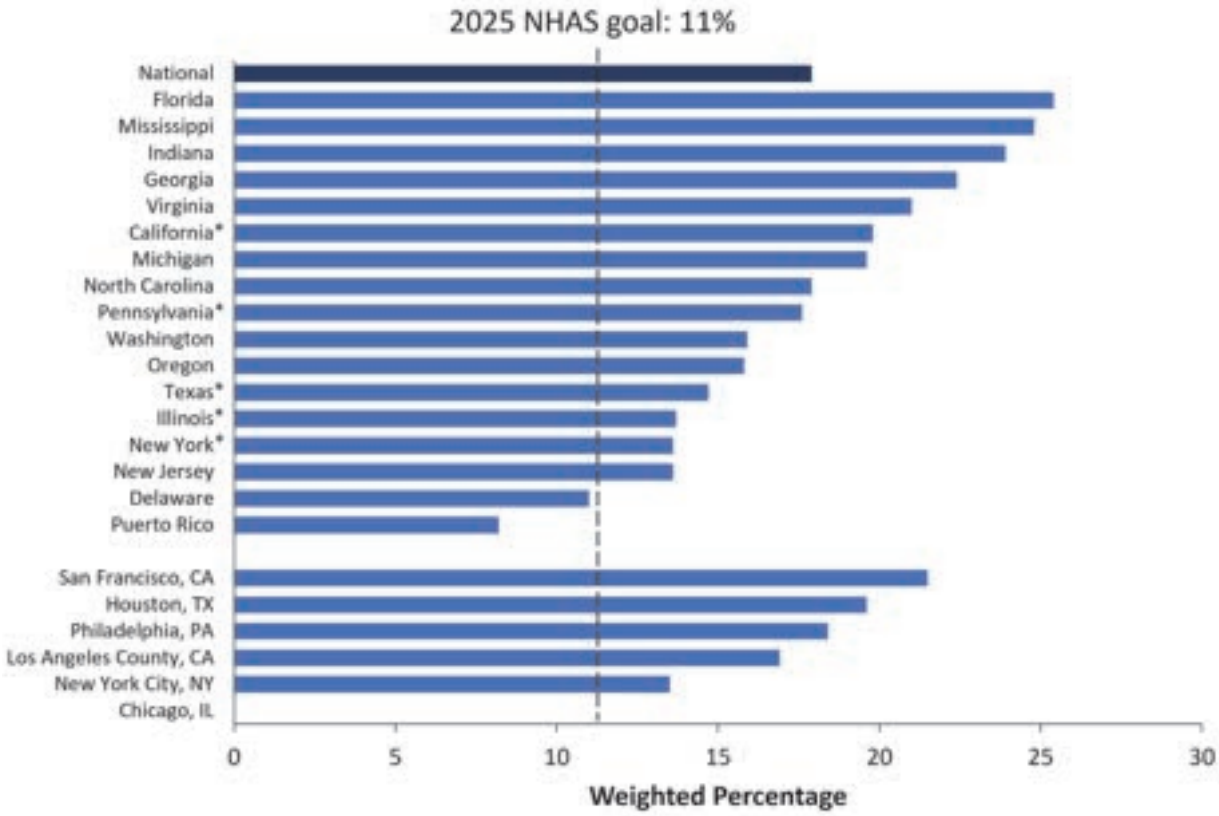


Abbreviations: NHAS, National HIV/AIDS Strategy; MMP, Medical Monitoring Project.

Note. "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size <30. Estimates with an absolute CI width >30, estimates with an absolute CI width between 5 and 30 and a relative CI width >130%, and estimates of 0% or 100% are marked with an asterisk (*) and should be interpreted with caution.

† Includes separately funded jurisdictions within each state.

Figure 20. Unstable housing or homelessness among adults with diagnosed HIV, by jurisdiction—Medical Monitoring Project, United States, 2022

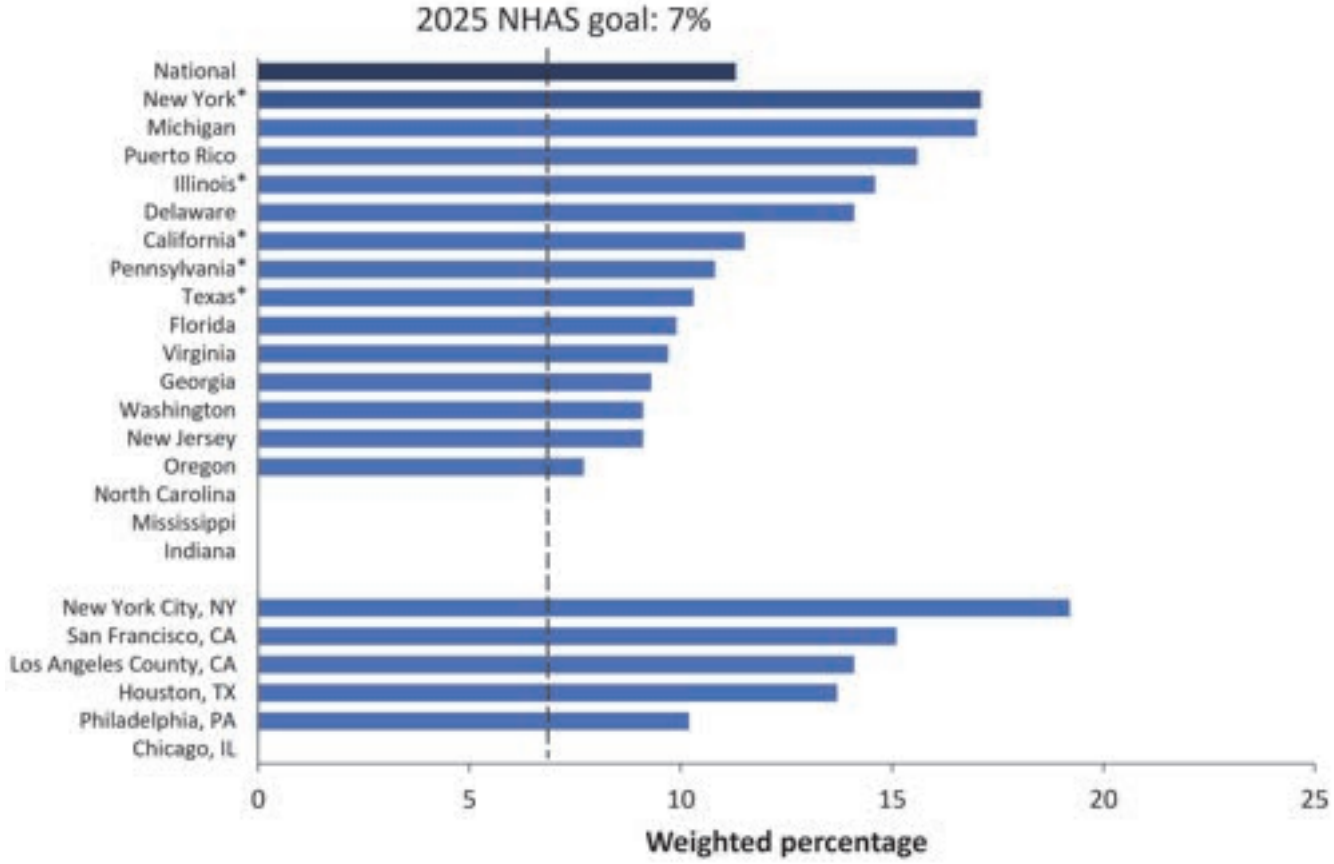


Abbreviations: NHAS, National HIV/AIDS Strategy; MMP, Medical Monitoring Project.

Note. "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size <30.

* Includes separately funded jurisdictions within each state.

Figure 21. Unemployment among adults with diagnosed HIV, by jurisdiction—Medical Monitoring Project, United States, 2022

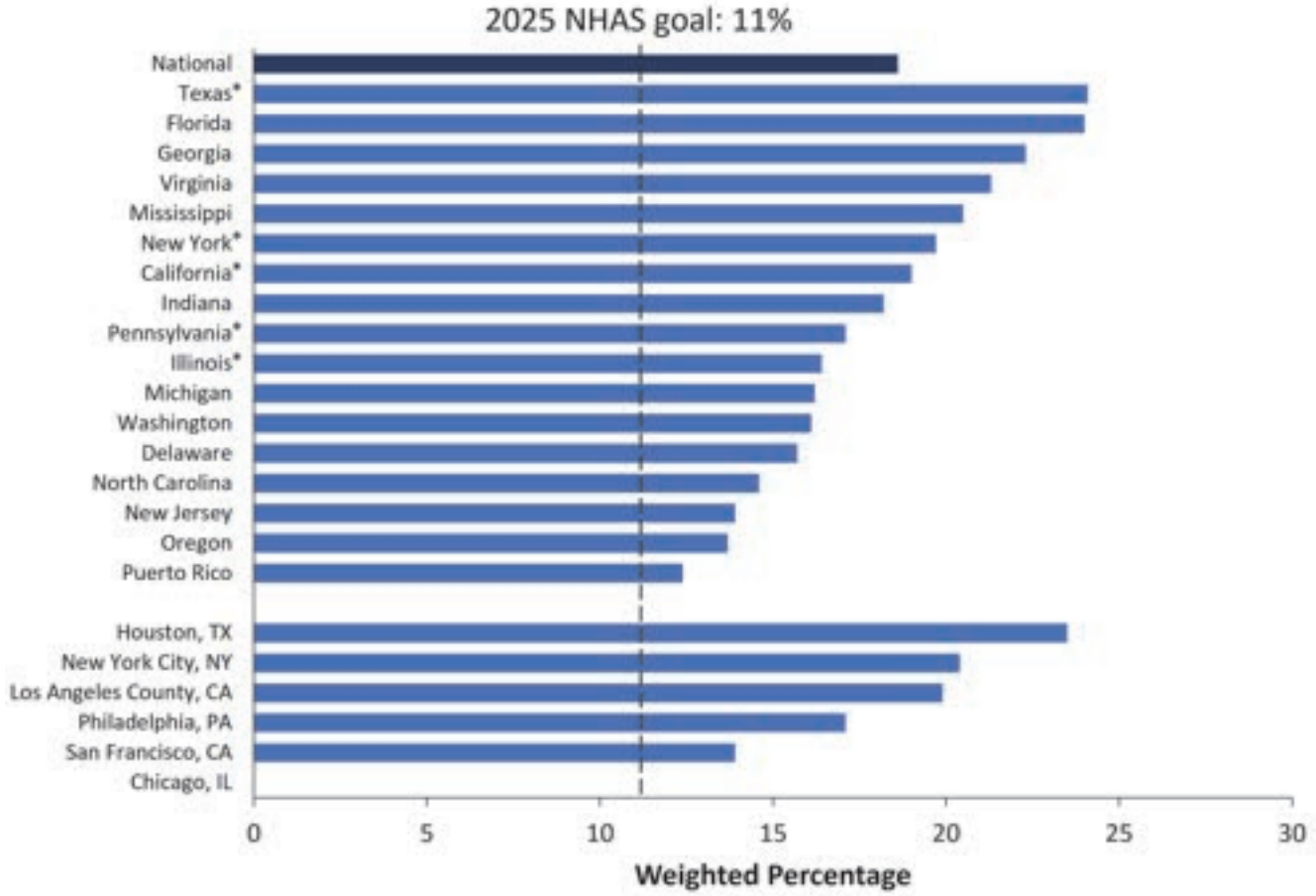


Abbreviations: NHAS, National HIV/AIDS Strategy; MMP, Medical Monitoring Project.

Note. Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size <30.

* Includes separately funded jurisdictions within each state.

Figure 22. Hunger or food insecurity among adults with diagnosed HIV, by jurisdiction—Medical Monitoring Project, United States, 2022

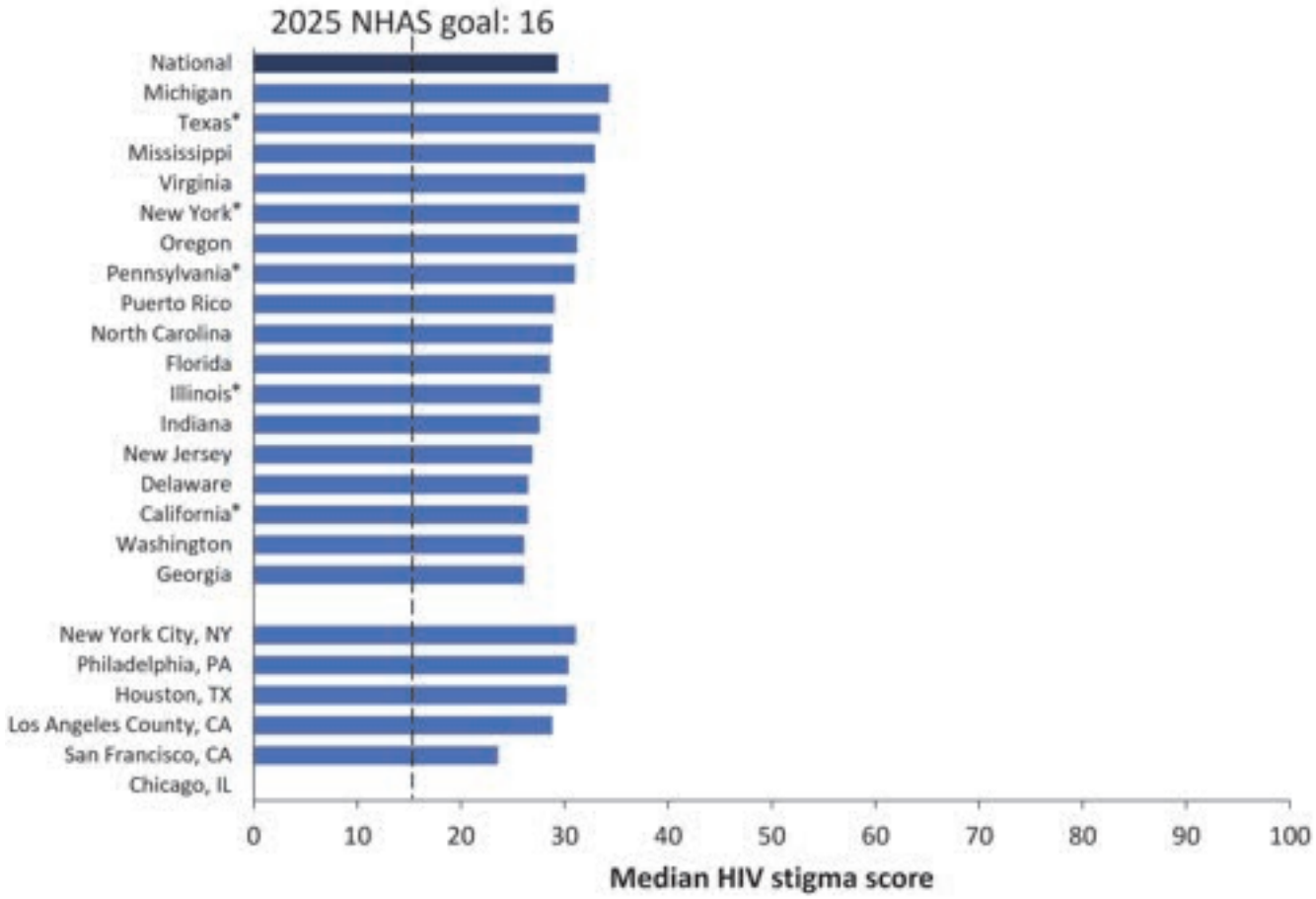


Abbreviations: NHAS, National HIV/AIDS Strategy; MMP, Medical Monitoring Project.

Note. "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months. Estimates were suppressed if they had a coefficient of variation ≥0.30 or were based on a denominator sample size <30.

* Includes separately funded jurisdictions within each state.

Figure 23. Median HIV stigma score among adults with diagnosed HIV, by jurisdiction—Medical Monitoring Project, United States, 2022



Abbreviations: NHAS, National HIV/AIDS Strategy; MMP, Medical Monitoring Project.

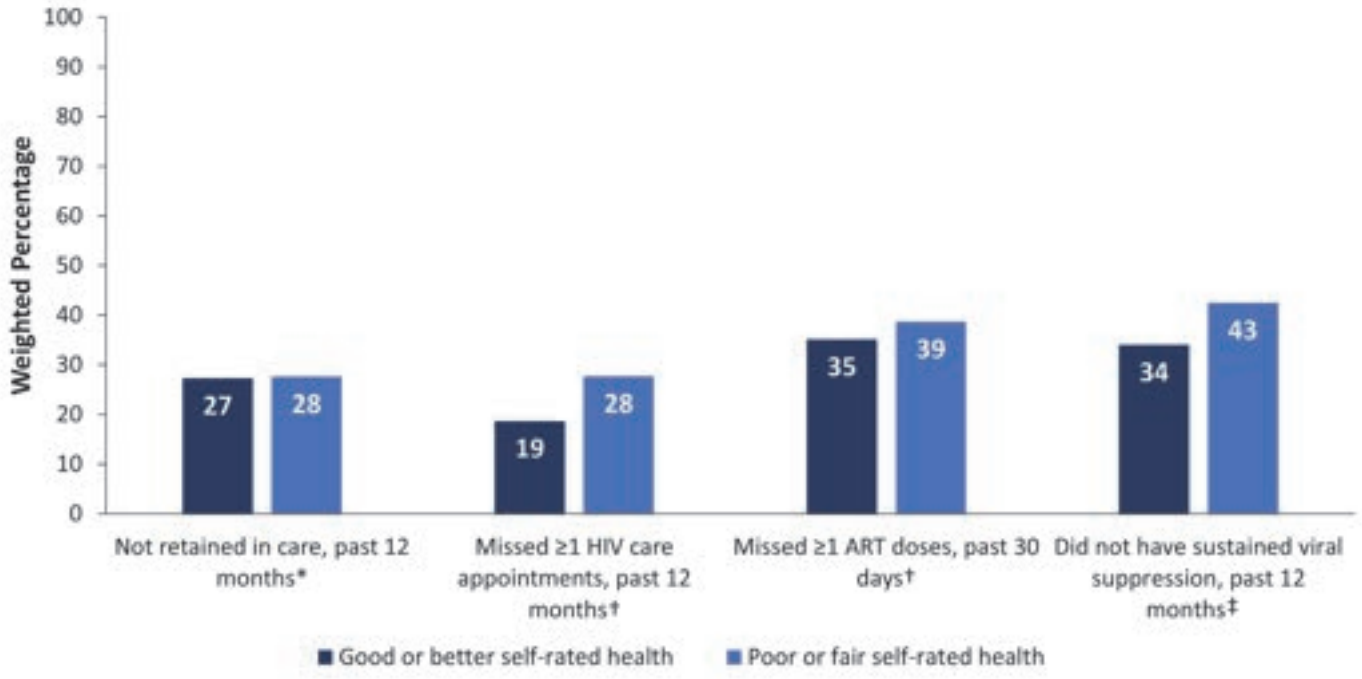
Note. "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. Estimates were suppressed if they were based on a denominator sample size <30.

* Includes separately funded jurisdictions within each state.

Prevalence of Adverse HIV Outcomes by NHAS QoL Indicators

The prevalence of not being retained in care was similar among those who had good or better self-rated health (27%) and those who had poor or fair self-rated health (28%) (Table 9; Figure 24). The prevalence of certain adverse HIV outcomes was lower among persons with good or better self-rated health than those with poor or fair self-rated health, including missing ≥1 HIV care appointments during the past 12 months (19% vs. 28%) and not having sustained viral suppression during the past 12 months (34% vs. 43%).

Figure 24. Prevalence of adverse clinical outcomes among adults with diagnosed HIV, by self-rated health—Medical Monitoring Project, United States, 2022



Note. Self-rated health evaluated at the time of interview.

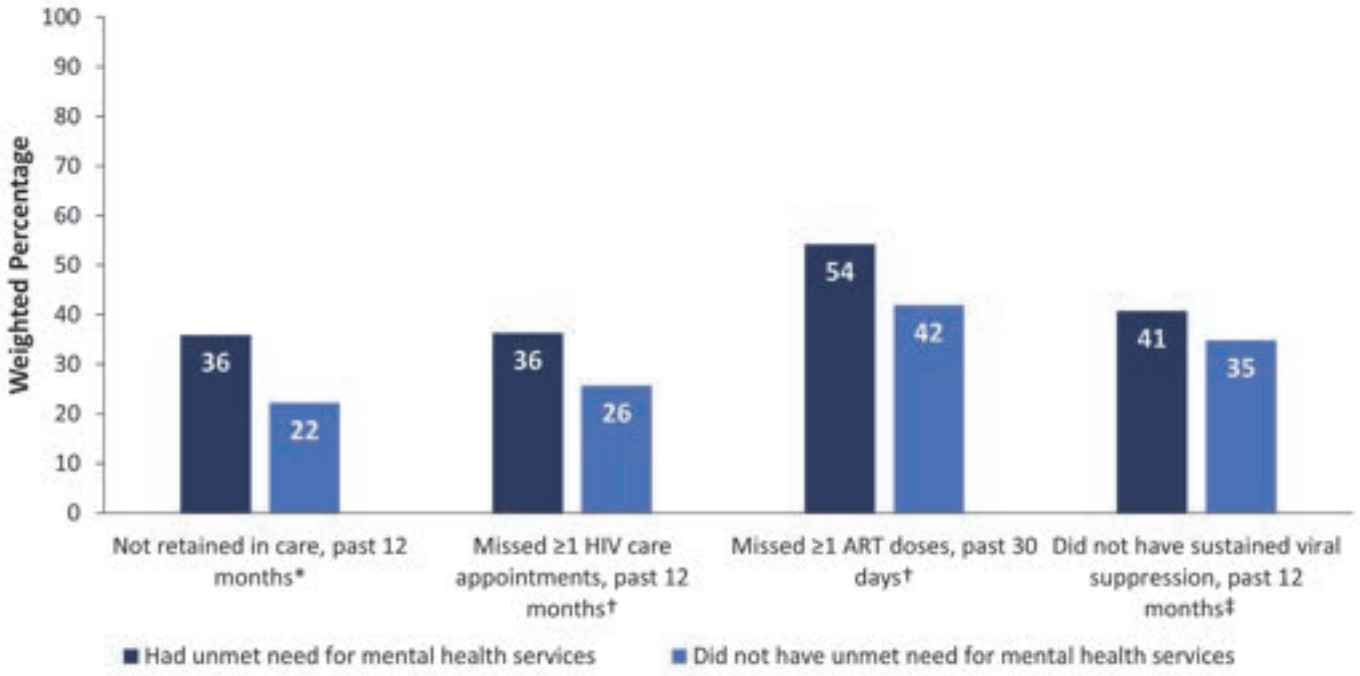
* Defined as not having 2 or more elements of outpatient HIV care at least 90 days apart during the past 12 months.

† Based on self-report.

‡ Defined as having ≥1 viral load measurements documented detectable or ≥200 copies/mL during the past 12 months.

The prevalence of certain adverse HIV outcomes was higher among persons with unmet needs for services from a mental health professional among those who needed it than those who did not, including not being retained in care during the past 12 months (36% vs. 22%), missing ≥1 HIV care appointments during the past 12 months (36% vs. 26%), and missing ≥1 ART doses during the past 30 days (54% vs. 42%) (Table 9; Figure 25).

Figure 25. Prevalence of adverse clinical outcomes among adults with diagnosed HIV, by whether or not persons experienced unmet needs for mental health services among those who needed them—Medical Monitoring Project, United States, 2022



Note. "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

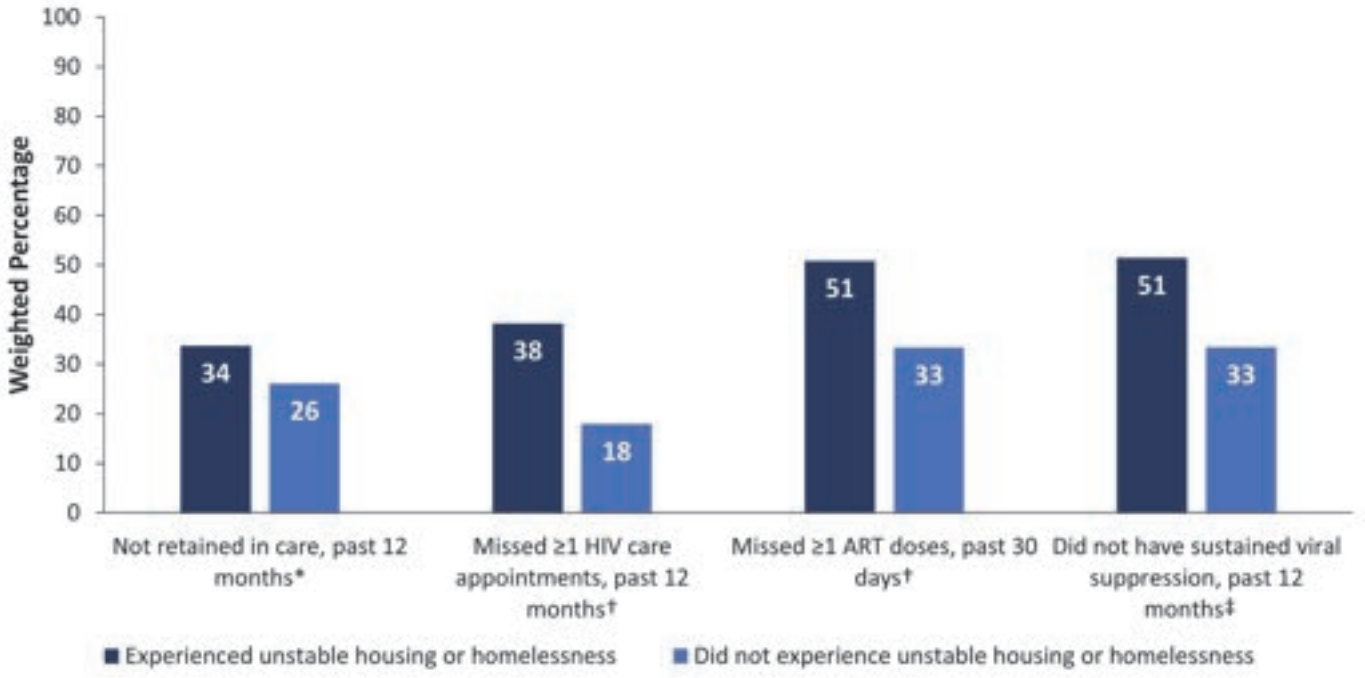
* Defined as not having 2 or more elements of outpatient HIV care at least 90 days apart during the past 12 months.

† Based on self-report.

‡ Defined as having ≥1 viral load measurements documented detectable or ≥200 copies/mL during the past 12 months.

The prevalence of certain adverse HIV outcomes was higher among persons who experienced unstable housing or homelessness during the past 12 months than those who did not, including not being retained in HIV care during the past 12 months (34% vs. 26%), missing ≥1 HIV care appointments during the past 12 months (38% vs. 18%), missing ≥1 ART doses during the past 30 days (51% vs. 33%), and not having sustained viral suppression during the past 12 months (51% vs. 33%) (Table 9; Figure 26).

Figure 26. Prevalence of adverse clinical outcomes among adults with diagnosed HIV, by whether or not persons experienced unstable housing or homelessness—Medical Monitoring Project, United States, 2022



Note. "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

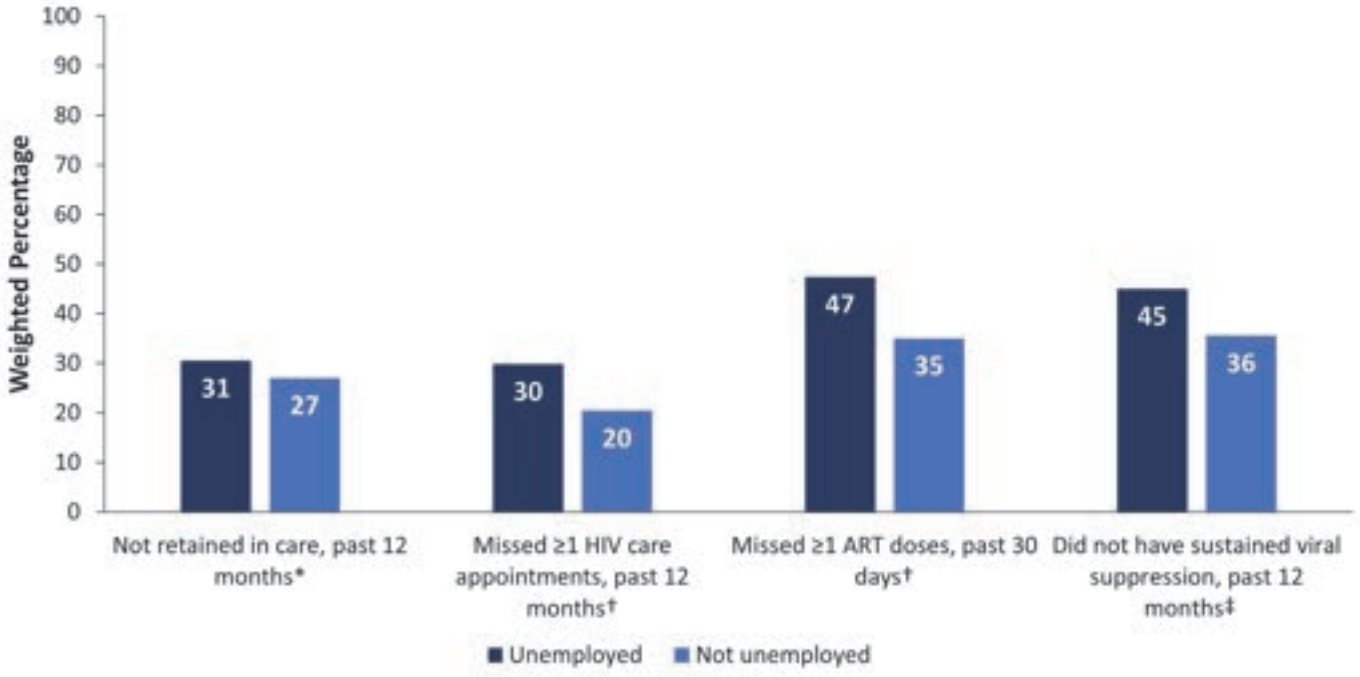
* Defined as not having 2 or more elements of outpatient HIV care at least 90 days apart during the past 12 months.

† Based on self-report.

‡ Defined as having ≥1 viral load measurements documented detectable or ≥200 copies/mL during the past 12 months.

The prevalence of certain adverse HIV outcomes was also higher among persons who were unemployed than those who were not, including missing ≥1 HIV care appointments during the past 12 months (30% vs. 20%), missing ≥1 ART doses during the past 30 days (47% vs. 35%), and not having sustained viral suppression during the past 12 months (45% vs. 36%) (Table 9; Figure 27).

Figure 27. Prevalence of adverse clinical outcomes among adults with diagnosed HIV, by whether or not persons were unemployed—Medical Monitoring Project, United States, 2022



Note. Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

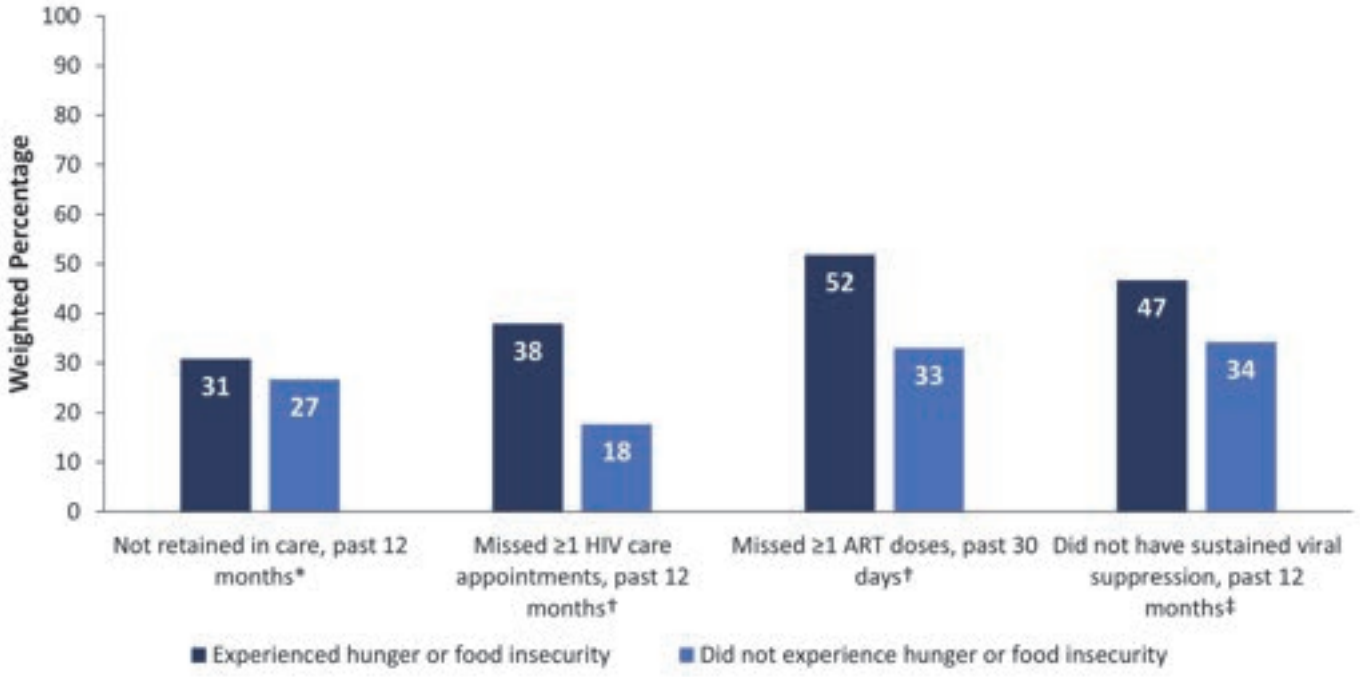
* Defined as not having 2 or more elements of outpatient HIV care at least 90 days apart during the past 12 months.

† Based on self-report.

‡ Defined as having ≥1 viral load measurements documented detectable or ≥200 copies/mL during the past 12 months.

The prevalence of certain adverse HIV outcomes was higher among persons who experienced hunger or food insecurity during the past 12 months than those who did not, including missing ≥1 HIV care appointments during the past 12 months (38% vs. 18%), missing ≥1 ART doses during the past 30 days (52% vs. 33%), and not having sustained viral suppression during the past 12 months (47% vs. 34%) (Table 9; Figure 28).

Figure 28. Prevalence of adverse clinical outcomes among adults with diagnosed HIV, by whether or not persons experienced hunger or food insecurity—Medical Monitoring Project, United States, 2022



Note. "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

* Defined as not having 2 or more elements of outpatient HIV care at least 90 days apart during the past 12 months.

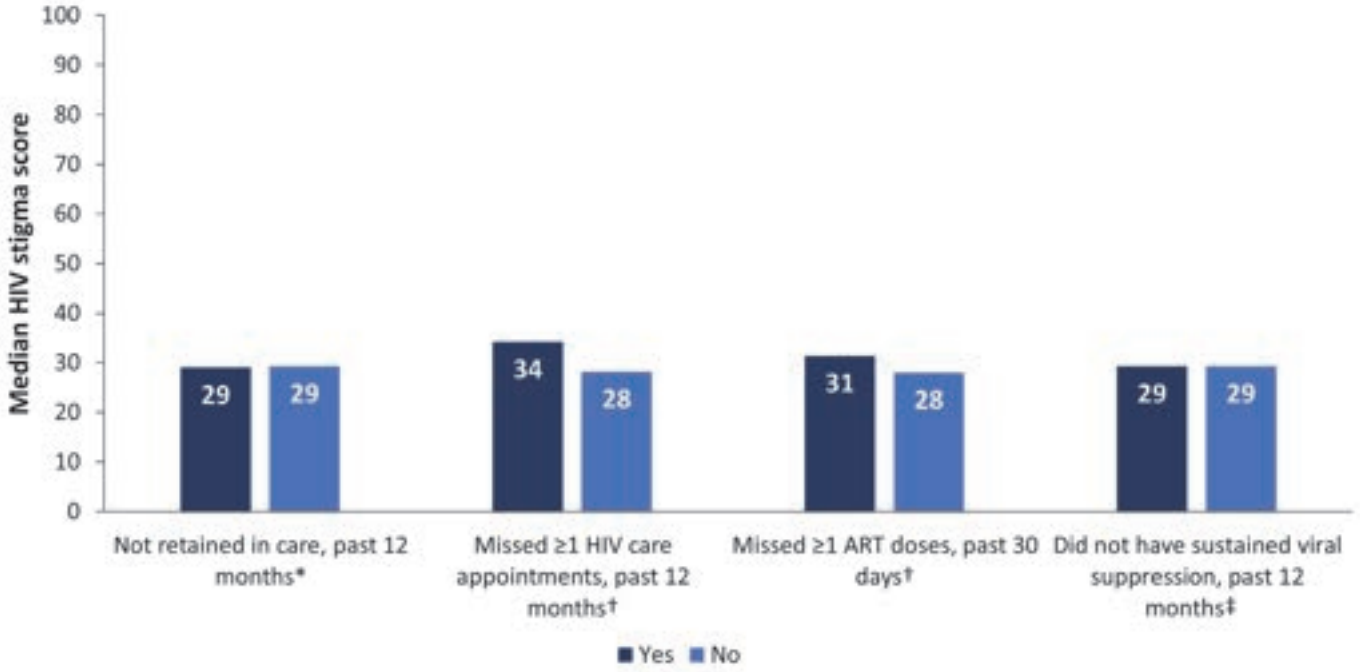
† Based on self-report.

‡ Defined as having ≥1 viral load measurements documented detectable or ≥200 copies/mL during the past 12 months.

HIV Stigma by HIV Outcomes

Median HIV stigma scores were higher among those who missed ≥1 HIV care appointments during the past 12 months versus those who did not (34 vs. 28) or missed ≥1 ART doses during the past 30 days versus those who did not (31 vs. 28; Figure 29). Median scores were similar by retention in care (not retained in care: 29, retained in care: 29) and viral suppression status (did not have sustained viral suppression: 29, had sustained viral suppression: 29) (Table 10; Figure 29).

Figure 29. Median HIV stigma scores among adults with diagnosed HIV, by selected HIV outcomes—Medical Monitoring Project, United States, 2022



Note. "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico.

* Defined as not having 2 or more elements of outpatient HIV care at least 90 days apart during the past 12 months.

† Based on self-report.

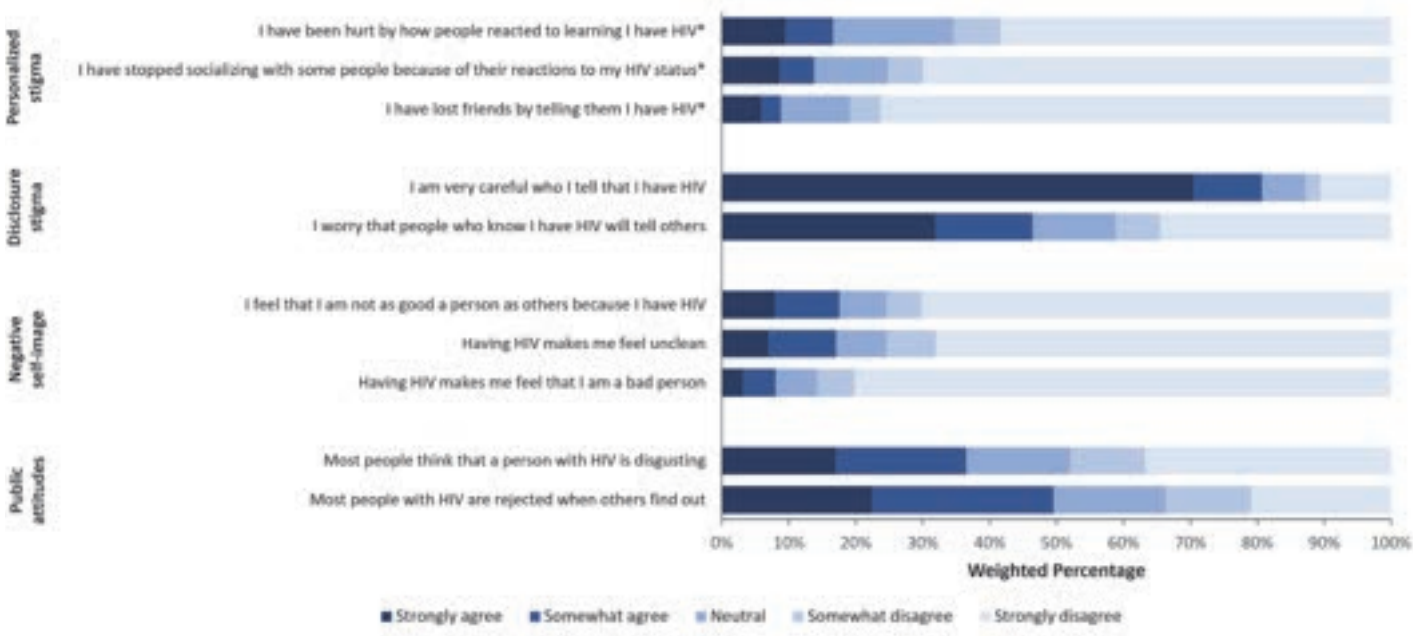
‡ Defined as having ≥1 viral load measurements documented detectable or ≥200 copies/mL during the past 12 months.

HIV Stigma Scale Responses by Stigma Domain

During 2022, the most highly endorsed "strongly agree" responses to the HIV stigma scale questions were within the disclosure domain (Table 11; Figure 30). Specifically, 70% of PWH strongly agreed with the statement "I am very careful who I tell that I have HIV," and 32% strongly agreed with the statement "I worry that people who know I have HIV will tell others."

During 2022, the most highly endorsed "strongly disagree" responses were within negative self-image and personalized stigma domains. Specifically, 80% of PWH strongly disagreed with the statement "Having HIV makes me feel that I am a bad person, and 76% strongly disagreed with the statement "During the past 12 months, I have lost friends by telling them I have HIV."

Figure 30. Experiences with HIV-related stigma among adults with diagnosed HIV, by domain—Medical Monitoring Project, United States, 2022



* During the past 12 months.

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5. Office of Infectious Disease and HIV/AIDS Policy, U.S. Department of Health and Human Services. EHE overview. https://www.hiv.gov/federal-response/ending-the-hiv-epidemic/overview/. Updated December 2023. Accessed October 4, 2024.

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Table 1. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by cycle year — Medical Monitoring Project, United States, 2015–2022

	2015			2016			2017			2018		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Total	**3,654**			**4,038**			**4,222**			**4,050**		
National HIV/AIDS Strategy indicators related to social determinants of health												
Quality of life												
Physical health												
Self-reported health status[a]												
Good, very good, excellent	N/A	N/A	N//A	N/A	N/A	N/A	N/A	N/A	N/A	2,825	71.5	(69.4–73.6)
Poor, fair	N/A	N/A	N//A	N/A	N/A	N/A	N/A	N/A	N/A	1,196	28.5	(26.4–30.6)
Mental or emotional health												
Unmet needs for services from a mental health professional among those who needed services, past 12 months[b]												
Yes	347	24.0	(20.9–27.1)	350	23.8	(20.7–26.9)	372	24.2	(21.0–27.5)	317	19.8	(17.1–22.5)
No	1,206	76.0	(72.9–79.1)	1,274	76.2	(73.1–79.3)	1,311	75.8	(72.5–79.0)	1,346	80.2	(77.5–82.9)
Structural or subsistence factors												
Unstable housing or homelessness, past 12 months[c]												
Yes	N/A	N/A	N//A	N/A	N/A	N/A	N/A	N/A	N/A	870	21.0	(19.5–22.6)
No	N/A	N/A	N//A	N/A	N/A	N/A	N/A	N/A	N/A	3,157	79.0	(77.4–80.5)
Unemployment[d]												
Yes	574	16.8	(15.2–18.5)	640	15.7	(14.2–17.3)	634	14.9	(13.5–16.4)	550	13.9	(12.6–15.1)
No	3,061	83.2	(81.5–84.8)	3,386	84.3	(82.7–85.8)	3,566	85.1	(83.6–86.5)	3,483	86.1	(84.9–87.4)
Hunger or food insecurity, past 12 months[e]												
Yes	771	21.5	(19.6–23.3)	865	21.2	(19.6–22.9)	866	21.1	(19.2–22.9)	802	19.5	(18.2–20.8)
No	2,862	78.5	(76.7–80.4)	3,164	78.8	(77.1–80.4)	3,340	78.9	(77.1–80.8)	3,234	80.5	(79.2–81.8)
HIV stigma, past 12 months **(n, median score, 95% CI)**[f]	N/A	N/A	N//A	N/A	N/A	N/A	N/A	N/A	N/A	3,824	31.2	(30.3–32.1)
Other factors important for health, including those that affect quality of life												
Economic stability												
Household income with respect to poverty guidelines[g]												
<100% FPL	1,608	46.4	(42.4–50.4)	1,633	42.1	(37.7–46.5)	1,661	41.6	(37.0–46.3)	1,651	42.9	(40.1–45.6)
100%–138% FPL	294	8.7	(7.5–9.9)	314	8.3	(7.5–9.1)	329	8.7	(7.8–9.6)	455	13.0	(11.7–14.3)
139%–399% FPL	1,109	33.4	(30.5–36.3)	1,291	35.5	(33.1–37.9)	1,383	35.7	(32.1–39.3)	1,186	33.2	(31.1–35.3)
≥400% FPL	416	11.5	(9.6–13.5)	508	14.1	(11.2–16.9)	554	14.0	(11.4–16.5)	414	10.9	(8.8–13.0)
Education												
Educational attainment												
Less than high school diploma	721	19.9	(17.4–22.3)	724	17.2	(14.8–19.6)	691	16.6	(15.1–18.1)	715	16.9	(14.9–18.9)
High school diploma or equivalent	916	24.2	(22.3–26.0)	1,029	25.6	(23.7–27.4)	1,116	27.3	(25.2–29.5)	1,088	27.1	(25.2–29.0)
Greater than high school	1,995	55.9	(52.7–59.2)	2,273	57.2	(53.9–60.6)	2,396	56.1	(53.3–58.8)	2,237	56.1	(53.0–59.2)
Health-related factors												
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[h]												
Any private	1,224	34.6	(31.4–37.7)	1,406	36.2	(33.3–39.1)	1,483	35.4	(32.0–38.9)	1,383	35.0	(31.8–38.3)
Public only, excluding RWHAP only	2,061	55.0	(50.4–59.6)	2,247	54.2	(51.1–57.2)	2,315	53.8	(50.3–57.4)	2,248	54.2	(49.7–58.8)
Uninsured or RWHAP only	309	10.4	(6.8–14.1)	335	9.6	(7.2–12.1)	381	10.7	(7.5–14.0)	373	10.8	(7.6–13.9)
Received RWHAP assistance, past 12 months												
Yes	1,693	45.1	(42.8–47.4)	1,900	44.4	(42.1–46.7)	1,988	45.9	(42.9–49.0)	1,925	45.7	(44.1–47.2)
No	1,854	54.9	(52.6–57.2)	2,051	55.6	(53.3–57.9)	2,116	54.1	(51.0–57.1)	2,007	54.3	(52.8–55.9)
Confidence in completing health forms												
Somewhat, a little bit, not at all	802	23.0	(21.0–25.0)	907	22.6	(20.8–24.5)	957	23.0	(21.4–24.7)	1,113	27.2	(25.5–28.9)
Extremely, quite a bit	2,826	77.0	(75.0–79.0)	3,104	77.4	(75.5–79.2)	3,237	77.0	(75.3–78.6)	2,916	72.8	(71.1–74.5)

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Table 1. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by cycle year—Medical Monitoring Project, United States, 2015–2022 *(cont)*

	2015			2016			2017			2018		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Health-related factors (cont)												
Has a disability[i]												
Yes	1,633	45.3	(42.4–48.3)	1,879	46.5	(43.8–49.2)	1,886	44.5	(42.7–46.4)	1,815	43.9	(41.5–46.3)
No	1,994	54.7	(51.7–57.6)	2,146	53.5	(50.8–56.2)	2,316	55.5	(53.6–57.3)	2,222	56.1	(53.7–58.5)
Any unmet HIV ancillary service need, past 12 months[j]												
Yes	N/A	N/A	N//A	N/A	N/A	N/A	N/A	N/A	N/A	1,880	47.3	(44.7–50.0)
No	N/A	N/A	N//A	N/A	N/A	N/A	N/A	N/A	N/A	2,143	52.7	(50.0–55.3)
Neighborhood and built environment												
Any met or unmet need for transportation assistance, past 12 months[k]												
Yes	1,222	32.1	(29.9–34.3)	1,301	30.4	(28.4–32.3)	1,352	31.4	(29.4–33.4)	1,408	32.9	(31.0–34.9)
No	2,406	67.9	(65.7–70.1)	2,705	69.6	(67.7–71.6)	2,838	68.6	(66.6–70.6)	2,604	67.1	(65.1–69.0)
Social and community context												
HIV health care discrimination among persons who received care, past 12 months[l]												
Yes	N/A	N/A	N//A	N/A	N/A	N/A	N/A	N/A	N/A	967	24.6	(21.9–27.2)
No	N/A	N/A	N//A	N/A	N/A	N/A	N/A	N/A	N/A	2,883	75.4	(72.8–78.1)
English proficiency												
Speaks English less than well	—	—	—	—	—	—	283	5.9	(2.6–9.2)	—	—	—
Speaks English well	3,379	93.0	(88.2–97.8)	3,775	93.6	(88.8–98.4)	3,924	94.1	(90.8–97.4)	3,770	93.3	(89.3–97.4)
Experiences of physical violence by an intimate partner or forced sex, lifetime[m]												
Yes	1,217	33.2	(30.5–36.0)	1,330	33.0	(30.5–35.6)	1,347	32.0	(29.3–34.7)	1,337	34.0	(30.6–37.4)
No	2,390	66.8	(64.0–69.5)	2,654	67.0	(64.4–69.5)	2,810	68.0	(65.3–70.7)	2,637	66.0	(62.6–69.4)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[m]												
Yes	192	5.7	(4.8–6.6)	200	4.9	(4.2–5.5)	185	4.8	(4.1–5.5)	187	4.7	(3.8–5.6)
No	3,407	94.3	(93.4–95.2)	3,767	95.1	(94.5–95.8)	3,961	95.2	(94.5–95.9)	3,775	95.3	(94.4–96.2)
Incarcerated >24 hours, past 12 months												
Yes	188	5.1	(3.9–6.2)	198	5.2	(4.3–6.2)	213	5.4	(4.5–6.4)	181	4.7	(3.7–5.8)
No	3,447	94.9	(93.8–96.1)	3,829	94.8	(93.8–95.7)	3,993	94.6	(93.6–95.5)	3,853	95.3	(94.2–96.3)

	2019			2020			2021			2022		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Total	**4,100**			**3,710**			**3,995**			**3,818**		
National HIV/AIDS Strategy indicators related to social determinants of health												
Quality of life												
Physical health												
Self-reported health status[a]												
Good, very good, excellent	2,848	70.6	(68.7–72.5)	2,621	71.5	(70.0–73.1)	2,697	68.8	(67.4–70.3)	2,562	69.9	(68.5–71.2)
Poor, fair	1,233	29.4	(27.5–31.3)	1,071	28.5	(26.9–30.0)	1,275	31.2	(29.7–32.6)	1,123	30.1	(28.8–31.5)
Mental or emotional health												
Unmet needs for services from a mental health professional among those who needed services, past 12 months[b]												
Yes	336	20.8	(17.4–24.3)	275	21.0	(18.2–23.8)	389	27.7	(22.9–32.5)	354	26.8	(23.0–30.6)
No	1,352	79.2	(75.7–82.6)	1,124	79.0	(76.2–81.8)	1,120	72.3	(67.5–77.1)	1,123	73.2	(69.4–77.0)
Structural or subsistence factors												
Unstable housing or homelessness, past 12 months[c]												
Yes	791	19.8	(18.0–21.6)	630	17.2	(15.2–19.2)	651	17.0	(15.3–18.6)	613	17.9	(16.5–19.3)
No	3,298	80.2	(78.4–82.0)	3,061	82.8	(80.8–84.8)	3,330	83.0	(81.4–84.7)	3,073	82.1	(80.7–83.5)

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Table 1. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by cycle/year—Medical Monitoring Project, United States, 2015–2022 *(cont)*

	2019			2020			2021			2022		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Structural or subsistence factors *(cont)*												
Unemployment[d]												
Yes	556	13.7	(12.2–15.3)	644	18.1	(16.5–19.7)	558	14.7	(13.4–16.0)	427	11.3	(9.4–13.2)
No	3,522	86.3	(84.7–87.8)	3,039	81.9	(80.3–83.5)	3,417	85.3	(84.0–86.6)	3,250	88.7	(86.8–90.6)
Hunger or food insecurity, past 12 months[e]												
Yes	781	19.9	(18.0–21.8)	592	16.4	(15.2–17.6)	607	15.7	(14.2–17.3)	651	18.6	(17.3–19.9)
No	3,302	80.1	(78.2–82.0)	3,101	83.6	(82.4–84.8)	3,369	84.3	(82.7–85.8)	3,038	81.4	(80.1–82.7)
HIV stigma, past 12 months **(n, median score, 95% CI)**[f]	3,904	30.7	(29.2–32.1)	3,518	28.4	(27.7–29.2)	3,712	28.8	(27.6–30.1)	3,319	29.3	(27.9–30.7)
Other factors important for health, including those that affect quality of life												
Economic stability												
Household income with respect to poverty guidelines[g]												
<100% FPL	1,593	41.6	(38.4–44.9)	1,189	35.6	(31.9–39.2)	1,373	38.0	(33.3–42.8)	1,106	33.0	(29.5–36.5)
100%–138% FPL	422	11.4	(10.3–12.5)	443	13.2	(11.9–14.6)	383	10.9	(9.2–12.7)	449	13.5	(12.1–14.9)
139%–399% FPL	1,235	34.3	(32.0–36.7)	1,218	35.8	(33.5–38.0)	1,279	36.5	(33.9–39.1)	1,200	37.2	(35.3–39.0)
≥400% FPL	488	12.6	(11.1–14.2)	526	15.4	(13.4–17.4)	543	14.5	(12.0–17.0)	572	16.3	(14.0–18.6)
Education												
Educational attainment												
Less than high school diploma	688	16.3	(15.0–17.6)	550	14.6	(12.9–16.3)	583	14.9	(12.4–17.4)	500	13.5	(11.9–15.1)
High school diploma or equivalent	1,103	26.7	(25.0–28.5)	899	25.0	(22.8–27.3)	1,039	25.9	(24.1–27.7)	987	26.9	(25.1–28.8)
Greater than high school	2,296	57.0	(54.7–59.2)	2,240	60.4	(57.7–63.1)	2,354	59.2	(56.0–62.5)	2,209	59.5	(56.9–62.2)
Health-related factors												
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[h]												
Any private	1,388	33.5	(30.7–36.2)	1,445	39.6	(37.2–42.0)	1,609	41.5	(38.7–44.3)	1,539	42.1	(39.2–45.1)
Public only, excluding RWHAP only	2,259	54.8	(50.8–58.8)	1,912	50.9	(47.5–54.3)	1,990	48.9	(44.3–53.6)	1,813	49.3	(45.1–53.4)
Uninsured or RWHAP only	396	11.7	(8.9–14.5)	295	9.5	(7.7–11.3)	314	9.6	(6.5–12.7)	264	8.6	(6.7–10.5)
Received RWHAP assistance, past 12 months												
Yes	1,950	46.1	(43.4–48.8)	1,796	47.2	(44.6–49.8)	1,897	47.1	(44.2–50.0)	1,738	46.8	(42.9–50.8)
No	2,030	53.9	(51.2–56.6)	1,791	52.8	(50.2–55.4)	1,926	52.9	(50.0–55.8)	1,803	53.2	(49.2–57.1)
Confidence in completing health forms												
Somewhat, a little bit, not at all	1,078	26.5	(24.9–28.2)	998	27.1	(24.9–29.3)	952	24.1	(22.2–25.9)	905	24.9	(23.3–26.4)
Extremely, quite a bit	2,999	73.5	(71.8–75.1)	2,689	72.9	(70.7–75.1)	3,017	75.9	(74.1–77.8)	2,782	75.1	(73.6–76.7)
Has a disability[i]												
Yes	1,797	42.6	(40.7–44.4)	1,507	39.7	(36.8–42.6)	1,674	40.6	(38.4–42.9)	1,547	42.1	(40.2–44.1)
No	2,288	57.4	(55.6–59.3)	2,178	60.3	(57.4–63.2)	2,303	59.4	(57.1–61.6)	2,141	57.9	(55.9–59.8)
Any unmet HIV ancillary service need, past 12 months[j]												
Yes	1,757	45.0	(41.0–49.1)	1,467	41.4	(39.6–43.2)	1,815	47.5	(44.9–50.1)	1,748	49.0	(45.6–52.5)
No	2,316	55.0	(50.9–59.0)	2,208	58.6	(56.8–60.4)	2,138	52.5	(49.9–55.1)	1,918	51.0	(47.5–54.4)
Neighborhood and built environment												
Any met or unmet need for transportation assistance, past 12 months[k]												
Yes	1,335	32.1	(30.2–34.1)	999	26.1	(24.5–27.7)	1,108	27.1	(25.6–28.6)	1,082	29.5	(27.8–31.3)
No	2,730	67.9	(65.9–69.8)	2,675	73.9	(72.3–75.5)	2,838	72.9	(71.4–74.4)	2,548	70.5	(68.7–72.2)
Social and community context												
HIV health care discrimination among persons who received care, past 12 months[l]												
Yes	843	21.7	(18.9–24.4)	724	20.4	(17.3–23.4)	815	21.8	(19.3–24.4)	781	23.4	(20.8–26.0)
No	3,061	78.3	(75.6–81.1)	2,734	79.6	(76.6–82.7)	2,858	78.2	(75.6–80.7)	2,647	76.6	(74.0–79.2)

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Table 1. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by cycle year—Medical Monitoring Project, United States, 2015–2022 *(cont)*

	2019			2020			2021			2022		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Social and community context (cont)												
English proficiency												
Speaks English less than well	292	7.1	(2.9–11.3)	284	7.1	(3.4–10.7)	327	7.4	(3.9–10.9)	298	7.2	(4.0–10.5)
Speaks English well	3,794	92.9	(88.7–97.1)	3,411	92.9	(89.3–96.6)	3,657	92.6	(89.1–96.1)	3,398	92.8	(89.5–96.0)
Experiences of physical violence by an intimate partner or forced sex, lifetime[m]												
Yes	1,291	31.4	(29.1–33.8)	1,138	31.9	(28.2–35.5)	1,292	34.5	(32.2–36.8)	1,228	35.1	(32.7–37.5)
No	2,736	68.6	(66.2–70.9)	2,492	68.1	(64.5–71.8)	2,586	65.5	(63.2–67.8)	2,368	64.9	(62.5–67.3)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[m]												
Yes	208	5.1	(4.4–5.9)	161	4.8	(4.0–5.6)	182	5.7	(4.6–6.7)	182	5.9	(5.0–6.9)
No	3,806	94.9	(94.1–95.6)	3,456	95.2	(94.4–96.0)	3,673	94.3	(93.3–95.4)	3,383	94.1	(93.1–95.0)
Incarcerated >24 hours, past 12 months												
Yes	148	3.9	(3.0–4.8)	107	3.5	(2.4–4.6)	93	2.8	(2.2–3.5)	100	3.0	(2.3–3.6)
No	3,938	96.1	(95.2–97.0)	3,588	96.5	(95.4–97.6)	3,886	97.2	(96.5–97.8)	3,597	97.0	(96.4–97.7)

Abbreviations: n, number; col, column; CI, confidence interval; N/A, not applicable; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, U.S. Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. Unweighted numbers and weighted percentages are presented. CIs incorporate weighted percentages. Excluded are estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30.

[a] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[b] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[c] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[d] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[e] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[f] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[g] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[h] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city-, county-, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[i] Self-reported, and includes physical, mental, and emotional disabilities.

[j] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[k] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[l] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[m] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

Table 2a. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by age—Medical Monitoring Project, United States, 2022

	18–29 years			30–39 years			40–49 years			50–64 years			≥65 years		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Total (row %)	**256**	**7.2**	**(5.9–8.5)**	**675**	**18.4**	**(17.3–19.6)**	**651**	**19.1**	**(17.7–20.4)**	**1,625**	**40.5**	**(38.7–42.2)**	**611**	**14.8**	**(13.7–15.9)**
National HIV/AIDS Strategy indicators related to social determinants of health															
Quality of life															
Physical health															
Self-reported health status[a]															
Good, very good, excellent	192	80.6	(76.1–85.1)	513	78.4	(74.3–82.5)	443	71.9	(68.6–75.1)	1,022	64.5	(62.0–66.9)	392	66.4	(62.2–70.5)
Poor, fair	46	19.4	(14.9–23.9)	142	21.6	(17.5–25.7)	178	28.1	(24.9–31.4)	560	35.5	(33.1–38.0)	197	33.6	(29.5–37.8)
Mental or emotional health															
Unmet needs for services from a mental health professional among those who needed services, past 12 months[b]															
Yes	30	32.5	(24.1–40.8)	98	32.5	(27.5–37.5)	74	31.5	(23.7–39.2)	127	23.0	(17.9–28.1)	25	14.4	(7.4–21.4)
No	73	67.5	(59.2–75.9)	220	67.5	(62.5–72.5)	186	68.5	(60.8–76.3)	510	77.0	(71.9–82.1)	134	85.6	(78.6–92.6)
Structural or subsistence factors															
Unstable housing or homelessness, past 12 months[c]															
Yes	80	32.3	(26.7–38.0)	156	26.9	(22.6–31.2)	119	19.5	(16.0–23.0)	206	13.7	(11.6–15.7)	52	9.3	(6.8–11.8)
No	161	67.7	(62.0–73.3)	499	73.1	(68.8–77.4)	501	80.5	(77.0–84.0)	1,375	86.3	(84.3–88.4)	537	90.7	(88.2–93.2)
Unemployment[d]															
Yes	40	16.4	(11.5–21.4)	103	15.5	(11.6–19.4)	97	14.8	(11.2–18.4)	162	9.7	(7.8–11.6)	25	3.4	(1.5–5.3)
No	196	83.6	(78.6–88.5)	549	84.5	(80.6–88.4)	524	85.2	(81.6–88.8)	1,419	90.3	(88.4–92.2)	562	96.6	(94.7–98.5)
Hunger or food insecurity, past 12 months[e]															
Yes	63	26.3	(19.5–33.1)	160	24.4	(21.5–27.3)	140	23.3	(19.4–27.2)	255	17.1	(15.1–19.0)	33	6.0	(3.8–8.2)
No	176	73.7	(66.9–80.5)	495	75.6	(72.7–78.5)	484	76.7	(72.8–80.6)	1,328	82.9	(81.0–84.9)	555	94.0	(91.8–96.2)
HIV stigma, past 12 months **(n, median score, 95% CI)**[f]	227	36.4	(32.8–40.0)	601	33.2	(30.8–35.6)	554	30.4	(27.2–33.6)	1,420	28.6	(27.0–30.2)	517	23.1	(20.7–25.4)
Other factors important for health, including those that affect quality of life															
Economic stability															
Household income with respect to poverty guidelines[g]															
<100% FPL	56	31.2	(23.7–38.6)	177	29.8	(24.6–35.0)	166	30.0	(24.3–35.8)	538	36.8	(32.4–41.1)	169	31.0	(25.5–36.5)
100%–138% FPL	21	10.4	(6.0–14.9)	66	12.7	(9.6–15.9)	79	14.3	(11.5–17.0)	204	13.8	(11.5–16.2)	79	14.0	(11.2–16.8)
139%–399% FPL	104	50.3	(43.6–57.0)	224	41.0	(35.9–46.1)	215	39.6	(35.7–43.5)	451	32.0	(28.5–35.4)	206	37.9	(32.7–43.1)
≥400% FPL	17	8.1	(4.5–11.7)	101	16.4	(11.4–21.4)	103	16.1	(11.4–20.7)	257	17.4	(15.0–19.9)	94	17.1	(13.7–20.5)
Education															
Educational attainment															
Less than high school diploma	18	8.2	(3.9–12.4)	63	9.6	(7.0–12.3)	89	14.1	(10.6–17.5)	247	15.1	(13.0–17.2)	83	15.9	(11.0–20.8)
High school diploma or equivalent	97	40.3	(33.5–47.0)	181	29.7	(25.0–34.5)	166	26.8	(21.5–32.2)	415	25.5	(23.4–27.6)	128	21.1	(17.9–24.4)
Greater than high school	126	51.5	(45.3–57.7)	412	60.7	(55.6–65.7)	371	59.1	(53.0–65.3)	921	59.4	(56.7–62.1)	379	63.0	(57.7–68.2)
Health-related factors															
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[h]															
Any private	102	42.9	(37.1–48.6)	301	46.4	(40.0–52.8)	275	42.6	(38.2–47.1)	641	42.0	(38.4–45.6)	220	36.1	(31.6–40.6)
Public only, excluding RWHAP only	98	42.3	(34.3–50.3)	268	40.9	(32.8–49.1)	279	45.7	(39.5–51.9)	823	51.3	(47.4–55.1)	345	62.4	(57.8–67.0)
Uninsured or RWHAP only	31	14.9	(9.3–20.4)	71	12.6	(9.3–16.0)	65	11.7	(6.7–16.7)	88	6.8	(5.2–8.3)	-	-	-
Received RWHAP assistance, past 12 months															
Yes	107	45.1	(35.4–54.7)	324	47.8	(43.3–52.2)	308	50.4	(45.0–55.9)	748	46.5	(41.7–51.4)	251	42.4	(36.5–48.4)
No	116	54.9	(45.3–64.6)	305	52.2	(47.8–56.7)	294	49.6	(44.1–55.0)	777	53.5	(48.6–58.3)	311	57.6	(51.6–63.5)
Confidence in completing health forms															
Somewhat, a little bit, not at all	53	23.4	(16.6–30.3)	128	19.9	(15.6–24.1)	152	24.5	(20.3–28.7)	414	25.9	(23.7–28.2)	158	29.3	(24.2–34.3)
Extremely, quite a bit	185	76.6	(69.7–83.4)	527	80.1	(75.9–84.4)	472	75.5	(71.3–79.7)	1,168	74.1	(71.8–76.3)	430	70.7	(65.7–75.8)
Has a disability[i]															
Yes	70	28.5	(22.6–34.3)	203	31.1	(26.7–35.4)	237	40.9	(35.5–46.2)	743	47.9	(45.3–50.4)	294	48.4	(44.1–52.7)
No	171	71.5	(65.7–77.4)	453	68.9	(64.6–73.3)	385	59.1	(53.8–64.5)	837	52.1	(49.6–54.7)	295	51.6	(47.3–55.9)
Any unmet HIV ancillary service need, past 12 months[j]															
Yes	150	63.1	(56.7–69.5)	377	60.0	(55.1–64.8)	304	49.2	(43.8–54.5)	723	47.1	(43.4–50.9)	194	33.8	(28.8–38.8)
No	85	36.9	(30.5–43.3)	274	40.0	(35.2–44.9)	313	50.8	(45.5–56.2)	854	52.9	(49.1–56.6)	392	66.2	(61.2–71.2)

Table 2a. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by age—Medical Monitoring Project, United States, 2022 *(cont)*

	18–29 years			30–39 years			40–49 years			50–64 years			≥65 years		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Neighborhood and built environment															
Any met or unmet need for transportation assistance, past 12 months[k]															
Yes	57	24.8	(18.4–31.3)	169	26.7	(23.6–29.9)	161	27.8	(23.6–32.0)	507	32.1	(29.5–34.7)	188	30.4	(26.6–34.2)
No	176	75.2	(68.7–81.6)	472	73.3	(70.1–76.4)	451	72.2	(68.0–76.4)	1,053	67.9	(65.3–70.5)	396	69.6	(65.8–73.4)
Social and community context															
HIV health care discrimination among persons who received care, past 12 months[l]															
Yes	53	26.4	(17.6–35.3)	163	28.2	(24.5–31.9)	150	26.3	(21.0–31.7)	325	22.4	(19.2–25.6)	90	15.5	(11.5–19.6)
No	167	73.6	(64.7–82.4)	424	71.8	(68.1–75.5)	428	73.7	(68.3–79.0)	1,165	77.6	(74.4–80.8)	463	84.5	(80.4–88.5)
English proficiency															
Speaks English less than well	—	—	—	45	6.3	(3.9–8.7)	55	8.6	(5.6–11.6)	—	—	—	—	—	—
Speaks English well	234	98.1	(96.5–99.8)	611	93.7	(91.3–96.1)	570	91.4	(88.4–94.4)	1,441	91.9	(87.1–96.7)	542	93.1	(88.6–97.6)
Experiences of physical violence by an intimate partner or forced sex, lifetime[m]															
Yes	94	41.3	(35.6–47.1)	256	40.3	(36.3–44.2)	243	42.6	(38.4–46.9)	503	32.4	(28.7–36.2)	132	23.2	(18.6–27.8)
No	139	58.7	(52.9–64.4)	385	59.7	(55.8–63.7)	361	57.4	(53.1–61.6)	1,042	67.6	(63.8–71.3)	441	76.8	(72.2–81.4)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[m]															
Yes	26	11.8	(8.0–15.7)	71	11.5	(8.9–14.1)	31	7.1	(4.5–9.6)	50	3.8	(2.3–5.3)	—	—	—
No	202	88.2	(84.3–92.0)	565	88.5	(85.9–91.1)	565	92.9	(90.4–95.5)	1,485	96.2	(94.7–97.7)	566	99.4	(98.9–100)
Incarcerated >24 hours, past 12 months															
Yes	14	6.5	(3.3–9.6)	26	4.1	(2.7–5.6)	22	2.8	(1.6–4.1)	31	2.6	(1.6–3.6)	—	—	—
No	227	93.5	(90.4–96.7)	630	95.9	(94.4–97.3)	603	97.2	(95.9–98.4)	1,553	97.4	(96.4–98.4)	584	98.8	(98.0–99.7)

Abbreviations: n, number; col, column; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, U.S. Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. Unweighted numbers and weighted percentages are presented. CIs incorporate weighted percentages. Excluded are estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30.

[a] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[b] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[c] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[d] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[e] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[f] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[g] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[h] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[i] Self-reported, and includes physical, mental, and emotional disabilities.

[j] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[k] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[l] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[m] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

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Table 2b. Relative and absolute differences in individual-level social determinants of health and quality of life among adults with diagnosed HIV, by age—Medical Monitoring Project, United States, 2022

	18–29 years vs. ≥65 years				30–39 years vs. ≥65 years				40–49 years vs. ≥65 years				50–59 years vs. ≥65 years			
	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
National HIV/AIDS Strategy indicators related to social determinants of health																
Quality of life																
Physical health																
Self-reported health status[a]																
Good, very good, excellent	1.21	(1.12–1.32)	14.24	(8.36– 20.12)	1.18	(1.07–1.30)	12.03	(5.21– 18.85)	1.08	(1.00–1.18)	5.52	(-0.25– 11.29)	0.97	(0.91–1.04)	-1.89	(-6.41– 2.62)
Poor, fair	0.58	(0.45–0.74)	-14.24	(-20.12– -8.36)	0.64	(0.49–0.83)	-12.03	(-18.85– -5.21)	0.84	(0.69–1.01)	-5.52	(-11.29– 0.25)	1.06	(0.93–1.21)	1.89	(-2.62– 6.41)
Mental or emotional health																
Unmet needs for services from a mental health professional among those who needed services, past 12 months[b]																
Yes	2.25	(1.34–3.79)	18.04	(7.85– 28.24)	2.25	(1.35–3.75)	18.08	(9.51– 26.66)	2.18	(1.40–3.41)	17.05	(9.05– 25.04)	1.60	(1.03–2.47)	8.59	(1.96– 15.22)
No	0.79	(0.69–0.91)	-18.04	(-28.24– -7.85)	0.79	(0.71–0.88)	-18.08	(-26.66– -9.51)	0.80	(0.72–0.89)	-17.05	(-25.04– -9.05)	0.90	(0.83–0.97)	-8.59	(-15.22– -1.96)
Structural or subsistence factors																
Unstable housing or homelessness, past 12 months[c]																
Yes	3.49	(2.52–4.83)	23.07	(16.80– 29.35)	2.90	(2.16–3.90)	17.65	(12.94– 22.36)	2.10	(1.53–2.89)	10.22	(5.98– 14.45)	1.48	(1.09–2.00)	4.42	(1.23– 7.61)
No	0.75	(0.68–0.82)	-23.07	(-29.35– -16.80)	0.81	(0.76–0.86)	-17.65	(-22.36– -12.94)	0.89	(0.84–0.93)	-10.22	(-14.45– -5.98)	0.95	(0.92–0.99)	-4.42	(-7.61– -1.23)
Unemployment[d]																
Yes	4.84	(2.78–8.43)	13.02	(8.27– 17.76)	4.56	(2.70–7.71)	12.09	(8.47– 15.70)	4.37	(2.33–8.18)	11.42	(7.26– 15.57)	2.87	(1.58–5.21)	6.33	(3.63– 9.02)
No	0.87	(0.82–0.92)	-13.02	(-17.76– -8.27)	0.87	(0.84–0.91)	-12.09	(-15.70– -8.47)	0.88	(0.84–0.92)	-11.42	(-15.57– -7.26)	0.93	(0.91–0.96)	-6.33	(-9.02– -3.63)
Hunger or food insecurity, past 12 months[e]																
Yes	4.40	(2.95–6.57)	20.34	(13.63– 27.04)	4.08	(2.78–6.00)	18.42	(14.79– 22.05)	3.90	(2.62–5.80)	17.30	(12.89– 21.72)	2.86	(1.95–4.18)	11.08	(8.18– 13.99)
No	0.78	(0.72–0.86)	-20.34	(-27.04– -13.63)	0.80	(0.77–0.84)	-18.42	(-22.05– -14.79)	0.82	(0.77–0.86)	-17.30	(-21.72– -12.89)	0.88	(0.85–0.91)	-11.08	(-13.99– -8.18)
HIV stigma, past 12 months **(n, median score, 95% CI)**[f]																
Other factors important for health, including those that affect quality of life																
Economic stability																
Household income with respect to poverty guidelines[g]																
<100% FPL	1.01	(0.80–1.27)	0.16	(-7.13– 7.45)	0.96	(0.75–1.23)	-1.16	(-8.69– 6.37)	0.97	(0.80–1.18)	-0.96	(-6.98– 5.06)	1.19	(1.02–1.38)	5.77	(1.04– 10.51)
100%–138% FPL	0.75	(0.47–1.18)	-3.55	(-8.65– 1.55)	0.91	(0.65–1.27)	-1.26	(-5.66– 3.13)	1.02	(0.78–1.34)	0.27	(-3.56– 4.10)	0.99	(0.78–1.25)	-0.16	(-3.38– 3.07)
139%–399% FPL	1.33	(1.13–1.56)	12.42	(5.25– 19.58)	1.08	(0.89–1.32)	3.09	(-4.73– 10.91)	1.05	(0.88–1.24)	1.72	(-4.87– 8.30)	0.84	(0.72–0.98)	-5.94	(-11.40– -0.49)
≥400% FPL	0.47	(0.29–0.77)	-9.03	(-13.96– -4.09)	0.96	(0.68–1.36)	-0.66	(-6.38– 5.05)	0.94	(0.69–1.29)	-1.03	(-6.17– 4.11)	1.02	(0.82–1.27)	0.33	(-3.45– 4.10)
Education																
Educational attainment																
Less than high school diploma	0.51	(0.28–0.95)	-7.71	(-14.31– -1.11)	0.61	(0.38–0.96)	-6.28	(-12.43– -0.12)	0.88	(0.62–1.26)	-1.84	(-7.23– 3.55)	0.95	(0.70–1.29)	-0.80	(-5.59– 3.99)
High school diploma or equivalent	1.91	(1.49–2.44)	19.14	(11.14– 27.14)	1.41	(1.13–1.74)	8.57	(2.98– 14.16)	1.27	(0.97–1.65)	5.68	(-0.85– 12.21)	1.21	(1.02–1.42)	4.39	(0.75– 8.03)
Greater than high school	0.82	(0.71–0.95)	-11.43	(-19.70– -3.17)	0.96	(0.86–1.08)	-2.30	(-9.38– 4.79)	0.94	(0.85–1.04)	-3.84	(-10.00– 2.32)	0.94	(0.87–1.03)	-3.59	(-8.96– 1.77)
Health-related factors																
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[h]																
Any private	1.19	(0.99–1.42)	6.78	(-0.29– 13.85)	1.29	(1.06–1.56)	10.35	(2.26– 18.44)	1.18	(1.01–1.39)	6.55	(0.29– 12.81)	1.16	(1.01–1.34)	5.90	(0.59– 11.20)
Public only, excluding RWHAP only	0.68	(0.55–0.83)	-20.11	(-29.50– -10.72)	0.66	(0.53–0.82)	-21.45	(-31.24– -11.66)	0.73	(0.62–0.86)	-16.69	(-24.98– -8.41)	0.82	(0.74–0.91)	-11.14	(-16.93– -5.34)
Uninsured or RWHAP only	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Received RWHAP assistance, past 12 months																
Yes	1.06	(0.84–1.34)	2.61	(-7.71– 12.92)	1.13	(0.98–1.29)	5.32	(-0.64– 11.27)	1.19	(1.02–1.39)	7.99	(0.87– 15.10)	1.10	(0.95–1.26)	4.09	(-2.13– 10.31)
No	0.95	(0.79–1.15)	-2.61	(-12.92– 7.71)	0.91	(0.82–1.01)	-5.32	(-11.27– 0.64)	0.86	(0.75–0.98)	-7.99	(-15.10– -0.87)	0.93	(0.83–1.04)	-4.09	(-10.31– 2.13)
Confidence in completing health forms																
Somewhat, a little bit, not at all	0.80	(0.56–1.15)	-5.85	(-14.89– 3.19)	0.68	(0.49–0.94)	-9.41	(-17.23– -1.59)	0.84	(0.67–1.04)	-4.75	(-10.69– 1.18)	0.89	(0.73–1.08)	-3.32	(-8.92– 2.28)
Extremely, quite a bit	1.08	(0.96–1.22)	5.85	(-3.19– 14.89)	1.13	(1.02–1.26)	9.41	(1.59– 17.23)	1.07	(0.98–1.16)	4.75	(-1.18– 10.69)	1.05	(0.97–1.13)	3.32	(-2.28– 8.92)
Has a disability[i]																
Yes	0.59	(0.47–0.73)	-19.90	(-26.92– -12.89)	0.64	(0.54–0.76)	-17.32	(-23.75– -10.89)	0.85	(0.72–0.99)	-7.48	(-14.44– -0.52)	0.99	(0.90–1.09)	-0.51	(-5.10– 4.09)
No	1.39	(1.24–1.55)	19.90	(12.89– 26.92)	1.34	(1.20–1.49)	17.32	(10.89– 23.75)	1.14	(1.01–1.30)	7.48	(0.52– 14.44)	1.01	(0.92–1.10)	0.51	(-4.09– 5.10)
Any unmet HIV ancillary service need, past 12 months[j]																
Yes	1.87	(1.57–2.21)	29.28	(21.59– 36.96)	1.77	(1.52–2.08)	26.15	(19.76– 32.54)	1.46	(1.25–1.70)	15.38	(9.31– 21.45)	1.39	(1.22–1.59)	13.34	(8.72– 17.97)
No	0.56	(0.47–0.67)	-29.28	(-36.96– -21.59)	0.60	(0.53–0.69)	-26.15	(-32.54– -19.76)	0.77	(0.69–0.86)	-15.38	(-21.45– -9.31)	0.80	(0.74–0.86)	-13.34	(-17.97– -8.72)

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Table 2b. Relative and absolute differences in individual-level social determinants of health and quality of life among adults with diagnosed HIV, by age—Medical Monitoring Project, United States, 2022 *(cont)*

	18–29 years vs. ≥65 years				30–39 years vs. ≥65 years				40–49 years vs. ≥65 years				50–59 years vs. ≥65 years			
	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
Neighborhood and built environment																
Any met or unmet need for transportation assistance, past 12 months[k]																
Yes	0.82	(0.61–1.09)	-5.57	(-12.97– 1.83)	0.88	(0.74–1.05)	-3.66	(-8.68– 1.37)	0.91	(0.76–1.10)	-2.61	(-7.85– 2.63)	1.06	(0.93–1.20)	1.69	(-2.38– 5.77)
No	1.08	(0.98–1.19)	5.57	(-1.83– 12.97)	1.05	(0.98–1.13)	3.66	(-1.37– 8.68)	1.04	(0.96–1.12)	2.61	(-2.63– 7.85)	0.98	(0.92–1.03)	-1.69	(-5.77– 2.38)
Social and community context																
HIV health care discrimination among persons who received care, past 12 months[l]																
Yes	1.70	(1.13–2.55)	10.91	(1.48– 20.33)	1.82	(1.41–2.33)	12.67	(8.16– 17.18)	1.70	(1.29–2.23)	10.81	(5.27– 16.34)	1.44	(1.15–1.81)	6.87	(3.14– 10.59)
No	0.87	(0.77–0.99)	-10.91	(-20.33– -1.48)	0.85	(0.80–0.90)	-12.67	(-17.18– -8.16)	0.87	(0.81–0.94)	-10.81	(-16.34– -5.27)	0.92	(0.88–0.96)	-6.87	(-10.59– -3.14)
English proficiency																
Speaks English less than well	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Speaks English well	1.05	(1.01–1.10)	5.01	(0.96– 9.06)	1.01	(0.97–1.05)	0.58	(-3.19– 4.35)	0.98	(0.94–1.02)	-1.72	(-5.62– 2.19)	0.99	(0.96–1.01)	-1.21	(-3.77– 1.36)
Experiences of physical violence by an intimate partner or forced sex, lifetime[m]																
Yes	1.78	(1.38–2.30)	18.17	(10.41– 25.94)	1.74	(1.39–2.17)	17.10	(11.03– 23.17)	1.84	(1.52–2.23)	19.47	(14.28– 24.65)	1.40	(1.17–1.67)	9.25	(4.81– 13.70)
No	0.76	(0.68–0.86)	-18.17	(-25.94– -10.41)	0.78	(0.71–0.85)	-17.10	(-23.17– -11.03)	0.75	(0.69–0.81)	-19.47	(-24.65– -14.28)	0.88	(0.83–0.93)	-9.25	(-13.70– -4.81)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[m]																
Yes	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
No	0.89	(0.85–0.93)	-11.25	(-15.05– -7.45)	0.89	(0.86–0.92)	-10.96	(-13.53– -8.39)	0.93	(0.91–0.96)	-6.51	(-9.20– -3.81)	0.97	(0.95–0.98)	-3.26	(-4.89– -1.63)
Incarcerated >24 hours, past 12 months																
Yes	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
No	0.95	(0.91–0.98)	-5.31	(-8.52– -2.10)	0.97	(0.95–0.99)	-2.98	(-4.63– -1.32)	0.98	(0.97–1.00)	-1.68	(-3.20– -0.15)	0.99	(0.97–1.00)	-1.43	(-2.81– -0.04)

Abbreviations: PR, prevalence ratio; PD, prevalence difference; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, U.S. Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. persons aged ≥65 years were the referent group for each disparity assessment. Excluded are prevalence ratios and prevalence differences that are based on estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30.

[a] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[b] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[c] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[d] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[e] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[f] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[g] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[h] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[i] Self-reported, and includes physical, mental, and emotional disabilities.

[j] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[k] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[l] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[m] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

Table 3a. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by current gender identity—Medical Monitoring Project, United States, 2022

	Cisgender men[a]			Cisgender women[a]			Transgender persons[a]		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Total (row %)	**2,861**	**75.0**	**(72.8–77.2)**	**875**	**23.0**	**(20.7–25.3)**	**80**	**2.0**	**(1.5–2.5)**
National HIV/AIDS Strategy indicators related to social determinants of health									
Quality of life									
Physical health									
Self-reported health status[b]									
Good, very good, excellent	1,984	72.6	(70.9–74.2)	524	61.5	(58.1–65.0)	53	64.5	(53.4–75.5)
Poor, fair	770	27.4	(25.8–29.1)	325	38.5	(35.0–41.9)	27	35.5	(24.5–46.6)
Mental or emotional health									
Unmet needs for services from a mental health professional among those who needed services, past 12 months[c]									
Yes	276	28.1	(23.5–32.7)	69	23.9	(18.5–29.4)	—	—	—
No	796	71.9	(67.3–76.5)	288	76.1	(70.6–81.5)	38	81.2	(69.3–93.2)
Structural or subsistence factors									
Unstable housing or homelessness, past 12 months[d]									
Yes	456	17.5	(15.9–19.1)	137	18.3	(15.4–21.2)	19	29.0	(17.9–40.2)
No	2,301	82.5	(80.9–84.1)	711	81.7	(78.8–84.6)	60	71.0	(59.8–82.1)
Unemployment[e]									
Yes	321	11.2	(9.3–13.0)	92	11.3	(8.0–14.7)	14	15.6	(6.6–24.6)
No	2,427	88.8	(87.0–90.7)	756	88.7	(85.3–92.0)	65	84.4	(75.4–93.4)
Hunger or food insecurity, past 12 months[f]									
Yes	474	18.6	(17.1–20.0)	157	18.0	(15.1–21.0)	20	27.2	(17.5–36.9)
No	2,283	81.4	(80.0–82.9)	693	82.0	(79.0–84.9)	60	72.8	(63.1–82.5)
HIV stigma, past 12 months **(n, median score, 95% CI)**[g]	2,490	28.2	(26.8–29.6)	751	32.9	(30.6–35.2)	76	35.1	(27.1–43.1)
Other factors important for health, including those that affect quality of life									
Economic stability									
Household income with respect to poverty guidelines[h]									
<100% FPL	680	27.0	(24.4–29.7)	389	51.9	(45.7–58.0)	35	45.4*	(28.1–62.7)
100%–138% FPL	329	12.8	(11.3–14.3)	109	15.6	(12.4–18.8)	—	—	—
139%–399% FPL	966	39.8	(37.8–41.8)	210	28.5	(24.0–33.1)	24	34.1	(19.7–48.4)
≥400% FPL	533	20.4	(17.7–23.0)	36	4.0	(1.8–6.2)	—	—	—
Education									
Educational attainment									
Less than high school diploma	276	10.6	(9.0–12.3)	206	22.1	(19.2–24.9)	17	23.3	(11.5–35.0)
High school diploma or equivalent	685	25.2	(22.7–27.8)	275	32.2	(27.3–37.1)	27	30.6	(21.1–40.1)
Greater than high school	1,802	64.1	(60.9–67.4)	370	45.8	(41.9–49.7)	36	46.1	(34.0–58.3)
Health-related factors									
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[i]									
Any private	1,246	45.2	(42.5–47.9)	273	33.6	(28.7–38.4)	20	26.1	(15.4–36.8)
Public only, excluding RWHAP only	1,255	45.6	(41.7–49.5)	505	59.8	(53.9–65.6)	51	66.5	(54.8–78.2)
Uninsured or RWHAP only	205	9.2	(7.2–11.2)	54	6.7	(3.9–9.4)	—	—	—
Received RWHAP assistance, past 12 months									
Yes	1,293	47.2	(43.2–51.1)	406	45.4	(39.7–51.0)	38	48.8*	(32.8–64.8)
No	1,351	52.8	(48.9–56.8)	413	54.6	(49.0–60.3)	38	51.2*	(35.2–67.2)
Confidence in completing health forms									
Somewhat, a little bit, not at all	640	24.2	(22.3–26.1)	241	26.8	(23.4–30.1)	23	28.6	(19.0–38.2)
Extremely, quite a bit	2,115	75.8	(73.9–77.7)	609	73.2	(69.9–76.6)	57	71.4	(61.8–81.0)
Has a disability[j]									
Yes	1,047	38.3	(36.0–40.6)	458	53.7	(50.2–57.3)	41	51.6	(39.2–64.0)
No	1,711	61.7	(59.4–64.0)	390	46.3	(42.7–49.8)	39	48.4	(36.0–60.8)
Any unmet HIV ancillary service need, past 12 months[k]									
Yes	1,278	48.2	(44.6–51.8)	421	50.9	(46.1–55.6)	48	59.5	(47.8–71.1)
No	1,463	51.8	(48.2–55.4)	422	49.1	(44.4–53.9)	32	40.5	(28.9–52.2)

Table 3a. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by current gender identity—Medical Monitoring Project, United States, 2022 *(cont)*

	Cisgender men[a]			Cisgender women[a]			Transgender persons[a]		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Neighborhood and built environment									
Any met or unmet need for transportation assistance, past 12 months[l]									
Yes	703	25.8	(23.9–27.7)	338	39.8	(36.0–43.6)	40	50.5	(37.8–63.2)
No	2,010	74.2	(72.3–76.1)	499	60.2	(56.4–64.0)	38	49.5	(36.8–62.2)
Social and community context									
HIV health care discrimination among persons who received care, past 12 months[m]									
Yes	605	24.2	(21.2–27.1)	159	20.9	(17.0–24.9)	17	22.9	(12.0–33.8)
No	1,961	75.8	(72.9–78.8)	623	79.1	(75.1–83.0)	61	77.1	(66.2–88.0)
English proficiency									
Speaks English less than well	187	6.9	(3.9–9.8)	103	8.5	(3.7–13.2)	—	—	—
Speaks English well	2,576	93.1	(90.2–96.1)	748	91.5	(86.8–96.3)	73	92.6	(85.5–99.7)
Experiences of physical violence by an intimate partner or forced sex, lifetime[n]									
Yes	830	31.4	(28.7–34.2)	358	45.5	(41.6–49.4)	39	52.6	(40.2–65.0)
No	1,866	68.6	(65.8–71.3)	460	54.5	(50.6–58.4)	41	47.4	(35.0–59.8)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[n]									
Yes	134	5.8	(4.6–7.0)	39	5.6	(3.8–7.5)	—	—	—
No	2,548	94.2	(93.0–95.4)	763	94.4	(92.5–96.2)	70	85.2	(74.8–95.6)
Incarcerated >24 hours, past 12 months									
Yes	85	3.3	(2.6–4.0)	12	1.8	(0.8–2.7)	—	—	—
No	2,679	96.7	(96.0–97.4)	839	98.2	(97.3–99.2)	77	95.9	(91.2–100)

Abbreviations: n, number; col, column; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, U.S. Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. Unweighted numbers and weighted percentages are presented. CIs incorporate weighted percentages. Excluded are estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30. Estimates with an absolute CI width >30, estimates with an absolute CI width between 5 and 30 and a relative CI width >130%, and estimates of 0% or 100% are marked with an asterisk (*) and should be interpreted with caution.

[a] Persons were classified as cisgender if sex at birth and gender reported by the person were the same. Persons were classified as transgender if sex at birth and gender reported by the person were different, or if the person chose "transgender" in response to the question about self-identified gender.

[b] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[c] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[d] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[e] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[f] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[g] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[h] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[i] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[j] Self-reported, and includes physical, mental, and emotional disabilities.

[k] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[l] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[m] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[n] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

Table 3b. Relative and absolute differences in individual-level social determinants of health and quality of life among adults with diagnosed HIV, by current gender identity—Medical Monitoring Project, United States, 2022

	Cisgender women vs. cisgender men[a]				Transgender persons vs. cisgender men[a]			
	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
National HIV/AIDS Strategy indicators related to social determinants of health								
Quality of life								
Physical health								
Self-reported health status[b]								
Good, very good, excellent	0.85	(0.80–0.90)	-11.06	(-15.10– -7.01)	0.89	(0.75–1.06)	-8.12	(-19.45– 3.21)
Poor, fair	1.40	(1.25–1.57)	11.06	(7.01– 15.10)	1.30	(0.94–1.79)	8.12	(-3.21– 19.45)
Mental or emotional health								
Unmet needs for services from a mental health professional among those who needed services, past 12 months[c]								
Yes	0.85	(0.64–1.12)	-4.21	(-11.23– 2.82)	—	—	—	—
No	1.06	(0.96–1.16)	4.21	(-2.82– 11.23)	1.13	(0.99–1.30)	9.36	(-1.70– 20.42)
Structural or subsistence factors								
Unstable housing or homelessness, past 12 months[d]								
Yes	1.05	(0.87–1.26)	0.82	(-2.57– 4.20)	1.66	(1.15–2.40)	11.54	(0.78– 22.31)
No	0.99	(0.95–1.03)	-0.82	(-4.20– 2.57)	0.86	(0.74–1.00)	-11.54	(-22.31– -0.78)
Unemployment[e]								
Yes	1.01	(0.78–1.32)	0.15	(-2.86– 3.16)	1.39	(0.79–2.47)	4.39	(-4.43– 13.22)
No	1.00	(0.96–1.03)	-0.15	(-3.16– 2.86)	0.95	(0.86–1.06)	-4.39	(-13.22– 4.43)
Hunger or food insecurity, past 12 months[f]								
Yes	0.97	(0.81–1.16)	-0.52	(-3.74– 2.69)	1.47	(1.01–2.12)	8.65	(-1.23– 18.53)
No	1.01	(0.97–1.05)	0.52	(-2.69– 3.74)	0.89	(0.78–1.02)	-8.65	(-18.53– 1.23)
HIV stigma, past 12 months								
(n, median score, 95% CI)[g]								
Other factors important for health, including those that affect quality of life								
Economic stability								
Household income with respect to poverty guidelines[h]								
<100% FPL	1.92	(1.73–2.12)	24.81	(19.68– 29.93)	1.68*	(1.20–2.34)	18.33*	(2.46– 34.20)
100%–138% FPL	1.22	(0.98–1.53)	2.84	(-0.53– 6.21)	—	—	—	—
139%–399% FPL	0.72	(0.61–0.85)	-11.26	(-16.34– -6.18)	0.86	(0.56–1.30)	-5.74	(-20.09– 8.60)
≥400% FPL	0.20	(0.11–0.33)	-16.39	(-19.46– -13.32)	—	—	—	—
Education								
Educational attainment								
Less than high school diploma	2.08	(1.70–2.53)	11.44	(8.17– 14.70)	2.19	(1.35–3.57)	12.67	(1.26– 24.08)
High school diploma or equivalent	1.27	(1.03–1.58)	6.90	(0.51– 13.30)	1.21	(0.86–1.71)	5.35	(-4.88– 15.58)
Greater than high school	0.71	(0.64–0.80)	-18.34	(-23.98– -12.70)	0.72	(0.56–0.93)	-18.02	(-29.82– -6.22)
Health-related factors								
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[i]								
Any private	0.74	(0.66–0.84)	-11.63	(-15.53– -7.73)	0.58	(0.39–0.86)	-19.10	(-29.39– -8.81)
Public only, excluding RWHAP only	1.31	(1.22–1.41)	14.17	(10.09– 18.25)	1.46	(1.23–1.73)	20.94	(9.78– 32.11)
Uninsured or RWHAP only	0.72	(0.52–1.02)	-2.54	(-4.82– -0.26)	—	—	—	—
Received RWHAP assistance, past 12 months								
Yes	0.96	(0.86–1.08)	-1.80	(-7.08– 3.48)	1.03*	(0.77–1.39)	1.62*	(-12.88– 16.12)
No	1.03	(0.94–1.14)	1.80	(-3.48– 7.08)	0.97*	(0.73–1.29)	-1.62*	(-16.12– 12.88)
Confidence in completing health forms								
Somewhat, a little bit, not at all	1.11	(0.95–1.29)	2.59	(-1.43– 6.60)	1.18	(0.84–1.66)	4.45	(-5.17– 14.06)
Extremely, quite a bit	0.97	(0.91–1.02)	-2.59	(-6.60– 1.43)	0.94	(0.82–1.08)	-4.45	(-14.06– 5.17)
Has a disability[j]								
Yes	1.40	(1.29–1.52)	15.40	(11.57– 19.23)	1.35	(1.05–1.72)	13.29	(0.76– 25.82)
No	0.75	(0.69–0.81)	-15.40	(-19.23– -11.57)	0.78	(0.61–1.01)	-13.29	(-25.82– -0.76)
Any unmet HIV ancillary service need, past 12 months[k]								
Yes	1.05	(0.96–1.16)	2.64	(-2.03– 7.31)	1.23	(1.03–1.48)	11.25	(0.31– 22.19)
No	0.95	(0.86–1.04)	-2.64	(-7.31– 2.03)	0.78	(0.60–1.03)	-11.25	(-22.19– -0.31)

Table 3b. Relative and absolute differences in individual-level social determinants of health and quality of life among adults with diagnosed HIV, by current gender identity—Medical Monitoring Project, United States, 2022 *(cont)*

	Cisgender women vs. cisgender men[a]				Transgender persons vs. cisgender men[a]			
	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
Neighborhood and built environment								
Any met or unmet need for transportation assistance, past 12 months[l]								
Yes	1.54	(1.38–1.73)	14.00	(9.98– 18.01)	1.96	(1.51–2.54)	24.69	(11.86– 37.52)
No	0.81	(0.76–0.87)	-14.00	(-18.01– -9.98)	0.67	(0.52–0.86)	-24.69	(-37.52– -11.86)
Social and community context								
HIV health care discrimination among persons who received care, past 12 months[m]								
Yes	0.87	(0.70–1.07)	-3.22	(-7.75– 1.31)	0.95	(0.60–1.50)	-1.23	(-11.74– 9.28)
No	1.04	(0.98–1.10)	3.22	(-1.31– 7.75)	1.02	(0.89–1.16)	1.23	(-9.28– 11.74)
English proficiency								
Speaks English less than well	1.23	(0.91–1.66)	1.59	(-1.12– 4.30)	—	—	—	—
Speaks English well	0.98	(0.95–1.01)	-1.59	(-4.30– 1.12)	0.99	(0.94–1.05)	-0.54	(-5.87– 4.79)
Experiences of physical violence by an intimate partner or forced sex, lifetime[n]								
Yes	1.45	(1.31–1.60)	14.07	(10.02– 18.12)	1.67	(1.34–2.09)	21.17	(9.36– 32.99)
No	0.79	(0.74–0.85)	-14.07	(-18.12– -10.02)	0.69	(0.54–0.89)	-21.17	(-32.99– -9.36)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[n]								
Yes	0.97	(0.64–1.47)	-0.18	(-2.54– 2.19)	—	—	—	—
No	1.00	(0.98–1.03)	0.18	(-2.19– 2.54)	0.90	(0.80–1.02)	-9.00	(-19.39– 1.39)
Incarcerated >24 hours, past 12 months								
Yes	0.54	(0.31–0.94)	-1.53	(-2.66– -0.39)	—	—	—	—
No	1.02	(1.00–1.03)	1.53	(0.39– 2.66)	0.99	(0.95–1.04)	-0.74	(-5.38– 3.89)

Abbreviations: PR, prevalence ratio; PD, prevalence difference; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, U.S. Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. Cisgender males were the referent group for each disparity assessment. Excluded are prevalence ratios and prevalence differences that are based on estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30. Prevalence ratios and prevalence differences that are based on one or more estimates with an absolute CI width >30, estimates with an absolute CI width between 5 and 30 and a relative CI width >130%, and estimates of 0% or 100% are marked with an asterisk (*) and should be interpreted with caution.

[a] Persons were classified as cisgender if sex at birth and gender reported by the person were the same. Persons were classified as transgender if sex at birth and gender reported by the person were different, or if the person chose "transgender" in response to the question about self-identified gender.

[b] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[c] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[d] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[e] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[f] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[g] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[h] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[i] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[j] Self-reported, and includes physical, mental, and emotional disabilities.

[k] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[l] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[m] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[n] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

Table 4a. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by sexual orientation—Medical Monitoring Project, United States, 2022

	Bisexual			Gay or lesbian			Heterosexual			Other		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Total (row %)	**322**	**9.6**	**(8.5–10.8)**	**1,647**	**43.7**	**(40.0–47.4)**	**1,575**	**43.7**	**(40.3–47.1)**	**108**	**3.0**	**(2.3–3.7)**
National HIV/AIDS Strategy indicators related to social determinants of health												
Quality of life												
Physical health												
Self-reported health status[a]												
Good, very good, excellent	207	65.8	(59.2–72.4)	1,258	76.5	(74.0–79.0)	1,006	64.7	(62.4–67.0)	66	63.9	(56.3–71.5)
Poor, fair	114	34.2	(27.6–40.8)	387	23.5	(21.0–26.0)	562	35.3	(33.0–37.6)	40	36.1	(28.5–43.7)
Mental or emotional health												
Unmet needs for services from a mental health professional among those who needed services, past 12 months[b]												
Yes	37	31.1	(21.5–40.7)	185	28.6	(23.6–33.6)	115	23.6	(19.1–28.1)	11	20.4	(11.4–29.4)
No	103	68.9	(59.3–78.5)	508	71.4	(66.4–76.4)	456	76.4	(71.9–80.9)	44	79.6	(70.6–88.6)
Structural or subsistence factors												
Unstable housing or homelessness, past 12 months[c]												
Yes	73	21.4	(17.0–25.9)	243	16.4	(14.3–18.5)	263	18.0	(15.9–20.0)	24	25.9	(16.8–34.9)
No	248	78.6	(74.1–83.0)	1,400	83.6	(81.5–85.7)	1,306	82.0	(80.0–84.1)	83	74.1	(65.1–83.2)
Unemployment[d]												
Yes	48	15.4	(10.4–20.4)	174	10.6	(8.2–13.1)	187	10.9	(8.8–13.0)	—	—	—
No	271	84.6	(79.6–89.6)	1,466	89.4	(86.9–91.8)	1,378	89.1	(87.0–91.2)	100	92.5	(85.4–99.5)
Hunger or food insecurity, past 12 months[e]												
Yes	95	31.2	(26.1–36.4)	238	16.2	(14.1–18.3)	273	17.2	(15.4–18.9)	32	31.3	(23.5–39.0)
No	227	68.8	(63.6–73.9)	1,408	83.8	(81.7–85.9)	1,296	82.8	(81.1–84.6)	75	68.7	(61.0–76.5)
HIV stigma, past 12 months **(n, median score, 95% CI)**[f]	291	37.1	(32.8–41.4)	1,529	26.3	(24.9–27.7)	1,380	30.7	(29.0–32.4)	82	33.4	(27.9–38.8)
Other factors important for health, including those that affect quality of life												
Economic stability												
Household income with respect to poverty guidelines[g]												
<100% FPL	90	34.4	(27.6–41.1)	294	18.3	(15.1–21.6)	672	47.2	(42.3–52.1)	39	42.7	(32.6–52.8)
100%–138% FPL	56	18.9	(14.4–23.5)	167	10.7	(9.1–12.2)	210	15.4	(12.6–18.2)	8	8.2	(4.1–12.3)
139%–399% FPL	112	37.2	(30.4–44.0)	618	43.3	(40.5–46.1)	415	30.5	(26.5–34.5)	43	39.4	(29.3–49.6)
≥400% FPL	30	9.5	(5.5–13.4)	441	27.7	(24.0–31.4)	92	6.8	(5.1–8.6)	—	—	—
Education												
Educational attainment												
Less than high school diploma	35	10.7	(7.6–13.8)	86	5.7	(4.2–7.2)	350	21.6	(19.1–24.0)	—	—	—
High school diploma or equivalent	90	28.4	(23.7–33.0)	314	19.8	(17.4–22.3)	546	34.0	(31.6–36.5)	21	19.1	(11.2–27.0)
Greater than high school	197	60.9	(55.1–66.8)	1,246	74.5	(71.5–77.4)	677	44.4	(41.1–47.7)	73	68.1	(56.9–79.3)
Health-related factors												
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[h]												
Any private	125	39.1	(32.0–46.2)	854	51.5	(48.2–54.7)	496	33.1	(28.8–37.4)	51	47.3	(32.7–61.9)
Public only, excluding RWHAP only	165	51.1	(42.6–59.6)	651	39.7	(35.8–43.5)	920	58.5	(53.0–64.1)	52	47.9	(33.2–62.5)
Uninsured or RWHAP only	—	—	—	118	8.9	(6.9–10.9)	116	8.4	(6.1–10.6)	—	—	—
Received RWHAP assistance, past 12 months												
Yes	166	52.1	(44.4–59.9)	764	46.3	(41.8–50.8)	738	46.2	(41.1–51.4)	47	43.9	(35.7–52.1)
No	141	47.9	(40.1–55.6)	836	53.7	(49.2–58.2)	751	53.8	(48.6–58.9)	56	56.1	(47.9–64.3)
Confidence in completing health forms												
Somewhat, a little bit, not at all	77	24.0	(19.5–28.6)	289	17.8	(15.6–20.0)	491	31.5	(28.9–34.1)	29	27.8	(17.6–37.9)
Extremely, quite a bit	244	76.0	(71.4–80.5)	1,357	82.2	(80.0–84.4)	1,078	68.5	(65.9–71.1)	77	72.2	(62.1–82.4)
Has a disability[i]												
Yes	152	45.7	(39.2–52.2)	548	33.9	(31.1–36.6)	758	48.3	(45.4–51.1)	63	58.4	(47.4–69.4)
No	169	54.3	(47.8–60.8)	1,096	66.1	(63.4–68.9)	811	51.7	(48.9–54.6)	45	41.6	(30.6–52.6)
Any unmet HIV ancillary service need, past 12 months[j]												
Yes	184	59.3	(53.6–65.0)	710	45.2	(41.4–49.0)	763	49.6	(45.8–53.5)	63	60.0	(48.6–71.4)
No	137	40.7	(35.0–46.4)	928	54.8	(51.0–58.6)	794	50.4	(46.5–54.2)	43	40.0	(28.6–51.4)

Table 4a. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by sexual orientation—Medical Monitoring Project, United States, 2022 *(cont)*

	Bisexual			Gay or lesbian			Heterosexual			Other		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Neighborhood and built environment												
Any met or unmet need for transportation assistance, past 12 months[k]												
Yes	121	39.8	(31.1–48.6)	332	20.4	(18.0–22.8)	570	35.8	(33.0–38.6)	38	35.2	(26.2–44.3)
No	195	60.2	(51.4–68.9)	1,291	79.6	(77.2–82.0)	974	64.2	(61.4–67.0)	66	64.8	(55.7–73.8)
Social and community context												
HIV health care discrimination among persons who received care, past 12 months[l]												
Yes	89	29.3	(23.4–35.1)	382	25.5	(22.6–28.4)	270	19.3	(16.2–22.3)	30	33.0	(23.6–42.4)
No	210	70.7	(64.9–76.6)	1,173	74.5	(71.6–77.4)	1,170	80.7	(77.7–83.8)	64	67.0	(57.6–76.4)
English proficiency												
Speaks English less than well	—	—	—	76	4.8	(2.3–7.4)	191	9.8	(4.7–15.0)	—	—	—
Speaks English well	308	95.0	(91.6–98.3)	1,571	95.2	(92.6–97.7)	1,383	90.2	(85.0–95.3)	99	93.0	(86.3–99.7)
Experiences of physical violence by an intimate partner or forced sex, lifetime[m]												
Yes	117	38.5	(32.7–44.3)	599	38.6	(35.7–41.6)	459	30.5	(27.9–33.1)	45	43.1	(28.7–57.6)
No	199	61.5	(55.7–67.3)	1,019	61.4	(58.4–64.3)	1,057	69.5	(66.9–72.1)	59	56.9	(42.4–71.3)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[m]												
Yes	25	10.1	(4.2–16.0)	91	6.8	(5.5–8.2)	55	3.8	(2.8–4.9)	10	11.3	(5.6–17.1)
No	287	89.9	(84.0–95.8)	1,515	93.2	(91.8–94.5)	1,448	96.2	(95.1–97.2)	92	88.7	(82.9–94.4)
Incarcerated >24 hours, past 12 months												
Yes	18	5.1	(2.3–7.9)	29	2.1	(1.3–3.0)	47	3.2	(2.1–4.3)	—	—	—
No	304	94.9	(92.1–97.7)	1,618	97.9	(97.0–98.7)	1,526	96.8	(95.7–97.9)	103	95.1	(90.9–99.2)

Abbreviations: n, number; col, column; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, U.S. Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. Unweighted numbers and weighted percentages are presented. CIs incorporate weighted percentages. Excluded are estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30.

[a] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[b] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[c] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[d] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[e] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[f] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[g] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[h] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[i] Self-reported, and includes physical, mental, and emotional disabilities.

[j] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[k] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[l] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[m] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

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Table 4b. Relative and absolute differences in individual-level social determinants of health and quality of life among adults with diagnosed HIV, by sexual orientation—Medical Monitoring Project, United States, 2022

	Bisexual vs. gay or lesbian persons				Heterosexual vs. gay or lesbian persons				Persons who identify as other sexual orientation vs. gay or lesbian persons			
	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
National HIV/AIDS Strategy indicators related to social determinants of health												
Quality of life												
Physical health												
Self-reported health status[a]												
Good, very good, excellent	0.86	(0.78–0.95)	-10.72	(-17.52– -3.93)	0.85	(0.80–0.89)	-11.81	(-15.59– -8.02)	0.84	(0.74–0.95)	-12.56	(-20.56– -4.55)
Poor, fair	1.46	(1.18–1.80)	10.72	(3.93– 17.52)	1.50	(1.31–1.72)	11.81	(8.02– 15.59)	1.53	(1.21–1.94)	12.56	(4.55– 20.56)
Mental or emotional health												
Unmet needs for services from a mental health professional among those who needed services, past 12 months[b]												
Yes	1.09	(0.80–1.49)	2.52	(-7.06– 12.10)	0.83	(0.66–1.04)	-4.96	(-10.94– 1.02)	0.71	(0.45–1.12)	-8.19	(-17.97– 1.58)
No	0.96	(0.84–1.11)	-2.52	(-12.10– 7.06)	1.07	(0.99–1.16)	4.96	(-1.02– 10.94)	1.11	(0.98–1.26)	8.19	(-1.58– 17.97)
Structural or subsistence factors												
Unstable housing or homelessness, past 12 months[c]												
Yes	1.31	(1.05–1.62)	5.03	(0.57– 9.49)	1.10	(0.93–1.29)	1.56	(-1.27– 4.39)	1.58	(1.08–2.31)	9.47	(0.05– 18.89)
No	0.94	(0.89–0.99)	-5.03	(-9.49– -0.57)	0.98	(0.95–1.02)	-1.56	(-4.39– 1.27)	0.89	(0.78–1.01)	-9.47	(-18.89– -0.05)
Unemployment[d]												
Yes	1.45	(1.06–1.98)	4.75	(0.16– 9.35)	1.03	(0.80–1.32)	0.29	(-2.40– 2.98)	—	—	—	—
No	0.95	(0.90–1.00)	-4.75	(-9.35– -0.16)	1.00	(0.97–1.03)	-0.29	(-2.98– 2.40)	1.03	(0.95–1.13)	3.09	(-4.68– 10.86)
Hunger or food insecurity, past 12 months[e]												
Yes	1.93	(1.53–2.42)	15.04	(9.12– 20.96)	1.06	(0.90–1.25)	0.97	(-1.73– 3.68)	1.93	(1.45–2.57)	15.07	(6.92– 23.21)
No	0.82	(0.75–0.89)	-15.04	(-20.96– -9.12)	0.99	(0.96–1.02)	-0.97	(-3.68– 1.73)	0.82	(0.73–0.92)	-15.07	(-23.21– -6.92)
HIV stigma, past 12 months **(n, median score, 95% CI)**[f]												
Other factors important for health, including those that affect quality of life												
Economic stability												
Household income with respect to poverty guidelines[g]												
<100% FPL	1.87	(1.46–2.40)	16.04	(8.88– 23.20)	2.57	(2.18–3.04)	28.86	(24.16– 33.56)	2.33	(1.77–3.05)	24.33	(14.22– 34.45)
100%–138% FPL	1.77	(1.36–2.31)	8.24	(3.62– 12.87)	1.44	(1.14–1.83)	4.72	(1.44– 7.99)	0.76	(0.45–1.29)	-2.52	(-6.91– 1.88)
139%–399% FPL	0.86	(0.70–1.06)	-6.06	(-14.03– 1.91)	0.71	(0.60–0.84)	-12.74	(-18.52– -6.97)	0.91	(0.71–1.16)	-3.88	(-13.45– 5.70)
≥400% FPL	0.34	(0.22–0.52)	-18.22	(-23.33– -13.11)	0.25	(0.19–0.32)	-20.84	(-24.36– -17.31)	—	—	—	—
Education												
Educational attainment												
Less than high school diploma	1.87	(1.35–2.59)	4.97	(1.93– 8.00)	3.77	(2.85–4.99)	15.85	(13.02– 18.68)	—	—	—	—
High school diploma or equivalent	1.43	(1.20–1.71)	8.54	(3.85– 13.22)	1.72	(1.48–1.99)	14.18	(10.55– 17.81)	0.96	(0.61–1.51)	-0.72	(-9.36– 7.93)
Greater than high school	0.82	(0.75–0.89)	-13.50	(-18.91– -8.10)	0.60	(0.55–0.65)	-30.03	(-34.74– -25.33)	0.91	(0.76–1.10)	-6.38	(-18.81– 6.04)
Health-related factors												
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[h]												
Any private	0.76	(0.62–0.93)	-12.36	(-20.82– -3.89)	0.64	(0.58–0.71)	-18.35	(-21.90– -14.80)	0.92	(0.67–1.25)	-4.19	(-18.78– 10.40)
Public only, excluding RWHAP only	1.29	(1.10–1.52)	11.49	(3.41– 19.57)	1.48	(1.36–1.60)	18.89	(14.60– 23.18)	1.21	(0.90–1.62)	8.25	(-5.78– 22.28)
Uninsured or RWHAP only	—	—	—	—	0.94	(0.71–1.23)	-0.54	(-2.88– 1.80)	—	—	—	—
Received RWHAP assistance, past 12 months												
Yes	1.13	(0.98–1.29)	5.83	(-1.10– 12.76)	1.00	(0.88–1.13)	-0.06	(-5.89– 5.76)	0.95	(0.77–1.17)	-2.42	(-11.69– 6.85)
No	0.89	(0.77–1.03)	-5.83	(-12.76– 1.10)	1.00	(0.90–1.12)	0.06	(-5.76– 5.89)	1.05	(0.88–1.24)	2.42	(-6.85– 11.69)
Confidence in completing health forms												
Somewhat, a little bit, not at all	1.35	(1.09–1.67)	6.21	(1.37– 11.06)	1.77	(1.54–2.03)	13.71	(10.52– 16.90)	1.56	(1.04–2.34)	9.94	(-0.80– 20.69)
Extremely, quite a bit	0.92	(0.87–0.98)	-6.21	(-11.06– -1.37)	0.83	(0.80–0.87)	-13.71	(-16.90– -10.52)	0.88	(0.76–1.02)	-9.94	(-20.69– 0.80)
Has a disability[i]												
Yes	1.35	(1.15–1.59)	11.83	(4.83– 18.84)	1.43	(1.29–1.57)	14.40	(10.56– 18.24)	1.72	(1.39–2.15)	24.54	(12.70– 36.38)
No	0.82	(0.72–0.93)	-11.83	(-18.84– -4.83)	0.78	(0.73–0.84)	-14.40	(-18.24– -10.56)	0.63	(0.48–0.83)	-24.54	(-36.38– -12.70)
Any unmet HIV ancillary service need, past 12 months[j]												
Yes	1.31	(1.17–1.48)	14.13	(7.82– 20.44)	1.10	(1.02–1.18)	4.42	(1.07– 7.77)	1.33	(1.12–1.58)	14.81	(4.38– 25.24)
No	0.74	(0.64–0.86)	-14.13	(-20.44– -7.82)	0.92	(0.86–0.98)	-4.42	(-7.77– -1.07)	0.73	(0.56–0.95)	-14.81	(-25.24– -4.38)

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Table 4b. Relative and absolute differences in individual-level social determinants of health and quality of life among adults with diagnosed HIV, by sexual orientation—Medical Monitoring Project, United States, 2022 *(cont)*

	Bisexual vs. gay or lesbian persons				Heterosexual vs. gay or lesbian persons				Persons who identify as other sexual orientation vs. gay or lesbian persons			
	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI	PR	95% CI	PD	95% CI
Neighborhood and built environment												
Any met or unmet need for transportation assistance, past 12 months[k]												
Yes	1.95	(1.61–2.37)	19.43	(11.49– 27.36)	1.76	(1.52–2.02)	15.41	(11.69– 19.12)	1.73	(1.28–2.33)	14.82	(5.13– 24.52)
No	0.76	(0.66–0.86)	-19.43	(-27.36– -11.49)	0.81	(0.76–0.85)	-15.41	(-19.12– -11.69)	0.81	(0.70–0.94)	-14.82	(-24.52– -5.13)
Social and community context												
HIV health care discrimination among persons who received care, past 12 months[l]												
Yes	1.15	(0.96–1.37)	3.78	(-1.33– 8.89)	0.76	(0.65–0.88)	-6.23	(-9.56– -2.90)	1.30	(0.96–1.75)	7.56	(-2.12– 17.25)
No	0.95	(0.88–1.02)	-3.78	(-8.89– 1.33)	1.08	(1.04–1.13)	6.23	(2.90– 9.56)	0.90	(0.78–1.04)	-7.56	(-17.25– 2.12)
English proficiency												
Speaks English less than well	—	—	—	—	2.05	(1.52–2.75)	5.03	(1.74– 8.33)	—	—	—	—
Speaks English well	1.00	(0.96–1.04)	-0.21	(-4.11– 3.68)	0.95	(0.91–0.98)	-5.03	(-8.33– -1.74)	0.98	(0.91–1.05)	-2.18	(-8.63– 4.27)
Experiences of physical violence by an intimate partner or forced sex, lifetime[m]												
Yes	1.00	(0.85–1.17)	-0.11	(-6.23– 6.00)	0.79	(0.72–0.87)	-8.14	(-11.37– -4.91)	1.12	(0.82–1.53)	4.52	(-9.09– 18.13)
No	1.00	(0.91–1.11)	0.11	(-6.00– 6.23)	1.13	(1.08–1.19)	8.14	(4.91– 11.37)	0.93	(0.73–1.18)	-4.52	(-18.13– 9.09)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[m]												
Yes	1.49	(0.83–2.67)	3.31	(-2.53– 9.16)	0.56	(0.41–0.77)	-2.98	(-4.60– -1.37)	1.66	(0.95–2.92)	4.51	(-1.53– 10.55)
No	0.96	(0.90–1.03)	-3.31	(-9.16– 2.53)	1.03	(1.01–1.05)	2.98	(1.37– 4.60)	0.95	(0.89–1.02)	-4.51	(-10.55– 1.53)
Incarcerated >24 hours, past 12 months												
Yes	2.38	(1.21–4.66)	2.95	(0.02– 5.89)	1.50	(0.88–2.56)	1.07	(-0.34– 2.47)	—	—	—	—
No	0.97	(0.94–1.00)	-2.95	(-5.89– -0.02)	0.99	(0.97–1.00)	-1.07	(-2.47– 0.34)	0.97	(0.93–1.02)	-2.79	(-7.37– 1.79)

Abbreviations: PR, prevalence ratio; PD, prevalence difference; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, U.S. Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. Gay or lesbian persons were the referent group for each disparity assessment. Excluded are prevalence ratios and prevalence differences that are based on estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30.

[a] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[b] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[c] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[d] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[e] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[f] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[g] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[h] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[i] Self-reported, and includes physical, mental, and emotional disabilities.

[j] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[k] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[l] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[m] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

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Table 5a. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by racial/ethnic identity—Medical Monitoring Project, United States, 2022

	American Indian/ Alaska Native			Asian			Black/African American			Hispanic/Latino[a]			Native Hawaiian/ other Pacific Islander			White			Multiple races		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Total (row %)	—	—	—	**57**	**1.3**	**(0.9–1.8)**	**1,497**	**40.8**	**(32.5–49.2)**	**937**	**23.6**	**(16.2–31.0)**	—	—	—	**1,117**	**28.5**	**(24.2–32.9)**	**194**	**5.1**	**(4.0–6.3)**
National HIV/AIDS Strategy indicators related to social determinants of health																					
Quality of life																					
Physical health																					
Self-reported health status[b]																					
Good, very good, excellent	—	—	—	43	83.6	(74.7–92.4)	999	69.8	(67.1–72.4)	634	69.4	(66.0–72.7)	—	—	—	759	70.5	(67.0–74.0)	115	63.2	(55.1–71.2)
Poor, fair	—	—	—	13	16.4	(7.6–25.3)	425	30.2	(27.6–32.9)	281	30.6	(27.3–34.0)	—	—	—	325	29.5	(26.0–33.0)	75	36.8	(28.8–44.9)
Mental or emotional health																					
Unmet needs for services from a mental health professional among those who needed services, past 12 months[c]																					
Yes	—	—	—	—	—	—	130	28.4	(23.7–33.2)	82	22.7	(13.9–31.5)	—	—	—	105	26.6	(21.2–31.9)	28	36.5	(25.5–47.4)
No	—	—	—	—	—	—	365	71.6	(66.8–76.3)	334	77.3	(68.5–86.1)	—	—	—	342	73.4	(68.1–78.8)	60	63.5	(52.6–74.5)
Structural or subsistence factors																					
Unstable housing or homelessness, past 12 months[d]																					
Yes	—	—	—	—	—	—	290	21.5	(19.0–24.0)	143	17.7	(14.1–21.4)	—	—	—	137	13.3	(11.6–15.1)	36	19.3	(12.9–25.6)
No	—	—	—	52	96.9	(92.3–100)	1,138	78.5	(76.0–81.0)	770	82.3	(78.6–85.9)	—	—	—	947	86.7	(84.9–88.4)	154	80.7	(74.4–87.1)
Unemployment[e]																					
Yes	—	—	—	—	—	—	192	12.4	(9.6–15.1)	116	12.0	(9.2–14.8)	—	—	—	86	8.5	(5.8–11.3)	24	14.6	(8.6–20.6)
No	—	—	—	48	91.9	(84.4–99.3)	1,229	87.6	(84.9–90.4)	798	88.0	(85.2–90.8)	—	—	—	996	91.5	(88.7–94.2)	165	85.4	(79.4–91.4)
Hunger or food insecurity, past 12 months[f]																					
Yes	—	—	—	—	—	—	266	19.1	(16.4–21.8)	192	23.0	(18.3–27.8)	—	—	—	133	13.8	(10.6–17.0)	53	26.1	(19.2–33.0)
No	—	—	—	52	94.6	(88.0–100)	1,161	80.9	(78.2–83.6)	723	77.0	(72.2–81.7)	—	—	—	952	86.2	(83.0–89.4)	137	73.9	(67.0–80.8)
HIV stigma, past 12 months **(n, median score, 95% CI)[g]**	—	—	—	45	34.6	(25.9–43.2)	1,281	30.4	(28.3–32.6)	807	29.7	(27.8–31.6)	—	—	—	1,001	27.7	(25.2–30.1)	170	29.0	(24.1–33.9)
Other factors important for health, including those that affect quality of life																					
Economic stability																					
Household income with respect to poverty guidelines[h]																					
<100% FPL	—	—	—	—	—	—	485	39.8	(36.7–42.8)	339	38.9	(30.7–47.0)	—	—	—	193	18.5	(15.4–21.7)	77	43.4	(32.8–53.9)
100%–138% FPL	—	—	—	—	—	—	169	12.9	(11.0–14.7)	116	15.0	(11.7–18.3)	—	—	—	134	13.6	(10.9–16.3)	24	12.4	(7.5–17.3)
139%–399% FPL	—	—	—	18	33.2	(19.6–46.9)	453	36.5	(32.8–40.3)	261	34.3	(30.8–37.7)	—	—	—	410	41.7	(38.7–44.8)	54	29.4	(22.5–36.4)
≥400% FPL	—	—	—	22	51.6*	(35.7–67.4)	142	10.8	(9.3–12.3)	92	11.8	(6.8–16.9)	—	—	—	291	26.1	(22.7–29.5)	24	14.8	(7.0–22.6)
Education																					
Educational attainment																					
Less than high school diploma	—	—	—	—	—	—	205	14.2	(11.8–16.7)	211	22.9	(19.1–26.8)	—	—	—	54	5.5	(3.7–7.2)	25	12.0	(5.4–18.7)
High school diploma or equivalent	—	—	—	—	—	—	485	33.1	(30.8–35.5)	230	25.7	(22.1–29.3)	—	—	—	208	19.5	(16.7–22.3)	54	29.0	(21.8–36.1)
Greater than high school	—	—	—	49	86.3	(77.0–95.7)	742	52.7	(49.2–56.2)	475	51.4	(45.7–57.1)	—	—	—	823	75.0	(72.2–77.8)	112	59.0	(52.0–66.0)
Health-related factors																					
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[i]																					
Any private	—	—	—	33	63.6*	(46.4–80.7)	580	40.6	(37.9–43.3)	297	33.9	(28.7–39.0)	—	—	—	549	50.3	(46.5–54.1)	74	39.7	(31.1–48.3)
Public only, excluding RWHAP only	—	—	—	19	29.9*	(14.2–45.7)	702	50.0	(45.6–54.4)	495	52.4	(43.5–61.3)	—	—	—	484	45.5	(41.2–49.7)	105	57.2	(48.1–66.3)
Uninsured or RWHAP only	—	—	—	—	—	—	112	9.4	(6.7–12.1)	106	13.7	(8.4–19.0)	—	—	—	36	4.3	(2.4–6.1)	—	—	—
Received RWHAP assistance, past 12 months																					
Yes	—	—	—	20	35.7*	(20.2–51.2)	665	44.7	(40.5–48.9)	501	56.0	(47.5–64.5)	—	—	—	469	44.3	(38.4–50.3)	77	40.8	(31.0–50.6)
No	—	—	—	35	64.3*	(48.8–79.8)	713	55.3	(51.1–59.5)	358	44.0	(35.5–52.5)	—	—	—	585	55.7	(49.7–61.6)	103	59.2	(49.4–69.0)
Confidence in completing health forms																					
Somewhat, a little bit, not at all	—	—	—	11	19.4	(8.2–30.6)	347	25.2	(22.7–27.7)	320	35.5	(31.7–39.2)	—	—	—	173	16.1	(14.2–18.1)	49	23.2	(16.3–30.1)
Extremely, quite a bit	—	—	—	45	80.6	(69.4–91.8)	1,080	74.8	(72.3–77.3)	595	64.5	(60.8–68.3)	—	—	—	911	83.9	(81.9–85.8)	140	76.8	(69.9–83.7)
Has a disability[j]																					
Yes	—	—	—	—	—	—	572	40.9	(37.8–43.9)	406	43.9	(40.5–47.4)	—	—	—	447	42.1	(39.0–45.2)	103	50.5	(43.2–57.9)
No	—	—	—	47	88.1	(79.5–96.7)	857	59.1	(56.1–62.2)	510	56.1	(52.6–59.5)	—	—	—	634	57.9	(54.8–61.0)	87	49.5	(42.1–56.8)
Any unmet HIV ancillary service need, past 12 months[k]																					
Yes	—	—	—	22	34.4	(22.2–46.6)	787	55.7	(51.3–60.2)	419	48.2	(40.2–56.1)	—	—	—	409	39.4	(35.0–43.9)	103	57.9	(49.9–66.0)
No	—	—	—	33	65.6	(53.4–77.8)	631	44.3	(39.8–48.7)	490	51.8	(43.9–59.8)	—	—	—	672	60.6	(56.1–65.0)	84	42.1	(34.0–50.1)

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Table 5a. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by racial/ethnic identity — Medical Monitoring Project, United States, 2022 *(cont)*

	American Indian/ Alaska Native			Asian			Black/African American			Hispanic/Latino[a]			Native Hawaiian/ other Pacific Islander			White			Multiple races		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Neighborhood and built environment																					
Any met or unmet need for transportation assistance, past 12 months[l]																					
Yes	—	—	—	—	—	—	506	35.4	(32.0–38.9)	260	28.7	(25.3–32.2)	—	—	—	227	21.2	(17.4–25.1)	73	38.3	(31.1–45.5)
No	—	—	—	44	85.4	(75.6–95.3)	899	64.6	(61.1–68.0)	638	71.3	(67.8–74.7)	—	—	—	844	78.8	(74.9–82.6)	113	61.7	(54.5–68.9)
Social and community context																					
HIV health care discrimination among persons who received care, past 12 months[m]																					
Yes	—	—	—	—	—	—	252	20.5	(17.3–23.7)	180	21.7	(18.6–24.7)	—	—	—	275	27.8	(24.0–31.6)	58	31.5	(23.4–39.6)
No	—	—	—	42	84.6	(74.2–94.9)	1,065	79.5	(76.3–82.7)	679	78.3	(75.3–81.4)	—	—	—	740	72.2	(68.4–76.0)	113	68.5	(60.4–76.6)
English proficiency																					
Speaks English less than well	—	—	—	—	—	—	27	2.0	(1.1–2.9)	259	26.1	(19.2–32.9)	—	—	—	—	—	—	—	—	—
Speaks English well	—	—	—	50	88.1	(79.2–96.9)	1,403	98.0	(97.1–98.9)	659	73.9	(67.1–80.8)	—	—	—	1,081	99.8	(99.6–100)	190	99.5	(98.5–100)
Experiences of physical violence by an intimate partner or forced sex, lifetime[n]																					
Yes	—	—	—	21	37.8*	(22.8–52.8)	422	30.9	(28.4–33.4)	271	31.2	(26.1–36.2)	—	—	—	422	42.0	(38.4–45.5)	83	46.4	(37.5–55.2)
No	—	—	—	33	62.2*	(47.2–77.2)	960	69.1	(66.6–71.6)	625	68.8	(63.8–73.9)	—	—	—	641	58.0	(54.5–61.6)	102	53.6	(44.8–62.5)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[n]																					
Yes	—	—	—	—	—	—	61	5.1	(4.0–6.2)	49	6.4	(3.7–9.2)	—	—	—	49	6.2	(4.3–8.1)	—	—	—
No	—	—	—	50	95.3	(89.7–100)	1,309	94.9	(93.8–96.0)	841	93.6	(90.8–96.3)	—	—	—	1,004	93.8	(91.9–95.7)	167	91.4	(86.4–96.5)
Incarcerated >24 hours, past 12 months																					
Yes	—	—	—	0	0.0*	—	41	3.2	(1.8–4.7)	20	2.6	(1.5–3.8)	—	—	—	29	2.8	(1.9–3.8)	—	—	—
No	—	—	—	56	100*	(100–100)	1,391	96.8	(95.3–98.2)	897	97.4	(96.2–98.5)	—	—	—	1,056	97.2	(96.2–98.1)	181	95.6	(92.1–99.2)

Abbreviations: n, number; col, column; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, U.S. Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. Unweighted numbers and weighted percentages are presented. CIs incorporate weighted percentages. Excluded are estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30. Estimates with an absolute CI width >30, estimates with an absolute CI width between 5 and 30 and a relative CI width >130%, and estimates of 0% or 100% are marked with an asterisk (*) and should be interpreted with caution.

[a] Hispanic or Latino persons can be of any race. Persons are classified in only 1 race/ethnicity category.

[b] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[c] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[d] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[e] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[f] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[g] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[h] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[i] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[j] Self-reported, and includes physical, mental, and emotional disabilities.

[k] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[l] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[m] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[n] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

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Table 5b. Relative and absolute differences in individual-level social determinants of health and quality of life among adults with diagnosed HIV, by racial/ethnic identity—Medical Monitoring Project, United States, 2022

	Black/African American persons vs. White persons				Hispanic/Latino[a] persons vs. White persons				Multiracial persons vs. White persons			
	PR	col %	PD	95% CI	PR	col %	PD	95% CI	PR	col %	PD	95% CI
National HIV/AIDS Strategy indicators related to social determinants of health												
Quality of life												
Physical health												
Self-reported health status[b]												
Good, very good, excellent	0.99	(0.92–1.07)	-0.75	(-6.02– 4.52)	0.98	(0.91–1.06)	-1.15	(-6.22– 3.92)	0.90	(0.78–1.03)	-7.38	(-16.55– 1.80)
Poor, fair	1.03	(0.86–1.22)	0.75	(-4.52– 6.02)	1.04	(0.88–1.23)	1.15	(-3.92– 6.22)	1.25	(0.96–1.62)	7.38	(-1.80– 16.55)
Mental or emotional health												
Unmet needs for services from a mental health professional among those who needed services, past 12 months[c]												
Yes	1.07	(0.84–1.36)	1.89	(-4.61– 8.39)	0.85	(0.53–1.39)	-3.87	(-15.38– 7.64)	1.37	(0.98–1.93)	9.90	(-1.66– 21.45)
No	0.97	(0.89–1.07)	-1.89	(-8.39– 4.61)	1.05	(0.90–1.22)	3.87	(-7.64– 15.38)	0.87	(0.72–1.03)	-9.90	(-21.45– 1.66)
Structural or subsistence factors												
Unstable housing or homelessness, past 12 months[d]												
Yes	1.61	(1.36–1.92)	8.18	(5.15– 11.22)	1.33	(1.05–1.69)	4.42	(0.44– 8.40)	1.45	(1.02–2.05)	5.95	(-0.56– 12.46)
No	0.91	(0.87–0.94)	-8.18	(-11.22– -5.15)	0.95	(0.90–1.00)	-4.42	(-8.40– -0.44)	0.93	(0.86–1.01)	-5.95	(-12.46– 0.56)
Unemployment[e]												
Yes	1.45	(1.03–2.04)	3.85	(0.47– 7.24)	1.41	(0.95–2.08)	3.48	(-0.36– 7.32)	1.71	(1.13–2.58)	6.06	(0.53– 11.59)
No	0.96	(0.92–0.99)	-3.85	(-7.24– -0.47)	0.96	(0.92–1.00)	-3.48	(-7.32– 0.36)	0.93	(0.88–1.00)	-6.06	(-11.59– -0.53)
Hunger or food insecurity, past 12 months[f]												
Yes	1.38	(1.01–1.88)	5.27	(0.44– 10.09)	1.67	(1.23–2.27)	9.22	(3.53– 14.90)	1.89	(1.37–2.61)	12.28	(5.12– 19.43)
No	0.94	(0.89–0.99)	-5.27	(-10.09– -0.44)	0.89	(0.83–0.96)	-9.22	(-14.90– -3.53)	0.86	(0.78–0.94)	-12.28	(-19.43– -5.12)
HIV stigma, past 12 months **(n, median score, 95% CI)[g]**												
Other factors important for health, including those that affect quality of life												
Economic stability												
Household income with respect to poverty guidelines[h]												
<100% FPL	2.15	(1.77–2.60)	21.25	(16.69– 25.80)	2.10	(1.62–2.71)	20.33	(11.93– 28.73)	2.34	(1.87–2.93)	24.82	(15.31– 34.33)
100%–138% FPL	0.95	(0.75–1.20)	-0.72	(-3.84– 2.41)	1.11	(0.83–1.48)	1.43	(-2.76– 5.62)	0.92	(0.55–1.53)	-1.15	(-7.68– 5.38)
139%–399% FPL	0.88	(0.76–1.01)	-5.20	(-10.59– 0.19)	0.82	(0.73–0.93)	-7.47	(-11.91– -3.03)	0.70	(0.55–0.91)	-12.33	(-20.23– -4.43)
≥400% FPL	0.41	(0.34–0.50)	-15.33	(-19.00– -11.65)	0.45	(0.29–0.70)	-14.29	(-20.11– -8.47)	0.57	(0.34–0.93)	-11.34	(-18.68– -4.00)
Education												
Educational attainment												
Less than high school diploma	2.61	(1.72–3.95)	8.76	(5.23– 12.28)	4.21	(3.01–5.87)	17.48	(13.53– 21.44)	2.21	(1.22–3.99)	6.58	(-0.03– 13.19)
High school diploma or equivalent	1.70	(1.42–2.02)	13.58	(9.47– 17.68)	1.32	(1.09–1.59)	6.18	(1.84– 10.51)	1.48	(1.06–2.08)	9.44	(0.61– 18.27)
Greater than high school	0.70	(0.64–0.77)	-22.33	(-27.48– -17.19)	0.68	(0.61–0.77)	-23.66	(-29.75– -17.57)	0.79	(0.70–0.89)	-16.02	(-23.34– -8.71)
Health-related factors												
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[i]												
Any private	0.81	(0.74–0.89)	-9.67	(-13.94– -5.39)	0.67	(0.57–0.79)	-16.42	(-22.46– -10.37)	0.79	(0.64–0.97)	-10.59	(-18.95– -2.22)
Public only, excluding RWHAP only	1.10	(1.00–1.21)	4.56	(0.03– 9.09)	1.15	(0.97–1.37)	6.97	(-1.80– 15.75)	1.26	(1.09–1.45)	11.74	(3.78– 19.70)
Uninsured or RWHAP only	2.20	(1.51–3.21)	5.11	(2.73– 7.48)	3.22	(1.83–5.66)	9.44	(3.92– 14.97)	—	—	—	—
Received RWHAP assistance, past 12 months												
Yes	1.01	(0.86–1.18)	0.37	(-6.45– 7.19)	1.26	(1.04–1.54)	11.64	(1.60– 21.69)	0.92	(0.73–1.16)	-3.53	(-13.18– 6.13)
No	0.99	(0.88–1.12)	-0.37	(-7.19– 6.45)	0.79	(0.64–0.98)	-11.64	(-21.69– -1.60)	1.06	(0.90–1.25)	3.53	(-6.13– 13.18)
Confidence in completing health forms												
Somewhat, a little bit, not at all	1.56	(1.34–1.82)	9.05	(5.96– 12.14)	2.20	(1.88–2.58)	19.36	(15.19– 23.52)	1.44	(1.04–2.00)	7.10	(-0.23– 14.44)
Extremely, quite a bit	0.89	(0.86–0.93)	-9.05	(-12.14– -5.96)	0.77	(0.72–0.82)	-19.36	(-23.52– -15.19)	0.92	(0.83–1.01)	-7.10	(-14.44– 0.23)
Has a disability[j]												
Yes	0.97	(0.88–1.08)	-1.21	(-5.48– 3.05)	1.04	(0.94–1.16)	1.83	(-2.58– 6.25)	1.20	(1.02–1.41)	8.40	(0.61– 16.20)
No	1.02	(0.95–1.10)	1.21	(-3.05– 5.48)	0.97	(0.90–1.05)	-1.83	(-6.25– 2.58)	0.85	(0.73–1.00)	-8.40	(-16.20– -0.61)
Any unmet HIV ancillary service need, past 12 months[k]												
Yes	1.41	(1.29–1.55)	16.30	(12.32– 20.27)	1.22	(1.00–1.50)	8.75	(-0.58– 18.09)	1.47	(1.24–1.74)	18.49	(9.76– 27.21)
No	0.73	(0.67–0.79)	-16.30	(-20.27– -12.32)	0.86	(0.72–1.02)	-8.75	(-18.09– 0.58)	0.69	(0.57–0.85)	-18.49	(-27.21– -9.76)

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Table 5b. Relative and absolute differences in individual-level social determinants of health and quality of life among adults with diagnosed HIV, by racial/ethnic identity—Medical Monitoring Project, United States, 2022 *(cont)*

	Black/African American persons vs. White persons				Hispanic/Latino[a] persons vs. White persons				Multiracial persons vs. White persons			
	PR	col %	PD	95% CI	PR	col %	PD	95% CI	PR	col %	PD	95% CI
Neighborhood and built environment												
Any met or unmet need for transportation assistance, past 12 months[l]												
Yes	1.67	(1.41–1.97)	14.19	(10.25– 18.12)	1.35	(1.07–1.71)	7.48	(1.84– 13.11)	1.81	(1.38–2.36)	17.10	(8.76– 25.43)
No	0.82	(0.78–0.87)	-14.19	(-18.12– -10.25)	0.91	(0.84–0.98)	-7.48	(-13.11– -1.84)	0.78	(0.69–0.89)	-17.10	(-25.43– -8.76)
Social and community context												
HIV health care discrimination among persons who received care, past 12 months[m]												
Yes	0.74	(0.61–0.89)	-7.27	(-11.78– -2.76)	0.78	(0.66–0.92)	-6.11	(-10.09– -2.12)	1.13	(0.85–1.51)	3.73	(-5.09– 12.54)
No	1.10	(1.04–1.17)	7.27	(2.76– 11.78)	1.08	(1.03–1.14)	6.11	(2.12– 10.09)	0.95	(0.83–1.08)	-3.73	(-12.54– 5.09)
English proficiency												
Speaks English less than well	—	—	—	—	—	—	—	—	—	—	—	—
Speaks English well	0.98	(0.97–0.99)	-1.76	(-2.68– -0.85)	0.74	(0.68–0.81)	-25.85	(-32.68– -19.02)	1.00	(0.99–1.01)	-0.33	(-1.39– 0.73)
Experiences of physical violence by an intimate partner or forced sex, lifetime[n]												
Yes	0.74	(0.66–0.81)	-11.10	(-14.92– -7.29)	0.74	(0.63–0.88)	-10.80	(-16.46– -5.14)	1.10	(0.89–1.37)	4.39	(-5.28– 14.07)
No	1.19	(1.12–1.27)	11.10	(7.29– 14.92)	1.19	(1.09–1.29)	10.80	(5.14– 16.46)	0.92	(0.77–1.10)	-4.39	(-14.07– 5.28)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[n]												
Yes	0.82	(0.58–1.16)	-1.10	(-3.10– 0.90)	1.04	(0.62–1.75)	0.25	(-3.08– 3.57)	—	—	—	—
No	1.01	(0.99–1.03)	1.10	(-0.90– 3.10)	1.00	(0.96–1.03)	-0.25	(-3.57– 3.08)	0.97	(0.92–1.04)	-2.36	(-7.92– 3.21)
Incarcerated >24 hours, past 12 months												
Yes	1.14	(0.62–2.09)	0.40	(-1.47– 2.27)	0.93	(0.52–1.67)	-0.20	(-1.78– 1.38)	—	—	—	—
No	1.00	(0.98–1.02)	-0.40	(-2.27– 1.47)	1.00	(0.99–1.02)	0.20	(-1.38– 1.78)	0.98	(0.95–1.02)	-1.53	(-5.36– 2.29)

Abbreviations: PR, prevalence ratio; PD, prevalence difference; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, U.S. Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. White persons were the referent group for each disparity assessment. Due to sample size issues with other racial/ethnic groups, disparities could only be assessed for Black/African American persons and Hispanic/Latino persons, versus White persons. Excluded are prevalence ratios and prevalence differences that are based on estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30.

[a] Hispanic or Latino persons can be of any race. Persons are classified in only 1 race/ethnicity category.

[b] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[c] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[d] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[e] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[f] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[g] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[h] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[i] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[j] Self-reported, and includes physical, mental, and emotional disabilities.

[k] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[l] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[m] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[n] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

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Table 6. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by National HIV/AIDS Strategy priority populations—Medical Monitoring Project, United States, 2022

	All MSM[a]			Black/African American MSM[b]			Hispanic/Latino MSM[c]			AI/AN MSM[d]			Black/African American cisgender women[e]			Transgender women[f]			Persons aged 18–24 years[g]			Persons who inject drugs[h]		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Total (row %)	**1,950**	**51.4**	**(48.0–54.7)**	**543**	**15.0**	**(12.1–17.9)**	**475**	**12.8**	**(8.8–16.9)**	**—**	**—**	**—**	**477**	**13.3**	**(10.5–16.1)**	**68**	**1.7**	**(1.2–2.2)**	**59**	**1.8**	**(1.2–2.4)**	**120**	**3.0**	**(2.0–4.1)**
National HIV/AIDS Strategy indicators related to social determinants of health																								
Quality of life																								
Physical health																								
Self-reported health status[i]																								
Good, very good, excellent	1,467	75.8	(73.4–78.1)	428	78.2	(73.7–82.7)	357	75.6	(71.8–79.4)	—	—	—	298	65.5	(61.6–69.4)	47	67.6	(55.9–79.3)	46	85.9	(77.2–94.6)	69	61.1	(51.5–70.7)
Poor, fair	479	24.2	(21.9–26.6)	113	21.8	(17.3–26.3)	117	24.4	(20.6–28.2)	—	—	—	161	34.5	(30.6–38.4)	21	32.4	(20.7–44.1)	—	—	—	51	38.9	(29.3–48.5)
Mental or emotional health																								
Unmet needs for services from a mental health professional among those who needed services, past 12 months[j]																								
Yes	220	28.6	(24.0–33.3)	69	36.6	(26.2–47.0)	51	23.5	(15.3–31.7)	—	—	—	30	19.2	(13.2–25.3)	—	—	—	—	—	—	24	37.1	(23.6–50.6)
No	611	71.4	(66.7–76.0)	139	63.4	(53.0–73.8)	170	76.5	(68.3–84.7)	—	—	—	137	80.8	(74.7–86.8)	32	82.7	(70.4–95.0)	—	—	—	59	62.9	(49.4–76.4)
Structural or subsistence factors																								
Unstable housing or homelessness, past 12 months[k]																								
Yes	306	16.7	(14.8–18.6)	118	22.4	(18.0–26.8)	73	17.1	(12.9–21.2)	—	—	—	75	17.8	(13.5–22.2)	17	30.7	(18.4–43.0)	18	31.6	(19.3–43.8)	58	50.8	(40.5–61.2)
No	1,638	83.3	(81.4–85.2)	424	77.6	(73.2–82.0)	399	82.9	(78.8–87.1)	—	—	—	384	82.2	(77.8–86.5)	50	69.3	(57.0–81.6)	38	68.4	(56.2–80.7)	62	49.2	(38.8–59.5)
Unemployment[l]																								
Yes	215	11.0	(8.6–13.4)	76	13.4	(9.5–17.3)	59	12.1	(8.2–16.0)	—	—	—	56	11.4	(8.1–14.7)	—	—	—	14	22.9	(11.6–34.1)	28	25.5	(15.7–35.2)
No	1,724	89.0	(86.6–91.4)	463	86.6	(82.7–90.5)	413	87.9	(84.0–91.8)	—	—	—	403	88.6	(85.3–91.9)	55	84.6	(75.5–93.8)	41	77.1	(65.9–88.4)	92	74.5	(64.8–84.3)
Hunger or food insecurity, past 12 months[m]																								
Yes	316	17.7	(15.8–19.6)	114	21.4	(15.6–27.2)	88	20.5	(15.5–25.6)	—	—	—	69	13.9	(10.4–17.3)	18	29.2	(16.8–41.5)	12	18.2	(8.2–28.1)	51	44.4	(33.0–55.8)
No	1,632	82.3	(80.4–84.2)	428	78.6	(72.8–84.4)	386	79.5	(74.4–84.5)	—	—	—	391	86.1	(82.7–89.6)	50	70.8	(58.5–83.2)	44	81.8	(71.9–91.8)	69	55.6	(44.2–67.0)
HIV stigma, past 12 months **(n, median score, 95% CI)[n]**	1,793	27.5	(26.0–28.9)	505	27.1	(25.1–29.2)	426	29.3	(27.0–31.6)	—	—	—	403	34.2	(31.1–37.3)	65	34.9	(28.1–41.7)	52	37.1	(30.3–44.0)	108	30.2	(21.7–38.7)
Other factors important for health, including those that affect quality of life																								
Economic stability																								
Household income with respect to poverty guidelines[o]																								
<100% FPL	354	19.4	(16.8–22.0)	107	21.2	(16.9–25.4)	114	25.8	(19.8–31.9)	—	—	—	202	53.4	(46.5–60.3)	28	44.6*	(26.6–62.6)	14	43.2*	(21.6–64.7)	52	44.1	(34.2–54.1)
100%–138% FPL	212	11.6	(10.1–13.0)	52	9.9	(7.6–12.2)	57	12.5	(9.2–15.8)	—	—	—	55	14.5	(10.4–18.7)	—	—	—	—	—	—	—	—	—
139%–399% FPL	743	43.3	(40.7–45.8)	221	47.6	(43.1–52.0)	177	43.4	(38.2–48.5)	—	—	—	117	28.8	(23.8–33.9)	21	34.6*	(19.6–49.7)	23	45.7*	(24.7–66.7)	31	31.1	(20.3–41.9)
≥400% FPL	479	25.8	(22.5–29.1)	98	21.4	(17.2–25.6)	76	18.3	(11.1–25.5)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Education																								
Educational attainment																								
Less than high school diploma	100	5.6	(4.3–6.9)	30	5.1	(3.1–7.1)	42	9.7	(6.3–13.1)	—	—	—	91	18.8	(15.2–22.3)	14	23.8	(11.1–36.5)	—	—	—	—	—	—
High school diploma or equivalent	393	21.0	(18.7–23.3)	156	27.7	(24.4–30.9)	100	23.4	(16.7–30.1)	—	—	—	160	34.9	(27.6–42.1)	22	28.5	(17.6–39.5)	21	42.4*	(25.6–59.2)	29	26.5	(15.7–37.3)
Greater than high school	1,456	73.4	(70.7–76.1)	357	67.3	(63.8–70.7)	332	66.9	(58.4–75.4)	—	—	—	209	46.3	(39.9–52.8)	32	47.7	(35.6–59.8)	29	46.4*	(28.0–64.8)	80	63.8	(54.3–73.3)
Health-related factors																								
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[p]																								
Any private	995	51.4	(48.4–54.3)	278	53.3	(47.3–59.4)	198	41.6	(36.1–47.0)	—	—	—	166	36.5	(31.2–41.7)	19	28.1	(16.6–39.5)	29	50.3	(37.8–62.9)	39	34.2	(23.0–45.5)
Public only, excluding RWHAP only	779	39.8	(35.7–43.8)	203	37.0	(30.5–43.5)	205	42.6	(34.7–50.6)	—	—	—	255	56.7	(50.5–63.0)	41	63.5	(51.0–76.0)	21	40.4	(27.1–53.7)	78	63.5	(51.5–75.5)
Uninsured or RWHAP only	142	8.9	(6.9–10.9)	48	9.7	(6.7–12.6)	64	15.8	(8.8–22.8)	—	—	—	28	6.8	(3.4–10.2)	—	—	—	—	—	—	—	—	—
Received RWHAP assistance, past 12 months																								
Yes	916	47.4	(43.3–51.5)	265	47.9	(43.5–52.4)	258	54.8	(45.1–64.5)	—	—	—	216	44.0	(37.0–50.9)	31	47.4*	(31.9–63.0)	25	42.2*	(25.5–58.8)	61	49.5	(36.6–62.4)
No	971	52.6	(48.5–56.7)	259	52.1	(47.6–56.5)	198	45.2	(35.5–54.9)	—	—	—	232	56.0	(49.1–63.0)	33	52.6*	(37.0–68.1)	29	57.8*	(41.2–74.5)	55	50.5	(37.6–63.4)
Confidence in completing health forms																								
Somewhat, a little bit, not at all	355	18.8	(16.9–20.7)	100	18.0	(14.7–21.4)	121	26.6	(21.3–32.0)	—	—	—	119	27.0	(21.9–32.0)	22	32.8	(21.7–43.8)	15	33.1	(19.0–47.2)	30	19.9	(9.4–30.4)
Extremely, quite a bit	1,593	81.2	(79.3–83.1)	443	82.0	(78.6–85.3)	353	73.4	(68.0–78.7)	—	—	—	341	73.0	(68.0–78.1)	46	67.2	(56.2–78.3)	40	66.9	(52.8–81.0)	90	80.1	(69.6–90.6)
Has a disability[q]																								
Yes	673	34.9	(32.4–37.4)	159	30.3	(25.1–35.6)	171	36.8	(31.6–42.0)	—	—	—	231	49.3	(45.0–53.7)	34	51.5	(38.3–64.8)	18	28.1	(16.1–40.1)	74	65.6	(53.7–77.4)
No	1,273	65.1	(62.6–67.6)	384	69.7	(64.4–74.9)	304	63.2	(58.0–68.4)	—	—	—	228	50.7	(46.3–55.0)	34	48.5	(35.2–61.7)	38	71.9	(59.9–83.9)	45	34.4	(22.6–46.3)
Any unmet HIV ancillary service need, past 12 months[r]																								
Yes	879	46.7	(43.0–50.4)	310	57.9	(50.6–65.2)	200	43.0	(37.1–48.8)	—	—	—	239	50.4	(43.5–57.4)	42	60.6	(48.6–72.6)	32	49.9*	(33.9–65.9)	89	75.0	(67.0–83.0)
No	1,060	53.3	(49.6–57.0)	230	42.1	(34.8–49.4)	271	57.0	(51.2–62.9)	—	—	—	218	49.6	(42.6–56.5)	26	39.4	(27.4–51.4)	24	50.1*	(34.1–66.1)	30	25.0	(17.0–33.0)

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Table 6. Individual-level social determinants of health and quality of life among adults with diagnosed HIV, by National HIV/AIDS Strategy priority populations—Medical Monitoring Project, United States, 2022 *(cont)*

	All MSM[a]			Black/African American MSM[b]			Hispanic/Latino MSM[c]			AI/AN MSM[d]			Black/African American cisgender women[e]			Transgender women[f]			Persons aged 18–24 years[g]			Persons who inject drugs[h]		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Neighborhood and built environment																								
Any met or unmet need for transportation assistance, past 12 months[s]																								
Yes	424	22.0	(19.3–24.8)	159	30.0	(23.0–37.0)	86	18.7	(15.1–22.3)	—	—	—	181	37.6	(33.3–42.0)	32	48.4	(35.7–61.0)	14	26.2	(11.8–40.6)	60	48.0	(35.6–60.5)
No	1,495	78.0	(75.2–80.7)	374	70.0	(63.0–77.0)	377	81.3	(77.7–84.9)	—	—	—	273	62.4	(58.0–66.7)	34	51.6	(39.0–64.3)	41	73.8	(59.4–88.2)	58	52.0	(39.5–64.4)
Social and community context																								
HIV health care discrimination among persons who received care, past 12 months[t]																								
Yes	466	26.1	(22.8–29.4)	113	23.6	(18.5–28.7)	103	23.6	(19.6–27.7)	—	—	—	72	19.3	(14.3–24.2)	15	22.6	(11.1–34.1)	13	30.4	(17.9–42.9)	47	37.3	(22.8–51.7)
No	1,362	73.9	(70.6–77.2)	390	76.4	(71.3–81.5)	342	76.4	(72.3–80.4)	—	—	—	354	80.7	(75.8–85.7)	51	77.4	(65.9–88.9)	37	69.6	(57.1–82.1)	57	62.7	(48.3–77.2)
English proficiency																								
Speaks English less than well	84	4.6	(2.4–6.9)	—	—	—	79	17.7	(12.3–23.0)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Speaks English well	1,865	95.4	(93.1–97.6)	541	99.8	(99.5–100)	396	82.3	(77.0–87.7)	—	—	—	446	97.3	(95.1–99.5)	62	92.4	(85.4–99.3)	55	98.3	(95.1–100)	119	99.4	(98.3–100)
Experiences of physical violence by an intimate partner or forced sex, lifetime[u]																								
Yes	695	37.2	(34.4–40.0)	186	35.2	(30.6–39.7)	137	32.0	(25.4–38.5)	—	—	—	160	35.9	(31.6–40.2)	36	57.5	(43.9–71.1)	24	46.8	(33.5–60.0)	69	57.8	(48.1–67.6)
No	1,219	62.8	(60.0–65.6)	348	64.8	(60.3–69.4)	324	68.0	(61.5–74.6)	—	—	—	278	64.1	(59.8–68.4)	32	42.5	(28.9–56.1)	30	53.2	(40.0–66.5)	49	42.2	(32.4–51.9)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[u]																								
Yes	116	7.1	(5.6–8.5)	34	6.7	(4.2–9.2)	31	7.7	(3.5–11.9)	—	—	—	—	—	—	—	—	—	—	—	—	22	20.8	(11.5–30.1)
No	1,786	92.9	(91.5–94.4)	496	93.3	(90.8–95.8)	429	92.3	(88.1–96.5)	—	—	—	416	96.4	(94.0–98.8)	58	82.8	(70.8–94.7)	46	87.3	(79.2–95.3)	94	79.2	(69.9–88.5)
Incarcerated >24 hours, past 12 months																								
Yes	49	2.8	(2.1–3.5)	16	3.6	(1.5–5.8)	14	3.5	(1.5–5.4)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
No	1,901	97.2	(96.5–97.9)	527	96.4	(94.2–98.5)	461	96.5	(94.6–98.5)	—	—	—	459	99.3	(98.2–100)	66	97.0	(92.7–100)	54	96.8	(92.7–100)	111	92.4	(87.8–96.9)

Abbreviations: MSM, men who have sex with men; AI/AN, American Indian/Alaska Native; n, number; col, column; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. Unweighted numbers and weighted percentages are presented. CIs incorporate weighted percentages. Excluded are estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30. Estimates with an absolute CI width >30, estimates with an absolute CI width between 5 and 30 and a relative CI width >130%, and estimates of 0% or 100% are marked with an asterisk (*) and should be interpreted with caution.

[a] Includes cisgender men with diagnosed HIV who reported having sex with ≥1 cisgender men in the past 12 months (among persons who had sex during the past 12 months) and cisgender men with diagnosed HIV who reported identifying as gay or bisexual (among those who did not have sex during the past 12 months).

[b] Includes MSM with diagnosed HIV who identified as non-Hispanic/Latino Black/African American race/ethnicity.

[c] Includes MSM who identified as Hispanic/Latino race/ethnicity. Hispanic or Latino MSM can be of any race.

[d] Includes MSM who identified as American Indian/Alaska Native race/ethnicity.

[e] Includes cisgender women with diagnosed HIV who identified as non-Hispanic Black/African American race/ethnicity.

[f] Persons with diagnosed HIV were classified as transgender women if the person reported that their sex assigned at birth was male but identified as female or transgender.

[g] Priority population for youths includes persons with diagnosed HIV aged 13–24 years; however, data from MMP are only available and presented for persons aged 18–24 years.

[h] Includes persons with diagnosed HIV who reported injecting drugs during the past 12 months.

[i] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[j] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[k] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[l] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[m] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[n] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[o] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[p] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[q] Self-reported, and includes physical, mental, and emotional disabilities.

[r] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[s] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[t] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on seven forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[u] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

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Table 7. National HIV/AIDS Strategy indicators among adults with diagnosed HIV, by other individual-level social determinants of health — Medical Monitoring Project, United States, 2022

	Good or better self-rated health[a]			Unmet needs for services from a mental health professional among those who needed services[b]			Unstable housing or homelessness[c]			Unemployment[d]			Hunger/food insecurity[e]			Median HIV stigma score[f]		
	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	Median score	95% CI
Total (row %)	**2,562**	**69.9**	**(68.5–71.2)**	**354**	**26.8**	**(23.0–30.6)**	**613**	**17.9**	**(16.5–19.3)**	**427**	**11.3**	**(9.4–13.2)**	**651**	**18.6**	**(17.3–19.9)**	**3,319**	**29.3**	**(27.9–30.7)**
Economic stability																		
Household income with respect to poverty guidelines[g]																		
<100% FPL	594	53.7	(50.1–57.3)	111	24.9	(19.8–30.0)	269	26.7	(22.8–30.7)	216	18.1	(14.9–21.4)	314	30.7	(26.6–34.8)	981	34.5	(32.5–36.6)
100%–138% FPL	287	65.2	(59.9–70.6)	46	30.2	(22.7–37.6)	84	19.4	(15.7–23.2)	36	8.5	(5.9–11.0)	98	22.5	(18.5–26.6)	416	31.2	(28.4–34.1)
139%–399% FPL	918	77.6	(75.0–80.2)	112	26.9	(20.1–33.6)	166	14.8	(12.7–17.0)	88	7.7	(5.8–9.5)	156	13.2	(10.3–16.1)	1,095	26.2	(24.7–27.6)
≥400% FPL	514	89.6	(86.6–92.7)	46	26.6	(18.6–34.6)	24	4.4	(2.8–5.9)	—	—	—	13	2.0	(1.0–3.1)	540	25.6	(22.9–28.2)
Education																		
Educational attainment																		
Less than high school diploma	252	51.5	(47.6–55.5)	35	18.7	(12.3–25.1)	126	27.3	(22.5–32.0)	72	13.0	(8.5–17.4)	128	28.3	(23.1–33.4)	437	33.4	(30.4–36.4)
High school diploma or equivalent	647	67.2	(63.7–70.6)	81	27.0	(21.0–32.9)	193	20.8	(17.8–23.9)	133	14.0	(10.4–17.7)	184	19.6	(17.2–22.0)	873	30.2	(28.3–32.2)
Greater than high school	1,662	75.3	(73.5–77.1)	238	28.5	(24.1–33.0)	292	14.3	(12.8–15.9)	222	9.7	(7.8–11.6)	337	15.9	(14.4–17.4)	2,009	28.1	(26.7–29.5)
Health-related factors																		
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[h]																		
Any private	1,252	81.7	(79.0–84.4)	143	29.3	(24.8–33.9)	179	12.7	(10.6–14.7)	104	7.1	(5.1–9.0)	174	12.1	(10.0–14.3)	1,404	28.3	(26.8–29.7)
Public only, excluding RWHAP only	1,062	59.0	(56.2–61.8)	176	24.2	(19.0–29.5)	345	20.2	(17.8–22.6)	269	14.4	(12.3–16.5)	380	21.7	(19.7–23.6)	1,621	29.3	(27.4–31.2)
Uninsured or RWHAP only	202	76.7	(71.6–81.8)	29	32.9	(20.5–45.4)	67	28.2	(21.7–34.7)	43	13.1	(9.4–16.9)	74	30.5	(25.1–36.0)	234	33.8	(29.8–37.8)
Received RWHAP assistance, past 12 months																		
Yes	1,185	68.7	(66.4–71.0)	155	23.9	(18.1–29.6)	318	20.0	(17.7–22.3)	207	11.4	(9.6–13.3)	351	21.5	(19.8–23.3)	1,552	29.5	(28.2–30.9)
No	1,276	71.0	(68.6–73.4)	186	30.0	(25.4–34.7)	257	15.5	(13.6–17.3)	195	10.7	(8.3–13.2)	263	15.8	(13.9–17.7)	1,639	28.7	(26.8–30.7)
Confidence in completing health forms																		
Somewhat, a little bit, not at all	470	53.0	(49.5–56.5)	99	25.3	(19.6–31.0)	210	23.0	(20.1–25.9)	118	11.3	(8.2–14.3)	227	25.0	(22.0–28.0)	779	36.9	(34.1–39.6)
Extremely, quite a bit	2,091	75.4	(74.0–76.9)	255	27.4	(23.3–31.4)	399	16.2	(14.3–18.0)	306	11.2	(9.4–13.0)	422	16.5	(14.9–18.0)	2,538	27.6	(26.3–29.0)
Has a disability[i]																		
Yes	766	50.2	(47.5–53.0)	183	25.7	(21.1–30.3)	361	24.2	(22.1–26.3)	199	12.0	(9.6–14.4)	422	27.7	(25.5–29.9)	1,359	33.7	(31.5–35.9)
No	1,793	84.2	(82.2–86.2)	171	28.2	(23.0–33.4)	252	13.4	(11.5–15.4)	227	10.7	(8.7–12.7)	228	12.0	(10.5–13.6)	1,955	26.6	(25.4–27.8)
Any unmet HIV ancillary service need, past 12 months[j]																		
Yes	1,070	62.1	(59.4–64.8)	N/A	N/A	N/A	441	26.7	(24.3–29.0)	272	15.3	(12.9–17.7)	497	29.6	(27.6–31.6)	1,579	34.1	(32.4–35.8)
No	1,473	77.2	(75.3–79.2)	N/A	N/A	N/A	165	9.5	(8.2–10.9)	152	7.4	(5.3–9.5)	148	7.9	(6.8–9.1)	1,736	25.5	(23.7–27.4)
Neighborhood and built environment																		
Any met or unmet need for transportation assistance, past 12 months[k]																		
Yes	557	51.3	(47.7–54.9)	142	26.8	(21.8–31.8)	301	28.7	(26.3–31.1)	179	17.3	(14.4–20.2)	354	34.7	(31.7–37.7)	972	34.8	(32.5–37.0)
No	1,966	77.6	(75.8–79.4)	210	26.8	(22.6–30.9)	293	13.1	(11.5–14.7)	241	8.8	(6.9–10.7)	281	11.7	(10.2–13.2)	2,337	27.7	(26.5–29.0)

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Table 7. National HIV/AIDS Strategy indicators among adults with diagnosed HIV, by other individual-level social determinants of health — Medical Monitoring Project, United States, 2022

	Good or better self-rated health[a]			Unmet needs for services from a mental health professional among those who needed services[b]			Unstable housing or homelessness[c]			Unemployment[d]			Hunger/food insecurity[e]			Median HIV stigma score[f]		
	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	Median score	95% CI
Social and community context																		
HIV health care discrimination among persons who received care, past 12 months[l]																		
Yes	475	62.3	(58.4–66.1)	119	29.9	(24.9–35.0)	171	21.9	(19.0–24.8)	86	10.3	(7.7–12.9)	222	27.5	(24.4–30.7)	724	38.7	(36.0–41.4)
No	1,926	73.1	(71.5–74.7)	195	21.6	(17.5–25.7)	374	15.3	(13.2–17.3)	297	10.8	(8.8–12.7)	359	14.4	(13.0–15.8)	2,417	27.1	(25.9–28.2)
English proficiency																		
Speaks English less than well	176	59.8	(54.2–65.3)	—	—	—	38	13.8	(8.9–18.7)	35	9.2	(5.1–13.2)	64	25.4	(16.2–34.7)	256	34.2	(30.2–38.2)
Speaks English well	2,386	70.7	(69.1–72.2)	340	27.6	(24.4–30.8)	574	18.2	(16.8–19.6)	392	11.4	(9.6–13.3)	587	18.1	(16.6–19.6)	3,063	29.0	(27.5–30.5)
Experiences of physical violence by an intimate partner or forced sex, lifetime[m]																		
Yes	799	66.0	(63.3–68.7)	179	29.9	(24.9–35.0)	279	23.1	(20.4–25.7)	165	13.5	(10.4–16.5)	321	26.8	(24.0–29.6)	1,132	34.0	(32.2–35.9)
No	1,708	72.3	(70.4–74.2)	172	24.0	(19.0–29.0)	307	14.6	(13.0–16.3)	249	10.0	(8.2–11.8)	308	14.0	(12.5–15.5)	2,142	27.2	(25.4–29.0)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[m]																		
Yes	111	61.1	(53.1–69.0)	36	33.2	(23.6–42.8)	76	43.6	(36.2–51.1)	38	20.4	(13.4–27.3)	93	53.6	(44.5–62.6)	167	46.7	(39.4–54.0)
No	2,378	70.7	(69.1–72.3)	311	26.0	(21.8–30.3)	504	16.0	(14.6–17.4)	370	10.6	(8.7–12.5)	525	16.1	(14.6–17.6)	3,083	28.5	(27.0–30.0)
Incarcerated >24 hours, past 12 months																		
Yes	60	59.7	(49.8–69.7)	11	22.9	(9.6–36.3)	53	59.4	(49.5–69.3)	29	26.9	(17.7–36.0)	44	45.3	(35.8–54.9)	93	39.1	(31.0–47.2)
No	2,502	70.2	(68.8–71.6)	343	27.0	(23.0–30.9)	560	16.7	(15.3–18.0)	398	10.8	(9.0–12.7)	606	17.8	(16.4–19.1)	3,225	29.1	(27.7–30.6)

Abbreviations: n, number; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; HHS, U.S. Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. Unweighted numbers and weighted percentages are presented. CIs incorporate weighted percentages. Excluded are estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30.

[a] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[b] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[c] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[d] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[e] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[f] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[g] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[h] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance includes Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[i] Self-reported, and includes physical, mental, and emotional disabilities.

[j] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[k] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[l] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on 7 forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[m] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

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Table 8. National HIV/AIDS Strategy indicators among adults with diagnosed HIV, by project area—Medical Monitoring Project, United States, 2022

Jurisdiction[g]	Good or better self-rated health[a]			Unmet needs for services from a mental health professional among those who needed services[b]			Unstable housing or homelessness[c]			Unemployment[d]			Hunger/food insecurity[e]			Median HIV stigma score[f]		
	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	Median score	95% CI
California	414	72.8	(68.4–77.2)	60	28.3	(20.8–35.7)	102	19.8	(15.6–24.0)	62	11.5	(8.2–14.7)	97	19.0	(15.0–23.0)	489	26.5	(24.3–28.7)
Chicago, IL	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Delaware	135	68.9	(61.6–76.2)	—	—	—	26	11.0	(6.7–15.4)	32	14.1	(9.2–19.0)	28	15.7	(8.2–23.2)	192	26.5	(22.6–30.3)
Florida	158	69.9	(63.4–76.4)	26	35.3	(23.4–47.2)	57	25.4	(19.2–31.7)	25	9.9	(5.7–14.1)	50	24.0	(17.8–30.2)	199	28.6	(25.1–32.2)
Georgia	107	67.4	(59.9–75.0)	—	—	—	33	22.4	(15.3–29.5)	16	9.3	(4.7–14.0)	32	22.3	(15.3–29.4)	152	26.1	(23.7–28.4)
Houston, TX	125	69.4	(61.5–77.3)	19	28.5	(16.5–40.5)	29	19.6	(12.2–26.9)	24	13.7	(8.0–19.4)	38	23.5	(16.1–31.0)	156	30.2	(25.2–35.1)
Illinois	67	73.4	(64.1–82.7)	—	—	—	12	13.7	(5.7–21.7)	15	14.6	(7.3–21.8)	12	16.4	(6.9–25.9)	84	27.7	(24.4–31.0)
Indiana	66	71.5	(62.3–80.8)	9	27.2*	(11.6–42.8)	21	23.9	(14.3–33.4)	—	—	—	16	18.2	(9.4–27.0)	82	27.6	(19.8–35.5)
Los Angeles County, CA	135	73.9	(67.5–80.4)	11	16.4	(7.5–25.4)	30	16.9	(11.3–22.5)	26	14.1	(8.9–19.2)	37	19.9	(14.0–25.7)	161	28.8	(26.2–31.5)
Michigan	122	66.1	(59.0–73.2)	23	28.5	(18.3–38.8)	39	19.6	(13.6–25.5)	33	17.0	(11.3–22.7)	33	16.2	(10.6–21.7)	176	34.3	(28.9–39.6)
Mississippi	68	69.6	(60.5–78.7)	11	36.5*	(19.0–54.0)	25	24.8	(16.2–33.5)	—	—	—	21	20.5	(12.5–28.5)	81	32.9	(30.1–35.7)
New Jersey	156	68.7	(61.5–75.9)	26	27.1	(17.0–37.1)	29	13.6	(7.9–19.4)	22	9.1	(4.9–13.2)	34	13.9	(8.8–18.9)	208	26.9	(23.6–30.2)
New York	260	68.8	(63.8–73.8)	33	19.9	(13.4–26.3)	51	13.6	(9.8–17.3)	64	17.1	(13.1–21.1)	78	19.7	(15.5–23.9)	337	31.4	(28.1–34.7)
New York City, NY	194	68.0	(62.0–73.9)	24	19.9	(12.3–27.6)	39	13.5	(9.2–17.9)	55	19.2	(14.3–24.2)	62	20.4	(15.5–25.4)	249	31.1	(27.6–34.7)
North Carolina	126	73.7	(67.1–80.3)	—	—	—	29	17.9	(11.8–24.0)	—	—	—	27	14.6	(9.3–19.9)	169	28.8	(24.0–33.6)
Oregon	132	70.0	(63.2–76.8)	28	33.1	(22.7–43.4)	26	15.8	(8.0–23.6)	15	7.7	(3.7–11.7)	28	13.7	(8.7–18.6)	186	31.2	(27.5–34.9)
Pennsylvania	150	66.9	(59.7–74.2)	22	20.9	(11.8–30.0)	40	17.6	(11.8–23.4)	26	10.8	(6.5–15.2)	38	17.1	(11.3–22.8)	187	31.0	(25.7–36.3)
Philadelphia, PA	101	69.8	(61.8–77.9)	15	28.9	(15.9–41.9)	27	18.4	(11.8–25.1)	16	10.2	(5.3–15.2)	25	17.1	(10.6–23.6)	124	30.4	(24.0–36.8)
Puerto Rico	145	76.1	(69.7–82.4)	—	—	—	18	8.2	(4.3–12.1)	28	15.6	(9.7–21.6)	25	12.4	(7.5–17.4)	183	29.0	(25.9–32.0)
San Francisco, CA	105	69.0	(61.2–76.9)	20	25.3	(15.1–35.6)	29	21.5	(13.4–29.7)	19	15.1	(7.4–22.7)	21	13.9	(8.1–19.7)	143	23.6	(18.6–28.5)
Texas	241	71.5	(66.1–77.0)	40	29.6	(20.9–38.2)	50	14.7	(10.5–19.0)	38	10.3	(6.8–13.9)	75	24.1	(18.9–29.4)	310	33.4	(30.7–36.0)
Virginia	100	69.8	(62.3–77.3)	18	35.5	(22.1–48.8)	28	21.0	(13.9–28.1)	13	9.7	(4.6–14.8)	30	21.3	(14.4–28.2)	136	32.0	(27.2–36.8)
Washington	115	69.4	(62.3–76.5)	20	31.8	(20.2–43.5)	27	15.9	(10.3–21.5)	15	9.1	(4.6–13.5)	27	16.1	(10.4–21.7)	148	26.1	(21.5–30.6)
National	**2,562**	**69.9**	**(68.5–71.2)**	**354**	**26.8**	**(23.0–30.6)**	**613**	**17.9**	**(16.5–19.3)**	**427**	**11.3**	**(9.4–13.2)**	**651**	**18.6**	**(17.3–19.9)**	**3,319**	**29.3**	**(27.9–30.7)**

Abbreviations: n, number; CI, confidence interval.

Note. Unweighted numbers and weighted percentages are presented. CIs incorporate weighted percentages. Excluded are estimates with a coefficient of variation ≥0.30 and those based on a denominator sample size <30. Estimates with an absolute CI width >30, estimates with an absolute CI width between 5 and 30 and a relative CI width >130%, and estimates of 0% or 100% are marked with an asterisk (*) and should be interpreted with caution.

[a] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[b] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[c] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[d] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[e] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[f] "Median HIV stigma score" defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2001277/ [Wright K, Naar-King S, Lam P, Templin T, Frey M. Stigma scale revised: reliability and validity of a brief measure of stigma for HIV+ youth. *J Adolesc Health* 2007;40(1):96–98].

[g] States include separately funded jurisdictions within those states.

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Table 9. Key clinical outcomes among adults with diagnosed HIV, by individual-level social determinants of health and quality of life — Medical Monitoring Project, United States, 2022

	Not retained in HIV care, past 12 months[a]			Missed ≥1 appointments, past 12 months			Missed ≥1 ART doses, past 30 days[b]			Virally unsuppressed at last test, past 12 months[c]			Did not have sustained viral suppression, past 12 months[d]			Had ≥1 unmet needs for HIV ancillary services, past 12 months[e]			Had ≥1 emergency room visits, past 12 months			Had ≥1 hospitalizations, past 12 months		
	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI
Total (row %)	**782**	**27.5**	**(25.5–29.5)**	**750**	**21.5**	**(19.7–23.2)**	**1,269**	**36.3**	**(34.1–38.4)**	**1,007**	**32.8**	**(29.9–35.7)**	**1,170**	**36.6**	**(33.6–39.6)**	**1,748**	**49.0**	**(45.6–52.5)**	**1,423**	**39.0**	**(37.0–41.0)**	**617**	**15.9**	**(14.5–17.3)**
National HIV/AIDS Strategy indicators related to social determinants of health																								
Quality of life																								
Physical health																								
Self-reported health status[f]																								
Good, very good, excellent	521	27.3	(24.8–29.9)	443	18.7	(16.8–20.7)	855	35.1	(32.7–37.6)	614	30.6	(27.0–34.2)	714	34.0	(30.3–37.8)	1,070	43.6	(39.6–47.7)	839	33.7	(31.7–35.8)	302	11.1	(9.8–12.4)
Poor, fair	231	27.6	(23.9–31.3)	305	27.7	(24.3–31.1)	410	38.7	(35.3–42.1)	361	38.0	(33.1–42.9)	417	42.5	(38.1–46.8)	674	61.6	(57.9–65.2)	580	51.0	(47.6–54.5)	313	27.0	(24.2–29.8)
Mental or emotional health																								
Unmet needs for services from a mental health professional among those who needed services, past 12 months[g]																								
Yes	89	35.9	(30.0–41.9)	118	36.3	(30.1–42.6)	172	54.2	(48.8–59.6)	101	37.4	(30.9–43.9)	117	40.7	(33.9–47.4)	N/A	N/A	N/A	161	44.8	(38.7–50.9)	53	13.3	(9.0–17.6)
No	200	22.2	(18.7–25.6)	279	25.7	(22.9–28.4)	450	41.9	(38.1–45.6)	303	30.9	(27.0–34.8)	354	34.8	(30.8–38.8)	N/A	N/A	N/A	509	47.7	(43.7–51.8)	232	21.0	(18.5–23.5)
Structural or subsistence factors																								
Unstable housing or homelessness, past 12 months[h]																								
Yes	156	33.7	(29.8–37.6)	221	38.2	(33.6–42.7)	270	50.8	(45.0–56.6)	242	46.3	(41.6–51.0)	281	51.4	(47.4–55.5)	441	72.9	(67.7–78.1)	342	56.7	(52.1–61.3)	173	25.2	(21.2–29.2)
No	595	26.1	(23.8–28.4)	527	17.9	(15.9–20.0)	996	33.3	(31.1–35.6)	735	29.9	(26.9–32.9)	852	33.4	(30.2–36.7)	1,299	43.7	(40.5–46.9)	1,078	35.1	(33.0–37.2)	443	13.9	(12.5–15.2)
Unemployment[i]																								
Yes	91	30.5	(24.7–36.3)	126	29.8	(25.2–34.4)	185	47.4	(41.2–53.6)	131	39.4	(33.2–45.6)	165	45.0	(38.8–51.2)	272	66.6	(59.3–73.8)	187	43.9	(38.5–49.2)	78	16.0	(11.9–20.0)
No	657	27.0	(24.8–29.1)	620	20.4	(18.6–22.2)	1,080	35.0	(32.8–37.1)	841	32.0	(29.1–34.9)	961	35.5	(32.5–38.4)	1,468	46.8	(43.6–50.1)	1,231	38.4	(36.3–40.4)	536	15.9	(14.5–17.2)
Hunger or food insecurity, past 12 months[j]																								
Yes	145	30.8	(26.5–35.0)	246	37.9	(32.6–43.1)	310	51.8	(47.6–56.0)	220	40.3	(36.4–44.3)	268	46.7	(42.8–50.7)	497	78.2	(74.2–82.3)	351	51.7	(47.7–55.8)	165	22.8	(19.2–26.4)
No	608	26.7	(24.4–28.9)	502	17.7	(15.9–19.5)	958	33.0	(30.7–35.3)	756	31.1	(27.8–34.4)	864	34.2	(30.8–37.7)	1,251	42.4	(39.1–45.7)	1,071	36.1	(33.9–38.2)	451	14.3	(12.9–15.7)
Other factors important for health, including those that affect quality of life																								
Economic stability																								
Household income with respect to poverty guidelines[k]																								
<100% FPL	225	27.4	(22.6–32.1)	297	27.9	(24.8–30.9)	393	38.9	(34.8–42.9)	325	35.5	(30.8–40.3)	386	40.7	(36.2–45.2)	601	57.2	(51.5–62.9)	507	46.0	(42.3–49.7)	247	20.2	(17.7–22.7)
100%–138% FPL	80	24.2	(18.9–29.5)	80	18.5	(13.6–23.5)	163	38.4	(32.2–44.5)	113	32.0	(24.1–39.9)	136	36.5	(28.8–44.3)	248	56.4	(51.1–61.7)	184	41.2	(35.6–46.8)	84	19.0	(14.5–23.4)
139%–399% FPL	241	27.1	(24.0–30.1)	244	21.3	(18.5–24.1)	426	37.7	(34.7–40.7)	310	32.1	(28.3–35.8)	351	34.9	(30.8–39.1)	551	47.2	(41.3–53.0)	430	36.3	(33.3–39.4)	160	13.3	(11.1–15.6)
≥400% FPL	133	30.7	(26.1–35.3)	53	9.6	(6.4–12.7)	176	28.8	(25.0–32.6)	131	29.0	(23.9–34.1)	140	30.3	(25.4–35.2)	143	25.0	(20.6–29.4)	156	28.2	(23.9–32.6)	53	9.6	(7.0–12.2)
Education																								
Educational attainment																								
Less than high school diploma	88	24.9	(19.9–29.9)	138	29.1	(24.7–33.6)	145	32.6	(28.4–36.8)	151	36.4	(31.3–41.5)	178	42.0	(37.2–46.7)	263	56.6	(50.9–62.4)	225	47.9	(42.4–53.3)	120	25.2	(20.8–29.7)
High school diploma or equivalent	198	25.7	(22.4–28.9)	220	22.9	(18.9–26.9)	323	34.9	(29.9–39.9)	270	31.9	(27.9–35.9)	325	37.4	(33.0–41.7)	501	53.2	(49.2–57.3)	406	40.6	(37.5–43.7)	187	16.3	(13.4–19.3)
Greater than high school	466	28.8	(26.6–31.0)	390	19.0	(17.2–20.8)	800	37.6	(35.0–40.2)	558	32.4	(29.0–35.9)	633	35.1	(31.5–38.7)	981	45.4	(41.7–49.0)	792	36.3	(33.8–38.9)	309	13.6	(12.2–15.1)
Health-related factors																								
Health insurance or coverage (including Ryan White HIV/AIDS Program [RWHAP] assistance), past 12 months[l]																								
Any private	331	28.3	(26.0–30.6)	250	17.5	(15.7–19.4)	532	35.7	(32.8–38.6)	383	30.7	(27.9–33.5)	436	33.8	(31.0–36.7)	626	41.7	(38.0–45.3)	531	34.9	(31.9–37.9)	209	13.3	(11.5–15.0)
Public only, excluding RWHAP only	359	27.4	(24.0–30.9)	418	24.1	(21.7–26.5)	628	37.0	(34.0–40.0)	496	34.3	(30.3–38.4)	579	38.2	(34.1–42.3)	920	52.7	(47.9–57.4)	771	43.3	(40.3–46.3)	364	19.3	(17.1–21.4)
Uninsured or RWHAP only	50	23.4	(16.8–30.1)	57	23.1	(16.5–29.7)	84	34.6	(28.2–41.0)	74	34.6	(26.8–42.4)	89	39.7	(32.4–47.1)	155	61.0	(54.4–67.6)	87	34.4	(27.9–40.8)	31	10.1	(6.0–14.2)
Received RWHAP assistance, past 12 months																								
Yes	285	21.2	(18.0–24.4)	397	24.0	(21.5–26.5)	624	38.0	(34.5–41.5)	405	28.0	(25.5–30.6)	479	32.1	(29.1–35.0)	841	50.3	(45.5–55.0)	676	38.6	(35.3–41.9)	307	16.6	(14.1–19.1)
No	436	32.7	(30.1–35.4)	320	19.0	(17.0–21.1)	591	34.6	(31.8–37.3)	527	36.8	(32.9–40.8)	597	40.1	(36.3–43.9)	827	47.4	(44.2–50.6)	687	39.3	(36.2–42.5)	285	15.4	(13.5–17.3)
Confidence in completing health forms																								
Somewhat, a little bit, not at all	174	24.7	(20.6–28.7)	240	28.4	(24.5–32.3)	327	37.8	(32.6–42.9)	257	33.1	(29.8–36.4)	299	37.2	(33.6–40.8)	502	55.5	(50.8–60.2)	400	44.3	(39.5–49.1)	205	23.0	(18.6–27.5)
Extremely, quite a bit	579	28.4	(25.9–30.8)	510	19.2	(17.0–21.4)	942	35.8	(33.9–37.7)	717	32.7	(29.0–36.3)	831	36.3	(32.9–39.7)	1,246	47.0	(43.4–50.5)	1,022	37.2	(35.1–39.2)	411	13.5	(12.2–14.8)
Has a disability[m]																								
Yes	325	27.6	(24.7–30.4)	411	27.8	(25.4–30.3)	587	40.2	(37.0–43.4)	465	35.9	(32.4–39.5)	533	39.7	(36.0–43.4)	889	58.7	(55.5–61.9)	755	48.1	(45.2–50.9)	380	22.7	(20.7–24.8)
No	428	27.4	(24.9–30.0)	339	16.9	(14.5–19.4)	681	33.5	(31.4–35.7)	513	30.7	(27.5–34.0)	601	34.4	(31.2–37.7)	858	42.1	(37.6–46.6)	665	32.4	(29.6–35.2)	234	10.9	(8.9–12.8)
Any unmet HIV ancillary service need, past 12 months[n]																								
Yes	384	29.3	(26.7–31.9)	491	29.3	(25.5–33.2)	730	45.1	(41.9–48.2)	499	34.8	(31.9–37.7)	588	39.3	(36.4–42.2)	N/A	N/A	N/A	801	46.0	(43.1–48.8)	345	18.1	(16.0–20.2)
No	359	25.3	(22.2–28.3)	255	14.1	(12.6–15.7)	532	28.3	(25.7–30.8)	469	30.9	(26.9–34.9)	535	33.9	(29.8–37.9)	N/A	N/A	N/A	608	32.0	(29.3–34.7)	267	13.7	(12.1–15.4)

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Table 9. Key clinical outcomes among adults with diagnosed HIV, by individual-level social determinants of health and quality of life — Medical Monitoring Project, United States, 2022 *(cont)*

	Not retained in HIV care, past 12 months[a]			Missed ≥1 appointments, past 12 months			Missed ≥1 ART doses, past 30 days[b]			Virally unsuppressed at last test, past 12 months[c]			Did not have sustained viral suppression, past 12 months[d]			Had ≥1 unmet needs for HIV ancillary services, past 12 months[e]			Had ≥1 emergency room visits, past 12 months			Had ≥1 hospitalizations, past 12 months		
	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI	n	row %	95% CI
Neighborhood and built environment																								
Any met or unmet need for transportation assistance, past 12 months[o]																								
Yes	219	27.0	(23.9–30.1)	332	33.3	(29.7–36.9)	434	43.3	(39.3–47.3)	318	35.7	(32.0–39.5)	385	41.3	(37.8–44.9)	739	70.8	(67.3–74.2)	570	52.4	(49.0–55.8)	294	25.1	(22.1–28.1)
No	519	27.5	(24.9–30.0)	405	16.5	(14.5–18.5)	821	33.4	(30.9–35.9)	633	31.2	(27.6–34.8)	718	34.1	(30.5–37.7)	1,003	40.6	(37.1–44.1)	828	33.4	(31.2–35.5)	313	12.1	(10.6–13.6)
Social and community context																								
HIV health care discrimination among persons who received care, past 12 months[p]																								
Yes	139	23.8	(20.1–27.5)	224	29.1	(25.5–32.7)	348	45.4	(42.4–48.5)	200	30.9	(25.6–36.2)	239	35.2	(29.5–40.8)	490	62.5	(58.6–66.3)	368	46.7	(41.9–51.5)	159	19.2	(16.3–22.1)
No	454	21.4	(19.4–23.5)	447	17.5	(15.1–19.9)	836	32.3	(30.0–34.5)	628	27.8	(24.9–30.6)	741	31.8	(28.9–34.7)	1,116	43.3	(39.8–46.8)	951	36.6	(34.5–38.7)	413	15.1	(13.3–17.0)
English proficiency																								
Speaks English less than well	37	18.2	(9.4–27.0)	64	21.9	(16.8–26.9)	80	27.0	(22.2–31.9)	66	25.7	(17.7–33.8)	77	30.8	(20.4–41.2)	119	43.4	(31.8–55.0)	95	28.0	(21.3–34.7)	41	11.8	(6.8–16.8)
Speaks English well	718	28.3	(26.6–30.0)	685	21.4	(19.6–23.3)	1,188	37.0	(34.5–39.4)	915	33.5	(30.3–36.6)	1,061	37.2	(33.9–40.5)	1,629	49.5	(46.2–52.8)	1,327	39.8	(37.7–41.9)	575	16.2	(14.7–17.7)
Experiences of physical violence by an intimate partner or forced sex, lifetime[q]																								
Yes	277	30.7	(27.0–34.4)	314	26.8	(23.6–30.0)	533	44.9	(42.0–47.7)	364	37.1	(32.4–41.8)	424	41.2	(36.3–46.1)	730	59.7	(55.0–64.4)	557	45.3	(41.8–48.8)	226	17.1	(14.8–19.4)
No	458	25.7	(22.7–28.7)	416	18.6	(16.4–20.7)	715	31.7	(29.4–34.1)	583	30.3	(26.7–33.9)	676	33.9	(30.5–37.3)	986	43.7	(39.9–47.6)	830	35.5	(33.0–38.0)	370	15.1	(13.6–16.6)
Experiences of physical violence by an intimate partner or forced sex, past 12 months[q]																								
Yes	49	39.0	(29.8–48.2)	80	44.1	(36.5–51.7)	104	60.6	(54.4–66.8)	69	47.2	(37.7–56.7)	79	51.0	(41.8–60.3)	135	75.9	(66.8–85.1)	106	57.8	(48.0–67.6)	42	20.4	(15.1–25.7)
No	681	26.7	(24.6–28.9)	639	20.0	(18.1–21.8)	1,128	34.6	(32.4–36.8)	869	31.7	(28.9–34.5)	1,008	35.3	(32.4–38.3)	1,563	47.5	(44.3–50.8)	1,268	37.7	(35.8–39.6)	547	15.5	(14.0–16.9)
Incarcerated >24 hours, past 12 months																								
Yes	30	36.9	(27.4–46.5)	39	37.7	(28.1–47.3)	38	45.8	(33.7–57.9)	41	46.6	(35.7–57.6)	46	51.3	(40.4–62.2)	64	70.2	(58.6–81.8)	54	57.2	(46.6–67.8)	28	25.3	(17.1–33.6)
No	725	27.2	(25.2–29.3)	711	21.0	(19.2–22.8)	1,231	36.0	(33.8–38.3)	940	32.5	(29.6–35.3)	1,092	36.3	(33.3–39.2)	1,684	48.4	(45.1–51.7)	1,369	38.4	(36.4–40.4)	589	15.6	(14.2–17.0)

Abbreviations: n, number; CI, confidence interval; FPL, federal poverty level; RWHAP, Ryan White HIV/AIDS Program; CD4, CD4+ T-lymphocyte count (cells/mm^3 or cells/μL) or percentage [footnotes only]; ART, antiretroviral therapy [footnotes only]; PCP, *Pneumocystis* pneumonia [footnotes only]; MAC, *Mycobacterium avium* complex [footnotes only]; ADAP, AIDS Drug Assistance Program [footnotes only]; SNAP, Supplemental Nutrition Assistance Program [footnotes only]; WIC, Special Supplemental Nutrition Program for Women, Infants, and Children [footnotes only]; HHS, Department of Health and Human Services [footnotes only]; VA, Veterans Administration [footnotes only].

Note. Unweighted numbers and weighted percentages are presented. CIs incorporate weighted percentages.

[a] Defined as not having 2 or more elements of outpatient HIV care at least 90 days apart in the past 12 months. Outpatient care was defined as any documentation of the following: encounter with an HIV care provider, viral load test result, CD4 test result, HIV resistance test or tropism assay, ART prescription, PCP prophylaxis, or MAC prophylaxis.

[b] Based on self-report.

[c] Defined as having most recent viral load documented in medical record as detectable or ≥200 copies/mL

[d] Defined as having ≥1 viral load measurements documented as detectable or ≥200 copies/mL

[e] Defined as needing, but not receiving, ≥1 HIV ancillary services related to HIV support (i.e., HIV case management, medicine through ADAP, adherence support, patient navigation, HIV peer group support), non-HIV medical services (i.e., dental care, mental health services, drug or alcohol counseling or treatment, domestic violence services), or subsistence services (i.e., SNAP or WIC, meal or food services, transportation assistance, shelter or housing services). Calculated among all persons.

[f] "Good or better self-rated health" defined as rating one's health as good, very good, or excellent (as opposed to poor or fair) at the time of interview.

[g] "Unmet need for mental health services from a mental health professional" defined as needing, but not receiving, services from a mental health professional among those who indicated needing mental health services (i.e., receiving or needing but not receiving) during the past 12 months.

[h] "Unstable housing or homelessness" defined as experiencing unstable housing (i.e., moving in with others due to financial issues, moving 2 or more times, or being evicted) or homelessness (living on the street, in a shelter, in a single-room–occupancy hotel, or in a car) at any time during the past 12 months.

[i] Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV.

[j] "Hunger/food insecurity" defined as going without food due to lack of money during the past 12 months.

[k] Poverty guidelines defined by HHS. For persons interviewed in a particular calendar year, the HHS poverty guidelines from the previous year were used. For instance, the 2020 guidelines were used for persons interviewed in 2021. More information regarding HHS poverty guidelines can be found at https://aspe.hhs.gov/frequently-asked-questions-related-poverty-guidelines-and-poverty.

[l] Persons could select more than 1 response for health insurance or coverage. Mutually exclusive categories are presented based on responses. Private coverage defined as receiving health insurance through a person's employer or a family member's employer or purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance included Medicaid, Medicare, VA, RWHAP, or other city, county, or state-funded insurance. Uninsured or RWHAP only category includes those who did not report having any insurance, or received RWHAP assistance only, without coverage through any other insurance categories.

[m] Self-reported, and includes physical, mental, and emotional disabilities.

[n] Represents those who needed, but did not receive, ≥1 HIV ancillary services, among all persons.

[o] Represents those who needed transportation assistance, regardless of whether that assistance was received, among all persons.

[p] HIV health care discrimination among those who received HIV care during the previous 12 months was assessed based on seven forms of discrimination, including: being treated with less courtesy than other persons, being treated with less respect than other persons, receiving poorer service than others, having a doctor or nurse act as if he or she believed they were not smart, having a doctor or nurse act as if he or she were afraid of them, having a doctor or nurse act as if he or she were better than them, and having a doctor or nurse not listen to what they were saying. Respondents were asked if they experienced these forms of discrimination never, rarely, some of the time, most of the time, or all the time. Respondents who reported experiencing at least one form of health care discrimination rarely, some of the time, most of the time, or all of time were considered to have experienced discrimination in an HIV health care setting.

[q] Physical violence by an intimate partner defined as ever being slapped, punched, shoved, kicked, choked, or otherwise physically hurt by a romantic or sexual partner. Forced sex defined as ever being threatened with harm or physically forced to have unwanted vaginal, anal, or oral sex.

Table 10. Median HIV stigma scores by key clinical outcomes among adults with diagnosed HIV—Medical Monitoring Project, 2022

	n	Median score	95% CI
Not retained in care, past 12 months[a]			
Yes	682	29.0	(26.3–31.8)
No	2,534	29.3	(28.1–30.6)
Missed ≥1 HIV care appointments, past 12 months[b]			
Yes	668	34.2	(29.9–38.4)
No	2,635	28.2	(26.7–29.7)
Missed ≥1 ART doses, past 30 days[b]			
Yes	1,160	31.4	(29.8–33.1)
No	2,054	28.0	(26.5–29.4)
Virally unsuppressed at last test, past 12 months[c]			
Yes	865	29.2	(26.3–32.1)
No	2,454	29.4	(28.3–30.5)
Did not have sustained viral suppression, past 12 months[d]			
Yes	1,005	29.3	(26.6–32.0)
No	2,314	29.3	(28.2–30.4)
Had ≥1 unmet needs for HIV ancillary services, past 12 months[e]			
Yes	1,579	34.1	(32.4–35.8)
No	1,736	25.5	(23.7–27.4)
Had ≥1 emergency room visits, past 12 months			
Yes	1,296	31.8	(28.6–34.9)
No	2,012	28.2	(26.8–29.5)
Had ≥1 hospitalizations, past 12 months			
Yes	553	29.5	(26.7–32.3)
No	2,758	29.3	(27.8–30.7)

Abbreviation: n, number; CI, confidence interval; ART, antiretroviral therapy; CD4, CD4+ T-lymphocyte count (cells/mm^3 or cells/μL) or percentage [footnotes only]; PCP, *Pneumocystis* pneumonia [footnotes only]; MAC, *Mycobacterium avium* complex [footnotes only]; ADAP, AIDS Drug Assistance Program [footnotes only]; SNAP, Supplemental Nutrition Assistance Program [footnotes only]; WIC, Special Supplemental Nutrition Program for Women, Infants, and Children [footnotes only].

Note. Unweighted numbers and weighted median scores are presented. CIs incorporate weighted medians.

HIV stigma scores were based on a 10-item scale that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about people living with HIV.

[a] Defined as not having 2 or more elements of outpatient HIV care at least 90 days apart in each 12-month period. Outpatient care was defined as any documentation of the following: encounter with an HIV care provider, viral load test result, CD4 test result, HIV resistance test or tropism assay, ART prescription, PCP prophylaxis, or MAC prophylaxis.

[b] Based on self-report.

[c] Defined as having most recent viral load documented in medical record as detectable or ≥200 copies/mL.

[d] Defined as having ≥1 viral load measurements documented as detectable or ≥200 copies/mL.

[e] Defined as needing, but not receiving, ≥1 HIV ancillary services related to HIV support (i.e., HIV case management, medicine through ADAP, adherence support, patient navigation, HIV peer group support), non-HIV medical services (i.e., dental care, mental health services, drug or alcohol counseling or treatment, domestic violence services), or subsistence services (i.e., SNAP or WIC, meal or food services, transportation assistance, shelter or housing services). Calculated among all persons.

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Table 11. Experiences with HIV-related stigma among adults with diagnosed HIV, by domain — Medical Monitoring Project, United States, 2022

	Strongly disagree			Somewhat disagree			Neutral			Somewhat agree			Strongly agree		
	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI	n	col %	95% CI
Personalized stigma															
During the past 12 months, I have been hurt by how people reacted to learning I have HIV	2,107	58.4	(55.0–61.8)	225	7.0	(6.1–7.9)	617	18.0	(15.7–20.3)	257	7.1	(5.9–8.3)	335	9.5	(8.6–10.5)
During the past 12 months, I have stopped socializing with some people because of their reactions to my HIV status	2,516	70.0	(67.8–72.3)	167	5.2	(4.4–6.1)	382	11.0	(9.5–12.5)	180	5.2	(4.2–6.1)	302	8.6	(7.6–9.5)
During the past 12 months, I have lost friends by telling them I have HIV	2,757	76.4	(74.0–78.7)	145	4.6	(3.5–5.6)	349	10.3	(9.0–11.7)	97	2.9	(2.3–3.5)	202	5.9	(5.0–6.7)
Disclosure stigma															
I am very careful who I tell that I have HIV	387	10.6	(9.2–12.1)	97	2.2	(1.6–2.9)	232	6.5	(5.6–7.4)	374	10.2	(8.8–11.7)	2,529	70.4	(67.8–73.0)
I worry that people who know I have HIV will tell others	1,239	34.6	(32.0–37.3)	238	6.6	(5.7–7.5)	436	12.4	(11.0–13.7)	526	14.5	(13.3–15.8)	1,161	31.9	(29.2–34.5)
Negative self-image															
I feel that I am not as good a person as others because I have HIV	2,574	70.1	(68.3–72.0)	193	5.3	(4.5–6.0)	243	7.0	(6.0–8.1)	331	9.6	(8.4–10.8)	273	7.9	(7.1–8.7)
Having HIV makes me feel unclean	2,495	68.0	(65.6–70.4)	254	7.4	(6.4–8.4)	240	7.5	(6.6–8.5)	366	10.1	(8.5–11.8)	251	6.9	(5.5–8.2)
Having HIV makes me feel that I am a bad person	2,941	80.1	(78.0–82.2)	185	5.6	(4.3–7.0)	205	6.2	(5.3–7.2)	176	4.9	(4.0–5.9)	110	3.1	(2.5–3.6)
Public attitudes															
Most people think that a person with HIV is disgusting	1,348	36.8	(33.9–39.8)	381	11.1	(9.5–12.6)	537	15.6	(14.1–17.1)	672	19.5	(17.5–21.5)	586	17.0	(14.4–19.6)
Most people with HIV are rejected when others find out	784	20.9	(19.0–22.7)	459	12.8	(10.8–14.9)	583	16.8	(14.6–19.1)	913	27.1	(25.4–28.8)	794	22.4	(20.0–24.7)

Abbreviations: n, number; col, column; CI, confidence interval.

Note. All numbers are unweighted and all percentages are weighted percentages; CIs incorporate weighted percentages.

Technical Notes & Appendix

TECHNICAL NOTES

Population of Inference

For the 2022 Medical Monitoring Project (MMP) data collection cycle (data collected June 1, 2022–May 31, 2023), the population of inference was adults with diagnosed HIV (aged ≥18 years) living in the United States.

A total of 23 areas were funded to conduct data collection for the 2022 cycle: California (including the separately funded jurisdictions of Los Angeles County and San Francisco), Delaware, Florida, Georgia, Illinois (including the separately funded jurisdiction of Chicago), Indiana, Michigan, Mississippi, New Jersey, New York (including the separately funded jurisdiction of New York City), North Carolina, Oregon, Pennsylvania (including the separately funded jurisdiction of Philadelphia), Puerto Rico, Texas (including the separately funded jurisdiction of Houston), Virginia, and Washington.

Data Collection

Persons with diagnosed HIV were sampled for MMP by using data from the National HIV Surveillance System (NHSS). Sampled persons were recruited by mail, by telephone, or in person. To be eligible to be included in MMP's 2022 data cycle, the person had to be, as of December 31, 2021: living with diagnosed HIV infection, aged ≥18 years, and residing in an MMP project area. The participant eligibility criteria were the same in all participating project areas.

A trained interviewer conducted an interview via telephone, in-person, or video format. English and Spanish versions of the questionnaire were used in the 2022 cycle. Persons speaking a language other than English or Spanish were offered an interview in their native language if an interpreter was available.

Persons who agreed to participate were offered an interview over the telephone or in person or video in a private location (e.g., at home or in a clinic). The interview (approximately 40 minutes) included questions about demographic characteristics, social determinants of health, health care use, met and unmet needs for ancillary services, sexual behavior, symptoms of depression and anxiety, gynecologic and reproductive history, substance use, and use of HIV/STD prevention services. Respondents were given a token of appreciation of no more than $50 in cash or the equivalent for participation; type of token differed by project area according to local considerations.

After the interview, MMP staff abstracted clinical data from the medical records of respondents at the health care facility identified by the respondents as their most frequent source of HIV care. Abstracted information included diagnoses of AIDS-defining conditions, prescription of antiretroviral therapy (ART) medications, laboratory results, and health care use in the 24 months before the interview.

For further technical details, please see the appendix.

APPENDIX

Methods

The Medical Monitoring Project (MMP) uses a stratified, 2-stage sampling design. States were sampled first, with probability proportional to size (PPS). All 50 states, the District of Columbia, and Puerto Rico (defined as primary sampling units [PSUs]) were eligible for selection.

From these 52 PSUs, 20 were selected by using PPS sampling based on AIDS prevalence at the end of 2002. According to the PPS sampling method, states with a higher AIDS prevalence had a higher probability of selection, and those with a lower AIDS prevalence had a lower probability of selection [1, 2]. Six municipal jurisdictions receive separate funding for HIV surveillance (Chicago, Illinois; Houston, Texas; Los Angeles County, California; New York City, New York; Philadelphia, Pennsylvania; and San Francisco, California); these areas were included with the state for first-stage sampling and constituted a city-state unit. If a state included a city with independent HIV surveillance authority (e.g., Texas, which includes Houston), selection of the state included selection of the city (i.e., city-state units were selected together).

In 2004, 19 states (including the 6 separately funded areas within those states) and Puerto Rico were selected from the 52 PSUs, resulting in 26 MMP project areas. Because of funding constraints for the 2009 data collection cycle, 3 project areas (Maryland, Massachusetts, and South Carolina) were randomly selected to discontinue participation in MMP, and the total number of MMP areas was reduced to 23.

Analyses carried out in 2014 and subsequently in 2021 found that the original measure of size with which states were originally sampled (i.e., AIDS prevalence in 2002) was still a reasonable proxy for the distribution of HIV prevalence. The selected sample of states was still sufficiently representative of the population of persons with diagnosed HIV; consequently, selecting a new sample for the 2015 and subsequent data collection cycles was unwarranted. In addition, the change in the sampling frame and the availability of national totals from the National HIV Surveillance System (NHSS) presented new options for calibrating weights, further lessening the need for any adjustments to the sample of states.

At the second stage, persons with a reported diagnosis in NHSS were sampled after the selection of the states. The sampling frame was the national case surveillance data set containing records submitted to the Centers for Disease Control and Prevention (CDC) as of December 31, 2021. Using NHSS data, the initial national frame dataset was created for persons who were alive, had diagnosed HIV infection, were aged 18 years or older, and were living in the United States, the District of Columbia, or Puerto Rico on the sampling date (i.e., December 31, 2021). Each case was assigned to a surveillance jurisdiction based on the most recently reported residence in NHSS. These addresses primarily came from case report forms and HIV-related laboratory reports. From this initial national frame, CDC staff drew simple random samples for each of the 23 project areas; project area staff then linked their samples to local case surveillance systems and extracted contact information for use in locating sampled persons, whom they then attempted to recruit.

Eligibility and Response Classifications

Persons were eligible for participation if, as of the sampling date, they had received a diagnosis of HIV, were aged ≥18 years, were alive, and were a resident of an MMP project area. Sampled persons were presumed to be eligible based on their information in NHSS unless data from another source contradicted this status. Persons were classified into 4 categories: (1) eligible respondents, (2) contacted nonrespondents, (3) nonrespondents who were not contacted, and (4) ineligible persons. These categories were used in calculating final response rates and contact rates following standard formulas [3].

Weighting

Overview

For the 2022 MMP cycle, sets of weights were produced nationally, for the city-state combinations, and for each project area. This report presents national weighted data and, thus, represents all adults with diagnosed HIV infection living in the United States. Nationally, data were weighted based on known probabilities of selection at the state or jurisdiction level and person level and then adjusted for multiplicity and nonresponse. After adjusting for nonresponse, the weights were poststratified to population totals from the NHSS frame. Extreme weights, if present, were trimmed, and the weights were adjusted to the same population totals.

For the weighting process, an updated sampling frame was obtained from NHSS data approximately a year and a half after sampling, during which time additional information reported to NHSS may have become available for sampled persons and additional diagnoses may have been reported. This updated sampling frame added records that would have been eligible if their information had been reported to NHSS on the date the initial sample was drawn; primarily, these were diagnoses that occurred during the year prior to the MMP sampling date (for the 2022 cycle, December 31, 2021). Additionally, some persons were found to have had multiple records at the time of sampling that were later identified as duplicate records. In some cases, updated information indicated that a person originally judged eligible and included on the original frame was ineligible. The updated sampling frame data also provided descriptive information for all sampled persons regardless of response and were the source of data used for nonresponse analysis and weighting.

Adjustments for unequal selection probabilities

The first step in the computation of weights was the calculation of base weights that reflect the sampling design probabilities. The base weight for each sampled person incorporates both the probability of selecting a project area and the probability of selecting a person within a project area. A person who was sampled from one jurisdiction but lived in another area at the time of sampling retained the original base weight. Prior to weighting, such cross-jurisdictional records were grouped with their project area of residence at the time of sampling. This moving of records did not affect the national weights but did affect the project area weight totals, increasing some while decreasing others.

Adjustments for multiplicity

A multiplicity factor was applied to the person weight for persons with records found to be present more than once after the original frame was compared to the updated sampling frame. This factor, which accounts for some persons' multiple opportunities for being sampled, was capped at 2.0 and was applicable for only 30 persons.

Adjustments for nonresponse

A nonresponse adjustment factor was applied to the multiplicity-adjusted base weight based on an analysis of nonresponse. In 2022, updated sampling frame data provided descriptive information about all sampled persons, which was used to assess how these characteristics were associated with nonresponse. The potential predictors of nonresponse were: race/ethnicity, male-to-male sexual contact (MMSC) HIV transmission category, HIV/AIDS disease stage, disease progression measured by most recent viral load test reported to NHSS, time since HIV diagnosis, age of most recent contact information, the person's frequency of receipt of HIV care (as indicated by NHSS records), movement to a different MMP jurisdiction since the time of sampling, non-U.S. birthplace, sex at birth, and age at sampling date. The nonresponse analysis followed a 2-step process. First, a bivariate analysis was conducted to determine which characteristics were potential predictors of nonresponse; then, a multivariate analysis using the significant characteristics from the bivariate analysis was conducted to identify independent predictors of nonresponse. Three significant predictors from this multivariate analysis were used to create weighting classes for the national data. In 2022, the significant predictors of nonresponse were: disease progression measured by the most recent viral load test reported to NHSS, time since HIV diagnosis, and the person's frequency of receipt of HIV care, as indicated by NHSS

records. Within weighting classes, the adjustment factor for nonresponse was the ratio of the sum of the multiplicity-adjusted base weights for eligible sampled cases to the sum of these weights for eligible respondents. The multiplicity adjusted weight within each nonresponse weighting class was then multiplied by the nonresponse adjustment factor to produce the nonresponse adjusted weights.

Poststratification and trimming

Poststratification methods ensure that weighted totals sum to known population totals and, therefore, minimize the potential for biases due to nonresponse and noncoverage. However, poststratification can also add additional variance to the weights. Thus, trimming procedures are used to control weight variability and reduce its impact on survey variances. MMP used an iterative approach that combines poststratification and trimming so that trimmed weights retain their variance-reducing features after poststratification and ensures that poststratified weights add up to known population totals.

The nonresponse adjusted weights were first poststratified to population totals from the updated sampling frame. The poststratification cells were defined by crossing sex at birth, race/ethnicity, and age group. Nationally, there were 32 poststratification cells. Poststratification adjustments were performed within each poststratification cell so that the weighted sum was preserved in each cell. To reduce additional variance added to poststratified weights, cells were collapsed and the need for weight trimming was evaluated. Poststratified cells were collapsed when cells had 2 or fewer respondents or had 5 or fewer respondents with an extreme adjustment factor ($\geq$1.75). The need for trimming was then assessed. If the design effect due to weighting (measured as $1 + CV^2$, where CV is the coefficient of variation of the weights) had exceeded 1.75, we would have capped the weights at the median weight plus 4 times the interquartile range of the weights; where trimming occurred, the weights were redistributed and poststratified again to the population totals. However, no trimming was needed for the 2022 MMP national weights.

Design variables

Nationally, design variables indicating strata and cluster membership for each participating person accounting for the sample design were created. Many project areas were sampled with certainty because of higher AIDS prevalence, and each of these was defined as its own stratum. Elsewhere, strata were created by grouping 2 to 3 project areas (PSUs in the stratified PPS design) that had similar selection probabilities. Among the 23 project areas, 14 were sampled with certainty. The 14 certainty project areas each represent a stratum, and each person within the stratum is a cluster. The remaining 9 noncertainty project areas were grouped to create strata, and each noncertainty project area was a cluster within the stratum. Multiple project areas within certainty states were effectively substrata, and each project area remained its own stratum. For local estimates, variance estimation was conditional on the initial sampling of states as PSUs, meaning that this stage of sampling was ignored. Respondents were treated as having come from a simple random sample with replacement, although the various adjustment factors induced unequal weights.

Definitions

NHAS indicators

- **Good or better self-rated health**: Self-rated health is assessed using a single question that captures the respondent's self-perceived general health at the time of interview using a Likert-type scale with the following responses: poor, fair, good, very good, or excellent. Self-rated health was dichotomized as good or better health (i.e., good, very good, or excellent) versus less than good health (i.e., poor, fair). This measure is also used in several other national initiatives and surveys examining self-rated health among the general U.S. population (e.g., Healthy People 2030, National Health and Nutrition Examination Survey [NHANES], Behavioral Risk Factor Surveillance System [BRFSS]) [4, 5, 6]. The 2025 NHAS target for good or better self-rated health is 95%.

- **Unmet needs for mental health services from a mental health professional among persons who needed services**: This measure was assessed through 2 questions. First, respondents were asked if they saw or talked to a mental health professional (e.g., psychologist, psychiatrist, psychiatric nurse, or clinical social worker) about their health during the past 12 months. Next, they were asked if they needed to see or talk to a mental health professional about their health. The denominator represents persons who needed mental health services (i.e., those with a met or unmet need), and was defined as those who received services (met need) and those who needed, but did not receive, services (unmet need). The numerator represents those who needed, but did not receive, services (unmet need). The 2025 NHAS target for unmet needs for mental health services from a mental health professional among persons who needed services is approximately 12%.
- **Hunger/food insecurity**: Persons who reported being hungry and not eating because there was not enough money for food in the past 12 months were considered to be food insecure. The 2025 NHAS target for hunger/food insecurity is approximately 11%.
- **Unemployment**: Unemployed persons included those who reported being unemployed at the time of interview, excluding persons who are unable to work, calculated among all adults with HIV. The 2025 NHAS target for unemployment is approximately 7%.
- **Unstable housing or homelessness**: Persons were considered to have experienced unstable housing if they reported moving in with others due to financial issues, moving 2 or more times, or being evicted at any time during the past 12 months. Persons were considered to have experienced homelessness if they reported living on the street, in a shelter, in a single-room-occupancy hotel, or in a car during the past 12 months. Persons were considered to have experienced unstable housing or homelessness if they reported any form of unstable housing or homelessness during the past 12 months. The 2025 NHAS target for unstable housing or homelessness is approximately 11%.
- **HIV stigma**: Defined as the weighted median score on a 10-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures 4 dimensions of HIV stigma: personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about persons living with HIV, measured among persons aged ≥18 years with diagnosed HIV infection living in the United States and Puerto Rico. The HIV stigma scale used for this indicator is discussed in Wright, et al [7]. The 2025 NHAS target for the median HIV stigma score is approximately 16.

Demographic characteristics and additional social determinants of health

- **Gender**: Categories were cisgender men, cisgender women, and transgender. Respondents were classified as cisgender if sex at birth and gender reported by the person were the same. Respondents were classified as transgender if reported sex at birth and current gender as reported by the respondent were not the same or if the respondent answered “transgender” to the interview question regarding self-identified gender.
- **Race/ethnicity**: Respondents were asked about whether they considered themselves as being of Hispanic, Latino/a, or Spanish origin. They were also asked about racial groups they identified as; respondents could check all categories that applied to them. These data were used to create the following analytic racial/ethnic categories: American Indian/Alaska Native, Asian, Black/African American, Hispanic/Latino, Native Hawaiian/other Pacific Islander, White, and multiple races. Hispanic/Latino persons could be of any race.

NHAS priority populations

- **Gay, bisexual, or other men who had sex with men (MSM)**: Included cisgender men with diagnosed HIV who reported having sex with ≥1 cisgender men in the past 12 months (among persons who had sex during the past 12 months) and cisgender men with diagnosed HIV who reported identifying as gay or bisexual (among those who did not have sex during the past 12 months).
- **Black/African American MSM**: Included MSM with diagnosed HIV who identified as non-Hispanic/Latino Black/African American race/ethnicity.

- **Hispanic/Latino MSM**: Included MSM with diagnosed HIV who identified as Hispanic/Latino race/ethnicity. Hispanic or Latino MSM could be of any race.
- **American Indian/Alaska Native MSM**: Included MSM with diagnosed HIV who identified as American Indian/Alaska Native race/ethnicity.
- **Black/African American cisgender women**: Included cisgender women with diagnosed HIV who identified as non-Hispanic Black/African American race/ethnicity.
- **Transgender women**: Persons with diagnosed HIV were classified as transgender women if the person reported that their sex assigned at birth was male but identified as female or transgender.
- **Persons aged 18–24 years**: Priority population for youths includes persons with diagnosed HIV aged 13–24 years; however, data from MMP are only available and presented for persons aged 18–24 years.
- **Persons who inject drugs**: Included persons with diagnosed HIV who reported injecting drugs for nonmedical purposes during the past 12 months.

Other factors related to social determinants of health

- **Federal poverty guidelines**: Respondents were asked about their combined monthly or yearly household income (in U.S.$) from all sources during the calendar year prior to the interview date. The number of persons meeting the current federal poverty threshold was determined by using the U.S. Department of Health and Human Services poverty guidelines that corresponded to the calendar year for which income was asked. These guidelines are issued yearly for the 48 contiguous states and Washington, D.C., and are an indicator used for determining eligibility for many federal and state programs. The 2021 guidelines were used for respondents interviewed in 2022, and the 2022 guidelines were used for persons interviewed in 2023 [8]. Because the poverty guidelines are not defined for the territory of Puerto Rico, the guidelines for the contiguous states and Washington, D.C., were used for this jurisdiction. Respondents were asked to specify their income range, and household income was assumed to be the midpoint of the income range.
- **Health insurance or coverage (including receipt of Ryan White HIV/AIDS Program [RWHAP] assistance)**: Respondents were asked whether they had health insurance or coverage during the 12 months before interview—including assistance through the RWHAP, a federally-funded comprehensive care program that provides HIV primary care, medications, and essential support services for low-income persons with HIV [9]. Respondents could select more than 1 response for health insurance or coverage. Responses to these questions were combined and categorized as having any private health insurance; having public insurance only; and being uninsured or being covered through RWHAP only. Private insurance included receipt of health insurance through a person's employer or family member's employer, or health insurance purchased through the Health Insurance Marketplace or directly from a health insurance company. Public insurance included Medicaid, Medicare, TRICARE/CHAMPUS, Veterans Administration insurance, and other public health insurance plans. Those who only received RWHAP assistance were considered to not have health insurance.
- **Disability**: Defined as having a physical, mental, and/or emotional disability. Respondents were considered to have a disability if they reported being deaf or having serious difficulty hearing; being blind or having serious difficulty seeing, even when wearing glasses; having serious difficulty concentrating, remembering, or making decisions because of a physical, mental, or emotional condition; having serious difficulty walking or climbing stairs; having difficulty dressing or bathing; or having difficulty completing errands alone such as visiting a doctor's office or shopping because of a physical, mental, or emotional condition.

Clinical outcomes

- **Outpatient HIV medical care**: Defined as documentation of any of the following at the most frequent source of HIV care: encounter with an HIV care provider, viral load test result, CD4 test result, HIV resistance test or tropism assay, ART prescription, pneumocystis pneumonia (PCP) prophylaxis, or

Mycobacterium avium complex (MAC) prophylaxis. All were measured through documentation in the person's medical record; an encounter with an HIV care provider was also measured based on interview self-report.

- **Retention in HIV care**: Persons were considered to be retained in care if they had 2 or more elements of outpatient HIV care at least 90 days apart in each 12-month period reviewed.
- **ART dose adherence**: Respondents were asked about how many days they missed at least 1 dose of their HIV medicines during the 30 days before interview as part of a 3-item ART adherence scale developed by Wilson and colleagues [10]. Respondents were considered ART dose adherent if they reported not missing any doses of their HIV medicines during the 30 days before interview.
- **Viral suppression**: Viral loads were abstracted from medical records from the facility where respondents most frequently received HIV care. Lack of viral suppression was assessed based on two measures. Lack of viral suppression at last test was defined as having the viral load measurement at last test documented as detectable or ≥200 copies/mL. Lack of sustained viral suppression was defined as having any viral load measurement during the past 12 months documented as detectable or ≥200 copies/mL. Those with no viral load tests were considered to be unsuppressed.
- **Unmet needs for ancillary services**: Ancillary services were defined as services that support retention in routine HIV medical care and viral suppression, such as HIV case management, dental care, and mental health services [11]. Ancillary services include services that support HIV medical care more directly, or those that support a person's general health through other types of services. Ancillary services included: HIV case management; medicine through the AIDS Drug Assistance Program (ADAP); adherence support services; HIV peer group support; and patient navigation services (patient navigation services could have been for HIV medical care or other types of care); dental care; mental health services; drug or alcohol counseling or treatment; and domestic violence services; Supplemental Nutrition Assistance Program (SNAP) or Special Supplemental Nutrition Program for Women, Infants, and Children (WIC); transportation assistance; meal or food services; and shelter or housing services. Needs for SSI, SSDI, interpreter services, and lawyer/legal services were dropped after the 2017 cycle and could not be incorporated in estimates for unmet needs for ≥1 ancillary services from 2018 cycle onwards. For this reason, estimates for unmet needs for ≥1 ancillary services were not reported from 2015–2017.

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Weddle Declaration
Exhibit C

Ryan White HIV/AIDS Program

Annual Data Report

Ryan White HIV/AIDS Program Services Report

2022

HRSA
Ryan White HIV/AIDS Program

The *Ryan White HIV/AIDS Program Annual Data Report* is published by the Division of Policy and Data, HIV/AIDS Bureau (HAB), Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services, Rockville, Maryland.

Data presented are for clients reported to the HRSA HAB Ryan White Services Report (RSR; non-AIDS Drug Assistance Program [ADAP]) data system for calendar years 2018 through 2022.

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Information about the Ryan White HIV/AIDS Program: ryanwhite.hrsa.gov

Educational and technical assistance materials about HIV and the Ryan White HIV/AIDS Program: targethiv.org

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COMMENTARY

The Ryan White HIV/AIDS Program (RWHAP) supports direct health care and support services for more than half a million people with HIV—more than half of all people with diagnosed HIV in the United States [1]. The RWHAP funds and coordinates with cities, counties, states, and local community-based organizations to deliver efficient and effective HIV care, treatment, and support services for people with HIV who have lower incomes. Since it was established, the RWHAP has developed a comprehensive system of safety net services within a network of providers who deliver high-quality, direct health care and support services. The RWHAP is critical to ensuring that individuals with HIV are linked to and retained in care, adhere to medication schedules, and remain virally suppressed. People with HIV who take HIV medication as prescribed and reach and maintain viral suppression cannot sexually transmit the virus to their partner (also known as “U=U” for “Undetectable = Untransmittable”) and can live longer and healthier lives. RWHAP services are crucial for attaining optimal HIV health outcomes among people with HIV, preventing further transmission of the virus, and—ultimately—ending the HIV epidemic in the United States.

Background

The U.S. Department of Health and Human Services (HHS), Health Resources and Services Administration (HRSA), HIV/AIDS Bureau (HAB) administers the RWHAP. In 1990, Congress passed the Ryan White Comprehensive AIDS Resources Emergency (CARE) Act to address the crisis of the HIV epidemic in the United States. This statute was amended and reauthorized in 1996, 2000, 2006, and, most recently, in 2009 as the Ryan White HIV/AIDS Treatment Extension Act of 2009.

The RWHAP was funded at $2.49 billion in fiscal year (FY) 2022 and is the largest federal program focused exclusively on HIV care, treatment, and support services. The RWHAP leverages other funding sources and health care coverage opportunities for people with HIV (e.g., state and/or local funds, program income, pharmaceutical rebates).

The RWHAP has five statutorily defined Parts that provide funding for medical and support services, technical assistance, clinical training, and the development of innovative models of care to meet the needs of different communities and populations affected by HIV:

- **Part A** provides funding to Eligible Metropolitan Areas (EMAs) and Transitional Grant Areas (TGAs) severely affected by the HIV epidemic. Grant funds assist eligible jurisdictions to develop or enhance access to a comprehensive continuum of high-quality, community-based care for people with HIV who have lower incomes through the provision of formula, supplemental, and Minority AIDS Initiative funds. Eligibility for RWHAP Part A grants is based, in part, on the number of confirmed Stage 3 HIV (AIDS) cases within a statutorily specified “metropolitan area.” HHS uses the Office of Management and Budget (OMB) census-based definitions of a metropolitan statistical area (MSA) to determine the geographic boundaries of an RWHAP metropolitan area, based on the boundaries in effect when a jurisdiction initially received RWHAP Part A funding. For all newly eligible areas, HHS bases the boundaries on current OMB MSA boundary definitions. To qualify for EMA status, an area must have reported more than 2,000 AIDS cases in the most recent five years and have a population of at least 50,000. To be eligible for TGA status, an area must have reported 1,000 to 1,999 AIDS cases in the most recent five years and have a population of at least 50,000. EMAs and TGAs range in size from one city or county to more than 26 different geographic entities; 11 EMAs or TGAs have service areas that cross state lines.

- **Part B** provides funding to all 50 states, the District of Columbia, the Commonwealth of Puerto Rico (hereafter referred to as Puerto Rico), the Northern Mariana Islands, American Samoa, Guam, the U.S. Virgin Islands, the Federated States of Micronesia, the Republic of the Marshall Islands, and the Republic of Palau—hereafter referred to collectively as state(s)/territory(ies)—to support HIV care and treatment services for people with HIV who have lower incomes.
  - The RWHAP Part B grants include funding for the AIDS Drug Assistance Program (ADAP) to fund medication and health care coverage.
- **Part C** provides funding to local community-based organizations, community health centers, health departments, academic medical centers, and hospitals in 49 states, the District of Columbia, Puerto Rico, and the U.S. Virgin Islands to provide comprehensive primary medical care and support services in an outpatient setting for people with HIV who have lower incomes. The RWHAP Part C funds also support capacity development grants to strengthen organizational infrastructure and develop, enhance, or expand access to high-quality primary medical care for people with HIV.
- **Part D** provides funding to local community-based organizations, community health centers, health departments, academic medical centers, and hospitals in 39 states and Puerto Rico to support family-centered HIV primary medical care and support services in an outpatient setting (directly or through contracts or memoranda of understanding) for women, infants, children, and youth with HIV who have lower incomes and their affected family members.
- **Part F** provides funds for the following programs:
  - The Special Projects of National Significance (SPNS) Program supports the development, implementation, and evaluation of evidence-based, evidence-informed, and emerging interventions to improve and enhance HIV care and effective service delivery systems for people with HIV. The RWHAP SPNS Program also supports the dissemination of successful interventions and supports the adaptation, replication, and integration of these interventions by RWHAP-funded recipients.
  - The AIDS Education and Training Center (AETC) Program works to increase the number of health care providers who can counsel, diagnose, treat, and medically manage individuals with HIV by providing education, training, consultation, and clinical decision support to health care professionals at the local and regional levels.
  - The Dental Programs provide funding for oral health care for people with HIV and support training dental and dental hygiene providers.
  - The Minority AIDS Initiative provides funding to evaluate and address the disproportionate impact of HIV on racial and ethnic minority populations.

Together, the Parts of the RWHAP provide the public health infrastructure needed to ensure access to a wide range of core medical services (e.g., outpatient/ambulatory health services, medical case management, mental health services, outpatient care for substance use) and support services (e.g., non-medical case management, housing, transportation, food bank/home delivered meals) aimed at early diagnosis of HIV, linkage to care, retention in care, medically appropriate treatment, and sustained viral suppression.

Ending the HIV Epidemic in the U.S.

The RWHAP goals align with two complementary national efforts to reduce new HIV infections: the *Ending the HIV Epidemic in the U.S. (EHE)* initiative [2] and the *National HIV/AIDS Strategy (NHAS)*

2022–2025 [3]. The EHE initiative focuses on increased linkage to, reengagement in, and retention in HIV care and treatment. Reducing new infections to this level essentially would mean that HIV transmissions would be rare and would meet the definition of ending the epidemic. In 2021, HAB EHE-funded providers served 22,413 people with HIV who were new to care and 15,318 people who were estimated to be re-engaged in care [4,5]. Correspondingly, *NHAS 2022–2025*, which was released in December 2021, aims to prevent new HIV infections, improve HIV-related health outcomes for those with HIV, reduce HIV-related disparities and health inequities, and achieve integrated and coordinated efforts to address the HIV epidemic. HRSA's RWHAP plays a key role in providing care and treatment to people with new HIV diagnoses, people with HIV who are re-engaged in care, and people with HIV who are in care but not virally suppressed, as well as continued care for the more than half a million people served by the RWHAP annually.

2022 Ryan White HIV/AIDS Program Annual Data Report Overview

This report is HRSA HAB's annual publication of national RWHAP client-level data from the RWHAP Services Report (RSR). The RSR data are HRSA HAB's primary source of annual, client-level data reported by more than 2,000 funded grant recipients and subrecipients.

Client-level RSR data collection began in 2010, and the data are used to assess the numbers and demographics of clients receiving RWHAP services, understand client HIV-related outcomes, and identify and address HIV-related disparities. This information is a crucial component of data-driven program decision-making and for informing action to advance health equity. Project officers at HRSA HAB discuss the data with recipients to monitor and support their progress to improve HIV care and treatment for people with HIV. It is through the dedicated work of RWHAP recipients, subrecipients, and the RWHAP community that clients receive HIV services every day.

This report includes data submitted to HRSA HAB through the RSR system for all clients served by RWHAP Parts A, B, C, and D during calendar years 2018 through 2022, regardless of the source of RWHAP funding. The data presented are not specific to any one Part, regardless of geographic area presented (e.g., state-level, EMA/TGA-level). RSR data do not include information about ADAP; all ADAP-related information is reported through the RWHAP ADAP Data Report and is disseminated in another publication [6]. Although data presented here are "non-ADAP," many clients also receive ADAP services.

The RSR data presented in this report highlight the state of the RWHAP and include the demographic composition of clients served; socioeconomic factors, such as federal poverty level (FPL), health care coverage, and housing status; and the results of focused analyses to measure progress toward achieving select HIV-related clinical outcome indicators [7,8]. The data are inclusive of the overall RWHAP client population and priority populations. This report does not include the specific services provided to individuals. All tables include all clients served, regardless of the RWHAP services rendered (unless otherwise noted, e.g., viral suppression tables) or source of RWHAP funding (i.e., data from Parts A, B, C, and D are included in all tables).

Tables displaying demographic and socioeconomic data (Table 1a, Tables 2 through 8, and Tables 20a through 26b) include all RWHAP clients, regardless of HIV serostatus[1] (hereafter referred to as *HIV status)*. The data include people with HIV, as well as clients missing HIV status information (e.g., clients who receive services that do not require HIV status to be reported, such as medical transportation services) and clients who do not have HIV (i.e., the families of people with HIV are able to receive certain RWHAP services). In 2022, people with HIV represented 98.3% of all clients. Table 1b and tables displaying retention in care and viral suppression data (Tables 9 through 19b and

[1] "The state of either having or not having detectable antibodies against a specific antigen, as measured by a blood test (serologic test). For example, *HIV seropositive* means that a person has detectable antibodies to HIV; *HIV seronegative* means that a person does not have detectable HIV antibodies" (https://clinicalinfo.hiv.gov/en/glossary/serostatus*)*.

Tables 27a through 36b) include only people with HIV who meet the criteria for the specified analysis (see Technical Notes). The tables include data reported from 50 states, the District of Columbia, Guam, Puerto Rico, and the U.S. Virgin Islands. However, due to reporting challenges during the coronavirus disease 2019 (COVID-19) pandemic, Guam's 2019 and 2020 RSR data are unavailable. Tables 20a through 36b display data by state and EMA/TGA. Readers are encouraged to review all table titles and footnotes carefully to ensure a complete understanding of the data presented.

Readers should interpret RWHAP retention in care and viral suppression data carefully. RWHAP recipients and subrecipients report RSR client-level data annually, and the data are de-identified when reported. As a result, it is not possible to link client-level data across years, which affects how HIV-related outcomes are calculated in this report (i.e., outcomes are calculated separately for each calendar year and compared across years). Specifically, HRSA HAB measures retention in care among RWHAP clients with HIV who received at least one Outpatient Ambulatory Health Services (OAHS) visit before September 1 of the calendar year (i.e., January 1 through August 31), thereby allowing a second care visit to occur at least 90 days later during that calendar year. HRSA HAB measures viral suppression among RWHAP clients who received at least one OAHS visit any time during the calendar year and who had at least one viral load test result reported; that is, viral suppression is measured among people with HIV who received medical care from RWHAP providers during the year and had at least one viral load test.

As a result of the above specifications about the retention in care and viral suppression calculations, the numbers of people with HIV included in these analyses are not equal to the total number of people with HIV served by the RWHAP; the subset of clients for retention in care analyses is 63% of the total RWHAP client population with HIV, and the subset for viral suppression is 66%. Clients not included in retention in care or viral suppression calculations may have received any other RWHAP service (e.g., medical or non-medical case management, housing, transportation, food bank/home delivered meals). It is also important to note that many of the clients not included in calculations for retention in care and viral suppression (i.e., those who did not receive RWHAP OAHS services) receive medical care at RWHAP-supported organizations, where primary medical care services are covered using non-RWHAP funding sources (e.g., private, public, or other health care coverage types), or receive care from providers outside the RWHAP system; these clients should not be presumed to be "out of care" [9].

Monitoring HIV-Related Health Outcomes

RWHAP recipients and subrecipients submit select client-level HIV-related clinical data (e.g., OAHS visit dates and viral load test results) to HRSA HAB that monitors progress toward achieving the goals of the EHE initiative and NHAS. HRSA HAB uses these data to calculate retention in HIV medical care and viral suppression among clients receiving RWHAP OAHS. This report displays these data for the RWHAP client population of people with HIV who are receiving OAHS by demographics, state, and EMA or TGA (Tables 9, 10, and 27a through 36b).

Because of notable disparities, HRSA HAB enhanced its efforts to improve HIV-related health outcomes among several priority populations, as detailed in Tables 11a through 19b. These tables also display retention in care ("a" tables) and viral suppression ("b" tables) for priority populations (except for Tables 12a–d, where retention in care for men and gay, bisexual, and other men who have sex with men are displayed in the "a" and "b" tables, respectively, and viral suppression in the "c" and "d" tables, respectively).

Report Considerations

HRSA HAB periodically updates the RSR to measure the full investment of the RWHAP more precisely and demonstrate its impact at the state and local levels. As a payor of last resort, RWHAP funds cannot be used to pay for services that have been or reasonably can be expected to be

covered by another payment source. However, more recipients have been funding services with RWHAP-related funding (i.e., program income, pharmaceutical rebates) to be used for specified allowable costs. To fully measure RWHAP investments and their impact, beginning with the 2019 data, HRSA HAB encourages recipients and subrecipients to include RSR data on clients receiving services provided using RWHAP-related funding; this became a reporting requirement for all RWHAP recipients and subrecipients beginning with the 2021 data submission. It is important to note that this new reporting requirement does not replace the previous eligible scope reporting requirement, but rather expands on the previous requirement.

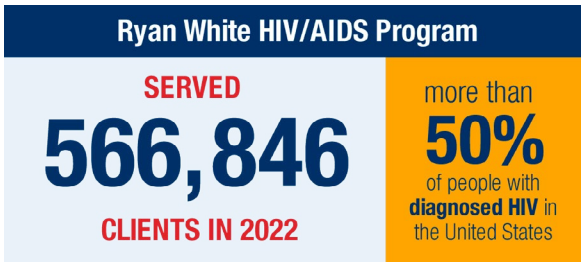
Client-level data for people with HIV who received HAB EHE–funded services and RWHAP FY 2020 Coronavirus Aid, Relief, and Economic Security (CARES) Act–funded services were included in the RSR data submission for 2020–2021 (EHE- and CARES Act–funded services) and 2022 (EHE-funded services only). Collectively, these reporting changes may explain some fluctuations in the numbers of clients since 2019.

Because of reporting challenges, data for the state of Indiana are not included in the state-level data tables ("a" tables from 20a to 36a). Additionally, race/ethnicity data for the states of Maryland and Texas and the Baltimore, MD, and Dallas, TX, EMAs are not included in this report because of data quality issues (Tables 22a–22b, Tables 31a–31b, and Tables 32a–32b).

Ryan White HIV/AIDS Program Client Highlights

Client Demographics

The RWHAP serves more than half a million people each year. In 2022, 566,846 clients received services from RWHAP-funded providers (Table 1a). Among all RWHAP clients served in 2022, 98.3% (557,394) were people with HIV (Table 1b), which has been relatively consistent since 2018.

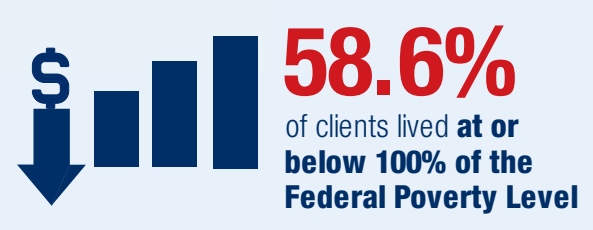


Nearly half of RWHAP clients are aged 50 years and older. In 2022, people aged 50 years and older accounted for 48.2% of all RWHAP clients, an increase from 46.1% of clients in 2018. People aged 65 years and older accounted for 11.6% of all RWHAP clients, an increase from 7.6% of clients in 2018.

Nearly three-quarters of RWHAP clients are from racial and ethnic minority groups. The percentage distribution of client race and ethnicity populations has remained consistent since 2018. In 2022, 44.5% of clients self-identified as Black/African American, 25.8% as White, 25.3% as Hispanic/Latino, and less than 2% each as American Indian/Alaska Native, Asian, Native Hawaiian/Pacific Islander, or people of multiple races (Table 1a).

The majority of RWHAP clients are male. In 2022, 72.1% of clients were cisgender male (hereafter referred to as *male*), 25.2% were cisgender female (hereafter referred to as *female*), and 2.8% identified as transgender (2.3% transgender female; 0.3% transgender male; 0.2% clients with another gender identity; Table 1a). The gender distribution of RWHAP clients has remained largely consistent since 2018. However, the gender distribution differs by race and ethnicity (Table 2) and by age group (Table 3). See Technical Notes for additional information about gender categories.

Socioeconomic Factors and Health Care Coverage



More than half of RWHAP clients are living at or below 100% FPL. In 2022, 58.6% of clients were living at or below 100% FPL, a slight decrease from 61.3% in 2018 (Table 1a).

The percentages of clients living below 100% FPL differ by race/ethnicity. The percentages of Black/African American, American Indian/Alaska Native, Hispanic/Latino, and multiracial clients living at or below 100% FPL (63.2%, 62.5%, 61.1%, and 59.1%, respectively) were higher than those among clients of other races (Native Hawaiian/Pacific Islander, 53.6%; Asian, 52.1%; White, 48.7%; Table 5, percentages presented in the table are column percentages, and those presented here are row percentages).

Higher percentages of female and transgender female clients are living below 100% FPL compared to male clients. In 2022, 66.8% of female clients and 72.5% of transgender female clients were living at or below 100% FPL (Table 3). Comparatively, 55.2% of male clients were living at or below 100% FPL.

Approximately 18% of RWHAP clients lack health care coverage and nearly 50% are covered by Medicare and/or Medicaid. Among all RWHAP clients in 2022, 31.4% were covered by Medicaid, 10.3% were covered by Medicare, 10.4% had multiple forms of coverage, 10.2% had private employer coverage, and 9.4% had private individual coverage (Table 1a); multiple coverages include any combination of health care coverage types, *except* those who had Medicaid *and* Medicare (dual eligibility), which is displayed separately (7.6% of clients). See Technical Notes for additional information. Nearly one-fifth (18.2%) of RWHAP clients had no health care coverage in 2022, which is lower than in 2018 (20.1%).

Approximately 7% of RWHAP clients have temporary housing and approximately 5% have unstable housing. The distribution of RWHAP clients by housing status has remained relatively stable since 2018 (Table 1a). Nearly 90% of RWHAP clients had stable housing in 2022.

In 2022, the highest proportions of clients with temporary or unstable housing were among those aged 20–24 years (9.6% and 5.7%, respectively), 25–29 years (9.6% and 6.9%), 30–34 years (9.1% and 7.3%), 35–39 years (8.7% and 7.1%), and 40–44 years (8.0% and 6.4%) (Table 6; percentages presented in the table are column percentages, and those presented here and below are row percentages). In addition, a relatively high proportion of youth aged 15–19 years had temporary housing in 2022 (7.9%).

Retention in Care and Viral Suppression Highlights

Retention in HIV Medical Care

HRSA HAB calculates retention in care among RWHAP patients with HIV who had at least one OAHS visit by September 1 of the measurement calendar year; patients are considered retained in care if they had a second visit at least 90 days after.

Retention in care remained relatively stable at approximately 80% year-to-year during 2018 through 2022. In 2022, 77.5% of 352,115 OAHS patients were retained in HIV care (Table 9), a slight decrease (0.8 percentage points) compared to 2021. These data do not delineate the factors contributing to this decrease, and similar minor fluctuations occurred in years prior.

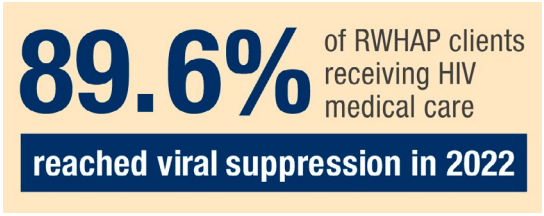
Across subpopulations, retention in care was generally consistent with the overall average (Table 9). However, a few subpopulations had lower retention in care percentages (lower than the national RWHAP average of 77.5% by at least 5 percentage points): patients in each 5-year age group aged 25–34 years (71.1% and 71.9%, respectively), patients with a race/ethnicity of Native Hawaiian/Pacific Islander (70.1%), transgender male patients (70.6%), patients with another gender identity (61.5%), patients with Veterans Administration (72.5%) or Indian Health Service (63.8%) health care coverage, and patients with unstable housing (71.8%).

When examining retention in care among subpopulations from 2018 through 2022, the percentage of patients retained in care by 5-year age groups forms a reverse bell curve, with older and younger populations more likely to be retained and the lowest percentage occurring among those aged 25–29 years.

Viral Suppression

Viral suppression was calculated among people with HIV who had at least one OAHS visit and at least one viral load test during the measurement calendar year. Viral suppression was defined as a most recent viral load test result of <200 copies/mL.

Nearly 90% of RWHAP OAHS patients reached viral suppression in 2022. In 2022, 89.6% of 367,846 OAHS patients had a suppressed viral load at their most recent test (Table 10). From 2018 through 2022, viral suppression increased nearly 3 percentage points, from 87.1% in 2018 to 89.6% in 2022.



Young people aged 15−24 years made great progress improving viral suppression from 2018 through 2022. In 2022, viral suppression was 83.6% among patients aged 15–19 years and 83.7% among those aged 20–24 years (Table 10). Although these percentages are the lowest by age group, they reflect approximately 7 percentage point increases each for these groups from 2018 through 2022.

The percentage of transgender women (aged >13 years) reaching viral suppression continues to increase. In 2022, 86.0% of transgender women reached viral suppression, which reflects a 4.9 percentage point increase from 2018 (81.1%; Table 10).

Viral suppression improved for OAHS patients with unstable housing. In 2022, 77.9% of patients with unstable housing reached viral suppression, compared with 72.4% in 2018 (Table 10). There were also small gains in viral suppression from 2018 through 2022 for patients with temporary housing (from 80.7% to 84.1%) and for patients with stable housing (from 88.4% to 90.6%). Patients with unstable and temporary housing continue to have disparately lower levels of viral suppression than those with stable housing.

Retention in Care and Viral Suppression Among Priority Populations

This section reviews overall retention in care and viral suppression in 2022 for each priority population and highlights the subpopulations with the lowest percentages. Generally, this includes subpopulations with outcomes at least 5 percentage points lower than that of the overall priority population. Data for subpopulations with less than 100 patients are not included in the highlights because of the variability in percentages resulting from small numbers.

Black/African American women (Tables 11a/b): Overall, the percentages of Black/African American women retained in care (79.0%) and virally suppressed (89.1%) were relatively consistent with the national RWHAP averages (77.5% and 89.6%, respectively).

Among Black/African American women, retention in care was lowest among those aged 25–29 and 30–34 years (72.4% and 72.4%, respectively), those with unstable housing (73.0%), and those in HHS Regions 5 and 8 (71.9% and 71.0%, respectively; see Technical Notes for states and territories included in each region).

Viral suppression among Black/African American women was lowest among those in each 5-year age group from 15 to 39 years (range: 79.9%–84.1%), those with perinatal HIV (77.1%), and those with unstable housing (77.5%). In most subpopulations of women, viral suppression was lower among Black/African American women than among women overall in that subpopulation.

Black/African American men (Tables 12a/c): The overall percentage of Black/African American men who were retained in care (75.3%) was relatively consistent with the national RWHAP average (77.5%) and the average among all men (76.8%). The percentage of those who achieved viral suppression (86.2%) was lower than the RWHAP average (89.6%) and the average among men overall (89.6%).

Retention in care was lowest among those aged 25–29 years (69.3%); those with health care coverage though the Veterans Administration (66.7%); those with unstable housing (66.5%); and those in HHS Regions 5, 7, and 10 (68.7%, 70.0%, and 69.6%, respectively).

Viral suppression was lowest among Black/African American men aged 25–29 years (81.1%), those with perinatal HIV (77.2%), those with no health care coverage (79.6%), and those with temporary (80.1%) or unstable (74.2%) housing.

The proportions of Black/African American men who were virally suppressed (86.2%) were lower than those of Hispanic/Latino (91.3%) and White men (92.9%). This gap was the widest among those aged 25–39 years, those with perinatal HIV or male-to-male sexual contact transmission categories; those living at or below 100% FPL; those with Medicaid, other plan, and no health care coverage; and those with temporary housing.

Hispanic/Latina women (Tables 11a/b): Overall, larger percentages of Hispanic/Latina women were retained in care (84.5%) and virally suppressed (91.6%) than the national RWHAP averages (77.5% and 89.6%, respectively).

Among Hispanic/Latina women, retention in care was lowest among each 5-year age group from 20–39 years (range: 76.4%–79.5%); those living at greater than 400% FPL (74.5%); those with temporary housing (79.3%); and those in HHS Regions 7 and 10 (75.8% and 76.1%, respectively).

The lowest percentages of viral suppression were among Hispanic/Latina women aged 20–24 (83.3%), 25–29 (82.3%), and 35–39 (85.6%) years; those with perinatal HIV (78.5%); and those with unstable housing (85.1%).

Hispanic/Latino men (Tables 12a/c): Overall, retention in care (80.5%) and viral suppression (91.3%) among Hispanic/Latino men were higher than the national RWHAP averages (77.5% and 89.6%, respectively).

Retention in care was lowest among Hispanic/Latino men in each 5-year age group from 20 to 34 years (range: 74.3%–75.1%); those with temporary housing (75.3%); and those in HHS Regions 5 and 10 (73.9% and 73.2%, respectively).

Viral suppression was lowest among Hispanic/Latino men aged 15–19 and 20–24 years (82.8% and 85.8%, respectively), those with perinatal HIV (83.4%), and those with unstable housing (83.7%).

Gay, bisexual, and other men who have sex with men (Tables 12b/d): Overall, retention in care (76.9%) and viral suppression (90.2%) for males with HIV attributed to male-to-male sexual contact (i.e., gay, bisexual, and other men who have sex with men) were relatively consistent with the national

RWHAP averages (77.5% and 89.6%, respectively). It is important to note that data presented for gay, bisexual, and other men who have sex with men are based on the reported risk factor most likely to have been responsible for the original transmission of HIV (i.e., male-to-male sexual contact).

Retention in care among gay, bisexual, and other men who have sex with men by race/ethnicity was lowest among American Indian/Alaska Native patients (72.3%), Black/African American patients (74.5%), and Native Hawaiian/Pacific Islander patients (71.6%).

The lowest percentage of viral suppression among gay, bisexual, and other men who have sex with men by race/ethnicity was among Black/African American patients (85.7%), particularly among those aged 15–19 years (80.6%), those with no health care coverage (78.9%), and those with temporary (79.3%) or unstable (73.6%) housing. Viral suppression also was lower than the overall average among American Indian/Alaska Native patients aged 30–34 years (85.0%) and those with no health care coverage (83.2%). Among all gay, bisexual, and other men who have sex with men, regardless of race/ethnicity, viral suppression was consistently lowest among those with temporary (84.6%) or unstable (79.7%) housing.

Transgender adults and adolescents (Tables 13a/b): Overall, retention in care (73.5%) and viral suppression (86.4%) for transgender adults and adolescents were lower than the national RWHAP averages (77.5% and 89.6%, respectively).

Among transgender patients, retention in care was lowest among those with HIV attributed at diagnosis to sexual contact and injection drug use (64.9%), those with private employer health care coverage (68.1%), those with temporary (68.3%) or unstable (67.5%) housing, and those in HHS Regions 5 and 8 (67.3% and 46.0%, respectively).

Viral suppression was lowest among patients with unstable housing (73.6%). Generally, Black/African American transgender patients had lower percentages of viral suppression (overall 83.3%) across demographic subgroups than Hispanic/Latino (88.4%) and White (91.8%) transgender patients.

Given the low numbers within the various subpopulations for transgender people, caution should be used in interpreting the percentages in Tables 13a/b.

Older adults aged 50 years and older (14a/b): Overall, retention in care (81.1%) and viral suppression (92.9%) for older adults with HIV were higher than the national RWHAP averages (77.5% and 89.6%, respectively).

Retention in care among older adults by race/ethnicity was lowest among American Indian/Alaska Native patients (77.6%), Native Hawaiian/Pacific Islander patients (72.7%), and White patients (78.6%). Regardless of race/ethnicity, retention in care was lowest among those with health care coverage through the Veterans Administration (74.8%) and those with temporary (77.0%) or unstable (76.2%) housing.

Viral suppression was lower among transgender older adults with HIV attributed to sexual contact and injection drug use (88.1%), compared to older adults overall. In addition, viral suppression was lower among older adults with temporary (88.0%) or unstable (82.1%) housing, particularly for Black/African American older adults (86.2% and 79.5%, respectively), and was low among White older adults with unstable housing (81.1%).

Given the low numbers within various subpopulations for older adults, caution should be used in interpreting the percentages in Tables 14a/b.

Youth aged 13–24 years (Tables 15a/b): Among youth overall, retention in care (74.6%) and viral suppression (83.8%) were lower than the national RWHAP averages (77.5% and 89.6%, respectively).

The lowest percentages of retention in care were among transgender youth (68.5%), transgender youth with HIV attributed at diagnosis to sexual contact (69.9%), and youth with unstable housing (69.1%).

Viral suppression was lowest among transgender youth (81.0%), transgender youth with HIV attributed at diagnosis to sexual contact (79.7%), and youth with unstable housing (75.3%).

Given the low numbers within the various subpopulations for youth, caution should be used in interpreting the percentages in Tables 15a/b.

Young Black/African American gay, bisexual, and other men who have sex with men, aged 13–24 years (Tables 16a/b): Overall, retention in care for young Black/African American gay, bisexual, and other men who have sex with men (73.3%) was lower than the national RWHAP average (77.5%), but consistent with the average for young gay, bisexual, and other men who have sex with men overall (74.2%). Viral suppression for young Black/African American gay, bisexual, and other men who have sex with men (83.0%) was lower than the national RWHAP average (89.6%) by a considerable difference of 6.6 percentage points, but slightly lower than the average for young gay, bisexual, and other men who have sex with men overall (84.8%).

For young Black/African American gay, bisexual, and other men who have sex with men, the lowest percentage of retention in care was among those with unstable housing (61.6%), and viral suppression was lowest among those with no health care coverage (77.4%) or unstable housing (77.0%).

Young Black/African American gay, bisexual, and other men who have sex with men living at or below 100% FPL had notably lower viral suppression compared with other racial/ethnic groups. Specifically, viral suppression among young Black/African American gay, bisexual, and other men who have sex with men living at or below 100% FPL (81.2%) was 3.6 percentage points lower than that among young Hispanic/Latino gay, bisexual, and other men who have sex with men (84.8%) and 8.7 percentage points lower than that among young White gay, bisexual, and other men who have sex with men (89.9%).

Given the low numbers within the various subpopulations of young gay, bisexual, and other men who have sex with men and young Black/African American gay, bisexual, and other men who have sex with men, caution should be used in interpreting the percentages in Tables 16a/b.

Young Black/African American women, aged 13–24 years (Tables 17a/b): Overall, retention in care for young Black/African American women (79.4%) was consistent with the national RWHAP average (77.5%) and slightly higher than the average for young women overall (78.9%). Viral suppression for young Black/African American women (81.8%) was considerably lower than the national RWHAP average (89.6%) and lower than the average for young women overall (82.8%).

Given the low numbers within the various subpopulations of young women and young Black/African American women, caution should be used in interpreting the percentages in Tables 17a/b.

Patients with HIV attributed at diagnosis to injection drug use (Tables 18a/b): Overall, for patients with HIV attributed at diagnosis to injection drug use, retention in care (77.4%) and viral suppression (88.5%) were consistent with the national RWHAP averages (77.5% and 89.6%, respectively).

Among all patients with HIV attributed at diagnosis to injection drug use, retention in care was lower among patients in each 5-year age group from 20 to 44 years (range: 54.7%–69.6%), those with “other plan” health care coverage (70.2%) or no health care coverage (68.7%), and those with temporary (69.5%) or unstable (64.0%) housing. By race/ethnicity, retention in care was lowest among White patients (72.4%) and American Indian/Alaska Native patients (71.6%).

Viral suppression was lower than the overall average for patients with HIV attributed at diagnosis to injection drug use (88.5%) among American Indian/Alaska Native (82.6%) and White patients (86.7%). Regardless of race/ethnicity, low viral suppression was seen among patients in each 5-year age group from 20 to 49 years (range: 75.0%–82.9%), those with no health care coverage (80.0%), and those with temporary (82.0%) or unstable (73.1%) housing. By race/ethnicity, patients with temporary or unstable housing had lower viral suppression than patients in that population overall. Viral suppression for those with temporary housing was 81.0% among White patients, 82.6% among Black/African American patients, and 83.1% among Hispanic/Latino patients; viral suppression among those with unstable housing was 70.5% among White patients, 76.4% among Black/African American patients, and 74.5% among Hispanic/Latino patients.

Data for patients with HIV attributed at diagnosis to injection drug use are based on patients who reported “injection drug use” as their transmission category at diagnosis and may not reflect current behavior.

Housing status (Tables 19a/b): Among RWHAP patients, those with temporary or unstable housing consistently have lower retention in care and viral suppression than those with stable housing.

Overall, retention in care was higher among patients with stable housing (78.4%) than among those with temporary (72.6%) or unstable (71.8%) housing. Among patients with temporary housing, retention in care was lowest among patients aged 25–29 years (66.8%) and 30–34 years (67.6%), male patients with HIV attributed at diagnosis to male-to-male sexual contact and injection drug use (66.9%), and male patients with HIV attributed at diagnosis to perinatal transmission (68.8%). Among patients with unstable housing, retention in care was lowest among patients aged 25–29 years (63.4%), patients of multiple races (63.4%), and male and female patients with HIV attributed at diagnosis to injection drug use (62.6% and 66.6%, respectively).

Overall, the highest percentage of viral suppression was among patients with stable housing (90.6%), while percentages among patients with temporary (84.1%) or unstable (77.9%) housing were substantially lower. Among patients with temporary housing, viral suppression was lowest among male and female patients with perinatal HIV (70.5% and 76.4%, respectively). Among patients with unstable housing, viral suppression was lowest among patients aged 25–29 years (72.2%), patients of multiple races (72.8%), and male patients with HIV attributed at diagnosis to injection drug use (72.9%).

Across all genders, a substantially greater proportion of patients with stable housing reached viral suppression compared with those who had temporary or unstable housing. For example, viral suppression among transgender females with stable housing (87.7%) was 5.9 percentage points higher than that among transgender females with temporary housing (81.8%) and 14.3 percentage points higher than that among those with unstable housing (73.4%). There were similar percentage point differences for male and female patients.

TECHNICAL NOTES

Ryan White HIV/AIDS Program Data

The Ryan White HIV/AIDS Program (RWHAP) Services Report (RSR) is the U.S. Department of Health and Human Services (HHS), Health Resources and Services Administration (HRSA), HIV/AIDS Bureau's (HAB) primary source of annual, client-level data reported by more than 2,000 grant recipients and subrecipients. These data allow HRSA HAB and its stakeholders to assess the numbers and demographics of clients receiving services, understand client HIV-related outcomes, and identify and address HIV-related disparities. Client-level RSR data have been used since 2010. Each year, HRSA HAB requires grant recipients and subrecipients that use RWHAP funds to provide core medical or support services during the reporting period to submit data in a specified format [10].

This report includes data reported to the RSR for all clients served by the RWHAP Parts A through D during calendar years 2018 through 2022. Beginning with the 2016 calendar year data collection period, recipients and subrecipients reported data for all clients who met the recipient's eligibility requirements for RWHAP participation (which varies by recipient and is based on such criteria as HIV status, income, and residency) and received at least one of the core medical or support services for which the recipient or subrecipient received RWHAP funding. The data are reported regardless of the actual funding used to pay for the services (i.e., some services may have been paid for by sources other than the RWHAP). Because more recipients have been moving toward funding services with RWHAP-related funding (i.e., program income; pharmaceutical rebates), beginning with the 2019 data, HRSA HAB encourages recipients and subrecipients to include RSR data on clients receiving services provided using RWHAP-related funding; this became a reporting requirement for all RWHAP recipients and subrecipients beginning with the 2021 data submission. This reporting requirement did not replace the previous eligible scope reporting requirement, but rather expanded on the previous requirement.

In addition to the expanded scope of reporting clients served using RWHAP-related funds, recent RSR data include information for people with HIV receiving RWHAP fiscal year 2020 Coronavirus Aid, Relief, and Economic Security (CARES) Act–funded services (2020 and 2021) and HAB *Ending the HIV Epidemic in the U.S. (EHE)* initiative–funded services (2020–2022).

RSR data do not include information about the AIDS Drug Assistance Program (ADAP), which is reported through another data system. Although data presented in this report are "non-ADAP," many clients included in the RSR data also receive ADAP services.

After removing personally identifying information, recipients and subrecipients submit data to HRSA HAB. Data are reported by RWHAP grant recipients and subrecipients in 50 states, the District of Columbia, and three territories—Guam, Puerto Rico, and the U.S. Virgin Islands. Of the six U.S. Pacific territories, only Guam submits client-level data; only Guam, therefore, is included in this report.

Presentation of Data

The data in this report include information received by HRSA HAB for clients served during calendar years 2018 through 2022. Data are organized into four sections:

- Section 1 (Tables 1–8): National-level numbers and percentages of clients served by the RWHAP (non-ADAP), presented by selected demographics.

- Section 2 (Tables 9–19b): National-level retention in care and viral suppression among patients receiving outpatient ambulatory health services (OAHS), presented by selected demographics and priority populations.
- Section 3 (Tables 20a–26b): State- and Eligible Metropolitan Area or Transitional Grant Area (EMA/TGA)–level numbers and percentages of clients served by the RWHAP (non-ADAP), presented by selected demographics.
- Section 4 (Tables 27a–36b): State- and EMA/TGA-level retention in care and viral suppression among patients receiving OAHS, presented by selected demographics.

Tables 1–3 and 5–8 display subtotals for each subpopulation, as well as the overall total. Subtotals are displayed to reflect the denominator used for the percentage calculation of each subpopulation. Because of missing data, the values in each column may not sum to the column total.

HIV Status

RSR data include de-identified client-level information about people who received services from RWHAP-funded providers. RWHAP clients include people with HIV, as well as people who are affected by HIV (e.g., families and partners of people with HIV served by the RWHAP). Families of people with HIV can receive certain services through RWHAP Part D. The data presented in Table 1a, Tables 2 through 8, and Tables 20a through 26b include all RWHAP clients, regardless of HIV status. Table 1b and tables displaying retention in care and viral suppression (Tables 9 through 19b and Tables 27a through 36b) include only people with HIV.

Presumed HIV-positive status

Table 1b displays demographic data only about clients with HIV; however, many clients receive services that do not require HIV status to be reported (e.g., Medical Transportation) and, therefore, may be missing HIV status information. HRSA HAB applied an algorithm to estimate a “presumed HIV positive” status for Table 1b. That is, only six RWHAP-funded service categories are available to clients without HIV (i.e., Child Care Services, Early Intervention Services, Food Bank/Home-Delivered Meals, Other Professional Services, Outreach Services, and Psychosocial Support Services) [11]. Clients aged 13 years and older who received only one or a combination of these six services, without receiving another service available to only people with HIV, were presumed to be HIV negative. All other clients (aged 13 years and older) were presumed to have HIV and were included in Table 1b. Clients younger than 13 years were not included in the algorithm because of an inconsistency in data reporting between 2014 and later years; however, testing the algorithm for 2017 and 2018 for the <13 age group produced effectively no difference from the number of clients with a reported HIV status. Therefore, the HIV status variable was used for clients aged <13 years across all years.

Age Group

RWHAP grant recipients and subrecipients report client birth year, which is used to calculate the client’s age during the designated year as a discrete variable. For tables displaying age groups (Tables 1a–14b and 18a–19b), client ages were categorized to align with the Centers for Disease Control and Prevention (CDC) National HIV Surveillance System (NHSS) age group delineations: <13 years (if applicable), 13–14, 15–19, 20–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64, and ≥65 years [1].

In Tables 21a/b (state and EMA/TGA by age group), data are displayed using broader age group delineations: <13 years, 13–24, 25–34, 35–44, 45–54, 55–64, and ≥65 years.

Tables displaying retention in care and viral suppression for priority populations (Tables 11a–19b) include only clients aged 13 years and older. Tables 14a–14b focus on older adults (aged 50 years and older), and Tables 15a–17b focus on youth and young adults aged 13–24 years.

Race/Ethnicity

Recipients and subrecipients report race/ethnicity information for RWHAP clients according to Office of Management and Budget (OMB) standards [12]. The OMB standards have five categories for race: American Indian or Alaska Native; Asian; Black or African American; Native Hawaiian or Other Pacific Islander; and White. The data on ethnicity have two categories: (1) Hispanic or Latino and (2) not Hispanic or Latino. Race and ethnicity are submitted as separate variables and combined for analysis.

The race/ethnicity variable is categorized as American Indian or Alaska Native, Asian, Black or African American, Hispanic or Latino, Native Hawaiian or other Pacific Islander, White, and multiple races (two or more categories of race reported).

In this report, clients categorized as Hispanic/Latino may have had race reported as well. Clients categorized by race (e.g., Black/African American) are non-Hispanic/Latino; however, the number of clients reported in each “non-Hispanic/Latino” race category may include clients with missing data for Hispanic/Latino ethnicity.

HRSA HAB expects RWHAP grant recipients and subrecipients to make every effort to obtain and report race and ethnicity based on each client’s self-report. Self-identification is the preferred means of obtaining this information.

Gender

Gender designations in this report are cisgender (non-transgender) male, cisgender female, or transgender. Transgender is a term for people whose gender identity and/or expression is different from their sex assigned at birth. Because of the unique health needs of transgender people with HIV, they are discussed separately from cisgender people and are specifically identified as being transgender. HRSA HAB collaborated with the transgender community and other experts in sexual orientation and gender identity data collection methods to successfully designate transgender people receiving HIV care and treatment from RWHAP providers, to best inform program decisions.

Reporting and analysis to determine transgender identity

Transgender variable options for RSR data reporting include transgender female-to-male, transgender male-to-female, or transgender other, which includes people who do not identify with the provided transgender variable options and/or who do not identify with the binary options of male/female (e.g., nonbinary, two-spirit, genderqueer). Self-identification is the preferred means of obtaining this information.

During the period 2010 through 2013, RSR variables for gender included *current gender,* with the options of male, female, and transgender, and a subsequent variable for *transgender identity* (this variable captured transgender female-to-male, transgender male-to-female, and transgender unknown). In 2014, HRSA HAB began requiring recipients and subrecipients report gender using a multistep method: *sex assigned at birth (*male or female) was added, and the *current gender* variable was replaced with *current gender identity* (male, female, transgender); the *transgender identity* variable remained intact. Beginning with 2017 reporting, HRSA HAB further refined the *current gender identity* variable to include the options of male, female, transgender female-to-male, transgender male-to-female, and transgender other (previously *transgender unknown*); the transgender identity variable was removed, thus creating a two-step method for reporting and determining gender (i.e., sex assigned at birth and current gender identity).

Gender data in this report use the two-step method (i.e., the 2017 method); when the reported *current gender identity* is different from the *sex assigned at birth*, the analysis determines gender using an algorithm designed specifically for this purpose.

Language used in this report

In this report and in the accompanying data tables, for analyses that include clients of all ages, cisgender male clients are referred to as *male*, cisgender female clients as *female*, transgender female-to-male clients as *transgender male*, and transgender male-to-female clients as *transgender female*. For analyses that include only clients aged 13 years and older, clients are referred to as *men, women, transgender men,* and *transgender women,* respectively.

Clients designated under the *transgender other* variable option are referred throughout as *clients with another gender identity,* or in the data tables as *other gender identity.*

Transmission Category

Transmission category is the term for the classification that summarizes a client's possible HIV risk factor(s) at the time of HIV acquisition; the summary classification results from selecting—from a presumed hierarchical order of probability—the single risk factor most likely to have been responsible for transmission.

It is important to note that data by transmission category presented in this report are based on the reported risk factor *most likely to have been responsible for the original transmission of HIV;* data may not reflect current behavior (e.g., injection drug use).

For tables displaying data for all clients served by the RWHAP (Table 1a, Tables 2 through 8, and Tables 20a through 26b), transmission category data include clients with known positive HIV status and those who have unknown HIV status (e.g., children with indeterminate status and clients with transmission category information but missing HIV status data).

Transmission categories are presented separately by gender (i.e., male, female, transgender).

- For male clients, transmission categories include male-to-male sexual contact, injection drug use, male-to-male sexual contact *and* injection drug use, heterosexual contact, perinatal, and other.
- For female clients, transmission categories include heterosexual contact, injection drug use, perinatal, and other.
- For transgender clients, transmission categories have been modified to better reflect the transgender experience of transmission risk while continuing to follow a relative hierarchy of likelihood for transmission. That is, transmission category data for transgender clients are presented as sexual contact, injection drug use, sexual contact *and* injection drug use, perinatal, and other.

HRSA HAB adapted the definitions of transmission risk categories from the CDC's NHSS definitions for transmission categories [1]. Clients with more than one reported risk factor are classified in the transmission category listed first in the hierarchy. The only exceptions are (1) men who had sexual contact with other men and who injected drugs and (2) perinatal; these groups make up separate transmission categories. The transmission categories are defined, in order of the hierarchy, as follows:

- *Male-to-male sexual contact:* Male clients who report sexual contact with other men and males who report sexual contact with both men and women.

- *Injection drug use:* Clients who report use of drugs intravenously or through skin popping.
- *Male-to-male sexual contact and injection drug use:* Male clients who report sexual contact with other men or sexual contact with both men and women *and* report the use of drugs intravenously or through skin popping.
- *Heterosexual contact:* Clients who report specific heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
- *Perinatal:* This category is exclusively for clients with perinatally acquired HIV. This category includes clients born after 1980 who are known to have HIV and whose HIV is attributed to perinatal transmission at diagnosis, as well as infants with indeterminate HIV status.
- *Other:* Clients who report transmission from the receipt of transfusion of blood, blood components, or tissue and clients who report hemophilia/coagulation disorder. Beginning with 2014 data collection, unknown risk factor was no longer included in the classification of *other* transmission risk, nor was it collected as a separate category for the RSR. All analyses in this report include only blood transfusion or hemophilia/coagulation disorder in the *other* transmission category.

For transgender clients, the following transmission category hierarchy is used:

- *Sexual contact:* Transgender clients who report any sexual transmission risk.
- Injection drug use: Transgender clients who report use of drugs intravenously or through skin popping.
- *Sexual contact and injection drug use:* Transgender clients who report sexual contact *and* report the use of drugs intravenously or through skin popping.
- *Perinatal:* As above.
- *Other:* As above.

Tables 12b/d and 16a/b display retention in care and viral suppression among gay, bisexual, and other men who have sex with men aged 13 years and older and among young gay, bisexual, and other men who have sex with men aged 13–24 years, respectively. These tables include only those clients with infection attributed at diagnosis to male-to-male sexual contact and exclude male-to-male sexual contact *and* injection drug use. Tables 18a and 18b display retention in care and viral suppression among people with HIV attributed at diagnosis to injection drug use, respectively. These tables include only those clients whose reported transmission category is injection drug use; male clients with male-to-male sexual contact *and* injection drug use and transgender clients with sexual contact *and* injection drug use as their transmission category are not included.

Federal Poverty Level

Federal poverty level (FPL) characterizes the client's income as a percentage of the FPL [13] at the end of the reporting period. In this report, FPL categories are 0–100% FPL, 101–138% FPL, 139–250% FPL, 251–400% FPL, and >400% FPL.

Health Care Coverage

RWHAP grant recipients and subrecipients report all sources of health care coverage that each client had for any part of the reporting period. These data are categorized further for analysis. Health care coverage was categorized as private employer, private individual, Medicare, Medicaid, Medicare and

Medicaid (dual eligibility), Veterans Administration, Indian Health Service, other plan, no coverage, and multiple coverages. The Medicaid classification also includes the Children's Health Insurance Program (CHIP) and other public state health care coverage programs.

Housing Status

The housing status variable captures the client's housing status at the end of the reporting period and is categorized as stable (e.g., permanent) housing, temporary housing, or unstable housing. The definitions for each of these categories are based on the Housing Opportunities for Persons with AIDS Program Annual Progress Report Measuring Performance Outcomes: form HUD-40110C and the McKinney-Vento Act, Title 42 US Code, Sec. 11302, General definition of homeless individual [14,15].

Region

HHS uses 10 geographic designations for classifying regions of the United States, which encompass all states and territories. The classification of states and territories within these regions is as follows:

- **Region 1:** Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont
- **Region 2:** New Jersey, New York, Puerto Rico, U.S. Virgin Islands
- **Region 3:** Delaware, District of Columbia, Maryland, Pennsylvania, Virginia, West Virginia
- **Region 4:** Alabama, Florida, Georgia, Kentucky, Mississippi, North Carolina, South Carolina, Tennessee
- **Region 5:** Illinois, Indiana, Michigan, Minnesota, Ohio, Wisconsin
- **Region 6:** Arkansas, Louisiana, New Mexico, Oklahoma, Texas
- **Region 7:** Iowa, Kansas, Missouri, Nebraska
- **Region 8:** Colorado, Montana, North Dakota, South Dakota, Utah, Wyoming
- **Region 9:** Arizona, California, Guam, Hawaii, Nevada
- **Region 10:** Alaska, Idaho, Oregon, Washington

The six U.S. Pacific territories are included in HHS Region 9. However, only Guam submits client-level data; only Guam, therefore, is included in this report.

It is important to note that the COVID-19 pandemic emerged during the 2019 RSR data submission period and continued through the 2021 period, shifting the priorities for RWHAP recipients and subrecipients. Because of these challenges, the U.S. territory of Guam was unable to submit data by the deadline needed for data processing in 2019 and 2020. Therefore, the 2019 and 2020 data do not include Guam's data; in addition, these data are not shown for state/territory-specific tables that show these data years (i.e., Tables 20a, 27a, and 28a).

State

State data are displayed in "a" tables from 20a through 36a. State-level delineation of data is based on provider location rather than client location. Clients receiving services in multiple states are not included in state-specific totals; these clients make up less than 2% of the total RWHAP population.

In addition, state-level analyses include data submitted for all Parts of the RWHAP. That is, data presented by state are not limited to entities receiving RWHAP Part B funding; all tables include data for all clients served by RWHAP providers in the state, regardless of the source of RWHAP funding (i.e., data from Parts A, B, C, and D are included).

Eligible Metropolitan Areas (EMAs) and Transitional Grant Areas (TGAs)

Part A of the RWHAP provides emergency assistance to EMAs and TGAs that are most severely affected by the HIV epidemic. To qualify for EMA status, an area must have reported at least 2,000 Stage 3 HIV (AIDS) cases in the most recent five years and have a population of at least 50,000. To be eligible for TGA status, an area must have reported 1,000–1,999 AIDS cases in the most recent five years and have a population of at least 50,000.

EMAs and TGAs range in size from one city or county to more than 26 different geographic entities; 11 include parts of more than one state.

The boundaries of EMAs and TGAs are based on the U.S. Census Bureau delineation of the metropolitan statistical area at the time of first eligibility. Client-level data are reported based on provider location, rather than client location.

EMA and TGA data are displayed in “b” tables from 20b through 36b. It is important to note that data shown for EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and TGAs. In addition, data presented for EMAs and TGAs are not limited to entities receiving RWHAP Part A funding; all tables include data for all clients served by RWHAP providers in the EMA or TGA, regardless of the source of RWHAP funding (i.e., Parts A, B, C, and D data are included).

Tables 22b, 31b, and 32b display EMA and TGA data by race/ethnicity. To protect the confidentiality of clients, values less than five (5) were suppressed. In addition, to ensure values less than 5 cannot be calculated, all data on clients of multiple races have been suppressed. In Table 22b, the “Total” column on which percentages were based includes all clients with reported race/ethnicity information.

Similarly, Table 23b displays data by gender. To protect the confidentiality of clients, values less than 5 were suppressed and all data on clients whose gender is “other gender identity” have been suppressed. The Total column on which percentages were based includes all clients with reported gender information.

Retention in Care and Viral Suppression

Retention in HIV medical care was defined as people with HIV having at least two medical visits that were at least 90 days apart in the measurement year. Because the data sets are restricted to one calendar year of data each, the first of these HIV medical care visits in the year must have occurred before September 1 of the measurement year, thus giving the client an opportunity to meet the retention criteria by December 31.

Viral suppression was based on data for people with HIV who had at least one OAHS visit and at least one viral load test during the measurement year. Viral suppression was defined as the most recently reported HIV RNA test result of <200 copies/mL.

Priority Populations

Although anyone can have HIV, all people and communities are not impacted equally. HRSA HAB has enhanced its efforts to focus on communities where HIV is most concentrated. These priority populations include women; transgender women; gay, bisexual, and other men who have sex with men; Blacks/African Americans; Hispanics/Latinos; adults aged 50 years and older; youth; young

Black/African American gay, bisexual, and other men who have sex with men; young Black/African American women; people with HIV attributed at diagnosis to injection drug use; and people with unstable or temporary housing. Tables 11a through 19b display retention in care (“a” tables) and viral suppression (“b” tables) for these priority populations (except for Tables 12a–d, where retention in care for men and for gay, bisexual, and other men who have sex with men are displayed in the “a” and “b” tables, respectively, and viral suppression in the “c” and “d” tables, respectively).

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Additional Resources

Centers for Disease Control and Prevention, HIV prevention resources: cdc.gov/hiv

Health Resources and Services Administration, HIV/AIDS programs: ryanwhite.hrsa.gov

HIV.gov, the nation’s source for timely and relevant federal HIV policies, programs, and resources: HIV.gov

Ryan White HIV/AIDS Program Compass Dashboard, a user-friendly, interactive data tool to visualize the reach, impact, and outcomes of the program: ryanwhite.hrsa.gov/data/dashboard

TargetHIV, tools for the Ryan White HIV/AIDS Program Community: targethiv.org

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Section 1.

National-Level Data: Client Characteristics

Table 1a. Ryan White HIV/AIDS Program clients (non-ADAP), by year and selected characteristics, 2018–2022—United States and 3 territories

	2018		2019		2020		2021		2022	
	N	%	N	%	N	%	N	%	N	%
Age group (yrs)										
<13	4,303	0.8	3,617	0.6	3,423	0.6	3,284	0.6	3,107	0.5
13–14	611	0.1	507	0.1	456	0.1	371	0.1	345	0.1
15–19	3,282	0.6	3,147	0.6	2,651	0.5	2,499	0.4	2,414	0.4
20–24	18,085	3.4	18,441	3.2	16,593	3.0	16,401	2.8	15,635	2.8
25–29	44,378	8.3	45,932	8.1	42,270	7.5	41,333	7.2	39,269	6.9
30–34	51,045	9.6	57,715	10.2	59,373	10.6	62,683	10.9	63,049	11.1
35–39	51,949	9.7	55,768	9.8	55,139	9.8	58,224	10.1	59,275	10.5
40–44	51,175	9.6	54,577	9.6	54,979	9.8	57,550	10.0	57,004	10.1
45–49	62,809	11.8	62,480	11.0	57,580	10.3	55,581	9.6	53,381	9.4
50–54	79,932	15.0	79,293	14.0	74,823	13.3	71,865	12.5	65,782	11.6
55–59	75,839	14.2	82,416	14.5	82,127	14.6	82,483	14.3	77,683	13.7
60–64	49,854	9.3	55,743	9.8	58,780	10.5	63,152	11.0	64,357	11.4
≥65	40,378	7.6	48,167	8.5	53,222	9.5	60,650	10.5	65,545	11.6
Subtotal	**533,640**	**100.0**	**567,803**	**100.0**	**561,416**	**100.0**	**576,076**	**100.0**	**566,846**	**100.0**
Race/ethnicity										
American Indian/Alaska Native	2,681	0.5	3,070	0.5	2,796	0.5	3,107	0.5	3,729	0.7
Asian	7,592	1.4	8,259	1.5	8,195	1.5	8,788	1.5	9,591	1.7
Black/African American	249,832	47.1	261,734	46.6	258,186	46.6	260,682	45.8	248,574	44.5
Hispanic/Latino[a]	122,848	23.2	131,225	23.3	131,033	23.6	137,112	24.1	141,214	25.3
Native Hawaiian/Pacific Islander	924	0.2	1,058	0.2	1,074	0.2	1,159	0.2	1,111	0.2
White	139,667	26.3	149,804	26.6	146,648	26.4	151,902	26.7	143,711	25.8
Multiple races	6,882	1.3	6,968	1.2	6,618	1.2	6,852	1.2	10,117	1.8
Subtotal	**530,426**	**100.0**	**562,118**	**100.0**	**554,550**	**100.0**	**569,602**	**100.0**	**558,047**	**100.0**
Gender										
Male	382,052	71.6	406,312	71.6	404,079	72.0	415,486	72.2	407,765	72.1
Female	141,363	26.5	148,452	26.2	145,441	25.9	146,177	25.4	142,469	25.2
Transgender male	981	0.2	1,676	0.3	1,011	0.2	1,422	0.2	1,562	0.3
Transgender female	8,974	1.7	10,712	1.9	10,174	1.8	11,594	2.0	12,787	2.3
Other gender identity	223	<0.1	400	0.1	424	0.1	982	0.2	1,214	0.2
Subtotal	**533,593**	**100.0**	**567,552**	**100.0**	**561,129**	**100.0**	**575,661**	**100.0**	**565,797**	**100.0**
Transmission category										
Male client										
Male-to-male sexual contact	225,540	65.7	232,029	65.7	234,809	66.7	236,920	67.4	237,281	67.9
Injection drug use	19,823	5.8	19,845	5.6	19,105	5.4	18,415	5.2	17,170	4.9
Male-to-male sexual contact and injection drug use	11,059	3.2	11,138	3.2	11,055	3.1	10,942	3.1	10,920	3.1
Heterosexual contact[b]	80,948	23.6	83,664	23.7	81,038	23.0	78,988	22.5	78,351	22.4
Perinatal	4,205	1.2	4,162	1.2	4,150	1.2	4,130	1.2	3,875	1.1
Other[c]	1,968	0.6	2,108	0.6	2,090	0.6	2,064	0.6	2,088	0.6
Subtotal[d]	**343,543**	**100.0**	**352,946**	**100.0**	**352,247**	**100.0**	**351,459**	**100.0**	**349,685**	**100.0**
Female client										
Injection drug use	10,251	8.2	10,364	8.1	10,148	8.1	9,965	8.1	9,417	7.7
Heterosexual contact[b]	107,707	86.5	111,330	86.7	108,929	86.8	107,149	86.6	106,352	87.2
Perinatal	5,232	4.2	5,101	4.0	4,945	3.9	5,049	4.1	4,720	3.9
Other[c]	1,359	1.1	1,540	1.2	1,534	1.2	1,589	1.3	1,464	1.2
Subtotal[d]	**124,549**	**100.0**	**128,335**	**100.0**	**125,556**	**100.0**	**123,752**	**100.0**	**121,953**	**100.0**
Transgender client										
Sexual contact[e]	7,872	92.7	9,925	93.4	8,800	93.2	9,965	93.4	11,085	93.6
Injection drug use	119	1.4	163	1.5	119	1.3	143	1.3	156	1.3
Sexual contact[e] and injection drug use	419	4.9	402	3.8	434	4.6	454	4.3	487	4.1
Perinatal	52	0.6	96	0.9	55	0.6	64	0.6	67	0.6
Other[c]	27	0.3	45	0.4	33	0.3	43	0.4	45	0.4
Subtotal[d]	**8,489**	**100.0**	**10,631**	**100.0**	**9,441**	**100.0**	**10,669**	**100.0**	**11,840**	**100.0**

Table 1a. Ryan White HIV/AIDS Program clients (non-ADAP), by year and selected characteristics, 2018–2022—United States and 3 territories *(cont.)*

	2018		2019		2020		2021		2022	
	N	%	N	%	N	%	N	%	N	%
Federal poverty level										
0–100%	304,082	61.3	316,202	60.7	313,693	60.9	305,817	59.2	304,976	58.6
101–138%	56,982	11.5	58,250	11.2	56,293	10.9	53,206	10.3	54,092	10.4
139–250%	84,533	17.0	91,892	17.6	90,399	17.6	94,247	18.3	93,101	17.9
251–400%	36,179	7.3	42,257	8.1	41,267	8.0	45,856	8.9	49,733	9.6
>400%	14,251	2.9	12,427	2.4	13,107	2.5	17,094	3.3	18,541	3.6
Subtotal	**496,027**	**100.0**	**521,028**	**100.0**	**514,759**	**100.0**	**516,220**	**100.0**	**520,443**	**100.0**
Health care coverage										
Private employer	52,389	10.2	54,163	10.0	53,927	10.1	54,439	10.0	54,775	10.2
Private individual	41,412	8.1	45,888	8.5	50,210	9.4	54,489	10.0	50,734	9.4
Medicare	53,230	10.3	57,880	10.7	56,561	10.6	57,092	10.5	55,575	10.3
Medicaid	162,098	31.5	166,738	30.8	164,343	30.8	171,022	31.5	168,848	31.4
Medicare and Medicaid	40,612	7.9	41,786	7.7	40,144	7.5	40,986	7.5	40,684	7.6
Veterans Administration	1,317	0.3	1,313	0.2	1,180	0.2	1,258	0.2	1,041	0.2
Indian Health Service	201	<0.1	170	<0.1	90	<0.1	231	<0.1	212	<0.1
Other plan	8,146	1.6	9,018	1.7	10,749	2.0	10,812	2.0	11,607	2.2
No coverage	103,350	20.1	110,645	20.4	103,746	19.4	98,307	18.1	97,786	18.2
Multiple coverages	51,548	10.0	54,037	10.0	52,493	9.8	55,066	10.1	55,992	10.4
Subtotal	**514,303**	**100.0**	**541,638**	**100.0**	**533,443**	**100.0**	**543,702**	**100.0**	**537,254**	**100.0**
Housing status										
Stable	436,227	87.0	455,641	87.0	458,508	88.3	465,003	88.4	458,688	87.9
Temporary	38,436	7.7	38,830	7.4	35,678	6.9	34,885	6.6	36,075	6.9
Unstable	26,815	5.3	28,978	5.5	25,177	4.8	26,346	5.0	27,199	5.2
Subtotal	**501,478**	**100.0**	**523,449**	**100.0**	**519,363**	**100.0**	**526,234**	**100.0**	**521,962**	**100.0**
Total[f]	**533,758**	—	**567,803**	—	**561,416**	—	**576,076**	—	**566,846**	—

[a] Hispanics/Latinos can be of any race.
[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[c] Includes hemophilia and blood transfusion.
[d] Subtotals are reflective of available gender and transmission category information. The values may not sum to the subtotals for gender overall.
[e] Includes any sexual transmission category reported by transgender clients.
[f] Subtotals for each subpopulation are displayed to reflect the denominator used for the percentage calculation of each subpopulation; due to missing data, the values in each column may not sum to the column total.

Table 1b. Ryan White HIV/AIDS Program clients with HIV (non-ADAP), by year and selected characteristics, 2018–2022—United States and 3 territories

	2018		2019		2020		2021		2022	
	N	%	N	%	N	%	N	%	N	%
Age group (yrs)										
<13	1,089	0.2	1,000	0.2	869	0.2	779	0.1	726	0.1
13–14	412	0.1	391	0.1	367	0.1	327	0.1	271	<0.1
15–19	2,672	0.5	2,748	0.5	2,371	0.4	2,274	0.4	2,160	0.4
20–24	17,114	3.3	17,682	3.2	16,087	2.9	15,806	2.8	15,086	2.7
25–29	43,040	8.3	45,095	8.1	41,785	7.5	40,436	7.1	38,390	6.9
30–34	49,837	9.6	56,894	10.2	58,898	10.6	61,658	10.9	62,067	11.1
35–39	50,664	9.8	54,894	9.9	54,685	9.9	57,329	10.1	58,470	10.5
40–44	50,153	9.7	53,823	9.7	54,659	9.9	56,841	10.0	56,357	10.1
45–49	61,773	11.9	61,649	11.1	57,206	10.3	55,032	9.7	52,870	9.5
50–54	78,778	15.2	78,229	14.1	74,385	13.4	71,167	12.6	65,213	11.7
55–59	74,593	14.4	81,322	14.6	81,612	14.7	81,765	14.4	77,118	13.8
60–64	49,064	9.5	54,973	9.9	58,355	10.5	62,575	11.1	63,885	11.5
≥65	39,514	7.6	47,328	8.5	52,674	9.5	59,927	10.6	64,781	11.6
Subtotal	**518,703**	**100.0**	**556,028**	**100.0**	**553,953**	**100.0**	**565,916**	**100.0**	**557,394**	**100.0**
Race/ethnicity										
American Indian/Alaska Native	2,604	0.5	3,006	0.5	2,768	0.5	3,048	0.5	3,670	0.7
Asian	7,397	1.4	8,171	1.5	8,104	1.5	8,616	1.5	9,418	1.7
Black/African American	241,210	46.8	256,091	46.4	254,246	46.4	256,792	45.8	244,675	44.5
Hispanic/Latino[a]	120,625	23.4	129,452	23.5	129,771	23.7	135,144	24.1	139,413	25.4
Native Hawaiian/Pacific Islander	891	0.2	1,044	0.2	1,065	0.2	1,140	0.2	1,087	0.2
White	137,170	26.6	147,760	26.8	145,642	26.6	149,377	26.6	141,497	25.7
Multiple races	6,051	1.2	6,060	1.1	6,334	1.2	6,555	1.2	9,812	1.8
Subtotal	**515,948**	**100.0**	**551,584**	**100.0**	**547,930**	**100.0**	**560,672**	**100.0**	**549,572**	**100.0**
Gender										
Male	373,239	72.0	399,634	71.9	399,835	72.2	408,839	72.3	402,270	72.2
Female	135,531	26.1	143,650	25.8	142,408	25.7	142,973	25.3	139,409	25.0
Transgender male	938	0.2	1,639	0.3	981	0.2	1,364	0.2	1,529	0.3
Transgender female	8,750	1.7	10,554	1.9	10,077	1.8	11,463	2.0	12,591	2.3
Other gender identity	186	<0.1	369	0.1	404	0.1	922	0.2	1,183	0.2
Subtotal	**518,644**	**100.0**	**555,846**	**100.0**	**553,705**	**100.0**	**565,561**	**100.0**	**556,982**	**100.0**
Transmission category										
Male client										
Male-to-male sexual contact	225,326	65.8	231,923	65.9	234,797	66.8	236,902	67.6	237,272	68.0
Injection drug use	19,821	5.8	19,836	5.6	19,105	5.4	18,415	5.3	17,167	4.9
Male-to-male sexual contact and injection drug use	11,059	3.2	11,109	3.2	11,054	3.1	10,942	3.1	10,919	3.1
Heterosexual contact[b]	80,915	23.6	83,571	23.7	81,009	23.1	78,974	22.5	78,345	22.5
Perinatal	3,376	1.0	3,383	1.0	3,366	1.0	3,329	0.9	3,118	0.9
Other[c]	1,967	0.6	2,108	0.6	2,090	0.6	2,064	0.6	2,088	0.6
Subtotal[d]	**342,464**	**100.0**	**351,930**	**100.0**	**351,421**	**100.0**	**350,626**	**100.0**	**348,909**	**100.0**
Female client										
Injection drug use	10,251	8.3	10,361	8.1	10,146	8.1	9,965	8.1	9,417	7.8
Heterosexual contact[b]	107,680	87.1	111,227	87.3	108,898	87.2	107,130	87.1	106,348	87.8
Perinatal	4,356	3.5	4,345	3.4	4,252	3.4	4,281	3.5	3,946	3.3
Other[c]	1,359	1.1	1,540	1.2	1,534	1.2	1,589	1.3	1,464	1.2
Subtotal[d]	**123,646**	**100.0**	**127,473**	**100.0**	**124,830**	**100.0**	**122,965**	**100.0**	**121,175**	**100.0**
Transgender client										
Sexual contact[e]	7,864	92.8	9,914	93.4	8,796	93.2	9,965	93.4	11,085	93.7
Injection drug use	118	1.4	162	1.5	119	1.3	143	1.3	156	1.3
Sexual contact[e] and injection drug use	419	4.9	402	3.8	434	4.6	454	4.3	487	4.1
Perinatal	47	0.6	87	0.8	51	0.5	62	0.6	61	0.5
Other[c]	27	0.3	45	0.4	33	0.3	43	0.4	45	0.4
Subtotal[d]	**8,475**	**100.0**	**10,610**	**100.0**	**9,433**	**100.0**	**10,667**	**100.0**	**11,834**	**100.0**

Table 1b. Ryan White HIV/AIDS Program clients with HIV (non-ADAP), by year and selected characteristics, 2018–2022—United States and 3 territories *(cont.)*

	2018		2019		2020		2021		2022	
	N	%	N	%	N	%	N	%	N	%
Federal poverty level										
0–100%	301,411	61.2	313,925	60.6	311,596	60.9	304,288	59.2	303,457	58.6
101–138%	56,703	11.5	58,018	11.2	56,087	11.0	53,038	10.3	53,861	10.4
139–250%	84,180	17.1	91,643	17.7	90,070	17.6	93,905	18.3	92,815	17.9
251–400%	36,032	7.3	42,198	8.1	41,220	8.1	45,795	8.9	49,669	9.6
>400%	14,207	2.9	12,397	2.4	13,050	2.5	17,009	3.3	18,453	3.6
Subtotal	**492,533**	**100.0**	**518,181**	**100.0**	**512,023**	**100.0**	**514,035**	**100.0**	**518,255**	**100.0**
Health care coverage										
Private employer	51,968	10.2	53,916	10.1	53,709	10.1	54,212	10.0	54,531	10.2
Private individual	41,210	8.1	45,784	8.5	50,077	9.5	54,342	10.1	50,677	9.5
Medicare	53,036	10.5	57,798	10.8	56,501	10.7	57,042	10.6	55,475	10.4
Medicaid	158,347	31.2	163,884	30.6	162,012	30.6	168,750	31.2	166,435	31.2
Medicare and Medicaid	40,578	8.0	41,764	7.8	40,120	7.6	40,938	7.6	40,652	7.6
Veterans Administration	1,291	0.3	1,304	0.2	1,168	0.2	1,245	0.2	1,025	0.2
Indian Health Service	200	<0.1	169	<0.1	78	<0.1	227	<0.1	207	<0.1
Other plan	8,012	1.6	8,840	1.6	10,708	2.0	10,792	2.0	11,559	2.2
No coverage	101,305	20.0	108,776	20.3	102,603	19.4	97,547	18.1	96,877	18.2
Multiple coverages	51,448	10.1	53,989	10.1	52,447	9.9	55,021	10.2	55,949	10.5
Subtotal	**507,395**	**100.0**	**536,224**	**100.0**	**529,423**	**100.0**	**540,116**	**100.0**	**533,387**	**100.0**
Housing status										
Stable	432,851	86.9	452,944	87.0	455,884	88.2	462,776	88.3	456,396	87.8
Temporary	38,333	7.7	38,755	7.4	35,569	6.9	34,791	6.6	35,972	6.9
Unstable	26,756	5.4	28,913	5.6	25,133	4.9	26,297	5.0	27,169	5.2
Subtotal	**497,940**	**100.0**	**520,612**	**100.0**	**516,586**	**100.0**	**523,864**	**100.0**	**519,537**	**100.0**
Total[f]	**518,728**	**—**	**556,028**	**—**	**553,953**	**—**	**565,916**	**—**	**557,394**	**—**

[a] Hispanics/Latinos can be of any race.
[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[c] Includes hemophilia and blood transfusion.
[d] Subtotals are reflective of available gender and transmission category information. The values may not sum to the subtotals for gender overall.
[e] Includes any sexual transmission category reported by transgender clients.
[f] Subtotals for each subpopulation are displayed to reflect the denominator used for the percentage calculation of each subpopulation; due to missing data, the values in each column may not sum to the column total.

Table 2. Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native		Asian		Black/ African American		Hispanic/Latino[a]		Native Hawaiian/ Pacific Islander		White		Multiple races	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Age group (yrs)														
<13	7	0.2	60	0.6	2,109	0.8	523	0.4	4	0.4	252	0.2	51	0.5
13–14	4	0.1	25	0.3	223	0.1	41	<0.1	1	0.1	34	<0.1	8	0.1
15–19	8	0.2	81	0.8	1,445	0.6	535	0.4	4	0.4	226	0.2	63	0.6
20–24	93	2.5	267	2.8	8,456	3.4	4,142	2.9	30	2.7	1,964	1.4	328	3.2
25–29	244	6.5	726	7.6	19,216	7.7	11,015	7.8	112	10.1	6,285	4.4	833	8.2
30–34	420	11.3	1,178	12.3	30,616	12.3	16,801	11.9	162	14.6	11,514	8.0	1,246	12.3
35–39	379	10.2	1,234	12.9	26,333	10.6	16,641	11.8	138	12.4	12,467	8.7	1,096	10.8
40–44	395	10.6	1,169	12.2	23,756	9.6	16,530	11.7	126	11.3	13,207	9.2	942	9.3
45–49	326	8.7	1,188	12.4	22,011	8.9	15,575	11.0	105	9.5	12,564	8.7	850	8.4
50–54	469	12.6	1,250	13.0	26,876	10.8	16,922	12.0	105	9.5	18,225	12.7	1,037	10.3
55–59	573	15.4	1,001	10.4	32,224	13.0	17,317	12.3	148	13.3	24,042	16.7	1,321	13.1
60–64	448	12.0	689	7.2	27,390	11.0	12,857	9.1	90	8.1	20,877	14.5	1,156	11.4
≥65	363	9.7	723	7.5	27,919	11.2	12,315	8.7	86	7.7	22,054	15.3	1,186	11.7
Subtotal	**3,729**	**100.0**	**9,591**	**100.0**	**248,574**	**100.0**	**141,214**	**100.0**	**1,111**	**100.0**	**143,711**	**100.0**	**10,117**	**100.0**
Gender														
Male	2,804	75.3	7,339	76.7	157,438	63.4	108,036	76.6	821	74.1	118,217	82.5	6,920	68.7
Female	791	21.2	1,942	20.3	83,695	33.7	28,275	20.0	196	17.7	22,875	16.0	2,797	27.8
Transgender male	14	0.4	27	0.3	626	0.3	451	0.3	6	0.5	344	0.2	26	0.3
Transgender female	105	2.8	222	2.3	6,272	2.5	3,908	2.8	79	7.1	1,618	1.1	309	3.1
Other gender identity	9	0.2	33	0.3	376	0.2	421	0.3	6	0.5	307	0.2	22	0.2
Subtotal	**3,723**	**100.0**	**9,563**	**100.0**	**248,407**	**100.0**	**141,091**	**100.0**	**1,108**	**100.0**	**143,361**	**100.0**	**10,074**	**100.0**
Transmission category														
Male client														
Male-to-male sexual contact	1,428	70.2	4,237	72.7	82,887	59.8	64,966	69.8	526	78.6	77,793	76.6	3,858	65.5
Injection drug use	140	6.9	170	2.9	5,778	4.2	4,777	5.1	29	4.3	5,710	5.6	500	8.5
Male-to-male sexual contact and injection drug use	163	8.0	101	1.7	2,039	1.5	2,202	2.4	21	3.1	6,036	5.9	320	5.4
Heterosexual contact[b]	256	12.6	1,139	19.5	44,802	32.3	19,877	21.4	81	12.1	10,726	10.6	1,095	18.6
Perinatal	25	1.2	84	1.4	2,408	1.7	783	0.8	10	1.5	437	0.4	87	1.5
Other[c]	23	1.1	101	1.7	614	0.4	453	0.5	2	0.3	850	0.8	33	0.6
Subtotal[d]	**2,035**	**100.0**	**5,832**	**100.0**	**138,528**	**100.0**	**93,058**	**100.0**	**669**	**100.0**	**101,552**	**100.0**	**5,893**	**100.0**
Female client														
Injection drug use	132	21.2	33	2.4	3,563	4.9	1,645	6.9	11	6.9	3,664	18.5	335	13.9
Heterosexual contact[b]	474	76.2	1,213	86.6	65,730	89.9	21,109	87.9	139	87.4	15,359	77.7	1,917	79.3
Perinatal	7	1.1	99	7.1	3,020	4.1	925	3.9	8	5.0	475	2.4	131	5.4
Other[c]	9	1.4	55	3.9	772	1.1	324	1.3	1	0.6	260	1.3	33	1.4
Subtotal[d]	**622**	**100.0**	**1,400**	**100.0**	**73,085**	**100.0**	**24,003**	**100.0**	**159**	**100.0**	**19,758**	**100.0**	**2,416**	**100.0**
Transgender client														
Sexual contact[e]	84	86.6	192	95.0	5,647	95.6	3,373	94.1	67	93.1	1,419	87.0	191	86.4
Injection drug use	2	2.1	2	1.0	54	0.9	51	1.4	2	2.8	34	2.1	6	2.7
Sexual contact[e] and injection drug use	10	10.3	6	3.0	153	2.6	137	3.8	3	4.2	152	9.3	20	9.0
Perinatal	1	1.0	1	0.5	34	0.6	8	0.2	0	0.0	17	1.0	2	0.9
Other[c]	0	0.0	1	0.5	17	0.3	16	0.4	0	0.0	9	0.6	2	0.9
Subtotal[d]	**97**	**100.0**	**202**	**100.0**	**5,905**	**100.0**	**3,585**	**100.0**	**72**	**100.0**	**1,631**	**100.0**	**221**	**100.0**
Total[f]	**3,729**	**—**	**9,591**	**—**	**248,574**	**—**	**141,214**	**—**	**1,111**	**—**	**143,711**	**—**	**10,117**	**—**

[a] Hispanics/Latinos can be of any race.
[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[c] Includes hemophilia and blood transfusion.
[d] Subtotals are reflective of available gender and transmission category information. The values may not sum to the subtotals for gender overall.
[e] Includes any sexual transmission category reported by transgender clients.
[f] Subtotals for each subpopulation are displayed to reflect the denominator used for the percentage calculation of each subpopulation; due to missing data, the values in each column may not sum to the column total.

Table 3. Ryan White HIV/AIDS Program clients (non-ADAP), by gender and selected characteristics, 2022—United States and 3 territories

	Male		Female		Transgender male		Transgender female		Other gender identity		Total[a]	
	N	%	N	%	N	%	N	%	N	%	N	%
Age group (yrs)												
<13	1,495	0.4	1,598	1.1	*	*	*	*	*	*	3,093	0.5
13–14	162	<0.1	183	0.1	*	*	*	*	*	*	345	0.1
15–19	1,473	0.4	848	0.6	11	0.7	62	0.5	7	0.6	2,401	0.4
20–24	12,073	3.0	2,569	1.8	94	6.0	755	5.9	77	6.3	15,568	2.8
25–29	31,218	7.7	5,788	4.1	195	12.5	1,647	12.9	236	19.4	39,084	6.9
30–34	50,213	12.3	9,650	6.8	263	16.8	2,457	19.2	272	22.4	62,855	11.1
35–39	44,612	10.9	12,106	8.5	204	13.1	1,996	15.6	193	15.9	59,111	10.4
40–44	39,695	9.7	15,339	10.8	165	10.6	1,560	12.2	127	10.5	56,886	10.1
45–49	35,206	8.6	16,717	11.7	123	7.9	1,189	9.3	71	5.8	53,306	9.4
50–54	44,612	10.9	19,703	13.8	145	9.3	1,165	9.1	74	6.1	65,699	11.6
55–59	55,433	13.6	20,978	14.7	137	8.8	991	7.8	78	6.4	77,617	13.7
60–64	45,512	11.2	18,081	12.7	111	7.1	566	4.4	46	3.8	64,316	11.4
≥65	46,061	11.3	18,909	13.3	108	6.9	396	3.1	33	2.7	65,507	11.6
Subtotal	**407,765**	**100.0**	**142,469**	**100.0**	**1,562**	**100.0**	**12,787**	**100.0**	**1,214**	**100.0**	**565,788**	**100.0**
Race/ethnicity												
American Indian/Alaska Native	2,804	0.7	791	0.6	14	0.9	105	0.8	9	0.8	3,723	0.7
Asian	7,339	1.8	1,942	1.4	27	1.8	222	1.8	33	2.8	9,563	1.7
Black/African American	157,438	39.2	83,695	59.5	626	41.9	6,272	50.1	376	32.0	248,407	44.6
Hispanic/Latino[b]	108,036	26.9	28,275	20.1	451	30.2	3,908	31.2	421	35.9	141,091	25.3
Native Hawaiian/Pacific Islander	821	0.2	196	0.1	6	0.4	79	0.6	6	0.5	1,108	0.2
White	118,217	29.4	22,875	16.3	344	23.0	1,618	12.9	307	26.1	143,361	25.7
Multiple races	6,920	1.7	2,797	2.0	26	1.7	309	2.5	22	1.9	10,074	1.8
Subtotal	**401,575**	**100.0**	**140,571**	**100.0**	**1,494**	**100.0**	**12,513**	**100.0**	**1,174**	**100.0**	**557,327**	**100.0**
Transmission category												
Male-to-male sexual contact	237,281	67.9	—	—	—	—	—	—	—	—	237,281	49.1
Injection drug use	17,170	4.9	9,417	7.7	38	3.5	108	1.1	10	1.3	26,743	5.5
Male-to-male sexual contact and injection drug use	10,920	3.1	—	—	—	—	—	—	—	—	10,920	2.3
Heterosexual contact[c]	78,351	22.4	106,352	87.2	—	—	—	—	—	—	184,703	38.2
Perinatal	3,875	1.1	4,720	3.9	30	2.8	31	0.3	6	0.8	8,662	1.8
Other[d]	2,088	0.6	1,464	1.2	6	0.6	35	0.4	4	0.5	3,597	0.7
Sexual contact[e]	—	—	—	—	961	89.3	9,415	94.3	709	91.0	11,085	2.3
Sexual contact[e] and injection drug use	—	—	—	—	41	3.8	396	4.0	50	6.4	487	0.1
Subtotal	**349,685**	**100.0**	**121,953**	**100.0**	**1,076**	**100.0**	**9,985**	**100.0**	**779**	**100.0**	**483,478**	**100.0**
Federal poverty level												
0–100%	206,997	55.2	87,610	66.8	880	64.2	8,520	72.5	703	72.8	304,710	58.6
101–138%	39,614	10.6	13,410	10.2	125	9.1	881	7.5	50	5.2	54,080	10.4
139–250%	72,004	19.2	19,274	14.7	184	13.4	1,472	12.5	126	13.0	93,060	17.9
251–400%	40,942	10.9	7,990	6.1	103	7.5	627	5.3	56	5.8	49,718	9.6
>400%	15,349	4.1	2,828	2.2	78	5.7	245	2.1	31	3.2	18,531	3.6
Subtotal	**374,906**	**100.0**	**131,112**	**100.0**	**1,370**	**100.0**	**11,745**	**100.0**	**966**	**100.0**	**520,099**	**100.0**

Table 3. Ryan White HIV/AIDS Program clients (non-ADAP), by gender and selected characteristics, 2022—United States and 3 territories *(cont.)*

	Male		Female		Transgender male		Transgender female		Other gender identity		Total[a]	
	N	%	N	%	N	%	N	%	N	%	N	%
Housing status												
Stable	328,602	87.5	118,878	89.9	1,151	84.1	9,248	79.0	666	79.2	458,545	87.9
Temporary	26,577	7.1	8,042	6.1	135	9.9	1,209	10.3	90	10.7	36,053	6.9
Unstable	20,442	5.4	5,245	4.0	83	6.1	1,248	10.7	85	10.1	27,103	5.2
Subtotal	**375,621**	**100.0**	**132,165**	**100.0**	**1,369**	**100.0**	**11,705**	**100.0**	**841**	**100.0**	**521,701**	**100.0**
Total[f]	**407,765**	**—**	**142,469**	**—**	**1,562**	**—**	**12,787**	**—**	**1,214**	**—**	**565,797**	**—**

* To ensure confidentiality, data have been suppressed.
[a] Row totals include clients in the specified subpopulation with reported gender information.
[b] Hispanics/Latinos can be of any race.
[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[d] Includes hemophilia and blood transfusion.
[e] Includes any sexual transmission category reported by transgender clients.
[f] Subtotals for each subpopulation are displayed to reflect the denominator used for the percentage calculation of each subpopulation; due to missing data, the values in each column may not sum to the column total.

Table 4a. Male clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and age group, 2022—United States and 3 territories

	Male-to-male sexual contact		Injection drug use		Male-to-male sexual contact and injection drug use		Heterosexual contact[a]		Perinatal		Other[b]	
	N	%	N	%	N	%	N	%	N	%	N	%
Age group (yrs)												
<13	—	—	—	—	—	—	—	—	1,024	26.4	3	0.1
13–14	4	<0.1	0	0.0	0	0.0	0	0.0	110	2.8	1	<0.1
15–19	670	0.3	3	<0.1	6	0.1	79	0.1	383	9.9	5	0.2
20–24	8,665	3.7	70	0.4	107	1.0	853	1.1	516	13.3	18	0.9
25–29	22,242	9.4	348	2.0	589	5.4	2,542	3.2	769	19.8	61	2.9
30–34	35,584	15.0	752	4.4	1,154	10.6	4,771	6.1	736	19.0	96	4.6
35–39	29,861	12.6	935	5.4	1,261	11.5	5,737	7.3	289	7.5	131	6.3
40–44	24,058	10.1	1,145	6.7	1,255	11.5	7,389	9.4	48	1.2	180	8.6
45–49	19,423	8.2	1,225	7.1	1,104	10.1	8,331	10.6	—	—	179	8.6
50–54	23,982	10.1	1,822	10.6	1,393	12.8	11,020	14.1	—	—	255	12.2
55–59	29,494	12.4	2,916	17.0	1,663	15.2	13,454	17.2	—	—	367	17.6
60–64	22,420	9.4	3,537	20.6	1,269	11.6	11,759	15.0	—	—	346	16.6
≥65	20,878	8.8	4,417	25.7	1,119	10.2	12,416	15.8	—	—	446	21.4
Total	**237,281**	**100.0**	**17,170**	**100.0**	**10,920**	**100.0**	**78,351**	**100.0**	**3,875**	**100.0**	**2,088**	**100.0**

[a] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[b] Includes hemophilia and blood transfusion.

Table 4b. Female clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and age group, 2022—United States and 3 territories

	Injection drug use		Heterosexual contact[a]		Perinatal		Other[b]	
	N	%	N	%	N	%	N	%
Age group (yrs)								
<13	—	—	—	—	1,116	23.6	2	0.1
13–14	0	0.0	5	<0.1	125	2.6	0	0.0
15–19	6	0.1	149	0.1	477	10.1	5	0.3
20–24	43	0.5	1,336	1.3	672	14.2	10	0.7
25–29	211	2.2	3,466	3.3	1,043	22.1	27	1.8
30–34	458	4.9	6,622	6.2	927	19.6	48	3.3
35–39	608	6.5	9,189	8.6	331	7.0	90	6.1
40–44	762	8.1	12,192	11.5	29	0.6	113	7.7
45–49	761	8.1	13,493	12.7	—	—	121	8.3
50–54	1,236	13.1	15,682	14.7	—	—	191	13.0
55–59	1,732	18.4	16,280	15.3	—	—	224	15.3
60–64	1,804	19.2	13,733	12.9	—	—	236	16.1
≥65	1,796	19.1	14,205	13.4	—	—	397	27.1
Total	**9,417**	**100.0**	**106,352**	**100.0**	**4,720**	**100.0**	**1,464**	**100.0**

[a] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[b] Includes hemophilia and blood transfusion.

Table 4c. Transgender clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and age group, 2022—United States and 3 territories

	Sexual contact[a]		Injection drug use		Sexual contact[a] and injection drug use		Perinatal		Other[b]	
	N	%	N	%	N	%	N	%	N	%
Age group (yrs)										
<13	—	—	—	—	—	—	*	*	*	*
13–14	*	*	*	*	*	*	*	*	*	*
15–19	46	0.4	0	0.0	1	0.2	0	0.0	0	0.0
20–24	656	5.9	4	2.6	9	1.8	11	18.0	0	0.0
25–29	1,476	13.3	15	9.6	42	8.6	15	24.6	6	13.3
30–34	2,237	20.2	19	12.2	63	12.9	24	39.3	5	11.1
35–39	1,712	15.4	14	9.0	73	15.0	11	18.0	5	11.1
40–44	1,315	11.9	19	12.2	61	12.5	—	—	2	4.4
45–49	999	9.0	11	7.1	43	8.8	—	—	3	6.7
50–54	976	8.8	20	12.8	53	10.9	—	—	4	8.9
55–59	819	7.4	23	14.7	70	14.4	—	—	10	22.2
60–64	496	4.5	21	13.5	48	9.9	—	—	4	8.9
≥65	353	3.2	10	6.4	24	4.9	—	—	6	13.3
Total	**11,085**	**100.0**	**156**	**100.0**	**487**	**100.0**	**61**	**100.0**	**45**	**100.0**

* To ensure confidentiality, data have been suppressed.
[a] Includes any reported sexual transmission category reported by transgender clients.
[b] Includes hemophilia and blood transfusion.

Table 5. Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and selected characteristics, 2022—United States and 3 territories

	0–100% FPL		101–138% FPL		139–250% FPL		251–400% FPL		>400% FPL	
	N	%	N	%	N	%	N	%	N	%
Age group (yrs)										
<13	1,692	0.6	265	0.5	342	0.4	103	0.2	134	0.7
13–14	139	<0.1	24	<0.1	43	<0.1	34	0.1	19	0.1
15–19	1,359	0.4	183	0.3	266	0.3	109	0.2	70	0.4
20–24	9,041	3.0	1,148	2.1	2,576	2.8	1,008	2.0	261	1.4
25–29	21,023	6.9	2,738	5.1	6,875	7.4	3,974	8.0	1,025	5.5
30–34	34,419	11.3	4,214	7.8	10,131	10.9	6,738	13.5	2,071	11.2
35–39	32,441	10.6	4,334	8.0	9,340	10.0	6,027	12.1	2,176	11.7
40–44	31,417	10.3	4,636	8.6	8,855	9.5	5,470	11.0	2,118	11.4
45–49	29,275	9.6	4,665	8.6	8,473	9.1	4,942	9.9	1,916	10.3
50–54	35,957	11.8	6,303	11.7	10,327	11.1	5,902	11.9	2,340	12.6
55–59	42,191	13.8	8,509	15.7	12,087	13.0	6,386	12.8	2,647	14.3
60–64	34,356	11.3	7,687	14.2	10,721	11.5	4,759	9.6	1,968	10.6
≥65	31,666	10.4	9,386	17.4	13,065	14.0	4,281	8.6	1,796	9.7
Subtotal	**304,976**	**100.0**	**54,092**	**100.0**	**93,101**	**100.0**	**49,733**	**100.0**	**18,541**	**100.0**
Race/ethnicity										
American Indian/Alaska Native	2,096	0.7	384	0.7	587	0.6	210	0.4	78	0.4
Asian	4,504	1.5	849	1.6	1,689	1.8	1,083	2.2	517	2.8
Black/African American	144,892	48.0	22,326	41.9	36,715	39.9	18,972	38.6	6,280	34.4
Hispanic/Latino[a]	80,415	26.6	12,857	24.1	23,247	25.3	11,675	23.8	3,475	19.0
Native Hawaiian/Pacific Islander	550	0.2	94	0.2	208	0.2	123	0.3	52	0.3
White	64,174	21.3	15,884	29.8	28,040	30.5	16,139	32.8	7,546	41.3
Multiple races	5,253	1.7	907	1.7	1,453	1.6	944	1.9	333	1.8
Subtotal	**301,884**	**100.0**	**53,301**	**100.0**	**91,939**	**100.0**	**49,146**	**100.0**	**18,281**	**100.0**
Gender										
Male	206,997	67.9	39,614	73.3	72,004	77.4	40,942	82.3	15,349	82.8
Female	87,610	28.8	13,410	24.8	19,274	20.7	7,990	16.1	2,828	15.3
Transgender male	880	0.3	125	0.2	184	0.2	103	0.2	78	0.4
Transgender female	8,520	2.8	881	1.6	1,472	1.6	627	1.3	245	1.3
Other gender identity	703	0.2	50	0.1	126	0.1	56	0.1	31	0.2
Subtotal	**304,710**	**100.0**	**54,080**	**100.0**	**93,060**	**100.0**	**49,718**	**100.0**	**18,531**	**100.0**
Transmission category										
Male client										
Male-to-male sexual contact	117,355	62.5	24,737	68.3	48,681	74.3	29,051	78.3	10,849	80.2
Injection drug use	12,486	6.7	1,542	4.3	1,702	2.6	721	1.9	249	1.8
Male-to-male sexual contact and injection drug use	6,879	3.7	1,137	3.1	1,577	2.4	792	2.1	252	1.9
Heterosexual contact[b]	47,578	25.4	8,131	22.5	12,582	19.2	6,009	16.2	1,942	14.4
Perinatal	2,288	1.2	370	1.0	572	0.9	321	0.9	141	1.0
Other[c]	1,039	0.6	275	0.8	426	0.7	199	0.5	94	0.7
Subtotal[d]	**187,625**	**100.0**	**36,192**	**100.0**	**65,540**	**100.0**	**37,093**	**100.0**	**13,527**	**100.0**
Female client										
Injection drug use	7,282	9.2	732	6.0	737	4.2	258	3.6	97	4.0
Heterosexual contact[b]	68,450	86.2	10,829	88.9	15,816	90.1	6,540	91.0	2,114	87.0
Perinatal	2,814	3.5	460	3.8	752	4.3	291	4.1	186	7.7
Other[c]	894	1.1	165	1.4	255	1.5	95	1.3	34	1.4
Subtotal[d]	**79,440**	**100.0**	**12,186**	**100.0**	**17,560**	**100.0**	**7,184**	**100.0**	**2,431**	**100.0**

Table 5. Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and selected characteristics, 2022—United States and 3 territories *(cont.)*

	0–100% FPL		101–138% FPL		139–250% FPL		251–400% FPL		>400% FPL	
	N	%	N	%	N	%	N	%	N	%
Transgender client										
Sexual contact[e]	7,690	93.0	842	94.0	1,429	95.6	597	97.1	208	95.4
Injection drug use	119	1.4	13	1.5	9	0.6	5	0.8	5	2.3
Sexual contact[e] and injection drug use	390	4.7	28	3.1	40	2.7	10	1.6	2	0.9
Perinatal	44	0.5	6	0.7	10	0.7	2	0.3	2	0.9
Other[c]	30	0.4	7	0.8	6	0.4	1	0.2	1	0.5
Subtotal[d]	**8,273**	**100.0**	**896**	**100.0**	**1,494**	**100.0**	**615**	**100.0**	**218**	**100.0**
Health care coverage										
Private employer	13,361	4.4	3,013	5.6	13,133	14.3	15,146	30.9	7,090	38.5
Private individual	18,248	6.0	4,169	7.8	12,986	14.1	9,381	19.1	3,531	19.2
Medicare	23,346	7.7	11,394	21.3	13,571	14.8	3,188	6.5	1,096	6.0
Medicaid	126,308	41.8	12,763	23.9	16,788	18.3	4,617	9.4	2,036	11.1
Medicare and Medicaid	27,767	9.2	6,752	12.6	4,151	4.5	614	1.3	382	2.1
Veterans Administration	336	0.1	174	0.3	237	0.3	132	0.3	57	0.3
Indian Health Service	180	0.1	4	<0.1	7	<0.1	5	<0.1	3	<0.1
Other plan	5,668	1.9	1,000	1.9	2,267	2.5	1,246	2.5	643	3.5
No coverage	60,250	20.0	8,038	15.0	16,494	17.9	7,119	14.5	1,494	8.1
Multiple coverages	26,418	8.8	6,131	11.5	12,352	13.4	7,593	15.5	2,060	11.2
Subtotal	**301,882**	**100.0**	**53,438**	**100.0**	**91,986**	**100.0**	**49,041**	**100.0**	**18,392**	**100.0**
Housing status										
Stable	250,516	83.5	48,707	92.1	86,156	93.8	46,873	95.9	17,225	96.2
Temporary	27,277	9.1	2,668	5.0	3,668	4.0	1,309	2.7	438	2.4
Unstable	22,225	7.4	1,528	2.9	2,065	2.2	694	1.4	239	1.3
Subtotal	**300,018**	**100.0**	**52,903**	**100.0**	**91,889**	**100.0**	**48,876**	**100.0**	**17,902**	**100.0**
Total[f]	**304,976**	**—**	**54,092**	**—**	**93,101**	**—**	**49,733**	**—**	**18,541**	**—**

Abbreviation: FPL, federal poverty level.
[a] Hispanics/Latinos can be of any race.
[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[c] Includes hemophilia and blood transfusion.
[d] Subtotals are reflective of available gender and transmission category information. The values may not sum to the subtotals for gender overall.
[e] Includes any sexual transmission category reported by transgender clients.
[f] Subtotals for each subpopulation are displayed to reflect the denominator used for the percentage calculation of each subpopulation; due to missing data, the values in each column may not sum to the column total.

Table 6. Ryan White HIV/AIDS Program clients (non-ADAP), by housing status and selected characteristics, 2022—United States and 3 territories

	Stable		Temporary		Unstable	
	N	%	N	%	N	%
Age group (yrs)						
<13	2,568	0.6	104	0.3	19	0.1
13–14	273	0.1	5	<0.1	2	<0.1
15–19	1,828	0.4	162	0.4	73	0.3
20–24	11,991	2.6	1,359	3.8	804	3.0
25–29	29,929	6.5	3,425	9.5	2,453	9.0
30–34	48,246	10.5	5,281	14.6	4,220	15.5
35–39	45,804	10.0	4,760	13.2	3,875	14.2
40–44	45,051	9.8	4,192	11.6	3,370	12.4
45–49	43,129	9.4	3,525	9.8	2,756	10.1
50–54	53,786	11.7	4,012	11.1	3,175	11.7
55–59	64,513	14.1	4,180	11.6	3,243	11.9
60–64	54,697	11.9	2,898	8.0	2,020	7.4
≥65	56,873	12.4	2,172	6.0	1,189	4.4
Subtotal	**458,688**	**100.0**	**36,075**	**100.0**	**27,199**	**100.0**
Race/ethnicity						
American Indian/Alaska Native	2,814	0.6	218	0.6	306	1.1
Asian	7,880	1.7	479	1.4	233	0.9
Black/African American	202,847	44.7	16,715	47.2	11,392	42.3
Hispanic/Latino[a]	114,536	25.2	9,369	26.4	7,852	29.2
Native Hawaiian/Pacific Islander	888	0.2	77	0.2	68	0.3
White	117,116	25.8	7,967	22.5	6,611	24.6
Multiple races	7,970	1.8	625	1.8	462	1.7
Subtotal	**454,051**	**100.0**	**35,450**	**100.0**	**26,924**	**100.0**
Gender						
Male	328,602	71.7	26,577	73.7	20,442	75.4
Female	118,878	25.9	8,042	22.3	5,245	19.4
Transgender male	1,151	0.3	135	0.4	83	0.3
Transgender female	9,248	2.0	1,209	3.4	1,248	4.6
Other gender identity	666	0.1	90	0.2	85	0.3
Subtotal	**458,545**	**100.0**	**36,053**	**100.0**	**27,103**	**100.0**
Transmission category						
Male client						
Male-to-male sexual contact	204,612	68.4	14,685	63.1	11,625	63.4
Injection drug use	13,490	4.5	1,694	7.3	1,537	8.4
Male-to-male sexual contact and injection drug use	8,052	2.7	1,312	5.6	1,287	7.0
Heterosexual contact[b]	67,697	22.6	5,243	22.5	3,665	20.0
Perinatal	3,371	1.1	239	1.0	155	0.8
Other[c]	1,863	0.6	101	0.4	70	0.4
Subtotal[d]	**299,085**	**100.0**	**23,274**	**100.0**	**18,339**	**100.0**
Female client						
Injection drug use	7,517	6.9	849	12.4	806	18.7
Heterosexual contact[b]	95,282	87.9	5,636	82.4	3,372	78.2
Perinatal	4,230	3.9	278	4.1	108	2.5
Other[c]	1,334	1.2	77	1.1	28	0.6
Subtotal[d]	**108,363**	**100.0**	**6,840**	**100.0**	**4,314**	**100.0**
Transgender client						
Sexual contact[e]	8,519	94.6	1,015	90.2	1,045	90.2
Injection drug use	103	1.1	21	1.9	24	2.1
Sexual contact[e] and injection drug use	295	3.3	79	7.0	82	7.1
Perinatal	54	0.6	6	0.5	5	0.4
Other[c]	38	0.4	4	0.4	3	0.3
Subtotal[d]	**9,009**	**100.0**	**1,125**	**100.0**	**1,159**	**100.0**

Table 6. Ryan White HIV/AIDS Program clients (non-ADAP), by housing status and selected characteristics, 2022— United States and 3 territories *(cont.)*

	Stable		Temporary		Unstable	
	N	%	N	%	N	%
Health care coverage						
Private employer	49,354	10.9	1,315	3.8	1,376	5.2
Private individual	45,245	10.0	2,352	6.8	1,153	4.3
Medicare	49,359	10.9	1,907	5.5	1,217	4.6
Medicaid	135,719	30.0	13,937	40.1	12,279	46.0
Medicare and Medicaid	35,781	7.9	2,171	6.2	1,644	6.2
Veterans Administration	855	0.2	60	0.2	44	0.2
Indian Health Service	160	<0.1	7	<0.1	30	0.1
Other plan	9,331	2.1	860	2.5	576	2.2
No coverage	78,570	17.3	8,606	24.7	6,084	22.8
Multiple coverages	48,705	10.7	3,575	10.3	2,315	8.7
Subtotal	**453,079**	**100.0**	**34,790**	**100.0**	**26,718**	**100.0**
Total[f]	**458,688**	**—**	**36,075**	**—**	**27,199**	**—**

[a] Hispanics/Latinos can be of any race.
[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[c] Includes hemophilia and blood transfusion.
[d] Subtotals are reflective of available gender and transmission category information. The values may not sum to the subtotals for gender overall.
[e] Includes any sexual transmission category reported by transgender clients.
[f] Subtotals for each subpopulation are displayed to reflect the denominator used for the percentage calculation of each subpopulation; due to missing data, the values in each column may not sum to the column total.

Table 7. Ryan White HIV/AIDS Program clients (non-ADAP), by health care coverage and selected characteristics, 2022—United States and 3 territories

	Private employer		Private individual		Medicare		Medicaid		Medicare & Medicaid		Veterans Administration		Indian Health Service		Other plan		No coverage		Multiple coverages	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Age group (yrs)																				
<13	242	0.4	48	0.1	10	<0.1	2,232	1.3	8	<0.1	6	0.6	0	0.0	30	0.3	106	0.1	69	0.1
13–14	71	0.1	10	<0.1	0	0.0	169	0.1	2	<0.1	4	0.4	0	0.0	1	<0.1	15	<0.1	19	<0.1
15–19	254	0.5	93	0.2	11	<0.1	1,325	0.8	8	<0.1	11	1.1	0	0.0	36	0.3	265	0.3	150	0.3
20–24	1,540	2.8	1,359	2.7	74	0.1	5,681	3.4	91	0.2	30	2.9	9	4.2	331	2.9	4,174	4.3	1,289	2.3
25–29	4,291	7.8	3,791	7.5	313	0.6	12,392	7.3	449	1.1	48	4.6	16	7.5	869	7.5	11,269	11.5	3,252	5.8
30–34	7,234	13.2	6,200	12.2	874	1.6	20,334	12.0	1,073	2.6	65	6.2	39	18.4	1,452	12.5	16,708	17.1	5,405	9.7
35–39	6,794	12.4	6,127	12.1	1,288	2.3	18,960	11.2	1,439	3.5	59	5.7	20	9.4	1,451	12.5	14,225	14.5	5,561	9.9
40–44	6,317	11.5	6,098	12.0	1,981	3.6	18,079	10.7	2,042	5.0	55	5.3	22	10.4	1,485	12.8	12,591	12.9	5,431	9.7
45–49	6,008	11.0	5,709	11.3	2,732	4.9	16,309	9.7	2,574	6.3	59	5.7	16	7.5	1,380	11.9	10,583	10.8	5,358	9.6
50–54	7,055	12.9	6,878	13.6	5,073	9.1	20,603	12.2	4,603	11.3	103	9.9	28	13.2	1,436	12.4	10,228	10.5	6,673	11.9
55–59	7,459	13.6	7,233	14.3	8,964	16.1	24,624	14.6	7,502	18.4	158	15.2	28	13.2	1,434	12.4	8,763	9.0	7,891	14.1
60–64	5,323	9.7	5,577	11.0	9,814	17.7	19,806	11.7	7,479	18.4	204	19.6	21	9.9	1,039	9.0	5,583	5.7	6,688	11.9
≥65	2,187	4.0	1,611	3.2	24,441	44.0	8,334	4.9	13,414	33.0	239	23.0	13	6.1	663	5.7	3,276	3.4	8,206	14.7
Subtotal	**54,775**	**100.0**	**50,734**	**100.0**	**55,575**	**100.0**	**168,848**	**100.0**	**40,684**	**100.0**	**1,041**	**100.0**	**212**	**100.0**	**11,607**	**100.0**	**97,786**	**100.0**	**55,992**	**100.0**
Race/ethnicity																				
American Indian/Alaska Native	258	0.5	229	0.5	464	0.8	1,039	0.6	232	0.6	17	1.7	178	84.8	29	0.3	534	0.6	481	0.9
Asian	1,225	2.3	1,104	2.2	491	0.9	2,549	1.5	399	1.0	23	2.2	0	0.0	265	2.3	1,696	1.8	1,132	2.0
Black/African American	23,825	43.9	21,469	42.5	24,321	44.1	82,751	49.6	18,286	45.1	458	44.5	9	4.3	3,850	33.8	41,232	42.6	21,597	38.9
Hispanic/Latino[a]	10,474	19.3	11,545	22.9	7,496	13.6	42,440	25.4	7,490	18.5	94	9.1	10	4.8	4,637	40.7	37,777	39.1	12,859	23.2
Native Hawaiian/Pacific Islander	132	0.2	82	0.2	73	0.1	401	0.2	67	0.2	10	1.0	0	0.0	33	0.3	127	0.1	134	0.2
White	17,373	32.0	15,571	30.8	21,695	39.3	34,636	20.7	12,995	32.0	410	39.8	7	3.3	2,492	21.9	14,212	14.7	17,964	32.3
Multiple races	1,013	1.9	483	1.0	672	1.2	3,142	1.9	1,102	2.7	18	1.7	6	2.9	80	0.7	1,132	1.2	1,378	2.5
Subtotal	**54,300**	**100.0**	**50,483**	**100.0**	**55,212**	**100.0**	**166,958**	**100.0**	**40,571**	**100.0**	**1,030**	**100.0**	**210**	**100.0**	**11,386**	**100.0**	**96,710**	**100.0**	**55,545**	**100.0**
Gender																				
Male	43,324	79.2	39,719	78.3	41,235	74.2	107,951	64.0	27,380	67.3	848	81.5	159	75.0	8,837	76.2	76,343	78.2	41,293	73.8
Female	10,583	19.3	10,048	19.8	13,638	24.6	54,391	32.2	12,584	30.9	180	17.3	50	23.6	2,347	20.2	18,220	18.7	13,222	23.6
Transgender male	102	0.2	106	0.2	146	0.3	485	0.3	77	0.2	3	0.3	0	0.0	40	0.3	380	0.4	133	0.2
Transgender female	554	1.0	804	1.6	495	0.9	5,451	3.2	602	1.5	10	1.0	3	1.4	337	2.9	2,557	2.6	1,174	2.1
Other gender identity	158	0.3	48	0.1	38	0.1	500	0.3	33	0.1	0	0.0	0	0.0	35	0.3	130	0.1	158	0.3
Subtotal	**54,721**	**100.0**	**50,725**	**100.0**	**55,552**	**100.0**	**168,778**	**100.0**	**40,676**	**100.0**	**1,041**	**100.0**	**212**	**100.0**	**11,596**	**100.0**	**97,630**	**100.0**	**55,980**	**100.0**
Transmission category																				
Male client																				
Male-to-male sexual contact	30,013	78.4	26,621	76.6	22,263	61.7	58,913	60.5	14,873	59.3	461	63.6	100	70.9	5,203	70.5	47,470	71.3	28,121	73.4
Injection drug use	603	1.6	653	1.9	2,482	6.9	7,350	7.5	2,365	9.4	45	6.2	9	6.4	233	3.2	1,518	2.3	1,616	4.2
Male-to-male sexual contact and injection drug use	617	1.6	698	2.0	1,057	2.9	4,164	4.3	1,186	4.7	20	2.8	11	7.8	168	2.3	1,226	1.8	1,617	4.2
Heterosexual contact[b]	6,445	16.8	6,449	18.6	9,782	27.1	24,378	25.0	6,236	24.9	182	25.1	21	14.9	1,664	22.6	15,645	23.5	6,455	16.8
Perinatal	398	1.0	189	0.5	106	0.3	2,185	2.2	146	0.6	8	1.1	0	0.0	71	1.0	448	0.7	278	0.7
Other[c]	204	0.5	154	0.4	396	1.1	447	0.5	274	1.1	9	1.2	0	0.0	37	0.5	296	0.4	237	0.6
Subtotal[d]	**38,280**	**100.0**	**34,764**	**100.0**	**36,086**	**100.0**	**97,437**	**100.0**	**25,080**	**100.0**	**725**	**100.0**	**141**	**100.0**	**7,376**	**100.0**	**66,603**	**100.0**	**38,324**	**100.0**
Female client																				
Injection drug use	256	2.7	297	3.4	993	8.1	4,771	9.7	1,335	11.5	5	3.3	15	32.6	117	6.1	564	3.7	883	7.2
Heterosexual contact[b]	8,533	90.9	8,014	92.7	10,892	89.0	41,006	83.7	9,928	85.4	135	88.8	30	65.2	1,711	89.3	14,049	92.7	10,742	87.8
Perinatal	504	5.4	224	2.6	122	1.0	2,759	5.6	197	1.7	12	7.9	0	0.0	61	3.2	338	2.2	454	3.7
Other[c]	96	1.0	108	1.2	232	1.9	458	0.9	163	1.4	0	0.0	1	2.2	26	1.4	205	1.4	155	1.3
Subtotal[d]	**9,389**	**100.0**	**8,643**	**100.0**	**12,239**	**100.0**	**48,994**	**100.0**	**11,623**	**100.0**	**152**	**100.0**	**46**	**100.0**	**1,915**	**100.0**	**15,156**	**100.0**	**12,234**	**100.0**

Table 7. Ryan White HIV/AIDS Program clients (non-ADAP), by health care coverage and selected characteristics, 2022—United States and 3 territories *(cont.)*

	Private employer		Private individual		Medicare		Medicaid		Medicare & Medicaid		Veterans Administration		Indian Health Service		Other plan		No coverage		Multiple coverages	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Transgender client																				
Sexual contact[e]	638	96.7	768	97.0	492	90.4	4,800	92.5	539	91.0	12	92.3	3	100.0	203	93.5	2,436	96.9	1,023	89.8
Injection drug use	4	0.6	6	0.8	13	2.4	81	1.6	6	1.0	0	0.0	0	0.0	2	0.9	21	0.8	21	1.8
Sexual contact[e] and injection drug use	14	2.1	13	1.6	25	4.6	251	4.8	41	6.9	1	7.7	0	0.0	8	3.7	43	1.7	86	7.6
Perinatal	2	0.3	2	0.3	5	0.9	37	0.7	3	0.5	0	0.0	0	0.0	3	1.4	7	0.3	8	0.7
Other[c]	2	0.3	3	0.4	9	1.7	20	0.4	3	0.5	0	0.0	0	0.0	1	0.5	6	0.2	1	0.1
Subtotal[d]	**660**	**100.0**	**792**	**100.0**	**544**	**100.0**	**5,189**	**100.0**	**592**	**100.0**	**13**	**100.0**	**3**	**100.0**	**217**	**100.0**	**2,513**	**100.0**	**1,139**	**100.0**
Total[f]	**54,775**	**—**	**50,734**	**—**	**55,575**	**—**	**168,848**	**—**	**40,684**	**—**	**1,041**	**—**	**212**	**—**	**11,607**	**—**	**97,786**	**—**	**55,992**	**—**

[a] Hispanics/Latinos can be of any race.
[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[c] Includes hemophilia and blood transfusion.
[d] Subtotals are reflective of available gender and transmission category information. The values may not sum to the subtotals for gender overall.
[e] Includes any sexual transmission category reported by transgender clients.
[f] Subtotals for each subpopulation are displayed to reflect the denominator used for the percentage calculation of each subpopulation; due to missing data, the values in each column may not sum to the column total.

Table 8. Ryan White HIV/AIDS Program clients (non-ADAP), by HHS region and selected characteristics, 2022—United States and 3 territories

	Region 1		Region 2		Region 3		Region 4		Region 5		Region 6		Region 7		Region 8		Region 9		Region 10	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Age group (yrs)																				
<13	110	0.5	445	0.6	367	0.6	980	0.7	437	0.7	301	0.4	69	0.5	83	0.7	276	0.4	13	0.1
13–14	11	<0.1	25	<0.1	35	0.1	117	0.1	58	0.1	38	0.1	5	<0.1	17	0.1	29	<0.1	3	<0.1
15–19	62	0.3	267	0.3	265	0.4	701	0.5	309	0.5	272	0.4	80	0.6	86	0.7	229	0.3	70	0.4
20–24	359	1.6	1,628	2.1	1,355	2.2	4,697	3.2	1,947	3.2	2,465	3.5	400	3.0	319	2.8	1,438	2.1	464	2.6
25–29	928	4.0	4,276	5.5	3,449	5.6	11,336	7.7	4,648	7.7	5,812	8.2	976	7.4	948	8.2	4,313	6.3	1,146	6.4
30–34	1,614	7.0	7,121	9.2	5,871	9.6	17,531	11.9	7,505	12.4	9,288	13.1	1,510	11.4	1,328	11.5	7,196	10.5	1,852	10.4
35–39	1,858	8.1	7,037	9.1	5,917	9.7	15,477	10.5	6,560	10.8	8,545	12.0	1,405	10.6	1,385	12.0	7,276	10.7	1,918	10.8
40–44	1,930	8.4	6,949	9.0	5,481	9.0	14,822	10.1	6,228	10.3	8,097	11.4	1,428	10.8	1,320	11.5	7,016	10.3	1,986	11.2
45–49	2,154	9.3	6,751	8.7	5,368	8.8	13,869	9.4	5,696	9.4	7,202	10.1	1,336	10.1	1,174	10.2	6,571	9.6	1,793	10.1
50–54	2,956	12.8	8,940	11.6	7,173	11.7	17,127	11.6	6,808	11.2	8,097	11.4	1,560	11.8	1,300	11.3	8,038	11.8	2,124	11.9
55–59	3,852	16.7	11,759	15.2	9,189	15.0	19,639	13.3	7,808	12.9	8,482	12.0	1,797	13.6	1,407	12.2	9,623	14.1	2,337	13.1
60–64	3,460	15.0	10,332	13.4	8,021	13.1	15,943	10.8	6,458	10.6	6,613	9.3	1,409	10.7	1,100	9.5	7,728	11.3	1,911	10.7
≥65	3,776	16.4	11,837	15.3	8,614	14.1	15,128	10.3	6,206	10.2	5,759	8.1	1,240	9.4	1,056	9.2	8,497	12.5	2,176	12.2
Subtotal	**23,070**	**100.0**	**77,367**	**100.0**	**61,105**	**100.0**	**147,367**	**100.0**	**60,668**	**100.0**	**70,971**	**100.0**	**13,215**	**100.0**	**11,523**	**100.0**	**68,230**	**100.0**	**17,793**	**100.0**
Race/ethnicity																				
American Indian/Alaska Native	80	0.4	156	0.2	180	0.3	352	0.2	253	0.4	1,259	1.8	70	0.5	192	1.7	643	1.0	463	2.7
Asian	370	1.6	1,266	1.7	544	0.9	914	0.6	854	1.4	1,820	2.6	200	1.5	172	1.5	2,638	3.9	608	3.5
Black/African American	6,915	30.6	30,122	39.6	35,183	58.2	85,273	58.9	30,610	51.5	29,712	42.5	5,544	42.1	2,057	18.2	12,935	19.1	2,938	17.0
Hispanic/Latino[a]	7,137	31.6	34,533	45.4	7,445	12.3	22,237	15.4	9,040	15.2	21,811	31.2	1,331	10.1	3,446	30.5	28,514	42.1	3,401	19.7
Native Hawaiian/Pacific Islander	28	0.1	106	0.1	48	0.1	93	0.1	90	0.2	72	0.1	22	0.2	24	0.2	493	0.7	122	0.7
White	7,797	34.5	9,372	12.3	13,125	21.7	34,683	24.0	17,222	29.0	14,659	21.0	5,756	43.7	5,169	45.7	21,347	31.5	9,207	53.4
Multiple races	279	1.2	492	0.6	3,954	6.5	1,147	0.8	1,362	2.3	526	0.8	259	2.0	240	2.1	1,110	1.6	504	2.9
Subtotal	**22,606**	**100.0**	**76,047**	**100.0**	**60,479**	**100.0**	**144,699**	**100.0**	**59,431**	**100.0**	**69,859**	**100.0**	**13,182**	**100.0**	**11,300**	**100.0**	**67,680**	**100.0**	**17,243**	**100.0**
Gender																				
Male	15,317	66.4	49,561	64.1	40,014	65.5	105,230	71.4	45,215	74.9	52,320	73.7	9,978	75.5	8,855	76.9	55,984	82.1	13,634	79.3
Female	7,180	31.1	24,476	31.6	19,422	31.8	39,280	26.7	13,285	22.0	17,019	24.0	2,918	22.1	2,110	18.3	10,076	14.8	3,156	18.4
Transgender male	178	0.8	184	0.2	183	0.3	242	0.2	169	0.3	343	0.5	11	0.1	25	0.2	144	0.2	55	0.3
Transgender female	340	1.5	2,769	3.6	1,370	2.2	2,480	1.7	1,606	2.7	1,183	1.7	308	2.3	156	1.4	1,992	2.9	290	1.7
Other gender identity	54	0.2	371	0.5	77	0.1	48	<0.1	119	0.2	98	0.1	0	0.0	370	3.2	14	<0.1	52	0.3
Subtotal	**23,069**	**100.0**	**77,361**	**100.0**	**61,066**	**100.0**	**147,280**	**100.0**	**60,394**	**100.0**	**70,963**	**100.0**	**13,215**	**100.0**	**11,516**	**100.0**	**68,210**	**100.0**	**17,187**	**100.0**
Transmission category																				
Male client																				
Male-to-male sexual contact	8,045	58.1	24,662	56.2	20,624	60.4	63,496	67.1	27,204	73.6	28,667	71.1	6,946	73.6	5,010	68.3	39,208	77.3	4,850	68.0
Injection drug use	1,881	13.6	3,355	7.6	2,945	8.6	2,626	2.8	1,252	3.4	1,490	3.7	404	4.3	339	4.6	2,033	4.0	414	5.8
Male-to-male sexual contact and injection drug use	381	2.8	701	1.6	756	2.2	1,751	1.9	731	2.0	1,279	3.2	123	1.3	1,102	15.0	2,838	5.6	799	11.2
Heterosexual contact[b]	3,169	22.9	14,189	32.3	8,965	26.3	25,242	26.7	7,154	19.4	8,398	20.8	1,796	19.0	755	10.3	6,063	12.0	902	12.6
Perinatal	241	1.7	666	1.5	591	1.7	985	1.0	404	1.1	312	0.8	66	0.7	110	1.5	300	0.6	112	1.6
Other[c]	125	0.9	300	0.7	243	0.7	516	0.5	217	0.6	187	0.5	107	1.1	24	0.3	251	0.5	58	0.8
Subtotal[d]	**13,842**	**100.0**	**43,873**	**100.0**	**34,124**	**100.0**	**94,616**	**100.0**	**36,962**	**100.0**	**40,333**	**100.0**	**9,442**	**100.0**	**7,340**	**100.0**	**50,693**	**100.0**	**7,135**	**100.0**
Female client																				
Injection drug use	978	15.1	1,613	7.6	1,899	11.5	1,537	4.3	664	6.1	843	6.7	148	5.4	294	16.7	943	10.5	235	14.4
Heterosexual contact[b]	5,140	79.3	18,606	87.1	13,648	82.8	32,478	91.4	9,568	87.4	11,238	89.0	2,494	90.4	1,343	76.3	7,529	83.9	1,318	81.0
Perinatal	264	4.1	798	3.7	734	4.5	1,229	3.5	583	5.3	389	3.1	82	3.0	112	6.4	367	4.1	54	3.3
Other[c]	101	1.6	339	1.6	198	1.2	290	0.8	132	1.2	157	1.2	36	1.3	12	0.7	134	1.5	20	1.2
Subtotal[d]	**6,483**	**100.0**	**21,356**	**100.0**	**16,479**	**100.0**	**35,534**	**100.0**	**10,947**	**100.0**	**12,627**	**100.0**	**2,760**	**100.0**	**1,761**	**100.0**	**8,973**	**100.0**	**1,627**	**100.0**

Table 8. Ryan White HIV/AIDS Program clients (non-ADAP), by HHS region and selected characteristics, 2022—United States and 3 territories *(cont.)*

	Region 1		Region 2		Region 3		Region 4		Region 5		Region 6		Region 7		Region 8		Region 9		Region 10	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Transgender client																				
Sexual contact[e]	405	88.8	1,944	94.1	1,054	94.2	2,388	96.4	1,366	95.5	1,212	96.2	292	96.7	317	83.2	1,643	89.4	167	83.1
Injection drug use	22	4.8	42	2.0	13	1.2	11	0.4	10	0.7	13	1.0	5	1.7	5	1.3	33	1.8	2	1.0
Sexual contact[e] and injection drug use	24	5.3	47	2.3	38	3.4	52	2.1	42	2.9	31	2.5	3	1.0	58	15.2	150	8.2	28	13.9
Perinatal	4	0.9	14	0.7	12	1.1	16	0.6	9	0.6	3	0.2	1	0.3	0	0.0	3	0.2	4	2.0
Other[c]	1	0.2	18	0.9	2	0.2	9	0.4	4	0.3	1	0.1	1	0.3	1	0.3	8	0.4	0	0.0
Subtotal[d]	**456**	**100.0**	**2,065**	**100.0**	**1,119**	**100.0**	**2,476**	**100.0**	**1,431**	**100.0**	**1,260**	**100.0**	**302**	**100.0**	**381**	**100.0**	**1,837**	**100.0**	**201**	**100.0**
Federal poverty level																				
0–100%	11,980	58.4	51,932	70.2	30,440	57.0	76,327	55.4	30,883	57.1	35,861	57.7	6,986	54.7	6,071	59.7	37,298	57.1	6,905	46.3
101–138%	2,088	10.2	6,078	8.2	5,582	10.5	14,961	10.9	4,428	8.2	8,195	13.2	1,282	10.0	938	9.2	7,644	11.7	1,511	10.1
139–250%	3,374	16.4	11,019	14.9	9,191	17.2	27,638	20.1	8,655	16.0	11,570	18.6	2,670	20.9	1,623	16.0	12,117	18.6	2,784	18.7
251–400%	1,858	9.0	3,441	4.7	5,622	10.5	16,034	11.6	5,156	9.5	5,179	8.3	1,500	11.8	1,088	10.7	6,325	9.7	2,435	16.3
>400%	1,231	6.0	1,478	2.0	2,567	4.8	2,790	2.0	4,982	9.2	1,357	2.2	323	2.5	455	4.5	1,904	2.9	1,291	8.6
Subtotal	**20,531**	**100.0**	**73,948**	**100.0**	**53,402**	**100.0**	**137,750**	**100.0**	**54,104**	**100.0**	**62,162**	**100.0**	**12,761**	**100.0**	**10,175**	**100.0**	**65,288**	**100.0**	**14,926**	**100.0**
Health care coverage																				
Private employer	1,381	6.3	4,586	6.1	6,085	10.8	17,286	12.5	8,063	13.9	6,708	10.1	1,652	13.0	1,646	15.4	3,853	5.8	2,465	15.9
Private individual	2,498	11.4	2,837	3.8	4,062	7.2	23,302	16.8	4,529	7.8	5,266	7.9	1,869	14.7	928	8.7	2,848	4.3	1,166	7.5
Medicare	2,117	9.7	6,631	8.8	7,693	13.7	16,442	11.9	6,168	10.7	7,858	11.8	840	6.6	888	8.3	3,628	5.5	2,080	13.4
Medicaid	9,078	41.5	40,182	53.2	23,599	42.0	19,498	14.1	22,309	38.5	12,856	19.4	2,911	22.9	3,742	35.1	25,877	38.9	4,585	29.6
Medicare and Medicaid	2,794	12.8	5,926	7.8	4,757	8.5	7,860	5.7	4,315	7.5	3,011	4.5	1,773	13.9	593	5.6	6,424	9.7	1,600	10.3
Veterans Administration	21	0.1	24	<0.1	168	0.3	387	0.3	45	0.1	109	0.2	54	0.4	41	0.4	124	0.2	50	0.3
Indian Health Service	0	0.0	3	<0.1	0	0.0	10	<0.1	4	<0.1	7	<0.1	1	<0.1	4	<0.1	18	<0.1	160	1.0
Other plan	378	1.7	2,030	2.7	511	0.9	3,105	2.2	700	1.2	1,460	2.2	43	0.3	181	1.7	2,629	4.0	323	2.1
No coverage	1,013	4.6	7,361	9.7	4,529	8.1	39,988	28.9	6,171	10.7	25,656	38.6	732	5.8	1,058	9.9	8,618	13.0	784	5.1
Multiple coverages	2,618	12.0	5,927	7.8	4,766	8.5	10,668	7.7	5,578	9.6	3,458	5.2	2,841	22.3	1,595	14.9	12,463	18.7	2,283	14.7
Subtotal	**21,898**	**100.0**	**75,507**	**100.0**	**56,170**	**100.0**	**138,546**	**100.0**	**57,882**	**100.0**	**66,389**	**100.0**	**12,716**	**100.0**	**10,676**	**100.0**	**66,482**	**100.0**	**15,496**	**100.0**
Housing status																				
Stable	17,964	87.9	63,874	87.8	50,087	92.7	127,229	91.1	49,843	89.9	51,738	82.9	11,071	87.6	7,625	78.5	55,530	84.3	11,862	86.8
Temporary	1,501	7.3	6,206	8.5	2,021	3.7	7,670	5.5	3,137	5.7	6,138	9.8	831	6.6	1,584	16.3	4,452	6.8	804	5.9
Unstable	967	4.7	2,706	3.7	1,952	3.6	4,748	3.4	2,433	4.4	4,537	7.3	729	5.8	507	5.2	5,859	8.9	998	7.3
Subtotal	**20,432**	**100.0**	**72,786**	**100.0**	**54,060**	**100.0**	**139,647**	**100.0**	**55,413**	**100.0**	**62,413**	**100.0**	**12,631**	**100.0**	**9,716**	**100.0**	**65,841**	**100.0**	**13,664**	**100.0**
Total[f]	**23,070**	**—**	**77,367**	**—**	**61,105**	**—**	**147,367**	**—**	**60,668**	**—**	**70,971**	**—**	**13,215**	**—**	**11,523**	**—**	**68,230**	**—**	**17,793**	**—**

Note: See Technical Notes for the states/territories included in each region.
[a] Hispanics/Latinos can be of any race.
[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[c] Includes hemophilia and blood transfusion.
[d] Subtotals are reflective of available gender and transmission category information. The values may not sum to the subtotals for gender overall.
[e] Includes any sexual transmission category reported by transgender clients.
[f] Subtotals for each subpopulation are displayed to reflect the denominator used for the percentage calculation of each subpopulation; due to missing data, the values in each column may not sum to the column total.

Section 2.

National-Level Data: Retention in Care and Viral Suppression

Table 9. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by year and selected characteristics, 2018–2022—United States and 3 territories

	2018			2019			2020			2021			2022		
		Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)															
<13	784	691	88.1	643	562	87.4	548	470	85.8	527	454	86.1	505	429	85.0
13–14	309	273	88.3	261	218	83.5	222	186	83.8	215	170	79.1	181	156	86.2
15–19	1,711	1,408	82.3	1,659	1,331	80.2	1,451	1,170	80.6	1,397	1,119	80.1	1,363	1,088	79.8
20–24	11,092	8,352	75.3	11,063	8,347	75.4	10,131	7,649	75.5	9,857	7,165	72.7	9,306	6,845	73.6
25–29	28,394	21,018	74.0	28,402	21,089	74.3	26,316	19,487	74.1	25,313	18,032	71.2	23,742	16,870	71.1
30–34	33,442	25,331	75.7	36,353	27,389	75.3	37,295	28,097	75.3	38,530	28,058	72.8	39,051	28,068	71.9
35–39	33,975	26,435	77.8	35,284	27,215	77.1	34,982	26,959	77.1	36,061	26,728	74.1	37,105	27,169	73.2
40–44	34,180	27,468	80.4	34,834	27,824	79.9	35,063	27,294	77.8	36,104	27,728	76.8	36,085	27,218	75.4
45–49	41,753	34,052	81.6	39,947	32,509	81.4	36,591	29,243	79.9	35,384	27,900	78.8	34,309	26,680	77.8
50–54	51,957	43,179	83.1	49,794	41,254	82.8	46,777	37,855	80.9	44,827	35,892	80.1	42,003	33,238	79.1
55–59	48,564	41,102	84.6	51,116	42,994	84.1	50,442	41,309	81.9	50,559	41,314	81.7	49,049	39,517	80.6
60–64	31,591	27,132	85.9	34,222	29,272	85.5	35,727	29,682	83.1	38,137	31,662	83.0	40,012	32,801	82.0
≥65	24,921	21,648	86.9	28,901	24,970	86.4	31,251	25,881	82.8	35,330	29,564	83.7	39,404	32,682	82.9
Race/ethnicity															
American Indian/Alaska Native	1,526	1,176	77.1	1,566	1,172	74.8	1,453	1,084	74.6	1,645	1,223	74.3	1,693	1,253	74.0
Asian	4,883	4,058	83.1	5,106	4,268	83.6	5,258	4,196	79.8	5,541	4,422	79.8	5,482	4,295	78.3
Black/African American	163,905	131,402	80.2	170,079	136,164	80.1	163,804	129,579	79.1	166,050	128,848	77.6	162,720	124,502	76.5
Hispanic/Latino[a]	83,249	70,507	84.7	84,668	71,298	84.2	86,260	71,310	82.7	88,689	72,414	81.6	90,695	73,714	81.3
Native Hawaiian/Pacific Islander	468	365	78.0	522	423	81.0	550	416	75.6	619	443	71.6	551	386	70.1
White	83,617	66,692	79.8	85,393	67,656	79.2	83,968	64,648	77.0	84,014	64,345	76.6	82,329	62,140	75.5
Multiple races	3,579	2,817	78.7	3,166	2,486	78.5	3,210	2,412	75.1	3,212	2,344	73.0	6,037	4,659	77.2
Gender															
Male	243,509	195,963	80.5	249,224	199,831	80.2	247,150	194,474	78.7	251,540	195,111	77.6	250,408	192,298	76.8
Female	93,190	77,447	83.1	95,686	79,104	82.7	93,300	75,912	81.4	92,874	74,745	80.5	92,933	74,030	79.7
Transgender male	604	478	79.1	1,160	955	82.3	501	385	76.8	690	495	71.7	712	503	70.6
Transgender female	5,293	4,139	78.2	6,214	4,924	79.2	5,636	4,355	77.3	6,534	4,996	76.5	7,206	5,405	75.0
Other gender identity	83	68	81.9	177	145	81.9	178	138	77.5	499	389	78.0	725	446	61.5
Transmission category															
Male client															
Male-to-male sexual contact	151,047	121,119	80.2	153,048	122,565	80.1	152,688	120,322	78.8	155,653	121,211	77.9	158,534	121,930	76.9
Injection drug use	12,974	10,681	82.3	12,920	10,576	81.9	12,180	9,726	79.9	11,761	9,245	78.6	11,463	8,869	77.4
Male-to-male sexual contact and injection drug use	7,071	5,535	78.3	6,873	5,370	78.1	6,995	5,370	76.8	6,773	5,019	74.1	6,893	5,154	74.8
Heterosexual contact[b]	57,158	46,839	81.9	58,519	47,805	81.7	55,277	44,485	80.5	54,689	43,721	79.9	55,624	43,825	78.8
Perinatal	2,439	1,995	81.8	2,349	1,907	81.2	2,300	1,799	78.2	2,299	1,795	78.1	2,242	1,706	76.1
Other[c]	1,214	976	80.4	1,233	983	79.7	1,201	957	79.7	1,202	957	79.6	1,250	974	77.9
Female client															
Injection drug use	7,010	5,730	81.7	7,046	5,776	82.0	6,704	5,421	80.9	6,552	5,155	78.7	6,412	4,973	77.6
Heterosexual contact[b]	77,671	64,827	83.5	79,511	66,077	83.1	76,553	62,645	81.8	75,592	61,522	81.4	76,998	61,800	80.3
Perinatal	3,227	2,686	83.2	3,095	2,557	82.6	2,969	2,406	81.0	3,014	2,417	80.2	2,891	2,305	79.7
Other[c]	878	744	84.7	946	791	83.6	926	762	82.3	991	805	81.2	934	776	83.1
Transgender client															
Sexual contact[d]	4,948	3,885	78.5	6,420	5,164	80.4	5,255	4,108	78.2	6,158	4,736	76.9	6,817	5,069	74.4
Injection drug use	57	46	80.7	95	75	78.9	52	39	75.0	60	46	76.7	61	47	77.0
Sexual contact[d] and injection drug use	245	200	81.6	211	159	75.4	231	183	79.2	244	194	79.5	279	181	64.9
Perinatal	35	30	85.7	60	45	75.0	33	26	78.8	38	31	81.6	40	28	70.0
Other[c]	14	12	85.7	27	25	92.6	19	13	68.4	22	15	68.2	23	19	82.6

Table 9. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by year and selected characteristics, 2018–2022—United States and 3 territories *(cont.)*

	2018			2019			2020			2021			2022		
		Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Federal poverty level															
0–100%	206,781	167,656	81.1	211,356	170,431	80.6	209,021	166,404	79.6	202,135	158,284	78.3	204,555	157,618	77.1
101–138%	37,211	31,035	83.4	37,817	31,532	83.4	35,599	29,003	81.5	33,911	27,410	80.8	34,472	27,594	80.0
139–250%	53,592	43,874	81.9	57,856	47,498	82.1	56,340	45,112	80.1	60,400	48,255	79.9	59,934	47,813	79.8
251–400%	22,962	18,526	80.7	26,402	21,368	80.9	25,403	19,955	78.6	28,603	22,558	78.9	31,070	24,336	78.3
>400%	11,216	8,988	80.1	9,122	7,300	80.0	9,420	7,231	76.8	11,769	9,053	76.9	13,000	9,692	74.6
Health care coverage															
Private employer	36,566	28,849	78.9	37,346	29,598	79.3	35,329	27,226	77.1	36,107	27,554	76.3	38,145	28,850	75.6
Private individual	26,439	20,864	78.9	28,341	22,773	80.4	29,197	22,714	77.8	32,250	25,118	77.9	30,284	23,022	76.0
Medicare	34,585	28,900	83.6	36,265	30,239	83.4	35,134	28,502	81.1	34,755	28,312	81.5	34,988	28,311	80.9
Medicaid	104,683	85,387	81.6	104,997	84,478	80.5	105,109	83,093	79.1	109,158	84,861	77.7	107,933	82,149	76.1
Medicare and Medicaid	25,087	21,651	86.3	25,587	21,951	85.8	24,328	20,322	83.5	24,419	20,409	83.6	24,482	20,361	83.2
Veterans Administration	404	291	72.0	430	315	73.3	375	259	69.1	347	234	67.4	385	279	72.5
Indian Health Service	124	91	73.4	100	66	66.0	17	11	64.7	147	100	68.0	149	95	63.8
Other plan	4,932	3,908	79.2	5,278	4,120	78.1	6,651	5,503	82.7	6,467	4,926	76.2	7,486	5,947	79.4
No coverage	73,713	58,380	79.2	76,277	60,462	79.3	74,328	58,732	79.0	70,716	54,365	76.9	68,787	52,571	76.4
Multiple coverages	33,616	28,211	83.9	35,110	29,332	83.5	34,019	27,564	81.0	35,157	28,374	80.7	36,993	29,820	80.6
Housing status															
Stable	297,941	244,651	82.1	303,351	248,524	81.9	303,417	243,691	80.3	309,290	245,336	79.3	308,868	242,227	78.4
Temporary	23,447	17,902	76.4	22,666	17,120	75.5	20,850	15,568	74.7	19,603	14,207	72.5	20,823	15,112	72.6
Unstable	14,495	10,837	74.8	15,182	11,144	73.4	13,739	9,985	72.7	14,895	10,674	71.7	15,649	11,230	71.8
HHS region[e]															
Region 1	13,054	10,839	83.0	13,276	10,845	81.7	13,279	10,604	79.9	13,717	11,059	80.6	13,482	10,547	78.2
Region 2	46,949	40,748	86.8	51,950	45,064	86.7	51,052	43,792	85.8	50,776	43,556	85.8	53,520	45,096	84.3
Region 3	40,703	32,938	80.9	41,605	33,832	81.3	39,612	31,731	80.1	39,421	30,803	78.1	40,479	31,307	77.3
Region 4	95,558	78,742	82.4	97,751	80,876	82.7	92,081	74,130	80.5	95,179	76,106	80.0	99,785	79,205	79.4
Region 5	37,118	28,811	77.6	39,266	30,040	76.5	38,047	27,242	71.6	42,077	29,757	70.7	36,885	25,755	69.8
Region 6	42,717	31,794	74.4	42,878	32,579	76.0	44,068	34,187	77.6	41,927	30,546	72.9	40,672	30,247	74.4
Region 7	6,701	5,467	81.6	6,985	5,496	78.7	6,934	5,432	78.3	6,570	5,265	80.1	6,710	4,876	72.7
Region 8	6,228	5,034	80.8	6,525	5,082	77.9	6,158	4,278	69.5	6,125	4,455	72.7	6,615	4,697	71.0
Region 9	39,442	32,262	81.8	38,085	30,228	79.4	41,811	33,564	80.3	42,674	33,743	79.1	38,043	28,985	76.2
Region 10	5,680	4,605	81.1	6,447	4,868	75.5	6,235	4,272	68.5	5,826	4,216	72.4	5,919	4,267	72.1
Total[f]	**342,688**	**278,101**	**81.2**	**352,479**	**284,974**	**80.8**	**346,796**	**275,282**	**79.4**	**352,241**	**275,786**	**78.3**	**352,115**	**272,761**	**77.5**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
[a] Hispanics/Latinos can be of any race.
[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[c] Includes hemophilia and blood transfusion.
[d] Includes any sexual transmission category reported by transgender clients.
[e] See Technical Notes for the states/territories in each region.
[f] Because column totals were calculated independently of the values for the subpopulations, the values in each column may not sum to the column total.

Table 10. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by year and selected characteristics, 2018–2022—United States and 3 territories

	2018			2019			2020			2021			2022		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)															
<13	797	698	87.6	671	600	89.4	559	495	88.6	522	474	90.8	510	461	90.4
13–14	320	282	88.1	273	251	91.9	232	211	90.9	216	194	89.8	177	164	92.7
15–19	1,998	1,517	75.9	1,937	1,540	79.5	1,622	1,316	81.1	1,583	1,294	81.7	1,534	1,283	83.6
20–24	12,475	9,482	76.0	12,411	9,814	79.1	11,175	9,091	81.4	10,958	9,066	82.7	10,517	8,805	83.7
25–29	30,994	24,554	79.2	30,997	25,100	81.0	28,166	23,478	83.4	27,467	23,152	84.3	25,955	21,794	84.0
30–34	35,861	29,413	82.0	39,143	32,504	83.0	39,316	33,299	84.7	41,165	35,092	85.2	41,908	35,687	85.2
35–39	36,078	30,379	84.2	37,599	31,984	85.1	36,442	31,625	86.8	37,973	32,898	86.6	39,318	34,005	86.5
40–44	35,936	30,982	86.2	36,749	31,956	87.0	36,132	31,872	88.2	37,744	33,433	88.6	37,821	33,321	88.1
45–49	43,503	38,189	87.8	41,744	37,055	88.8	37,633	33,762	89.7	36,631	32,964	90.0	35,597	31,921	89.7
50–54	53,695	47,886	89.2	51,752	46,570	90.0	47,926	43,586	90.9	46,148	42,043	91.1	43,459	39,522	90.9
55–59	49,809	45,373	91.1	52,595	48,264	91.8	51,241	47,336	92.4	51,811	47,902	92.5	50,305	46,379	92.2
60–64	32,297	30,134	93.3	35,010	32,678	93.3	36,144	33,959	94.0	38,860	36,465	93.8	40,866	38,232	93.6
≥65	25,323	24,033	94.9	29,238	27,888	95.4	31,326	29,985	95.7	35,778	34,251	95.7	39,879	38,069	95.5
Race/ethnicity															
American Indian/Alaska Native	1,577	1,366	86.6	1,677	1,473	87.8	1,524	1,311	86.0	1,733	1,520	87.7	1,762	1,555	88.3
Asian	5,101	4,787	93.8	5,360	5,077	94.7	5,455	5,183	95.0	5,800	5,564	95.9	5,672	5,379	94.8
Black/African American	172,625	145,114	84.1	178,897	152,365	85.2	169,553	147,065	86.7	173,150	151,029	87.2	170,250	148,255	87.1
Hispanic/Latino[a]	86,641	77,194	89.1	88,865	80,079	90.1	88,748	80,971	91.2	92,480	84,551	91.4	95,234	86,919	91.3
Native Hawaiian/Pacific Islander	508	449	88.4	552	487	88.2	557	505	90.7	658	578	87.8	576	518	89.9
White	87,351	79,459	91.0	89,372	82,022	91.8	86,430	79,917	92.5	87,147	80,794	92.7	85,644	79,222	92.5
Multiple races	3,765	3,250	86.3	3,335	2,901	87.0	3,281	2,947	89.8	3,373	2,986	88.5	6,150	5,531	89.9
Gender															
Male	255,906	223,654	87.4	262,716	232,133	88.4	256,150	229,367	89.5	262,820	236,135	89.8	262,781	235,496	89.6
Female	96,920	84,151	86.8	99,436	87,440	87.9	95,198	85,099	89.4	95,900	86,200	89.9	95,864	86,205	89.9
Transgender male	629	545	86.6	1,208	1,017	84.2	520	453	87.1	728	611	83.9	754	656	87.0
Transgender female	5,552	4,502	81.1	6,551	5,434	82.9	5,848	4,922	84.2	6,810	5,760	84.6	7,635	6,567	86.0
Other gender identity	84	76	90.5	187	161	86.1	160	141	88.1	507	451	89.0	665	599	90.1
Transmission category															
Male client															
Male-to-male sexual contact	159,318	140,387	88.1	161,840	144,166	89.1	158,884	143,472	90.3	163,121	147,764	90.6	166,653	150,301	90.2
Injection drug use	13,405	11,660	87.0	13,352	11,644	87.2	12,290	10,819	88.0	11,997	10,607	88.4	11,749	10,383	88.4
Male-to-male sexual contact and injection drug use	7,366	6,238	84.7	7,212	6,220	86.2	7,118	6,236	87.6	6,975	6,101	87.5	7,142	6,233	87.3
Heterosexual contact[b]	59,911	52,076	86.9	61,305	53,777	87.7	57,160	50,886	89.0	56,922	50,832	89.3	58,316	51,972	89.1
Perinatal	2,559	1,909	74.6	2,469	1,905	77.2	2,362	1,851	78.4	2,395	1,911	79.8	2,318	1,873	80.8
Other[c]	1,272	1,181	92.8	1,292	1,189	92.0	1,237	1,145	92.6	1,257	1,183	94.1	1,313	1,217	92.7
Female client															
Injection drug use	7,210	6,139	85.1	7,226	6,274	86.8	6,593	5,833	88.5	6,579	5,836	88.7	6,473	5,738	88.6
Heterosexual contact[b]	80,921	70,849	87.6	82,661	73,162	88.5	78,336	70,462	89.9	78,210	70,780	90.5	79,581	72,026	90.5
Perinatal	3,352	2,481	74.0	3,234	2,447	75.7	3,056	2,388	78.1	3,095	2,455	79.3	2,976	2,381	80.0
Other[c]	902	813	90.1	974	899	92.3	945	877	92.8	1,012	942	93.1	958	899	93.8
Transgender client															
Sexual contact[d]	5,213	4,282	82.1	6,772	5,648	83.4	5,471	4,627	84.6	6,393	5,483	85.8	7,157	6,196	86.6
Injection drug use	57	52	91.2	89	73	82.0	47	37	78.7	65	51	78.5	66	56	84.8
Sexual contact[d] and injection drug use	252	211	83.7	217	180	82.9	226	189	83.6	242	197	81.4	272	222	81.6
Perinatal	35	24	68.6	61	45	73.8	33	25	75.8	38	31	81.6	39	34	87.2
Other[c]	14	13	92.9	30	26	86.7	20	16	80.0	25	19	76.0	25	22	88.0

Table 10. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by year and selected characteristics, 2018–2022—United States and 3 territories *(cont.)*

	2018			2019			2020			2021			2022		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Federal poverty level															
0–100%	217,406	183,906	84.6	222,493	190,526	85.6	215,658	187,725	87.0	210,972	184,498	87.5	214,536	187,421	87.4
101–138%	38,697	34,888	90.2	39,400	35,744	90.7	36,678	33,720	91.9	35,086	32,268	92.0	35,539	32,718	92.1
139–250%	56,182	51,243	91.2	60,818	55,851	91.8	58,594	54,483	93.0	62,962	58,355	92.7	62,560	57,900	92.6
251–400%	23,997	22,396	93.3	27,797	26,108	93.9	26,504	25,134	94.8	29,984	28,363	94.6	32,537	30,612	94.1
>400%	11,689	11,062	94.6	9,535	9,164	96.1	9,753	9,386	96.2	12,332	11,809	95.8	13,553	12,891	95.1
Health care coverage															
Private employer	38,526	35,820	93.0	39,488	36,992	93.7	36,917	34,891	94.5	37,928	35,911	94.7	39,809	37,602	94.5
Private individual	27,645	25,534	92.4	29,705	27,650	93.1	30,526	28,643	93.8	33,391	31,341	93.9	31,457	29,409	93.5
Medicare	35,531	32,468	91.4	37,197	34,240	92.1	35,593	33,127	93.1	35,395	32,942	93.1	35,664	33,239	93.2
Medicaid	108,755	91,569	84.2	109,781	93,359	85.0	107,328	92,883	86.5	112,922	98,250	87.0	112,099	97,674	87.1
Medicare and Medicaid	25,627	23,032	89.9	26,055	23,782	91.3	24,449	22,389	91.6	24,777	22,906	92.4	24,954	23,017	92.2
Veterans Administration	421	391	92.9	472	437	92.6	383	352	91.9	358	331	92.5	404	377	93.3
Indian Health Service	138	120	87.0	119	102	85.7	21	14	66.7	167	147	88.0	162	145	89.5
Other plan	5,181	4,543	87.7	5,607	4,899	87.4	6,932	6,238	90.0	6,800	6,088	89.5	7,859	7,112	90.5
No coverage	79,959	65,555	82.0	83,124	69,300	83.4	79,360	67,695	85.3	76,405	65,410	85.6	74,999	63,835	85.1
Multiple coverages	34,735	31,686	91.2	35,918	33,177	92.4	34,539	32,173	93.1	36,137	33,646	93.1	37,919	35,070	92.5
Housing status															
Stable	311,565	275,413	88.4	317,808	283,810	89.3	313,689	283,456	90.4	321,816	292,101	90.8	322,650	292,294	90.6
Temporary	25,167	20,317	80.7	24,417	20,060	82.2	21,898	18,345	83.8	21,068	17,603	83.6	22,522	18,946	84.1
Unstable	15,621	11,309	72.4	16,404	12,223	74.5	14,364	11,037	76.8	15,843	12,252	77.3	16,616	12,952	77.9
HHS region[e]															
Region 1	13,150	12,187	92.7	13,676	12,821	93.7	13,010	12,260	94.2	13,736	13,022	94.8	13,480	12,777	94.8
Region 2	48,793	42,601	87.3	53,660	47,300	88.1	52,267	46,729	89.4	52,046	46,716	89.8	55,398	50,174	90.6
Region 3	42,366	37,601	88.8	43,181	38,643	89.5	39,997	36,293	90.7	40,300	36,671	91.0	41,624	37,646	90.4
Region 4	100,779	86,483	85.8	103,000	89,439	86.8	96,342	85,075	88.3	99,805	88,555	88.7	105,299	93,042	88.4
Region 5	39,034	34,434	88.2	41,471	37,003	89.2	38,883	34,868	89.7	43,931	39,820	90.6	38,654	35,070	90.7
Region 6	45,331	38,070	84.0	46,297	39,178	84.6	47,122	41,038	87.1	44,708	38,645	86.4	43,162	37,380	86.6
Region 7	7,482	6,618	88.5	7,443	6,686	89.8	7,452	6,741	90.5	7,183	6,541	91.1	7,076	6,442	91.0
Region 8	6,383	5,799	90.9	6,648	6,114	92.0	5,875	5,437	92.5	6,101	5,699	93.4	6,381	5,989	93.9
Region 9	40,757	36,094	88.6	39,865	35,681	89.5	42,547	38,649	90.8	44,447	40,406	90.9	39,834	36,007	90.4
Region 10	5,918	5,398	91.2	6,602	6,226	94.3	6,379	5,919	92.8	6,123	5,674	92.7	6,358	5,830	91.7
Total[f]	**359,101**	**312,937**	**87.1**	**370,119**	**326,204**	**88.1**	**357,914**	**320,015**	**89.4**	**366,856**	**329,228**	**89.7**	**367,846**	**329,643**	**89.6**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.

[a] Hispanics/Latinos can be of any race.

[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[c] Includes hemophilia and blood transfusion.

[d] Includes any sexual transmission category reported by transgender clients.

[e] See Technical Notes for the states/territories in each region.

[f] Because column totals were calculated independently of the values for the subpopulations, the values in each column may not sum to the column total.

Table 11a. Retention in care among women (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latina[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)																								
13–14	0	—	—	8	7	87.5	65	56	86.2	8	7	87.5	1	1	100.0	8	5	62.5	2	2	100.0	95	80	84.2
15–19	0	—	—	23	20	87.0	322	255	79.2	93	80	86.0	0	—	—	63	49	77.8	5	4	80.0	510	410	80.4
20–24	4	4	100.0	16	13	81.3	935	739	79.0	283	225	79.5	5	5	100.0	183	128	69.9	41	33	80.5	1,479	1,155	78.1
25–29	12	9	75.0	37	30	81.1	2,183	1,581	72.4	705	552	78.3	7	4	57.1	499	357	71.5	70	44	62.9	3,540	2,597	73.4
30–34	22	15	68.2	80	64	80.0	3,719	2,694	72.4	1,108	846	76.4	9	5	55.6	945	677	71.6	143	100	69.9	6,080	4,440	73.0
35–39	29	15	51.7	145	120	82.8	4,680	3,503	74.9	1,497	1,179	78.8	10	6	60.0	1,204	835	69.4	140	102	72.9	7,751	5,787	74.7
40–44	56	44	78.6	186	141	75.8	5,888	4,522	76.8	2,105	1,746	82.9	15	10	66.7	1,530	1,114	72.8	192	150	78.1	10,019	7,767	77.5
45–49	41	33	80.5	173	131	75.7	6,752	5,296	78.4	2,424	2,035	84.0	8	6	75.0	1,566	1,178	75.2	191	145	75.9	11,204	8,855	79.0
50–54	65	50	76.9	150	108	72.0	7,890	6,283	79.6	2,769	2,351	84.9	12	9	75.0	2,057	1,580	76.8	254	204	80.3	13,256	10,627	80.2
55–59	63	49	77.8	111	95	85.6	8,560	6,972	81.4	2,925	2,546	87.0	13	9	69.2	2,090	1,638	78.4	280	233	83.2	14,085	11,573	82.2
60–64	47	37	78.7	96	83	86.5	7,326	6,003	81.9	2,623	2,318	88.4	7	5	71.4	1,742	1,383	79.4	255	212	83.1	12,129	10,064	83.0
≥65	46	37	80.4	106	90	84.9	7,417	6,137	82.7	2,941	2,577	87.6	8	6	75.0	1,641	1,295	78.9	277	241	87.0	12,500	10,432	83.5
Transmission category																								
Injection drug use	73	53	72.6	16	10	62.5	2,530	2,011	79.5	1,164	950	81.6	6	5	83.3	2,340	1,713	73.2	265	220	83.0	6,412	4,973	77.6
Heterosexual contact[c]	277	211	76.2	863	697	80.8	47,922	38,085	79.5	16,044	13,692	85.3	77	53	68.8	10,123	7,744	76.5	1,441	1,137	78.9	76,998	61,800	80.3
Perinatal	2	2	100.0	50	41	82.0	1,662	1,308	78.7	535	436	81.5	2	1	50.0	276	213	77.2	87	65	74.7	2,630	2,079	79.0
Other[d]	2	2	100.0	37	29	78.4	507	419	82.6	205	174	84.9	1	1	100.0	154	128	83.1	20	16	80.0	933	775	83.1
Federal poverty level																								
0–100%	276	207	75.0	612	497	81.2	36,138	28,591	79.1	14,444	12,251	84.8	61	38	62.3	8,202	6,116	74.6	1,151	926	80.5	61,122	48,798	79.8
101–138%	32	25	78.1	121	93	76.9	5,545	4,434	80.0	1,615	1,382	85.6	10	8	80.0	1,490	1,196	80.3	173	143	82.7	9,047	7,324	81.0
139–250%	56	43	76.8	190	158	83.2	8,267	6,684	80.9	2,271	1,921	84.6	16	12	75.0	2,045	1,615	79.0	254	201	79.1	13,177	10,699	81.2
251–400%	7	7	100.0	125	99	79.2	3,214	2,564	79.8	656	548	83.5	4	4	100.0	972	747	76.9	177	132	74.6	5,168	4,108	79.5
>400%	8	7	87.5	40	34	85.0	1,149	861	74.9	216	161	74.5	1	1	100.0	425	316	74.4	76	58	76.3	1,925	1,447	75.2
Health care coverage																								
Private employer	13	12	92.3	135	102	75.6	4,846	3,727	76.9	894	734	82.1	10	6	60.0	1,266	957	75.6	196	156	79.6	7,392	5,714	77.3
Private individual	18	14	77.8	105	83	79.0	4,283	3,344	78.1	883	706	80.0	3	3	100.0	1,082	811	75.0	64	49	76.6	6,461	5,026	77.8
Medicare	29	17	58.6	39	32	82.1	6,216	5,073	81.6	1,468	1,286	87.6	6	4	66.7	1,624	1,284	79.1	114	93	81.6	9,541	7,821	82.0
Medicaid	145	107	73.8	410	338	82.4	21,509	16,594	77.1	8,236	6,937	84.2	41	24	58.5	4,983	3,687	74.0	612	478	78.1	36,152	28,325	78.3
Medicare and Medicaid	32	26	81.3	35	31	88.6	4,809	4,027	83.7	1,484	1,310	88.3	2	1	50.0	1,456	1,178	80.9	251	224	89.2	8,083	6,809	84.2
Veterans Administration	5	5	100.0	5	5	100.0	50	36	72.0	12	12	100.0	2	2	100.0	25	19	76.0	5	3	60.0	104	82	78.8
Indian Health Service	36	25	69.4	0	—	—	1	0	0.0	1	1	100.0	0	—	—	0	—	—	0	—	—	38	26	68.4
Other plan	2	1	50.0	34	25	73.5	840	698	83.1	469	393	83.8	4	4	100.0	223	165	74.0	16	12	75.0	1,606	1,308	81.4
No coverage	41	32	78.0	222	172	77.5	7,248	5,711	78.8	4,092	3,426	83.7	12	9	75.0	1,340	977	72.9	230	172	74.8	13,214	10,519	79.6
Multiple coverages	62	52	83.9	131	107	81.7	5,551	4,611	83.1	1,854	1,605	86.6	14	12	85.7	1,434	1,113	77.6	319	268	84.0	9,418	7,808	82.9

Table 11a. Retention in care among women (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latina[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Housing status																								
Stable	306	231	75.5	1,042	839	80.5	50,288	40,041	79.6	17,615	14,971	85.0	85	59	69.4	11,787	9,054	76.8	1,736	1,401	80.7	83,204	66,849	80.3
Temporary	23	20	87.0	47	36	76.6	3,005	2,309	76.8	950	753	79.3	5	3	60.0	802	578	72.1	73	47	64.4	4,917	3,752	76.3
Unstable	42	31	73.8	11	8	72.7	1,568	1,144	73.0	756	625	82.7	4	3	75.0	724	486	67.1	29	17	58.6	3,147	2,325	73.9
HHS region[e]																								
Region 1	17	16	94.1	52	45	86.5	1,754	1,404	80.0	1,516	1,219	80.4	2	2	100.0	831	625	75.2	46	32	69.6	4,248	3,366	79.2
Region 2	25	24	96.0	168	146	86.9	8,193	6,823	83.3	7,610	6,722	88.3	15	13	86.7	1,320	1,056	80.0	123	108	87.8	17,581	14,996	85.3
Region 3	41	33	80.5	92	74	80.4	8,673	6,828	78.7	1,441	1,238	85.9	4	3	75.0	1,781	1,340	75.2	1,119	921	82.3	13,212	10,480	79.3
Region 4	60	48	80.0	155	134	86.5	19,971	16,102	80.6	2,540	2,152	84.7	12	11	91.7	4,179	3,237	77.5	187	139	74.3	27,144	21,854	80.5
Region 5	14	7	50.0	110	81	73.6	5,501	3,954	71.9	920	711	77.3	5	2	40.0	1,254	877	69.9	105	61	58.1	7,979	5,739	71.9
Region 6	66	45	68.2	186	147	79.0	6,418	4,909	76.5	2,354	1,911	81.2	8	7	87.5	1,316	988	75.1	60	46	76.7	10,470	8,090	77.3
Region 7	7	3	42.9	44	31	70.5	992	735	74.1	120	91	75.8	2	2	100.0	448	304	67.9	33	24	72.7	1,646	1,190	72.3
Region 8	24	17	70.8	30	20	66.7	435	309	71.0	272	217	79.8	3	1	33.3	326	226	69.3	20	16	80.0	1,121	816	72.8
Region 9	53	43	81.1	211	161	76.3	1,781	1,353	76.0	2,301	1,865	81.1	36	18	50.0	1,318	1,038	78.8	89	68	76.4	5,812	4,560	78.5
Region 10	70	52	74.3	50	34	68.0	476	378	79.4	117	89	76.1	6	6	100.0	318	221	69.5	28	22	78.6	1,082	808	74.7
Total[b]	**385**	**293**	**76.1**	**1,131**	**902**	**79.8**	**55,737**	**44,041**	**79.0**	**19,481**	**16,462**	**84.5**	**95**	**66**	**69.5**	**13,528**	**10,239**	**75.7**	**1,850**	**1,470**	**79.5**	**92,648**	**73,787**	**79.6**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.

[a] Hispanics/Latinas can be of any race.

[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.

[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[d] Includes hemophilia and blood transfusion.

[e] See Technical Notes for the states/territories in each region.

Table 11b. Viral suppression among women (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latina[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)																								
13–14	0	—	—	8	8	100.0	64	59	92.2	7	5	71.4	1	1	100.0	6	6	100.0	2	2	100.0	92	85	92.4
15–19	0	—	—	22	21	95.5	343	281	81.9	96	87	90.6	0	—	—	62	58	93.5	6	6	100.0	533	456	85.6
20–24	6	4	66.7	16	13	81.3	1,015	823	81.1	323	269	83.3	5	4	80.0	214	177	82.7	46	33	71.7	1,636	1,331	81.4
25–29	16	11	68.8	38	33	86.8	2,338	1,869	79.9	763	628	82.3	8	6	75.0	527	447	84.8	72	65	90.3	3,795	3,086	81.3
30–34	25	19	76.0	78	74	94.9	3,952	3,243	82.1	1,170	1,022	87.4	10	8	80.0	1,010	880	87.1	154	119	77.3	6,446	5,404	83.8
35–39	31	23	74.2	155	150	96.8	4,924	4,141	84.1	1,568	1,342	85.6	9	9	100.0	1,291	1,101	85.3	144	126	87.5	8,165	6,927	84.8
40–44	59	47	79.7	184	177	96.2	6,113	5,329	87.2	2,208	1,946	88.1	16	14	87.5	1,593	1,382	86.8	195	178	91.3	10,418	9,117	87.5
45–49	40	36	90.0	164	156	95.1	6,962	6,177	88.7	2,492	2,283	91.6	8	6	75.0	1,618	1,433	88.6	190	176	92.6	11,522	10,311	89.5
50–54	59	54	91.5	147	139	94.6	8,147	7,305	89.7	2,833	2,627	92.7	13	12	92.3	2,106	1,936	91.9	246	225	91.5	13,602	12,345	90.8
55–59	59	57	96.6	111	108	97.3	8,750	8,008	91.5	2,988	2,799	93.7	13	12	92.3	2,139	1,989	93.0	277	261	94.2	14,379	13,274	92.3
60–64	48	44	91.7	93	89	95.7	7,439	6,919	93.0	2,664	2,527	94.9	8	7	87.5	1,799	1,699	94.4	247	234	94.7	12,333	11,552	93.7
≥65	42	39	92.9	105	102	97.1	7,539	7,134	94.6	2,961	2,849	96.2	8	7	87.5	1,662	1,605	96.6	274	261	95.3	12,655	12,057	95.3
Transmission category																								
Injection drug use	73	57	78.1	14	14	100.0	2,553	2,289	89.7	1,176	1,072	91.2	6	5	83.3	2,377	2,057	86.5	255	230	90.2	6,473	5,738	88.6
Heterosexual contact[c]	285	253	88.8	891	857	96.2	49,526	44,373	89.6	16,572	15,272	92.2	79	69	87.3	10,536	9,648	91.6	1,447	1,333	92.1	79,581	72,026	90.5
Perinatal	2	2	100.0	52	49	94.2	1,712	1,320	77.1	549	431	78.5	3	3	100.0	279	252	90.3	90	64	71.1	2,706	2,136	78.9
Other[d]	3	3	100.0	33	31	93.9	516	479	92.8	214	202	94.4	1	1	100.0	160	153	95.6	21	21	100.0	957	898	93.8
Federal poverty level																								
0–100%	283	244	86.2	609	577	94.7	37,496	32,874	87.7	14,873	13,541	91.0	63	53	84.1	8,505	7,484	88.0	1,149	1,022	88.9	63,235	56,022	88.6
101–138%	34	30	88.2	122	115	94.3	5,663	5,155	91.0	1,666	1,558	93.5	11	11	100.0	1,541	1,443	93.6	170	152	89.4	9,247	8,501	91.9
139–250%	47	42	89.4	190	187	98.4	8,534	7,846	91.9	2,350	2,200	93.6	17	14	82.4	2,119	2,020	95.3	266	253	95.1	13,600	12,629	92.9
251–400%	9	8	88.9	125	117	93.6	3,315	3,117	94.0	679	632	93.1	4	4	100.0	1,030	989	96.0	176	169	96.0	5,350	5,048	94.4
>400%	6	6	100.0	41	41	100.0	1,188	1,089	91.7	224	203	90.6	1	1	100.0	445	427	96.0	76	75	98.7	1,995	1,855	93.0
Health care coverage																								
Private employer	15	14	93.3	146	141	96.6	5,020	4,693	93.5	906	852	94.0	10	10	100.0	1,331	1,275	95.8	195	189	96.9	7,654	7,203	94.1
Private individual	16	15	93.8	106	104	98.1	4,373	4,063	92.9	909	861	94.7	3	3	100.0	1,116	1,056	94.6	65	61	93.8	6,613	6,186	93.5
Medicare	30	29	96.7	37	37	100.0	6,341	5,840	92.1	1,480	1,399	94.5	7	7	100.0	1,678	1,600	95.4	114	103	90.4	9,732	9,058	93.1
Medicaid	151	123	81.5	412	386	93.7	22,221	19,212	86.5	8,444	7,658	90.7	43	35	81.4	5,169	4,527	87.6	621	541	87.1	37,255	32,648	87.6
Medicare and Medicaid	25	24	96.0	35	33	94.3	4,912	4,500	91.6	1,514	1,438	95.0	2	1	50.0	1,483	1,377	92.9	252	233	92.5	8,241	7,623	92.5
Veterans Administration	5	5	100.0	6	6	100.0	53	49	92.5	12	12	100.0	2	2	100.0	28	28	100.0	7	7	100.0	113	109	96.5
Indian Health Service	37	32	86.5	0	—	—	0	—	—	1	1	100.0	0	—	—	0	—	—	0	—	—	38	33	86.8
Other plan	2	2	100.0	36	35	97.2	869	768	88.4	491	448	91.2	4	3	75.0	233	207	88.8	17	14	82.4	1,669	1,492	89.4
No coverage	39	31	79.5	196	184	93.9	7,762	6,694	86.2	4,335	3,876	89.4	12	10	83.3	1,452	1,224	84.3	236	222	94.1	14,070	12,276	87.2
Multiple coverages	63	58	92.1	134	132	98.5	5,648	5,145	91.1	1,888	1,764	93.4	14	13	92.9	1,446	1,338	92.5	314	288	91.7	9,564	8,788	91.9

Table 11b. Viral suppression among women (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latina[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Housing status																								
Stable	306	278	90.8	1,043	998	95.7	52,004	46,649	89.7	18,150	16,720	92.1	89	78	87.6	12,221	11,273	92.2	1,734	1,599	92.2	85,914	77,926	90.7
Temporary	23	19	82.6	51	49	96.1	3,216	2,728	84.8	996	874	87.8	5	5	100.0	859	732	85.2	74	52	70.3	5,243	4,472	85.3
Unstable	46	31	67.4	10	8	80.0	1,652	1,280	77.5	770	655	85.1	4	2	50.0	748	529	70.7	39	29	74.4	3,283	2,546	77.6
HHS region[e]																								
Region 1	17	17	100.0	50	49	98.0	1,776	1,672	94.1	1,547	1,467	94.8	4	4	100.0	818	772	94.4	39	38	97.4	4,280	4,043	94.5
Region 2	25	25	100.0	181	173	95.6	8,478	7,599	89.6	7,770	7,120	91.6	15	14	93.3	1,362	1,270	93.2	127	115	90.6	18,092	16,434	90.8
Region 3	30	27	90.0	95	92	96.8	8,803	7,907	89.8	1,487	1,364	91.7	4	3	75.0	1,820	1,650	90.7	1,102	1,008	91.5	13,404	12,108	90.3
Region 4	65	59	90.8	159	152	95.6	20,802	18,374	88.3	2,627	2,414	91.9	12	12	100.0	4,361	3,903	89.5	187	168	89.8	28,261	25,125	88.9
Region 5	15	10	66.7	110	105	95.5	5,706	5,080	89.0	975	910	93.3	5	3	60.0	1,338	1,233	92.2	109	101	92.7	8,337	7,512	90.1
Region 6	70	56	80.0	148	140	94.6	6,611	5,786	87.5	2,434	2,164	88.9	8	7	87.5	1,423	1,234	86.7	66	57	86.4	10,786	9,470	87.8
Region 7	8	7	87.5	44	44	100.0	1,037	933	90.0	134	121	90.3	2	2	100.0	460	429	93.3	34	31	91.2	1,719	1,567	91.2
Region 8	22	19	86.4	34	31	91.2	429	397	92.5	276	257	93.1	2	2	100.0	313	293	93.6	20	18	90.0	1,106	1,026	92.8
Region 9	51	45	88.2	214	203	94.9	1,809	1,633	90.3	2,397	2,179	90.9	39	31	79.5	1,365	1,245	91.2	101	92	91.1	6,001	5,448	90.8
Region 10	72	60	83.3	53	49	92.5	529	493	93.2	123	116	94.3	6	6	100.0	314	284	90.4	28	25	89.3	1,143	1,050	91.9
Total[b]	**385**	**334**	**86.8**	**1,121**	**1,070**	**95.5**	**57,586**	**51,288**	**89.1**	**20,073**	**18,384**	**91.6**	**99**	**86**	**86.9**	**14,027**	**12,713**	**90.6**	**1,853**	**1,686**	**91.0**	**95,576**	**85,945**	**89.9**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.

[a] Hispanics/Latinas can be of any race.

[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.

[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[d] Includes hemophilia and blood transfusion.

[e] See Technical Notes for the states/territories in each region.

Table 12a. Retention in care among men (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)																								
13–14	3	2	66.7	2	2	100.0	54	46	85.2	10	10	100.0	0	—	—	12	11	91.7	2	2	100.0	86	76	88.4
15–19	4	2	50.0	24	20	83.3	517	421	81.4	187	147	78.6	1	1	100.0	65	48	73.8	15	13	86.7	825	659	79.9
20–24	38	20	52.6	107	87	81.3	4,150	3,017	72.7	1,978	1,469	74.3	12	9	75.0	843	607	72.0	135	91	67.4	7,340	5,361	73.0
25–29	100	62	62.0	324	220	67.9	9,596	6,650	69.3	5,564	4,164	74.8	43	26	60.5	2,872	1,996	69.5	379	266	70.2	19,078	13,506	70.8
30–34	156	108	69.2	553	418	75.6	15,311	10,838	70.8	8,873	6,665	75.1	61	42	68.9	5,477	3,767	68.8	543	390	71.8	31,264	22,430	71.7
35–39	125	91	72.8	517	384	74.3	11,938	8,472	71.0	8,700	6,761	77.7	56	37	66.1	5,917	4,156	70.2	421	298	70.8	27,941	20,374	72.9
40–44	135	103	76.3	526	395	75.1	9,406	6,880	73.1	8,287	6,558	79.1	49	34	69.4	6,021	4,296	71.4	346	259	74.9	24,995	18,678	74.7
45–49	115	86	74.8	551	448	81.3	7,748	5,871	75.8	7,565	6,159	81.4	33	25	75.8	5,807	4,265	73.4	306	226	73.9	22,310	17,216	77.2
50–54	147	101	68.7	604	486	80.5	9,781	7,616	77.9	8,103	6,720	82.9	37	31	83.8	8,732	6,631	75.9	369	276	74.8	27,966	22,000	78.7
55–59	173	133	76.9	437	362	82.8	12,638	9,998	79.1	8,337	7,039	84.4	59	41	69.5	11,894	9,239	77.7	545	437	80.2	34,282	27,387	79.9
60–64	142	120	84.5	263	212	80.6	10,690	8,615	80.6	5,743	4,969	86.5	26	18	69.2	9,969	7,964	79.9	509	420	82.5	27,486	22,413	81.5
≥65	104	83	79.8	252	211	83.7	10,568	8,680	82.1	5,186	4,538	87.5	26	18	69.2	9,838	7,946	80.8	490	421	85.9	26,615	22,012	82.7
Transmission category																								
Male-to-male sexual contact	788	570	72.3	2,637	2,031	77.0	58,252	43,409	74.5	44,218	35,779	80.9	289	207	71.6	48,872	37,347	76.4	2,457	1,833	74.6	158,534	121,930	76.9
Injection drug use	68	48	70.6	111	93	83.8	3,994	3,137	78.5	3,346	2,710	81.0	11	6	54.5	3,495	2,513	71.9	397	335	84.4	11,463	8,869	77.4
Male-to-male sexual contact and injection drug use	86	69	80.2	48	37	77.1	1,359	995	73.2	1,413	1,078	76.3	10	5	50.0	3,773	2,818	74.7	179	133	74.3	6,893	5,154	74.8
Heterosexual contact[c]	150	115	76.7	841	696	82.8	32,012	24,787	77.4	14,492	12,069	83.3	40	24	60.0	7,007	5,306	75.7	830	663	79.9	55,624	43,825	78.8
Perinatal	13	8	61.5	36	30	83.3	1,234	927	75.1	425	327	76.9	7	7	100.0	263	187	71.1	51	38	74.5	2,040	1,534	75.2
Other[d]	7	5	71.4	63	50	79.4	363	295	81.3	285	227	79.6	1	1	100.0	501	372	74.3	20	16	80.0	1,248	973	78.0
Federal poverty level																								
0–100%	742	530	71.4	2,077	1,617	77.9	60,489	45,039	74.5	39,488	31,697	80.3	187	125	66.8	30,784	22,700	73.7	2,272	1,768	77.8	137,073	104,195	76.0
101–138%	119	85	71.4	361	289	80.1	9,590	7,515	78.4	6,699	5,540	82.7	31	21	67.7	7,379	5,868	79.5	410	317	77.3	24,752	19,747	79.8
139–250%	204	163	79.9	799	638	79.8	16,960	13,281	78.3	12,807	10,483	81.9	91	69	75.8	13,673	10,740	78.5	682	515	75.5	45,549	36,154	79.4
251–400%	101	82	81.2	518	406	78.4	9,525	7,345	77.1	6,201	5,006	80.7	52	36	69.2	8,392	6,505	77.5	464	339	73.1	25,368	19,807	78.1
>400%	49	38	77.6	312	233	74.7	3,117	2,305	73.9	2,094	1,603	76.6	26	18	69.2	4,933	3,642	73.8	182	131	72.0	10,813	8,047	74.4
Health care coverage																								
Private employer	127	100	78.7	631	489	77.5	11,842	8,831	74.6	6,191	4,930	79.6	60	41	68.3	10,465	7,727	73.8	529	389	73.5	30,110	22,684	75.3
Private individual	68	49	72.1	512	385	75.2	9,605	7,215	75.1	4,728	3,625	76.7	34	26	76.5	7,974	6,014	75.4	230	173	75.2	23,273	17,564	75.5
Medicare	126	97	77.0	170	142	83.5	10,878	8,722	80.2	3,486	2,942	84.4	24	9	37.5	9,971	7,978	80.0	268	213	79.5	25,068	20,204	80.6
Medicaid	347	248	71.5	1,156	905	78.3	30,175	21,984	72.9	19,103	15,372	80.5	125	87	69.6	14,893	10,877	73.0	1,241	906	73.0	67,817	50,925	75.1
Medicare and Medicaid	76	65	85.5	144	130	90.3	6,606	5,425	82.1	3,241	2,793	86.2	19	16	84.2	5,411	4,371	80.8	495	427	86.3	16,044	13,269	82.7
Veterans Administration	4	4	100.0	6	5	83.3	108	72	66.7	29	19	65.5	2	1	50.0	119	86	72.3	5	5	100.0	275	194	70.5
Indian Health Service	97	59	60.8	0	—	—	3	2	66.7	4	2	50.0	0	—	—	5	4	80.0	1	1	100.0	110	68	61.8
Other plan	14	13	92.9	127	89	70.1	1,791	1,435	80.1	2,284	1,869	81.8	10	7	70.0	1,224	898	73.4	29	20	69.0	5,583	4,412	79.0
No coverage	186	130	69.9	832	628	75.5	21,403	15,694	73.3	22,358	17,874	79.9	68	49	72.1	7,973	5,686	71.3	582	429	73.7	53,595	40,616	75.8
Multiple coverages	181	140	77.3	557	459	82.4	9,244	7,323	79.2	6,689	5,504	82.3	57	42	73.7	8,959	7,041	78.6	629	518	82.4	26,545	21,204	79.9

Table 12a. Retention in care among men (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Housing status																								
Stable	1,047	777	74.2	3,733	2,933	78.6	89,076	68,089	76.4	59,158	47,974	81.1	352	250	71.0	59,668	45,711	76.6	3,635	2,800	77.0	218,134	169,611	77.8
Temporary	81	55	67.9	232	170	73.3	6,936	4,887	70.5	4,310	3,245	75.3	24	18	75.0	3,338	2,288	68.5	214	167	78.0	15,217	10,883	71.5
Unstable	83	58	69.9	100	75	75.0	4,621	3,075	66.5	4,118	3,326	80.8	20	9	45.0	2,606	1,744	66.9	170	108	63.5	11,774	8,427	71.6
HHS region[e]																								
Region 1	26	22	84.6	178	142	79.8	1,860	1,477	79.4	2,726	2,172	79.7	8	6	75.0	3,978	3,020	75.9	114	92	80.7	9,002	7,002	77.8
Region 2	63	46	73.0	731	626	85.6	11,041	8,870	80.3	16,671	14,541	87.2	54	42	77.8	4,627	3,767	81.4	169	139	82.2	34,017	28,556	83.9
Region 3	76	66	86.8	299	235	78.6	13,741	10,284	74.8	3,210	2,608	81.2	15	14	93.3	7,301	5,561	76.2	1,616	1,320	81.7	26,425	20,200	76.4
Region 4	183	141	77.0	452	378	83.6	40,154	31,309	78.0	10,963	9,088	82.9	51	35	68.6	18,089	14,272	78.9	610	476	78.0	70,625	55,797	79.0
Region 5	112	75	67.0	434	313	72.1	13,337	9,165	68.7	4,727	3,492	73.9	55	40	72.7	8,260	5,676	68.7	459	261	56.9	27,667	19,189	69.4
Region 6	279	209	74.9	429	300	69.9	10,941	7,788	71.2	11,040	8,443	76.5	30	20	66.7	6,061	4,373	72.1	223	165	74.0	29,237	21,450	73.4
Region 7	21	11	52.4	87	71	81.6	1,852	1,296	70.0	583	454	77.9	9	5	55.6	2,241	1,646	73.4	92	68	73.9	4,887	3,552	72.7
Region 8	76	52	68.4	66	50	75.8	624	452	72.4	1,565	1,204	76.9	8	3	37.5	2,576	1,803	70.0	79	55	69.6	5,113	3,699	72.3
Region 9	237	178	75.1	1,207	919	76.1	4,772	3,375	70.7	14,675	11,382	77.6	139	91	65.5	9,449	7,210	76.3	468	351	75.0	31,095	23,594	75.9
Region 10	149	99	66.4	173	129	74.6	728	507	69.6	989	724	73.2	29	22	75.9	2,405	1,725	71.7	119	89	74.8	4,688	3,347	71.4
Total[b]	**1,242**	**911**	**73.3**	**4,160**	**3,245**	**78.0**	**102,397**	**77,104**	**75.3**	**68,533**	**55,199**	**80.5**	**403**	**282**	**70.0**	**67,447**	**50,926**	**75.5**	**4,060**	**3,099**	**76.3**	**250,188**	**192,112**	**76.8**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.

[a] Hispanics/Latinos can be of any race.

[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.

[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[d] Includes hemophilia and blood transfusion.

[e] See Technical Notes for the states/territories in each region.

Table 12b. Retention in care among gay, bisexual, and other men who have sex with men (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)																								
13–14	1	0	0.0	0	—	—	1	1	100.0	0	—	—	0	—	—	0	—	—	0	—	—	2	1	50.0
15–19	4	2	50.0	5	4	80.0	248	191	77.0	102	81	79.4	0	—	—	26	21	80.8	12	10	83.3	400	311	77.8
20–24	29	15	51.7	76	64	84.2	3,332	2,432	73.0	1,546	1,180	76.3	6	4	66.7	652	479	73.5	109	76	69.7	5,789	4,281	74.0
25–29	71	48	67.6	267	183	68.5	7,713	5,424	70.3	4,393	3,350	76.3	35	21	60.0	2,160	1,537	71.2	316	225	71.2	15,053	10,846	72.1
30–34	113	77	68.1	420	320	76.2	12,242	8,777	71.7	7,039	5,375	76.4	47	31	66.0	4,031	2,805	69.6	441	314	71.2	24,476	17,812	72.8
35–39	88	64	72.7	362	270	74.6	8,822	6,337	71.8	6,521	5,161	79.1	38	28	73.7	4,234	3,015	71.2	318	225	70.8	20,536	15,206	74.0
40–44	87	64	73.6	324	242	74.7	5,805	4,299	74.1	5,678	4,577	80.6	39	28	71.8	4,242	3,054	72.0	225	171	76.0	16,538	12,537	75.8
45–49	81	60	74.1	311	247	79.4	3,923	3,004	76.6	4,723	3,902	82.6	23	18	78.3	4,039	3,015	74.6	171	119	69.6	13,364	10,437	78.1
50–54	81	56	69.1	356	277	77.8	4,399	3,438	78.2	4,852	4,070	83.9	23	21	91.3	6,166	4,730	76.7	218	163	74.8	16,197	12,834	79.2
55–59	99	71	71.7	261	220	84.3	5,272	4,213	79.9	4,656	3,961	85.1	41	30	73.2	8,784	6,883	78.4	266	214	80.5	19,492	15,680	80.4
60–64	77	66	85.7	142	110	77.5	3,728	3,028	81.2	2,756	2,401	87.1	20	15	75.0	7,233	5,835	80.7	224	181	80.8	14,249	11,682	82.0
≥65	57	47	82.5	113	94	83.2	2,767	2,265	81.9	1,952	1,721	88.2	17	11	64.7	7,305	5,973	81.8	157	135	86.0	12,438	10,303	82.8
Federal poverty level																								
0–100%	464	320	69.0	1,268	977	77.1	32,162	23,625	73.5	23,656	19,032	80.5	125	86	68.8	20,670	15,464	74.8	1,271	964	75.8	80,093	60,815	75.9
101–138%	71	50	70.4	218	170	78.0	5,356	4,125	77.0	4,397	3,642	82.8	25	17	68.0	5,443	4,351	79.9	236	178	75.4	15,855	12,607	79.5
139–250%	132	108	81.8	504	402	79.8	10,826	8,399	77.6	9,074	7,478	82.4	70	53	75.7	10,534	8,307	78.9	462	348	75.3	31,811	25,272	79.4
251–400%	76	62	81.6	352	271	77.0	6,525	4,989	76.5	4,733	3,848	81.3	37	28	75.7	6,669	5,194	77.9	316	226	71.5	18,782	14,673	78.1
>400%	25	21	84.0	244	181	74.2	1,999	1,494	74.7	1,620	1,252	77.3	22	15	68.2	4,012	3,008	75.0	137	95	69.3	8,133	6,124	75.3
Health care coverage																								
Private employer	99	78	78.8	449	348	77.5	8,142	6,055	74.4	4,782	3,847	80.4	40	31	77.5	8,284	6,179	74.6	355	258	72.7	22,294	16,897	75.8
Private individual	45	34	75.6	342	248	72.5	6,182	4,613	74.6	3,436	2,647	77.0	25	19	76.0	6,386	4,847	75.9	178	133	74.7	16,663	12,588	75.5
Medicare	77	59	76.6	92	75	81.5	4,568	3,623	79.3	1,602	1,331	83.1	19	7	36.8	7,378	5,974	81.0	151	126	83.4	13,963	11,250	80.6
Medicaid	213	143	67.1	675	513	76.0	15,743	11,259	71.5	11,010	8,823	80.1	87	61	70.1	9,640	7,119	73.8	734	517	70.4	38,514	28,746	74.6
Medicare and Medicaid	39	34	87.2	82	77	93.9	2,831	2,319	81.9	1,618	1,406	86.9	9	8	88.9	3,783	3,076	81.3	223	184	82.5	8,617	7,128	82.7
Veterans Administration	2	2	100.0	3	2	66.7	60	41	68.3	18	10	55.6	0	—	—	77	57	74.0	1	1	100.0	161	113	70.2
Indian Health Service	66	41	62.1	0	—	—	3	2	66.7	1	1	100.0	0	—	—	4	3	75.0	1	1	100.0	75	48	64.0
Other plan	7	7	100.0	88	64	72.7	977	792	81.1	1,511	1,269	84.0	6	4	66.7	834	631	75.7	17	11	64.7	3,503	2,830	80.8
No coverage	114	77	67.5	520	389	74.8	13,644	10,027	73.5	15,182	12,311	81.1	55	39	70.9	5,374	3,903	72.6	413	303	73.4	35,383	27,100	76.6
Multiple coverages	121	94	77.7	375	311	82.9	5,707	4,475	78.4	4,861	4,013	82.6	46	36	78.3	6,845	5,409	79.0	364	290	79.7	18,457	14,738	79.9
Housing status																								
Stable	670	489	73.0	2,359	1,836	77.8	50,980	38,501	75.5	37,926	30,818	81.3	257	183	71.2	44,038	34,025	77.3	2,196	1,646	75.0	139,229	108,124	77.7
Temporary	54	36	66.7	138	98	71.0	3,716	2,609	70.2	2,805	2,144	76.4	18	14	77.8	2,069	1,464	70.8	134	102	76.1	8,978	6,497	72.4
Unstable	47	34	72.3	76	58	76.3	2,516	1,685	67.0	2,929	2,427	82.9	9	6	66.7	1,387	952	68.6	99	66	66.7	7,085	5,242	74.0

Table 12b. Retention in care among gay, bisexual, and other men who have sex with men (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
HHS region[c]																								
Region 1	15	12	80.0	119	90	75.6	690	555	80.4	1,338	1,086	81.2	8	6	75.0	3,064	2,326	75.9	72	57	79.2	5,368	4,168	77.6
Region 2	34	26	76.5	450	395	87.8	4,918	3,938	80.1	8,909	7,832	87.9	40	31	77.5	3,193	2,655	83.2	93	75	80.6	18,047	15,300	84.8
Region 3	33	27	81.8	180	139	77.2	6,900	4,980	72.2	1,590	1,287	80.9	12	11	91.7	5,323	4,099	77.0	734	569	77.5	14,843	11,160	75.2
Region 4	124	94	75.8	282	231	81.9	23,871	18,457	77.3	7,723	6,374	82.5	39	28	71.8	13,605	10,827	79.6	451	351	77.8	46,155	36,413	78.9
Region 5	89	58	65.2	262	185	70.6	8,339	5,756	69.0	3,206	2,353	73.4	37	28	75.7	6,189	4,308	69.6	324	187	57.7	18,559	12,952	69.8
Region 6	171	128	74.9	210	136	64.8	6,208	4,390	70.7	7,182	5,716	79.6	20	14	70.0	3,906	2,901	74.3	168	131	78.0	18,034	13,527	75.0
Region 7	12	6	50.0	39	30	76.9	1,172	832	71.0	415	326	78.6	9	5	55.6	1,733	1,294	74.7	68	52	76.5	3,450	2,546	73.8
Region 8	43	31	72.1	46	36	78.3	295	209	70.8	1,040	803	77.2	6	3	50.0	1,749	1,233	70.5	47	32	68.1	3,243	2,360	72.8
Region 9	152	111	73.0	883	670	75.9	3,089	2,195	71.1	11,111	8,673	78.1	93	62	66.7	6,620	5,091	76.9	333	253	76.0	22,347	17,095	76.5
Region 10	101	68	67.3	113	82	72.6	336	227	67.6	656	507	77.3	22	17	77.3	1,604	1,159	72.3	78	60	76.9	2,961	2,149	72.6
Total[b]	**788**	**570**	**72.3**	**2,637**	**2,031**	**77.0**	**58,252**	**43,409**	**74.5**	**44,218**	**35,779**	**80.9**	**289**	**207**	**71.6**	**48,872**	**37,347**	**76.4**	**2,457**	**1,833**	**74.6**	**158,534**	**121,930**	**76.9**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Note: Data are included only for males with the transmission category male-to-male sexual contact; data do not include male clients who reported male-to-male sexual contact *and* injection drug use.
[a] Hispanics/Latinos can be of any race.
[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.
[c] See Technical Notes for the states/territories in each region.

Table 12c. Viral suppression among men (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)																								
13–14	3	3	100.0	2	2	100.0	56	51	91.1	11	10	90.9	0	—	—	9	9	100.0	2	2	100.0	85	79	92.9
15–19	4	3	75.0	25	24	96.0	616	501	81.3	227	188	82.8	1	1	100.0	68	61	89.7	15	13	86.7	968	799	82.5
20–24	42	35	83.3	132	116	87.9	4,689	3,873	82.6	2,303	1,977	85.8	13	13	100.0	944	835	88.5	143	126	88.1	8,343	7,040	84.4
25–29	107	94	87.9	369	339	91.9	10,475	8,498	81.1	6,248	5,466	87.5	48	43	89.6	3,115	2,771	89.0	393	336	85.5	20,948	17,714	84.6
30–34	182	152	83.5	585	561	95.9	16,477	13,451	81.6	9,616	8,563	89.0	67	60	89.6	5,867	5,228	89.1	576	506	87.8	33,663	28,773	85.5
35–39	138	122	88.4	543	497	91.5	12,712	10,630	83.6	9,247	8,318	90.0	61	53	86.9	6,275	5,615	89.5	433	371	85.7	29,678	25,836	87.1
40–44	138	123	89.1	548	524	95.6	9,877	8,425	85.3	8,713	7,885	90.5	49	48	98.0	6,386	5,721	89.6	363	318	87.6	26,290	23,231	88.4
45–49	116	101	87.1	563	546	97.0	8,114	7,042	86.8	7,888	7,210	91.4	32	28	87.5	6,048	5,528	91.4	316	280	88.6	23,256	20,892	89.8
50–54	163	140	85.9	619	593	95.8	10,165	8,979	88.3	8,387	7,814	93.2	37	34	91.9	9,118	8,376	91.9	378	345	91.3	29,049	26,443	91.0
55–59	175	163	93.1	441	418	94.8	13,031	11,600	89.0	8,579	8,042	93.7	63	57	90.5	12,196	11,507	94.4	545	495	90.8	35,219	32,457	92.2
60–64	140	130	92.9	265	256	96.6	10,962	9,954	90.8	5,862	5,502	93.9	26	25	96.2	10,235	9,832	96.1	502	466	92.8	28,127	26,294	93.5
≥65	96	89	92.7	256	245	95.7	10,685	9,952	93.1	5,254	5,056	96.2	29	26	89.7	9,977	9,760	97.8	495	475	96.0	26,934	25,737	95.6
Transmission category																								
Male-to-male sexual contact	850	763	89.8	2,770	2,629	94.9	61,638	52,849	85.7	46,813	43,002	91.9	313	288	92.0	50,711	47,574	93.8	2,554	2,286	89.5	166,653	150,301	90.2
Injection drug use	65	57	87.7	114	109	95.6	4,107	3,647	88.8	3,389	3,020	89.1	12	11	91.7	3,636	3,154	86.7	387	350	90.4	11,749	10,383	88.4
Male-to-male sexual contact and injection drug use	91	76	83.5	53	49	92.5	1,400	1,186	84.7	1,450	1,267	87.4	10	8	80.0	3,919	3,457	88.2	190	166	87.4	7,142	6,233	87.3
Heterosexual contact[c]	160	138	86.3	870	829	95.3	33,566	29,292	87.3	15,168	13,829	91.2	39	34	87.2	7,407	6,858	92.6	838	767	91.5	58,316	51,972	89.1
Perinatal	13	10	76.9	38	33	86.8	1,288	994	77.2	439	366	83.4	6	6	100.0	267	227	85.0	53	42	79.2	2,115	1,688	79.8
Other[d]	9	9	100.0	66	63	95.5	381	349	91.6	301	273	90.7	1	1	100.0	527	498	94.5	20	17	85.0	1,311	1,215	92.7
Federal poverty level																								
0–100%	760	659	86.7	2,164	2,038	94.2	64,064	53,546	83.6	41,791	37,435	89.6	199	175	87.9	32,223	28,927	89.8	2,346	2,051	87.4	144,590	125,736	87.0
101–138%	130	121	93.1	380	356	93.7	9,900	8,871	89.6	6,985	6,483	92.8	34	31	91.2	7,634	7,228	94.7	413	375	90.8	25,600	23,579	92.1
139–250%	225	202	89.8	832	804	96.6	17,846	15,944	89.3	13,463	12,624	93.8	95	89	93.7	14,184	13,493	95.1	714	655	91.7	47,701	44,118	92.5
251–400%	111	100	90.1	539	509	94.4	10,016	9,187	91.7	6,517	6,175	94.8	58	56	96.6	8,797	8,467	96.2	464	439	94.6	26,625	25,047	94.1
>400%	49	46	93.9	322	312	96.9	3,303	3,047	92.2	2,214	2,125	96.0	26	25	96.2	5,099	4,973	97.5	173	165	95.4	11,291	10,792	95.6
Health care coverage																								
Private employer	136	128	94.1	680	654	96.2	12,421	11,424	92.0	6,475	6,187	95.6	60	59	98.3	10,948	10,607	96.9	541	512	94.6	31,515	29,812	94.6
Private individual	74	71	95.9	543	519	95.6	10,019	9,090	90.7	4,977	4,754	95.5	38	37	97.4	8,252	7,884	95.5	242	227	93.8	24,267	22,695	93.5
Medicare	125	110	88.0	169	157	92.9	10,992	9,979	90.8	3,591	3,382	94.2	27	25	92.6	10,245	9,822	95.9	272	250	91.9	25,552	23,843	93.3
Medicaid	362	310	85.6	1,195	1,130	94.6	31,674	26,628	84.1	19,761	17,646	89.3	130	112	86.2	15,571	13,945	89.6	1,277	1,101	86.2	70,724	61,509	87.0
Medicare and Medicaid	76	72	94.7	145	140	96.6	6,813	6,094	89.4	3,278	3,063	93.4	19	17	89.5	5,462	5,161	94.5	506	468	92.5	16,346	15,058	92.1
Veterans Administration	4	4	100.0	6	5	83.3	105	93	88.6	29	27	93.1	2	2	100.0	131	124	94.7	6	5	83.3	285	262	91.9
Indian Health Service	107	98	91.6	0	—	—	3	2	66.7	4	3	75.0	0	—	—	5	4	80.0	2	2	100.0	122	110	90.2
Other plan	15	14	93.3	127	124	97.6	1,857	1,590	85.6	2,434	2,266	93.1	9	9	100.0	1,301	1,210	93.0	32	29	90.6	5,886	5,338	90.7
No coverage	203	167	82.3	867	802	92.5	23,692	18,858	79.6	24,410	21,783	89.2	74	66	89.2	8,674	7,383	85.1	616	533	86.5	58,737	49,770	84.7
Multiple coverages	190	171	90.0	574	553	96.3	9,551	8,572	89.7	6,902	6,533	94.7	62	56	90.3	9,172	8,660	94.4	635	578	91.0	27,300	25,319	92.7

Table 12c. Viral suppression among men (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Housing status																								
Stable	1,102	985	89.4	3,885	3,691	95.0	93,711	81,796	87.3	62,393	57,477	92.1	370	338	91.4	62,113	58,373	94.0	3,709	3,370	90.9	228,822	207,395	90.6
Temporary	81	72	88.9	248	234	94.4	7,564	6,055	80.1	4,720	4,132	87.5	29	28	96.6	3,565	3,064	85.9	234	197	84.2	16,531	13,861	83.8
Unstable	94	72	76.6	110	100	90.9	5,027	3,731	74.2	4,214	3,526	83.7	21	16	76.2	2,845	2,208	77.6	180	132	73.3	12,548	9,825	78.3
HHS region[e]																								
Region 1	24	24	100.0	181	171	94.5	1,916	1,762	92.0	2,789	2,644	94.8	7	7	100.0	3,850	3,718	96.6	108	102	94.4	8,966	8,514	95.0
Region 2	60	54	90.0	742	717	96.6	11,559	10,066	87.1	17,219	15,809	91.8	54	51	94.4	4,767	4,493	94.3	177	154	87.0	35,261	31,939	90.6
Region 3	66	57	86.4	321	304	94.7	14,205	12,572	88.5	3,395	3,108	91.5	18	17	94.4	7,547	7,106	94.2	1,620	1,481	91.4	27,339	24,787	90.7
Region 4	196	171	87.2	483	452	93.6	42,578	36,292	85.2	11,773	10,820	91.9	56	50	89.3	18,996	17,581	92.6	642	575	89.6	74,872	66,065	88.2
Region 5	112	103	92.0	449	432	96.2	13,982	12,264	87.7	5,028	4,739	94.3	55	51	92.7	8,687	8,218	94.6	459	404	88.0	29,043	26,461	91.1
Region 6	319	278	87.1	423	385	91.0	11,674	9,697	83.1	11,879	10,439	87.9	32	30	93.8	6,626	5,871	88.6	246	213	86.6	31,352	27,052	86.3
Region 7	23	22	95.7	92	91	98.9	1,989	1,751	88.0	631	586	92.9	10	10	100.0	2,326	2,169	93.3	100	87	87.0	5,173	4,717	91.2
Region 8	65	60	92.3	69	65	94.2	622	569	91.5	1,564	1,470	94.0	8	7	87.5	2,488	2,369	95.2	77	72	93.5	4,971	4,684	94.2
Region 9	252	218	86.5	1,296	1,224	94.4	4,964	4,294	86.5	15,479	14,024	90.6	149	130	87.2	9,819	9,034	92.0	482	435	90.2	32,628	29,515	90.5
Region 10	164	147	89.6	187	178	95.2	791	709	89.6	1,110	1,036	93.3	31	30	96.8	2,549	2,340	91.8	122	101	82.8	5,061	4,642	91.7
Total[b]	**1,304**	**1,155**	**88.6**	**4,348**	**4,121**	**94.8**	**107,859**	**92,956**	**86.2**	**72,335**	**66,031**	**91.3**	**426**	**388**	**91.1**	**70,238**	**65,243**	**92.9**	**4,161**	**3,733**	**89.7**	**262,560**	**235,295**	**89.6**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.

[a] Hispanics/Latinos can be of any race.

[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.

[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[d] Includes hemophilia and blood transfusion.

[e] See Technical Notes for the states/territories in each region.

Table 12d. Viral suppression among gay, bisexual, and other men who have sex with men (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)																								
13–14	1	1	100.0	0	—	—	2	1	50.0	0	—	—	0	—	—	0	—	—	0	—	—	3	2	66.7
15–19	4	3	75.0	5	5	100.0	325	262	80.6	135	109	80.7	0	—	—	29	28	96.6	12	10	83.3	515	419	81.4
20–24	36	29	80.6	94	84	89.4	3,767	3,135	83.2	1,824	1,574	86.3	8	8	100.0	737	666	90.4	114	101	88.6	6,617	5,626	85.0
25–29	80	71	88.8	305	281	92.1	8,385	6,888	82.1	4,914	4,336	88.2	40	36	90.0	2,337	2,112	90.4	333	290	87.1	16,495	14,106	85.5
30–34	133	113	85.0	452	435	96.2	13,110	10,773	82.2	7,575	6,833	90.2	52	47	90.4	4,290	3,897	90.8	471	414	87.9	26,237	22,644	86.3
35–39	97	89	91.8	384	354	92.2	9,359	7,865	84.0	6,907	6,267	90.7	45	40	88.9	4,478	4,061	90.7	328	281	85.7	21,747	19,094	87.8
40–44	90	81	90.0	336	318	94.6	6,076	5,210	85.7	5,946	5,456	91.8	40	39	97.5	4,467	4,064	91.0	236	210	89.0	17,323	15,497	89.5
45–49	81	71	87.7	312	303	97.1	4,078	3,554	87.2	4,929	4,574	92.8	21	20	95.2	4,206	3,887	92.4	181	160	88.4	13,902	12,653	91.0
50–54	95	85	89.5	369	358	97.0	4,535	4,076	89.9	5,035	4,750	94.3	24	22	91.7	6,413	5,965	93.0	224	208	92.9	16,789	15,552	92.6
55–59	103	96	93.2	254	239	94.1	5,414	4,909	90.7	4,766	4,516	94.8	45	41	91.1	8,967	8,516	95.0	271	246	90.8	19,926	18,663	93.7
60–64	77	74	96.1	142	140	98.6	3,787	3,526	93.1	2,806	2,674	95.3	20	19	95.0	7,410	7,143	96.4	225	214	95.1	14,530	13,850	95.3
≥65	53	50	94.3	117	112	95.7	2,800	2,650	94.6	1,976	1,913	96.8	18	16	88.9	7,377	7,235	98.1	159	152	95.6	12,569	12,195	97.0
Federal poverty level																								
0–100%	481	425	88.4	1,334	1,259	94.4	34,302	28,331	82.6	25,229	22,729	90.1	136	122	89.7	21,566	19,610	90.9	1,345	1,170	87.0	84,894	74,095	87.3
101–138%	82	76	92.7	230	216	93.9	5,508	4,903	89.0	4,582	4,257	92.9	26	23	88.5	5,621	5,354	95.2	242	219	90.5	16,369	15,122	92.4
139–250%	154	139	90.3	536	516	96.3	11,431	10,141	88.7	9,554	8,984	94.0	76	71	93.4	10,914	10,417	95.4	478	434	90.8	33,360	30,900	92.6
251–400%	84	77	91.7	365	346	94.8	6,898	6,306	91.4	4,964	4,717	95.0	44	43	97.7	6,969	6,727	96.5	326	308	94.5	19,731	18,597	94.3
>400%	31	29	93.5	249	240	96.4	2,132	1,977	92.7	1,716	1,652	96.3	22	21	95.5	4,146	4,045	97.6	130	124	95.4	8,504	8,162	96.0
Health care coverage																								
Private employer	101	96	95.0	483	466	96.5	8,601	7,904	91.9	4,995	4,762	95.3	41	40	97.6	8,662	8,415	97.1	370	351	94.9	23,393	22,168	94.8
Private individual	50	48	96.0	358	342	95.5	6,455	5,826	90.3	3,623	3,468	95.7	30	30	100.0	6,567	6,297	95.9	188	178	94.7	17,344	16,257	93.7
Medicare	80	72	90.0	94	86	91.5	4,616	4,189	90.7	1,653	1,557	94.2	21	19	90.5	7,554	7,259	96.1	151	141	93.4	14,233	13,384	94.0
Medicaid	226	194	85.8	703	667	94.9	16,572	13,879	83.7	11,453	10,308	90.0	93	82	88.2	10,027	9,110	90.9	759	658	86.7	40,228	35,244	87.6
Medicare and Medicaid	41	40	97.6	82	79	96.3	2,939	2,595	88.3	1,637	1,538	94.0	8	7	87.5	3,835	3,636	94.8	233	212	91.0	8,803	8,133	92.4
Veterans Administration	2	2	100.0	3	2	66.7	60	52	86.7	18	17	94.4	0	—	—	85	82	96.5	2	1	50.0	170	156	91.8
Indian Health Service	75	70	93.3	0	—	—	3	2	66.7	1	1	100.0	0	—	—	4	3	75.0	2	2	100.0	86	79	91.9
Other plan	8	7	87.5	87	86	98.9	1,009	872	86.4	1,610	1,506	93.5	5	5	100.0	869	821	94.5	19	17	89.5	3,673	3,375	91.9
No coverage	137	114	83.2	559	514	91.9	15,089	11,908	78.9	16,614	14,909	89.7	61	55	90.2	5,840	5,036	86.2	443	377	85.1	38,841	32,998	85.0
Multiple coverages	127	117	92.1	387	373	96.4	5,923	5,302	89.5	5,011	4,779	95.4	52	48	92.3	7,016	6,672	95.1	372	335	90.1	19,019	17,749	93.3
Housing status																								
Stable	730	661	90.5	2,476	2,352	95.0	53,971	46,839	86.8	40,182	37,202	92.6	277	256	92.4	45,745	43,268	94.6	2,272	2,058	90.6	146,518	133,423	91.1
Temporary	53	48	90.6	150	141	94.0	4,052	3,214	79.3	3,095	2,740	88.5	23	22	95.7	2,212	1,940	87.7	149	124	83.2	9,780	8,270	84.6
Unstable	54	41	75.9	81	76	93.8	2,753	2,027	73.6	2,972	2,547	85.7	10	7	70.0	1,528	1,207	79.0	107	81	75.7	7,532	6,006	79.7

Table 12d. Viral suppression among gay, bisexual, and other men who have sex with men (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
HHS region[c]																								
Region 1	15	15	100.0	119	113	95.0	703	635	90.3	1,389	1,325	95.4	7	7	100.0	2,952	2,865	97.1	67	64	95.5	5,299	5,070	95.7
Region 2	31	30	96.8	459	441	96.1	5,134	4,508	87.8	9,233	8,595	93.1	39	38	97.4	3,260	3,090	94.8	96	81	84.4	18,674	17,165	91.9
Region 3	32	28	87.5	191	182	95.3	7,178	6,341	88.3	1,720	1,602	93.1	15	14	93.3	5,525	5,267	95.3	751	683	90.9	15,489	14,186	91.6
Region 4	132	118	89.4	307	289	94.1	25,516	21,627	84.8	8,315	7,682	92.4	44	40	90.9	14,218	13,282	93.4	480	434	90.4	49,085	43,537	88.7
Region 5	88	80	90.9	268	261	97.4	8,788	7,661	87.2	3,430	3,238	94.4	38	35	92.1	6,520	6,208	95.2	327	288	88.1	19,576	17,880	91.3
Region 6	212	185	87.3	223	199	89.2	6,577	5,422	82.4	7,710	6,797	88.2	22	20	90.9	4,233	3,795	89.7	183	159	86.9	19,273	16,681	86.6
Region 7	14	14	100.0	44	43	97.7	1,266	1,111	87.8	446	420	94.2	10	10	100.0	1,792	1,672	93.3	75	67	89.3	3,649	3,338	91.5
Region 8	36	35	97.2	45	43	95.6	289	258	89.3	1,023	966	94.4	6	5	83.3	1,678	1,619	96.5	45	43	95.6	3,138	2,982	95.0
Region 9	160	138	86.3	943	893	94.7	3,227	2,810	87.1	11,689	10,649	91.1	104	93	89.4	6,858	6,377	93.0	346	311	89.9	23,409	21,339	91.2
Region 10	113	104	92.0	117	112	95.7	357	324	90.8	745	698	93.7	24	23	95.8	1,708	1,586	92.9	79	67	84.8	3,197	2,966	92.8
Total[b]	**850**	**763**	**89.8**	**2,770**	**2,629**	**94.9**	**61,638**	**52,849**	**85.7**	**46,813**	**43,002**	**91.9**	**313**	**288**	**92.0**	**50,711**	**47,574**	**93.8**	**2,554**	**2,286**	**89.5**	**166,653**	**150,301**	**90.2**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Note: Data are included only for males with the transmission category male-to-male sexual contact; data do not include male clients who reported male-to-male sexual contact *and* injection drug use.
[a] Hispanics/Latinos can be of any race.
[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.
[c] See Technical Notes for the states/territories in each region.

Table 13a. Retention in care among transgender adults and adolescents (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Gender																								
Transgender male	2	1	50.0	13	7	53.8	312	213	68.3	203	148	72.9	2	1	50.0	158	118	74.7	10	7	70.0	712	503	70.6
Transgender female	59	45	76.3	125	101	80.8	3,690	2,702	73.2	2,130	1,665	78.2	45	33	73.3	933	701	75.1	101	70	69.3	7,206	5,405	75.0
Other gender identity	4	2	50.0	22	12	54.5	192	126	65.6	259	160	61.8	5	3	60.0	206	115	55.8	7	6	85.7	725	446	61.5
Age group (yrs)																								
13–14	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
15–19	0	—	—	0	—	—	14	9	64.3	11	7	63.6	0	—	—	2	2	100.0	0	—	—	27	18	66.7
20–24	2	2	100.0	4	2	50.0	281	193	68.7	134	92	68.7	0	—	—	36	23	63.9	12	9	75.0	477	327	68.6
25–29	10	8	80.0	17	12	70.6	579	396	68.4	303	218	71.9	8	7	87.5	146	93	63.7	19	14	73.7	1,098	756	68.9
30–34	17	8	47.1	37	24	64.9	942	672	71.3	421	300	71.3	8	7	87.5	207	141	68.1	23	12	52.2	1,681	1,182	70.3
35–39	11	10	90.9	22	17	77.3	726	526	72.5	408	297	72.8	11	7	63.6	167	104	62.3	17	10	58.8	1,398	996	71.2
40–44	4	3	75.0	21	16	76.2	485	339	69.9	364	276	75.8	4	3	75.0	151	104	68.9	10	7	70.0	1,060	765	72.2
45–49	6	5	83.3	21	15	71.4	285	212	74.4	318	254	79.9	11	6	54.5	116	88	75.9	10	9	90.0	784	601	76.7
50–54	5	5	100.0	12	10	83.3	300	221	73.7	287	238	82.9	6	4	66.7	142	113	79.6	7	6	85.7	771	605	78.5
55–59	7	5	71.4	15	13	86.7	270	222	82.2	195	158	81.0	1	1	100.0	158	130	82.3	9	6	66.7	671	548	81.7
60–64	2	2	100.0	7	7	100.0	171	140	81.9	90	75	83.3	1	1	100.0	107	84	78.5	4	4	100.0	391	321	82.1
≥65	1	0	0.0	4	4	100.0	141	111	78.7	61	58	95.1	2	1	50.0	65	52	80.0	7	6	85.7	285	235	82.5
Transmission category																								
Sexual contact[c]	48	33	68.8	122	92	75.4	3,517	2,587	73.6	2,028	1,566	77.2	43	29	67.4	902	652	72.3	96	68	70.8	6,817	5,069	74.4
Injection drug use	0	—	—	1	1	100.0	17	13	76.5	21	17	81.0	1	1	100.0	17	12	70.6	3	2	66.7	61	47	77.0
Sexual contact[c] and injection drug use	8	7	87.5	3	3	100.0	90	54	60.0	78	54	69.2	1	1	100.0	86	54	62.8	10	7	70.0	279	181	64.9
Perinatal	0	—	—	0	—	—	19	14	73.7	4	3	75.0	0	—	—	14	9	64.3	2	1	50.0	40	28	70.0
Other[d]	0	—	—	0	—	—	12	9	75.0	5	5	100.0	0	—	—	6	5	83.3	0	—	—	23	19	82.6
Federal poverty level																								
0–100%	50	35	70.0	103	76	73.8	3,048	2,196	72.0	1,774	1,324	74.6	35	22	62.9	770	537	69.7	84	58	69.0	5,976	4,324	72.4
101–138%	6	5	83.3	11	6	54.5	257	191	74.3	204	162	79.4	4	3	75.0	118	95	80.5	8	6	75.0	618	476	77.0
139–250%	7	6	85.7	21	18	85.7	506	381	75.3	382	321	84.0	3	3	100.0	177	134	75.7	15	10	66.7	1,135	896	78.9
251–400%	2	2	100.0	13	12	92.3	214	166	77.6	123	99	80.5	6	6	100.0	119	91	76.5	9	7	77.8	492	387	78.7
>400%	0	—	—	9	7	77.8	84	64	76.2	52	34	65.4	3	3	100.0	60	50	83.3	2	2	100.0	220	165	75.0
Health care coverage																								
Private employer	5	2	40.0	15	9	60.0	222	160	72.1	151	97	64.2	3	2	66.7	124	84	67.7	7	5	71.4	530	361	68.1
Private individual	1	1	100.0	7	5	71.4	296	236	79.7	126	97	77.0	1	1	100.0	98	74	75.5	7	6	85.7	538	422	78.4
Medicare	10	7	70.0	3	2	66.7	200	148	74.0	59	45	76.3	2	1	50.0	95	74	77.9	3	2	66.7	374	281	75.1
Medicaid	31	22	71.0	67	52	77.6	1,874	1,328	70.9	1,005	759	75.5	30	21	70.0	454	302	66.5	53	38	71.7	3,605	2,589	71.8
Medicare and Medicaid	5	5	100.0	2	2	100.0	186	149	80.1	69	56	81.2	1	0	0.0	76	59	77.6	8	6	75.0	350	280	80.0
Veterans Administration	0	—	—	1	1	100.0	1	0	0.0	0	—	—	0	—	—	4	2	50.0	0	—	—	6	3	50.0
Indian Health Service	1	1	100.0	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	1	1	100.0
Other plan	0	—	—	14	10	71.4	91	65	71.4	95	70	73.7	4	4	100.0	72	61	84.7	0	—	—	287	220	76.7
No coverage	3	3	100.0	36	27	75.0	899	638	71.0	791	615	77.7	2	1	50.0	130	88	67.7	18	12	66.7	1,891	1,391	73.6
Multiple coverages	9	7	77.8	14	11	78.6	393	304	77.4	272	222	81.6	9	7	77.8	233	184	79.0	19	11	57.9	989	771	78.0

Table 13a. Retention in care among transgender adults and adolescents (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Housing status																								
Stable	47	34	72.3	131	102	77.9	3,418	2,559	74.9	2,093	1,643	78.5	41	30	73.2	1,030	784	76.1	91	63	69.2	6,990	5,321	76.1
Temporary	6	4	66.7	10	7	70.0	344	228	66.3	192	141	73.4	4	1	25.0	79	54	68.4	12	9	75.0	656	448	68.3
Unstable	10	9	90.0	13	10	76.9	345	217	62.9	203	152	74.9	6	5	83.3	85	55	64.7	14	10	71.4	686	463	67.5
HHS region[e]																								
Region 1	1	1	100.0	13	10	76.9	46	35	76.1	87	64	73.6	1	1	100.0	53	41	77.4	7	6	85.7	210	160	76.2
Region 2	9	9	100.0	46	35	76.1	696	541	77.7	715	592	82.8	9	9	100.0	267	217	81.3	4	4	100.0	1,864	1,497	80.3
Region 3	2	2	100.0	5	4	80.0	501	357	71.3	125	94	75.2	3	2	66.7	99	76	76.8	24	19	79.2	766	558	72.8
Region 4	2	1	50.0	11	10	90.9	1,236	948	76.7	287	231	80.5	1	1	100.0	242	171	70.7	11	9	81.8	1,792	1,372	76.6
Region 5	18	9	50.0	17	15	88.2	700	463	66.1	191	132	69.1	9	9	100.0	144	101	70.1	25	14	56.0	1,119	753	67.3
Region 6	8	7	87.5	9	5	55.6	466	332	71.2	352	268	76.1	2	1	50.0	85	65	76.5	5	3	60.0	931	683	73.4
Region 7	1	1	100.0	1	1	100.0	99	73	73.7	21	17	81.0	2	1	50.0	32	23	71.9	4	2	50.0	160	118	73.8
Region 8	5	2	40.0	6	3	50.0	49	20	40.8	154	74	48.1	2	1	50.0	143	64	44.8	0	—	—	365	168	46.0
Region 9	10	10	100.0	43	31	72.1	249	156	62.7	586	443	75.6	16	8	50.0	150	113	75.3	22	16	72.7	1,086	782	72.0
Region 10	7	4	57.1	7	4	57.1	28	22	78.6	43	36	83.7	7	4	57.1	47	36	76.6	9	6	66.7	149	112	75.2
Total[b]	**65**	**48**	**73.8**	**160**	**120**	**75.0**	**4,194**	**3,041**	**72.5**	**2,592**	**1,973**	**76.1**	**52**	**37**	**71.2**	**1,297**	**934**	**72.0**	**118**	**83**	**70.3**	**8,643**	**6,354**	**73.5**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
* To ensure confidentiality, data have been suppressed.
[a] Hispanics/Latinos can be of any race.
[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.
[c] Includes any sexual transmission category reported by transgender clients.
[d] Includes hemophilia and blood transfusion.
[e] See Technical Notes for the states/territories in each region.

Table 13b. Viral suppression among transgender adults and adolescents (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Gender																								
Transgender male	3	3	100.0	14	14	100.0	329	281	85.4	211	177	83.9	2	2	100.0	170	158	92.9	12	10	83.3	753	656	87.1
Transgender female	66	59	89.4	134	122	91.0	3,902	3,238	83.0	2,283	2,022	88.6	42	36	85.7	969	885	91.3	108	87	80.6	7,635	6,567	86.0
Other gender identity	3	3	100.0	20	18	90.0	184	157	85.3	240	218	90.8	6	5	83.3	175	163	93.1	7	7	100.0	665	599	90.1
Age group (yrs)																								
13–14	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*
15–19	0	—	—	0	—	—	17	14	82.4	13	11	84.6	0	—	—	2	2	100.0	1	1	100.0	33	28	84.8
20–24	2	2	100.0	5	4	80.0	316	248	78.5	141	120	85.1	0	—	—	41	37	90.2	15	10	66.7	530	428	80.8
25–29	12	10	83.3	18	16	88.9	622	470	75.6	335	295	88.1	8	6	75.0	150	138	92.0	23	20	87.0	1,183	969	81.9
30–34	18	18	100.0	40	38	95.0	1,010	811	80.3	435	379	87.1	8	7	87.5	210	192	91.4	21	17	81.0	1,773	1,490	84.0
35–39	13	11	84.6	23	21	91.3	747	613	82.1	439	378	86.1	9	8	88.9	173	150	86.7	18	13	72.2	1,458	1,228	84.2
40–44	4	3	75.0	20	16	80.0	500	434	86.8	383	343	89.6	5	5	100.0	153	137	89.5	11	8	72.7	1,099	965	87.8
45–49	7	6	85.7	24	21	87.5	298	251	84.2	322	287	89.1	11	9	81.8	113	102	90.3	10	10	100.0	804	705	87.7
50–54	5	4	80.0	12	12	100.0	309	277	89.6	306	279	91.2	5	5	100.0	141	130	92.2	7	7	100.0	797	725	91.0
55–59	7	7	100.0	15	15	100.0	280	257	91.8	202	179	88.6	1	1	100.0	163	155	95.1	9	8	88.9	692	635	91.8
60–64	3	3	100.0	7	7	100.0	172	166	96.5	96	87	90.6	1	1	100.0	105	101	96.2	5	4	80.0	397	377	95.0
≥65	1	1	100.0	4	4	100.0	144	135	93.8	62	59	95.2	2	1	50.0	63	62	98.4	7	6	85.7	287	272	94.8
Transmission category																								
Sexual contact[c]	54	48	88.9	127	116	91.3	3,731	3,109	83.3	2,118	1,896	89.5	43	36	83.7	912	845	92.7	107	88	82.2	7,157	6,196	86.6
Injection drug use	0	—	—	1	1	100.0	19	16	84.2	23	18	78.3	0	—	—	18	17	94.4	4	3	75.0	66	56	84.8
Sexual contact[c] and injection drug use	8	7	87.5	3	3	100.0	85	69	81.2	83	65	78.3	1	1	100.0	81	68	84.0	8	6	75.0	272	222	81.6
Perinatal	0	—	—	0	—	—	19	15	78.9	3	2	66.7	0	—	—	14	14	100.0	2	2	100.0	39	34	87.2
Other[d]	0	—	—	0	—	—	12	11	91.7	7	6	85.7	0	—	—	6	5	83.3	0	—	—	25	22	88.0
Federal poverty level																								
0–100%	54	49	90.7	109	99	90.8	3,232	2,629	81.3	1,897	1,649	86.9	33	27	81.8	778	693	89.1	87	70	80.5	6,307	5,319	84.3
101–138%	7	6	85.7	10	9	90.0	266	238	89.5	203	191	94.1	3	3	100.0	126	118	93.7	9	8	88.9	633	582	91.9
139–250%	9	9	100.0	21	19	90.5	523	468	89.5	400	364	91.0	3	3	100.0	182	176	96.7	17	16	94.1	1,180	1,079	91.4
251–400%	2	1	50.0	14	14	100.0	229	204	89.1	130	119	91.5	6	6	100.0	121	117	96.7	10	7	70.0	518	474	91.5
>400%	0	—	—	10	9	90.0	85	72	84.7	48	43	89.6	4	4	100.0	63	61	96.8	3	3	100.0	224	202	90.2
Health care coverage																								
Private employer	6	5	83.3	14	13	92.9	231	207	89.6	144	133	92.4	2	2	100.0	118	113	95.8	8	7	87.5	526	483	91.8
Private individual	1	1	100.0	8	7	87.5	313	281	89.8	130	122	93.8	2	2	100.0	102	95	93.1	7	6	85.7	565	516	91.3
Medicare	10	10	100.0	3	3	100.0	200	176	88.0	60	49	81.7	2	0	0.0	93	89	95.7	4	3	75.0	374	332	88.8
Medicaid	32	29	90.6	70	63	90.0	1,962	1,618	82.5	1,057	933	88.3	28	27	96.4	452	394	87.2	59	45	76.3	3,754	3,192	85.0
Medicare and Medicaid	6	6	100.0	2	2	100.0	194	177	91.2	69	64	92.8	1	1	100.0	77	69	89.6	8	8	100.0	361	331	91.7
Veterans Administration	0	—	—	1	1	100.0	1	1	100.0	0	—	—	0	—	—	4	4	100.0	0	—	—	6	6	100.0
Indian Health Service	2	2	100.0	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	2	2	100.0
Other plan	0	—	—	15	13	86.7	87	79	90.8	101	93	92.1	4	4	100.0	75	74	98.7	1	1	100.0	295	275	93.2
No coverage	7	4	57.1	39	37	94.9	990	752	76.0	871	753	86.5	3	1	33.3	149	131	87.9	19	15	78.9	2,092	1,706	81.5
Multiple coverages	8	8	100.0	14	13	92.9	408	361	88.5	280	255	91.1	8	6	75.0	236	229	97.0	18	16	88.9	1,012	925	91.4

Table 13b. Viral suppression among transgender adults and adolescents (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Housing status																								
Stable	54	51	94.4	139	131	94.2	3,593	3,053	85.0	2,208	1,975	89.4	39	34	87.2	1,068	1,002	93.8	101	86	85.1	7,351	6,468	88.0
Temporary	6	5	83.3	10	7	70.0	368	301	81.8	227	190	83.7	4	3	75.0	81	65	80.2	13	10	76.9	716	588	82.1
Unstable	11	8	72.7	13	10	76.9	382	260	68.1	214	175	81.8	6	5	83.3	87	69	79.3	12	7	58.3	735	541	73.6
HHS region[e]																								
Region 1	1	1	100.0	13	13	100.0	42	37	88.1	94	92	97.9	0	—	—	55	52	94.5	7	4	57.1	214	201	93.9
Region 2	9	8	88.9	49	45	91.8	742	628	84.6	765	680	88.9	9	9	100.0	282	266	94.3	5	5	100.0	1,989	1,756	88.3
Region 3	3	2	66.7	6	5	83.3	526	439	83.5	128	112	87.5	3	2	66.7	103	90	87.4	28	24	85.7	802	679	84.7
Region 4	2	2	100.0	12	11	91.7	1,333	1,102	82.7	318	283	89.0	1	1	100.0	257	239	93.0	11	11	100.0	1,936	1,651	85.3
Region 5	20	19	95.0	19	18	94.7	723	595	82.3	190	178	93.7	8	7	87.5	144	131	91.0	24	19	79.2	1,141	978	85.7
Region 6	12	8	66.7	8	8	100.0	491	398	81.1	371	322	86.8	2	2	100.0	97	84	86.6	8	6	75.0	994	832	83.7
Region 7	1	1	100.0	1	1	100.0	100	81	81.0	24	21	87.5	2	2	100.0	36	34	94.4	4	4	100.0	168	144	85.7
Region 8	4	4	100.0	4	4	100.0	38	36	94.7	124	109	87.9	3	3	100.0	108	101	93.5	0	—	—	287	263	91.6
Region 9	11	11	100.0	47	43	91.5	255	216	84.7	631	544	86.2	17	13	76.5	153	135	88.2	23	18	78.3	1,149	992	86.3
Region 10	7	7	100.0	7	4	57.1	29	28	96.6	53	44	83.0	5	4	80.0	44	43	97.7	9	8	88.9	154	138	89.6
Total[b]	**72**	**65**	**90.3**	**168**	**154**	**91.7**	**4,415**	**3,676**	**83.3**	**2,734**	**2,417**	**88.4**	**50**	**43**	**86.0**	**1,314**	**1,206**	**91.8**	**127**	**104**	**81.9**	**9,053**	**7,822**	**86.4**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
* To ensure confidentiality, data have been suppressed.
[a] Hispanics/Latinos can be of any race.
[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.
[c] Includes any sexual transmission category reported by transgender clients.
[d] Includes hemophilia and blood transfusion.
[e] See Technical Notes for the states/territories in each region.

Table 14a. Retention in care among older adults (aged 50 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)																								
50–54	217	156	71.9	766	604	78.9	17,976	14,123	78.6	11,161	9,311	83.4	55	44	80.0	10,932	8,324	76.1	631	487	77.2	42,003	33,238	79.1
55–59	243	187	77.0	563	470	83.5	21,476	17,199	80.1	11,458	9,744	85.0	73	51	69.9	14,143	11,008	77.8	834	676	81.1	49,049	39,517	80.6
60–64	191	159	83.2	367	303	82.6	18,189	14,760	81.1	8,456	7,362	87.1	34	24	70.6	11,819	9,431	79.8	768	636	82.8	40,012	32,801	82.0
≥65	151	120	79.5	362	305	84.3	18,126	14,928	82.4	8,189	7,174	87.6	36	25	69.4	11,544	9,293	80.5	774	668	86.3	39,404	32,682	82.9
Gender																								
Male	566	437	77.2	1,556	1,271	81.7	43,677	34,909	79.9	27,369	23,266	85.0	148	108	73.0	40,433	31,780	78.6	1,913	1,554	81.2	116,349	93,812	80.6
Female	221	173	78.3	463	376	81.2	31,193	25,395	81.4	11,258	9,792	87.0	40	29	72.5	7,530	5,896	78.3	1,066	890	83.5	51,970	42,696	82.2
Transgender	15	12	80.0	38	34	89.5	882	694	78.7	633	529	83.6	10	7	70.0	472	379	80.3	27	22	81.5	2,118	1,709	80.7
Transmission category																								
Male client																								
Male-to-male sexual contact	314	240	76.4	872	701	80.4	16,166	12,944	80.1	14,216	12,153	85.5	101	77	76.2	29,488	23,421	79.4	865	693	80.1	62,376	50,499	81.0
Injection drug use	45	30	66.7	43	37	86.0	3,598	2,878	80.0	2,583	2,170	84.0	7	4	57.1	2,086	1,596	76.5	347	301	86.7	8,733	7,034	80.5
Male-to-male sexual contact and injection drug use	42	34	81.0	18	16	88.9	807	633	78.4	611	512	83.8	2	2	100.0	1,938	1,536	79.3	82	64	78.0	3,509	2,804	79.9
Heterosexual contact[c]	99	80	80.8	440	374	85.0	20,692	16,636	80.4	8,454	7,310	86.5	26	17	65.4	4,559	3,562	78.1	555	454	81.8	34,952	28,518	81.6
Perinatal	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
Other[d]	4	4	100.0	33	25	75.8	235	204	86.8	159	133	83.6	1	1	100.0	379	287	75.7	15	11	73.3	832	670	80.5
Female client																								
Injection drug use	42	33	78.6	6	5	83.3	2,208	1,782	80.7	843	708	84.0	6	5	83.3	1,259	985	78.2	218	189	86.7	4,595	3,715	80.8
Heterosexual contact[c]	157	120	76.4	367	299	81.5	27,030	22,144	81.9	9,534	8,357	87.7	28	20	71.4	5,822	4,571	78.5	815	672	82.5	43,879	36,278	82.7
Perinatal	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
Other[d]	2	2	100.0	23	17	73.9	370	303	81.9	144	127	88.2	1	1	100.0	115	95	82.6	14	12	85.7	673	561	83.4
Transgender client																								
Sexual contact[e]	9	7	77.8	27	26	96.3	704	564	80.1	498	418	83.9	9	6	66.7	318	253	79.6	20	17	85.0	1,596	1,300	81.5
Injection drug use	0	—	—	0	—	—	8	8	100.0	7	7	100.0	0	—	—	7	5	71.4	1	1	100.0	23	21	91.3
Sexual contact[e] and injection drug use	3	2	66.7	2	2	100.0	45	28	62.2	27	22	81.5	0	—	—	28	23	82.1	4	3	75.0	110	80	72.7
Perinatal	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
Other[d]	0	—	—	0	—	—	6	6	100.0	2	2	100.0	0	—	—	3	2	66.7	0	—	—	11	10	90.9
Federal poverty level																								
0–100%	498	378	75.9	1,144	934	81.6	47,729	38,283	80.2	25,834	22,131	85.7	102	69	67.6	21,641	16,778	77.5	1,723	1,438	83.5	99,155	80,350	81.0
101–138%	88	69	78.4	213	177	83.1	8,450	6,920	81.9	3,856	3,324	86.2	25	18	72.0	6,462	5,263	81.4	367	301	82.0	19,544	16,135	82.6
139–250%	131	107	81.7	374	307	82.1	11,016	9,113	82.7	5,919	5,071	85.7	32	25	78.1	10,140	8,173	80.6	471	381	80.9	28,291	23,353	82.5
251–400%	41	34	82.9	186	152	81.7	4,837	3,970	82.1	2,243	1,918	85.5	17	14	82.4	5,267	4,187	79.5	302	235	77.8	12,938	10,542	81.5
>400%	29	26	89.7	95	82	86.3	1,822	1,425	78.2	815	674	82.7	13	10	76.9	3,302	2,542	77.0	117	96	82.1	6,234	4,884	78.3

Table 14a. Retention in care among older adults (aged 50 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Health care coverage																								
Private employer	54	42	77.8	217	175	80.6	6,405	4,992	77.9	2,479	2,113	85.2	25	16	64.0	6,219	4,750	76.4	324	256	79.0	15,819	12,402	78.4
Private individual	33	27	81.8	199	155	77.9	5,413	4,310	79.6	2,046	1,675	81.9	19	17	89.5	4,800	3,717	77.4	94	77	81.9	12,664	10,017	79.1
Medicare	136	100	73.5	181	153	84.5	14,454	11,857	82.0	4,446	3,846	86.5	29	11	37.9	10,592	8,509	80.3	312	253	81.1	30,298	24,839	82.0
Medicaid	221	163	73.8	653	540	82.7	23,501	18,446	78.5	13,818	11,881	86.0	54	38	70.4	9,616	7,430	77.3	757	615	81.2	48,951	39,367	80.4
Medicare and Medicaid	94	80	85.1	151	135	89.4	9,074	7,660	84.4	4,036	3,539	87.7	17	16	94.1	5,753	4,702	81.7	599	530	88.5	19,774	16,701	84.5
Veterans Administration	5	5	100.0	4	4	100.0	73	53	72.6	22	16	72.7	4	3	75.0	98	72	73.5	7	6	85.7	214	160	74.8
Indian Health Service	61	40	65.6	0	—	—	2	0	0.0	2	2	100.0	0	—	—	4	3	75.0	0	—	—	69	45	65.2
Other plan	8	7	87.5	62	49	79.0	1,078	907	84.1	1,033	879	85.1	4	4	100.0	738	556	75.3	17	11	64.7	2,975	2,436	81.9
No coverage	64	55	85.9	303	246	81.2	8,102	6,490	80.1	7,196	6,059	84.2	20	19	95.0	3,650	2,769	75.9	297	230	77.4	19,694	15,909	80.8
Multiple coverages	116	99	85.3	277	216	78.0	7,167	5,982	83.5	4,017	3,473	86.5	23	17	73.9	6,654	5,369	80.7	542	467	86.2	18,924	15,718	83.1
Housing status																								
Stable	671	526	78.4	1,872	1,543	82.4	67,926	55,223	81.3	35,435	30,442	85.9	174	130	74.7	43,956	34,854	79.3	2,847	2,352	82.6	153,651	125,649	81.8
Temporary	41	30	73.2	95	74	77.9	4,139	3,184	76.9	1,727	1,388	80.4	11	7	63.6	1,836	1,364	74.3	84	67	79.8	7,962	6,131	77.0
Unstable	62	47	75.8	47	36	76.6	2,534	1,835	72.4	1,670	1,445	86.5	8	3	37.5	1,368	980	71.6	52	36	69.2	5,771	4,397	76.2
HHS region[f]																								
Region 1	23	22	95.7	111	94	84.7	2,201	1,770	80.4	2,471	2,013	81.5	6	4	66.7	3,371	2,577	76.4	89	69	77.5	8,330	6,588	79.1
Region 2	54	45	83.3	383	337	88.0	11,588	9,840	84.9	14,335	12,931	90.2	33	31	93.9	3,915	3,276	83.7	162	140	86.4	30,861	26,915	87.2
Region 3	75	64	85.3	159	138	86.8	12,452	9,895	79.5	2,218	1,930	87.0	8	6	75.0	5,828	4,575	78.5	1,738	1,497	86.1	22,568	18,169	80.5
Region 4	114	93	81.6	210	184	87.6	27,254	22,432	82.3	4,800	4,139	86.2	19	15	78.9	12,812	10,463	81.7	294	234	79.6	45,556	37,598	82.5
Region 5	48	30	62.5	186	148	79.6	8,320	6,223	74.8	2,224	1,768	79.5	17	12	70.6	5,480	3,966	72.4	232	136	58.6	16,622	12,353	74.3
Region 6	139	102	73.4	215	159	74.0	6,827	5,315	77.9	4,411	3,549	80.5	16	12	75.0	3,773	2,864	75.9	101	81	80.2	15,567	12,140	78.0
Region 7	12	6	50.0	33	27	81.8	1,189	888	74.7	234	182	77.8	3	3	100.0	1,597	1,202	75.3	26	20	76.9	3,095	2,328	75.2
Region 8	53	41	77.4	36	25	69.4	497	365	73.4	641	534	83.3	0	—	—	1,637	1,199	73.2	35	28	80.0	2,926	2,209	75.5
Region 9	162	134	82.7	611	477	78.1	3,137	2,408	76.8	7,116	5,877	82.6	77	47	61.0	6,967	5,574	80.0	236	192	81.4	18,373	14,754	80.3
Region 10	113	79	69.9	83	71	85.5	616	489	79.4	388	308	79.4	18	13	72.2	1,565	1,181	75.5	55	41	74.5	2,885	2,202	76.3
Total[b]	**802**	**622**	**77.6**	**2,058**	**1,682**	**81.7**	**75,767**	**61,010**	**80.5**	**39,264**	**33,591**	**85.6**	**198**	**144**	**72.7**	**48,438**	**38,056**	**78.6**	**3,007**	**2,467**	**82.0**	**170,468**	**138,238**	**81.1**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.

[a] Hispanics/Latinos can be of any race.

[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.

[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[d] Includes hemophilia and blood transfusion.

[e] Includes any sexual transmission category reported by transgender clients.

[f] See Technical Notes for the states/territories in each region.

Table 14b. Viral suppression among older adults (aged 50 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)																								
50–54	227	198	87.2	778	744	95.6	18,627	16,567	88.9	11,528	10,722	93.0	55	51	92.7	11,365	10,442	91.9	632	577	91.3	43,459	39,522	90.9
55–59	241	227	94.2	567	541	95.4	22,069	19,872	90.0	11,771	11,022	93.6	77	70	90.9	14,499	13,652	94.2	831	764	91.9	50,305	46,379	92.2
60–64	191	177	92.7	366	353	96.4	18,575	17,041	91.7	8,622	8,116	94.1	35	33	94.3	12,140	11,633	95.8	754	704	93.4	40,866	38,232	93.6
≥65	139	129	92.8	365	351	96.2	18,368	17,221	93.8	8,278	7,965	96.2	39	34	87.2	11,702	11,427	97.6	776	742	95.6	39,879	38,069	95.5
Gender																								
Male	574	522	90.9	1,581	1,512	95.6	44,843	40,485	90.3	28,082	26,414	94.1	155	142	91.6	41,526	39,475	95.1	1,920	1,781	92.8	119,329	110,931	93.0
Female	208	194	93.3	456	438	96.1	31,875	29,366	92.1	11,446	10,802	94.4	42	38	90.5	7,706	7,229	93.8	1,044	981	94.0	52,969	49,228	92.9
Transgender	16	15	93.8	38	38	100.0	905	835	92.3	666	604	90.7	9	8	88.9	472	448	94.9	28	25	89.3	2,173	2,009	92.5
Transmission category																								
Male client																								
Male-to-male sexual contact	328	305	93.0	882	849	96.3	16,536	15,161	91.7	14,583	13,853	95.0	107	98	91.6	30,167	28,859	95.7	879	820	93.3	63,814	60,260	94.4
Injection drug use	43	39	90.7	43	41	95.3	3,670	3,285	89.5	2,610	2,397	91.8	8	7	87.5	2,152	1,966	91.4	338	311	92.0	8,887	8,066	90.8
Male-to-male sexual contact and injection drug use	45	39	86.7	20	17	85.0	822	732	89.1	617	566	91.7	2	2	100.0	1,982	1,821	91.9	84	77	91.7	3,581	3,261	91.1
Heterosexual contact[c]	101	87	86.1	447	426	95.3	21,283	19,043	89.5	8,675	8,116	93.6	26	23	88.5	4,753	4,495	94.6	556	516	92.8	35,966	32,818	91.2
Perinatal	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
Other[d]	5	5	100.0	33	32	97.0	248	232	93.5	161	151	93.8	1	1	100.0	397	379	95.5	14	12	85.7	863	816	94.6
Female client																								
Injection drug use	39	35	89.7	5	5	100.0	2,218	2,008	90.5	849	795	93.6	6	5	83.3	1,275	1,164	91.3	206	189	91.7	4,611	4,212	91.3
Heterosexual contact[c]	153	145	94.8	376	366	97.3	27,635	25,538	92.4	9,710	9,181	94.6	30	28	93.3	5,972	5,637	94.4	805	760	94.4	44,802	41,770	93.2
Perinatal	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
Other[d]	3	3	100.0	20	18	90.0	377	357	94.7	147	141	95.9	1	1	100.0	118	115	97.5	13	13	100.0	684	653	95.5
Transgender client																								
Sexual contact[e]	10	9	90.0	27	27	100.0	729	673	92.3	519	472	90.9	8	7	87.5	315	300	95.2	20	19	95.0	1,639	1,518	92.6
Injection drug use	0	—	—	0	—	—	9	9	100.0	7	7	100.0	0	—	—	7	7	100.0	2	1	50.0	25	24	96.0
Sexual contact[e] and injection drug use	3	3	100.0	2	2	100.0	42	38	90.5	29	25	86.2	0	—	—	28	24	85.7	4	3	75.0	109	96	88.1
Perinatal	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
Other[d]	0	—	—	0	—	—	6	6	100.0	3	2	66.7	0	—	—	3	3	100.0	0	—	—	12	11	91.7
Federal poverty level																								
0–100%	496	451	90.9	1,150	1,094	95.1	49,029	43,902	89.5	26,428	24,624	93.2	102	91	89.2	22,221	20,610	92.8	1,708	1,559	91.3	101,613	92,771	91.3
101–138%	100	93	93.0	215	204	94.9	8,579	8,003	93.3	3,959	3,781	95.5	27	25	92.6	6,622	6,348	95.9	362	336	92.8	19,928	18,853	94.6
139–250%	124	113	91.1	383	374	97.7	11,304	10,591	93.7	6,048	5,804	96.0	32	30	93.8	10,428	10,037	96.3	491	471	95.9	29,021	27,615	95.2
251–400%	41	38	92.7	187	177	94.7	4,972	4,744	95.4	2,317	2,237	96.5	22	21	95.5	5,463	5,319	97.4	297	288	97.0	13,341	12,866	96.4
>400%	24	23	95.8	99	98	99.0	1,884	1,775	94.2	847	818	96.6	14	14	100.0	3,387	3,323	98.1	112	110	98.2	6,410	6,202	96.8

Table 14b. Viral suppression among older adults (aged 50 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Health care coverage																								
Private employer	60	56	93.3	234	224	95.7	6,567	6,223	94.8	2,530	2,445	96.6	24	24	100.0	6,453	6,299	97.6	324	313	96.6	16,287	15,677	96.3
Private individual	37	36	97.3	196	189	96.4	5,563	5,196	93.4	2,134	2,070	97.0	21	21	100.0	4,920	4,761	96.8	95	92	96.8	13,020	12,416	95.4
Medicare	132	122	92.4	179	169	94.4	14,633	13,588	92.9	4,537	4,312	95.0	33	30	90.9	10,865	10,481	96.5	317	290	91.5	30,836	29,120	94.4
Medicaid	221	194	87.8	664	633	95.3	24,031	21,295	88.6	14,038	13,029	92.8	56	47	83.9	9,892	9,109	92.1	747	677	90.6	49,964	45,270	90.6
Medicare and Medicaid	87	83	95.4	152	146	96.1	9,260	8,589	92.8	4,098	3,894	95.0	17	15	88.2	5,814	5,520	94.9	606	574	94.7	20,083	18,868	94.0
Veterans Administration	5	5	100.0	5	5	100.0	75	70	93.3	21	21	100.0	4	4	100.0	104	100	96.2	6	6	100.0	220	211	95.9
Indian Health Service	65	63	96.9	0	—	—	1	1	100.0	2	2	100.0	0	—	—	4	3	75.0	0	—	—	72	69	95.8
Other plan	8	8	100.0	63	63	100.0	1,090	982	90.1	1,050	997	95.0	4	4	100.0	758	725	95.6	18	18	100.0	3,028	2,832	93.5
No coverage	57	48	84.2	292	276	94.5	8,673	7,592	87.5	7,527	6,977	92.7	20	18	90.0	3,837	3,419	89.1	303	281	92.7	20,774	18,671	89.9
Multiple coverages	117	108	92.3	279	272	97.5	7,259	6,724	92.6	4,097	3,933	96.0	24	22	91.7	6,744	6,438	95.5	541	504	93.2	19,181	18,114	94.4
Housing status																								
Stable	670	620	92.5	1,886	1,811	96.0	69,633	63,907	91.8	36,299	34,342	94.6	179	164	91.6	45,171	43,146	95.5	2,830	2,650	93.6	157,446	147,365	93.6
Temporary	40	38	95.0	105	104	99.0	4,356	3,757	86.2	1,809	1,622	89.7	14	14	100.0	1,926	1,721	89.4	88	79	89.8	8,366	7,359	88.0
Unstable	65	53	81.5	47	38	80.9	2,659	2,115	79.5	1,671	1,465	87.7	8	5	62.5	1,452	1,177	81.1	57	40	70.2	5,991	4,920	82.1
HHS region[f]																								
Region 1	23	23	100.0	112	108	96.4	2,197	2,077	94.5	2,491	2,404	96.5	7	7	100.0	3,262	3,175	97.3	80	77	96.3	8,215	7,912	96.3
Region 2	52	47	90.4	389	376	96.7	11,890	10,734	90.3	14,536	13,640	93.8	34	32	94.1	4,011	3,829	95.5	167	157	94.0	31,467	29,167	92.7
Region 3	61	57	93.4	162	158	97.5	12,621	11,596	91.9	2,277	2,149	94.4	10	9	90.0	5,964	5,702	95.6	1,705	1,598	93.7	22,888	21,349	93.3
Region 4	119	108	90.8	215	202	94.0	28,067	25,441	90.6	4,955	4,680	94.5	18	17	94.4	13,230	12,505	94.5	295	273	92.5	46,959	43,281	92.2
Region 5	50	47	94.0	190	182	95.8	8,563	7,940	92.7	2,344	2,263	96.5	16	16	100.0	5,758	5,530	96.0	231	211	91.3	17,269	16,300	94.4
Region 6	144	128	88.9	193	185	95.9	7,023	6,273	89.3	4,603	4,239	92.1	15	14	93.3	4,024	3,684	91.6	105	89	84.8	16,168	14,672	90.7
Region 7	13	11	84.6	33	33	100.0	1,236	1,145	92.6	251	237	94.4	3	3	100.0	1,636	1,565	95.7	29	26	89.7	3,202	3,020	94.3
Region 8	46	43	93.5	37	35	94.6	489	458	93.7	635	603	95.0	0	—	—	1,562	1,509	96.6	34	33	97.1	2,817	2,695	95.7
Region 9	163	150	92.0	628	599	95.4	3,164	2,871	90.7	7,263	6,814	93.8	84	72	85.7	7,088	6,686	94.3	249	237	95.2	18,710	17,494	93.5
Region 10	118	109	92.4	87	82	94.3	646	600	92.9	408	383	93.9	18	17	94.4	1,617	1,526	94.4	58	51	87.9	3,001	2,817	93.9
Total[b]	**798**	**731**	**91.6**	**2,076**	**1,989**	**95.8**	**77,639**	**70,701**	**91.1**	**40,199**	**37,825**	**94.1**	**206**	**188**	**91.3**	**49,706**	**47,154**	**94.9**	**2,993**	**2,787**	**93.1**	**174,509**	**162,202**	**92.9**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.

[a] Hispanics/Latinos can be of any race.

[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.

[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[d] Includes hemophilia and blood transfusion.

[e] Includes any sexual transmission category reported by transgender clients.

[f] See Technical Notes for the states/territories in each region.

Table 15a. Retention in care among youth and young adults (aged 13–24 years) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Gender																								
Male	45	24	53.3	133	109	82.0	4,721	3,484	73.8	2,175	1,626	74.8	13	10	76.9	920	666	72.4	152	106	69.7	8,251	6,096	73.9
Female	4	4	100.0	47	40	85.1	1,322	1,050	79.4	384	312	81.3	6	6	100.0	254	182	71.7	48	39	81.3	2,084	1,645	78.9
Transgender	2	2	100.0	4	2	50.0	295	202	68.5	145	99	68.3	0	—	—	38	25	65.8	12	9	75.0	504	345	68.5
Transmission category																								
Male client																								
Male-to-male sexual contact	34	17	50.0	81	68	84.0	3,581	2,624	73.3	1,648	1,261	76.5	6	4	66.7	678	500	73.7	121	86	71.1	6,191	4,593	74.2
Injection drug use	0	—	—	2	2	100.0	8	6	75.0	8	4	50.0	1	1	100.0	22	11	50.0	2	0	0.0	43	24	55.8
Male-to-male sexual contact and injection drug use	2	1	50.0	0	—	—	25	14	56.0	23	14	60.9	0	—	—	25	16	64.0	1	0	0.0	76	45	59.2
Heterosexual contact[c]	0	—	—	8	6	75.0	368	262	71.2	148	97	65.5	1	0	0.0	59	44	74.6	9	6	66.7	600	421	70.2
Perinatal	3	2	66.7	26	24	92.3	497	394	79.3	135	108	80.0	4	4	100.0	71	51	71.8	12	10	83.3	753	598	79.4
Other[d]	0	—	—	0	—	—	8	7	87.5	4	3	75.0	0	—	—	2	2	100.0	0	—	—	14	12	85.7
Female client																								
Injection drug use	1	1	100.0	0	—	—	1	0	0.0	4	2	50.0	0	—	—	15	10	66.7	2	0	0.0	23	13	56.5
Heterosexual contact[c]	2	2	100.0	4	3	75.0	612	471	77.0	187	149	79.7	5	5	100.0	130	93	71.5	25	20	80.0	971	747	76.9
Perinatal	0	—	—	40	34	85.0	629	518	82.4	154	130	84.4	1	1	100.0	96	73	76.0	20	18	90.0	949	781	82.3
Other[d]	0	—	—	0	—	—	7	5	71.4	5	4	80.0	0	—	—	1	1	100.0	0	—	—	13	10	76.9
Transgender client																								
Sexual contact[e]	2	2	100.0	4	2	50.0	248	175	70.6	119	82	68.9	0	—	—	28	19	67.9	11	8	72.7	418	292	69.9
Injection drug use	0	—	—	0	—	—	1	0	0.0	1	0	0.0	0	—	—	1	1	100.0	0	—	—	3	1	33.3
Sexual contact[e] and injection drug use	0	—	—	0	—	—	1	1	100.0	0	—	—	0	—	—	2	1	50.0	0	—	—	3	2	66.7
Perinatal	0	—	—	0	—	—	5	3	60.0	1	1	100.0	0	—	—	2	2	100.0	1	1	100.0	9	7	77.8
Other[d]	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
Federal poverty level																								
0–100%	33	17	51.5	109	90	82.6	3,969	2,889	72.8	1,683	1,231	73.1	13	10	76.9	693	491	70.9	132	98	74.2	6,703	4,883	72.8
101–138%	2	2	100.0	18	11	61.1	566	454	80.2	204	162	79.4	1	1	100.0	91	63	69.2	17	13	76.5	912	714	78.3
139–250%	9	8	88.9	28	23	82.1	1,098	879	80.1	507	402	79.3	4	4	100.0	233	171	73.4	36	28	77.8	1,930	1,528	79.2
251–400%	4	3	75.0	17	17	100.0	351	265	75.5	189	153	81.0	0	—	—	122	96	78.7	16	8	50.0	703	544	77.4
>400%	1	0	0.0	8	6	75.0	151	120	79.5	51	44	86.3	0	—	—	24	16	66.7	7	6	85.7	244	193	79.1
Health care coverage																								
Private employer	6	4	66.7	35	27	77.1	709	536	75.6	194	146	75.3	1	1	100.0	224	167	74.6	31	22	71.0	1,218	916	75.2
Private individual	1	1	100.0	18	17	94.4	555	416	75.0	160	125	78.1	2	1	50.0	148	107	72.3	12	7	58.3	901	676	75.0
Medicare	0	—	—	1	0	0.0	25	21	84.0	10	8	80.0	0	—	—	6	5	83.3	1	0	0.0	45	35	77.8
Medicaid	24	16	66.7	56	49	87.5	2,821	2,136	75.7	1,006	754	75.0	8	8	100.0	417	293	70.3	96	67	69.8	4,478	3,364	75.1
Medicare and Medicaid	0	—	—	2	1	50.0	33	24	72.7	16	13	81.3	0	—	—	3	1	33.3	2	2	100.0	56	41	73.2
Veterans Administration	0	—	—	3	3	100.0	20	14	70.0	2	2	100.0	0	—	—	4	3	75.0	0	—	—	29	22	75.9
Indian Health Service	4	2	50.0	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	4	2	50.0
Other plan	0	—	—	5	3	60.0	90	69	76.7	92	66	71.7	1	1	100.0	26	19	73.1	3	2	66.7	221	164	74.2
No coverage	10	4	40.0	31	23	74.2	1,552	1,117	72.0	982	745	75.9	6	4	66.7	211	140	66.4	35	24	68.6	2,855	2,075	72.7
Multiple coverages	6	3	50.0	30	27	90.0	501	385	76.8	218	164	75.2	0	—	—	172	137	79.7	30	29	96.7	972	757	77.9

Table 15a. Retention in care among youth and young adults (aged 13–24 years) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Housing status																								
Stable	44	25	56.8	174	142	81.6	5,503	4,147	75.4	2,259	1,713	75.8	17	14	82.4	1,055	772	73.2	184	133	72.3	9,317	7,009	75.2
Temporary	3	1	33.3	5	5	100.0	470	358	76.2	244	177	72.5	0	—	—	93	59	63.4	17	12	70.6	835	615	73.7
Unstable	2	2	100.0	1	0	0.0	247	160	64.8	149	116	77.9	1	1	100.0	45	30	66.7	8	6	75.0	466	322	69.1
HHS region[f]																								
Region 1	0	—	—	7	6	85.7	107	83	77.6	92	61	66.3	0	—	—	40	31	77.5	6	6	100.0	255	188	73.7
Region 2	0	—	—	19	14	73.7	477	355	74.4	514	413	80.4	2	2	100.0	71	50	70.4	13	11	84.6	1,113	859	77.2
Region 3	2	1	50.0	12	11	91.7	745	593	79.6	149	122	81.9	0	—	—	99	72	72.7	50	40	80.0	1,064	843	79.2
Region 4	3	2	66.7	27	23	85.2	2,603	1,976	75.9	516	404	78.3	6	4	66.7	392	282	71.9	49	30	61.2	3,618	2,742	75.8
Region 5	11	8	72.7	17	12	70.6	902	647	71.7	194	146	75.3	2	2	100.0	143	92	64.3	28	19	67.9	1,332	946	71.0
Region 6	15	9	60.0	26	19	73.1	720	502	69.7	546	391	71.6	3	2	66.7	164	119	72.6	16	11	68.8	1,513	1,067	70.5
Region 7	2	1	50.0	8	5	62.5	160	119	74.4	38	31	81.6	0	—	—	39	29	74.4	13	10	76.9	260	195	75.0
Region 8	5	4	80.0	8	8	100.0	80	68	85.0	69	46	66.7	1	1	100.0	45	35	77.8	6	5	83.3	221	174	78.7
Region 9	7	3	42.9	43	39	90.7	245	166	67.8	472	335	71.0	4	4	100.0	137	96	70.1	16	12	75.0	932	662	71.0
Region 10	5	2	40.0	7	6	85.7	33	23	69.7	29	23	79.3	0	—	—	33	25	75.8	4	1	25.0	115	84	73.0
Total[b]	**51**	**30**	**58.8**	**184**	**151**	**82.1**	**6,340**	**4,736**	**74.7**	**2,704**	**2,037**	**75.3**	**19**	**16**	**84.2**	**1,213**	**873**	**72.0**	**212**	**154**	**72.6**	**10,850**	**8,089**	**74.6**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.

[a] Hispanics/Latinos can be of any race.

[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.

[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[d] Includes hemophilia and blood transfusion.

[e] Includes any sexual transmission category reported by transgender clients.

[f] See Technical Notes for the states/territories in each region.

Table 15b. Viral suppression among youth and young adults (aged 13–24 years) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Gender																								
Male	49	41	83.7	159	142	89.3	5,361	4,425	82.5	2,541	2,175	85.6	14	14	100.0	1,021	905	88.6	160	141	88.1	9,396	7,918	84.3
Female	6	4	66.7	46	42	91.3	1,422	1,163	81.8	426	361	84.7	6	5	83.3	282	241	85.5	54	41	75.9	2,261	1,872	82.8
Transgender	2	2	100.0	5	4	80.0	333	262	78.7	154	131	85.1	0	—	—	43	39	90.7	16	11	68.8	563	456	81.0
Transmission category																								
Male client																								
Male-to-male sexual contact	41	33	80.5	99	89	89.9	4,094	3,398	83.0	1,959	1,683	85.9	8	8	100.0	766	694	90.6	126	111	88.1	7,135	6,047	84.8
Injection drug use	0	—	—	2	2	100.0	9	7	77.8	9	6	66.7	1	1	100.0	22	17	77.3	2	2	100.0	45	35	77.8
Male-to-male sexual contact and injection drug use	1	1	100.0	0	—	—	28	21	75.0	22	18	81.8	0	—	—	27	22	81.5	1	1	100.0	80	63	78.8
Heterosexual contact[c]	0	—	—	8	7	87.5	432	346	80.1	166	135	81.3	0	—	—	69	50	72.5	11	11	100.0	693	555	80.1
Perinatal	3	3	100.0	27	24	88.9	521	434	83.3	141	125	88.7	4	4	100.0	69	62	89.9	13	10	76.9	783	667	85.2
Other[d]	0	—	—	1	1	100.0	9	8	88.9	5	5	100.0	0	—	—	5	3	60.0	0	—	—	20	17	85.0
Female client																								
Injection drug use	1	1	100.0	0	—	—	2	2	100.0	5	3	60.0	0	—	—	19	12	63.2	2	2	100.0	29	20	69.0
Heterosexual contact[c]	4	2	50.0	4	2	50.0	679	574	84.5	228	193	84.6	5	4	80.0	149	123	82.6	29	20	69.0	1,104	922	83.5
Perinatal	0	—	—	40	38	95.0	650	517	79.5	156	130	83.3	1	1	100.0	97	90	92.8	21	17	81.0	975	801	82.2
Other[d]	0	—	—	0	—	—	6	6	100.0	6	6	100.0	0	—	—	1	1	100.0	1	1	100.0	14	14	100.0
Transgender client																								
Sexual contact[e]	2	2	100.0	4	4	100.0	284	216	76.1	124	107	86.3	0	—	—	33	30	90.9	15	10	66.7	469	374	79.7
Injection drug use	0	—	—	0	—	—	1	1	100.0	1	1	100.0	0	—	—	1	1	100.0	0	—	—	3	3	100.0
Sexual contact[e] and injection drug use	0	—	—	0	—	—	1	1	100.0	1	0	0.0	0	—	—	2	2	100.0	0	—	—	4	3	75.0
Perinatal	0	—	—	0	—	—	5	5	100.0	1	1	100.0	0	—	—	2	2	100.0	1	1	100.0	9	9	100.0
Other[d]	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
Federal poverty level																								
0–100%	33	28	84.8	123	113	91.9	4,517	3,628	80.3	1,962	1,656	84.4	14	14	100.0	772	658	85.2	142	117	82.4	7,634	6,275	82.2
101–138%	2	2	100.0	19	17	89.5	617	527	85.4	233	202	86.7	1	1	100.0	106	98	92.5	19	16	84.2	1,005	870	86.6
139–250%	13	11	84.6	34	29	85.3	1,222	1,039	85.0	567	510	89.9	4	3	75.0	265	238	89.8	43	38	88.4	2,165	1,879	86.8
251–400%	5	4	80.0	19	16	84.2	411	356	86.6	226	195	86.3	0	—	—	129	124	96.1	15	13	86.7	813	713	87.7
>400%	0	—	—	8	8	100.0	155	138	89.0	59	51	86.4	0	—	—	28	27	96.4	7	6	85.7	259	231	89.2
Health care coverage																								
Private employer	6	5	83.3	39	39	100.0	785	691	88.0	222	203	91.4	1	1	100.0	236	223	94.5	34	30	88.2	1,341	1,207	90.0
Private individual	2	1	50.0	24	21	87.5	609	542	89.0	180	168	93.3	1	1	100.0	160	144	90.0	14	11	78.6	994	891	89.6
Medicare	0	—	—	1	1	100.0	30	25	83.3	11	9	81.8	0	—	—	8	6	75.0	1	1	100.0	53	44	83.0
Medicaid	27	21	77.8	60	52	86.7	3,110	2,524	81.2	1,105	940	85.1	8	8	100.0	453	390	86.1	104	83	79.8	4,918	4,055	82.5
Medicare and Medicaid	0	—	—	2	2	100.0	36	30	83.3	16	15	93.8	0	—	—	4	4	100.0	2	2	100.0	60	53	88.3
Veterans Administration	0	—	—	3	3	100.0	21	17	81.0	2	1	50.0	0	—	—	6	5	83.3	0	—	—	33	27	81.8
Indian Health Service	5	4	80.0	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	5	4	80.0
Other plan	0	—	—	5	4	80.0	104	86	82.7	103	91	88.3	1	1	100.0	30	25	83.3	4	3	75.0	252	215	85.3
No coverage	13	12	92.3	37	32	86.5	1,847	1,428	77.3	1,205	1,008	83.7	8	7	87.5	260	211	81.2	39	34	87.2	3,432	2,751	80.2
Multiple coverages	4	4	100.0	32	29	90.6	534	476	89.1	248	214	86.3	0	—	—	186	174	93.5	30	27	90.0	1,048	936	89.3

Table 15b. Viral suppression among youth and young adults (aged 13–24 years) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Housing status																								
Stable	52	43	82.7	192	174	90.6	6,186	5,105	82.5	2,611	2,249	86.1	18	17	94.4	1,171	1,044	89.2	203	173	85.2	10,524	8,876	84.3
Temporary	2	2	100.0	7	6	85.7	544	448	82.4	289	245	84.8	0	—	—	104	90	86.5	16	13	81.3	966	808	83.6
Unstable	3	2	66.7	2	2	100.0	274	208	75.9	173	135	78.0	1	1	100.0	52	33	63.5	7	5	71.4	522	393	75.3
HHS region[f]																								
Region 1	0	—	—	8	6	75.0	119	105	88.2	104	92	88.5	0	—	—	41	35	85.4	7	4	57.1	282	245	86.9
Region 2	0	—	—	24	21	87.5	536	431	80.4	570	495	86.8	2	2	100.0	77	69	89.6	14	12	85.7	1,241	1,043	84.0
Region 3	2	1	50.0	15	14	93.3	814	677	83.2	180	153	85.0	1	1	100.0	110	95	86.4	55	48	87.3	1,184	996	84.1
Region 4	5	4	80.0	30	27	90.0	2,943	2,380	80.9	596	524	87.9	5	5	100.0	442	385	87.1	52	45	86.5	4,093	3,386	82.7
Region 5	11	10	90.9	18	17	94.4	975	840	86.2	214	189	88.3	2	2	100.0	155	147	94.8	29	23	79.3	1,432	1,251	87.4
Region 6	20	17	85.0	27	22	81.5	830	667	80.4	635	529	83.3	3	2	66.7	182	155	85.2	20	17	85.0	1,734	1,423	82.1
Region 7	2	2	100.0	8	8	100.0	182	158	86.8	44	37	84.1	0	—	—	42	41	97.6	14	12	85.7	292	258	88.4
Region 8	3	3	100.0	9	8	88.9	85	78	91.8	71	61	85.9	1	1	100.0	49	48	98.0	5	5	100.0	231	211	91.3
Region 9	7	5	71.4	52	48	92.3	280	223	79.6	576	471	81.8	5	5	100.0	158	128	81.0	17	13	76.5	1,112	905	81.4
Region 10	6	4	66.7	8	7	87.5	42	35	83.3	39	35	89.7	0	—	—	36	33	91.7	5	4	80.0	142	123	86.6
Total[b]	**57**	**47**	**82.5**	**210**	**188**	**89.5**	**7,118**	**5,851**	**82.2**	**3,121**	**2,667**	**85.5**	**20**	**19**	**95.0**	**1,347**	**1,186**	**88.0**	**230**	**193**	**83.9**	**12,228**	**10,252**	**83.8**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.

[a] Hispanics/Latinos can be of any race.

[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.

[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[d] Includes hemophilia and blood transfusion.

[e] Includes any sexual transmission category reported by transgender clients.

[f] See Technical Notes for the states/territories in each region.

Table 16a. Retention in care among young gay, bisexual, and other men who have sex with men (aged 13–24 years) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Federal poverty level																								
0–100%	23	9	39.1	53	45	84.9	2,227	1,587	71.3	962	714	74.2	5	3	60.0	361	276	76.5	66	50	75.8	3,716	2,700	72.7
101–138%	0	—	—	10	8	80.0	296	233	78.7	122	95	77.9	0	—	—	50	32	64.0	12	9	75.0	496	381	76.8
139–250%	8	7	87.5	10	8	80.0	702	545	77.6	362	293	80.9	1	1	100.0	154	110	71.4	27	20	74.1	1,272	991	77.9
251–400%	1	1	100.0	7	7	100.0	219	166	75.8	136	110	80.9	0	—	—	77	60	77.9	12	5	41.7	454	349	76.9
>400%	0	—	—	1	0	0.0	63	51	81.0	33	29	87.9	0	—	—	16	12	75.0	3	2	66.7	117	95	81.2
Health care coverage																								
Private employer	4	2	50.0	10	9	90.0	393	291	74.0	144	112	77.8	1	1	100.0	134	98	73.1	23	15	65.2	718	535	74.5
Private individual	1	1	100.0	11	11	100.0	385	291	75.6	109	82	75.2	0	—	—	109	83	76.1	7	4	57.1	623	472	75.8
Medicare	0	—	—	1	0	0.0	13	10	76.9	2	2	100.0	0	—	—	3	3	100.0	0	—	—	19	15	78.9
Medicaid	18	10	55.6	17	15	88.2	1,298	945	72.8	502	374	74.5	2	2	100.0	188	141	75.0	47	32	68.1	2,091	1,535	73.4
Medicare and Medicaid	0	—	—	2	1	50.0	12	9	75.0	10	8	80.0	0	—	—	1	0	0.0	1	1	100.0	26	19	73.1
Veterans Administration	0	—	—	0	—	—	14	8	57.1	0	—	—	0	—	—	2	1	50.0	0	—	—	16	9	56.3
Indian Health Service	2	1	50.0	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	2	1	50.0
Other plan	0	—	—	2	1	50.0	57	42	73.7	62	49	79.0	0	—	—	13	9	69.2	1	1	100.0	138	105	76.1
No coverage	6	2	33.3	22	17	77.3	1,093	791	72.4	678	532	78.5	3	1	33.3	129	88	68.2	28	20	71.4	1,965	1,455	74.0
Multiple coverages	3	1	33.3	15	13	86.7	298	227	76.2	133	98	73.7	0	—	—	97	76	78.4	13	13	100.0	563	431	76.6
Housing status																								
Stable	29	14	48.3	77	64	83.1	3,107	2,281	73.4	1,400	1,079	77.1	5	3	60.0	605	446	73.7	109	78	71.6	5,359	3,989	74.4
Temporary	2	0	0.0	3	3	100.0	277	223	80.5	153	108	70.6	0	—	—	50	38	76.0	6	4	66.7	493	378	76.7
Unstable	2	2	100.0	0	—	—	138	85	61.6	81	64	79.0	1	1	100.0	15	12	80.0	5	3	60.0	243	168	69.1
HHS region[c]																								
Region 1	0	—	—	2	2	100.0	34	25	73.5	53	36	67.9	0	—	—	17	13	76.5	1	1	100.0	109	78	71.6
Region 2	0	—	—	13	13	100.0	206	154	74.8	250	199	79.6	1	1	100.0	30	24	80.0	4	4	100.0	510	400	78.4
Region 3	2	1	50.0	1	1	100.0	346	252	72.8	79	64	81.0	0	—	—	49	34	69.4	34	27	79.4	513	381	74.3
Region 4	1	1	100.0	15	12	80.0	1,644	1,228	74.7	346	279	80.6	1	0	0.0	220	165	75.0	32	19	59.4	2,266	1,710	75.5
Region 5	9	6	66.7	6	4	66.7	491	347	70.7	134	103	76.9	2	2	100.0	77	52	67.5	10	6	60.0	735	525	71.4
Region 6	9	4	44.4	6	3	50.0	444	320	72.1	328	247	75.3	2	1	50.0	96	68	70.8	10	7	70.0	909	659	72.5
Region 7	1	0	0.0	3	3	100.0	76	57	75.0	23	20	87.0	0	—	—	23	18	78.3	6	4	66.7	132	102	77.3
Region 8	2	2	100.0	0	—	—	16	12	75.0	40	30	75.0	0	—	—	28	21	75.0	3	3	100.0	89	68	76.4
Region 9	6	2	33.3	26	23	88.5	122	77	63.1	321	229	71.3	0	—	—	86	61	70.9	10	8	80.0	573	402	70.2
Region 10	3	1	33.3	5	5	100.0	10	6	60.0	18	13	72.2	0	—	—	21	16	76.2	4	1	25.0	64	45	70.3
Total[b]	**34**	**17**	**50.0**	**81**	**68**	**84.0**	**3,581**	**2,624**	**73.3**	**1,648**	**1,261**	**76.5**	**6**	**4**	**66.7**	**678**	**500**	**73.7**	**121**	**86**	**71.1**	**6,191**	**4,593**	**74.2**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Note: Data are included only for males with the transmission category male-to-male sexual contact; data do not include male clients who reported male-to-male sexual contact and injection drug use.
[a] Hispanics/Latinos can be of any race.
[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.
[c] See Technical Notes for the states/territories in each region.

Table 16b. Viral suppression among young gay, bisexual, and other men who have sex with men (aged 13–24 years) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Federal poverty level																								
0–100%	25	20	80.0	62	60	96.8	2,566	2,083	81.2	1,161	985	84.8	7	7	100.0	404	363	89.9	70	63	90.0	4,315	3,597	83.4
101–138%	1	1	100.0	12	10	83.3	322	288	89.4	143	123	86.0	0	—	—	59	54	91.5	13	11	84.6	554	490	88.4
139–250%	11	9	81.8	16	11	68.8	795	673	84.7	409	368	90.0	1	1	100.0	179	161	89.9	28	24	85.7	1,447	1,253	86.6
251–400%	1	1	100.0	8	7	87.5	262	224	85.5	166	143	86.1	0	—	—	82	79	96.3	11	10	90.9	535	466	87.1
>400%	0	—	—	1	1	100.0	67	60	89.6	40	35	87.5	0	—	—	20	19	95.0	3	2	66.7	132	118	89.4
Health care coverage																								
Private employer	3	3	100.0	12	12	100.0	456	396	86.8	171	155	90.6	1	1	100.0	148	144	97.3	25	22	88.0	823	737	89.6
Private individual	2	1	50.0	16	14	87.5	426	380	89.2	124	113	91.1	0	—	—	119	108	90.8	9	7	77.8	697	624	89.5
Medicare	0	—	—	1	1	100.0	16	13	81.3	2	2	100.0	0	—	—	3	3	100.0	0	—	—	22	19	86.4
Medicaid	19	14	73.7	22	20	90.9	1,478	1,227	83.0	565	482	85.3	2	2	100.0	207	184	88.9	47	42	89.4	2,363	1,988	84.1
Medicare and Medicaid	0	—	—	2	2	100.0	13	12	92.3	10	9	90.0	0	—	—	1	1	100.0	1	1	100.0	27	25	92.6
Veterans Administration	0	—	—	0	—	—	15	12	80.0	0	—	—	0	—	—	4	3	75.0	0	—	—	19	15	78.9
Indian Health Service	3	2	66.7	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	3	2	66.7
Other plan	0	—	—	1	1	100.0	61	51	83.6	70	65	92.9	0	—	—	16	14	87.5	1	1	100.0	152	135	88.8
No coverage	11	10	90.9	28	23	82.1	1,290	998	77.4	853	717	84.1	5	5	100.0	157	131	83.4	29	25	86.2	2,379	1,913	80.4
Multiple coverages	3	3	100.0	16	15	93.8	318	292	91.8	156	135	86.5	0	—	—	109	104	95.4	13	12	92.3	617	563	91.2
Housing status																								
Stable	36	29	80.6	94	84	89.4	3,562	2,966	83.3	1,667	1,440	86.4	7	7	100.0	678	617	91.0	115	103	89.6	6,193	5,271	85.1
Temporary	2	2	100.0	4	4	100.0	314	260	82.8	183	155	84.7	0	—	—	59	54	91.5	5	5	100.0	569	482	84.7
Unstable	3	2	66.7	0	—	—	152	117	77.0	95	76	80.0	1	1	100.0	20	15	75.0	4	2	50.0	277	214	77.3
HHS region[c]																								
Region 1	0	—	—	3	2	66.7	40	36	90.0	65	58	89.2	0	—	—	17	14	82.4	1	0	0.0	128	112	87.5
Region 2	0	—	—	15	14	93.3	230	201	87.4	288	248	86.1	1	1	100.0	35	31	88.6	4	4	100.0	579	504	87.0
Region 3	2	1	50.0	2	1	50.0	387	322	83.2	102	89	87.3	1	1	100.0	56	51	91.1	35	32	91.4	587	499	85.0
Region 4	2	2	100.0	18	16	88.9	1,888	1,539	81.5	409	363	88.8	1	1	100.0	246	222	90.2	34	29	85.3	2,606	2,178	83.6
Region 5	9	8	88.9	7	6	85.7	549	476	86.7	151	134	88.7	2	2	100.0	87	84	96.6	9	8	88.9	819	723	88.3
Region 6	14	12	85.7	11	8	72.7	525	425	81.0	404	336	83.2	2	2	100.0	111	98	88.3	11	10	90.9	1,085	896	82.6
Region 7	1	1	100.0	3	3	100.0	92	83	90.2	27	22	81.5	0	—	—	28	27	96.4	7	7	100.0	158	143	90.5
Region 8	1	1	100.0	0	—	—	16	15	93.8	43	39	90.7	0	—	—	31	31	100.0	3	3	100.0	95	89	93.7
Region 9	7	5	71.4	30	29	96.7	142	112	78.9	386	320	82.9	1	1	100.0	97	82	84.5	10	9	90.0	681	561	82.4
Region 10	4	2	50.0	5	5	100.0	12	11	91.7	24	21	87.5	0	—	—	23	21	91.3	4	3	75.0	75	66	88.0
Total[b]	**41**	**33**	**80.5**	**99**	**89**	**89.9**	**4,094**	**3,398**	**83.0**	**1,959**	**1,683**	**85.9**	**8**	**8**	**100.0**	**766**	**694**	**90.6**	**126**	**111**	**88.1**	**7,135**	**6,047**	**84.8**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Note: Data are included only for males with the transmission category male-to-male sexual contact; data do not include male clients who reported male-to-male sexual contact and injection drug use.
[a] Hispanics/Latinos can be of any race.
[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.
[c] See Technical Notes for the states/territories in each region.

Table 17a. Retention in care among young women (aged 13–24 years) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latina[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Transmission category																								
Injection drug use	1	1	100.0	0	—	—	1	0	0.0	4	2	50.0	0	—	—	15	10	66.7	2	0	0.0	23	13	56.5
Heterosexual contact[c]	2	2	100.0	4	3	75.0	612	471	77.0	187	149	79.7	5	5	100.0	130	93	71.5	25	20	80.0	971	747	76.9
Perinatal	0	—	—	40	34	85.0	629	518	82.4	154	130	84.4	1	1	100.0	96	73	76.0	20	18	90.0	949	781	82.3
Other[d]	0	—	—	0	—	—	7	5	71.4	5	4	80.0	0	—	—	1	1	100.0	0	—	—	13	10	76.9
Federal poverty level																								
0–100%	2	2	100.0	24	21	87.5	841	652	77.5	272	217	79.8	4	4	100.0	162	110	67.9	36	29	80.6	1,350	1,042	77.2
101–138%	1	1	100.0	4	2	50.0	130	108	83.1	32	29	90.6	0	—	—	21	16	76.2	3	3	100.0	194	161	83.0
139–250%	0	—	—	7	6	85.7	195	172	88.2	45	39	86.7	1	1	100.0	32	25	78.1	4	4	100.0	287	250	87.1
251–400%	1	1	100.0	5	5	100.0	50	40	80.0	10	7	70.0	0	—	—	20	17	85.0	3	2	66.7	89	72	80.9
>400%	0	—	—	5	4	80.0	44	35	79.5	11	9	81.8	0	—	—	6	3	50.0	1	1	100.0	67	52	77.6
Health care coverage																								
Private employer	1	1	100.0	14	11	78.6	149	120	80.5	20	13	65.0	0	—	—	42	33	78.6	5	4	80.0	233	183	78.5
Private individual	0	—	—	3	3	100.0	64	47	73.4	19	17	89.5	0	—	—	21	14	66.7	3	2	66.7	112	84	75.0
Medicare	0	—	—	0	—	—	8	7	87.5	1	0	0.0	0	—	—	2	1	50.0	0	—	—	11	8	72.7
Medicaid	2	2	100.0	18	15	83.3	813	650	80.0	216	178	82.4	3	3	100.0	120	80	66.7	25	20	80.0	1,207	956	79.2
Medicare and Medicaid	0	—	—	0	—	—	7	5	71.4	5	4	80.0	0	—	—	0	—	—	1	1	100.0	13	10	76.9
Veterans Administration	0	—	—	1	1	100.0	3	3	100.0	0	—	—	0	—	—	1	1	100.0	0	—	—	5	5	100.0
Indian Health Service	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
Other plan	0	—	—	1	1	100.0	8	6	75.0	6	3	50.0	0	—	—	5	3	60.0	1	0	0.0	21	13	61.9
No coverage	0	—	—	0	—	—	166	123	74.1	74	60	81.1	2	2	100.0	29	22	75.9	2	1	50.0	274	208	75.9
Multiple coverages	1	1	100.0	10	9	90.0	98	85	86.7	40	36	90.0	0	—	—	34	28	82.4	11	11	100.0	197	172	87.3
Housing status																								
Stable	3	3	100.0	45	38	84.4	1,151	926	80.5	317	261	82.3	5	5	100.0	216	157	72.7	40	32	80.0	1,794	1,433	79.9
Temporary	1	1	100.0	1	1	100.0	92	72	78.3	34	28	82.4	0	—	—	17	11	64.7	4	3	75.0	149	116	77.9
Unstable	0	—	—	0	—	—	48	34	70.8	20	15	75.0	0	—	—	16	10	62.5	3	3	100.0	88	63	71.6
HHS region[e]																								
Region 1	0	—	—	2	1	50.0	42	33	78.6	19	11	57.9	0	—	—	11	8	72.7	2	2	100.0	77	55	71.4
Region 2	0	—	—	2	1	50.0	121	96	79.3	103	90	87.4	0	—	—	15	10	66.7	5	4	80.0	249	203	81.5
Region 3	0	—	—	9	9	100.0	198	175	88.4	26	22	84.6	0	—	—	25	20	80.0	6	5	83.3	268	232	86.6
Region 4	0	—	—	7	7	100.0	460	364	79.1	69	53	76.8	2	2	100.0	92	66	71.7	10	6	60.0	645	503	78.0
Region 5	0	—	—	4	3	75.0	189	149	78.8	24	19	79.2	0	—	—	33	17	51.5	9	8	88.9	263	198	75.3
Region 6	2	2	100.0	7	7	100.0	122	88	72.1	60	47	78.3	1	1	100.0	28	24	85.7	4	4	100.0	226	175	77.4
Region 7	1	1	100.0	4	1	25.0	39	30	76.9	8	5	62.5	0	—	—	7	5	71.4	4	4	100.0	63	46	73.0
Region 8	0	—	—	4	4	100.0	36	30	83.3	6	6	100.0	1	1	100.0	8	8	100.0	1	1	100.0	56	50	89.3
Region 9	1	1	100.0	5	5	100.0	58	42	72.4	51	44	86.3	2	2	100.0	21	13	61.9	4	2	50.0	142	109	76.8
Region 10	0	—	—	1	0	0.0	13	9	69.2	2	2	100.0	0	—	—	5	4	80.0	0	—	—	21	15	71.4
Total[b]	**4**	**4**	**100.0**	**47**	**40**	**85.1**	**1,322**	**1,050**	**79.4**	**384**	**312**	**81.3**	**6**	**6**	**100.0**	**254**	**182**	**71.7**	**48**	**39**	**81.3**	**2,084**	**1,645**	**78.9**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.

[a] Hispanics/Latinas can be of any race.

[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.

[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[d] Includes hemophilia and blood transfusion.

[e] See Technical Notes for the states/territories in each region.

Table 17b. Viral suppression among young women (aged 13–24 years) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latina[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Transmission category																								
Injection drug use	1	1	100.0	0	—	—	2	2	100.0	5	3	60.0	0	—	—	19	12	63.2	2	2	100.0	29	20	69.0
Heterosexual contact[c]	4	2	50.0	4	2	50.0	679	574	84.5	228	193	84.6	5	4	80.0	149	123	82.6	29	20	69.0	1,104	922	83.5
Perinatal	0	—	—	40	38	95.0	650	517	79.5	156	130	83.3	1	1	100.0	97	90	92.8	21	17	81.0	975	801	82.2
Other[d]	0	—	—	0	—	—	6	6	100.0	6	6	100.0	0	—	—	1	1	100.0	1	1	100.0	14	14	100.0
Federal poverty level																								
0–100%	3	3	100.0	25	21	84.0	925	737	79.7	312	263	84.3	4	4	100.0	187	149	79.7	40	29	72.5	1,505	1,213	80.6
101–138%	0	—	—	3	3	100.0	141	117	83.0	33	29	87.9	0	—	—	23	23	100.0	3	2	66.7	206	177	85.9
139–250%	0	—	—	7	7	100.0	207	179	86.5	48	45	93.8	1	0	0.0	34	32	94.1	6	6	100.0	306	270	88.2
251–400%	2	1	50.0	5	5	100.0	53	48	90.6	12	8	66.7	0	—	—	21	21	100.0	3	2	66.7	97	86	88.7
>400%	0	—	—	5	5	100.0	44	40	90.9	11	9	81.8	0	—	—	6	6	100.0	1	1	100.0	67	61	91.0
Health care coverage																								
Private employer	2	1	50.0	15	15	100.0	156	140	89.7	20	18	90.0	0	—	—	43	40	93.0	5	4	80.0	243	220	90.5
Private individual	0	—	—	3	3	100.0	65	62	95.4	22	22	100.0	0	—	—	22	19	86.4	3	2	66.7	116	109	94.0
Medicare	0	—	—	0	—	—	10	10	100.0	1	1	100.0	0	—	—	3	2	66.7	0	—	—	14	13	92.9
Medicaid	4	3	75.0	16	13	81.3	869	691	79.5	229	189	82.5	3	3	100.0	135	109	80.7	29	21	72.4	1,295	1,036	80.0
Medicare and Medicaid	0	—	—	0	—	—	8	6	75.0	5	5	100.0	0	—	—	0	—	—	1	1	100.0	14	12	85.7
Veterans Administration	0	—	—	1	1	100.0	2	1	50.0	0	—	—	0	—	—	1	1	100.0	0	—	—	4	3	75.0
Indian Health Service	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
Other plan	0	—	—	1	1	100.0	10	8	80.0	8	5	62.5	0	—	—	5	3	60.0	2	1	50.0	26	18	69.2
No coverage	0	—	—	0	—	—	190	151	79.5	93	82	88.2	2	1	50.0	36	32	88.9	3	3	100.0	326	271	83.1
Multiple coverages	0	—	—	10	9	90.0	104	87	83.7	43	38	88.4	0	—	—	37	35	94.6	11	9	81.8	208	180	86.5
Housing status																								
Stable	6	4	66.7	44	40	90.9	1,245	1,018	81.8	354	305	86.2	5	4	80.0	243	214	88.1	46	34	73.9	1,960	1,632	83.3
Temporary	0	—	—	1	1	100.0	104	89	85.6	40	34	85.0	0	—	—	18	14	77.8	4	3	75.0	167	141	84.4
Unstable	0	—	—	0	—	—	51	41	80.4	24	17	70.8	0	—	—	17	9	52.9	3	3	100.0	96	71	74.0
HHS region[e]																								
Region 1	0	—	—	2	2	100.0	45	40	88.9	18	15	83.3	0	—	—	12	10	83.3	2	1	50.0	80	69	86.3
Region 2	0	—	—	2	2	100.0	134	101	75.4	113	101	89.4	0	—	—	15	15	100.0	5	3	60.0	272	223	82.0
Region 3	0	—	—	9	9	100.0	210	177	84.3	31	23	74.2	0	—	—	31	24	77.4	9	7	77.8	294	244	83.0
Region 4	2	1	50.0	7	7	100.0	499	392	78.6	77	65	84.4	2	2	100.0	101	89	88.1	10	8	80.0	703	568	80.8
Region 5	0	—	—	4	4	100.0	191	166	86.9	25	20	80.0	0	—	—	37	33	89.2	11	9	81.8	271	234	86.3
Region 6	3	2	66.7	5	4	80.0	133	113	85.0	63	52	82.5	1	0	0.0	31	25	80.6	5	4	80.0	243	202	83.1
Region 7	1	1	100.0	4	4	100.0	41	34	82.9	8	8	100.0	0	—	—	5	5	100.0	4	3	75.0	63	55	87.3
Region 8	0	—	—	5	4	80.0	36	31	86.1	7	6	85.7	1	1	100.0	9	8	88.9	1	1	100.0	59	51	86.4
Region 9	0	—	—	5	5	100.0	61	52	85.2	65	53	81.5	2	2	100.0	26	21	80.8	4	2	50.0	164	136	82.9
Region 10	0	—	—	1	0	0.0	19	16	84.2	3	3	100.0	0	—	—	5	4	80.0	0	—	—	28	23	82.1
Total[b]	**6**	**4**	**66.7**	**46**	**42**	**91.3**	**1,422**	**1,163**	**81.8**	**426**	**361**	**84.7**	**6**	**5**	**83.3**	**282**	**241**	**85.5**	**54**	**41**	**75.9**	**2,261**	**1,872**	**82.8**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.

[a] Hispanics/Latinas can be of any race.

[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.

[c] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[d] Includes hemophilia and blood transfusion.

[e] See Technical Notes for the states/territories in each region.

Table 18a. Retention in care among people with HIV attributed at diagnosis to injection drug use (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)																								
13–14	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
15–19	0	—	—	0	—	—	1	1	100.0	0	—	—	0	—	—	4	2	50.0	0	—	—	5	3	60.0
20–24	1	1	100.0	2	2	100.0	9	5	55.6	13	6	46.2	1	1	100.0	34	20	58.8	4	0	0.0	64	35	54.7
25–29	2	1	50.0	1	0	0.0	38	27	71.1	59	33	55.9	0	—	—	206	124	60.2	4	4	100.0	314	191	60.8
30–34	5	2	40.0	8	5	62.5	90	52	57.8	125	79	63.2	1	1	100.0	472	298	63.1	15	12	80.0	722	451	62.5
35–39	14	7	50.0	21	16	76.2	119	84	70.6	185	122	65.9	1	1	100.0	580	367	63.3	21	14	66.7	944	613	64.9
40–44	19	17	89.5	25	21	84.0	203	122	60.1	307	241	78.5	2	0	0.0	649	442	68.1	23	12	52.2	1,231	857	69.6
45–49	13	10	76.9	22	18	81.8	267	202	75.7	409	311	76.0	0	—	—	555	399	71.9	32	24	75.0	1,305	969	74.3
50–54	27	17	63.0	14	13	92.9	563	429	76.2	599	481	80.3	4	3	75.0	791	584	73.8	69	45	65.2	2,075	1,576	76.0
55–59	25	17	68.0	16	13	81.3	1,160	929	80.1	916	763	83.3	5	2	40.0	956	724	75.7	103	90	87.4	3,189	2,542	79.7
60–64	22	19	86.4	12	9	75.0	1,616	1,283	79.4	954	809	84.8	1	1	100.0	933	751	80.5	181	161	89.0	3,724	3,038	81.6
≥65	13	10	76.9	7	7	100.0	2,475	2,027	81.9	964	832	86.3	3	3	100.0	672	527	78.4	213	195	91.5	4,363	3,614	82.8
Gender																								
Male	68	48	70.6	111	93	83.8	3,994	3,137	78.5	3,346	2,710	81.0	11	6	54.5	3,495	2,513	71.9	397	335	84.4	11,463	8,869	77.4
Female	73	53	72.6	16	10	62.5	2,530	2,011	79.5	1,164	950	81.6	6	5	83.3	2,340	1,713	73.2	265	220	83.0	6,412	4,973	77.6
Transgender	0	—	—	1	1	100.0	17	13	76.5	21	17	81.0	1	1	100.0	17	12	70.6	3	2	66.7	61	47	77.0
Federal poverty level																								
0–100%	107	77	72.0	69	58	84.1	4,978	3,908	78.5	3,744	3,051	81.5	10	6	60.0	4,106	2,900	70.6	469	393	83.8	13,526	10,420	77.0
101–138%	15	11	73.3	19	14	73.7	569	465	81.7	252	204	81.0	1	1	100.0	537	426	79.3	75	65	86.7	1,475	1,191	80.7
139–250%	10	6	60.0	23	16	69.6	559	463	82.8	328	264	80.5	4	4	100.0	634	513	80.9	71	57	80.3	1,636	1,330	81.3
251–400%	2	2	100.0	12	11	91.7	208	171	82.2	108	85	78.7	2	0	0.0	304	224	73.7	37	31	83.8	673	524	77.9
>400%	4	3	75.0	3	3	100.0	72	53	73.6	35	28	80.0	1	1	100.0	118	85	72.0	9	9	100.0	243	182	74.9
Health care coverage																								
Private employer	2	2	100.0	11	11	100.0	227	178	78.4	97	80	82.5	5	2	40.0	275	201	73.1	39	38	97.4	659	513	77.8
Private individual	5	4	80.0	11	9	81.8	192	158	82.3	96	72	75.0	0	—	—	342	262	76.6	6	5	83.3	656	512	78.0
Medicare	7	3	42.9	1	1	100.0	1,319	1,069	81.0	494	428	86.6	1	1	100.0	615	488	79.3	48	35	72.9	2,493	2,033	81.5
Medicaid	59	43	72.9	57	43	75.4	2,670	2,058	77.1	2,550	2,076	81.4	9	6	66.7	2,543	1,779	70.0	225	179	79.6	8,143	6,202	76.2
Medicare and Medicaid	12	11	91.7	8	7	87.5	1,130	939	83.1	538	462	85.9	1	1	100.0	686	542	79.0	157	142	90.4	2,536	2,107	83.1
Veterans Administration	0	—	—	0	—	—	5	1	20.0	1	1	100.0	0	—	—	4	4	100.0	0	—	—	10	6	60.0
Indian Health Service	17	11	64.7	0	—	—	1	0	0.0	1	0	0.0	0	—	—	1	1	100.0	0	—	—	20	12	60.0
Other plan	2	1	50.0	3	3	100.0	71	56	78.9	67	48	71.6	0	—	—	103	63	61.2	4	4	100.0	252	177	70.2
No coverage	13	6	46.2	12	10	83.3	340	246	72.4	352	251	71.3	0	—	—	627	410	65.4	31	22	71.0	1,377	946	68.7
Multiple coverages	21	19	90.5	25	20	80.0	550	438	79.6	315	247	78.4	1	1	100.0	615	469	76.3	138	123	89.1	1,670	1,321	79.1
Housing status																								
Stable	100	70	70.0	115	93	80.9	5,577	4,488	80.5	3,916	3,239	82.7	15	11	73.3	4,536	3,432	75.7	609	520	85.4	14,916	11,886	79.7
Temporary	9	8	88.9	8	7	87.5	469	336	71.6	313	231	73.8	1	1	100.0	590	382	64.7	30	22	73.3	1,424	989	69.5
Unstable	30	21	70.0	3	2	66.7	407	282	69.3	256	176	68.8	2	0	0.0	635	374	58.9	21	13	61.9	1,360	871	64.0

Table 18a. Retention in care among people with HIV attributed at diagnosis to injection drug use (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
HHS region[c]																								
Region 1	5	5	100.0	2	2	100.0	414	333	80.4	759	578	76.2	1	1	100.0	537	404	75.2	18	13	72.2	1,746	1,342	76.9
Region 2	3	3	100.0	17	16	94.1	1,145	980	85.6	1,937	1,683	86.9	3	3	100.0	463	358	77.3	18	14	77.8	3,597	3,066	85.2
Region 3	5	4	80.0	7	6	85.7	1,884	1,489	79.0	486	418	86.0	0	—	—	931	668	71.8	489	430	87.9	3,807	3,020	79.3
Region 4	12	9	75.0	10	9	90.0	1,318	1,043	79.1	287	228	79.4	2	1	50.0	1,356	995	73.4	28	18	64.3	3,015	2,304	76.4
Region 5	6	3	50.0	6	5	83.3	560	418	74.6	189	145	76.7	1	1	100.0	408	264	64.7	17	10	58.8	1,199	854	71.2
Region 6	29	21	72.4	15	10	66.7	544	421	77.4	259	175	67.6	0	—	—	572	399	69.8	18	14	77.8	1,444	1,043	72.2
Region 7	4	2	50.0	10	9	90.0	79	49	62.0	22	14	63.6	0	—	—	170	112	65.9	7	3	42.9	292	189	64.7
Region 8	17	11	64.7	4	3	75.0	57	40	70.2	74	55	74.3	0	—	—	193	132	68.4	9	7	77.8	354	248	70.1
Region 9	30	22	73.3	42	31	73.8	348	251	72.1	440	316	71.8	7	3	42.9	805	614	76.3	44	35	79.5	1,728	1,279	74.0
Region 10	29	21	72.4	10	8	80.0	48	33	68.8	25	21	84.0	3	2	66.7	223	155	69.5	13	10	76.9	352	250	71.0
Total[b]	**141**	**101**	**71.6**	**128**	**104**	**81.3**	**6,541**	**5,161**	**78.9**	**4,531**	**3,677**	**81.2**	**18**	**12**	**66.7**	**5,852**	**4,238**	**72.4**	**665**	**557**	**83.8**	**17,936**	**13,889**	**77.4**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Notes: Data presented in this table represent clients who reported injection drug use as their transmission category; data may not be reflective of current injection drug use behavior.
Data are included only for clients with the transmission category injection drug use; data do not include male clients who reported male-to-male sexual contact and injection drug use or transgender clients who reported sexual contact and injection drug use.
[a] Hispanics/Latinos can be of any race.
[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.
[c] See Technical Notes for the states/territories in each region.

Table 18b. Viral suppression among people with HIV attributed at diagnosis to injection drug use (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)																								
13–14	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—	0	—	—
15–19	0	—	—	0	—	—	1	1	100.0	0	—	—	0	—	—	4	3	75.0	0	—	—	5	4	80.0
20–24	1	1	100.0	2	2	100.0	11	9	81.8	15	10	66.7	1	1	100.0	38	27	71.1	4	4	100.0	72	54	75.0
25–29	3	0	0.0	1	1	100.0	40	33	82.5	64	50	78.1	0	—	—	216	168	77.8	5	4	80.0	334	260	77.8
30–34	7	4	57.1	10	9	90.0	106	86	81.1	137	108	78.8	1	1	100.0	486	394	81.1	17	14	82.4	769	620	80.6
35–39	12	10	83.3	21	19	90.5	130	106	81.5	187	147	78.6	0	—	—	611	495	81.0	20	17	85.0	984	797	81.0
40–44	19	14	73.7	27	27	100.0	217	173	79.7	313	264	84.3	2	2	100.0	679	546	80.4	23	19	82.6	1,284	1,048	81.6
45–49	14	11	78.6	20	20	100.0	277	242	87.4	406	332	81.8	0	—	—	563	458	81.3	31	24	77.4	1,317	1,092	82.9
50–54	22	19	86.4	14	13	92.9	577	488	84.6	610	546	89.5	4	4	100.0	821	712	86.7	62	51	82.3	2,118	1,839	86.8
55–59	23	21	91.3	15	14	93.3	1,185	1,037	87.5	933	840	90.0	5	3	60.0	975	874	89.6	100	88	88.0	3,242	2,881	88.9
60–64	25	22	88.0	11	11	100.0	1,641	1,469	89.5	959	884	92.2	1	1	100.0	955	891	93.3	172	159	92.4	3,769	3,441	91.3
≥65	12	12	100.0	8	8	100.0	2,494	2,308	92.5	964	929	96.4	4	4	100.0	683	660	96.6	212	203	95.8	4,394	4,141	94.2
Gender																								
Male	65	57	87.7	114	109	95.6	4,107	3,647	88.8	3,389	3,020	89.1	12	11	91.7	3,636	3,154	86.7	387	350	90.4	11,749	10,383	88.4
Female	73	57	78.1	14	14	100.0	2,553	2,289	89.7	1,176	1,072	91.2	6	5	83.3	2,377	2,057	86.5	255	230	90.2	6,473	5,738	88.6
Transgender	0	—	—	1	1	100.0	19	16	84.2	23	18	78.3	0	—	—	18	17	94.4	4	3	75.0	66	56	84.8
Federal poverty level																								
0–100%	108	88	81.5	68	65	95.6	5,085	4,472	87.9	3,800	3,368	88.6	10	8	80.0	4,240	3,564	84.1	456	404	88.6	13,809	12,002	86.9
101–138%	15	14	93.3	19	17	89.5	577	529	91.7	255	237	92.9	1	1	100.0	558	513	91.9	69	64	92.8	1,502	1,383	92.1
139–250%	8	7	87.5	24	24	100.0	585	551	94.2	332	319	96.1	4	4	100.0	657	615	93.6	76	71	93.4	1,693	1,598	94.4
251–400%	2	1	50.0	12	12	100.0	211	201	95.3	110	102	92.7	2	2	100.0	317	303	95.6	34	33	97.1	688	654	95.1
>400%	2	2	100.0	4	4	100.0	71	68	95.8	34	32	94.1	1	1	100.0	118	115	97.5	8	8	100.0	239	231	96.7
Health care coverage																								
Private employer	1	0	0.0	12	12	100.0	225	212	94.2	98	96	98.0	5	5	100.0	282	268	95.0	39	38	97.4	665	634	95.3
Private individual	4	4	100.0	12	12	100.0	200	177	88.5	93	86	92.5	0	—	—	349	322	92.3	6	6	100.0	667	610	91.5
Medicare	6	5	83.3	1	1	100.0	1,336	1,237	92.6	499	476	95.4	1	1	100.0	638	606	95.0	46	43	93.5	2,535	2,377	93.8
Medicaid	58	47	81.0	57	53	93.0	2,735	2,373	86.8	2,559	2,247	87.8	8	6	75.0	2,617	2,174	83.1	224	197	87.9	8,288	7,120	85.9
Medicare and Medicaid	11	11	100.0	8	8	100.0	1,147	1,060	92.4	550	518	94.2	2	2	100.0	682	635	93.1	154	145	94.2	2,558	2,383	93.2
Veterans Administration	0	—	—	0	—	—	5	5	100.0	1	1	100.0	0	—	—	5	4	80.0	0	—	—	11	10	90.9
Indian Health Service	17	13	76.5	0	—	—	0	—	—	1	0	0.0	0	—	—	1	1	100.0	0	—	—	19	14	73.7
Other plan	2	2	100.0	3	2	66.7	72	61	84.7	66	58	87.9	0	—	—	113	97	85.8	4	3	75.0	262	225	85.9
No coverage	14	12	85.7	11	11	100.0	374	302	80.7	383	318	83.0	0	—	—	693	536	77.3	31	25	80.6	1,509	1,207	80.0
Multiple coverages	22	19	86.4	25	25	100.0	551	495	89.8	318	294	92.5	1	1	100.0	613	554	90.4	132	119	90.2	1,667	1,511	90.6
Housing status																								
Stable	98	84	85.7	117	114	97.4	5,667	5,137	90.6	3,950	3,603	91.2	14	13	92.9	4,662	4,184	89.7	591	540	91.4	15,146	13,716	90.6
Temporary	9	9	100.0	7	5	71.4	505	417	82.6	331	275	83.1	1	1	100.0	621	503	81.0	28	21	75.0	1,506	1,235	82.0
Unstable	29	19	65.5	3	3	100.0	424	324	76.4	267	199	74.5	2	1	50.0	672	474	70.5	23	18	78.3	1,425	1,041	73.1

Table 18b. Viral suppression among people with HIV attributed at diagnosis to injection drug use (aged 13 years and older) served by the Ryan White HIV/AIDS Program (non-ADAP), by race/ethnicity and selected characteristics, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/ African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races			Total[b]		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
HHS region[c]																								
Region 1	5	5	100.0	3	2	66.7	416	398	95.7	751	708	94.3	0	—	—	516	474	91.9	14	14	100.0	1,714	1,609	93.9
Region 2	3	3	100.0	18	18	100.0	1,171	1,028	87.8	1,948	1,734	89.0	3	3	100.0	475	427	89.9	19	16	84.2	3,649	3,237	88.7
Region 3	4	4	100.0	7	7	100.0	1,905	1,720	90.3	491	447	91.0	0	—	—	923	781	84.6	473	431	91.1	3,809	3,395	89.1
Region 4	13	11	84.6	10	10	100.0	1,371	1,192	86.9	303	275	90.8	2	2	100.0	1,435	1,215	84.7	26	24	92.3	3,162	2,731	86.4
Region 5	6	4	66.7	6	6	100.0	572	525	91.8	189	178	94.2	1	1	100.0	428	363	84.8	17	14	82.4	1,231	1,102	89.5
Region 6	30	25	83.3	12	12	100.0	573	490	85.5	269	216	80.3	0	—	—	634	533	84.1	21	16	76.2	1,547	1,299	84.0
Region 7	4	3	75.0	10	10	100.0	79	73	92.4	24	20	83.3	0	—	—	174	158	90.8	6	5	83.3	297	269	90.6
Region 8	14	14	100.0	5	5	100.0	60	55	91.7	70	63	90.0	0	—	—	190	168	88.4	9	8	88.9	348	313	89.9
Region 9	29	24	82.8	42	39	92.9	340	300	88.2	460	391	85.0	8	6	75.0	813	722	88.8	43	40	93.0	1,744	1,530	87.7
Region 10	28	19	67.9	11	10	90.9	46	38	82.6	28	25	89.3	3	3	100.0	232	204	87.9	15	12	80.0	364	312	85.7
Total[b]	**138**	**114**	**82.6**	**129**	**124**	**96.1**	**6,679**	**5,952**	**89.1**	**4,588**	**4,110**	**89.6**	**18**	**16**	**88.9**	**6,031**	**5,228**	**86.7**	**646**	**583**	**90.2**	**18,288**	**16,177**	**88.5**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Notes: Data presented in this table represent clients who reported injection drug use as their transmission category; data may not be reflective of current injection drug use behavior.
Data are included only for clients with the transmission category injection drug use; data do not include male clients who reported male-to-male sexual contact and injection drug use or transgender clients who reported sexual contact and injection drug use.
[a] Hispanics/Latinos can be of any race.
[b] Because totals were calculated independently of the values for the subpopulations, the values in each column and row may not sum to the column and row totals.
[c] See Technical Notes for the states/territories in each region.

Table 19a. Retention in care among clients served by the Ryan White HIV/AIDS Program (non-ADAP), by housing status and selected characteristics, 2022—United States and 3 territories

	Stable			Temporary			Unstable		
		Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)									
<13	465	394	84.7	24	22	91.7	1	0	0.0
13–14	171	146	85.4	1	1	100.0	0	—	—
15–19	1,197	965	80.6	81	66	81.5	39	27	69.2
20–24	7,949	5,898	74.2	753	548	72.8	427	295	69.1
25–29	20,081	14,530	72.4	1,862	1,244	66.8	1,335	846	63.4
30–34	32,953	24,054	73.0	2,944	1,989	67.6	2,310	1,561	67.6
35–39	31,399	23,355	74.4	2,714	1,845	68.0	2,197	1,508	68.6
40–44	31,027	23,716	76.4	2,438	1,730	71.0	1,909	1,369	71.7
45–49	29,975	23,520	78.5	2,044	1,536	75.1	1,660	1,227	73.9
50–54	36,990	29,534	79.8	2,390	1,801	75.4	1,863	1,401	75.2
55–59	43,634	35,505	81.4	2,498	1,895	75.9	1,970	1,492	75.7
60–64	36,356	30,004	82.5	1,760	1,397	79.4	1,217	938	77.1
≥65	36,671	30,606	83.5	1,314	1,038	79.0	721	566	78.5
Race/ethnicity									
American Indian/Alaska Native	1,401	1,043	74.4	110	79	71.8	135	98	72.6
Asian	4,936	3,901	79.0	289	213	73.7	124	93	75.0
Black/African American	143,134	110,974	77.5	10,307	7,443	72.2	6,540	4,438	67.9
Hispanic/Latino[a]	78,945	64,659	81.9	5,458	4,145	75.9	5,079	4,104	80.8
Native Hawaiian/Pacific Islander	479	340	71.0	33	22	66.7	30	17	56.7
White	72,536	55,587	76.6	4,222	2,922	69.2	3,418	2,286	66.9
Multiple races	5,471	4,271	78.1	299	223	74.6	213	135	63.4
Gender									
Male	218,339	169,783	77.8	15,227	10,892	71.5	11,774	8,427	71.6
Female	83,464	67,071	80.4	4,931	3,765	76.4	3,148	2,325	73.9
Transgender male	585	424	72.5	80	49	61.3	37	23	62.2
Transgender female	5,935	4,548	76.6	554	385	69.5	605	411	67.9
Other gender identity	470	349	74.3	22	14	63.6	44	29	65.9
Transmission category									
Male client									
Male-to-male sexual contact	139,229	108,124	77.7	8,978	6,497	72.4	7,085	5,242	74.0
Injection drug use	9,522	7,598	79.8	931	641	68.9	858	537	62.6
Male-to-male sexual contact and injection drug use	5,257	4,055	77.1	737	493	66.9	783	536	68.5
Heterosexual contact[b]	49,461	39,457	79.8	3,278	2,387	72.8	2,162	1,509	69.8
Perinatal	1,991	1,532	76.9	128	88	68.8	82	61	74.4
Other[c]	1,153	905	78.5	49	33	67.3	33	25	75.8
Female client									
Injection drug use	5,349	4,252	79.5	487	344	70.6	494	329	66.6
Heterosexual contact[b]	70,164	56,718	80.8	3,767	2,931	77.8	2,042	1,498	73.4
Perinatal	2,599	2,082	80.1	168	132	78.6	73	56	76.7
Other[c]	863	717	83.1	45	37	82.2	16	15	93.8
Transgender client									
Sexual contact[d]	5,555	4,258	76.7	495	346	69.9	545	371	68.1
Injection drug use	45	36	80.0	6	4	66.7	8	5	62.5
Sexual contact[d] and injection drug use	175	121	69.1	36	26	72.2	47	32	68.1
Perinatal	32	22	68.8	4	3	75.0	4	3	75.0
Other[c]	20	17	85.0	2	1	50.0	1	1	100.0

Table 19a. Retention in care among clients served by the Ryan White HIV/AIDS Program (non-ADAP), by housing status and selected characteristics, 2022—United States and 3 territories *(cont.)*

	Stable			Temporary			Unstable		
		Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%
Federal poverty level									
0–100%	173,923	135,973	78.2	15,945	11,440	71.7	12,565	8,774	69.8
101–138%	31,372	25,266	80.5	1,562	1,201	76.9	958	744	77.7
139–250%	55,962	44,734	79.9	2,100	1,594	75.9	1,381	1,134	82.1
251–400%	29,642	23,237	78.4	652	503	77.1	473	397	83.9
>400%	12,259	9,181	74.9	261	177	67.8	142	112	78.9
Health care coverage									
Private employer	35,468	26,823	75.6	846	619	73.2	1,117	990	88.6
Private individual	27,649	21,120	76.4	1,220	927	76.0	566	413	73.0
Medicare	32,482	26,458	81.5	1,177	892	75.8	726	542	74.7
Medicaid	91,568	70,920	77.5	7,960	5,638	70.8	6,479	4,393	67.8
Medicare and Medicaid	21,976	18,441	83.9	1,279	1,015	79.4	907	672	74.1
Veterans Administration	363	265	73.0	7	3	42.9	9	5	55.6
Indian Health Service	121	77	63.6	6	4	66.7	22	14	63.6
Other plan	6,470	5,217	80.6	541	419	77.4	384	258	67.2
No coverage	58,891	45,543	77.3	5,416	3,845	71.0	3,920	2,808	71.6
Multiple coverages	32,838	26,693	81.3	2,272	1,717	75.6	1,404	1,061	75.6
HHS region[e]									
Region 1	11,247	8,948	79.6	713	559	78.4	420	329	78.3
Region 2	47,910	40,699	84.9	3,782	2,981	78.8	1,317	1,034	78.5
Region 3	37,231	29,056	78.0	1,241	914	73.7	1,231	852	69.2
Region 4	91,615	73,435	80.2	4,256	3,120	73.3	2,853	2,017	70.7
Region 5	33,050	23,409	70.8	1,948	1,207	62.0	1,411	897	63.6
Region 6	32,017	23,812	74.4	3,993	2,833	70.9	3,453	2,801	81.1
Region 7	6,023	4,429	73.5	331	234	70.7	290	182	62.8
Region 8	4,821	3,541	73.4	669	466	69.7	247	168	68.0
Region 9	32,266	25,119	77.8	2,397	1,722	71.8	2,845	1,853	65.1
Region 10	5,071	3,698	72.9	294	202	68.7	429	293	68.3
Total[f]	**308,868**	**242,227**	**78.4**	**20,823**	**15,112**	**72.6**	**15,649**	**11,230**	**71.8**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.

[a] Hispanics/Latinos can be of any race.

[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[c] Includes hemophilia and blood transfusion.

[d] Includes any sexual transmission category reported by transgender clients.

[e] See Technical Notes for the states/territories in each region.

[f] Because column totals were calculated independently of the values for the subpopulations, the values in each column may not sum to the column total.

Table 19b. Viral suppression among clients served by the Ryan White HIV/AIDS Program (non-ADAP), by housing status and selected characteristics, 2022—United States and 3 territories

	Stable			Temporary			Unstable		
		Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%
Age group (yrs)									
<13	477	434	91.0	23	18	78.3	2	2	100.0
13–14	172	159	92.4	1	1	100.0	1	1	100.0
15–19	1,361	1,145	84.1	96	81	84.4	45	34	75.6
20–24	8,991	7,572	84.2	869	726	83.5	476	358	75.2
25–29	21,932	18,676	85.2	2,093	1,675	80.0	1,469	1,060	72.2
30–34	35,322	30,494	86.3	3,297	2,625	79.6	2,526	1,921	76.0
35–39	33,281	29,204	87.7	2,971	2,408	81.1	2,351	1,769	75.2
40–44	32,543	29,054	89.3	2,624	2,178	83.0	2,027	1,540	76.0
45–49	31,125	28,191	90.6	2,182	1,875	85.9	1,728	1,347	78.0
50–54	38,253	35,143	91.9	2,574	2,199	85.4	1,962	1,554	79.2
55–59	44,819	41,660	93.0	2,606	2,258	86.6	2,040	1,675	82.1
60–64	37,144	34,931	94.0	1,837	1,666	90.7	1,263	1,041	82.4
≥65	37,230	35,631	95.7	1,349	1,236	91.6	726	650	89.5
Race/ethnicity									
American Indian/Alaska Native	1,463	1,315	89.9	110	96	87.3	151	111	73.5
Asian	5,101	4,853	95.1	309	290	93.9	133	118	88.7
Black/African American	149,667	131,811	88.1	11,170	9,100	81.5	7,064	5,272	74.6
Hispanic/Latino[a]	82,832	76,249	92.1	5,949	5,201	87.4	5,201	4,359	83.8
Native Hawaiian/Pacific Islander	499	451	90.4	38	36	94.7	31	23	74.2
White	75,460	70,702	93.7	4,507	3,863	85.7	3,685	2,810	76.3
Multiple races	5,552	5,062	91.2	321	259	80.7	232	169	72.8
Gender									
Male	229,029	207,584	90.6	16,541	13,869	83.8	12,548	9,825	78.3
Female	86,183	78,171	90.7	5,256	4,482	85.3	3,285	2,548	77.6
Transgender male	629	554	88.1	77	64	83.1	38	28	73.7
Transgender female	6,259	5,491	87.7	615	503	81.8	653	479	73.4
Other gender identity	464	423	91.2	24	21	87.5	44	34	77.3
Transmission category									
Male client									
Male-to-male sexual contact	146,518	133,423	91.1	9,780	8,270	84.6	7,532	6,006	79.7
Injection drug use	9,706	8,787	90.5	987	804	81.5	914	666	72.9
Male-to-male sexual contact and injection drug use	5,438	4,879	89.7	768	646	84.1	832	617	74.2
Heterosexual contact[b]	51,737	46,606	90.1	3,558	2,946	82.8	2,336	1,807	77.4
Perinatal	2,051	1,682	82.0	139	98	70.5	94	65	69.1
Other[c]	1,211	1,126	93.0	51	47	92.2	39	33	84.6
Female client									
Injection drug use	5,392	4,888	90.7	512	425	83.0	502	368	73.3
Heterosexual contact[b]	72,534	66,108	91.1	3,990	3,436	86.1	2,185	1,697	77.7
Perinatal	2,674	2,160	80.8	178	136	76.4	77	51	66.2
Other[c]	888	836	94.1	45	40	88.9	17	15	88.2
Transgender client									
Sexual contact[d]	5,848	5,138	87.9	547	458	83.7	583	437	75.0
Injection drug use	48	41	85.4	7	6	85.7	9	7	77.8
Sexual contact[d] and injection drug use	169	147	87.0	39	33	84.6	52	31	59.6
Perinatal	31	27	87.1	4	3	75.0	4	4	100.0
Other[c]	22	19	86.4	2	2	100.0	1	1	100.0

Table 19b. Viral suppression among clients served by the Ryan White HIV/AIDS Program (non-ADAP), by housing status and selected characteristics, 2022—United States and 3 territories *(cont.)*

	Stable			Temporary			Unstable		
		Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%
Federal poverty level									
0–100%	181,847	161,112	88.6	17,309	14,376	83.1	13,456	10,229	76.0
101–138%	32,578	30,151	92.6	1,648	1,455	88.3	991	817	82.4
139–250%	58,452	54,266	92.8	2,249	1,968	87.5	1,413	1,250	88.5
251–400%	31,088	29,295	94.2	703	633	90.0	474	426	89.9
>400%	12,840	12,230	95.2	273	244	89.4	142	127	89.4
Health care coverage									
Private employer	37,197	35,228	94.7	902	794	88.0	1,118	1,022	91.4
Private individual	28,771	26,997	93.8	1,282	1,149	89.6	610	502	82.3
Medicare	33,191	31,113	93.7	1,230	1,062	86.3	752	603	80.2
Medicaid	95,169	84,095	88.4	8,507	7,031	82.6	6,888	5,198	75.5
Medicare and Medicaid	22,416	20,843	93.0	1,333	1,187	89.0	936	738	78.8
Veterans Administration	378	353	93.4	9	8	88.9	11	10	90.9
Indian Health Service	131	122	93.1	6	5	83.3	25	18	72.0
Other plan	6,745	6,169	91.5	600	513	85.5	423	353	83.5
No coverage	63,945	55,057	86.1	6,215	5,070	81.6	4,254	3,228	75.9
Multiple coverages	33,680	31,427	93.3	2,356	2,058	87.4	1,478	1,203	81.4
HHS region[e]									
Region 1	11,358	10,817	95.2	749	683	91.2	430	370	86.0
Region 2	49,423	45,166	91.4	4,079	3,479	85.3	1,384	1,075	77.7
Region 3	38,254	34,856	91.1	1,312	1,089	83.0	1,290	1,029	79.8
Region 4	96,376	85,978	89.2	4,722	3,837	81.3	3,176	2,333	73.5
Region 5	34,673	31,783	91.7	2,058	1,738	84.5	1,472	1,143	77.6
Region 6	34,564	30,251	87.5	4,396	3,604	82.0	3,506	2,882	82.2
Region 7	6,322	5,845	92.5	361	307	85.0	328	238	72.6
Region 8	4,777	4,561	95.5	657	600	91.3	257	193	75.1
Region 9	33,493	30,841	92.1	2,563	2,206	86.1	3,048	2,337	76.7
Region 10	5,412	5,035	93.0	324	288	88.9	474	370	78.1
Total[f]	**322,650**	**292,294**	**90.6**	**22,522**	**18,946**	**84.1**	**16,616**	**12,952**	**77.9**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.

[a] Hispanics/Latinos can be of any race.

[b] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).

[c] Includes hemophilia and blood transfusion.

[d] Includes any sexual transmission category reported by transgender clients.

[e] See Technical Notes for the states/territories in each region.

[f] Because column totals were calculated independently of the values for the subpopulations, the values in each column may not sum to the column total.

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Section 3.

State- and EMA/TGA-Level Data: Client Characteristics

Table 20a. Ryan White HIV/AIDS Program clients (non-ADAP), by year and state, 2018–2022—United States and 3 territories

	2018	2019	2020	2021	2022
State					
Alabama	9,389	10,092	9,989	10,542	10,707
Alaska	567	616	464	647	621
Arizona	7,956	9,463	9,731	9,582	9,331
Arkansas	2,553	2,682	2,833	3,005	3,103
California	55,884	57,172	56,188	57,078	52,676
Colorado	6,938	8,634	8,958	9,890	8,196
Connecticut	4,816	4,861	4,774	4,671	4,435
Delaware	1,998	2,143	2,100	2,162	2,076
District of Columbia	6,426	6,209	6,299	5,666	5,494
Florida	53,754	53,510	53,406	52,402	54,777
Georgia	22,982	24,706	23,361	26,011	25,661
Hawaii	1,123	1,171	1,361	1,321	1,183
Idaho	887	945	984	1,004	1,043
Illinois	25,119	26,108	26,256	25,870	25,376
Indiana[a]	4,169	7,965	6,071	8,069	—
Iowa	1,805	1,948	2,090	2,151	2,196
Kansas	691	1,014	1,129	951	1,129
Kentucky	5,099	5,493	5,643	5,743	5,772
Louisiana	12,372	13,549	13,007	13,347	12,838
Maine	849	933	1,220	1,059	923
Maryland	15,391	16,192	15,411	14,487	15,032
Massachusetts	12,550	14,311	13,288	13,495	13,432
Michigan	9,179	9,712	9,559	10,913	10,697
Minnesota	4,510	6,201	6,972	7,041	4,559
Mississippi	4,392	4,660	4,727	5,572	5,492
Missouri	8,656	8,665	8,494	8,520	8,449
Montana	404	478	487	487	475
Nebraska	937	1,172	1,198	1,332	1,441
Nevada	4,408	5,208	5,262	5,135	5,006
New Hampshire	900	1,017	1,112	1,119	1,038
New Jersey	15,204	16,060	15,290	15,024	15,326
New Mexico	2,127	2,168	2,275	2,476	2,113
New York	48,583	51,244	50,865	49,742	50,191
North Carolina	16,448	16,252	15,468	15,803	15,573
North Dakota	275	315	310	331	353
Ohio	11,582	13,172	13,505	13,861	13,300
Oklahoma	3,116	3,416	3,698	3,734	3,905
Oregon	3,423	3,644	3,700	7,466	7,771
Pennsylvania	23,995	25,558	24,436	25,745	26,298
Rhode Island	2,023	2,168	2,335	2,507	2,632
South Carolina	11,369	12,784	17,032	16,651	14,102
South Dakota	379	487	383	397	403
Tennessee	17,501	15,796	15,849	15,015	15,283
Texas	43,784	45,948	46,647	46,889	49,012
Utah	1,471	1,528	1,850	1,881	1,892
Vermont	579	604	621	631	610
Virginia	9,863	10,460	10,617	10,348	10,595
Washington	6,607	9,404	8,225	7,688	8,358
West Virginia	758	1,520	1,553	1,569	1,610
Wisconsin	5,000	5,375	2,299	5,395	5,337
Wyoming	247	233	209	203	204
Subtotal	**511,038**	**544,966**	**539,541**	**552,628**	**538,026**
Territory					
Guam[a]	35	—	—	35	34
Puerto Rico	11,381	12,309	11,542	12,332	11,592
U.S. Virgin Islands	226	232	266	251	258
Subtotal	**11,642**	**12,541**	**11,808**	**12,618**	**11,884**
Total	**522,680**	**557,507**	**551,349**	**565,246**	**549,910**

Note: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.

[a] 2022 data for Indiana are unavailable. 2019 and 2020 data for Guam are unavailable.

Table 20b. Ryan White HIV/AIDS Program clients (non-ADAP), by year and eligible metropolitan area and transitional grant area, 2018–2022—United States and Puerto Rico

State/Territory	EMA/TGA	2018	2019	2020	2021	2022
Arizona	Phoenix	5,402	6,285	6,307	5,916	6,276
California	Los Angeles	24,970	26,100	25,352	25,352	21,481
	Oakland	2,882	3,081	2,986	3,689	3,728
	Orange County	2,392	2,362	2,374	2,349	2,242
	Riverside–San Bernardino	3,693	3,324	3,306	2,964	3,122
	Sacramento	2,593	2,410	2,777	2,851	2,811
	San Diego	6,713	7,234	7,153	7,201	6,814
	San Francisco	6,031	5,932	5,832	5,714	5,402
	San Jose	2,048	1,877	1,845	1,682	1,730
Colorado	Denver	6,683	8,208	8,330	9,093	7,656
Connecticut	Hartford	2,518	2,057	2,135	2,041	1,964
	New Haven	1,231	2,750	2,594	2,524	2,367
District of Columbia	Washington[a]	11,940	11,977	11,781	11,216	11,152
Florida	Ft. Lauderdale	11,321	13,637	17,018	11,335	12,536
	Jacksonville	3,501	3,409	4,031	3,921	4,011
	Miami	12,364	11,606	10,013	11,031	11,051
	Orlando	4,927	4,858	4,575	5,445	5,559
	Tampa–St. Petersburg	6,894	7,076	6,546	6,723	8,458
	West Palm Beach	3,641	3,664	3,889	4,155	3,804
Georgia	Atlanta	15,768	16,858	15,481	18,020	17,360
Illinois	Chicago	23,336	24,114	24,064	24,190	23,838
Indiana	Indianapolis	3,755	7,382	5,513	6,840	4,243
Louisiana	Baton Rouge	3,728	4,024	5,199	4,672	4,511
	New Orleans	7,024	7,548	6,779	6,844	6,554
Maryland	Baltimore	13,330	14,113	13,436	12,266	12,766
Massachusetts	Boston[a]	11,034	12,885	11,775	12,151	12,292
Michigan	Detroit	5,668	5,771	5,490	6,631	6,512
Minnesota	Minneapolis–St. Paul[a]	4,687	6,214	7,027	7,083	4,620
Missouri	Kansas City[a]	2,841	2,791	2,692	2,818	2,840
	St. Louis[a]	8,320	8,141	7,903	10,037	9,284
Nevada	Las Vegas[a]	3,424	3,867	4,182	3,754	3,868
New Jersey	Bergen–Passaic	1,815	1,868	1,804	1,810	1,802
	Jersey City	2,032	1,791	1,671	1,652	1,798
	Middlesex	1,614	1,623	1,582	1,625	1,643
	Newark	6,729	7,206	6,724	6,837	6,747
New York	Nassau–Suffolk	2,933	3,132	2,989	3,039	3,162
	New York	42,475	43,893	43,353	42,092	42,379
North Carolina	Charlotte[a]	3,890	4,099	4,180	4,274	4,333
Ohio	Cleveland	3,478	3,552	3,640	3,815	3,859
	Columbus	5,447	6,972	6,965	7,011	6,572
Oregon	Portland[a]	2,530	2,744	2,665	4,393	4,597
Pennsylvania	Philadelphia[a]	19,025	20,404	18,847	18,654	19,039
Puerto Rico	San Juan	6,732	7,408	7,057	7,851	6,839
Tennessee	Memphis[a]	5,324	5,360	4,819	4,444	4,854
	Nashville	11,338	10,165	10,199	9,741	9,704
Texas	Austin	3,303	3,442	3,442	2,206	3,050
	Dallas	11,994	12,609	12,564	12,968	14,717
	Ft. Worth	3,368	3,274	3,699	3,824	3,682
	Houston	16,135	17,171	17,400	17,544	17,643
	San Antonio	3,406	3,527	3,653	3,541	3,901
Virginia	Norfolk[a]	3,339	3,438	3,257	3,316	3,485
Washington	Seattle	5,737	7,324	6,215	5,801	6,245

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location. Data shown for EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 21a. Ryan White HIV/AIDS Program clients (non-ADAP), by age group and state, 2022—United States and 3 territories

	<13 yrs		13–24 yrs		25–34 yrs		35–44 yrs		45–54 yrs		55–64 yrs		≥65 yrs		
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total N
State															
Alabama	57	0.5	420	3.9	2,241	20.9	2,375	22.2	2,291	21.4	2,395	22.4	928	8.7	10,707
Alaska	0	0.0	27	4.3	115	18.5	115	18.5	130	20.9	169	27.2	65	10.5	621
Arizona	81	0.9	336	3.6	1,725	18.5	1,873	20.1	1,951	20.9	2,243	24.0	1,122	12.0	9,331
Arkansas	1	<0.1	143	4.6	734	23.7	741	23.9	633	20.4	626	20.2	225	7.3	3,103
California	162	0.3	1,180	2.2	8,601	16.3	11,064	21.0	11,440	21.7	13,616	25.8	6,613	12.6	52,676
Colorado	78	1.0	329	4.0	1,664	20.3	1,895	23.1	1,685	20.6	1,774	21.6	771	9.4	8,196
Connecticut	17	0.4	91	2.1	466	10.5	618	13.9	943	21.3	1,524	34.4	776	17.5	4,435
Delaware	1	<0.1	37	1.8	241	11.6	315	15.2	400	19.3	698	33.6	384	18.5	2,076
District of Columbia	25	0.5	226	4.1	799	14.5	1,044	19.0	1,097	20.0	1,474	26.8	829	15.1	5,494
Florida	609	1.1	1,712	3.1	9,278	16.9	10,609	19.4	11,588	21.2	14,682	26.8	6,299	11.5	54,777
Georgia	102	0.4	1,222	4.8	6,127	23.9	5,784	22.5	4,922	19.2	5,328	20.8	2,176	8.5	25,661
Hawaii	1	0.1	10	0.8	107	9.0	185	15.6	217	18.3	408	34.5	255	21.6	1,183
Idaho	0	0.0	35	3.4	156	15.0	232	22.2	223	21.4	273	26.2	124	11.9	1,043
Illinois	176	0.7	879	3.5	5,424	21.4	5,582	22.0	5,206	20.5	5,645	22.2	2,464	9.7	25,376
Indiana[a]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Iowa	3	0.1	84	3.8	386	17.6	480	21.9	507	23.1	513	23.4	223	10.2	2,196
Kansas	1	0.1	41	3.6	167	14.8	231	20.5	256	22.7	298	26.4	135	12.0	1,129
Kentucky	19	0.3	191	3.3	1,177	20.4	1,262	21.9	1,282	22.2	1,288	22.3	553	9.6	5,772
Louisiana	9	0.1	437	3.4	2,378	18.5	3,011	23.5	2,824	22.0	2,885	22.5	1,294	10.1	12,838
Maine	3	0.3	10	1.1	79	8.6	157	17.0	221	23.9	281	30.4	172	18.6	923
Maryland	110	0.7	378	2.5	2,093	13.9	2,802	18.6	2,941	19.6	4,466	29.7	2,242	14.9	15,032
Massachusetts	71	0.5	246	1.8	1,568	11.7	2,301	17.1	2,961	22.0	4,139	30.8	2,146	16.0	13,432
Michigan	66	0.6	393	3.7	2,174	20.3	2,089	19.5	2,162	20.2	2,630	24.6	1,183	11.1	10,697
Minnesota	20	0.4	228	5.0	678	14.9	1,007	22.1	974	21.4	1,104	24.2	548	12.0	4,559
Mississippi	53	1.0	248	4.5	1,108	20.2	1,182	21.5	1,236	22.5	1,186	21.6	479	8.7	5,492
Missouri	64	0.8	316	3.7	1,688	20.0	1,792	21.2	1,781	21.1	2,052	24.3	756	8.9	8,449
Montana	0	0.0	5	1.1	69	14.5	102	21.5	98	20.6	150	31.6	51	10.7	475
Nebraska	1	0.1	44	3.1	245	17.0	330	22.9	352	24.4	343	23.8	126	8.7	1,441
Nevada	32	0.6	166	3.3	1,067	21.3	1,160	23.2	997	19.9	1,079	21.6	505	10.1	5,006
New Hampshire	4	0.4	20	1.9	105	10.1	168	16.2	225	21.7	349	33.6	167	16.1	1,038
New Jersey	164	1.1	410	2.7	2,344	15.3	2,735	17.8	2,932	19.1	4,450	29.0	2,291	14.9	15,326
New Mexico	3	0.1	63	3.0	312	14.8	351	16.6	434	20.5	606	28.7	344	16.3	2,113
New York	254	0.5	1,342	2.7	7,850	15.6	9,552	19.0	10,163	20.2	13,764	27.4	7,266	14.5	50,191
North Carolina	72	0.5	716	4.6	3,119	20.0	3,052	19.6	3,258	20.9	3,646	23.4	1,710	11.0	15,573
North Dakota	2	0.6	10	2.8	78	22.1	84	23.8	95	26.9	66	18.7	18	5.1	353
Ohio	89	0.7	512	3.8	2,527	19.0	2,743	20.6	2,756	20.7	3,263	24.5	1,410	10.6	13,300
Oklahoma	5	0.1	153	3.9	794	20.3	860	22.0	867	22.2	921	23.6	305	7.8	3,905
Oregon	4	0.1	314	4.0	1,541	19.8	1,733	22.3	1,595	20.5	1,650	21.2	934	12.0	7,771
Pennsylvania	194	0.7	663	2.5	3,916	14.9	4,742	18.0	5,544	21.1	7,498	28.5	3,741	14.2	26,298
Rhode Island	15	0.6	56	2.1	285	10.8	452	17.2	621	23.6	812	30.9	391	14.9	2,632
South Carolina	22	0.2	479	3.4	2,650	18.8	2,745	19.5	2,941	20.9	3,603	25.5	1,662	11.8	14,102
South Dakota	1	0.2	12	3.0	63	15.6	90	22.3	103	25.6	104	25.8	30	7.4	403
Tennessee	46	0.3	527	3.4	3,167	20.7	3,290	21.5	3,478	22.8	3,454	22.6	1,321	8.6	15,283
Texas	283	0.6	1,979	4.0	10,882	22.2	11,679	23.8	10,541	21.5	10,057	20.5	3,591	7.3	49,012

Table 21a. Ryan White HIV/AIDS Program clients (non-ADAP), by age group and state, 2022—United States and 3 territories *(cont.)*

	<13 yrs		13–24 yrs		25–34 yrs		35–44 yrs		45–54 yrs		55–64 yrs		≥65 yrs		
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total N
State															
Utah	2	0.1	64	3.4	379	20.0	495	26.2	441	23.3	358	18.9	153	8.1	1,892
Vermont	0	0.0	9	1.5	39	6.4	92	15.1	139	22.8	207	33.9	124	20.3	610
Virginia	35	0.3	327	3.1	2,023	19.1	2,151	20.3	2,180	20.6	2,637	24.9	1,242	11.7	10,595
Washington	9	0.1	161	1.9	1,186	14.2	1,824	21.8	1,969	23.6	2,156	25.8	1,053	12.6	8,358
West Virginia	2	0.1	24	1.5	248	15.4	344	21.4	379	23.5	437	27.1	176	10.9	1,610
Wisconsin	82	1.5	252	4.7	1,035	19.4	1,027	19.2	1,079	20.2	1,317	24.7	545	10.2	5,337
Wyoming	0	0.0	2	1.0	23	11.3	39	19.1	52	25.5	55	27.0	33	16.2	204
Subtotal	**3,050**	**0.6**	**17,529**	**3.3**	**97,121**	**18.1**	**110,586**	**20.6**	**113,110**	**21.0**	**134,679**	**25.0**	**61,951**	**11.5**	**538,026**
Territory															
Guam	0	0.0	4	11.8	9	26.5	10	29.4	4	11.8	5	14.7	2	5.9	34
Puerto Rico	26	0.2	163	1.4	1,186	10.2	1,654	14.3	2,535	21.9	3,803	32.8	2,225	19.2	11,592
U.S. Virgin Islands	1	0.4	5	1.9	17	6.6	45	17.4	61	23.6	74	28.7	55	21.3	258
Subtotal	**27**	**0.2**	**172**	**1.4**	**1,212**	**10.2**	**1,709**	**14.4**	**2,600**	**21.9**	**3,882**	**32.7**	**2,282**	**19.2**	**11,884**
Total	**3,077**	**0.6**	**17,701**	**3.2**	**98,333**	**17.9**	**112,295**	**20.4**	**115,710**	**21.0**	**138,561**	**25.2**	**64,233**	**11.7**	**549,910**

Notes: Percentages shown are based on the row total.
Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable.

Table 21b. Ryan White HIV/AIDS Program clients (non-ADAP), by age group and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		<13 yrs		13–24 yrs		25–34 yrs		35–44 yrs		45–54 yrs		55–64 yrs		≥65 yrs		
State/Territory	EMA/TGA	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total N
Arizona	Phoenix	81	1.3	267	4.3	1,353	21.6	1,407	22.4	1,307	20.8	1,314	20.9	547	8.7	6,276
California	Los Angeles	95	0.4	485	2.3	4,085	19.0	4,975	23.2	4,705	21.9	5,077	23.6	2,059	9.6	21,481
	Oakland	24	0.6	104	2.8	577	15.5	683	18.3	791	21.2	970	26.0	579	15.5	3,728
	Orange County	0	0.0	67	3.0	388	17.3	529	23.6	587	26.2	457	20.4	214	9.5	2,242
	Riverside–San Bernardino	0	0.0	63	2.0	433	13.9	501	16.0	609	19.5	992	31.8	524	16.8	3,122
	Sacramento	2	0.1	74	2.6	473	16.8	569	20.2	583	20.7	775	27.6	335	11.9	2,811
	San Diego	42	0.6	136	2.0	1,028	15.1	1,424	20.9	1,510	22.2	1,832	26.9	842	12.4	6,814
	San Francisco	0	0.0	50	0.9	580	10.7	986	18.3	1,128	20.9	1,610	29.8	1,048	19.4	5,402
	San Jose	0	0.0	37	2.1	305	17.6	414	23.9	379	21.9	402	23.2	193	11.2	1,730
Colorado	Denver	78	1.0	327	4.3	1,615	21.1	1,808	23.6	1,553	20.3	1,588	20.7	687	9.0	7,656
Connecticut	Hartford	17	0.9	54	2.7	202	10.3	248	12.6	407	20.7	696	35.4	340	17.3	1,964
	New Haven	0	0.0	41	1.7	279	11.8	359	15.2	516	21.8	771	32.6	401	16.9	2,367
District of Columbia	Washington[a]	48	0.4	351	3.1	1,674	15.0	2,247	20.1	2,457	22.0	2,832	25.4	1,543	13.8	11,152
Florida	Ft. Lauderdale	378	3.0	520	4.1	2,001	16.0	2,317	18.5	2,514	20.1	3,355	26.8	1,451	11.6	12,536
	Jacksonville	2	<0.1	109	2.7	792	19.7	829	20.7	904	22.5	995	24.8	380	9.5	4,011
	Miami	120	1.1	306	2.8	2,056	18.6	2,531	22.9	2,409	21.8	2,753	24.9	876	7.9	11,051
	Orlando	9	0.2	201	3.6	1,114	20.0	1,230	22.1	1,205	21.7	1,284	23.1	516	9.3	5,559
	Tampa–St. Petersburg	99	1.2	277	3.3	1,559	18.4	1,580	18.7	1,714	20.3	2,308	27.3	921	10.9	8,458
	West Palm Beach	2	0.1	79	2.1	557	14.6	668	17.6	808	21.2	1,078	28.3	612	16.1	3,804
Georgia	Atlanta	102	0.6	875	5.0	4,698	27.1	4,157	23.9	3,191	18.4	3,184	18.3	1,153	6.6	17,360
Illinois	Chicago	176	0.7	849	3.6	5,245	22.0	5,313	22.3	4,856	20.4	5,142	21.6	2,257	9.5	23,838
Indiana	Indianapolis	18	0.4	172	4.1	879	20.7	982	23.1	928	21.9	911	21.5	353	8.3	4,243
Louisiana	Baton Rouge	2	<0.1	119	2.6	649	14.4	998	22.1	1,016	22.5	1,126	25.0	601	13.3	4,511
	New Orleans	5	0.1	180	2.7	1,200	18.3	1,582	24.1	1,432	21.8	1,482	22.6	673	10.3	6,554
Maryland	Baltimore	107	0.8	330	2.6	1,817	14.2	2,334	18.3	2,380	18.6	3,870	30.3	1,928	15.1	12,766
Massachusetts	Boston[a]	74	0.6	238	1.9	1,510	12.3	2,180	17.7	2,686	21.9	3,703	30.1	1,901	15.5	12,292
Michigan	Detroit	66	1.0	288	4.4	1,512	23.2	1,291	19.8	1,220	18.7	1,444	22.2	691	10.6	6,512
Minnesota	Minneapolis–St. Paul[a]	20	0.4	232	5.0	710	15.4	1,023	22.1	977	21.1	1,115	24.1	543	11.8	4,620
Missouri	Kansas City[a]	2	0.1	106	3.7	602	21.2	649	22.9	609	21.4	637	22.4	235	8.3	2,840
	St. Louis[a]	60	0.6	343	3.7	1,824	19.6	1,932	20.8	1,976	21.3	2,292	24.7	857	9.2	9,284
Nevada	Las Vegas[a]	32	0.8	149	3.9	895	23.1	968	25.0	755	19.5	781	20.2	288	7.4	3,868
New Jersey	Bergen–Passaic	35	1.9	45	2.5	245	13.6	312	17.3	347	19.3	535	29.7	283	15.7	1,802
	Jersey City	9	0.5	41	2.3	311	17.3	344	19.1	356	19.8	484	26.9	253	14.1	1,798
	Middlesex	27	1.6	59	3.6	268	16.3	312	19.0	327	19.9	455	27.7	195	11.9	1,643
	Newark	43	0.6	194	2.9	1,068	15.8	1,224	18.1	1,289	19.1	1,909	28.3	1,020	15.1	6,747
New York	Nassau–Suffolk	35	1.1	203	6.4	460	14.5	498	15.7	609	19.3	836	26.4	521	16.5	3,162
	New York	219	0.5	1,008	2.4	6,859	16.2	8,383	19.8	8,508	20.1	11,420	26.9	5,982	14.1	42,379
North Carolina	Charlotte[a]	0	0.0	219	5.1	1,142	26.4	916	21.1	852	19.7	848	19.6	356	8.2	4,333
Ohio	Cleveland	5	0.1	163	4.2	724	18.8	716	18.6	765	19.8	1,008	26.1	478	12.4	3,859
	Columbus	83	1.3	252	3.8	1,287	19.6	1,396	21.2	1,358	20.7	1,564	23.8	632	9.6	6,572
Oregon	Portland[a]	1	<0.1	194	4.2	1,087	23.6	1,125	24.5	949	20.6	872	19.0	369	8.0	4,597
Pennsylvania	Philadelphia[a]	216	1.1	538	2.8	3,056	16.1	3,604	18.9	3,847	20.2	5,204	27.3	2,574	13.5	19,039
Puerto Rico	San Juan	25	0.4	111	1.6	660	9.7	947	13.8	1,476	21.6	2,311	33.8	1,309	19.1	6,839

Table 21b. Ryan White HIV/AIDS Program clients (non-ADAP), by age group and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico *(cont.)*

		<13 yrs		13–24 yrs		25–34 yrs		35–44 yrs		45–54 yrs		55–64 yrs		≥65 yrs		
State/Territory	**EMA/TGA**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**Total N**
Tennessee	Memphis[a]	25	0.5	239	4.9	1,104	22.7	1,123	23.1	1,054	21.7	948	19.5	361	7.4	4,854
	Nashville	22	0.2	294	3.0	1,952	20.1	2,031	20.9	2,222	22.9	2,335	24.1	848	8.7	9,704
Texas	Austin	0	0.0	99	3.2	610	20.0	701	23.0	674	22.1	706	23.1	260	8.5	3,050
	Dallas	78	0.5	476	3.2	3,158	21.5	3,583	24.3	3,181	21.6	3,138	21.3	1,103	7.5	14,717
	Ft. Worth	0	0.0	194	5.3	967	26.3	865	23.5	753	20.5	659	17.9	244	6.6	3,682
	Houston	173	1.0	810	4.6	4,048	22.9	4,218	23.9	3,740	21.2	3,396	19.2	1,258	7.1	17,643
	San Antonio	20	0.5	144	3.7	942	24.1	964	24.7	759	19.5	815	20.9	257	6.6	3,901
Virginia	Norfolk[a]	2	0.1	112	3.2	748	21.5	786	22.6	660	18.9	833	23.9	344	9.9	3,485
Washington	Seattle	4	0.1	125	2.0	854	13.7	1,392	22.3	1,508	24.1	1,593	25.5	769	12.3	6,245

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Notes: Percentages shown are based on the row total.
EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 22a. Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and state, 2022—United States and 3 territories

	American Indian/ Alaska Native		Asian		Black/ African American		Hispanic/Latino[a]		Native Hawaiian/ Pacific Islander		White		Multiple races		
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total N
State															
Alabama	16	0.2	35	0.3	7,305	69.2	343	3.3	13	0.1	2,786	26.4	52	0.5	10,550
Alaska	219	36.4	28	4.7	94	15.6	70	11.6	7	1.2	173	28.7	11	1.8	602
Arizona	278	3.0	146	1.6	1,534	16.5	3,255	34.9	19	0.2	3,828	41.1	260	2.8	9,320
Arkansas	9	0.3	18	0.6	1,405	45.3	278	9.0	10	0.3	1,351	43.5	32	1.0	3,103
California	326	0.6	2,152	4.1	9,999	19.2	23,334	44.7	247	0.5	15,525	29.8	565	1.1	52,148
Colorado	73	0.9	113	1.4	1,506	18.9	2,604	32.6	13	0.2	3,499	43.9	170	2.1	7,978
Connecticut	5	0.1	26	0.6	1,814	41.1	1,769	40.0	4	0.1	759	17.2	42	1.0	4,419
Delaware	3	0.1	9	0.4	1,285	61.9	179	8.6	1	<0.1	587	28.3	11	0.5	2,075
District of Columbia	6	0.1	21	0.4	4,403	80.5	676	12.4	1	<0.1	232	4.2	129	2.4	5,468
Florida	58	0.1	358	0.7	23,742	45.2	15,845	30.2	38	0.1	12,007	22.9	439	0.8	52,487
Georgia	32	0.1	157	0.6	19,605	76.9	1,895	7.4	9	<0.1	3,581	14.1	207	0.8	25,486
Hawaii	13	1.1	166	14.1	68	5.8	183	15.5	168	14.2	462	39.2	119	10.1	1,179
Idaho	12	1.2	14	1.3	100	9.6	193	18.5	4	0.4	706	67.7	14	1.3	1,043
Illinois	122	0.5	436	1.8	13,323	53.6	5,862	23.6	61	0.2	4,737	19.1	293	1.2	24,834
Indiana[b]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Iowa	10	0.5	70	3.2	597	27.6	259	12.0	7	0.3	1,173	54.2	49	2.3	2,165
Kansas	9	0.8	19	1.7	300	26.6	135	12.0	3	0.3	633	56.1	30	2.7	1,129
Kentucky	12	0.2	54	0.9	2,008	34.8	574	9.9	7	0.1	3,007	52.1	110	1.9	5,772
Louisiana	21	0.2	46	0.4	8,849	71.3	626	5.0	8	0.1	2,778	22.4	87	0.7	12,415
Maine	16	1.8	7	0.8	207	22.7	53	5.8	0	0.0	602	66.2	25	2.7	910
Maryland[b]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Massachusetts	31	0.2	249	1.9	4,072	31.1	4,367	33.3	10	0.1	4,216	32.2	155	1.2	13,100
Michigan	31	0.3	91	0.9	6,320	59.4	650	6.1	6	0.1	3,326	31.3	209	2.0	10,633
Minnesota	60	1.3	103	2.3	1,806	40.0	582	12.9	1	<0.1	1,452	32.1	514	11.4	4,518
Mississippi	15	0.3	9	0.2	4,380	79.8	101	1.8	0	0.0	969	17.7	15	0.3	5,489
Missouri	31	0.4	71	0.8	4,272	50.6	611	7.2	11	0.1	3,302	39.1	151	1.8	8,449
Montana	29	6.1	5	1.1	20	4.2	42	8.9	0	0.0	369	77.8	9	1.9	474
Nebraska	20	1.4	40	2.8	375	26.1	326	22.7	1	0.1	648	45.0	29	2.0	1,439
Nevada	26	0.5	161	3.2	1,334	26.7	1,742	34.8	39	0.8	1,531	30.6	166	3.3	4,999
New Hampshire	2	0.2	30	2.9	152	14.8	154	15.0	1	0.1	669	65.0	21	2.0	1,029
New Jersey	18	0.1	206	1.3	7,835	51.2	5,094	33.3	22	0.1	2,068	13.5	60	0.4	15,303
New Mexico	122	6.1	19	0.9	127	6.3	729	36.3	7	0.3	992	49.4	13	0.6	2,009
New York	137	0.3	1,056	2.2	22,090	45.2	18,062	36.9	84	0.2	7,071	14.5	401	0.8	48,901
North Carolina	160	1.0	101	0.6	10,087	64.9	1,725	11.1	10	0.1	3,357	21.6	104	0.7	15,544
North Dakota	16	4.6	1	0.3	158	45.0	24	6.8	0	0.0	130	37.0	22	6.3	351
Ohio	22	0.2	106	0.8	6,370	48.8	963	7.4	9	0.1	5,307	40.6	280	2.1	13,057
Oklahoma	225	5.8	86	2.2	987	25.4	454	11.7	8	0.2	1,944	50.1	176	4.5	3,880
Oregon	105	1.4	201	2.7	577	7.8	1,532	20.7	43	0.6	4,625	62.5	312	4.2	7,395
Pennsylvania	127	0.5	264	1.0	13,218	50.9	4,551	17.5	26	0.1	6,906	26.6	882	3.4	25,974
Rhode Island	18	0.7	44	1.7	600	23.5	758	29.7	12	0.5	1,087	42.6	31	1.2	2,550
South Carolina	26	0.2	58	0.4	9,898	70.2	708	5.0	9	0.1	3,263	23.2	129	0.9	14,091
South Dakota	30	7.4	4	1.0	161	40.0	34	8.4	0	0.0	158	39.2	16	4.0	403
Tennessee	33	0.2	142	0.9	8,248	54.0	1,046	6.8	7	<0.1	5,713	37.4	91	0.6	15,280
Texas[b]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

Table 22a. Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and state, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native		Asian		Black/ African American		Hispanic/Latino[a]		Native Hawaiian/ Pacific Islander		White		Multiple races		
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	Total N
State															
Utah	34	1.8	47	2.5	204	10.8	701	37.1	11	0.6	875	46.3	18	1.0	1,890
Vermont	8	1.3	14	2.3	70	11.7	36	6.0	1	0.2	464	77.6	5	0.8	598
Virginia	15	0.1	168	1.6	6,784	64.2	1,150	10.9	12	0.1	2,323	22.0	121	1.1	10,573
Washington	127	1.5	365	4.4	2,167	26.4	1,606	19.6	68	0.8	3,703	45.1	167	2.0	8,203
West Virginia	8	0.5	13	0.8	310	19.3	52	3.2	0	0.0	1,207	75.2	15	0.9	1,605
Wisconsin	16	0.3	81	1.6	2,156	43.1	822	16.4	11	0.2	1,881	37.6	35	0.7	5,002
Wyoming	10	4.9	2	1.0	8	3.9	41	20.1	0	0.0	138	67.6	5	2.5	204
Subtotal	**2,742**	**0.6**	**7,612**	**1.6**	**212,930**	**45.7**	**106,796**	**22.9**	**1,029**	**0.2**	**128,120**	**27.5**	**6,797**	**1.5**	**466,026**
Territory															
Guam	0	0.0	13	38.2	0	0.0	0	0.0	20	58.8	1	2.9	0	0.0	34
Puerto Rico	1	<0.1	2	<0.1	40	0.3	11,297	97.5	0	0.0	215	1.9	30	0.3	11,585
U.S. Virgin Islands	0	0.0	2	0.8	157	60.9	80	31.0	0	0.0	18	7.0	1	0.4	258
Subtotal	**1**	**<0.1**	**17**	**0.1**	**197**	**1.7**	**11,377**	**95.8**	**20**	**0.2**	**234**	**2.0**	**31**	**0.3**	**11,877**
Total	**2,743**	**0.6**	**7,629**	**1.6**	**213,127**	**44.6**	**118,173**	**24.7**	**1,049**	**0.2**	**128,354**	**26.9**	**6,828**	**1.4**	**477,903**

Notes: Percentages shown are based on the row total.
Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] Hispanics/Latinos can be of any race.
[b] 2022 data for Indiana are unavailable. 2022 race/ethnicity data for Maryland and Texas are unavailable.

Table 22b. Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		American Indian/ Alaska Native		Asian		Black/ African American		Hispanic/Latino[a]		Native Hawaiian/ Pacific Islander		White		
State/Territory	EMA/TGA	N	%	N	%	N	%	N	%	N	%	N	%	Total N[b]
Arizona	Phoenix	130	2.1	116	1.9	1,329	21.2	2,220	35.4	13	0.2	2,249	35.9	6,266
California	Los Angeles	93	0.4	810	3.8	4,930	23.0	10,830	50.5	64	0.3	4,567	21.3	21,455
	Oakland	26	0.7	204	5.6	1,701	46.4	1,039	28.3	26	0.7	627	17.1	3,665
	Orange County	5	0.2	142	6.4	108	4.9	1,377	62.3	9	0.4	546	24.7	2,212
	Riverside–San Bernardino	10	0.3	61	2.0	338	10.9	1,261	40.5	13	0.4	1,402	45.1	3,111
	Sacramento	22	0.8	103	3.7	635	22.8	744	26.8	20	0.7	1,197	43.1	2,779
	San Diego	34	0.5	201	3.0	840	12.5	3,284	49.0	28	0.4	2,258	33.7	6,707
	San Francisco	57	1.1	289	5.5	954	18.2	1,614	30.7	46	0.9	2,150	41.0	5,249
	San Jose	5	0.3	210	12.3	186	10.9	952	55.9	9	0.5	332	19.5	1,703
Colorado	Denver	62	0.8	101	1.4	1,509	20.3	2,449	32.9	11	0.1	3,131	42.1	7,440
Connecticut	Hartford	*	*	15	0.8	687	35.2	874	44.8	*	*	343	17.6	1,949
	New Haven	*	*	12	0.5	1,121	47.4	872	36.9	*	*	344	14.5	2,366
District of Columbia	Washington[c]	14	0.1	144	1.3	8,029	72.2	1,814	16.3	*	*	912	8.2	11,119
Florida	Ft. Lauderdale	5	<0.1	79	0.8	4,982	47.6	3,115	29.8	8	0.1	2,145	20.5	10,457
	Jacksonville	*	*	41	1.0	2,641	66.7	330	8.3	6	0.2	899	22.7	3,957
	Miami	7	0.1	23	0.2	3,826	34.7	6,472	58.6	*	*	690	6.3	11,040
	Orlando	8	0.1	43	0.8	2,331	42.0	1,953	35.2	6	0.1	1,122	20.2	5,554
	Tampa–St. Petersburg	7	0.1	90	1.1	3,334	39.5	1,948	23.1	5	0.1	2,941	34.8	8,447
	West Palm Beach	8	0.2	23	0.6	2,180	58.7	785	21.2	*	*	694	18.7	3,711
Georgia	Atlanta	28	0.2	133	0.8	13,476	78.2	1,575	9.1	8	<0.1	1,838	10.7	17,235
Illinois	Chicago	117	0.5	420	1.8	12,714	54.6	5,787	24.8	59	0.3	3,919	16.8	23,297
Indiana	Indianapolis	7	0.2	109	2.6	2,101	49.6	453	10.7	7	0.2	1,479	34.9	4,232
Louisiana	Baton Rouge	6	0.1	17	0.4	3,173	70.4	227	5.0	*	*	1,058	23.5	4,508
	New Orleans	10	0.2	27	0.4	4,466	68.2	475	7.3	*	*	1,518	23.2	6,549
Maryland	Baltimore[d]	—	—	—	—	—	—	—	—	—	—	—	—	—
Massachusetts	Boston[c]	29	0.2	246	2.1	3,887	32.5	3,594	30.0	11	0.1	4,047	33.8	11,974
Michigan	Detroit	5	0.1	22	0.3	5,029	77.5	272	4.2	*	*	1,071	16.5	6,486
Minnesota	Minneapolis–St. Paul[c]	57	1.2	102	2.2	1,854	40.5	589	12.9	*	*	1,462	31.9	4,582
Missouri	Kansas City[c]	9	0.3	34	1.2	1,228	43.2	409	14.4	*	*	1,083	38.1	2,840
	St. Louis[c]	34	0.4	70	0.8	4,743	51.1	652	7.0	11	0.1	3,615	38.9	9,284
Nevada	Las Vegas[c]	16	0.4	129	3.3	1,222	31.6	1,387	35.9	30	0.8	951	24.6	3,866
New Jersey	Bergen–Passaic	*	*	19	1.1	715	39.7	873	48.5	*	*	188	10.5	1,799
	Jersey City	*	*	49	2.7	640	35.7	916	51.0	*	*	180	10.0	1,795
	Middlesex	*	*	37	2.3	708	43.2	663	40.5	*	*	217	13.2	1,639
	Newark	8	0.1	56	0.8	4,347	64.4	1,819	27.0	13	0.2	487	7.2	6,747
New York	Nassau–Suffolk	*	*	86	2.7	1,262	39.9	967	30.6	*	*	782	24.8	3,159
	New York	102	0.2	881	2.1	19,036	46.3	16,383	39.9	77	0.2	4,346	10.6	41,100
North Carolina	Charlotte[c]	15	0.3	29	0.7	3,034	70.0	544	12.6	*	*	673	15.5	4,333
Ohio	Cleveland	*	*	19	0.5	2,267	58.7	364	9.4	*	*	1,160	30.1	3,859
	Columbus	12	0.2	55	0.9	2,629	41.5	479	7.6	7	0.1	2,955	46.6	6,342
Oregon	Portland[c]	41	0.9	134	3.1	430	9.8	978	22.3	24	0.5	2,532	57.8	4,380
Pennsylvania	Philadelphia[c]	107	0.6	208	1.1	11,361	60.6	3,147	16.8	19	0.1	3,147	16.8	18,753
Puerto Rico	San Juan	*	*	*	*	34	0.5	6,640	97.1	*	*	135	2.0	6,838

Table 22b. Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico *(cont.)*

		American Indian/ Alaska Native		Asian		Black/ African American		Hispanic/Latino[a]		Native Hawaiian/ Pacific Islander		White		
State/Territory	EMA/TGA	N	%	N	%	N	%	N	%	N	%	N	%	Total N[b]
Tennessee	Memphis[c]	9	0.2	7	0.1	4,241	87.4	168	3.5	*	*	393	8.1	4,854
	Nashville	18	0.2	115	1.2	4,716	48.6	757	7.8	*	*	4,033	41.6	9,701
Texas	Austin	12	0.4	39	1.3	799	26.3	1,253	41.2	*	*	899	29.6	3,038
	Dallas[d]	—	—	—	—	—	—	—	—	—	—	—	—	—
	Ft. Worth	15	0.4	54	1.5	1,785	49.1	947	26.1	5	0.1	796	21.9	3,632
	Houston	31	0.2	233	1.3	8,975	50.9	5,873	33.3	10	0.1	2,421	13.7	17,642
	San Antonio	13	0.3	44	1.1	633	16.2	2,556	65.6	*	*	635	16.3	3,899
Virginia	Norfolk[c]	*	*	28	0.8	2,618	75.1	165	4.7	*	*	612	17.6	3,484
Washington	Seattle	90	1.5	302	4.9	1,813	29.7	1,173	19.2	45	0.7	2,596	42.5	6,104

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Notes: Percentages shown are based on the row total.
EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
* To ensure confidentiality, values less than (<) 5 have been suppressed; in addition, all data for clients of multiple races have been suppressed. Therefore, the numbers for each subpopulation may not sum to the row total.
[a] Hispanics/Latinos can be of any race.
[b] Includes all clients with reported race/ethnicity information.
[c] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.
[d] 2022 race/ethnicity data for Baltimore, MD, and Dallas, TX, EMAs are unavailable.

Table 23a. Ryan White HIV/AIDS Program clients (non-ADAP), by gender and state, 2022—United States and 3 territories

	Male		Female		Transgender male		Transgender female		Other gender identity		
	N	%	N	%	N	%	N	%	N	%	Total N
State											
Alabama	7,532	70.7	2,958	27.8	8	0.1	147	1.4	3	<0.1	10,648
Alaska	452	72.8	150	24.2	1	0.2	11	1.8	7	1.1	621
Arizona	7,568	81.1	1,553	16.6	12	0.1	194	2.1	3	<0.1	9,330
Arkansas	2,363	76.2	701	22.6	4	0.1	35	1.1	0	0.0	3,103
California	43,368	82.4	7,544	14.3	120	0.2	1,621	3.1	6	<0.1	52,659
Colorado	6,268	76.5	1,413	17.3	19	0.2	122	1.5	367	4.5	8,189
Connecticut	2,625	59.2	1,722	38.8	6	0.1	76	1.7	6	0.1	4,435
Delaware	1,394	67.1	666	32.1	2	0.1	14	0.7	0	0.0	2,076
District of Columbia	3,362	61.2	1,869	34.0	47	0.9	208	3.8	8	0.1	5,494
Florida	38,646	70.6	15,177	27.7	105	0.2	816	1.5	7	<0.1	54,751
Georgia	18,399	71.7	6,632	25.8	40	0.2	570	2.2	20	0.1	25,661
Hawaii	1,000	84.6	151	12.8	2	0.2	27	2.3	2	0.2	1,182
Idaho	848	81.3	182	17.4	2	0.2	11	1.1	0	0.0	1,043
Illinois	19,184	75.6	5,054	19.9	126	0.5	917	3.6	81	0.3	25,362
Indiana[a]	—	—	—	—	—	—	—	—	—	—	—
Iowa	1,628	74.1	539	24.5	1	<0.1	28	1.3	0	0.0	2,196
Kansas	884	78.3	228	20.2	2	0.2	15	1.3	0	0.0	1,129
Kentucky	4,494	77.9	1,138	19.7	9	0.2	128	2.2	3	0.1	5,772
Louisiana	8,213	64.0	4,175	32.5	79	0.6	348	2.7	23	0.2	12,838
Maine	681	73.8	231	25.0	0	0.0	11	1.2	0	0.0	923
Maryland	9,218	61.3	5,491	36.5	48	0.3	264	1.8	10	0.1	15,031
Massachusetts	8,910	66.3	4,253	31.7	20	0.1	200	1.5	48	0.4	13,431
Michigan	8,114	75.9	2,385	22.3	10	0.1	184	1.7	3	<0.1	10,696
Minnesota	3,055	67.0	1,375	30.2	12	0.3	113	2.5	4	0.1	4,559
Mississippi	3,754	68.4	1,647	30.0	6	0.1	85	1.5	0	0.0	5,492
Missouri	6,372	75.4	1,839	21.8	7	0.1	231	2.7	0	0.0	8,449
Montana	398	83.8	72	15.2	0	0.0	5	1.1	0	0.0	475
Nebraska	1,094	75.9	312	21.7	1	0.1	34	2.4	0	0.0	1,441
Nevada	4,020	80.3	822	16.4	10	0.2	150	3.0	3	0.1	5,005
New Hampshire	766	73.8	256	24.7	1	0.1	15	1.4	0	0.0	1,038
New Jersey	9,810	64.0	5,293	34.5	18	0.1	202	1.3	3	<0.1	15,326
New Mexico	1,829	86.6	256	12.1	1	<0.1	26	1.2	1	<0.1	2,113
New York	31,606	63.0	15,565	31.0	144	0.3	2,506	5.0	364	0.7	50,185
North Carolina	11,006	70.7	4,269	27.4	22	0.1	268	1.7	6	<0.1	15,571
North Dakota	224	63.5	125	35.4	0	0.0	4	1.1	0	0.0	353
Ohio	9,915	75.5	2,963	22.6	11	0.1	218	1.7	31	0.2	13,138
Oklahoma	3,076	78.8	770	19.7	8	0.2	48	1.2	3	0.1	3,905
Oregon	5,864	81.8	1,114	15.5	27	0.4	120	1.7	41	0.6	7,166
Pennsylvania	17,542	66.8	7,959	30.3	61	0.2	645	2.5	53	0.2	26,260
Rhode Island	1,840	69.9	617	23.4	144	5.5	31	1.2	0	0.0	2,632
South Carolina	9,811	69.6	4,071	28.9	31	0.2	186	1.3	3	<0.1	14,102
South Dakota	241	59.8	157	39.0	0	0.0	5	1.2	0	0.0	403
Tennessee	11,588	75.8	3,388	22.2	21	0.1	280	1.8	6	<0.1	15,283
Texas	36,839	75.2	11,117	22.7	251	0.5	726	1.5	71	0.1	49,004

Table 23a. Ryan White HIV/AIDS Program clients (non-ADAP), by gender and state, 2022—United States and 3 territories *(cont.)*

	Male		Female		Transgender male		Transgender female		Other gender identity		
	N	%	N	%	N	%	N	%	N	%	Total N
State											
Utah	1,562	82.6	301	15.9	6	0.3	20	1.1	3	0.2	1,892
Vermont	495	81.1	101	16.6	7	1.1	7	1.1	0	0.0	610
Virginia	7,302	68.9	3,047	28.8	16	0.2	224	2.1	6	0.1	10,595
Washington	6,470	77.4	1,710	20.5	25	0.3	148	1.8	4	<0.1	8,357
West Virginia	1,196	74.3	390	24.2	9	0.6	15	0.9	0	0.0	1,610
Wisconsin	3,917	74.8	1,168	22.3	9	0.2	146	2.8	0	0.0	5,240
Wyoming	162	79.4	42	20.6	0	0.0	0	0.0	0	0.0	204
Subtotal	**386,905**	**72.1**	**134,958**	**25.1**	**1,511**	**0.3**	**12,405**	**2.3**	**1,199**	**0.2**	**536,978**
Territory											
Guam	28	82.4	6	17.6	0	0.0	0	0.0	0	0.0	34
Puerto Rico	7,999	69.0	3,507	30.3	22	0.2	60	0.5	4	<0.1	11,592
U.S. Virgin Islands	146	56.6	111	43.0	0	0.0	1	0.4	0	0.0	258
Subtotal	**8,173**	**68.8**	**3,624**	**30.5**	**22**	**0.2**	**61**	**0.5**	**4**	**<0.1**	**11,884**
Total	**395,078**	**72.0**	**138,582**	**25.2**	**1,533**	**0.3**	**12,466**	**2.3**	**1,203**	**0.2**	**548,862**

Notes: Percentages shown are based on the row total.
Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable.

Table 23b. Ryan White HIV/AIDS Program clients (non-ADAP), by gender and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		Male		Female		Transgender male		Transgender female		
State/Territory	EMA/TGA	N	%	N	%	N	%	N	%	Total N[a]
Arizona	Phoenix	5,039	80.3	1,098	17.5	6	0.1	129	2.1	6,276
California	Los Angeles	18,053	84.1	2,650	12.3	55	0.3	717	3.3	21,477
	Oakland	2,669	71.6	891	23.9	9	0.2	157	4.2	3,726
	Orange County	1,887	84.4	302	13.5	*	*	42	1.9	2,235
	Riverside–San Bernardino	2,750	88.1	324	10.4	7	0.2	41	1.3	3,122
	Sacramento	2,189	77.9	541	19.3	*	*	73	2.6	2,809
	San Diego	5,709	83.8	886	13.0	16	0.2	203	3.0	6,814
	San Francisco	4,469	82.7	632	11.7	14	0.3	286	5.3	5,401
	San Jose	1,443	83.4	252	14.6	*	*	31	1.8	1,730
Colorado	Denver	5,844	76.4	1,303	17.0	19	0.2	117	1.5	7,649
Connecticut	Hartford	1,179	60.0	751	38.2	*	*	28	1.4	1,964
	New Haven	1,393	58.9	920	38.9	*	*	48	2.0	2,367
District of Columbia	Washington[b]	6,785	60.8	4,031	36.1	55	0.5	271	2.4	11,152
Florida	Ft. Lauderdale	8,824	70.5	3,485	27.9	19	0.2	184	1.5	12,512
	Jacksonville	2,670	66.6	1,250	31.2	*	*	86	2.1	4,010
	Miami	8,389	75.9	2,520	22.8	11	0.1	130	1.2	11,050
	Orlando	4,036	72.6	1,360	24.5	29	0.5	134	2.4	5,559
	Tampa–St. Petersburg	6,315	74.7	1,976	23.4	11	0.1	153	1.8	8,458
	West Palm Beach	2,438	64.1	1,297	34.1	11	0.3	55	1.4	3,801
Georgia	Atlanta	13,222	76.2	3,636	20.9	36	0.2	448	2.6	17,360
Illinois	Chicago	18,111	76.0	4,637	19.5	118	0.5	877	3.7	23,824
Indiana	Indianapolis	3,082	72.6	1,050	24.7	*	*	102	2.4	4,243
Louisiana	Baton Rouge	2,905	64.4	1,503	33.3	24	0.5	75	1.7	4,511
	New Orleans	4,183	63.8	2,022	30.9	77	1.2	255	3.9	6,554
Maryland	Baltimore	7,956	62.3	4,510	35.3	44	0.3	246	1.9	12,765
Massachusetts	Boston[b]	8,187	66.6	3,857	31.4	19	0.2	181	1.5	12,291
Michigan	Detroit	4,840	74.3	1,517	23.3	5	0.1	146	2.2	6,511
Minnesota	Minneapolis–St. Paul[b]	3,120	67.5	1,368	29.6	14	0.3	113	2.4	4,620
Missouri	Kansas City[b]	2,191	77.1	557	19.6	*	*	90	3.2	2,840
	St. Louis[b]	7,006	75.5	2,020	21.8	10	0.1	248	2.7	9,284
Nevada	Las Vegas[b]	3,092	80.0	640	16.6	8	0.2	124	3.2	3,867
New Jersey	Bergen–Passaic	1,154	64.0	631	35.0	*	*	16	0.9	1,802
	Jersey City	1,295	72.0	473	26.3	6	0.3	24	1.3	1,798
	Middlesex	986	60.0	624	38.0	*	*	33	2.0	1,643
	Newark	4,162	61.7	2,490	36.9	7	0.1	88	1.3	6,747
New York	Nassau–Suffolk	1,504	47.6	1,564	49.5	*	*	87	2.8	3,162
	New York	27,176	64.1	12,441	29.4	123	0.3	2,298	5.4	42,373
North Carolina	Charlotte[b]	3,224	74.4	1,003	23.1	6	0.1	98	2.3	4,333
Ohio	Cleveland	2,940	76.2	815	21.1	*	*	97	2.5	3,858
	Columbus	4,879	76.1	1,433	22.4	5	0.1	76	1.2	6,410
Oregon	Portland[b]	3,360	84.0	501	12.5	21	0.5	85	2.1	3,998
Pennsylvania	Philadelphia[b]	12,557	66.1	5,793	30.5	54	0.3	547	2.9	19,001
Puerto Rico	San Juan	4,582	67.0	2,222	32.5	11	0.2	21	0.3	6,839
Tennessee	Memphis[b]	3,196	65.8	1,508	31.1	12	0.2	133	2.7	4,854
	Nashville	7,603	78.3	1,920	19.8	8	0.1	171	1.8	9,704
Texas	Austin	2,440	80.0	523	17.1	39	1.3	12	0.4	3,050
	Dallas	11,065	75.2	3,305	22.5	15	0.1	310	2.1	14,712
	Ft. Worth	2,742	74.5	866	23.5	10	0.3	63	1.7	3,681
	Houston	12,980	73.6	4,300	24.4	32	0.2	327	1.9	17,643
	San Antonio	3,165	81.2	623	16.0	92	2.4	16	0.4	3,900
Virginia	Norfolk[b]	2,415	69.3	972	27.9	*	*	92	2.6	3,485
Washington	Seattle	4,872	78.0	1,236	19.8	17	0.3	117	1.9	6,244

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Notes: Percentages shown are based on the row total.
EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
* To ensure confidentiality, values less than (<) 5 have been suppressed; in addition, data in the *Other gender identity* category are not included. Therefore, the numbers for each subpopulation may not sum to the row total.
[a] Includes all clients with reported gender information.
[b] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 24a-i. Male clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and state, 2022—United States and 3 territories

	Male-to-male sexual contact		Injection drug use		Male-to-male sexual contact and injection drug use		Heterosexual contact[a]		Perinatal		Other[b]		
	N	%	N	%	N	%	N	%	N	%	N	%	Total N
State													
Alabama	4,705	67.3	273	3.9	75	1.1	1,833	26.2	90	1.3	10	0.1	6,986
Alaska	260	66.2	18	4.6	25	6.4	85	21.6	2	0.5	3	0.8	393
Arizona	4,790	72.0	250	3.8	661	9.9	844	12.7	79	1.2	29	0.4	6,653
Arkansas	1,641	72.1	113	5.0	105	4.6	393	17.3	12	0.5	13	0.6	2,277
California	30,718	77.9	1,590	4.0	2,077	5.3	4,665	11.8	187	0.5	175	0.4	39,412
Colorado	3,669	69.1	232	4.4	796	15.0	508	9.6	90	1.7	16	0.3	5,311
Connecticut	1,109	45.0	494	20.0	57	2.3	742	30.1	44	1.8	18	0.7	2,464
Delaware	813	59.3	123	9.0	44	3.2	373	27.2	11	0.8	7	0.5	1,371
District of Columbia	1,670	62.3	193	7.2	24	0.9	733	27.4	58	2.2	2	0.1	2,680
Florida	22,052	65.5	811	2.4	534	1.6	9,589	28.5	418	1.2	258	0.8	33,662
Georgia	12,975	71.7	330	1.8	234	1.3	4,343	24.0	170	0.9	42	0.2	18,094
Hawaii	709	84.3	44	5.2	13	1.5	66	7.8	2	0.2	7	0.8	841
Idaho	535	67.7	56	7.1	72	9.1	109	13.8	3	0.4	15	1.9	790
Illinois	11,215	74.9	424	2.8	173	1.2	2,934	19.6	147	1.0	75	0.5	14,968
Indiana[c]	—	—	—	—	—	—	—	—	—	—	—	—	—
Iowa	942	66.2	80	5.6	94	6.6	271	19.1	10	0.7	25	1.8	1,422
Kansas	651	78.1	41	4.9	0	0.0	128	15.3	4	0.5	10	1.2	834
Kentucky	3,055	71.5	228	5.3	223	5.2	716	16.7	28	0.7	25	0.6	4,275
Louisiana	4,315	62.9	320	4.7	120	1.7	2,045	29.8	39	0.6	22	0.3	6,861
Maine	326	74.4	29	6.6	12	2.7	60	13.7	5	1.1	6	1.4	438
Maryland	3,686	53.2	805	11.6	107	1.5	2,116	30.5	171	2.5	46	0.7	6,931
Massachusetts	4,756	58.7	1,137	14.0	198	2.4	1,804	22.3	142	1.8	64	0.8	8,101
Michigan	4,913	73.0	177	2.6	171	2.5	1,351	20.1	78	1.2	37	0.6	6,727
Minnesota	1,497	63.3	109	4.6	173	7.3	523	22.1	45	1.9	17	0.7	2,364
Mississippi	2,229	60.5	82	2.2	76	2.1	1,240	33.7	42	1.1	14	0.4	3,683
Missouri	4,680	75.4	223	3.6	17	0.3	1,192	19.2	43	0.7	55	0.9	6,210
Montana	251	67.8	26	7.0	45	12.2	44	11.9	2	0.5	2	0.5	370
Nebraska	673	69.0	60	6.1	12	1.2	205	21.0	9	0.9	17	1.7	976
Nevada	2,974	79.1	149	4.0	84	2.2	481	12.8	31	0.8	40	1.1	3,759
New Hampshire	504	70.1	57	7.9	33	4.6	94	13.1	16	2.2	15	2.1	719
New Jersey	4,722	52.9	784	8.8	120	1.3	3,000	33.6	235	2.6	61	0.7	8,922
New Mexico	1,390	78.0	67	3.8	168	9.4	140	7.9	9	0.5	9	0.5	1,783
New York	16,055	59.4	1,577	5.8	515	1.9	8,348	30.9	335	1.2	199	0.7	27,029
North Carolina	6,634	64.4	337	3.3	293	2.8	2,871	27.9	122	1.2	51	0.5	10,308
North Dakota	120	58.8	12	5.9	21	10.3	50	24.5	1	0.5	0	0.0	204
Ohio	6,554	75.1	328	3.8	140	1.6	1,574	18.0	82	0.9	46	0.5	8,724
Oklahoma	2,053	71.2	165	5.7	209	7.2	411	14.3	20	0.7	25	0.9	2,883
Oregon	1,993	68.8	215	7.4	368	12.7	270	9.3	15	0.5	34	1.2	2,895
Pennsylvania	9,069	59.9	1,415	9.3	432	2.9	3,825	25.3	285	1.9	121	0.8	15,147
Rhode Island	987	59.4	142	8.5	60	3.6	425	25.6	29	1.7	18	1.1	1,661
South Carolina	6,096	64.8	287	3.0	117	1.2	2,769	29.4	63	0.7	78	0.8	9,410
South Dakota	147	63.4	4	1.7	47	20.3	32	13.8	1	0.4	1	0.4	232
Tennessee	5,750	70.1	278	3.4	199	2.4	1,881	22.9	52	0.6	38	0.5	8,198
Texas	19,268	72.6	825	3.1	677	2.6	5,409	20.4	232	0.9	118	0.4	26,529

Table 24a-i. Male clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and state, 2022—United States and 3 territories *(cont.)*

	Male-to-male sexual contact		Injection drug use		Male-to-male sexual contact and injection drug use		Heterosexual contact[a]		Perinatal		Other[b]		
	N	%	N	%	N	%	N	%	N	%	N	%	Total N
State													
Utah	770	67.5	56	4.9	178	15.6	115	10.1	16	1.4	5	0.4	1,140
Vermont	363	79.1	22	4.8	21	4.6	44	9.6	5	1.1	4	0.9	459
Virginia	4,619	67.5	259	3.8	101	1.5	1,753	25.6	59	0.9	54	0.8	6,845
Washington	2,062	67.5	125	4.1	334	10.9	438	14.3	92	3.0	6	0.2	3,057
West Virginia	767	66.7	150	13.0	48	4.2	165	14.3	7	0.6	13	1.1	1,150
Wisconsin	2,351	72.7	159	4.9	54	1.7	593	18.3	47	1.5	28	0.9	3,232
Wyoming	53	63.9	9	10.8	15	18.1	6	7.2	0	0.0	0	0.0	83
Subtotal	**224,136**	**68.0**	**15,690**	**4.8**	**10,372**	**3.1**	**73,606**	**22.3**	**3,685**	**1.1**	**1,974**	**0.6**	**329,463**
Territory													
Guam	17	60.7	0	0.0	3	10.7	7	25.0	1	3.6	0	0.0	28
Puerto Rico	3,835	49.3	986	12.7	65	0.8	2,763	35.5	95	1.2	40	0.5	7,784
U.S. Virgin Islands	50	36.2	8	5.8	1	0.7	78	56.5	1	0.7	0	0.0	138
Subtotal	**3,902**	**49.1**	**994**	**12.5**	**69**	**0.9**	**2,848**	**35.8**	**97**	**1.2**	**40**	**0.5**	**7,950**
Total	**228,038**	**67.6**	**16,684**	**4.9**	**10,441**	**3.1**	**76,454**	**22.7**	**3,782**	**1.1**	**2,014**	**0.6**	**337,413**

Notes: Percentages shown are based on the row total.
Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[b] Includes hemophilia and blood transfusion.
[c] 2022 data for Indiana are unavailable.

Table 24a-ii. Female clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and state, 2022—United States and 3 territories

	Injection drug use		Heterosexual contact[a]		Perinatal		Other[b]		
	N	%	N	%	N	%	N	%	Total N
State									
Alabama	130	4.7	2,554	92.9	50	1.8	14	0.5	2,748
Alaska	28	19.9	112	79.4	1	0.7	0	0.0	141
Arizona	170	12.1	1,151	82.2	68	4.9	11	0.8	1,400
Arkansas	63	9.3	593	87.2	17	2.5	7	1.0	680
California	720	10.8	5,602	83.8	254	3.8	107	1.6	6,683
Colorado	212	17.9	865	73.1	99	8.4	8	0.7	1,184
Connecticut	224	14.0	1,304	81.4	52	3.2	22	1.4	1,602
Delaware	92	14.1	530	81.4	22	3.4	7	1.1	651
District of Columbia	212	14.3	1,183	79.6	87	5.9	5	0.3	1,487
Florida	490	3.8	11,882	91.1	563	4.3	113	0.9	13,048
Georgia	175	2.7	6,053	93.1	220	3.4	51	0.8	6,499
Hawaii	13	11.0	101	85.6	3	2.5	1	0.8	118
Idaho	16	9.3	145	84.3	6	3.5	5	2.9	172
Illinois	229	5.8	3,442	86.9	236	6.0	56	1.4	3,963
Indiana[c]	—	—	—	—	—	—	—	—	—
Iowa	38	7.8	427	87.7	12	2.5	10	2.1	487
Kansas	18	8.3	190	88.0	7	3.2	1	0.5	216
Kentucky	130	12.0	910	84.3	32	3.0	8	0.7	1,080
Louisiana	196	5.7	3,202	92.6	47	1.4	14	0.4	3,459
Maine	11	7.5	125	85.0	5	3.4	6	4.1	147
Maryland	492	11.8	3,377	81.3	223	5.4	63	1.5	4,155
Massachusetts	604	15.7	3,016	78.6	162	4.2	56	1.5	3,838
Michigan	120	5.9	1,830	89.4	79	3.9	17	0.8	2,046
Minnesota	85	8.1	878	83.9	70	6.7	14	1.3	1,047
Mississippi	51	3.2	1,495	93.1	48	3.0	12	0.7	1,606
Missouri	80	4.5	1,622	91.4	54	3.0	19	1.1	1,775
Montana	15	22.1	52	76.5	0	0.0	1	1.5	68
Nebraska	12	4.3	255	90.4	9	3.2	6	2.1	282
Nevada	40	5.2	670	87.5	41	5.4	15	2.0	766
New Hampshire	46	20.2	161	70.6	15	6.6	6	2.6	228
New Jersey	430	9.2	3,926	84.3	237	5.1	65	1.4	4,658
New Mexico	46	18.7	182	74.0	10	4.1	8	3.3	246
New York	994	7.5	11,477	87.2	468	3.6	228	1.7	13,167
North Carolina	206	5.1	3,634	90.6	145	3.6	28	0.7	4,013
North Dakota	14	11.9	98	83.1	6	5.1	0	0.0	118
Ohio	152	5.7	2,332	88.1	140	5.3	22	0.8	2,646
Oklahoma	97	13.7	583	82.3	22	3.1	6	0.8	708
Oregon	99	19.3	402	78.5	6	1.2	5	1.0	512
Pennsylvania	821	11.8	5,763	82.7	309	4.4	76	1.1	6,969
Rhode Island	78	13.5	465	80.3	27	4.7	9	1.6	579
South Carolina	169	4.3	3,618	92.0	97	2.5	47	1.2	3,931
South Dakota	19	13.5	121	85.8	1	0.7	0	0.0	141
Tennessee	186	7.1	2,332	89.4	74	2.8	17	0.7	2,609
Texas	441	5.9	6,678	88.6	293	3.9	122	1.6	7,534
Utah	26	11.3	196	85.2	5	2.2	3	1.3	230
Vermont	15	16.9	69	77.5	3	3.4	2	2.2	89
Virginia	159	5.6	2,565	89.9	82	2.9	46	1.6	2,852
Washington	92	11.5	659	82.2	41	5.1	10	1.2	802
West Virginia	123	33.7	230	63.0	11	3.0	1	0.3	365
Wisconsin	52	5.5	822	87.0	52	5.5	19	2.0	945
Wyoming	8	40.0	11	55.0	1	5.0	0	0.0	20
Subtotal	**8,939**	**7.8**	**99,890**	**87.1**	**4,512**	**3.9**	**1,369**	**1.2**	**114,710**
Territory									
Guam	0	0.0	5	83.3	1	16.7	0	0.0	6
Puerto Rico	185	5.4	3,104	90.6	92	2.7	45	1.3	3,426
U.S. Virgin Islands	4	3.8	99	94.3	1	1.0	1	1.0	105
Subtotal	**189**	**5.3**	**3,208**	**90.7**	**94**	**2.7**	**46**	**1.3**	**3,537**
Total	**9,128**	**7.7**	**103,098**	**87.2**	**4,606**	**3.9**	**1,415**	**1.2**	**118,247**

Notes: Percentages shown are based on the row total.
Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[b] Includes hemophilia and blood transfusion.
[c] 2022 data for Indiana are unavailable.

Table 24a-iii. Transgender clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and state, 2022—United States and 3 territories

	Sexual contact[a]		Injection drug use		Sexual contact[a] and injection drug use		Perinatal		Other[b]		
	N	%	N	%	N	%	N	%	N	%	Total N
State											
Alabama	127	95.5	0	0.0	4	3.0	1	0.8	1	0.8	133
Alaska	14	87.5	0	0.0	2	12.5	0	0.0	0	0.0	16
Arizona	138	85.2	0	0.0	24	14.8	0	0.0	0	0.0	162
Arkansas	34	94.4	0	0.0	2	5.6	0	0.0	0	0.0	36
California	1,338	89.4	32	2.1	116	7.8	2	0.1	8	0.5	1,496
Colorado	293	83.0	5	1.4	54	15.3	0	0.0	1	0.3	353
Connecticut	71	87.7	3	3.7	7	8.6	0	0.0	0	0.0	81
Delaware	15	100.0	0	0.0	0	0.0	0	0.0	0	0.0	15
District of Columbia	142	97.9	0	0.0	3	2.1	0	0.0	0	0.0	145
Florida	772	96.3	4	0.5	17	2.1	7	0.9	2	0.2	802
Georgia	606	98.2	1	0.2	2	0.3	7	1.1	1	0.2	617
Hawaii	23	88.5	0	0.0	3	11.5	0	0.0	0	0.0	26
Idaho	10	83.3	0	0.0	2	16.7	0	0.0	0	0.0	12
Illinois	789	96.6	6	0.7	15	1.8	5	0.6	2	0.2	817
Indiana[c]	—	—	—	—	—	—	—	—	—	—	—
Iowa	24	88.9	1	3.7	2	7.4	0	0.0	0	0.0	27
Kansas	17	100.0	0	0.0	0	0.0	0	0.0	0	0.0	17
Kentucky	119	90.2	2	1.5	10	7.6	1	0.8	0	0.0	132
Louisiana	400	98.0	2	0.5	6	1.5	0	0.0	0	0.0	408
Maine	5	100.0	0	0.0	0	0.0	0	0.0	0	0.0	5
Maryland	183	94.8	5	2.6	3	1.6	2	1.0	0	0.0	193
Massachusetts	206	89.6	10	4.3	11	4.8	3	1.3	0	0.0	230
Michigan	149	94.3	0	0.0	8	5.1	1	0.6	0	0.0	158
Minnesota	80	87.0	0	0.0	12	13.0	0	0.0	0	0.0	92
Mississippi	89	98.9	0	0.0	0	0.0	0	0.0	1	1.1	90
Missouri	223	97.8	2	0.9	1	0.4	1	0.4	1	0.4	228
Montana	4	80.0	0	0.0	1	20.0	0	0.0	0	0.0	5
Nebraska	28	93.3	2	6.7	0	0.0	0	0.0	0	0.0	30
Nevada	144	94.1	1	0.7	7	4.6	1	0.7	0	0.0	153
New Hampshire	10	71.4	1	7.1	3	21.4	0	0.0	0	0.0	14
New Jersey	113	93.4	4	3.3	2	1.7	1	0.8	1	0.8	121
New Mexico	24	88.9	0	0.0	3	11.1	0	0.0	0	0.0	27
New York	1,750	94.1	37	2.0	43	2.3	13	0.7	17	0.9	1,860
North Carolina	263	96.3	1	0.4	8	2.9	0	0.0	1	0.4	273
North Dakota	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	1
Ohio	191	94.1	3	1.5	6	3.0	2	1.0	1	0.5	203
Oklahoma	52	98.1	0	0.0	1	1.9	0	0.0	0	0.0	53
Oregon	64	84.2	2	2.6	10	13.2	0	0.0	0	0.0	76
Pennsylvania	471	91.6	6	1.2	29	5.6	6	1.2	2	0.4	514
Rhode Island	101	88.6	8	7.0	3	2.6	1	0.9	1	0.9	114
South Carolina	205	96.7	2	0.9	2	0.9	0	0.0	3	1.4	212
South Dakota	4	100.0	0	0.0	0	0.0	0	0.0	0	0.0	4
Tennessee	207	95.4	1	0.5	9	4.1	0	0.0	0	0.0	217
Texas	702	95.4	11	1.5	19	2.6	3	0.4	1	0.1	736
Utah	15	83.3	0	0.0	3	16.7	0	0.0	0	0.0	18
Vermont	12	100.0	0	0.0	0	0.0	0	0.0	0	0.0	12
Virginia	223	97.4	1	0.4	2	0.9	3	1.3	0	0.0	229
Washington	79	81.4	0	0.0	14	14.4	4	4.1	0	0.0	97
West Virginia	20	87.0	1	4.3	1	4.3	1	4.3	0	0.0	23
Wisconsin	129	97.0	1	0.8	1	0.8	1	0.8	1	0.8	133
Wyoming	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0
Subtotal	**10,679**	**93.5**	**155**	**1.4**	**471**	**4.1**	**66**	**0.6**	**45**	**0.4**	**11,416**
Territory											
Guam	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0
Puerto Rico	80	96.4	1	1.2	2	2.4	0	0.0	0	0.0	83
U.S. Virgin Islands	1	100.0	0	0.0	0	0.0	0	0.0	0	0.0	1
Subtotal	**81**	**96.4**	**1**	**1.2**	**2**	**2.4**	**0**	**0.0**	**0**	**0.0**	**84**
Total	**10,760**	**93.6**	**156**	**1.4**	**473**	**4.1**	**66**	**0.6**	**45**	**0.4**	**11,500**

Notes: Percentages shown are based on the row total.
Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] Includes any sexual transmission category reported by transgender clients.
[b] Includes hemophilia and blood transfusion.
[c] 2022 data for Indiana are unavailable.

Table 24b-i. Male clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		Male-to-male sexual contact		Injection drug use		Male-to-male sexual contact and injection drug use		Heterosexual contact[a]		Perinatal		Other[b]		
State/Territory	EMA/TGA	N	%	N	%	N	%	N	%	N	%	N	%	Total N
Arizona	Phoenix	3,165	73.2	135	3.1	437	10.1	501	11.6	71	1.6	13	0.3	4,322
California	Los Angeles	14,115	81.8	359	2.1	779	4.5	1,860	10.8	82	0.5	52	0.3	17,247
	Oakland	1,563	70.5	97	4.4	106	4.8	410	18.5	25	1.1	16	0.7	2,217
	Orange County	1,359	78.2	65	3.7	58	3.3	248	14.3	4	0.2	3	0.2	1,737
	Riverside–San Bernardino	2,233	82.0	63	2.3	145	5.3	275	10.1	1	<0.1	6	0.2	2,723
	Sacramento	1,413	67.3	184	8.8	110	5.2	352	16.8	18	0.9	22	1.0	2,099
	San Diego	3,660	80.7	142	3.1	274	6.0	396	8.7	42	0.9	24	0.5	4,538
	San Francisco	2,755	73.6	360	9.6	417	11.1	186	5.0	7	0.2	16	0.4	3,741
	San Jose	893	76.8	40	3.4	42	3.6	180	15.5	1	0.1	7	0.6	1,163
Colorado	Denver	3,419	69.2	194	3.9	790	16.0	435	8.8	90	1.8	11	0.2	4,939
Connecticut	Hartford	473	44.3	242	22.7	33	3.1	289	27.1	26	2.4	4	0.4	1,067
	New Haven	634	47.1	239	17.7	21	1.6	420	31.2	21	1.6	12	0.9	1,347
District of Columbia	Washington[c]	3,472	60.6	315	5.5	56	1.0	1,759	30.7	88	1.5	38	0.7	5,728
Florida	Ft. Lauderdale	3,588	69.2	59	1.1	74	1.4	1,368	26.4	84	1.6	11	0.2	5,184
	Jacksonville	1,592	64.8	76	3.1	51	2.1	699	28.4	18	0.7	21	0.9	2,457
	Miami	5,735	70.2	115	1.4	61	0.7	2,114	25.9	114	1.4	25	0.3	8,164
	Orlando	2,652	70.2	95	2.5	65	1.7	920	24.4	33	0.9	13	0.3	3,778
	Tampa–St. Petersburg	4,366	71.0	199	3.2	167	2.7	1,277	20.8	93	1.5	50	0.8	6,152
	West Palm Beach	1,061	47.4	50	2.2	37	1.7	1,044	46.6	30	1.3	16	0.7	2,238
Georgia	Atlanta	10,121	77.7	173	1.3	177	1.4	2,389	18.4	144	1.1	14	0.1	13,018
Illinois	Chicago	10,591	75.3	366	2.6	164	1.2	2,741	19.5	139	1.0	65	0.5	14,066
Indiana	Indianapolis	2,185	74.0	91	3.1	59	2.0	564	19.1	25	0.8	29	1.0	2,953
Louisiana	Baton Rouge	1,324	59.4	107	4.8	54	2.4	718	32.2	21	0.9	5	0.2	2,229
	New Orleans	2,360	65.2	156	4.3	46	1.3	1,025	28.3	15	0.4	16	0.4	3,618
Maryland	Baltimore	3,134	53.1	762	12.9	102	1.7	1,702	28.9	162	2.7	35	0.6	5,897
Massachusetts	Boston[c]	4,446	60.2	931	12.6	217	2.9	1,590	21.5	137	1.9	64	0.9	7,385
Michigan	Detroit	2,791	70.6	99	2.5	79	2.0	918	23.2	57	1.4	10	0.3	3,954
Minnesota	Minneapolis–St. Paul[c]	1,572	64.4	109	4.5	177	7.3	521	21.3	48	2.0	14	0.6	2,441
Missouri	Kansas City[c]	1,659	76.8	71	3.3	5	0.2	407	18.8	5	0.2	14	0.6	2,161
	St. Louis[c]	5,178	76.0	230	3.4	32	0.5	1,265	18.6	52	0.8	53	0.8	6,810
Nevada	Las Vegas[c]	2,371	80.8	89	3.0	69	2.4	353	12.0	30	1.0	24	0.8	2,936
New Jersey	Bergen–Passaic	542	48.5	106	9.5	9	0.8	422	37.8	28	2.5	10	0.9	1,117
	Jersey City	826	64.9	74	5.8	6	0.5	332	26.1	21	1.7	13	1.0	1,272
	Middlesex	507	55.0	73	7.9	15	1.6	283	30.7	34	3.7	9	1.0	921
	Newark	1,912	52.1	285	7.8	41	1.1	1,304	35.5	110	3.0	19	0.5	3,671
New York	Nassau–Suffolk	552	54.7	60	5.9	13	1.3	335	33.2	41	4.1	9	0.9	1,010
	New York	14,091	59.8	1,233	5.2	425	1.8	7,381	31.3	287	1.2	136	0.6	23,553
North Carolina	Charlotte[c]	2,070	70.6	66	2.3	34	1.2	722	24.6	16	0.5	23	0.8	2,931
Ohio	Cleveland	2,004	73.7	95	3.5	44	1.6	547	20.1	21	0.8	9	0.3	2,720
	Columbus	3,142	78.6	111	2.8	87	2.2	579	14.5	53	1.3	24	0.6	3,996
Oregon	Portland[c]	1,475	74.5	109	5.5	247	12.5	128	6.5	11	0.6	11	0.6	1,981
Pennsylvania	Philadelphia[c]	5,962	57.5	987	9.5	240	2.3	2,910	28.1	233	2.2	40	0.4	10,372
Puerto Rico	San Juan	2,146	48.5	602	13.6	39	0.9	1,560	35.3	54	1.2	24	0.5	4,425

Table 24b-i. Male clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico *(cont.)*

		Male-to-male sexual contact		Injection drug use		Male-to-male sexual contact and injection drug use		Heterosexual contact[a]		Perinatal		Other[b]		
State/Territory	EMA/TGA	N	%	N	%	N	%	N	%	N	%	N	%	Total N
Tennessee	Memphis[c]	1,812	63.0	32	1.1	28	1.0	990	34.4	12	0.4	2	0.1	2,876
	Nashville	3,398	75.2	155	3.4	110	2.4	790	17.5	36	0.8	27	0.6	4,516
Texas	Austin	1,300	77.5	103	6.1	96	5.7	166	9.9	5	0.3	7	0.4	1,677
	Dallas	6,537	75.8	213	2.5	218	2.5	1,562	18.1	62	0.7	28	0.3	8,620
	Ft. Worth	1,767	71.8	66	2.7	65	2.6	554	22.5	4	0.2	4	0.2	2,460
	Houston	7,228	67.7	246	2.3	113	1.1	2,890	27.1	146	1.4	46	0.4	10,669
	San Antonio	1,048	80.5	72	5.5	40	3.1	128	9.8	5	0.4	9	0.7	1,302
Virginia	Norfolk[c]	1,662	69.9	84	3.5	29	1.2	572	24.1	14	0.6	16	0.7	2,377
Washington	Seattle	1,869	67.1	103	3.7	333	12.0	386	13.9	91	3.3	4	0.1	2,786

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Notes: Percentages shown are based on the row total.
EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[b] Includes hemophilia and blood transfusion.
[c] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 24b-ii. Female clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		Injection drug use		Heterosexual contact[a]		Perinatal		Other[b]		
State/Territory	EMA/TGA	N	%	N	%	N	%	N	%	Total N
Arizona	Phoenix	117	12.2	774	80.5	66	6.9	5	0.5	962
California	Los Angeles	131	5.3	2,183	88.5	113	4.6	40	1.6	2,467
	Oakland	67	10.0	551	82.1	40	6.0	13	1.9	671
	Orange County	24	9.0	231	86.5	7	2.6	5	1.9	267
	Riverside–San Bernardino	18	5.6	296	92.2	3	0.9	4	1.2	321
	Sacramento	62	12.0	426	82.7	18	3.5	9	1.7	515
	San Diego	81	10.6	634	82.7	43	5.6	9	1.2	767
	San Francisco	165	32.1	325	63.2	13	2.5	11	2.1	514
	San Jose	13	7.1	163	89.1	3	1.6	4	2.2	183
Colorado	Denver	202	18.6	781	71.8	98	9.0	7	0.6	1,088
Connecticut	Hartford	119	17.8	505	75.7	29	4.3	14	2.1	667
	New Haven	96	10.9	758	85.7	23	2.6	7	0.8	884
District of Columbia	Washington[c]	305	9.1	2,833	84.9	142	4.3	55	1.6	3,335
Florida	Ft. Lauderdale	32	1.6	1,839	91.1	134	6.6	13	0.6	2,018
	Jacksonville	58	4.9	1,086	92.4	25	2.1	6	0.5	1,175
	Miami	83	3.5	2,160	90.1	144	6.0	11	0.5	2,398
	Orlando	40	3.3	1,134	93.2	33	2.7	10	0.8	1,217
	Tampa–St. Petersburg	86	4.5	1,674	88.0	120	6.3	22	1.2	1,902
	West Palm Beach	27	2.2	1,143	94.1	35	2.9	10	0.8	1,215
Georgia	Atlanta	90	2.5	3,250	91.5	182	5.1	29	0.8	3,551
Illinois	Chicago	197	5.4	3,142	86.9	228	6.3	50	1.4	3,617
Indiana	Indianapolis	44	4.5	874	89.1	40	4.1	23	2.3	981
Louisiana	Baton Rouge	87	6.8	1,176	91.7	15	1.2	5	0.4	1,283
	New Orleans	77	4.6	1,555	93.7	20	1.2	8	0.5	1,660
Maryland	Baltimore	461	13.6	2,686	79.2	198	5.8	45	1.3	3,390
Massachusetts	Boston[c]	530	15.4	2,696	78.5	152	4.4	57	1.7	3,435
Michigan	Detroit	68	5.3	1,159	89.6	58	4.5	9	0.7	1,294
Minnesota	Minneapolis–St. Paul[c]	83	7.9	883	84.3	67	6.4	14	1.3	1,047
Missouri	Kansas City[c]	30	5.5	503	91.5	9	1.6	8	1.5	550
	St. Louis[c]	77	4.0	1,781	92.1	55	2.8	21	1.1	1,934
Nevada	Las Vegas[c]	31	5.2	526	88.1	32	5.4	8	1.3	597
New Jersey	Bergen–Passaic	44	7.3	525	87.4	22	3.7	10	1.7	601
	Jersey City	39	8.4	400	86.2	17	3.7	8	1.7	464
	Middlesex	52	9.3	460	81.9	44	7.8	6	1.1	562
	Newark	156	7.6	1,753	85.6	110	5.4	29	1.4	2,048
New York	Nassau–Suffolk	92	6.7	1,160	84.4	91	6.6	31	2.3	1,374
	New York	748	7.1	9,253	88.1	375	3.6	131	1.2	10,507
North Carolina	Charlotte[c]	24	2.6	858	93.4	21	2.3	16	1.7	919
Ohio	Cleveland	28	3.7	696	91.9	29	3.8	4	0.5	757
	Columbus	39	3.3	1,044	87.1	101	8.4	15	1.3	1,199
Oregon	Portland[c]	49	17.9	220	80.6	1	0.4	3	1.1	273
Pennsylvania	Philadelphia[c]	583	12.0	4,021	82.6	234	4.8	28	0.6	4,866
Puerto Rico	San Juan	124	5.7	1,949	90.1	62	2.9	28	1.3	2,163
Tennessee	Memphis[c]	34	2.5	1,309	95.1	31	2.3	3	0.2	1,377
	Nashville	89	7.1	1,105	88.1	48	3.8	12	1.0	1,254
Texas	Austin	50	15.8	249	78.8	6	1.9	11	3.5	316
	Dallas	120	5.2	2,091	90.6	71	3.1	26	1.1	2,308
	Ft. Worth	48	6.3	711	92.7	3	0.4	5	0.7	767
	Houston	100	2.8	3,222	90.7	184	5.2	46	1.3	3,552
	San Antonio	37	22.3	113	68.1	15	9.0	1	0.6	166
Virginia	Norfolk[c]	55	5.7	878	91.1	20	2.1	11	1.1	964
Washington	Seattle	75	11.1	554	82.2	41	6.1	4	0.6	674

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Notes: Percentages shown are based on the row total.
EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] Heterosexual contact with an individual with HIV or posing increased risk for HIV transmission (e.g., a person who injects drugs).
[b] Includes hemophilia and blood transfusion.
[c] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 24b-iii. Transgender clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		Sexual contact[a]		Injection drug use		Sexual contact[a] and injection drug use		Perinatal		Other[b]		
State/Territory	EMA/TGA	N	%	N	%	N	%	N	%	N	%	Total N
Arizona	Phoenix	108	91.5	0	0.0	10	8.5	0	0.0	0	0.0	118
California	Los Angeles	644	93.9	9	1.3	29	4.2	0	0.0	4	0.6	686
	Oakland	113	87.6	4	3.1	11	8.5	0	0.0	1	0.8	129
	Orange County	40	97.6	0	0.0	0	0.0	0	0.0	1	2.4	41
	Riverside–San Bernardino	44	95.7	0	0.0	2	4.3	0	0.0	0	0.0	46
	Sacramento	66	86.8	1	1.3	8	10.5	1	1.3	0	0.0	76
	San Diego	155	92.8	1	0.6	9	5.4	1	0.6	1	0.6	167
	San Francisco	187	73.6	15	5.9	52	20.5	0	0.0	0	0.0	254
	San Jose	16	88.9	1	5.6	0	0.0	0	0.0	1	5.6	18
Colorado	Denver	288	82.5	5	1.4	55	15.8	0	0.0	1	0.3	349
Connecticut	Hartford	23	74.2	2	6.5	6	19.4	0	0.0	0	0.0	31
	New Haven	48	96.0	1	2.0	1	2.0	0	0.0	0	0.0	50
District of Columbia	Washington[c]	205	98.6	0	0.0	3	1.4	0	0.0	0	0.0	208
Florida	Ft. Lauderdale	118	93.7	1	0.8	4	3.2	2	1.6	1	0.8	126
	Jacksonville	81	100.0	0	0.0	0	0.0	0	0.0	0	0.0	81
	Miami	127	96.9	0	0.0	4	3.1	0	0.0	0	0.0	131
	Orlando	141	94.6	2	1.3	4	2.7	2	1.3	0	0.0	149
	Tampa–St. Petersburg	154	95.7	0	0.0	6	3.7	1	0.6	0	0.0	161
	West Palm Beach	53	96.4	0	0.0	1	1.8	1	1.8	0	0.0	55
Georgia	Atlanta	481	98.2	1	0.2	1	0.2	6	1.2	1	0.2	490
Illinois	Chicago	752	96.7	6	0.8	14	1.8	4	0.5	2	0.3	778
Indiana	Indianapolis	102	97.1	0	0.0	2	1.9	1	1.0	0	0.0	105
Louisiana	Baton Rouge	83	98.8	0	0.0	1	1.2	0	0.0	0	0.0	84
	New Orleans	321	98.8	2	0.6	2	0.6	0	0.0	0	0.0	325
Maryland	Baltimore	163	94.2	5	2.9	3	1.7	2	1.2	0	0.0	173
Massachusetts	Boston[c]	186	87.7	9	4.2	14	6.6	3	1.4	0	0.0	212
Michigan	Detroit	118	95.9	0	0.0	4	3.3	1	0.8	0	0.0	123
Minnesota	Minneapolis–St. Paul[c]	82	86.3	0	0.0	13	13.7	0	0.0	0	0.0	95
Missouri	Kansas City[c]	90	100.0	0	0.0	0	0.0	0	0.0	0	0.0	90
	St. Louis[c]	243	98.4	2	0.8	1	0.4	1	0.4	0	0.0	247
Nevada	Las Vegas[c]	120	94.5	1	0.8	5	3.9	1	0.8	0	0.0	127
New Jersey	Bergen–Passaic	15	100.0	0	0.0	0	0.0	0	0.0	0	0.0	15
	Jersey City	29	96.7	0	0.0	0	0.0	0	0.0	1	3.3	30
	Middlesex	22	91.7	1	4.2	1	4.2	0	0.0	0	0.0	24
	Newark	8	72.7	1	9.1	1	9.1	1	9.1	0	0.0	11
New York	Nassau–Suffolk	24	85.7	1	3.6	2	7.1	1	3.6	0	0.0	28
	New York	1,640	94.7	28	1.6	39	2.3	12	0.7	13	0.8	1,732
North Carolina	Charlotte[c]	91	97.8	1	1.1	1	1.1	0	0.0	0	0.0	93
Ohio	Cleveland	95	96.9	1	1.0	1	1.0	0	0.0	1	1.0	98
	Columbus	47	90.4	1	1.9	3	5.8	1	1.9	0	0.0	52
Oregon	Portland[c]	45	84.9	1	1.9	7	13.2	0	0.0	0	0.0	53
Pennsylvania	Philadelphia[c]	384	93.4	5	1.2	17	4.1	4	1.0	1	0.2	411
Puerto Rico	San Juan	33	94.3	1	2.9	1	2.9	0	0.0	0	0.0	35

Table 24b-iii. Transgender clients served by the Ryan White HIV/AIDS Program (non-ADAP), by transmission category and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico *(cont.)*

		Sexual contact[a]		Injection drug use		Sexual contact[a] and injection drug use		Perinatal		Other[b]		
State/Territory	**EMA/TGA**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**Total N**
Tennessee	Memphis[c]	128	99.2	0	0.0	1	0.8	0	0.0	0	0.0	129
	Nashville	103	94.5	1	0.9	5	4.6	0	0.0	0	0.0	109
Texas	Austin	42	85.7	2	4.1	5	10.2	0	0.0	0	0.0	49
	Dallas	264	96.4	2	0.7	6	2.2	1	0.4	1	0.4	274
	Ft. Worth	62	95.4	0	0.0	3	4.6	0	0.0	0	0.0	65
	Houston	279	97.9	1	0.4	4	1.4	1	0.4	0	0.0	285
	San Antonio	38	92.7	2	4.9	1	2.4	0	0.0	0	0.0	41
Virginia	Norfolk[c]	93	96.9	1	1.0	2	2.1	0	0.0	0	0.0	96
Washington	Seattle	63	78.8	0	0.0	13	16.3	4	5.0	0	0.0	80

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Notes: Percentages shown are based on the row total.
EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] Includes any sexual transmission category reported by transgender clients.
[b] Includes hemophilia and blood transfusion.
[c] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 25a. Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and state, 2022—United States and 3 territories

	0–100% FPL		101–138% FPL		139–250% FPL		251–400% FPL		>400% FPL	
	N	%	N	%	N	%	N	%	N	%
State										
Alabama	5,928	58.5	1,070	10.6	1,840	18.1	1,011	10.0	292	2.9
Alaska	335	64.5	44	8.5	79	15.2	47	9.1	14	2.7
Arizona	3,997	46.8	1,068	12.5	1,691	19.8	1,350	15.8	435	5.1
Arkansas	1,411	46.2	387	12.7	659	21.6	445	14.6	155	5.1
California	30,449	60.0	5,937	11.7	9,036	17.8	3,933	7.8	1,380	2.7
Colorado	4,808	66.6	633	8.8	857	11.9	624	8.6	299	4.1
Connecticut	2,481	60.5	528	12.9	821	20.0	236	5.8	38	0.9
Delaware	853	42.7	246	12.3	415	20.8	301	15.1	185	9.3
District of Columbia	3,218	71.9	314	7.0	572	12.8	300	6.7	71	1.6
Florida	25,694	51.3	5,806	11.6	11,102	22.2	6,926	13.8	544	1.1
Georgia	14,084	57.3	2,962	12.1	4,942	20.1	2,232	9.1	342	1.4
Hawaii	628	53.8	161	13.8	262	22.4	116	9.9	1	0.1
Idaho	333	33.4	121	12.1	234	23.5	151	15.2	157	15.8
Illinois	13,295	57.3	1,442	6.2	3,010	13.0	1,773	7.6	3,682	15.9
Indiana[a]	—	—	—	—	—	—	—	—	—	—
Iowa	715	38.9	182	9.9	414	22.5	344	18.7	184	10.0
Kansas	626	55.5	90	8.0	183	16.2	165	14.6	63	5.6
Kentucky	2,937	53.3	524	9.5	1,042	18.9	718	13.0	285	5.2
Louisiana	6,160	56.9	1,850	17.1	1,880	17.4	757	7.0	186	1.7
Maine	314	53.4	63	10.7	107	18.2	82	13.9	22	3.7
Maryland	7,421	58.8	1,264	10.0	1,946	15.4	1,373	10.9	612	4.9
Massachusetts	7,490	62.2	1,081	9.0	1,750	14.5	1,053	8.7	676	5.6
Michigan	4,666	52.5	911	10.3	1,780	20.0	1,031	11.6	496	5.6
Minnesota	2,028	53.8	441	11.7	781	20.7	458	12.1	62	1.6
Mississippi	3,491	67.4	467	9.0	853	16.5	317	6.1	55	1.1
Missouri	5,020	60.0	849	10.1	1,699	20.3	747	8.9	58	0.7
Montana	178	40.5	54	12.3	98	22.3	70	15.9	40	9.1
Nebraska	625	44.0	161	11.3	374	26.3	244	17.2	18	1.3
Nevada	2,204	45.8	476	9.9	1,119	23.3	923	19.2	88	1.8
New Hampshire	233	34.1	83	12.2	159	23.3	156	22.8	52	7.6
New Jersey	8,996	61.7	1,576	10.8	2,551	17.5	1,114	7.6	351	2.4
New Mexico	874	41.7	243	11.6	469	22.4	336	16.0	176	8.4
New York	33,119	69.2	3,919	8.2	7,719	16.1	2,069	4.3	1,013	2.1
North Carolina	7,945	55.9	1,712	12.0	3,039	21.4	1,246	8.8	273	1.9
North Dakota	128	36.3	31	8.8	100	28.3	69	19.5	25	7.1
Ohio	6,468	54.4	1,163	9.8	2,279	19.2	1,420	12.0	552	4.6
Oklahoma	1,409	40.6	784	22.6	677	19.5	479	13.8	121	3.5
Oregon	2,505	46.8	530	9.9	1,022	19.1	857	16.0	443	8.3
Pennsylvania	13,414	58.7	2,510	11.0	3,872	16.9	2,076	9.1	995	4.4
Rhode Island	1,270	50.4	240	9.5	410	16.3	235	9.3	363	14.4
South Carolina	7,355	54.9	1,344	10.0	2,434	18.2	1,570	11.7	705	5.3
South Dakota	125	31.0	49	12.2	135	33.5	82	20.3	12	3.0
Tennessee	8,893	60.6	1,076	7.3	2,386	16.3	2,014	13.7	294	2.0
Texas	26,007	60.9	4,931	11.5	7,885	18.5	3,162	7.4	719	1.7
Utah	794	48.1	157	9.5	411	24.9	222	13.4	68	4.1
Vermont	192	32.7	93	15.8	127	21.6	96	16.3	80	13.6
Virginia	4,759	47.5	1,020	10.2	2,088	20.9	1,456	14.5	689	6.9
Washington	3,732	46.3	816	10.1	1,449	18.0	1,380	17.1	677	8.4
West Virginia	775	54.1	228	15.9	298	20.8	116	8.1	15	1.0
Wisconsin	3,645	72.3	346	6.9	535	10.6	343	6.8	174	3.5
Wyoming	38	35.8	14	13.2	22	20.8	21	19.8	11	10.4
Subtotal	**284,065**	**57.7**	**51,997**	**10.6**	**89,613**	**18.2**	**48,246**	**9.8**	**18,248**	**3.7**
Territory										
Guam	20	58.8	2	5.9	9	26.5	3	8.8	0	0.0
Puerto Rico	9,641	85.6	564	5.0	704	6.3	244	2.2	110	1.0
U.S. Virgin Islands	176	68.2	19	7.4	45	17.4	14	5.4	4	1.6
Subtotal	**9,837**	**85.1**	**585**	**5.1**	**758**	**6.6**	**261**	**2.3**	**114**	**1.0**
Total	**293,902**	**58.3**	**52,582**	**10.4**	**90,371**	**17.9**	**48,507**	**9.6**	**18,362**	**3.6**

Abbreviation: FPL, federal poverty level.
Notes: Percentages shown are based on the row total.
Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable.

Table 25b. Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		0–100% FPL		101–138% FPL		139–250% FPL		251–400% FPL		>400% FPL	
State/Territory	EMA/TGA	N	%	N	%	N	%	N	%	N	%
Arizona	Phoenix	2,741	49.3	661	11.9	1,075	19.3	893	16.1	186	3.3
California	Los Angeles	13,222	62.5	2,094	9.9	3,466	16.4	1,767	8.4	605	2.9
	Oakland	2,312	70.6	316	9.7	443	13.5	134	4.1	68	2.1
	Orange County	926	42.8	251	11.6	533	24.6	358	16.5	97	4.5
	Riverside–San Bernardino	1,647	53.0	536	17.2	703	22.6	196	6.3	26	0.8
	Sacramento	1,546	55.9	347	12.5	508	18.4	252	9.1	114	4.1
	San Diego	4,480	73.0	565	9.2	788	12.8	232	3.8	71	1.2
	San Francisco	2,746	51.5	958	18.0	1,189	22.3	341	6.4	95	1.8
	San Jose	935	56.4	165	9.9	308	18.6	205	12.4	46	2.8
Colorado	Denver	4,771	71.1	499	7.4	748	11.1	523	7.8	173	2.6
Connecticut	Hartford	1,136	63.6	216	12.1	341	19.1	84	4.7	8	0.4
	New Haven	1,323	59.7	280	12.6	447	20.2	139	6.3	28	1.3
District of Columbia	Washington[a]	5,572	58.5	823	8.6	1,669	17.5	1,075	11.3	392	4.1
Florida	Ft. Lauderdale	5,937	57.3	1,163	11.2	2,026	19.5	1,135	10.9	105	1.0
	Jacksonville	2,144	58.5	385	10.5	672	18.4	435	11.9	26	0.7
	Miami	4,686	45.4	1,273	12.3	2,522	24.4	1,793	17.4	41	0.4
	Orlando	3,258	61.1	492	9.2	952	17.9	568	10.7	59	1.1
	Tampa–St. Petersburg	4,007	50.2	947	11.9	1,844	23.1	1,122	14.1	58	0.7
	West Palm Beach	2,055	58.1	383	10.8	724	20.5	348	9.8	25	0.7
Georgia	Atlanta	9,399	56.6	2,058	12.4	3,555	21.4	1,464	8.8	133	0.8
Illinois	Chicago	12,609	58.2	1,265	5.8	2,641	12.2	1,569	7.2	3,580	16.5
Indiana	Indianapolis	2,534	60.5	408	9.7	886	21.1	340	8.1	22	0.5
Louisiana	Baton Rouge	1,824	50.7	493	13.7	839	23.3	363	10.1	82	2.3
	New Orleans	3,243	55.8	826	14.2	1,139	19.6	483	8.3	126	2.2
Maryland	Baltimore	6,491	60.3	1,099	10.2	1,592	14.8	1,115	10.4	474	4.4
Massachusetts	Boston[a]	6,533	59.8	1,027	9.4	1,670	15.3	1,042	9.5	654	6.0
Michigan	Detroit	3,188	58.9	537	9.9	1,001	18.5	550	10.2	140	2.6
Minnesota	Minneapolis–St. Paul[a]	2,125	55.2	445	11.6	772	20.1	443	11.5	62	1.6
Missouri	Kansas City[a]	1,570	55.3	294	10.4	613	21.6	340	12.0	21	0.7
	St. Louis[a]	5,499	59.7	953	10.4	1,858	20.2	829	9.0	68	0.7
Nevada	Las Vegas[a]	1,919	51.3	363	9.7	787	21.1	614	16.4	55	1.5
New Jersey	Bergen–Passaic	1,055	58.9	218	12.2	352	19.6	128	7.1	39	2.2
	Jersey City	1,013	57.1	216	12.2	342	19.3	159	9.0	44	2.5
	Middlesex	922	58.6	160	10.2	284	18.0	160	10.2	48	3.0
	Newark	4,579	68.1	649	9.6	995	14.8	390	5.8	114	1.7
New York	Nassau–Suffolk	1,397	53.3	285	10.9	510	19.5	277	10.6	151	5.8
	New York	28,976	71.3	3,143	7.7	6,482	16.0	1,274	3.1	752	1.9
North Carolina	Charlotte[a]	2,124	53.8	377	9.5	965	24.4	413	10.5	72	1.8
Ohio	Cleveland	2,237	63.2	297	8.4	621	17.6	304	8.6	78	2.2
	Columbus	2,634	47.5	640	11.5	1,200	21.6	816	14.7	259	4.7
Oregon	Portland[a]	1,682	57.9	232	8.0	433	14.9	360	12.4	198	6.8
Pennsylvania	Philadelphia[a]	9,991	63.7	1,626	10.4	2,477	15.8	1,142	7.3	456	2.9
Puerto Rico	San Juan	5,768	87.9	300	4.6	364	5.5	103	1.6	29	0.4

Table 25b. Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and eligible metropolitan area and transitional grant area, 2021—United States and Puerto Rico *(cont.)*

		0–100% FPL		101–138% FPL		139–250% FPL		251–400% FPL		>400% FPL	
State/Territory	**EMA/TGA**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Tennessee	Memphis[a]	2,882	65.5	337	7.7	661	15.0	511	11.6	7	0.2
	Nashville	5,923	62.2	597	6.3	1,449	15.2	1,296	13.6	259	2.7
Texas	Austin	1,734	61.6	273	9.7	487	17.3	263	9.3	57	2.0
	Dallas	7,733	63.6	1,617	13.3	2,057	16.9	614	5.0	140	1.2
	Ft. Worth	2,105	58.9	330	9.2	664	18.6	389	10.9	85	2.4
	Houston	10,688	61.9	1,877	10.9	3,157	18.3	1,289	7.5	245	1.4
	San Antonio	1,577	61.8	258	10.1	494	19.4	180	7.1	41	1.6
Virginia	Norfolk[a]	1,860	54.1	361	10.5	691	20.1	438	12.7	90	2.6
Washington	Seattle	2,884	48.3	533	8.9	952	15.9	1,020	17.1	583	9.8

Abbreviations: EMA, eligible metropolitan area; FPL, federal poverty level; TGA, transitional grant area.
Notes: Percentages shown are based on the row total.
EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 26a. Ryan White HIV/AIDS Program clients (non-ADAP), by housing status and state, 2022—United States and 3 territories

	Stable		Temporary		Unstable		
	N	%	N	%	N	%	Total N
State							
Alabama	9,294	90.8	640	6.3	301	2.9	10,235
Alaska	493	87.7	16	2.8	53	9.4	562
Arizona	7,736	89.8	230	2.7	645	7.5	8,611
Arkansas	2,919	95.5	104	3.4	34	1.1	3,057
California	42,570	83.1	3,872	7.6	4,797	9.4	51,239
Colorado	4,839	72.8	1,419	21.3	390	5.9	6,648
Connecticut	3,750	90.3	224	5.4	178	4.3	4,152
Delaware	1,931	94.8	50	2.5	55	2.7	2,036
District of Columbia	3,927	86.7	142	3.1	463	10.2	4,532
Florida	45,500	88.7	3,844	7.5	1,963	3.8	51,307
Georgia	23,030	93.4	701	2.8	928	3.8	24,659
Hawaii	1,080	92.3	30	2.6	60	5.1	1,170
Idaho	895	88.0	62	6.1	60	5.9	1,017
Illinois	21,478	89.4	1,639	6.8	906	3.8	24,023
Indiana[a]	—	—	—	—	—	—	—
Iowa	1,773	93.0	69	3.6	64	3.4	1,906
Kansas	968	89.8	32	3.0	78	7.2	1,078
Kentucky	4,960	89.2	342	6.2	258	4.6	5,560
Louisiana	9,114	89.7	668	6.6	381	3.7	10,163
Maine	702	89.7	42	5.4	39	5.0	783
Maryland	12,208	95.7	305	2.4	243	1.9	12,756
Massachusetts	9,834	86.3	959	8.4	599	5.3	11,392
Michigan	8,538	95.0	189	2.1	260	2.9	8,987
Minnesota	3,305	87.3	268	7.1	213	5.6	3,786
Mississippi	5,207	96.8	62	1.2	109	2.0	5,378
Missouri	7,061	85.9	653	7.9	509	6.2	8,223
Montana	408	90.5	8	1.8	35	7.8	451
Nebraska	1,269	89.1	77	5.4	78	5.5	1,424
Nevada	4,114	85.9	320	6.7	353	7.4	4,787
New Hampshire	930	90.6	60	5.8	37	3.6	1,027
New Jersey	12,312	83.7	1,941	13.2	458	3.1	14,711
New Mexico	1,933	91.6	101	4.8	77	3.6	2,111
New York	40,259	86.6	4,038	8.7	2,202	4.7	46,499
North Carolina	13,666	94.9	365	2.5	367	2.5	14,398
North Dakota	316	89.5	22	6.2	15	4.2	353
Ohio	10,938	90.1	721	5.9	480	4.0	12,139
Oklahoma	3,372	91.7	160	4.3	147	4.0	3,679
Oregon	3,627	87.1	261	6.3	276	6.6	4,164
Pennsylvania	20,968	91.2	1,190	5.2	838	3.6	22,996
Rhode Island	2,183	88.1	199	8.0	97	3.9	2,479
South Carolina	12,807	95.4	519	3.9	98	0.7	13,424
South Dakota	373	92.6	17	4.2	13	3.2	403
Tennessee	12,765	86.9	1,197	8.2	724	4.9	14,686
Texas	34,400	79.3	5,105	11.8	3,898	9.0	43,403
Utah	1,567	90.9	107	6.2	50	2.9	1,724
Vermont	565	94.3	17	2.8	17	2.8	599
Virginia	9,668	94.9	261	2.6	255	2.5	10,184
Washington	6,847	86.4	465	5.9	609	7.7	7,921
West Virginia	1,385	89.0	73	4.7	98	6.3	1,556
Wisconsin	4,445	86.3	233	4.5	475	9.2	5,153
Wyoming	122	89.1	11	8.0	4	2.9	137
Subtotal	**434,351**	**88.0**	**34,030**	**6.9**	**25,287**	**5.1**	**493,668**
Territory							
Guam	30	88.2	0	0.0	4	11.8	34
Puerto Rico	11,050	97.6	226	2.0	42	0.4	11,318
U.S. Virgin Islands	253	98.1	1	0.4	4	1.6	258
Subtotal	**11,333**	**97.6**	**227**	**2.0**	**50**	**0.4**	**11,610**
Total	**445,684**	**88.2**	**34,257**	**6.8**	**25,337**	**5.0**	**505,278**

Notes: Percentages shown are based on the row total.
Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable.

Table 26b. Ryan White HIV/AIDS Program clients (non-ADAP), by housing status and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		Stable		Temporary		Unstable		
State/Territory	EMA/TGA	N	%	N	%	N	%	Total N
Arizona	Phoenix	4,966	88.4	166	3.0	483	8.6	5,615
California	Los Angeles	18,347	86.5	592	2.8	2,277	10.7	21,216
	Oakland	2,896	79.1	274	7.5	491	13.4	3,661
	Orange County	1,854	85.8	204	9.4	104	4.8	2,162
	Riverside–San Bernardino	2,762	88.6	123	3.9	233	7.5	3,118
	Sacramento	2,056	76.6	244	9.1	383	14.3	2,683
	San Diego	4,692	75.5	862	13.9	660	10.6	6,214
	San Francisco	3,939	74.1	959	18.1	415	7.8	5,313
	San Jose	1,301	76.9	255	15.1	135	8.0	1,691
Colorado	Denver	4,248	69.2	1,475	24.0	418	6.8	6,141
Connecticut	Hartford	1,596	87.9	110	6.1	110	6.1	1,816
	New Haven	2,017	90.2	137	6.1	82	3.7	2,236
District of Columbia	Washington[a]	8,690	90.5	277	2.9	639	6.7	9,606
Florida	Ft. Lauderdale	8,226	78.7	1,987	19.0	246	2.4	10,459
	Jacksonville	3,269	89.3	214	5.8	177	4.8	3,660
	Miami	10,264	94.1	263	2.4	381	3.5	10,908
	Orlando	4,493	84.3	417	7.8	420	7.9	5,330
	Tampa–St. Petersburg	7,126	85.4	743	8.9	473	5.7	8,342
	West Palm Beach	3,121	85.1	329	9.0	218	5.9	3,668
Georgia	Atlanta	15,115	91.1	599	3.6	875	5.3	16,589
Illinois	Chicago	19,923	88.6	1,632	7.3	928	4.1	22,483
Indiana	Indianapolis	3,626	86.6	259	6.2	302	7.2	4,187
Louisiana	Baton Rouge	3,413	95.2	106	3.0	67	1.9	3,586
	New Orleans	5,103	88.5	395	6.9	268	4.6	5,766
Maryland	Baltimore	10,423	95.7	264	2.4	209	1.9	10,896
Massachusetts	Boston[a]	8,634	84.2	1,016	9.9	603	5.9	10,253
Michigan	Detroit	5,168	95.1	116	2.1	148	2.7	5,432
Minnesota	Minneapolis–St. Paul[a]	3,324	86.0	302	7.8	237	6.1	3,863
Missouri	Kansas City[a]	2,321	85.3	210	7.7	191	7.0	2,722
	St. Louis[a]	7,895	86.3	663	7.2	594	6.5	9,152
Nevada	Las Vegas[a]	3,107	83.2	298	8.0	328	8.8	3,733
New Jersey	Bergen–Passaic	1,690	94.3	46	2.6	56	3.1	1,792
	Jersey City	1,678	94.5	49	2.8	49	2.8	1,776
	Middlesex	1,364	85.0	109	6.8	132	8.2	1,605
	Newark	4,704	69.9	1,785	26.5	241	3.6	6,730
New York	Nassau–Suffolk	2,401	91.7	184	7.0	34	1.3	2,619
	New York	33,976	85.9	3,416	8.6	2,168	5.5	39,560
North Carolina	Charlotte[a]	3,780	95.5	97	2.5	80	2.0	3,957
Ohio	Cleveland	3,149	89.1	259	7.3	128	3.6	3,536
	Columbus	5,364	92.4	309	5.3	133	2.3	5,806
Oregon	Portland[a]	2,575	86.5	200	6.7	201	6.8	2,976
Pennsylvania	Philadelphia[a]	14,425	90.7	774	4.9	707	4.4	15,906
Puerto Rico	San Juan	6,392	96.6	193	2.9	34	0.5	6,619
Tennessee	Memphis[a]	4,180	94.6	97	2.2	142	3.2	4,419
	Nashville	7,750	81.4	1,180	12.4	596	6.3	9,526
Texas	Austin	2,204	76.8	486	16.9	178	6.2	2,868
	Dallas	6,652	53.7	2,743	22.2	2,988	24.1	12,383
	Ft. Worth	3,174	88.1	287	8.0	140	3.9	3,601
	Houston	15,401	88.6	1,387	8.0	604	3.5	17,392
	San Antonio	2,338	86.8	196	7.3	160	5.9	2,694
Virginia	Norfolk[a]	3,262	94.8	91	2.6	89	2.6	3,442
Washington	Seattle	4,969	85.5	324	5.6	516	8.9	5,809

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Notes: Percentages shown are based on the row total.
EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Section 4.

State- and EMA/TGA-Level Data: Retention in Care and Viral Suppression

Table 27a. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by year and state, 2018–2022—United States and 3 territories

	2018			2019			2020			2021			2022		
		Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State															
Alabama	7,572	6,319	83.5	5,498	4,584	83.4	5,250	3,991	76.0	5,636	4,669	82.8	8,570	6,270	73.2
Alaska	290	210	72.4	437	328	75.1	146	114	78.1	326	248	76.1	319	221	69.3
Arizona	4,107	3,424	83.4	4,940	3,844	77.8	5,109	4,331	84.8	5,318	4,482	84.3	5,745	4,936	85.9
Arkansas	2,050	1,673	81.6	1,251	832	66.5	1,140	801	70.3	1,254	944	75.3	1,324	1,022	77.2
California	32,560	26,578	81.6	30,085	24,041	79.9	33,538	27,060	80.7	34,126	26,979	79.1	29,600	22,259	75.2
Colorado	4,275	3,462	81.0	4,511	3,511	77.8	4,373	2,964	67.8	4,451	3,258	73.2	4,721	3,477	73.6
Connecticut	3,474	2,941	84.7	3,272	2,721	83.2	3,216	2,611	81.2	3,226	2,637	81.7	3,149	2,619	83.2
Delaware	1,548	1,283	82.9	1,594	1,284	80.6	1,521	1,221	80.3	1,535	1,214	79.1	1,549	1,164	75.1
District of Columbia	3,787	3,132	82.7	3,135	2,391	76.3	3,080	2,593	84.2	2,832	2,310	81.6	2,745	1,891	68.9
Florida	30,281	24,929	82.3	30,457	24,909	81.8	28,088	22,259	79.2	26,958	21,370	79.3	28,625	22,672	79.2
Georgia	19,277	16,223	84.2	21,183	18,004	85.0	19,901	16,747	84.2	22,569	18,074	80.1	22,217	18,354	82.6
Hawaii	270	205	75.9	407	269	66.1	341	257	75.4	577	300	52.0	124	1	0.8
Idaho	786	640	81.4	796	594	74.6	779	600	77.0	813	613	75.4	839	589	70.2
Illinois	16,632	13,063	78.5	16,483	12,959	78.6	15,883	11,811	74.4	16,934	12,092	71.4	16,911	12,202	72.2
Indiana[a]	1,788	1,430	80.0	2,031	1,679	82.7	2,585	2,115	81.8	2,625	2,192	83.5	—	—	—
Iowa	1,399	1,153	82.4	1,480	1,172	79.2	1,511	1,199	79.4	1,479	1,229	83.1	1,546	1,265	81.8
Kansas	427	366	85.7	549	467	85.1	569	416	73.1	392	309	78.8	522	423	81.0
Kentucky	4,208	3,289	78.2	4,316	3,462	80.2	4,101	3,041	74.2	4,095	3,028	73.9	3,872	2,873	74.2
Louisiana	7,617	6,059	79.5	8,276	6,109	73.8	7,275	5,387	74.0	6,949	5,010	72.1	6,845	5,206	76.1
Maine	435	368	84.6	379	277	73.1	461	375	81.3	492	417	84.8	507	405	79.9
Maryland	10,540	8,824	83.7	10,574	8,852	83.7	10,077	8,209	81.5	9,690	7,420	76.6	10,064	8,017	79.7
Massachusetts	6,348	5,270	83.0	6,739	5,570	82.7	6,770	5,457	80.6	6,970	5,420	77.8	6,863	5,069	73.9
Michigan	6,225	4,661	74.9	6,419	4,587	71.5	5,907	4,025	68.1	6,630	4,492	67.8	6,803	4,738	69.6
Minnesota	1,989	1,536	77.2	2,343	1,590	67.9	3,362	1,733	51.5	3,946	2,158	54.7	1,033	420	40.7
Mississippi	3,957	3,345	84.5	4,170	3,559	85.3	3,895	3,246	83.3	4,772	3,914	82.0	4,750	3,755	79.1
Missouri	4,130	3,399	82.3	4,293	3,372	78.5	4,172	3,304	79.2	3,974	3,196	80.4	3,911	2,648	67.7
Montana	332	260	78.3	356	273	76.7	397	308	77.6	397	285	71.8	363	274	75.5
Nebraska	745	549	73.7	663	485	73.2	682	513	75.2	725	531	73.2	731	540	73.9
Nevada	2,471	2,025	82.0	2,653	2,074	78.2	2,823	1,916	67.9	2,623	1,954	74.5	2,547	1,766	69.3
New Hampshire	696	555	79.7	743	561	75.5	695	452	65.0	804	756	94.0	748	718	96.0
New Jersey	7,941	6,568	82.7	11,439	9,779	85.5	10,965	9,280	84.6	10,934	9,074	83.0	11,320	9,370	82.8
New Mexico	1,804	1,597	88.5	1,376	1,189	86.4	1,950	1,743	89.4	1,916	1,583	82.6	1,288	1,052	81.7
New York	29,335	25,231	86.0	30,325	25,891	85.4	30,679	26,006	84.8	29,522	25,105	85.0	31,825	26,309	82.7
North Carolina	12,449	9,927	79.7	12,193	9,740	79.9	11,755	9,297	79.1	11,954	9,337	78.1	11,996	9,393	78.3
North Dakota	111	83	74.8	106	81	76.4	76	66	86.8	75	53	70.7	96	79	82.3
Ohio	7,224	5,512	76.3	8,534	6,386	74.8	8,573	6,163	71.9	8,510	6,172	72.5	7,899	5,305	67.2
Oklahoma	2,227	1,258	56.5	1,677	1,249	74.5	2,902	2,245	77.4	1,923	1,230	64.0	2,308	1,637	70.9
Oregon	1,162	928	79.9	1,212	953	78.6	1,225	921	75.2	1,217	854	70.2	1,225	887	72.4
Pennsylvania	18,665	15,677	84.0	19,134	15,919	83.2	17,970	14,535	80.9	17,816	14,443	81.1	18,677	14,957	80.1
Rhode Island	1,668	1,370	82.1	1,718	1,405	81.8	1,697	1,389	81.9	1,784	1,484	83.2	1,768	1,395	78.9
South Carolina	9,355	7,833	83.7	10,667	9,122	85.5	10,518	8,859	84.2	11,067	9,272	83.8	11,216	9,113	81.3
South Dakota	269	216	80.3	316	219	69.3	204	135	66.2	232	158	68.1	204	143	70.1
Tennessee	8,459	6,877	81.3	9,267	7,496	80.9	8,573	6,690	78.0	8,128	6,442	79.3	8,539	6,775	79.3
Texas	29,019	21,207	73.1	30,298	23,200	76.6	30,801	24,011	78.0	29,885	21,779	72.9	28,907	21,330	73.8

Table 27a. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by year and state, 2017–2021—United States and 3 territories *(cont.)*

	2018			2019			2020			2021			2022		
		Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State															
Utah	1,181	1,005	85.1	1,182	984	83.2	1,069	796	74.5	942	698	74.1	1,185	709	59.8
Vermont	433	335	77.4	425	311	73.2	440	320	72.7	441	345	78.2	447	341	76.3
Virginia	5,599	3,607	64.4	5,934	4,480	75.5	5,781	4,343	75.1	6,298	4,606	73.1	6,233	4,497	72.1
Washington	3,442	2,827	82.1	4,002	2,993	74.8	4,085	2,637	64.6	3,470	2,501	72.1	3,536	2,570	72.7
West Virginia	564	415	73.6	1,234	906	73.4	1,183	830	70.2	1,250	810	64.8	1,211	781	64.5
Wisconsin	3,260	2,609	80.0	3,456	2,839	82.1	1,737	1,395	80.3	3,432	2,651	77.2	3,686	2,683	72.8
Wyoming	60	8	13.3	54	14	25.9	39	9	23.1	28	3	10.7	46	15	32.6
Subtotal	**324,443**	**262,261**	**80.8**	**334,582**	**269,516**	**80.6**	**329,869**	**260,726**	**79.0**	**333,942**	**260,101**	**77.9**	**331,155**	**255,135**	**77.0**
Territory															
Guam	34	30	88.2	—	—	—	—	—	—	30	28	93.3	27	23	85.2
Puerto Rico	9,476	8,786	92.7	9,999	9,262	92.6	9,227	8,375	90.8	10,128	9,249	91.3	10,156	9,260	91.2
U.S. Virgin Islands	197	163	82.7	187	132	70.6	181	131	72.4	192	128	66.7	219	157	71.7
Subtotal	**9,707**	**8,979**	**92.5**	**10,186**	**9,394**	**92.2**	**9,408**	**8,506**	**90.4**	**10,350**	**9,405**	**90.9**	**10,402**	**9,440**	**90.8**
Total	**334,150**	**271,240**	**81.2**	**344,768**	**278,910**	**80.9**	**339,277**	**269,232**	**79.4**	**344,292**	**269,506**	**78.3**	**341,557**	**264,575**	**77.5**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Notes: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable. 2019 and 2020 data for Guam are unavailable.

Table 27b. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by year and eligible metropolitan area and transitional grant area, 2018–2022—United States and Puerto Rico

		2018			2019			2020			2021			2022		
			Retained			Retained			Retained			Retained			Retained	
State/Territory	EMA/TGA	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Arizona	Phoenix	2,276	1,933	84.9	3,220	2,592	80.5	3,831	3,284	85.7	3,781	3,184	84.2	4,164	3,513	84.4
California	Los Angeles	16,489	13,916	84.4	16,331	13,381	81.9	16,741	13,850	82.7	17,103	14,107	82.5	12,403	9,682	78.1
	Oakland	838	612	73.0	990	666	67.3	923	645	69.9	1,181	794	67.2	1,509	969	64.2
	Orange County	802	702	87.5	815	665	81.6	906	712	78.6	779	573	73.6	727	552	75.9
	Riverside–San Bernardino	1,046	735	70.3	446	310	69.5	1,002	797	79.5	849	661	77.9	1,029	717	69.7
	Sacramento	2,161	1,844	85.3	1,976	1,656	83.8	2,303	1,950	84.7	2,337	1,980	84.7	2,239	1,883	84.1
	San Diego	5,167	4,180	80.9	4,449	3,680	82.7	5,317	4,263	80.2	5,198	3,794	73.0	5,116	3,549	69.4
	San Francisco	1,935	1,335	69.0	1,662	980	59.0	2,010	1,485	73.9	2,065	1,485	71.9	1,958	1,329	67.9
	San Jose	1,206	885	73.4	277	68	24.5	1,221	804	65.8	1,176	903	76.8	1,121	884	78.9
Colorado	Denver	4,092	3,298	80.6	4,209	3,284	78.0	3,955	2,682	67.8	3,814	2,791	73.2	4,305	3,172	73.7
Connecticut	Hartford	1,838	1,590	86.5	1,382	1,193	86.3	1,510	1,227	81.3	1,456	1,119	76.9	1,486	1,230	82.8
	New Haven	837	693	82.8	1,925	1,557	80.9	1,738	1,402	80.7	1,761	1,507	85.6	1,652	1,380	83.5
District of Columbia	Washington[a]	7,381	6,113	82.8	6,880	5,380	78.2	6,702	5,536	82.6	6,345	4,922	77.6	6,274	4,612	73.5
Florida	Ft. Lauderdale	4,265	3,091	72.5	6,397	4,784	74.8	7,813	5,928	75.9	4,276	3,286	76.8	4,633	3,470	74.9
	Jacksonville	2,338	1,884	80.6	2,162	1,731	80.1	2,113	1,606	76.0	1,902	1,450	76.2	2,107	1,639	77.8
	Miami	7,274	6,010	82.6	7,378	6,036	81.8	5,862	4,846	82.7	6,480	5,211	80.4	6,453	5,367	83.2
	Orlando	2,958	2,513	85.0	2,829	2,428	85.8	2,691	2,301	85.5	3,188	2,553	80.1	3,228	2,615	81.0
	Tampa–St. Petersburg	4,354	3,755	86.2	4,350	3,762	86.5	3,459	2,707	78.3	3,775	2,947	78.1	5,096	4,112	80.7
	West Palm Beach	2,195	1,947	88.7	1,445	1,210	83.7	1,338	1,127	84.2	1,147	958	83.5	1,198	970	81.0
Georgia	Atlanta	12,784	10,698	83.7	14,029	11,764	83.9	12,877	10,705	83.1	15,294	11,775	77.0	14,652	11,939	81.5
Illinois	Chicago	16,423	12,916	78.6	16,042	12,655	78.9	15,233	11,371	74.6	16,327	11,632	71.2	16,449	11,919	72.5
Indiana	Indianapolis	1,918	1,529	79.7	2,163	1,782	82.4	2,795	2,278	81.5	2,794	2,323	83.1	2,546	2,030	79.7
Louisiana	Baton Rouge	2,497	2,101	84.1	2,688	2,137	79.5	3,028	2,358	77.9	2,458	1,996	81.2	2,347	1,911	81.4
	New Orleans	4,513	3,553	78.7	5,054	3,605	71.3	3,850	2,839	73.7	3,610	2,453	68.0	3,574	2,728	76.3
Maryland	Baltimore	9,490	7,989	84.2	9,724	8,198	84.3	9,269	7,616	82.2	8,792	6,827	77.7	9,152	7,346	80.3
Massachusetts	Boston[a]	5,175	4,269	82.5	5,671	4,722	83.3	5,685	4,706	82.8	6,001	4,874	81.2	6,076	4,630	76.2
Michigan	Detroit	4,145	2,947	71.1	4,189	2,911	69.5	3,743	2,548	68.1	4,171	2,781	66.7	4,378	3,078	70.3
Minnesota	Minneapolis–St. Paul[a]	2,111	1,629	77.2	2,416	1,634	67.6	3,457	1,788	51.7	4,055	2,222	54.8	1,128	471	41.8
Missouri	Kansas City[a]	1,406	1,100	78.2	1,462	1,113	76.1	1,456	1,083	74.4	1,409	1,046	74.2	1,341	944	70.4
	St. Louis[a]	4,471	3,756	84.0	4,315	3,466	80.3	3,887	3,146	80.9	5,166	4,213	81.6	4,843	3,420	70.6
Nevada	Las Vegas[a]	2,043	1,600	78.3	2,199	1,649	75.0	2,465	1,597	64.8	2,076	1,435	69.1	2,098	1,361	64.9
New Jersey	Bergen–Passaic	1,205	1,017	84.4	1,294	1,144	88.4	1,260	1,110	88.1	1,252	1,118	89.3	1,263	1,101	87.2
	Jersey City	1,509	1,360	90.1	1,415	1,271	89.8	1,303	1,176	90.3	1,358	1,232	90.7	1,487	1,301	87.5
	Middlesex	872	757	86.8	1,082	927	85.7	1,083	966	89.2	1,104	945	85.6	1,127	942	83.6
	Newark	2,094	1,566	74.8	5,105	4,311	84.4	5,034	4,135	82.1	5,338	4,478	83.9	5,271	4,357	82.7
New York	Nassau–Suffolk	1,178	929	78.9	1,157	892	77.1	1,075	811	75.4	1,170	923	78.9	1,182	939	79.4
	New York	26,162	22,636	86.5	26,925	22,962	85.3	27,243	23,148	85.0	26,916	22,972	85.3	27,816	23,073	82.9
North Carolina	Charlotte[a]	2,980	2,454	82.3	3,121	2,382	76.3	3,071	2,353	76.6	3,193	2,369	74.2	2,970	2,297	77.3
Ohio	Cleveland	2,452	2,029	82.7	2,661	2,191	82.3	2,683	2,087	77.8	2,773	2,165	78.1	2,575	1,971	76.5
	Columbus	2,675	1,966	73.5	3,872	2,815	72.7	3,796	2,609	68.7	3,533	2,480	70.2	3,252	1,898	58.4
Oregon	Portland[a]	1,269	1,008	79.4	1,293	1,015	78.5	1,307	985	75.4	1,291	915	70.9	1,326	965	72.8
Pennsylvania	Philadelphia[a]	13,811	11,529	83.5	14,162	11,699	82.6	12,905	10,380	80.4	12,822	10,206	79.6	13,199	10,361	78.5
Puerto Rico	San Juan	5,504	5,077	92.2	5,854	5,368	91.7	5,534	5,011	90.5	6,396	5,775	90.3	5,858	5,317	90.8

Table 27b. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by year and eligible metropolitan area and transitional grant area, 2018–2022—United States and Puerto Rico *(cont.)*

		2018			2019			2020			2021			2022		
			Retained			Retained			Retained			Retained			Retained	
State/Territory	EMA/TGA	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Tennessee	Memphis[a]	3,771	3,202	84.9	3,726	3,149	84.5	3,154	2,691	85.3	2,870	2,446	85.2	3,473	2,953	85.0
	Nashville	4,317	3,444	79.8	5,267	4,298	81.6	4,866	3,745	77.0	4,312	3,357	77.9	4,371	3,437	78.6
Texas	Austin	2,741	2,239	81.7	2,827	2,364	83.6	2,783	2,250	80.8	1,060	619	58.4	1,410	1,010	71.6
	Dallas	8,720	6,569	75.3	9,091	7,226	79.5	9,057	7,427	82.0	9,540	7,541	79.0	9,559	7,706	80.6
	Ft. Worth	1,431	983	68.7	1,570	1,225	78.0	1,916	1,638	85.5	2,135	1,720	80.6	2,007	1,638	81.6
	Houston	10,544	7,713	73.2	11,020	7,987	72.5	11,067	8,178	73.9	11,266	8,058	71.5	11,121	8,014	72.1
	San Antonio	1,683	1,111	66.0	1,549	1,085	70.0	1,752	1,295	73.9	1,674	1,077	64.3	1,858	1,158	62.3
Virginia	Norfolk[a]	2,413	1,079	44.7	2,458	1,637	66.6	2,343	1,511	64.5	2,529	1,657	65.5	2,477	1,469	59.3
Washington	Seattle	3,180	2,620	82.4	3,421	2,628	76.8	3,735	2,312	61.9	2,983	2,177	73.0	3,133	2,244	71.6

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for individual EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 28a. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by year and state, 2018–2022—United States and 3 territories

	2018			2019			2020			2021			2022		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State															
Alabama	7,870	6,779	86.1	5,718	4,912	85.9	5,227	4,595	87.9	5,978	5,289	88.5	8,672	7,762	89.5
Alaska	317	285	89.9	486	444	91.4	148	138	93.2	348	320	92.0	319	282	88.4
Arizona	4,327	3,971	91.8	5,224	4,790	91.7	5,413	5,042	93.1	5,811	5,382	92.6	6,023	5,558	92.3
Arkansas	1,921	1,588	82.7	1,278	1,093	85.5	1,272	1,102	86.6	1,364	1,196	87.7	1,406	1,211	86.1
California	33,411	29,440	88.1	31,212	27,848	89.2	33,743	30,515	90.4	35,166	31,886	90.7	30,882	27,781	90.0
Colorado	4,307	3,920	91.0	4,548	4,146	91.2	3,971	3,655	92.0	4,350	4,065	93.4	4,616	4,294	93.0
Connecticut	3,453	3,131	90.7	3,302	3,056	92.6	3,120	2,891	92.7	3,211	3,003	93.5	3,156	2,961	93.8
Delaware	1,624	1,467	90.3	1,616	1,458	90.2	1,630	1,509	92.6	1,629	1,503	92.3	1,607	1,485	92.4
District of Columbia	3,936	3,321	84.4	3,212	2,790	86.9	3,064	2,683	87.6	2,721	2,421	89.0	2,927	2,584	88.3
Florida	32,212	27,655	85.9	32,052	27,856	86.9	29,550	25,875	87.6	28,275	25,090	88.7	29,973	26,634	88.9
Georgia	20,340	16,974	83.5	22,381	18,946	84.7	20,910	18,245	87.3	23,763	20,556	86.5	23,697	20,328	85.8
Hawaii	268	262	97.8	485	428	88.2	352	307	87.2	588	520	88.4	122	102	83.6
Idaho	833	790	94.8	858	823	95.9	864	834	96.5	866	843	97.3	917	895	97.6
Illinois	17,470	15,252	87.3	17,040	15,017	88.1	15,858	14,051	88.6	17,461	15,691	89.9	17,255	15,613	90.5
Indiana[a]	1,874	1,645	87.8	2,177	1,915	88.0	2,610	2,345	89.8	2,657	2,400	90.3	—	—	—
Iowa	1,487	1,372	92.3	1,548	1,434	92.6	1,606	1,496	93.2	1,581	1,490	94.2	1,607	1,506	93.7
Kansas	462	402	87.0	606	547	90.3	608	554	91.1	414	391	94.4	551	492	89.3
Kentucky	4,306	3,805	88.4	4,462	4,048	90.7	4,050	3,738	92.3	4,236	3,921	92.6	4,152	3,792	91.3
Louisiana	8,073	6,991	86.6	8,679	7,567	87.2	7,849	6,991	89.1	7,188	6,390	88.9	6,540	5,783	88.4
Maine	322	304	94.4	415	401	96.6	461	445	96.5	486	468	96.3	504	482	95.6
Maryland	10,782	9,458	87.7	10,785	9,592	88.9	9,941	9,069	91.2	9,843	8,911	90.5	10,168	9,151	90.0
Massachusetts	6,477	6,028	93.1	6,913	6,486	93.8	6,540	6,187	94.6	6,923	6,573	94.9	6,857	6,498	94.8
Michigan	6,767	5,999	88.7	7,050	6,329	89.8	6,508	5,885	90.4	7,363	6,684	90.8	7,558	6,805	90.0
Minnesota	1,774	1,620	91.3	2,607	2,374	91.1	3,423	3,124	91.3	4,051	3,716	91.7	1,014	953	94.0
Mississippi	4,132	3,508	84.9	4,420	3,795	85.9	4,157	3,634	87.4	5,017	4,453	88.8	5,037	4,443	88.2
Missouri	4,724	4,132	87.5	4,565	4,064	89.0	4,492	4,021	89.5	4,413	3,947	89.4	4,130	3,716	90.0
Montana	341	315	92.4	383	363	94.8	407	377	92.6	396	371	93.7	375	358	95.5
Nebraska	809	712	88.0	724	641	88.5	746	670	89.8	775	713	92.0	788	728	92.4
Nevada	2,717	2,395	88.1	2,944	2,615	88.8	3,039	2,785	91.6	2,852	2,597	91.1	2,778	2,543	91.5
New Hampshire	752	710	94.4	799	754	94.4	741	703	94.9	772	735	95.2	715	688	96.2
New Jersey	8,519	7,354	86.3	11,919	10,403	87.3	11,408	10,178	89.2	11,327	10,223	90.3	12,011	10,798	89.9
New Mexico	1,846	1,712	92.7	1,402	1,318	94.0	1,940	1,824	94.0	2,036	1,873	92.0	1,345	1,225	91.1
New York	30,661	26,653	86.9	31,427	27,608	87.8	31,361	27,886	88.9	30,262	26,863	88.8	32,816	29,667	90.4
North Carolina	13,176	11,612	88.1	12,992	11,534	88.8	12,389	11,076	89.4	12,617	11,293	89.5	12,862	11,539	89.7
North Dakota	111	108	97.3	110	103	93.6	80	79	98.8	80	72	90.0	101	96	95.0
Ohio	7,703	6,789	88.1	9,036	8,082	89.4	8,656	7,792	90.0	8,776	7,981	90.9	8,309	7,560	91.0
Oklahoma	2,313	2,013	87.0	1,982	1,643	82.9	3,028	2,627	86.8	2,008	1,819	90.6	2,839	2,590	91.2
Oregon	1,227	1,096	89.3	1,275	1,140	89.4	1,203	1,090	90.6	1,280	1,149	89.8	1,315	1,170	89.0
Pennsylvania	19,331	17,482	90.4	19,808	17,877	90.3	17,866	16,333	91.4	18,194	16,666	91.6	18,989	17,318	91.2
Rhode Island	1,714	1,604	93.6	1,793	1,689	94.2	1,730	1,636	94.6	1,886	1,809	95.9	1,791	1,714	95.7
South Carolina	9,838	8,630	87.7	11,133	9,946	89.3	11,075	10,000	90.3	11,381	10,370	91.1	11,845	10,662	90.0
South Dakota	279	255	91.4	320	305	95.3	212	203	95.8	253	240	94.9	227	219	96.5
Tennessee	8,905	7,520	84.4	9,842	8,402	85.4	8,984	7,912	88.1	8,538	7,583	88.8	9,061	7,882	87.0
Texas	31,178	25,766	82.6	32,956	27,557	83.6	33,033	28,494	86.3	32,112	27,367	85.2	31,032	26,571	85.6

Table 28a. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by year and state, 2018–2022—United States and 3 territories *(cont.)*

	2018			2019			2020			2021			2022		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State															
Utah	1,264	1,125	89.0	1,230	1,144	93.0	1,159	1,082	93.4	988	921	93.2	1,007	970	96.3
Vermont	432	410	94.9	454	435	95.8	418	398	95.2	458	434	94.8	457	434	95.0
Virginia	6,108	5,343	87.5	6,382	5,692	89.2	6,220	5,545	89.1	6,652	6,038	90.8	6,615	5,930	89.6
Washington	3,541	3,227	91.1	3,983	3,819	95.9	4,164	3,857	92.6	3,629	3,362	92.6	3,807	3,483	91.5
West Virginia	585	530	90.6	1,378	1,234	89.6	1,276	1,154	90.4	1,261	1,132	89.8	1,318	1,178	89.4
Wisconsin	3,446	3,129	90.8	3,561	3,286	92.3	1,828	1,671	91.4	3,623	3,348	92.4	3,909	3,605	92.2
Wyoming	81	76	93.8	57	53	93.0	46	41	89.1	34	30	88.2	55	52	94.5
Subtotal	**340,346**	**296,665**	**87.2**	**351,529**	**309,802**	**88.1**	**340,376**	**304,344**	**89.4**	**347,893**	**312,098**	**89.7**	**346,057**	**310,091**	**89.6**
Territory															
Guam	34	26	76.5	—	—	—	—	—	—	30	21	70.0	29	23	79.3
Puerto Rico	9,415	8,424	89.5	10,127	9,125	90.1	9,303	8,497	91.3	10,295	9,486	92.1	10,318	9,488	92.0
U.S. Virgin Islands	198	170	85.9	187	164	87.7	195	168	86.2	162	144	88.9	253	221	87.4
Subtotal	**9,647**	**8,620**	**89.4**	**10,314**	**9,289**	**90.1**	**9,498**	**8,665**	**91.2**	**10,487**	**9,651**	**92.0**	**10,600**	**9,732**	**91.8**
Total	**349,993**	**305,285**	**87.2**	**361,843**	**319,091**	**88.2**	**349,874**	**313,009**	**89.5**	**358,380**	**321,749**	**89.8**	**356,657**	**319,823**	**89.7**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Note: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable. 2019 and 2020 data for Guam are unavailable.

Table 28b. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by year and eligible metropolitan area and transitional grant area, 2018–2022—United States and Puerto Rico

		2018			2019			2020			2021			2022		
			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
State/Territory	EMA/TGA	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Arizona	Phoenix	2,405	2,174	90.4	3,486	3,134	89.9	4,023	3,718	92.4	4,182	3,852	92.1	4,451	4,058	91.2
California	Los Angeles	16,677	14,465	86.7	16,969	14,957	88.1	16,888	15,131	89.6	17,458	15,719	90.0	12,616	11,258	89.2
	Oakland	974	848	87.1	1,137	1,002	88.1	991	892	90.0	1,556	1,398	89.8	1,677	1,518	90.5
	Orange County	871	771	88.5	867	780	90.0	816	758	92.9	826	732	88.6	795	692	87.0
	Riverside–San Bernardino	1,104	954	86.4	489	435	89.0	1,069	954	89.2	928	825	88.9	1,184	991	83.7
	Sacramento	2,060	1,796	87.2	1,875	1,643	87.6	2,137	1,886	88.3	2,156	1,909	88.5	2,182	1,927	88.3
	San Diego	5,245	4,833	92.1	4,519	4,161	92.1	5,338	4,946	92.7	5,225	4,864	93.1	5,557	5,156	92.8
	San Francisco	2,214	1,903	86.0	1,398	1,238	88.6	2,098	1,888	90.0	2,137	1,930	90.3	2,001	1,768	88.4
	San Jose	1,251	1,151	92.0	687	650	94.6	1,225	1,154	94.2	1,242	1,187	95.6	1,232	1,176	95.5
Colorado	Denver	4,092	3,697	90.3	4,211	3,827	90.9	3,435	3,137	91.3	3,672	3,406	92.8	4,158	3,834	92.2
Connecticut	Hartford	1,727	1,563	90.5	1,335	1,236	92.6	1,341	1,250	93.2	1,378	1,274	92.5	1,402	1,312	93.6
	New Haven	900	818	90.9	2,012	1,862	92.5	1,801	1,658	92.1	1,811	1,707	94.3	1,739	1,630	93.7
District of Columbia	Washington[a]	7,728	6,606	85.5	7,216	6,354	88.1	6,921	6,204	89.6	6,458	5,880	91.0	6,735	6,054	89.9
Florida	Ft. Lauderdale	4,727	3,919	82.9	6,975	6,023	86.4	8,708	7,543	86.6	4,778	4,180	87.5	4,935	4,355	88.2
	Jacksonville	2,526	2,131	84.4	2,271	1,912	84.2	2,235	1,894	84.7	2,049	1,757	85.7	2,241	1,965	87.7
	Miami	7,744	6,510	84.1	7,690	6,556	85.3	5,822	4,964	85.3	6,526	5,699	87.3	6,807	5,990	88.0
	Orlando	3,105	2,705	87.1	2,954	2,615	88.5	2,810	2,515	89.5	3,237	2,931	90.5	3,396	3,081	90.7
	Tampa–St. Petersburg	4,534	3,910	86.2	4,621	4,076	88.2	3,839	3,406	88.7	3,999	3,584	89.6	5,338	4,770	89.4
	West Palm Beach	2,302	2,052	89.1	1,466	1,284	87.6	1,329	1,201	90.4	1,151	1,028	89.3	1,192	1,047	87.8
Georgia	Atlanta	13,490	11,096	82.3	14,892	12,444	83.6	13,452	11,510	85.6	16,026	13,789	86.0	15,722	13,344	84.9
Illinois	Chicago	17,220	15,048	87.4	16,544	14,608	88.3	15,130	13,413	88.7	16,839	15,129	89.8	16,752	15,153	90.5
Indiana	Indianapolis	2,014	1,758	87.3	2,304	2,028	88.0	2,821	2,535	89.9	2,840	2,569	90.5	2,717	2,378	87.5
Louisiana	Baton Rouge	2,596	2,321	89.4	2,824	2,436	86.3	3,204	2,887	90.1	2,554	2,314	90.6	2,401	2,172	90.5
	New Orleans	4,790	4,182	87.3	5,246	4,699	89.6	4,364	3,872	88.7	3,862	3,394	87.9	3,725	3,267	87.7
Maryland	Baltimore	9,740	8,536	87.6	9,868	8,773	88.9	9,096	8,291	91.2	8,890	8,034	90.4	9,167	8,249	90.0
Massachusetts	Boston[a]	5,267	4,903	93.1	5,794	5,424	93.6	5,418	5,140	94.9	5,865	5,563	94.9	5,913	5,593	94.6
Michigan	Detroit	4,587	3,957	86.3	4,615	4,032	87.4	4,112	3,623	88.1	4,663	4,117	88.3	4,849	4,223	87.1
Minnesota	Minneapolis–St. Paul[a]	1,893	1,723	91.0	2,698	2,454	91.0	3,532	3,220	91.2	4,165	3,817	91.6	1,116	1,046	93.7
Missouri	Kansas City[a]	1,607	1,400	87.1	1,557	1,409	90.5	1,552	1,380	88.9	1,542	1,364	88.5	1,411	1,254	88.9
	St. Louis[a]	4,982	4,330	86.9	4,620	4,063	87.9	4,216	3,751	89.0	5,650	5,041	89.2	5,142	4,609	89.6
Nevada	Las Vegas[a]	2,330	2,043	87.7	2,478	2,227	89.9	2,692	2,453	91.1	2,317	2,109	91.0	2,359	2,152	91.2
New Jersey	Bergen–Passaic	1,261	1,100	87.2	1,360	1,197	88.0	1,304	1,188	91.1	1,310	1,189	90.8	1,337	1,213	90.7
	Jersey City	1,566	1,383	88.3	1,440	1,313	91.2	1,354	1,236	91.3	1,396	1,286	92.1	1,546	1,417	91.7
	Middlesex	906	802	88.5	1,128	1,018	90.2	1,112	1,014	91.2	1,132	1,034	91.3	1,157	1,062	91.8
	Newark	2,387	2,013	84.3	5,463	4,672	85.5	5,269	4,660	88.4	5,572	4,980	89.4	5,635	4,993	88.6
New York	Nassau–Suffolk	1,248	1,126	90.2	1,235	1,140	92.3	1,150	1,083	94.2	1,246	1,185	95.1	1,261	1,189	94.3
	New York	27,307	23,532	86.2	27,855	24,251	87.1	27,902	24,620	88.2	27,516	24,256	88.2	28,628	25,732	89.9
North Carolina	Charlotte[a]	3,252	2,859	87.9	3,381	2,950	87.3	3,325	2,981	89.7	3,393	3,020	89.0	3,282	2,894	88.2
Ohio	Cleveland	2,715	2,408	88.7	2,856	2,546	89.1	2,740	2,468	90.1	2,857	2,580	90.3	2,726	2,477	90.9
	Columbus	2,734	2,434	89.0	4,042	3,630	89.8	3,714	3,363	90.5	3,642	3,337	91.6	3,379	3,109	92.0
Oregon	Portland[a]	1,338	1,196	89.4	1,364	1,216	89.1	1,288	1,163	90.3	1,364	1,226	89.9	1,426	1,268	88.9
Pennsylvania	Philadelphia[a]	14,322	12,729	88.9	14,627	13,003	88.9	12,745	11,490	90.2	13,052	11,781	90.3	13,451	12,095	89.9
Puerto Rico	San Juan	5,476	4,838	88.3	5,934	5,269	88.8	5,521	4,984	90.3	6,550	5,966	91.1	5,987	5,461	91.2

Table 28b. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by year and eligible metropolitan area and transitional grant area, 2018–2022—United States and Puerto Rico *(cont.)*

		2018			2019			2020			2021			2022		
			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
State/Territory	EMA/TGA	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
Tennessee	Memphis[a]	3,941	3,034	77.0	3,948	3,098	78.5	3,145	2,547	81.0	3,045	2,496	82.0	3,643	2,891	79.4
	Nashville	4,559	3,994	87.6	5,561	4,907	88.2	5,199	4,712	90.6	4,510	4,125	91.5	4,646	4,222	90.9
Texas	Austin	2,876	2,511	87.3	2,993	2,655	88.7	2,895	2,594	89.6	1,192	1,084	90.9	1,575	1,389	88.2
	Dallas	9,320	7,586	81.4	9,767	8,195	83.9	9,421	8,113	86.1	10,017	8,526	85.1	9,715	8,398	86.4
	Ft. Worth	1,629	1,273	78.1	1,764	1,404	79.6	2,121	1,805	85.1	2,275	1,918	84.3	2,184	1,836	84.1
	Houston	11,344	9,354	82.5	12,032	9,874	82.1	12,198	10,472	85.9	12,251	10,380	84.7	12,277	10,447	85.1
	San Antonio	1,874	1,446	77.2	1,795	1,417	78.9	1,885	1,513	80.3	1,785	1,478	82.8	2,012	1,680	83.5
Virginia	Norfolk[a]	2,633	2,273	86.3	2,663	2,317	87.0	2,555	2,210	86.5	2,630	2,325	88.4	2,627	2,288	87.1
Washington	Seattle	3,260	2,972	91.2	3,344	3,236	96.8	3,795	3,537	93.2	3,115	2,900	93.1	3,371	3,091	91.7

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for individual EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 29a. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by age group and state, 2022—United States and 3 territories

	<13 yrs			13–24 yrs			25–34 yrs			35–44 yrs			45–54 yrs			55–64 yrs			≥65 yrs		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State																					
Alabama	8	7	87.5	320	231	72.2	1,723	1,228	71.3	1,885	1,362	72.3	1,898	1,402	73.9	1,961	1,480	75.5	775	560	72.3
Alaska	0	—	—	12	9	75.0	48	33	68.8	61	44	72.1	76	50	65.8	92	65	70.7	30	20	66.7
Arizona	12	12	100.0	203	169	83.3	1,034	840	81.2	1,221	1,017	83.3	1,298	1,138	87.7	1,353	1,210	89.4	624	550	88.1
Arkansas	0	—	—	60	45	75.0	337	239	70.9	349	258	73.9	276	221	80.1	234	200	85.5	68	59	86.8
California	31	31	100.0	637	436	68.4	4,844	3,251	67.1	6,424	4,585	71.4	6,838	5,263	77.0	7,593	6,015	79.2	3,233	2,678	82.8
Colorado	11	10	90.9	180	146	81.1	884	578	65.4	1,078	761	70.6	999	754	75.5	1,125	872	77.5	444	356	80.2
Connecticut	4	3	75.0	61	48	78.7	303	232	76.6	444	354	79.7	698	578	82.8	1,101	947	86.0	538	457	84.9
Delaware	0	—	—	29	22	75.9	176	109	61.9	256	185	72.3	293	226	77.1	526	409	77.8	269	213	79.2
District of Columbia	18	18	100.0	160	126	78.8	387	235	60.7	487	317	65.1	575	411	71.5	744	509	68.4	374	275	73.5
Florida	47	43	91.5	892	668	74.9	5,274	3,872	73.4	5,992	4,564	76.2	6,254	5,051	80.8	7,369	6,147	83.4	2,797	2,327	83.2
Georgia	49	43	87.8	967	773	79.9	5,139	3,991	77.7	4,985	4,015	80.5	4,334	3,680	84.9	4,774	4,134	86.6	1,969	1,718	87.3
Hawaii	0	—	—	1	0	0.0	10	0	0.0	21	0	0.0	30	1	3.3	48	0	0.0	14	0	0.0
Idaho	0	—	—	27	22	81.5	123	77	62.6	181	121	66.9	180	121	67.2	228	162	71.1	100	86	86.0
Illinois	27	21	77.8	583	423	72.6	3,640	2,358	64.8	3,837	2,616	68.2	3,554	2,627	73.9	3,668	2,846	77.6	1,602	1,311	81.8
Indiana[a]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Iowa	0	—	—	48	38	79.2	219	165	75.3	355	286	80.6	372	308	82.8	380	323	85.0	172	145	84.3
Kansas	1	1	100.0	15	14	93.3	58	38	65.5	89	62	69.7	117	99	84.6	167	143	85.6	75	66	88.0
Kentucky	5	5	100.0	107	67	62.6	714	495	69.3	832	602	72.4	891	658	73.8	940	742	78.9	383	304	79.4
Louisiana	5	5	100.0	236	172	72.9	1,212	823	67.9	1,637	1,191	72.8	1,540	1,194	77.5	1,548	1,271	82.1	667	550	82.5
Maine	2	2	100.0	4	3	75.0	45	36	80.0	90	72	80.0	137	109	79.6	144	111	77.1	85	72	84.7
Maryland	19	18	94.7	250	208	83.2	1,340	950	70.9	1,852	1,395	75.3	1,975	1,586	80.3	3,071	2,548	83.0	1,557	1,312	84.3
Massachusetts	12	11	91.7	134	98	73.1	799	575	72.0	1,166	862	73.9	1,536	1,140	74.2	2,163	1,607	74.3	1,053	776	73.7
Michigan	10	8	80.0	242	178	73.6	1,348	895	66.4	1,322	859	65.0	1,395	960	68.8	1,716	1,261	73.5	770	577	74.9
Minnesota	0	—	—	21	11	52.4	125	51	40.8	227	85	37.4	261	96	36.8	277	121	43.7	122	56	45.9
Mississippi	1	1	100.0	188	133	70.7	938	728	77.6	1,016	777	76.5	1,114	881	79.1	1,065	872	81.9	428	363	84.8
Missouri	15	14	93.3	176	129	73.3	799	508	63.6	832	554	66.6	820	544	66.3	907	645	71.1	362	254	70.2
Montana	0	—	—	3	2	66.7	50	36	72.0	75	53	70.7	70	51	72.9	123	95	77.2	42	37	88.1
Nebraska	1	1	100.0	21	14	66.7	119	84	70.6	167	118	70.7	181	135	74.6	181	146	80.7	61	42	68.9
Nevada	3	2	66.7	88	54	61.4	532	346	65.0	616	396	64.3	522	379	72.6	541	405	74.9	245	184	75.1
New Hampshire	2	2	100.0	15	15	100.0	70	66	94.3	121	115	95.0	172	162	94.2	250	243	97.2	118	115	97.5
New Jersey	24	21	87.5	325	240	73.8	1,708	1,313	76.9	2,060	1,626	78.9	2,231	1,886	84.5	3,278	2,795	85.3	1,694	1,489	87.9
New Mexico	0	—	—	43	39	90.7	197	148	75.1	209	166	79.4	262	208	79.4	376	314	83.5	201	177	88.1
New York	30	22	73.3	658	510	77.5	4,449	3,389	76.2	6,020	4,765	79.2	6,669	5,538	83.0	9,161	7,858	85.8	4,838	4,227	87.4
North Carolina	18	17	94.4	520	386	74.2	2,363	1,734	73.4	2,373	1,794	75.6	2,583	2,042	79.1	2,830	2,322	82.0	1,309	1,098	83.9
North Dakota	0	—	—	2	2	100.0	15	12	80.0	23	19	82.6	26	19	73.1	25	23	92.0	5	4	80.0
Ohio	18	17	94.4	322	218	67.7	1,459	880	60.3	1,605	1,010	62.9	1,684	1,133	67.3	1,962	1,402	71.5	849	645	76.0
Oklahoma	5	2	40.0	89	57	64.0	484	331	68.4	508	370	72.8	522	379	72.6	529	384	72.6	171	114	66.7
Oregon	0	—	—	20	11	55.0	172	113	65.7	315	221	70.2	319	238	74.6	300	229	76.3	99	75	75.8
Pennsylvania	35	30	85.7	453	372	82.1	2,551	1,885	73.9	3,237	2,435	75.2	4,062	3,259	80.2	5,560	4,595	82.6	2,779	2,381	85.7
Rhode Island	2	1	50.0	35	21	60.0	192	155	80.7	292	219	75.0	423	336	79.4	557	453	81.3	267	210	78.7
South Carolina	12	6	50.0	350	270	77.1	2,039	1,552	76.1	2,161	1,737	80.4	2,412	1,997	82.8	2,929	2,454	83.8	1,313	1,097	83.5
South Dakota	1	1	100.0	5	2	40.0	29	16	55.2	48	33	68.8	54	39	72.2	52	42	80.8	15	10	66.7
Tennessee	23	17	73.9	274	214	78.1	1,549	1,172	75.7	1,847	1,417	76.7	2,004	1,587	79.2	2,069	1,722	83.2	773	646	83.6
Texas	22	16	72.7	1,085	754	69.5	6,768	4,673	69.0	7,437	5,419	72.9	6,482	5,004	77.2	5,456	4,206	77.1	1,657	1,258	75.9

Table 29a. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by age group and state, 2022—United States and 3 territories *(cont.)*

	<13 yrs			13–24 yrs			25–34 yrs			35–44 yrs			45–54 yrs			55–64 yrs			≥65 yrs		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State																					
Utah	0	—	—	30	22	73.3	250	133	53.2	311	181	58.2	277	175	63.2	225	144	64.0	92	54	58.7
Vermont	0	—	—	6	3	50.0	25	19	76.0	60	41	68.3	105	80	76.2	161	126	78.3	90	72	80.0
Virginia	2	2	100.0	154	103	66.9	1,114	725	65.1	1,284	894	69.6	1,372	1,015	74.0	1,583	1,185	74.9	724	573	79.1
Washington	0	—	—	56	42	75.0	514	339	66.0	819	551	67.3	892	650	72.9	919	715	77.8	336	273	81.3
West Virginia	2	1	50.0	18	12	66.7	180	102	56.7	243	152	62.6	296	196	66.2	340	236	69.4	132	82	62.1
Wisconsin	5	2	40.0	141	97	68.8	741	508	68.6	720	505	70.1	780	580	74.4	937	707	75.5	362	284	78.5
Wyoming	0	—	—	1	0	0.0	3	1	33.3	8	3	37.5	13	3	23.1	14	6	42.9	7	2	28.6
Subtotal	**482**	**413**	**85.7**	**10,267**	**7,629**	**74.3**	**59,092**	**42,039**	**71.1**	**69,198**	**51,184**	**74.0**	**71,874**	**56,189**	**78.2**	**83,552**	**67,447**	**80.7**	**36,690**	**30,234**	**82.4**
Territory																					
Guam	0	—	—	3	3	100.0	7	5	71.4	7	6	85.7	4	3	75.0	4	4	100.0	2	2	100.0
Puerto Rico	1	1	100.0	126	108	85.7	1,011	888	87.8	1,428	1,277	89.4	2,226	2,004	90.0	3,397	3,153	92.8	1,967	1,829	93.0
U.S. Virgin Islands	0	—	—	4	1	25.0	12	8	66.7	34	24	70.6	53	38	71.7	66	44	66.7	50	42	84.0
Subtotal	**1**	**1**	**100.0**	**133**	**112**	**84.2**	**1,030**	**901**	**87.5**	**1,469**	**1,307**	**89.0**	**2,283**	**2,045**	**89.6**	**3,467**	**3,201**	**92.3**	**2,019**	**1,873**	**92.8**
Total	**483**	**414**	**85.7**	**10,400**	**7,741**	**74.4**	**60,122**	**42,940**	**71.4**	**70,667**	**52,491**	**74.3**	**74,157**	**58,234**	**78.5**	**87,019**	**70,648**	**81.2**	**38,709**	**32,107**	**82.9**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Note: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable.

Table 29b. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by age group and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		<13 yrs			13–24 yrs			25–34 yrs			35–44 yrs			45–54 yrs			55–64 yrs			≥65 yrs		
		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Arizona	Phoenix	13	13	100.0	172	139	80.8	884	710	80.3	1,032	852	82.6	938	811	86.5	835	738	88.4	290	250	86.2
California	Los Angeles	14	14	100.0	259	162	62.5	2,277	1,566	68.8	2,870	2,102	73.2	2,932	2,364	80.6	2,943	2,498	84.9	1,108	976	88.1
	Oakland	10	10	100.0	60	49	81.7	254	161	63.4	282	168	59.6	295	191	64.7	392	256	65.3	216	134	62.0
	Orange County	0	—	—	27	15	55.6	162	114	70.4	222	173	77.9	215	168	78.1	85	70	82.4	16	12	75.0
	Riverside–San Bernardino	0	—	—	36	20	55.6	252	163	64.7	242	160	66.1	245	174	71.0	214	166	77.6	40	34	85.0
	Sacramento	1	1	100.0	51	48	94.1	376	296	78.7	443	356	80.4	478	400	83.7	630	546	86.7	260	236	90.8
	San Diego	7	7	100.0	65	43	66.2	701	431	61.5	1,056	722	68.4	1,178	817	69.4	1,471	1,043	70.9	638	486	76.2
	San Francisco	0	—	—	22	15	68.2	268	165	61.6	441	281	63.7	429	303	70.6	521	358	68.7	277	207	74.7
	San Jose	0	—	—	21	16	76.2	175	121	69.1	259	198	76.4	270	216	80.0	274	226	82.5	122	107	87.7
Colorado	Denver	11	10	90.9	177	143	80.8	854	555	65.0	1,010	704	69.7	905	676	74.7	968	777	80.3	380	307	80.8
Connecticut	Hartford	4	3	75.0	41	34	82.9	143	105	73.4	186	148	79.6	320	260	81.3	541	464	85.8	251	216	86.1
	New Haven	0	—	—	23	17	73.9	171	133	77.8	257	206	80.2	378	319	84.4	545	467	85.7	278	238	85.6
District of Columbia	Washington[a]	21	21	100.0	226	173	76.5	927	622	67.1	1,255	898	71.6	1,464	1,119	76.4	1,582	1,167	73.8	799	612	76.6
Florida	Ft. Lauderdale	5	5	100.0	133	94	70.7	946	668	70.6	1,083	793	73.2	1,033	811	78.5	1,114	870	78.1	319	229	71.8
	Jacksonville	0	—	—	49	34	69.4	440	316	71.8	429	306	71.3	476	389	81.7	531	439	82.7	182	155	85.2
	Miami	16	15	93.8	217	174	80.2	1,275	1,034	81.1	1,472	1,179	80.1	1,318	1,104	83.8	1,599	1,386	86.7	556	475	85.4
	Orlando	7	5	71.4	126	105	83.3	689	518	75.2	736	589	80.0	728	603	82.8	715	601	84.1	227	194	85.5
	Tampa–St. Petersburg	19	18	94.7	219	175	79.9	1,029	731	71.0	1,048	814	77.7	1,081	895	82.8	1,278	1,105	86.5	422	374	88.6
	West Palm Beach	0	—	—	16	10	62.5	177	131	74.0	248	186	75.0	272	226	83.1	314	273	86.9	171	144	84.2
Georgia	Atlanta	49	43	87.8	685	554	80.9	3,904	3,010	77.1	3,502	2,791	79.7	2,736	2,290	83.7	2,769	2,376	85.8	1,007	875	86.9
Illinois	Chicago	27	21	77.8	584	424	72.6	3,614	2,356	65.2	3,757	2,573	68.5	3,428	2,544	74.2	3,506	2,740	78.2	1,533	1,261	82.3
Indiana	Indianapolis	16	10	62.5	105	81	77.1	547	413	75.5	618	482	78.0	590	488	82.7	506	415	82.0	164	141	86.0
Louisiana	Baton Rouge	1	1	100.0	75	53	70.7	346	262	75.7	534	406	76.0	542	454	83.8	565	485	85.8	284	250	88.0
	New Orleans	4	4	100.0	111	84	75.7	650	426	65.5	869	649	74.7	773	605	78.3	811	670	82.6	356	290	81.5
Maryland	Baltimore	16	15	93.8	235	199	84.7	1,238	888	71.7	1,661	1,251	75.3	1,739	1,406	80.9	2,832	2,367	83.6	1,431	1,220	85.3
Massachusetts	Boston[a]	13	12	92.3	131	100	76.3	759	566	74.6	1,075	820	76.3	1,366	1,035	75.8	1,850	1,427	77.1	882	670	76.0
Michigan	Detroit	10	8	80.0	188	143	76.1	966	646	66.9	859	538	62.6	842	591	70.2	1,017	758	74.5	496	394	79.4
Minnesota	Minneapolis–St. Paul[a]	0	—	—	25	13	52.0	150	66	44.0	247	95	38.5	284	107	37.7	297	132	44.4	125	58	46.4
Missouri	Kansas City[a]	0	—	—	48	38	79.2	308	207	67.2	308	202	65.6	281	197	70.1	295	222	75.3	101	78	77.2
	St. Louis[a]	16	15	93.8	204	152	74.5	973	648	66.6	1,016	699	68.8	1,042	730	70.1	1,148	849	74.0	444	327	73.6
Nevada	Las Vegas[a]	3	2	66.7	86	51	59.3	487	314	64.5	546	332	60.8	419	284	67.8	404	281	69.6	153	97	63.4
New Jersey	Bergen–Passaic	2	2	100.0	31	28	90.3	169	140	82.8	236	197	83.5	260	223	85.8	367	331	90.2	198	180	90.9
	Jersey City	2	1	50.0	33	27	81.8	235	179	76.2	296	256	86.5	308	280	90.9	391	352	90.0	222	206	92.8
	Middlesex	5	5	100.0	51	39	76.5	202	153	75.7	220	182	82.7	219	187	85.4	311	270	86.8	119	106	89.1
	Newark	10	8	80.0	155	112	72.3	829	642	77.4	969	751	77.5	1,020	856	83.9	1,490	1,285	86.2	798	703	88.1
New York	Nassau–Suffolk	5	4	80.0	76	66	86.8	128	100	78.1	137	105	76.6	227	170	74.9	357	294	82.4	252	200	79.4
	New York	25	18	72.0	528	411	77.8	4,055	3,084	76.1	5,482	4,355	79.4	5,789	4,850	83.8	7,824	6,738	86.1	4,113	3,617	87.9
North Carolina	Charlotte[a]	0	—	—	139	106	76.3	807	608	75.3	652	503	77.1	617	484	78.4	545	428	78.5	210	168	80.0
Ohio	Cleveland	2	2	100.0	107	80	74.8	434	314	72.4	448	325	72.5	520	407	78.3	715	552	77.2	349	291	83.4
	Columbus	16	15	93.8	153	96	62.7	684	384	56.1	725	400	55.2	667	387	58.0	728	446	61.3	279	170	60.9
Oregon	Portland[a]	0	—	—	23	13	56.5	200	138	69.0	351	248	70.7	337	250	74.2	315	240	76.2	100	76	76.0
Pennsylvania	Philadelphia[a]	27	27	100.0	387	311	80.4	2,036	1,501	73.7	2,407	1,768	73.5	2,725	2,131	78.2	3,784	3,080	81.4	1,833	1,543	84.2
Puerto Rico	San Juan	1	1	100.0	82	71	86.6	549	479	87.2	803	720	89.7	1,258	1,119	89.0	2,024	1,873	92.5	1,141	1,054	92.4

Table 29b. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by age group and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico *(cont.)*

		<13 yrs			13–24 yrs			25–34 yrs			35–44 yrs			45–54 yrs			55–64 yrs			≥65 yrs		
		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Tennessee	Memphis[a]	8	7	87.5	166	146	88.0	741	610	82.3	824	666	80.8	775	664	85.7	708	633	89.4	251	227	90.4
	Nashville	17	12	70.6	117	88	75.2	698	510	73.1	896	683	76.2	1,048	819	78.1	1,182	984	83.2	413	341	82.6
Texas	Austin	0	—	—	52	35	67.3	334	214	64.1	398	291	73.1	329	243	73.9	252	197	78.2	45	30	66.7
	Dallas	17	15	88.2	281	217	77.2	2,056	1,539	74.9	2,401	1,882	78.4	2,165	1,809	83.6	1,937	1,646	85.0	702	598	85.2
	Ft. Worth	0	—	—	119	87	73.1	617	491	79.6	555	456	82.2	410	345	84.1	253	218	86.2	53	41	77.4
	Houston	2	0	0.0	443	310	70.0	2,690	1,842	68.5	2,879	2,039	70.8	2,445	1,878	76.8	2,056	1,526	74.2	606	419	69.1
	San Antonio	2	1	50.0	84	59	70.2	560	347	62.0	554	344	62.1	368	232	63.0	257	157	61.1	33	18	54.5
Virginia	Norfolk[a]	0	—	—	64	36	56.3	512	283	55.3	533	296	55.5	469	274	58.4	638	405	63.5	261	175	67.0
Washington	Seattle	0	—	—	49	36	73.5	446	289	64.8	717	471	65.7	806	583	72.3	823	634	77.0	292	231	79.1

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for individual EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 30a. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by age group and state, 2022—United States and 3 territories

	<13 yrs			13–24 yrs			25–34 yrs			35–44 yrs			45–54 yrs			55–64 yrs			≥65 yrs		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State																					
Alabama	9	8	88.9	343	302	88.0	1,809	1,566	86.6	1,928	1,659	86.0	1,878	1,684	89.7	1,938	1,814	93.6	767	729	95.0
Alaska	0	—	—	12	8	66.7	55	43	78.2	60	56	93.3	75	65	86.7	89	84	94.4	28	26	92.9
Arizona	13	13	100.0	231	202	87.4	1,136	988	87.0	1,293	1,185	91.6	1,341	1,238	92.3	1,381	1,312	95.0	628	620	98.7
Arkansas	0	—	—	68	53	77.9	377	306	81.2	368	322	87.5	284	244	85.9	240	220	91.7	69	66	95.7
California	33	32	97.0	763	601	78.8	5,262	4,508	85.7	6,828	5,969	87.4	7,036	6,410	91.1	7,661	7,086	92.5	3,299	3,175	96.2
Colorado	12	11	91.7	189	170	89.9	867	785	90.5	1,040	945	90.9	976	916	93.9	1,099	1,050	95.5	433	417	96.3
Connecticut	3	3	100.0	69	63	91.3	318	284	89.3	448	410	91.5	693	654	94.4	1,092	1,031	94.4	533	516	96.8
Delaware	1	1	100.0	34	30	88.2	193	164	85.0	268	239	89.2	303	279	92.1	537	510	95.0	271	262	96.7
District of Columbia	19	17	89.5	173	136	78.6	434	361	83.2	516	443	85.9	612	549	89.7	775	708	91.4	398	370	93.0
Florida	47	42	89.4	960	794	82.7	5,714	4,815	84.3	6,321	5,546	87.7	6,535	5,842	89.4	7,569	6,944	91.7	2,827	2,651	93.8
Georgia	48	43	89.6	1,126	894	79.4	5,676	4,565	80.4	5,360	4,448	83.0	4,543	3,996	88.0	4,918	4,480	91.1	2,026	1,902	93.9
Hawaii	0	—	—	1	1	100.0	10	10	100.0	20	15	75.0	29	25	86.2	48	39	81.3	14	12	85.7
Idaho	0	—	—	34	32	94.1	136	134	98.5	206	198	96.1	196	190	96.9	241	238	98.8	104	103	99.0
Illinois	27	25	92.6	613	542	88.4	3,787	3,224	85.1	3,898	3,461	88.8	3,620	3,337	92.2	3,716	3,484	93.8	1,594	1,540	96.6
Indiana[a]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Iowa	0	—	—	53	48	90.6	239	218	91.2	365	333	91.2	388	369	95.1	389	366	94.1	173	172	99.4
Kansas	0	—	—	17	14	82.4	65	56	86.2	94	77	81.9	121	106	87.6	177	166	93.8	77	73	94.8
Kentucky	7	5	71.4	125	109	87.2	824	713	86.5	893	807	90.4	943	865	91.7	959	910	94.9	401	383	95.5
Louisiana	4	3	75.0	239	205	85.8	1,187	999	84.2	1,538	1,325	86.2	1,481	1,307	88.3	1,483	1,380	93.1	608	564	92.8
Maine	2	1	50.0	5	3	60.0	45	40	88.9	82	77	93.9	139	134	96.4	143	142	99.3	88	85	96.6
Maryland	20	17	85.0	279	233	83.5	1,355	1,120	82.7	1,927	1,672	86.8	1,988	1,818	91.4	3,071	2,844	92.6	1,528	1,447	94.7
Massachusetts	12	12	100.0	153	130	85.0	823	752	91.4	1,183	1,104	93.3	1,530	1,450	94.8	2,140	2,059	96.2	1,016	991	97.5
Michigan	10	9	90.0	278	245	88.1	1,518	1,267	83.5	1,481	1,287	86.9	1,559	1,430	91.7	1,873	1,749	93.4	839	818	97.5
Minnesota	0	—	—	20	19	95.0	122	107	87.7	226	203	89.8	256	244	95.3	271	265	97.8	119	115	96.6
Mississippi	1	1	100.0	232	187	80.6	1,031	845	82.0	1,086	951	87.6	1,155	1,031	89.3	1,092	1,002	91.8	440	426	96.8
Missouri	15	13	86.7	201	176	87.6	864	722	83.6	879	790	89.9	873	791	90.6	938	874	93.2	360	350	97.2
Montana	0	—	—	3	3	100.0	52	48	92.3	83	80	96.4	71	65	91.5	123	119	96.7	43	43	100.0
Nebraska	1	1	100.0	21	20	95.2	130	121	93.1	184	160	87.0	192	173	90.1	195	188	96.4	65	65	100.0
Nevada	5	3	60.0	113	97	85.8	612	539	88.1	660	601	91.1	561	519	92.5	578	546	94.5	249	238	95.6
New Hampshire	1	1	100.0	12	10	83.3	66	59	89.4	115	110	95.7	168	158	94.0	237	234	98.7	116	116	100.0
New Jersey	25	20	80.0	362	293	80.9	1,905	1,629	85.5	2,226	1,951	87.6	2,347	2,133	90.9	3,412	3,123	91.5	1,734	1,649	95.1
New Mexico	0	—	—	49	42	85.7	215	188	87.4	220	193	87.7	271	239	88.2	388	367	94.6	202	196	97.0
New York	27	23	85.2	736	628	85.3	4,745	4,082	86.0	6,260	5,566	88.9	6,850	6,208	90.6	9,304	8,512	91.5	4,894	4,648	95.0
North Carolina	19	18	94.7	589	503	85.4	2,608	2,206	84.6	2,557	2,236	87.4	2,750	2,481	90.2	2,982	2,796	93.8	1,357	1,299	95.7
North Dakota	0	—	—	2	2	100.0	17	16	94.1	24	23	95.8	27	26	96.3	25	24	96.0	6	5	83.3
Ohio	18	18	100.0	344	303	88.1	1,584	1,366	86.2	1,686	1,497	88.8	1,768	1,623	91.8	2,040	1,911	93.7	869	842	96.9
Oklahoma	0	—	—	101	89	88.1	589	526	89.3	636	572	89.9	640	584	91.3	662	618	93.4	211	201	95.3
Oregon	0	—	—	24	22	91.7	199	170	85.4	346	298	86.1	337	297	88.1	310	289	93.2	99	94	94.9
Pennsylvania	35	33	94.3	483	420	87.0	2,678	2,300	85.9	3,303	2,918	88.3	4,115	3,747	91.1	5,616	5,258	93.6	2,759	2,642	95.8
Rhode Island	2	2	100.0	38	34	89.5	198	187	94.4	318	301	94.7	419	395	94.3	557	539	96.8	259	256	98.8
South Carolina	13	12	92.3	406	337	83.0	2,232	1,933	86.6	2,293	2,007	87.5	2,525	2,262	89.6	3,042	2,838	93.3	1,334	1,273	95.4
South Dakota	1	1	100.0	5	5	100.0	33	32	97.0	53	48	90.6	61	59	96.7	59	59	100.0	15	15	100.0
Tennessee	23	21	91.3	312	260	83.3	1,691	1,383	81.8	1,974	1,664	84.3	2,105	1,837	87.3	2,164	1,976	91.3	792	741	93.6
Texas	24	22	91.7	1,277	1,034	81.0	7,471	6,069	81.2	8,032	6,711	83.6	6,830	6,002	87.9	5,713	5,145	90.1	1,685	1,588	94.2

Table 30a. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by age group and state, 2022—United States and 3 territories *(cont.)*

	<13 yrs			13–24 yrs			25–34 yrs			35–44 yrs			45–54 yrs			55–64 yrs			≥65 yrs		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State																					
Utah	0	—	—	31	30	96.8	228	220	96.5	265	255	96.2	232	221	95.3	181	175	96.7	70	69	98.6
Vermont	0	—	—	5	5	100.0	28	26	92.9	64	59	92.2	106	101	95.3	161	153	95.0	93	90	96.8
Virginia	2	2	100.0	194	163	84.0	1,207	999	82.8	1,383	1,236	89.4	1,439	1,298	90.2	1,644	1,532	93.2	746	700	93.8
Washington	0	—	—	72	61	84.7	587	532	90.6	895	790	88.3	957	877	91.6	941	881	93.6	355	342	96.3
West Virginia	2	2	100.0	21	14	66.7	191	154	80.6	268	232	86.6	329	295	89.7	365	346	94.8	142	135	95.1
Wisconsin	5	5	100.0	149	121	81.2	781	688	88.1	769	682	88.7	829	771	93.0	989	960	97.1	387	378	97.7
Wyoming	0	—	—	1	1	100.0	4	3	75.0	8	8	100.0	15	13	86.7	17	17	100.0	10	10	100.0
Subtotal	**486**	**440**	**90.5**	**11,568**	**9,694**	**83.8**	**63,898**	**54,068**	**84.6**	**72,930**	**63,720**	**87.4**	**74,498**	**67,358**	**90.4**	**85,545**	**79,363**	**92.8**	**37,132**	**35,448**	**95.5**
Territory																					
Guam	0	—	—	4	4	100.0	7	5	71.4	8	6	75.0	4	2	50.0	4	4	100.0	2	2	100.0
Puerto Rico	0	—	—	139	119	85.6	1,047	915	87.4	1,469	1,292	88.0	2,253	2,055	91.2	3,435	3,215	93.6	1,975	1,892	95.8
U.S. Virgin Islands	1	1	100.0	4	3	75.0	17	12	70.6	42	32	76.2	61	56	91.8	74	68	91.9	54	49	90.7
Subtotal	**1**	**1**	**100.0**	**147**	**126**	**85.7**	**1,071**	**932**	**87.0**	**1,519**	**1,330**	**87.6**	**2,318**	**2,113**	**91.2**	**3,513**	**3,287**	**93.6**	**2,031**	**1,943**	**95.7**
Total	**487**	**441**	**90.6**	**11,715**	**9,820**	**83.8**	**64,969**	**55,000**	**84.7**	**74,449**	**65,050**	**87.4**	**76,816**	**69,471**	**90.4**	**89,058**	**82,650**	**92.8**	**39,163**	**37,391**	**95.5**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Note: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable.

Table 30b. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by age group and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		<13 yrs			13–24 yrs			25–34 yrs			35–44 yrs			45–54 yrs			55–64 yrs			≥65 yrs		
		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Arizona	Phoenix	14	14	100.0	198	170	85.9	993	853	85.9	1,101	1,004	91.2	986	908	92.1	867	821	94.7	292	288	98.6
California	Los Angeles	14	13	92.9	293	227	77.5	2,391	2,055	85.9	2,991	2,600	86.9	2,933	2,662	90.8	2,895	2,657	91.8	1,099	1,044	95.0
	Oakland	12	12	100.0	64	57	89.1	288	249	86.5	321	284	88.5	327	295	90.2	416	381	91.6	249	240	96.4
	Orange County	0	—	—	37	25	67.6	198	166	83.8	236	206	87.3	221	200	90.5	86	79	91.9	17	16	94.1
	Riverside–San Bernardino	0	—	—	49	37	75.5	295	229	77.6	283	229	80.9	271	246	90.8	236	207	87.7	50	43	86.0
	Sacramento	1	1	100.0	55	44	80.0	366	311	85.0	452	382	84.5	465	416	89.5	599	541	90.3	244	232	95.1
	San Diego	7	7	100.0	102	82	80.4	809	729	90.1	1,158	1,056	91.2	1,254	1,167	93.1	1,553	1,459	93.9	674	656	97.3
	San Francisco	0	—	—	30	22	73.3	292	248	84.9	447	372	83.2	445	396	89.0	506	461	91.1	281	269	95.7
	San Jose	0	—	—	24	22	91.7	193	184	95.3	294	277	94.2	290	278	95.9	302	290	96.0	129	125	96.9
Colorado	Denver	12	11	91.7	187	168	89.8	828	745	90.0	966	868	89.9	866	805	93.0	935	888	95.0	364	349	95.9
Connecticut	Hartford	3	3	100.0	42	38	90.5	139	122	87.8	175	155	88.6	295	280	94.9	514	486	94.6	234	228	97.4
	New Haven	0	—	—	30	28	93.3	192	170	88.5	272	255	93.8	394	368	93.4	563	531	94.3	288	278	96.5
District of Columbia	Washington[a]	22	20	90.9	255	204	80.0	1,034	882	85.3	1,353	1,193	88.2	1,557	1,413	90.8	1,665	1,543	92.7	849	799	94.1
Florida	Ft. Lauderdale	6	5	83.3	152	129	84.9	1,025	850	82.9	1,154	1,031	89.3	1,101	973	88.4	1,172	1,068	91.1	325	299	92.0
	Jacksonville	0	—	—	57	45	78.9	479	405	84.6	437	363	83.1	519	463	89.2	558	512	91.8	191	177	92.7
	Miami	16	16	100.0	244	197	80.7	1,417	1,198	84.5	1,586	1,387	87.5	1,393	1,239	88.9	1,608	1,443	89.7	543	510	93.9
	Orlando	1	0	0.0	115	104	90.4	754	661	87.7	780	698	89.5	768	699	91.0	745	693	93.0	233	226	97.0
	Tampa–St. Petersburg	24	21	87.5	223	195	87.4	1,107	938	84.7	1,101	968	87.9	1,125	1,015	90.2	1,323	1,223	92.4	435	410	94.3
	West Palm Beach	0	—	—	18	16	88.9	181	142	78.5	244	210	86.1	267	240	89.9	312	285	91.3	170	154	90.6
Georgia	Atlanta	48	43	89.6	796	634	79.6	4,326	3,454	79.8	3,804	3,142	82.6	2,874	2,511	87.4	2,844	2,587	91.0	1,030	973	94.5
Illinois	Chicago	27	25	92.6	611	538	88.1	3,748	3,190	85.1	3,819	3,395	88.9	3,482	3,212	92.2	3,540	3,321	93.8	1,525	1,472	96.5
Indiana	Indianapolis	17	15	88.2	127	103	81.1	612	516	84.3	664	561	84.5	611	550	90.0	517	478	92.5	169	155	91.7
Louisiana	Baton Rouge	1	0	0.0	85	69	81.2	374	317	84.8	549	499	90.9	550	496	90.2	569	531	93.3	273	260	95.2
	New Orleans	3	3	100.0	111	98	88.3	705	600	85.1	909	763	83.9	810	700	86.4	835	777	93.1	352	326	92.6
Maryland	Baltimore	17	14	82.4	254	217	85.4	1,234	1,023	82.9	1,708	1,480	86.7	1,736	1,583	91.2	2,818	2,606	92.5	1,400	1,326	94.7
Massachusetts	Boston[a]	13	13	100.0	144	122	84.7	756	689	91.1	1,073	999	93.1	1,324	1,253	94.6	1,773	1,710	96.4	830	807	97.2
Michigan	Detroit	10	9	90.0	216	186	86.1	1,095	884	80.7	964	792	82.2	938	835	89.0	1,092	1,001	91.7	534	516	96.6
Minnesota	Minneapolis–St. Paul[a]	0	—	—	25	23	92.0	150	133	88.7	249	224	90.0	279	265	95.0	290	283	97.6	123	118	95.9
Missouri	Kansas City[a]	0	—	—	58	52	89.7	325	275	84.6	321	277	86.3	302	269	89.1	304	282	92.8	101	99	98.0
	St. Louis[a]	16	14	87.5	238	208	87.4	1,057	885	83.7	1,089	954	87.6	1,109	1,004	90.5	1,188	1,110	93.4	445	434	97.5
Nevada	Las Vegas[a]	5	3	60.0	109	93	85.3	568	502	88.4	611	543	88.9	463	430	92.9	442	426	96.4	161	155	96.3
New Jersey	Bergen–Passaic	2	1	50.0	38	34	89.5	191	168	88.0	256	224	87.5	266	245	92.1	382	342	89.5	202	199	98.5
	Jersey City	2	2	100.0	35	28	80.0	263	227	86.3	306	277	90.5	313	289	92.3	402	377	93.8	225	217	96.4
	Middlesex	5	3	60.0	53	43	81.1	210	187	89.0	230	215	93.5	228	210	92.1	319	295	92.5	112	109	97.3
	Newark	11	9	81.8	172	136	79.1	927	789	85.1	1,052	894	85.0	1,085	976	90.0	1,561	1,414	90.6	827	775	93.7
New York	Nassau–Suffolk	5	5	100.0	85	72	84.7	136	121	89.0	157	148	94.3	236	221	93.6	381	365	95.8	261	257	98.5
	New York	22	18	81.8	593	503	84.8	4,312	3,695	85.7	5,682	5,025	88.4	5,943	5,351	90.0	7,926	7,214	91.0	4,150	3,926	94.6
North Carolina	Charlotte[a]	0	—	—	165	140	84.8	910	760	83.5	706	613	86.8	679	612	90.1	591	553	93.6	231	216	93.5
Ohio	Cleveland	2	2	100.0	113	97	85.8	475	402	84.6	476	421	88.4	543	494	91.0	751	705	93.9	366	356	97.3
	Columbus	16	16	100.0	161	146	90.7	729	661	90.7	745	666	89.4	705	651	92.3	747	701	93.8	276	268	97.1
Oregon	Portland[a]	0	—	—	27	25	92.6	234	200	85.5	384	333	86.7	354	311	87.9	326	303	92.9	101	96	95.0
Pennsylvania	Philadelphia[a]	27	27	100.0	411	353	85.9	2,138	1,807	84.5	2,478	2,167	87.4	2,762	2,469	89.4	3,829	3,561	93.0	1,806	1,711	94.7
Puerto Rico	San Juan	0	—	—	92	80	87.0	572	492	86.0	824	705	85.6	1,289	1,158	89.8	2,054	1,919	93.4	1,156	1,107	95.8

Table 30b. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by age group and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico *(cont.)*

		<13 yrs			13–24 yrs			25–34 yrs			35–44 yrs			45–54 yrs			55–64 yrs			≥65 yrs		
		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Tennessee	Memphis[a]	8	6	75.0	186	150	80.6	793	571	72.0	876	667	76.1	800	640	80.0	724	629	86.9	256	228	89.1
	Nashville	17	16	94.1	133	120	90.2	777	688	88.5	963	852	88.5	1,093	992	90.8	1,243	1,159	93.2	420	395	94.0
Texas	Austin	0	—	—	61	54	88.5	382	338	88.5	450	392	87.1	360	314	87.2	275	245	89.1	47	46	97.9
	Dallas	19	17	89.5	325	256	78.8	2,127	1,731	81.4	2,466	2,083	84.5	2,167	1,927	88.9	1,936	1,745	90.1	675	639	94.7
	Ft. Worth	0	—	—	136	111	81.6	677	553	81.7	601	505	84.0	444	378	85.1	272	236	86.8	54	53	98.1
	Houston	2	2	100.0	542	437	80.6	3,079	2,484	80.7	3,168	2,615	82.5	2,639	2,323	88.0	2,204	1,986	90.1	643	600	93.3
	San Antonio	2	2	100.0	86	73	84.9	613	500	81.6	606	488	80.5	391	332	84.9	276	250	90.6	38	35	92.1
Virginia	Norfolk[a]	0	—	—	84	67	79.8	558	441	79.0	573	503	87.8	500	437	87.4	648	596	92.0	264	244	92.4
Washington	Seattle	0	—	—	64	55	85.9	511	466	91.2	784	687	87.6	856	786	91.8	844	794	94.1	312	303	97.1

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for individual EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 31a. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and state, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State																					
Alabama	13	9	69.2	29	19	65.5	5,821	4,152	71.3	266	218	82.0	11	7	63.6	2,343	1,805	77.0	41	24	58.5
Alaska	154	102	66.2	16	11	68.8	39	30	76.9	22	19	86.4	1	0	0.0	68	49	72.1	3	1	33.3
Arizona	121	96	79.3	102	91	89.2	978	824	84.3	2,202	1,920	87.2	12	11	91.7	2,172	1,861	85.7	156	133	85.3
Arkansas	2	0	0.0	8	5	62.5	685	535	78.1	149	111	74.5	5	2	40.0	458	357	77.9	17	12	70.6
California	169	133	78.7	1,259	957	76.0	5,226	3,718	71.1	14,343	11,066	77.2	116	81	69.8	7,962	5,947	74.7	344	248	72.1
Colorado	36	25	69.4	69	56	81.2	847	625	73.8	1,453	1,110	76.4	5	2	40.0	2,099	1,507	71.8	79	60	75.9
Connecticut	3	3	100.0	19	18	94.7	1,297	1,079	83.2	1,328	1,118	84.2	2	2	100.0	463	369	79.7	29	25	86.2
Delaware	1	1	100.0	6	5	83.3	973	716	73.6	144	113	78.5	1	1	100.0	418	324	77.5	5	3	60.0
District of Columbia	1	0	0.0	10	8	80.0	2,326	1,609	69.2	285	195	68.4	0	—	—	54	38	70.4	63	39	61.9
Florida	23	19	82.6	211	177	83.9	13,376	10,419	77.9	8,845	7,310	82.6	20	13	65.0	5,853	4,507	77.0	277	214	77.3
Georgia	24	18	75.0	132	115	87.1	16,986	13,899	81.8	1,652	1,444	87.4	8	4	50.0	3,140	2,644	84.2	186	153	82.3
Hawaii	3	0	0.0	16	0	0.0	12	0	0.0	21	0	0.0	29	0	0.0	40	0	0.0	3	1	33.3
Idaho	8	6	75.0	12	9	75.0	78	50	64.1	152	115	75.7	3	2	66.7	577	400	69.3	9	7	77.8
Illinois	101	66	65.3	342	253	74.0	9,038	6,498	71.9	4,012	3,020	75.3	57	43	75.4	3,051	2,138	70.1	201	119	59.2
Indiana[b]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Iowa	5	4	80.0	58	50	86.2	441	350	79.4	171	146	85.4	4	3	75.0	836	686	82.1	31	26	83.9
Kansas	1	0	0.0	9	7	77.8	123	94	76.4	51	40	78.4	2	1	50.0	328	276	84.1	8	5	62.5
Kentucky	8	7	87.5	34	28	82.4	1,239	863	69.7	396	305	77.0	5	4	80.0	2,126	1,625	76.4	64	41	64.1
Louisiana	4	4	100.0	16	13	81.3	5,158	3,965	76.9	318	234	73.6	3	2	66.7	1,141	863	75.6	39	29	74.4
Maine	13	12	92.3	5	3	60.0	100	93	93.0	31	26	83.9	0	—	—	333	255	76.6	15	11	73.3
Maryland[b]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Massachusetts	13	11	84.6	156	121	77.6	1,713	1,301	75.9	2,362	1,795	76.0	8	7	87.5	2,405	1,693	70.4	87	61	70.1
Michigan	16	12	75.0	54	39	72.2	4,301	2,979	69.3	381	271	71.1	1	1	100.0	1,908	1,345	70.5	133	85	63.9
Minnesota	5	0	0.0	19	8	42.1	474	181	38.2	227	137	60.4	0	—	—	225	73	32.4	83	21	25.3
Mississippi	10	8	80.0	7	6	85.7	3,788	3,003	79.3	89	73	82.0	0	—	—	845	656	77.6	11	9	81.8
Missouri	13	5	38.5	43	28	65.1	2,185	1,520	69.6	333	250	75.1	6	3	50.0	1,255	790	62.9	76	52	68.4
Montana	26	20	76.9	3	2	66.7	15	9	60.0	32	24	75.0	0	—	—	280	214	76.4	6	4	66.7
Nebraska	10	6	60.0	22	18	81.8	205	151	73.7	170	127	74.7	1	1	100.0	307	225	73.3	14	11	78.6
Nevada	8	3	37.5	82	62	75.6	605	360	59.5	1,006	714	71.0	18	12	66.7	752	562	74.7	76	53	69.7
New Hampshire	2	1	50.0	18	17	94.4	100	97	97.0	112	106	94.6	0	—	—	501	482	96.2	12	12.0	100.0
New Jersey	12	8	66.7	165	140	84.8	5,776	4,711	81.6	3,941	3,384	85.9	13	9	69.2	1,375	1,090	79.3	35	25	71.4
New Mexico	85	65	76.5	15	10	66.7	93	74	79.6	347	289	83.3	5	4	80.0	656	542	82.6	3	1	33.3
New York	84	70	83.3	777	665	85.6	14,020	11,426	81.5	11,056	9,351	84.6	65	55	84.6	4,693	3,832	81.7	233	200	85.8
North Carolina	133	103	77.4	79	70	88.6	7,729	5,994	77.6	1,436	1,195	83.2	6	6	100.0	2,521	1,949	77.3	76	65	85.5
North Dakota	2	2	100.0	1	1	100.0	50	40	80.0	4	4	100.0	0	—	—	36	29	80.6	2	2	100.0
Ohio	13	8	61.5	69	44	63.8	3,976	2,667	67.1	556	367	66.0	6	2	33.3	3,051	2,092	68.6	140	88	62.9
Oklahoma	122	90	73.8	69	51	73.9	585	384	65.6	294	235	79.9	2	1	50.0	1,124	797	70.9	102	77	75.5
Oregon	7	6	85.7	25	16	64.0	138	98	71.0	299	226	75.6	4	2	50.0	649	463	71.3	99	74	74.7
Pennsylvania	97	84	86.6	213	181	85.0	9,998	7,948	79.5	2,980	2,522	84.6	10	8	80.0	5,139	4,037	78.6	138	110	79.7
Rhode Island	10	9	90.0	36	32	88.9	414	322	77.8	476	393	82.6	0	—	—	810	621	76.7	21	18	85.7
South Carolina	22	17	77.3	46	39	84.8	7,921	6,410	80.9	574	501	87.3	9	9	100.0	2,538	2,055	81.0	103	80	77.7
South Dakota	16	9	56.3	3	2	66.7	83	61	73.5	18	15	83.3	0	—	—	81	55	67.9	3	1	33.3
Tennessee	12	9	75.0	86	74	86.0	4,681	3,761	80.3	545	438	80.4	5	4	80.0	3,157	2,449	77.6	53	40	75.5
Texas[b]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

Table 31a. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and state, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races		
		Retained			Retained			Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State																					
Utah	24	15	62.5	25	11	44.0	118	52	44.1	478	341	71.3	8	3	37.5	521	282	54.1	9	4	44.4
Vermont	3	3	100.0	10	7	70.0	48	36	75.0	25	21	84.0	1	0	0.0	353	268	75.9	4	3	75.0
Virginia	4	3	75.0	123	89	72.4	3,869	2,694	69.6	836	683	81.7	5	5	100.0	1,329	985	74.1	67	38	56.7
Washington	57	41	71.9	177	131	74.0	977	729	74.6	676	489	72.3	34	28	82.4	1,476	1,070	72.5	45	35	77.8
West Virginia	5	4	80.0	11	8	72.7	229	138	60.3	36	24	66.7	0	—	—	918	600	65.4	12	7	58.3
Wisconsin	8	5	62.5	61	51	83.6	1,491	1,073	72.0	607	496	81.7	5	5	100.0	1,286	903	70.2	23	14	60.9
Wyoming	1	0	0.0	2	2	100.0	3	1	33.3	10	4	40.0	0	—	—	30	8	26.7	0	—	—
Subtotal	**1,510**	**1,122**	**74.3**	**4,750**	**3,750**	**78.9**	**140,328**	**107,739**	**76.8**	**65,747**	**52,985**	**80.6**	**496**	**343**	**69.2**	**73,683**	**55,818**	**75.8**	**3,236**	**2,341**	**72.3**
Territory																					
Guam	0	—	—	9	8	88.9	0	—	—	0	—	—	17	14	82.4	1	1	100.0	0	—	—
Puerto Rico	1	1	100.0	1	1	100.0	31	28	90.3	9,950	9,085	91.3	0	—	—	138	112	81.2	28	26	92.9
U.S. Virgin Islands	0	—	—	2	1	50.0	133	91	68.4	70	54	77.1	0	—	—	13	10	76.9	1	1	100.0
Subtotal	**1**	**1**	**100.0**	**12**	**10**	**83.3**	**164**	**119**	**72.6**	**10,020**	**9,139**	**91.2**	**17**	**14**	**82.4**	**152**	**123**	**80.9**	**29**	**27**	**93.1**
Total	**1,511**	**1,123**	**74.3**	**4,762**	**3,760**	**79.0**	**140,492**	**107,858**	**76.8**	**75,767**	**62,124**	**82.0**	**513**	**357**	**69.6**	**73,835**	**55,941**	**75.8**	**3,265**	**2,368**	**72.5**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Note: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] Hispanics/Latinos can be of any race.
[b] 2022 data for Indiana are unavailable. 2022 race/ethnicity data for Maryland and Texas are unavailable.

Table 31b. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		American Indian/ Alaska Native			Asian			Black/African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White		
		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Arizona	Phoenix	77	57	74.0	88	79	89.8	900	753	83.7	1,622	1,403	86.5	8	7	87.5	1,331	1,100	82.6
California	Los Angeles	47	38	80.9	513	410	79.9	2,563	1,870	73.0	6,871	5,461	79.5	29	23	79.3	2,241	1,772	79.1
	Oakland	8	6	75.0	96	62	64.6	682	443	65.0	451	300	66.5	6	2	33.3	237	140	59.1
	Orange County	*	*	*	37	25	67.6	32	18	56.3	572	451	78.8	*	*	*	77	52	67.5
	Riverside–San Bernardino	*	*	*	19	13	68.4	150	91	60.7	610	470	77.0	6	1	16.7	233	135	57.9
	Sacramento	15	14	93.3	92	83	90.2	532	455	85.5	611	514	84.1	14	9	64.3	916	767	83.7
	San Diego	25	13	52.0	145	95	65.5	614	399	65.0	2,589	1,928	74.5	24	18	75.0	1,628	1,041	63.9
	San Francisco	19	14	73.7	115	75	65.2	327	207	63.3	704	479	68.0	13	8	61.5	670	472	70.4
	San Jose	*	*	*	147	111	75.5	120	96	80.0	631	507	80.3	*	*	*	204	156	76.5
Colorado	Denver	28	19	67.9	61	50	82.0	856	631	73.7	1,344	1,026	76.3	*	*	*	1,795	1,292	72.0
Connecticut	Hartford	*	*	*	10	9	90.0	508	427	84.1	692	569	82.2	*	*	*	245	200	81.6
	New Haven	*	*	*	8	8	100.0	805	669	83.1	640	547	85.5	*	*	*	188	146	77.7
District of Columbia	Washington[b]	*	*	*	101	79	78.2	4,511	3,267	72.4	1,074	865	80.5	*	*	*	461	320	69.4
Florida	Ft. Lauderdale	*	*	*	37	34	91.9	2,413	1,720	71.3	1,312	1,058	80.6	*	*	*	794	596	75.1
	Jacksonville	*	*	*	17	15	88.2	1,373	1,068	77.8	192	154	80.2	*	*	*	489	376	76.9
	Miami	*	*	*	14	11	78.6	2,536	2,070	81.6	3,534	2,995	84.7	*	*	*	346	268	77.5
	Orlando	*	*	*	26	23	88.5	1,366	1,107	81.0	1,234	1,017	82.4	*	*	*	529	418	79.0
	Tampa–St. Petersburg	*	*	*	60	44	73.3	2,195	1,762	80.3	1,340	1,117	83.4	*	*	*	1,416	1,126	79.5
	West Palm Beach	*	*	*	8	5	62.5	710	590	83.1	318	252	79.2	*	*	*	154	116	75.3
Georgia	Atlanta	22	18	81.8	111	96	86.5	11,394	9,167	80.5	1,361	1,184	87.0	8	4	50.0	1,551	1,297	83.6
Illinois	Chicago	100	65	65.0	334	248	74.3	8,852	6,372	72.0	4,006	3,029	75.6	56	42	75.0	2,787	1,972	70.8
Indiana	Indianapolis	*	*	*	94	83	88.3	1,392	1,109	79.7	325	272	83.7	*	*	*	687	524	76.3
Louisiana	Baton Rouge	*	*	*	6	5	83.3	1,873	1,524	81.4	109	91	83.5	*	*	*	349	281	80.5
	New Orleans	*	*	*	9	7	77.8	2,636	2,031	77.0	251	183	72.9	*	*	*	647	489	75.6
Maryland	Baltimore[c]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Massachusetts	Boston[b]	11	10	90.9	151	119	78.8	1,564	1,214	77.6	1,817	1,443	79.4	8	7	87.5	2,319	1,692	73.0
Michigan	Detroit	*	*	*	13	10	76.9	3,537	2,467	69.7	173	126	72.8	*	*	*	598	437	73.1
Minnesota	Minneapolis–St. Paul[b]	5	0	0.0	20	8	40.0	524	209	39.9	240	146	60.8	*	*	*	249	83	33.3
Missouri	Kansas City[b]	5	3	60.0	15	12	80.0	604	396	65.6	229	165	72.1	*	*	*	455	345	75.8
	St. Louis[b]	15	8	53.3	49	35	71.4	2,620	1,853	70.7	406	312	76.8	6	4	66.7	1,657	1,145	69.1
Nevada	Las Vegas[b]	8	3	37.5	81	63	77.8	612	366	59.8	866	592	68.4	16	10	62.5	451	285	63.2
New Jersey	Bergen–Passaic	*	*	*	12	12	100.0	514	443	86.2	639	560	87.6	*	*	*	95	83	87.4
	Jersey City	*	*	*	45	42	93.3	531	450	84.7	765	684	89.4	*	*	*	141	123	87.2
	Middlesex	*	*	*	30	22	73.3	464	386	83.2	507	424	83.6	*	*	*	121	106	87.6
	Newark	6	4	66.7	48	41	85.4	3,360	2,758	82.1	1,449	1,229	84.8	10	7	70.0	385	306	79.5
New York	Nassau–Suffolk	*	*	*	24	21	87.5	574	446	77.7	267	213	79.8	*	*	*	277	222	80.1
	New York	69	58	84.1	690	590	85.5	12,390	10,129	81.8	10,460	8,867	84.8	63	53	84.1	3,085	2,520	81.7
North Carolina	Charlotte[b]	9	6	66.7	22	19	86.4	2,053	1,563	76.1	423	354	83.7	*	*	*	440	334	75.9
Ohio	Cleveland	*	*	*	15	8	53.3	1,476	1,106	74.9	250	182	72.8	*	*	*	803	651	81.1
	Columbus	5	2	40.0	31	18	58.1	1,437	863	60.1	237	137	57.8	*	*	*	1,365	792	58.0
Oregon	Portland[b]	7	6	85.7	25	16	64.0	150	109	72.7	325	246	75.7	5	3	60.0	711	509	71.6
Pennsylvania	Philadelphia[b]	83	72	86.7	169	144	85.2	8,608	6,745	78.4	1,925	1,596	82.9	7	4	57.1	2,261	1,698	75.1
Puerto Rico	San Juan	*	*	*	*	*	*	25	22	88.0	5,723	5,205	90.9	*	*	*	83	65	78.3

Table 31b. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico *(cont.)*

		American Indian/ Alaska Native			Asian			Black/African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White		
		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Tennessee	Memphis[b]	*	*	*	6	6	100.0	3,062	2,599	84.9	118	104	88.1	*	*	*	256	220	85.9
	Nashville	*	*	*	62	56	90.3	2,123	1,673	78.8	331	265	80.1	*	*	*	1,822	1,420	77.9
Texas	Austin	*	*	*	19	14	73.7	320	204	63.8	682	519	76.1	*	*	*	368	256	69.6
	Dallas[c]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	Ft. Worth	6	4	66.7	26	18	69.2	959	757	78.9	629	556	88.4	*	*	*	361	284	78.7
	Houston	18	14	77.8	155	110	71.0	5,526	3,842	69.5	4,088	3,158	77.3	6	4	66.7	1,264	838	66.3
	San Antonio	6	5	83.3	23	16	69.6	286	169	59.1	1,301	823	63.3	*	*	*	230	139	60.4
Virginia	Norfolk[b]	*	*	*	20	13	65.0	1,826	1,086	59.5	116	73	62.9	*	*	*	475	278	58.5
Washington	Seattle	48	37	77.1	162	119	73.5	852	623	73.1	634	453	71.5	26	22	84.6	1,296	928	71.6

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for individual EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
* To ensure confidentiality, values less than (<) 5 have been suppressed; in addition, all data for clients of multiple races have been suppressed.
[a] Hispanics/Latinos can be of any race.
[b] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.
[c] 2022 race/ethnicity data for the Baltimore, MD, and Dallas, TX, EMAs are unavailable.

Table 32a. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and state, 2022—United States and 3 territories

	American Indian/ Alaska Native			Asian			Black/African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races		
	Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression	
	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
State																					
Alabama	12	11	91.7	31	30	96.8	5,858	5,142	87.8	274	253	92.3	10	9	90.0	2,391	2,231	93.3	42	38	90.5
Alaska	164	146	89.0	15	12	80.0	35	32	91.4	22	21	95.5	1	0	0.0	62	54	87.1	4	3	75.0
Arizona	135	115	85.2	109	101	92.7	1,024	914	89.3	2,334	2,172	93.1	12	11	91.7	2,237	2,086	93.2	170	157	92.4
Arkansas	2	2	100.0	9	8	88.9	724	609	84.1	153	131	85.6	5	4	80.0	496	443	89.3	17	14	82.4
California	168	149	88.7	1,337	1,267	94.8	5,350	4,655	87.0	15,060	13,553	90.0	129	110	85.3	8,268	7,551	91.3	347	309	89.0
Colorado	33	30	90.9	75	70	93.3	850	776	91.3	1,451	1,338	92.2	6	5	83.3	2,032	1,918	94.4	77	72	93.5
Connecticut	3	3	100.0	21	20	95.2	1,309	1,224	93.5	1,337	1,260	94.2	4	4	100.0	450	421	93.6	24	21	87.5
Delaware	1	1	100.0	9	8	88.9	1,005	914	90.9	155	144	92.9	1	1	100.0	429	410	95.6	6	6	100.0
District of Columbia	1	1	100.0	11	11	100.0	2,448	2,160	88.2	335	293	87.5	0	—	—	59	56	94.9	68	58	85.3
Florida	23	23	100.0	219	207	94.5	13,843	11,840	85.5	9,420	8,671	92.0	21	18	85.7	6,143	5,606	91.3	283	252	89.0
Georgia	28	24	85.7	140	131	93.6	18,115	15,301	84.5	1,783	1,632	91.5	8	8	100.0	3,320	2,967	89.4	193	172	89.1
Hawaii	3	2	66.7	16	12	75.0	12	11	91.7	21	20	95.2	29	22	75.9	39	35	89.7	2	0	0.0
Idaho	9	9	100.0	13	13	100.0	88	83	94.3	175	171	97.7	3	3	100.0	620	607	97.9	9	9	100.0
Illinois	99	90	90.9	355	345	97.2	9,113	7,963	87.4	4,213	3,963	94.1	53	49	92.5	3,115	2,939	94.3	188	159	84.6
Indiana[b]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Iowa	6	6	100.0	58	58	100.0	453	407	89.8	180	169	93.9	5	5	100.0	870	827	95.1	35	34	97.1
Kansas	1	1	100.0	10	9	90.0	133	109	82.0	61	55	90.2	2	2	100.0	336	309	92.0	8	7	87.5
Kentucky	9	9	100.0	41	40	97.6	1,366	1,199	87.8	426	393	92.3	6	6	100.0	2,233	2,080	93.1	71	65	91.5
Louisiana	5	5	100.0	13	13	100.0	4,978	4,385	88.1	322	289	89.8	3	3	100.0	1,140	1,014	88.9	42	38	90.5
Maine	14	14	100.0	5	5	100.0	97	92	94.8	32	29	90.6	0	—	—	331	319	96.4	16	16	100.0
Maryland[b]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Massachusetts	11	11	100.0	151	145	96.0	1,770	1,632	92.2	2,441	2,319	95.0	5	5	100.0	2,302	2,221	96.5	79	74	93.7
Michigan	19	17	89.5	54	54	100.0	4,739	4,140	87.4	437	410	93.8	2	2	100.0	2,155	2,043	94.8	142	129	90.8
Minnesota	5	4	80.0	17	17	100.0	466	435	93.3	233	220	94.4	0	—	—	212	205	96.7	81	72	88.9
Mississippi	12	12	100.0	8	6	75.0	4,021	3,520	87.5	96	85	88.5	0	—	—	886	807	91.1	13	12	92.3
Missouri	13	11	84.6	47	47	100.0	2,329	2,056	88.3	357	330	92.4	6	6	100.0	1,300	1,200	92.3	78	66	84.6
Montana	25	23	92.0	4	3	75.0	15	15	100.0	32	29	90.6	0	—	—	292	281	96.2	6	6	100.0
Nebraska	12	12	100.0	22	22	100.0	222	202	91.0	192	175	91.1	1	1	100.0	320	300	93.8	17	15	88.2
Nevada	9	9	100.0	91	89	97.8	665	584	87.8	1,103	1,012	91.7	19	18	94.7	803	751	93.5	87	79	90.8
New Hampshire	2	2	100.0	19	18	94.7	100	98	98.0	105	100	95.2	0	—	—	474	456	96.2	12	12.0	100.0
New Jersey	13	12	92.3	172	162	94.2	6,134	5,369	87.5	4,184	3,840	91.8	13	12	92.3	1,455	1,367	94.0	36	32	88.9
New Mexico	93	76	81.7	14	13	92.9	90	74	82.2	354	327	92.4	4	4	100.0	689	638	92.6	3	3	100.0
New York	80	74	92.5	797	770	96.6	14,490	12,784	88.2	11,407	10,425	91.4	65	62	95.4	4,797	4,516	94.1	245	217	88.6
North Carolina	143	120	83.9	88	81	92.0	8,337	7,363	88.3	1,520	1,397	91.9	10	9	90.0	2,667	2,484	93.1	80	70	87.5
North Dakota	2	2	100.0	1	1	100.0	53	50	94.3	4	4	100.0	0	—	—	38	36	94.7	2	2	100.0
Ohio	14	13	92.9	72	68	94.4	4,207	3,734	88.8	597	565	94.6	5	3	60.0	3,190	2,977	93.3	144	131	91.0
Oklahoma	148	133	89.9	76	73	96.1	725	642	88.6	354	329	92.9	5	4	80.0	1,390	1,285	92.4	121	107	88.4
Oregon	7	6	85.7	28	25	89.3	149	133	89.3	328	298	90.9	3	3	100.0	691	611	88.4	101	87	86.1
Pennsylvania	77	65	84.4	222	213	95.9	10,120	9,042	89.3	3,069	2,820	91.9	11	10	90.9	5,243	4,948	94.4	144	132	91.7
Rhode Island	9	9	100.0	36	34	94.4	421	389	92.4	494	475	96.2	1	1	100.0	810	788	97.3	19	17	89.5
South Carolina	22	21	95.5	47	43	91.5	8,363	7,435	88.9	621	558	89.9	9	9	100.0	2,673	2,497	93.4	107	96	89.7
South Dakota	14	14	100.0	3	3	100.0	90	86	95.6	22	22	100.0	0	—	—	93	91	97.8	5	3	60.0
Tennessee	14	12	85.7	88	84	95.5	4,987	4,119	82.6	594	543	91.4	5	4	80.0	3,318	3,067	92.4	55	53	96.4
Texas[b]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—

Table 32a. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and state, 2022—United States and 3 territories *(cont.)*

	American Indian/ Alaska Native			Asian			Black/African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White			Multiple races		
	Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression	
	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
State																					
Utah	16	14	87.5	23	22	95.7	87	80	92.0	445	434	97.5	7	7	100.0	421	405	96.2	7	7	100.0
Vermont	3	3	100.0	13	12	92.3	49	47	95.9	25	24	96.0	1	1	100.0	359	340	94.7	4	4	100.0
Virginia	6	6	100.0	132	123	93.2	4,112	3,621	88.1	891	822	92.3	7	7	100.0	1,396	1,286	92.1	71	65	91.5
Washington	63	53	84.1	191	181	94.8	1,077	982	91.2	761	706	92.8	35	34	97.1	1,534	1,395	90.9	45	35	77.8
West Virginia	5	5	100.0	12	12	100.0	251	220	87.6	37	33	89.2	0	—	—	998	895	89.7	14	12	85.7
Wisconsin	9	7	77.8	66	60	90.9	1,599	1,426	89.2	647	613	94.7	8	7	87.5	1,348	1,279	94.9	26	23	88.5
Wyoming	1	0	0.0	2	2	100.0	3	3	100.0	14	13	92.9	0	—	—	35	34	97.1	0	—	—
Subtotal	**1,563**	**1,387**	**88.7**	**4,983**	**4,743**	**95.2**	**146,472**	**128,097**	**87.5**	**69,118**	**63,485**	**91.9**	**520**	**469**	**90.2**	**76,460**	**71,076**	**93.0**	**3,346**	**2,991**	**89.4**
Territory																					
Guam	0	—	—	11	8	72.7	0	—	—	0	—	—	17	14	82.4	1	1	100.0	0	—	—
Puerto Rico	1	1	100.0	1	1	100.0	33	31	93.9	10,102	9,291	92.0	0	—	—	146	134	91.8	28	24	85.7
U.S. Virgin Islands	0	—	—	2	2	100.0	152	133	87.5	80	69	86.3	0	—	—	18	16	88.9	1	1	100.0
Subtotal	**1**	**1**	**100.0**	**14**	**11**	**78.6**	**185**	**164**	**88.6**	**10,182**	**9,360**	**91.9**	**17**	**14**	**82.4**	**165**	**151**	**91.5**	**29**	**25**	**86.2**
Total	**1,564**	**1,388**	**88.7**	**4,997**	**4,754**	**95.1**	**146,657**	**128,261**	**87.5**	**79,300**	**72,845**	**91.9**	**537**	**483**	**89.9**	**76,625**	**71,227**	**93.0**	**3,375**	**3,016**	**89.4**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Note: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] Hispanics/Latinos can be of any race.
[b] 2022 data for Indiana are unavailable. 2022 race/ethnicity data for Maryland and Texas are unavailable.

Table 32b. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		American Indian/ Alaska Native			Asian			Black/African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White		
		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Arizona	Phoenix	92	75	81.5	93	87	93.5	955	845	88.5	1,742	1,608	92.3	8	8	100.0	1,411	1,297	91.9
California	Los Angeles	44	36	81.8	527	509	96.6	2,545	2,203	86.6	7,072	6,319	89.4	30	25	83.3	2,255	2,039	90.4
	Oakland	9	9	100.0	107	103	96.3	756	690	91.3	488	426	87.3	9	7	77.8	277	257	92.8
	Orange County	*	*	*	45	39	86.7	36	31	86.1	612	542	88.6	*	*	*	92	71	77.2
	Riverside–San Bernardino	*	*	*	28	23	82.1	164	134	81.7	690	586	84.9	7	6	85.7	282	235	83.3
	Sacramento	16	15	93.8	89	84	94.4	496	426	85.9	616	542	88.0	15	14	93.3	893	799	89.5
	San Diego	24	23	95.8	164	156	95.1	672	601	89.4	2,780	2,586	93.0	26	22	84.6	1,778	1,667	93.8
	San Francisco	20	17	85.0	113	102	90.3	333	267	80.2	741	683	92.2	15	13	86.7	668	590	88.3
	San Jose	*	*	*	161	156	96.9	136	127	93.4	690	658	95.4	*	*	*	222	213	95.9
Colorado	Denver	25	22	88.0	64	59	92.2	857	777	90.7	1,335	1,225	91.8	*	*	*	1,701	1,589	93.4
Connecticut	Hartford	*	*	*	11	11	100.0	486	445	91.6	661	627	94.9	*	*	*	217	205	94.5
	New Haven	*	*	*	9	8	88.9	840	793	94.4	681	634	93.1	*	*	*	197	183	92.9
District of Columbia	Washington[b]	*	*	*	108	103	95.4	4,797	4,291	89.5	1,193	1,078	90.4	*	*	*	499	467	93.6
Florida	Ft. Lauderdale	*	*	*	39	36	92.3	2,547	2,171	85.2	1,409	1,313	93.2	*	*	*	857	764	89.1
	Jacksonville	*	*	*	18	18	100.0	1,455	1,254	86.2	214	193	90.2	*	*	*	515	467	90.7
	Miami	*	*	*	17	16	94.1	2,588	2,152	83.2	3,805	3,463	91.0	*	*	*	371	335	90.3
	Orlando	*	*	*	26	22	84.6	1,422	1,238	87.1	1,305	1,223	93.7	*	*	*	573	533	93.0
	Tampa–St. Petersburg	*	*	*	60	60	100.0	2,273	1,949	85.7	1,433	1,327	92.6	5	4	80.0	1,485	1,360	91.6
	West Palm Beach	*	*	*	8	7	87.5	696	598	85.9	325	298	91.7	*	*	*	154	137	89.0
Georgia	Atlanta	26	22	84.6	114	107	93.9	12,227	10,187	83.3	1,478	1,354	91.6	8	8	100.0	1,643	1,470	89.5
Illinois	Chicago	97	88	90.7	346	337	97.4	8,907	7,781	87.4	4,206	3,957	94.1	52	48	92.3	2,833	2,673	94.4
Indiana	Indianapolis	*	*	*	93	89	95.7	1,488	1,262	84.8	353	320	90.7	*	*	*	728	659	90.5
Louisiana	Baton Rouge	*	*	*	5	5	100.0	1,923	1,722	89.5	113	105	92.9	*	*	*	350	331	94.6
	New Orleans	*	*	*	7	7	100.0	2,744	2,394	87.2	255	232	91.0	*	*	*	682	602	88.3
Maryland	Baltimore[c]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Massachusetts	Boston[b]	10	10	100.0	143	137	95.8	1,588	1,463	92.1	1,825	1,731	94.8	5	5	100.0	2,166	2,082	96.1
Michigan	Detroit	*	*	*	13	13	100.0	3,912	3,371	86.2	196	178	90.8	*	*	*	667	607	91.0
Minnesota	Minneapolis–St. Paul[b]	5	4	80.0	18	18	100.0	517	481	93.0	249	235	94.4	*	*	*	239	230	96.2
Missouri	Kansas City[b]	5	5	100.0	16	16	100.0	636	559	87.9	244	228	93.4	*	*	*	474	413	87.1
	St. Louis[b]	15	13	86.7	52	52	100.0	2,808	2,463	87.7	431	399	92.6	6	6	100.0	1,735	1,596	92.0
Nevada	Las Vegas[b]	9	9	100.0	89	86	96.6	684	603	88.2	976	895	91.7	16	15	93.8	509	475	93.3
New Jersey	Bergen–Passaic	*	*	*	12	12	100.0	529	473	89.4	688	630	91.6	*	*	*	105	96	91.4
	Jersey City	*	*	*	48	45	93.8	553	479	86.6	793	747	94.2	*	*	*	147	141	95.9
	Middlesex	*	*	*	29	27	93.1	475	432	90.9	522	478	91.6	*	*	*	126	120	95.2
	Newark	7	6	85.7	52	48	92.3	3,584	3,118	87.0	1,566	1,415	90.4	10	10	100.0	402	384	95.5
New York	Nassau–Suffolk	*	*	*	29	29	100.0	601	560	93.2	292	275	94.2	*	*	*	298	286	96.0
	New York	67	61	91.0	699	673	96.3	12,786	11,205	87.6	10,772	9,832	91.3	63	60	95.2	3,140	2,934	93.4
North Carolina	Charlotte[b]	12	10	83.3	25	23	92.0	2,290	1,985	86.7	455	414	91.0	*	*	*	476	441	92.6
Ohio	Cleveland	*	*	*	14	13	92.9	1,565	1,381	88.2	267	255	95.5	*	*	*	845	798	94.4
	Columbus	5	5	100.0	34	31	91.2	1,499	1,354	90.3	251	237	94.4	*	*	*	1,422	1,333	93.7
Oregon	Portland[b]	7	6	85.7	28	25	89.3	163	144	88.3	354	323	91.2	*	*	*	761	672	88.3
Pennsylvania	Philadelphia[b]	63	52	82.5	178	174	97.8	8,757	7,762	88.6	1,981	1,816	91.7	8	7	87.5	2,312	2,151	93.0
Puerto Rico	San Juan	*	*	*	*	*	*	27	25	92.6	5,845	5,333	91.2	*	*	*	88	80	90.9

Table 32b. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by race/ethnicity and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico *(cont.)*

		American Indian/ Alaska Native			Asian			Black/African American			Hispanic/Latino[a]			Native Hawaiian/ Pacific Islander			White		
		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Tennessee	Memphis[b]	*	*	*	6	5	83.3	3,208	2,522	78.6	128	104	81.3	*	*	*	270	234	86.7
	Nashville	*	*	*	66	63	95.5	2,260	1,990	88.1	364	342	94.0	*	*	*	1,921	1,794	93.4
Texas	Austin	5	4	80.0	19	17	89.5	352	300	85.2	768	694	90.4	*	*	*	408	353	86.5
	Dallas[c]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	Ft. Worth	6	5	83.3	27	25	92.6	1,047	868	82.9	678	585	86.3	*	*	*	400	330	82.5
	Houston	21	16	76.2	166	153	92.2	6,112	5,065	82.9	4,507	3,957	87.8	6	6	100.0	1,392	1,191	85.6
	San Antonio	6	4	66.7	23	20	87.0	295	233	79.0	1,413	1,196	84.6	*	*	*	264	217	82.2
Virginia	Norfolk[b]	*	*	*	22	20	90.9	1,942	1,672	86.1	123	108	87.8	*	*	*	495	448	90.5
Washington	Seattle	54	46	85.2	177	167	94.4	941	859	91.3	711	656	92.3	27	26	96.3	1,339	1,223	91.3

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for individual EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
* To ensure confidentiality, values less than (<) 5 have been suppressed; in addition, all data for clients of multiple races have been suppressed.
[a] Hispanics/Latinos can be of any race.
[b] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.
[c] 2022 race/ethnicity data for the Baltimore, MD, and Dallas, TX, EMAs are unavailable.

Table 33a. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and state, 2022—United States and 3 territories

	0–100% FPL			101–138% FPL			139–250% FPL			251–400% FPL			>400% FPL		
		Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State															
Alabama	4,760	3,394	71.3	920	683	74.2	1,590	1,221	76.8	899	681	75.8	264	198	75.0
Alaska	221	149	67.4	15	14	93.3	32	28	87.5	12	11	91.7	5	5	100.0
Arizona	2,698	2,289	84.8	688	611	88.8	1,125	974	86.6	908	781	86.0	317	273	86.1
Arkansas	674	528	78.3	152	118	77.6	285	216	75.8	146	113	77.4	67	47	70.1
California	17,867	13,139	73.5	3,202	2,500	78.1	4,854	3,853	79.4	2,201	1,742	79.1	856	665	77.7
Colorado	3,202	2,407	75.2	343	256	74.6	444	331	74.5	310	227	73.2	188	126	67.0
Connecticut	1,897	1,582	83.4	377	311	82.5	631	525	83.2	183	160	87.4	33	28	84.8
Delaware	645	458	71.0	185	139	75.1	287	237	82.6	234	190	81.2	149	114	76.5
District of Columbia	1,983	1,338	67.5	181	132	72.9	338	248	73.4	186	137	73.7	43	32	74.4
Florida	15,747	12,162	77.2	2,848	2,347	82.4	5,517	4,572	82.9	3,165	2,587	81.7	316	237	75.0
Georgia	12,251	10,049	82.0	2,678	2,282	85.2	4,464	3,790	84.9	1,990	1,687	84.8	301	256	85.0
Hawaii	84	1	1.2	18	0	0.0	15	0	0.0	6	0	0.0	1	0	0.0
Idaho	255	171	67.1	91	69	75.8	188	133	70.7	129	97	75.2	143	101	70.6
Illinois	9,370	6,921	73.9	968	774	80.0	1,969	1,463	74.3	1,172	857	73.1	2,631	1,764	67.0
Indiana[a]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Iowa	536	422	78.7	149	127	85.2	313	266	85.0	273	235	86.1	157	125	79.6
Kansas	283	227	80.2	41	36	87.8	75	60	80.0	74	57	77.0	49	43	87.8
Kentucky	2,001	1,407	70.3	405	321	79.3	739	595	80.5	443	340	76.7	208	162	77.9
Louisiana	3,751	2,876	76.7	1,170	837	71.5	1,143	931	81.5	408	326	79.9	101	88	87.1
Maine	269	227	84.4	54	42	77.8	86	62	72.1	42	30	71.4	10	8	80.0
Maryland	5,727	4,562	79.7	993	832	83.8	1,500	1,211	80.7	1,086	858	79.0	518	394	76.1
Massachusetts	4,121	3,054	74.1	477	371	77.8	810	631	77.9	508	383	75.4	517	360	69.6
Michigan	3,449	2,404	69.7	678	505	74.5	1,291	924	71.6	808	546	67.6	410	270	65.9
Minnesota	489	194	39.7	136	65	47.8	254	95	37.4	147	65	44.2	7	1	14.3
Mississippi	3,030	2,372	78.3	418	345	82.5	760	640	84.2	291	251	86.3	48	38	79.2
Missouri	2,465	1,623	65.8	360	258	71.7	724	526	72.7	335	227	67.8	27	14	51.9
Montana	139	100	71.9	48	37	77.1	77	61	79.2	53	41	77.4	37	31	83.8
Nebraska	331	229	69.2	91	74	81.3	196	145	74.0	104	84	80.8	8	7	87.5
Nevada	1,116	724	64.9	240	176	73.3	612	448	73.2	531	402	75.7	39	16	41.0
New Hampshire	136	133	97.8	50	50	100.0	96	92	95.8	89	85	95.5	37	36	97.3
New Jersey	6,789	5,598	82.5	1,203	1,054	87.6	1,983	1,678	84.6	863	692	80.2	271	218	80.4
New Mexico	514	395	76.8	133	117	88.0	262	224	85.5	214	178	83.2	156	136	87.2
New York	20,803	17,000	81.7	2,412	2,079	86.2	5,827	4,916	84.4	1,522	1,285	84.4	841	698	83.0
North Carolina	6,389	4,928	77.1	1,381	1,133	82.0	2,455	1,966	80.1	1,064	856	80.5	248	213	85.9
North Dakota	36	30	83.3	5	5	100.0	25	21	84.0	23	17	73.9	7	6	85.7
Ohio	4,119	2,890	70.2	706	495	70.1	1,340	925	69.0	764	502	65.7	348	245	70.4
Oklahoma	862	645	74.8	474	285	60.1	398	302	75.9	308	226	73.4	96	73	76.0
Oregon	876	638	72.8	63	49	77.8	127	93	73.2	95	67	70.5	51	36	70.6
Pennsylvania	10,661	8,577	80.5	1,950	1,581	81.1	3,111	2,529	81.3	1,734	1,387	80.0	863	667	77.3
Rhode Island	869	690	79.4	186	160	86.0	321	247	76.9	201	151	75.1	188	146	77.7
South Carolina	5,998	4,792	79.9	1,125	941	83.6	2,086	1,754	84.1	1,369	1,126	82.2	595	471	79.2
South Dakota	49	33	67.3	25	18	72.0	69	50	72.5	50	34	68.0	11	8	72.7
Tennessee	4,873	3,821	78.4	673	531	78.9	1,400	1,155	82.5	1,335	1,078	80.7	251	184	73.3
Texas	17,592	12,881	73.2	3,237	2,508	77.5	5,073	3,765	74.2	1,805	1,301	72.1	398	276	69.3

Table 33a. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and state, 2022—United States and 3 territories *(cont.)*

	0–100% FPL			101–138% FPL			139–250% FPL			251–400% FPL			>400% FPL		
		Retained			Retained			Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State															
Utah	538	336	62.5	90	59	65.6	260	157	60.4	136	73	53.7	45	26	57.8
Vermont	138	108	78.3	68	50	73.5	88	70	79.5	83	58	69.9	70	55	78.6
Virginia	2,862	2,009	70.2	651	490	75.3	1,340	981	73.2	938	713	76.0	354	264	74.6
Washington	1,778	1,301	73.2	324	240	74.1	522	396	75.9	540	376	69.6	369	255	69.1
West Virginia	589	359	61.0	181	125	69.1	234	166	70.9	89	54	60.7	14	9	64.3
Wisconsin	2,587	1,893	73.2	237	190	80.2	363	264	72.7	254	180	70.9	131	89	67.9
Wyoming	19	9	47.4	3	1	33.3	12	2	16.7	8	1	12.5	4	2	50.0
Subtotal	**188,438**	**144,075**	**76.5**	**33,103**	**26,423**	**79.8**	**57,711**	**45,939**	**79.6**	**30,128**	**23,555**	**78.2**	**12,798**	**9,516**	**74.4**
Territory															
Guam	14	10	71.4	2	2	100.0	8	8	100.0	3	3	100.0	0	—	—
Puerto Rico	8,555	7,734	90.4	525	504	96.0	668	638	95.5	234	223	95.3	108	104	96.3
U.S. Virgin Islands	153	111	72.5	17	13	76.5	37	27	73.0	9	5	55.6	3	1	33.3
Subtotal	**8,722**	**7,855**	**90.1**	**544**	**519**	**95.4**	**713**	**673**	**94.4**	**246**	**231**	**93.9**	**111**	**105**	**94.6**
Total	**197,160**	**151,930**	**77.1**	**33,647**	**26,942**	**80.1**	**58,424**	**46,612**	**79.8**	**30,374**	**23,786**	**78.3**	**12,909**	**9,621**	**74.5**

Abbreviation: FPL, federal poverty level.
Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Note: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable.

Table 33b. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		0–100% FPL			101–138% FPL			139–250% FPL			251–400% FPL			>400% FPL		
		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Arizona	Phoenix	2,087	1,720	82.4	488	434	88.9	785	676	86.1	636	550	86.5	164	129	78.7
California	Los Angeles	7,277	5,494	75.5	1,222	997	81.6	2,212	1,834	82.9	1,193	958	80.3	402	318	79.1
	Oakland	1,162	740	63.7	126	82	65.1	151	107	70.9	42	21	50.0	24	18	75.0
	Orange County	353	259	73.4	77	61	79.2	173	138	79.8	87	72	82.8	21	16	76.2
	Riverside–San Bernardino	704	482	68.5	131	101	77.1	139	96	69.1	40	30	75.0	7	5	71.4
	Sacramento	1,225	1,024	83.6	288	249	86.5	401	349	87.0	202	168	83.2	88	73	83.0
	San Diego	3,643	2,557	70.2	420	288	68.6	543	384	70.7	148	107	72.3	54	30	55.6
	San Francisco	1,049	699	66.6	373	266	71.3	383	268	70.0	89	57	64.0	35	26	74.3
	San Jose	647	490	75.7	111	94	84.7	200	162	81.0	137	115	83.9	26	23	88.5
Colorado	Denver	3,181	2,380	74.8	225	179	79.6	358	262	73.2	242	179	74.0	81	52	64.2
Connecticut	Hartford	937	779	83.1	169	138	81.7	283	232	82.0	73	63	86.3	8	7	87.5
	New Haven	977	817	83.6	194	161	83.0	338	286	84.6	108	95	88.0	23	19	82.6
District of Columbia	Washington[a]	3,600	2,560	71.1	523	413	79.0	1,096	853	77.8	706	551	78.0	278	212	76.3
Florida	Ft. Lauderdale	3,360	2,476	73.7	320	248	77.5	594	472	79.5	325	265	81.5	19	7	36.8
	Jacksonville	1,241	928	74.8	218	181	83.0	369	307	83.2	249	206	82.7	20	15	75.0
	Miami	3,310	2,751	83.1	713	608	85.3	1,224	1,065	87.0	608	494	81.3	30	18	60.0
	Orlando	2,172	1,720	79.2	247	217	87.9	477	406	85.1	266	222	83.5	21	18	85.7
	Tampa–St. Petersburg	2,512	1,935	77.0	502	435	86.7	1,073	904	84.2	632	536	84.8	36	25	69.4
	West Palm Beach	789	637	80.7	105	90	85.7	211	169	80.1	85	68	80.0	8	6	75.0
Georgia	Atlanta	7,963	6,447	81.0	1,810	1,522	84.1	3,157	2,625	83.1	1,275	1,064	83.5	114	96	84.2
Illinois	Chicago	9,229	6,836	74.1	904	727	80.4	1,829	1,381	75.5	1,084	802	74.0	2,600	1,749	67.3
Indiana	Indianapolis	1,556	1,222	78.5	219	185	84.5	531	434	81.7	223	176	78.9	17	13	76.5
Louisiana	Baton Rouge	1,255	995	79.3	301	255	84.7	520	444	85.4	195	162	83.1	34	30	88.2
	New Orleans	2,057	1,569	76.3	535	391	73.1	664	525	79.1	222	178	80.2	53	43	81.1
Maryland	Baltimore	5,293	4,255	80.4	925	779	84.2	1,326	1,076	81.1	961	760	79.1	417	321	77.0
Massachusetts	Boston[a]	3,416	2,626	76.9	462	369	79.9	756	617	81.6	504	389	77.2	503	354	70.4
Michigan	Detroit	2,525	1,748	69.2	454	344	75.8	792	582	73.5	459	309	67.3	122	80	65.6
Minnesota	Minneapolis–St. Paul[a]	568	238	41.9	143	68	47.6	259	98	37.8	150	65	43.3	8	2	25.0
Missouri	Kansas City[a]	777	535	68.9	155	112	72.3	277	206	74.4	130	90	69.2	2	1	50.0
	St. Louis[a]	3,010	2,048	68.0	462	348	75.3	879	656	74.6	447	339	75.8	45	29	64.4
Nevada	Las Vegas[a]	1,010	610	60.4	184	123	66.8	469	327	69.7	398	287	72.1	31	14	45.2
New Jersey	Bergen–Passaic	738	624	84.6	149	142	95.3	255	229	89.8	89	76	85.4	32	30	93.8
	Jersey City	845	730	86.4	190	172	90.5	285	254	89.1	132	111	84.1	35	34	97.1
	Middlesex	673	561	83.4	110	101	91.8	207	168	81.2	107	89	83.2	30	23	76.7
	Newark	3,503	2,864	81.8	507	448	88.4	822	704	85.6	338	264	78.1	99	77	77.8
New York	Nassau–Suffolk	627	496	79.1	104	86	82.7	219	176	80.4	121	94	77.7	111	87	78.4
	New York	18,575	15,226	82.0	2,048	1,772	86.5	5,184	4,379	84.5	996	862	86.5	643	538	83.7
North Carolina	Charlotte[a]	1,606	1,232	76.7	269	208	77.3	688	534	77.6	318	253	79.6	67	59	88.1
Ohio	Cleveland	1,649	1,284	77.9	222	160	72.1	426	332	77.9	202	147	72.8	56	42	75.0
	Columbus	1,218	772	63.4	315	212	67.3	608	374	61.5	374	219	58.6	133	78	58.6
Oregon	Portland[a]	956	701	73.3	69	53	76.8	136	98	72.1	100	72	72.0	52	37	71.2
Pennsylvania	Philadelphia[a]	8,159	6,506	79.7	1,273	1,002	78.7	2,033	1,620	79.7	979	740	75.6	391	296	75.7
Puerto Rico	San Juan	5,045	4,537	89.9	278	269	96.8	342	330	96.5	98	95	96.9	29	29	100.0

Table 33b. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico *(cont.)*

		0–100% FPL			101–138% FPL			139–250% FPL			251–400% FPL			>400% FPL		
		Total	Retained		Total	Retained		Total	Retained		Total	Retained		Total	Retained	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Tennessee	Memphis[a]	2,285	1,937	84.8	260	221	85.0	517	449	86.8	397	334	84.1	7	6	85.7
	Nashville	2,464	1,931	78.4	280	215	76.8	650	518	79.7	758	610	80.5	219	163	74.4
Texas	Austin	844	590	69.9	90	76	84.4	237	185	78.1	142	107	75.4	31	15	48.4
	Dallas	5,503	4,343	78.9	1,265	1,057	83.6	1,565	1,303	83.3	516	433	83.9	112	94	83.9
	Ft. Worth	1,319	1,062	80.5	121	105	86.8	340	288	84.7	181	145	80.1	37	34	91.9
	Houston	7,444	5,407	72.6	1,197	884	73.9	1,831	1,311	71.6	534	345	64.6	85	47	55.3
	San Antonio	1,114	699	62.7	164	104	63.4	364	217	59.6	126	81	64.3	31	16	51.6
Virginia	Norfolk[a]	1,308	762	58.3	263	166	63.1	506	288	56.9	332	215	64.8	68	38	55.9
Washington	Seattle	1,626	1,166	71.7	265	197	74.3	405	303	74.8	482	335	69.5	352	241	68.5

Abbreviations: EMA, eligible metropolitan area; FPL, federal poverty level; TGA, transitional grant area.
Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for individual EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 34a. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and state, 2022—United States and 3 territories

	0–100% FPL			101–138% FPL			139–250% FPL			251–400% FPL			>400% FPL		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State															
Alabama	4,802	4,138	86.2	918	850	92.6	1,615	1,504	93.1	924	868	93.9	273	266	97.4
Alaska	233	202	86.7	15	15	100.0	31	28	90.3	12	11	91.7	5	5	100.0
Arizona	2,833	2,532	89.4	708	671	94.8	1,183	1,118	94.5	959	913	95.2	320	308	96.3
Arkansas	717	591	82.4	158	135	85.4	302	274	90.7	155	142	91.6	71	68	95.8
California	18,592	16,397	88.2	3,271	2,992	91.5	5,048	4,695	93.0	2,280	2,145	94.1	887	837	94.4
Colorado	3,120	2,862	91.7	353	336	95.2	457	443	96.9	323	310	96.0	201	194	96.5
Connecticut	1,916	1,781	93.0	373	358	96.0	626	595	95.0	184	174	94.6	33	31	93.9
Delaware	670	599	89.4	195	176	90.3	294	281	95.6	242	231	95.5	155	153	98.7
District of Columbia	2,103	1,845	87.7	191	174	91.1	367	327	89.1	202	183	90.6	48	44	91.7
Florida	16,616	14,349	86.4	2,982	2,764	92.7	5,730	5,252	91.7	3,305	3,111	94.1	314	289	92.0
Georgia	13,273	11,042	83.2	2,779	2,458	88.4	4,676	4,157	88.9	2,112	1,926	91.2	327	305	93.3
Hawaii	83	67	80.7	18	14	77.8	14	14	100.0	6	6	100.0	1	1	100.0
Idaho	289	273	94.5	98	96	98.0	203	200	98.5	139	138	99.3	154	154	100.0
Illinois	9,493	8,433	88.8	974	905	92.9	2,019	1,895	93.9	1,201	1,139	94.8	2,808	2,587	92.1
Indiana[a]	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Iowa	556	506	91.0	153	144	94.1	321	303	94.4	286	278	97.2	168	165	98.2
Kansas	303	260	85.8	43	37	86.0	75	71	94.7	78	73	93.6	52	51	98.1
Kentucky	2,184	1,913	87.6	420	405	96.4	778	729	93.7	470	457	97.2	217	211	97.2
Louisiana	3,801	3,288	86.5	915	832	90.9	1,173	1,066	90.9	401	376	93.8	98	90	91.8
Maine	259	242	93.4	53	53	100.0	87	85	97.7	44	43	97.7	11	11	100.0
Maryland	5,805	5,120	88.2	991	915	92.3	1,526	1,404	92.0	1,087	1,008	92.7	524	493	94.1
Massachusetts	4,229	3,965	93.8	481	464	96.5	812	779	95.9	494	477	96.6	475	466	98.1
Michigan	3,859	3,329	86.3	724	670	92.5	1,441	1,333	92.5	886	849	95.8	452	445	98.5
Minnesota	479	445	92.9	136	125	91.9	252	242	96.0	141	136	96.5	6	5	83.3
Mississippi	3,261	2,794	85.7	440	405	92.0	787	740	94.0	298	280	94.0	52	47	90.4
Missouri	2,621	2,319	88.5	376	344	91.5	750	693	92.4	354	334	94.4	29	26	89.7
Montana	142	132	93.0	48	47	97.9	83	78	94.0	57	56	98.2	39	39	100.0
Nebraska	360	315	87.5	94	92	97.9	213	203	95.3	111	108	97.3	9	9	100.0
Nevada	1,236	1,081	87.5	263	252	95.8	659	617	93.6	569	547	96.1	41	38	92.7
New Hampshire	136	128	94.1	49	48	98.0	97	95	97.9	88	86	97.7	37	36	97.3
New Jersey	7,245	6,377	88.0	1,269	1,186	93.5	2,087	1,932	92.6	901	838	93.0	288	267	92.7
New Mexico	539	457	84.8	136	130	95.6	269	257	95.5	230	221	96.1	161	157	97.5
New York	21,440	19,036	88.8	2,465	2,249	91.2	6,022	5,627	93.4	1,579	1,502	95.1	854	824	96.5
North Carolina	6,933	6,029	87.0	1,452	1,354	93.3	2,630	2,412	91.7	1,127	1,063	94.3	262	251	95.8
North Dakota	37	33	89.2	7	7	100.0	25	24	96.0	25	25	100.0	7	7	100.0
Ohio	4,351	3,842	88.3	730	677	92.7	1,401	1,322	94.4	819	780	95.2	371	361	97.3
Oklahoma	1,030	904	87.8	651	589	90.5	508	479	94.3	385	368	95.6	109	103	94.5
Oregon	932	813	87.2	68	61	89.7	137	132	96.4	106	99	93.4	62	58	93.5
Pennsylvania	10,841	9,667	89.2	1,979	1,832	92.6	3,133	2,925	93.4	1,768	1,696	95.9	895	872	97.4
Rhode Island	881	830	94.2	189	180	95.2	321	313	97.5	207	201	97.1	190	187	98.4
South Carolina	6,391	5,576	87.2	1,183	1,091	92.2	2,179	2,025	92.9	1,422	1,335	93.9	625	597	95.5
South Dakota	56	53	94.6	26	25	96.2	77	77	100.0	57	54	94.7	11	10	90.9
Tennessee	5,168	4,311	83.4	700	626	89.4	1,499	1,375	91.7	1,412	1,298	91.9	273	264	96.7
Texas	18,958	15,759	83.1	3,427	3,091	90.2	5,400	4,853	89.9	1,937	1,753	90.5	402	362	90.0

Table 34a. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and state, 2022—United States and 3 territories *(cont.)*

	0–100% FPL			101–138% FPL			139–250% FPL			251–400% FPL			>400% FPL		
		Viral suppression			Viral suppression			Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%	Total N	N	%
State															
Utah	486	458	94.2	75	74	98.7	218	214	98.2	114	111	97.4	33	33	100.0
Vermont	139	129	92.8	71	67	94.4	91	86	94.5	82	80	97.6	74	72	97.3
Virginia	3,052	2,625	86.0	694	644	92.8	1,417	1,298	91.6	1,002	938	93.6	370	355	95.9
Washington	1,931	1,701	88.1	329	307	93.3	568	533	93.8	591	561	94.9	385	378	98.2
West Virginia	636	530	83.3	196	188	95.9	251	243	96.8	97	95	97.9	14	13	92.9
Wisconsin	2,734	2,487	91.0	244	227	93.0	378	363	96.0	281	264	94.0	149	144	96.6
Wyoming	19	17	89.5	4	4	100.0	16	15	93.8	11	11	100.0	5	5	100.0
Subtotal	**197,770**	**172,582**	**87.3**	**34,114**	**31,386**	**92.0**	**60,246**	**55,726**	**92.5**	**31,561**	**29,698**	**94.1**	**13,347**	**12,694**	**95.1**
Territory															
Guam	15	9	60.0	2	2	100.0	9	9	100.0	3	3	100.0	0	—	—
Puerto Rico	8,694	7,936	91.3	537	503	93.7	682	662	97.1	234	223	95.3	109	107	98.2
U.S. Virgin Islands	172	145	84.3	19	18	94.7	44	41	93.2	14	13	92.9	4	4	100.0
Subtotal	**8,881**	**8,090**	**91.1**	**558**	**523**	**93.7**	**735**	**712**	**96.9**	**251**	**239**	**95.2**	**113**	**111**	**98.2**
Total	**206,651**	**180,672**	**87.4**	**34,672**	**31,909**	**92.0**	**60,981**	**56,438**	**92.6**	**31,812**	**29,937**	**94.1**	**13,460**	**12,805**	**95.1**

Abbreviation: FPL, federal poverty level.
Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Note: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable.

Table 34b. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		0–100% FPL			101–138% FPL			139–250% FPL			251–400% FPL			>400% FPL		
		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Arizona	Phoenix	2,236	1,994	89.2	513	479	93.4	835	773	92.6	681	639	93.8	172	163	94.8
California	Los Angeles	7,388	6,363	86.1	1,234	1,147	92.9	2,281	2,131	93.4	1,207	1,146	94.9	422	394	93.4
	Oakland	1,298	1,168	90.0	130	119	91.5	164	150	91.5	50	48	96.0	29	28	96.6
	Orange County	387	334	86.3	79	71	89.9	180	164	91.1	92	87	94.6	22	19	86.4
	Riverside–San Bernardino	800	676	84.5	157	134	85.4	162	130	80.2	43	35	81.4	13	8	61.5
	Sacramento	1,217	1,050	86.3	274	239	87.2	379	353	93.1	198	178	89.9	85	83	97.6
	San Diego	3,824	3,526	92.2	445	417	93.7	582	558	95.9	156	151	96.8	57	57	100.0
	San Francisco	1,080	937	86.8	364	323	88.7	390	352	90.3	100	93	93.0	35	34	97.1
	San Jose	707	670	94.8	124	119	96.0	219	210	95.9	155	150	96.8	27	27	100.0
Colorado	Denver	3,098	2,824	91.2	228	218	95.6	359	347	96.7	242	233	96.3	83	77	92.8
Connecticut	Hartford	894	834	93.3	147	141	95.9	268	251	93.7	70	66	94.3	8	6	75.0
	New Haven	1,036	953	92.0	210	203	96.7	349	337	96.6	112	106	94.6	23	23	100.0
District of Columbia	Washington[a]	3,871	3,402	87.9	559	519	92.8	1,183	1,090	92.1	764	706	92.4	297	285	96.0
Florida	Ft. Lauderdale	3,563	3,105	87.1	346	324	93.6	637	576	90.4	342	323	94.4	20	17	85.0
	Jacksonville	1,324	1,125	85.0	234	217	92.7	390	351	90.0	267	250	93.6	20	20	100.0
	Miami	3,532	3,024	85.6	753	684	90.8	1,281	1,167	91.1	640	588	91.9	28	25	89.3
	Orlando	2,314	2,059	89.0	256	249	97.3	494	464	93.9	290	274	94.5	21	20	95.2
	Tampa–St. Petersburg	2,646	2,276	86.0	529	497	94.0	1,120	1,047	93.5	656	623	95.0	36	31	86.1
	West Palm Beach	787	682	86.7	110	101	91.8	205	180	87.8	81	76	93.8	9	8	88.9
Georgia	Atlanta	8,694	7,189	82.7	1,889	1,646	87.1	3,323	2,893	87.1	1,364	1,220	89.4	121	114	94.2
Illinois	Chicago	9,331	8,285	88.8	905	841	92.9	1,872	1,765	94.3	1,111	1,055	95.0	2,771	2,551	92.1
Indiana	Indianapolis	1,680	1,410	83.9	230	214	93.0	554	516	93.1	235	220	93.6	17	17	100.0
Louisiana	Baton Rouge	1,321	1,155	87.4	291	276	94.8	532	496	93.2	191	182	95.3	35	33	94.3
	New Orleans	2,158	1,859	86.1	554	494	89.2	697	630	90.4	225	210	93.3	51	46	90.2
Maryland	Baltimore	5,311	4,690	88.3	920	848	92.2	1,336	1,229	92.0	951	886	93.2	421	392	93.1
Massachusetts	Boston[a]	3,409	3,186	93.5	458	440	96.1	742	710	95.7	478	459	96.0	455	446	98.0
Michigan	Detroit	2,828	2,369	83.8	479	434	90.6	879	797	90.7	501	472	94.2	133	128	96.2
Minnesota	Minneapolis–St. Paul[a]	563	520	92.4	144	133	92.4	258	248	96.1	144	139	96.5	7	6	85.7
Missouri	Kansas City[a]	827	714	86.3	158	144	91.1	289	270	93.4	135	124	91.9	2	2	100.0
	St. Louis[a]	3,225	2,824	87.6	484	447	92.4	912	846	92.8	472	449	95.1	49	43	87.8
Nevada	Las Vegas[a]	1,145	999	87.2	208	201	96.6	528	498	94.3	436	416	95.4	33	31	93.9
New Jersey	Bergen–Passaic	794	704	88.7	155	144	92.9	259	249	96.1	93	84	90.3	35	31	88.6
	Jersey City	886	792	89.4	193	186	96.4	295	275	93.2	136	130	95.6	36	34	94.4
	Middlesex	688	622	90.4	113	102	90.3	216	205	94.9	110	107	97.3	30	26	86.7
	Newark	3,767	3,273	86.9	539	505	93.7	878	795	90.5	345	323	93.6	105	96	91.4
New York	Nassau–Suffolk	678	626	92.3	115	107	93.0	231	226	97.8	121	116	95.9	116	114	98.3
	New York	19,098	16,859	88.3	2,088	1,891	90.6	5,353	4,993	93.3	1,038	985	94.9	648	622	96.0
North Carolina	Charlotte[a]	1,800	1,540	85.6	290	273	94.1	760	686	90.3	343	311	90.7	67	63	94.0
Ohio	Cleveland	1,739	1,548	89.0	221	204	92.3	455	428	94.1	218	207	95.0	60	58	96.7
	Columbus	1,285	1,148	89.3	325	309	95.1	619	587	94.8	403	379	94.0	140	137	97.9
Oregon	Portland[a]	1,021	892	87.4	74	67	90.5	147	139	94.6	111	104	93.7	63	59	93.7
Pennsylvania	Philadelphia[a]	8,296	7,322	88.3	1,317	1,213	92.1	2,048	1,895	92.5	993	937	94.4	414	396	95.7
Puerto Rico	San Juan	5,166	4,680	90.6	281	264	94.0	352	339	96.3	98	93	94.9	28	28	100.0

Table 34b. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by federal poverty level and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico *(cont.)*

		0–100% FPL			101–138% FPL			139–250% FPL			251–400% FPL			>400% FPL		
		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression		Total	Viral suppression	
State/Territory	EMA/TGA	N	N	%	N	N	%	N	N	%	N	N	%	N	N	%
Tennessee	Memphis[a]	2,401	1,839	76.6	268	223	83.2	541	459	84.8	417	355	85.1	7	7	100.0
	Nashville	2,594	2,291	88.3	292	270	92.5	708	664	93.8	811	765	94.3	241	232	96.3
Texas	Austin	939	809	86.2	99	88	88.9	257	239	93.0	154	146	94.8	34	32	94.1
	Dallas	5,633	4,702	83.5	1,287	1,173	91.1	1,592	1,437	90.3	520	478	91.9	91	84	92.3
	Ft. Worth	1,449	1,202	83.0	133	119	89.5	361	306	84.8	193	168	87.0	38	35	92.1
	Houston	8,237	6,814	82.7	1,303	1,175	90.2	2,020	1,820	90.1	582	523	89.9	93	82	88.2
	San Antonio	1,195	968	81.0	176	153	86.9	368	332	90.2	144	131	91.0	33	29	87.9
Virginia	Norfolk[a]	1,399	1,169	83.6	278	252	90.6	526	476	90.5	354	325	91.8	70	66	94.3
Washington	Seattle	1,767	1,553	87.9	269	251	93.3	445	425	95.5	519	497	95.8	368	362	98.4

Abbreviations: EMA, eligible metropolitan area; FPL, federal poverty level; TGA, transitional grant area.
Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for individual EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 35a. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by housing status and state, 2022—United States and 3 territories

	Stable			Temporary			Unstable		
		Retained			Retained			Retained	
	Total N	N	%	Total N	N	%	Total N	N	%
State									
Alabama	7,858	5,756	73.3	455	346	76.0	228	154	67.5
Alaska	278	191	68.7	9	8	88.9	30	22	73.3
Arizona	5,254	4,541	86.4	111	93	83.8	377	299	79.3
Arkansas	1,279	994	77.7	35	22	62.9	10	6	60.0
California	24,668	18,976	76.9	2,136	1,542	72.2	2,281	1,455	63.8
Colorado	3,157	2,449	77.6	571	409	71.6	188	131	69.7
Connecticut	2,876	2,419	84.1	137	100	73.0	126	97	77.0
Delaware	1,463	1,114	76.1	29	17	58.6	36	23	63.9
District of Columbia	2,384	1,669	70.0	37	24	64.9	307	191	62.2
Florida	25,518	20,472	80.2	1,891	1,386	73.3	1,064	729	68.5
Georgia	20,402	17,049	83.6	541	398	73.6	756	588	77.8
Hawaii	110	1	0.9	0	—	—	14	0	0.0
Idaho	737	542	73.5	42	27	64.3	47	15	31.9
Illinois	14,954	10,942	73.2	1,158	741	64.0	557	369	66.2
Indiana[a]	—	—	—	—	—	—	—	—	—
Iowa	1,397	1,172	83.9	42	31	73.8	45	31	68.9
Kansas	484	395	81.6	14	12	85.7	24	16	66.7
Kentucky	3,485	2,636	75.6	199	128	64.3	151	82	54.3
Louisiana	5,604	4,445	79.3	318	217	68.2	170	106	62.4
Maine	456	363	79.6	27	23	85.2	23	18	78.3
Maryland	9,526	7,630	80.1	169	139	82.2	148	113	76.4
Massachusetts	5,259	3,959	75.3	342	271	79.2	171	132	77.2
Michigan	6,444	4,529	70.3	122	75	61.5	141	85	60.3
Minnesota	900	375	41.7	97	34	35.1	36	11	30.6
Mississippi	4,632	3,686	79.6	46	26	56.5	64	39	60.9
Missouri	3,472	2,363	68.1	257	177	68.9	178	108	60.7
Montana	325	251	77.2	5	5	100.0	24	15	62.5
Nebraska	670	499	74.5	18	14	77.8	43	27	62.8
Nevada	2,211	1,582	71.6	150	87	58.0	169	95	56.2
New Hampshire	676	647	95.7	42	41	97.6	30	30	100.0
New Jersey	9,360	7,833	83.7	1,543	1,251	81.1	261	189	72.4
New Mexico	1,166	975	83.6	75	45	60.0	47	32	68.1
New York	28,377	23,612	83.2	2,086	1,604	76.9	1,017	812	79.8
North Carolina	11,213	8,893	79.3	242	165	68.2	241	159	66.0
North Dakota	91	75	82.4	4	4	100.0	1	0	0.0
Ohio	7,086	4,843	68.3	385	237	61.6	328	208	63.4
Oklahoma	2,145	1,541	71.8	85	48	56.5	78	48	61.5
Oregon	1,122	816	72.7	33	24	72.7	70	47	67.1
Pennsylvania	16,855	13,615	80.8	836	631	75.5	551	415	75.3
Rhode Island	1,553	1,234	79.5	155	117	75.5	60	44	73.3
South Carolina	10,717	8,725	81.4	397	312	78.6	87	70	80.5
South Dakota	191	134	70.2	11	7	63.6	2	2	100.0
Tennessee	7,790	6,218	79.8	485	359	74.0	262	196	74.8
Texas	21,823	15,857	72.7	3,480	2,501	71.9	3,148	2,609	82.9
Utah	1,018	620	60.9	72	38	52.8	31	20	64.5
Vermont	427	326	76.3	10	7	70.0	10	8	80.0
Virginia	5,911	4,299	72.7	117	81	69.2	123	80	65.0
Washington	2,934	2,149	73.2	210	143	68.1	282	209	74.1
West Virginia	1,092	729	66.8	53	22	41.5	66	30	45.5
Wisconsin	3,164	2,348	74.2	163	102	62.6	321	207	64.5
Wyoming	39	12	30.8	6	3	50.0	1	0	0.0
Subtotal	**290,553**	**226,501**	**78.0**	**19,448**	**14,094**	**72.5**	**14,425**	**10,372**	**71.9**
Territory									
Guam	23	19	82.6	0	—	—	4	4	100.0
Puerto Rico	9,959	9,101	91.4	152	126	82.9	35	29	82.9
U.S. Virgin Islands	214	153	71.5	1	0	0.0	4	4	100.0
Subtotal	**10,196**	**9,273**	**90.9**	**153**	**126**	**82.4**	**43**	**37**	**86.0**
Total	**300,749**	**235,774**	**78.4**	**19,601**	**14,220**	**72.5**	**14,468**	**10,409**	**71.9**

Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Note: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable.

Table 35b. Retention in care among Ryan White HIV/AIDS Program clients (non-ADAP), by housing status and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		Stable			Temporary			Unstable		
			Retained			Retained			Retained	
State/Territory	EMA/TGA	Total N	N	%	Total N	N	%	Total N	N	%
Arizona	Phoenix	3,756	3,198	85.1	99	82	82.8	306	231	75.5
California	Los Angeles	11,108	8,830	79.5	279	220	78.9	986	616	62.5
	Oakland	1,209	769	63.6	133	87	65.4	165	112	67.9
	Orange County	640	503	78.6	43	27	62.8	35	20	57.1
	Riverside–San Bernardino	903	662	73.3	48	24	50.0	77	31	40.3
	Sacramento	1,656	1,441	87.0	204	171	83.8	291	214	73.5
	San Diego	3,766	2,639	70.1	642	486	75.7	461	272	59.0
	San Francisco	1,313	909	69.2	408	263	64.5	195	133	68.2
	San Jose	865	693	80.1	175	128	73.1	77	60	77.9
Colorado	Denver	2,690	2,114	78.6	616	440	71.4	210	140	66.7
Connecticut	Hartford	1,336	1,122	84.0	67	46	68.7	82	61	74.4
	New Haven	1,500	1,270	84.7	89	65	73.0	54	43	79.6
District of Columbia	Washington[a]	5,678	4,252	74.9	122	84	68.9	406	255	62.8
Florida	Ft. Lauderdale	3,450	2,581	74.8	1,008	773	76.7	164	115	70.1
	Jacksonville	1,879	1,486	79.1	119	80	67.2	98	71	72.4
	Miami	5,959	4,985	83.7	180	145	80.6	260	196	75.4
	Orlando	2,755	2,265	82.2	238	184	77.3	189	133	70.4
	Tampa–St. Petersburg	4,452	3,688	82.8	345	220	63.8	298	203	68.1
	West Palm Beach	1,006	831	82.6	116	86	74.1	76	53	69.7
Georgia	Atlanta	13,085	10,775	82.3	446	343	76.9	709	559	78.8
Illinois	Chicago	14,454	10,627	73.5	1,169	753	64.4	582	387	66.5
Indiana	Indianapolis	2,236	1,808	80.9	137	111	81.0	173	111	64.2
Louisiana	Baton Rouge	2,185	1,804	82.6	65	47	72.3	40	26	65.0
	New Orleans	3,148	2,460	78.1	205	134	65.4	122	72	59.0
Maryland	Baltimore	8,630	6,970	80.8	152	126	82.9	150	115	76.7
Massachusetts	Boston[a]	4,398	3,453	78.5	391	312	79.8	196	158	80.6
Michigan	Detroit	4,186	2,966	70.9	83	48	57.8	92	53	57.6
Minnesota	Minneapolis–St. Paul[a]	956	408	42.7	119	45	37.8	53	18	34.0
Missouri	Kansas City[a]	1,148	822	71.6	100	62	62.0	93	60	64.5
	St. Louis[a]	4,292	3,059	71.3	311	210	67.5	240	151	62.9
Nevada	Las Vegas[a]	1,789	1,192	66.6	153	94	61.4	150	75	50.0
New Jersey	Bergen–Passaic	1,193	1,041	87.3	35	28	80.0	35	32	91.4
	Jersey City	1,416	1,249	88.2	35	23	65.7	36	29	80.6
	Middlesex	978	827	84.6	71	50	70.4	78	65	83.3
	Newark	3,666	3,053	83.3	1,454	1,196	82.3	150	108	72.0
New York	Nassau–Suffolk	1,079	855	79.2	91	74	81.3	12	10	83.3
	New York	24,795	20,706	83.5	1,802	1,390	77.1	1,026	815	79.4
North Carolina	Charlotte[a]	2,840	2,203	77.6	64	51	79.7	45	32	71.1
Ohio	Cleveland	2,303	1,778	77.2	173	126	72.8	79	61	77.2
	Columbus	2,986	1,770	59.3	115	72	62.6	70	44	62.9
Oregon	Portland[a]	1,180	863	73.1	50	35	70.0	96	67	69.8
Pennsylvania	Philadelphia[a]	11,836	9,383	79.3	540	417	77.2	479	350	73.1
Puerto Rico	San Juan	5,697	5,186	91.0	122	100	82.0	29	27	93.1
Tennessee	Memphis[a]	3,293	2,811	85.4	74	60	81.1	104	80	76.9
	Nashville	3,724	2,947	79.1	480	362	75.4	167	128	76.6
Texas	Austin	1,092	780	71.4	206	155	75.2	81	51	63.0
	Dallas	4,399	3,456	78.6	2,100	1,569	74.7	2,662	2,355	88.5
	Ft. Worth	1,745	1,444	82.8	161	119	73.9	99	75	75.8
	Houston	9,830	7,190	73.1	910	614	67.5	374	208	55.6
	San Antonio	1,635	1,010	61.8	128	89	69.5	86	52	60.5
Virginia	Norfolk[a]	2,382	1,406	59.0	49	32	65.3	46	31	67.4
Washington	Seattle	2,558	1,843	72.0	172	117	68.0	291	215	73.9

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Retention in care was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit by September 1 of the measurement year, with a second visit at least 90 days after.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for individual EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

Table 36a. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by housing status and state, 2022—United States and 3 territories

	Stable			Temporary			Unstable		
		Viral suppression			Viral suppression			Viral suppression	
	Total N	N	%	Total N	N	%	Total N	N	%
State									
Alabama	7,898	7,144	90.5	511	397	77.7	235	195	83.0
Alaska	279	254	91.0	8	7	87.5	32	21	65.6
Arizona	5,490	5,142	93.7	129	107	82.9	401	307	76.6
Arkansas	1,342	1,173	87.4	46	28	60.9	15	9	60.0
California	25,466	23,329	91.6	2,258	1,959	86.8	2,446	1,885	77.1
Colorado	3,213	3,049	94.9	566	517	91.3	198	143	72.2
Connecticut	2,871	2,711	94.4	143	128	89.5	134	115	85.8
Delaware	1,513	1,407	93.0	37	32	86.5	35	27	77.1
District of Columbia	2,545	2,257	88.7	46	39	84.8	321	275	85.7
Florida	26,610	23,971	90.1	2,060	1,714	83.2	1,173	854	72.8
Georgia	21,699	18,781	86.6	627	459	73.2	855	640	74.9
Hawaii	108	91	84.3	0	—	—	14	11	78.6
Idaho	795	780	98.1	54	50	92.6	54	51	94.4
Illinois	15,291	13,986	91.5	1,189	1,019	85.7	552	411	74.5
Indiana[a]	—	—	—	—	—	—	—	—	—
Iowa	1,453	1,382	95.1	48	43	89.6	45	32	71.1
Kansas	509	459	90.2	14	13	92.9	28	20	71.4
Kentucky	3,710	3,438	92.7	225	189	84.0	177	126	71.2
Louisiana	5,745	5,128	89.3	351	280	79.8	196	139	70.9
Maine	457	441	96.5	27	23	85.2	19	17	89.5
Maryland	9,629	8,701	90.4	178	140	78.7	150	125	83.3
Massachusetts	5,386	5,117	95.0	368	338	91.8	169	144	85.2
Michigan	7,137	6,461	90.5	137	110	80.3	173	131	75.7
Minnesota	884	840	95.0	96	85	88.5	34	28	82.4
Mississippi	4,901	4,342	88.6	55	40	72.7	74	55	74.3
Missouri	3,646	3,337	91.5	274	229	83.6	206	147	71.4
Montana	339	328	96.8	4	2	50.0	24	20	83.3
Nebraska	714	667	93.4	25	22	88.0	49	39	79.6
Nevada	2,404	2,258	93.9	176	140	79.5	183	132	72.1
New Hampshire	644	623	96.7	40	38	95.0	31	27	87.1
New Jersey	9,880	8,992	91.0	1,684	1,443	85.7	289	220	76.1
New Mexico	1,207	1,128	93.5	81	69	85.2	57	28	49.1
New York	29,172	26,637	91.3	2,241	1,899	84.7	1,055	825	78.2
North Carolina	11,987	10,822	90.3	300	244	81.3	285	204	71.6
North Dakota	96	92	95.8	4	3	75.0	1	1	100.0
Ohio	7,464	6,884	92.2	426	341	80.0	346	268	77.5
Oklahoma	2,619	2,419	92.4	120	95	79.2	100	76	76.0
Oregon	1,206	1,092	90.5	37	31	83.8	72	47	65.3
Pennsylvania	17,093	15,734	92.0	873	740	84.8	577	452	78.3
Rhode Island	1,566	1,509	96.4	161	148	91.9	64	57	89.1
South Carolina	11,315	10,232	90.4	427	357	83.6	91	64	70.3
South Dakota	213	207	97.2	12	10	83.3	2	2	100.0
Tennessee	8,256	7,248	87.8	517	437	84.5	286	195	68.2
Texas	23,651	20,403	86.3	3,798	3,132	82.5	3,138	2,630	83.8
Utah	868	839	96.7	65	63	96.9	31	26	83.9
Vermont	434	416	95.9	10	8	80.0	13	10	76.9
Virginia	6,281	5,664	90.2	125	102	81.6	135	101	74.8
Washington	3,132	2,909	92.9	225	200	88.9	316	251	79.4
West Virginia	1,193	1,093	91.6	53	36	67.9	72	49	68.1
Wisconsin	3,354	3,122	93.1	178	159	89.3	333	285	85.6
Wyoming	48	46	95.8	6	5	83.3	1	1	100.0
Subtotal	**303,713**	**275,085**	**90.6**	**21,035**	**17,670**	**84.0**	**15,287**	**11,918**	**78.0**
Territory									
Guam	25	21	84.0	0	—	—	4	2	50.0
Puerto Rico	10,123	9,319	92.1	153	137	89.5	36	27	75.0
U.S. Virgin Islands	248	218	87.9	1	0	0.0	4	3	75.0
Subtotal	**10,396**	**9,558**	**91.9**	**154**	**137**	**89.0**	**44**	**32**	**72.7**
Total	**314,109**	**284,643**	**90.6**	**21,189**	**17,807**	**84.0**	**15,331**	**11,950**	**77.9**

Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Note: Data are based on provider location. Clients receiving services in multiple states were not included in state-specific totals or column subtotals and totals.
[a] 2022 data for Indiana are unavailable.

Table 36b. Viral suppression among Ryan White HIV/AIDS Program clients (non-ADAP), by housing status and eligible metropolitan area and transitional grant area, 2022—United States and Puerto Rico

		Stable			Temporary			Unstable		
			Viral suppression			Viral suppression			Viral suppression	
State/Territory	EMA/TGA	Total N	N	%	Total N	N	%	Total N	N	%
Arizona	Phoenix	3,984	3,688	92.6	120	101	84.2	345	268	77.7
California	Los Angeles	11,225	10,179	90.7	285	235	82.5	1,068	816	76.4
	Oakland	1,338	1,228	91.8	154	131	85.1	182	156	85.7
	Orange County	669	613	91.6	53	43	81.1	38	22	57.9
	Riverside–San Bernardino	1,023	876	85.6	59	51	86.4	99	62	62.6
	Sacramento	1,631	1,492	91.5	201	164	81.6	274	204	74.5
	San Diego	3,953	3,736	94.5	691	631	91.3	493	413	83.8
	San Francisco	1,336	1,222	91.5	409	348	85.1	201	157	78.1
	San Jose	946	912	96.4	191	183	95.8	91	78	85.7
Colorado	Denver	2,696	2,540	94.2	615	559	90.9	222	164	73.9
Connecticut	Hartford	1,258	1,187	94.4	60	52	86.7	83	72	86.7
	New Haven	1,570	1,483	94.5	102	90	88.2	60	51	85.0
District of Columbia	Washington[a]	6,111	5,521	90.3	138	120	87.0	430	363	84.4
Florida	Ft. Lauderdale	3,649	3,273	89.7	1,087	943	86.8	183	135	73.8
	Jacksonville	1,987	1,773	89.2	138	104	75.4	109	86	78.9
	Miami	6,259	5,558	88.8	211	170	80.6	281	213	75.8
	Orlando	2,896	2,676	92.4	262	219	83.6	215	169	78.6
	Tampa–St. Petersburg	4,646	4,245	91.4	364	290	79.7	326	234	71.8
	West Palm Beach	995	882	88.6	122	101	82.8	75	64	85.3
Georgia	Atlanta	13,987	11,981	85.7	523	382	73.0	795	617	77.6
Illinois	Chicago	14,752	13,494	91.5	1,201	1,027	85.5	574	433	75.4
Indiana	Indianapolis	2,352	2,108	89.6	170	140	82.4	195	130	66.7
Louisiana	Baton Rouge	2,268	2,057	90.7	72	63	87.5	40	31	77.5
	New Orleans	3,274	2,917	89.1	233	182	78.1	149	105	70.5
Maryland	Baltimore	8,651	7,819	90.4	161	126	78.3	144	119	82.6
Massachusetts	Boston[a]	4,375	4,149	94.8	412	381	92.5	192	164	85.4
Michigan	Detroit	4,629	4,066	87.8	87	60	69.0	113	81	71.7
Minnesota	Minneapolis–St. Paul[a]	945	896	94.8	115	102	88.7	56	48	85.7
Missouri	Kansas City[a]	1,204	1,095	90.9	103	86	83.5	104	73	70.2
	St. Louis[a]	4,523	4,124	91.2	339	279	82.3	280	206	73.6
Nevada	Las Vegas[a]	1,991	1,864	93.6	181	153	84.5	179	128	71.5
New Jersey	Bergen–Passaic	1,266	1,157	91.4	34	28	82.4	37	28	75.7
	Jersey City	1,471	1,361	92.5	37	30	81.1	38	26	68.4
	Middlesex	999	923	92.4	75	67	89.3	83	72	86.7
	Newark	3,883	3,508	90.3	1,585	1,365	86.1	167	120	71.9
New York	Nassau–Suffolk	1,145	1,084	94.7	100	91	91.0	16	14	87.5
	New York	25,449	23,128	90.9	1,928	1,619	84.0	1,057	820	77.6
North Carolina	Charlotte[a]	3,120	2,768	88.7	77	64	83.1	64	41	64.1
Ohio	Cleveland	2,422	2,221	91.7	187	154	82.4	84	70	83.3
	Columbus	3,141	2,907	92.6	125	106	84.8	72	60	83.3
Oregon	Portland[a]	1,268	1,150	90.7	59	49	83.1	99	69	69.7
Pennsylvania	Philadelphia[a]	12,034	10,945	91.0	561	458	81.6	511	395	77.3
Puerto Rico	San Juan	5,831	5,325	91.3	120	107	89.2	30	24	80.0
Tennessee	Memphis[a]	3,447	2,753	79.9	80	63	78.8	114	73	64.0
	Nashville	3,955	3,644	92.1	508	435	85.6	183	143	78.1
Texas	Austin	1,204	1,077	89.5	241	208	86.3	99	76	76.8
	Dallas	4,550	3,924	86.2	2,211	1,863	84.3	2,570	2,257	87.8
	Ft. Worth	1,895	1,597	84.3	184	161	87.5	103	77	74.8
	Houston	10,802	9,345	86.5	1,039	821	79.0	426	274	64.3
	San Antonio	1,756	1,481	84.3	150	123	82.0	98	69	70.4
Virginia	Norfolk[a]	2,519	2,203	87.5	53	47	88.7	55	38	69.1
Washington	Seattle	2,729	2,536	92.9	187	169	90.4	319	261	81.8

Abbreviations: EMA, eligible metropolitan area; TGA, transitional grant area.
Viral suppression was based on data for people with HIV who had at least 1 outpatient ambulatory health services visit during the measurement year and whose most recent viral load test result was <200 copies/mL.
Notes: EMAs/TGAs are listed according to the primary state in which the jurisdiction resides. EMA/TGA delineations are based on provider location.
Data shown for individual EMAs and TGAs are not mutually exclusive; clients may have received services from providers in multiple EMAs and/or TGAs.
[a] The EMA/TGA service area crosses state boundaries. See Technical Notes for more information.

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Weddle Declaration
Exhibit D

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Health Communication in an Era of Disinformation: Perceived Source Credibility Among Transgender and Gender Diverse Individuals

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Abstract

This study examines perceived source credibility of health information in a moment of TGD health disinformation. Through thematic analysis of in-depth interviews with thirty transgender and gender diverse (TGD) individuals, findings suggest health information is marred by anti-TGD legislation, a sociopolitical force that bleeds into health information spaces. Disinformation and TGD health communication are intertwined in complex ways, whereby disinformation can undermine trust in healthcare institutions, lead to harmful behaviors, and contribute to the spread of diseases. Health communication practitioners need to center the safety and humanity of TGD people, addressing TGD health disinformation.

Keywords

transgender; gender diverse; health information seeking; source credibility; disinformation

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Introduction

Health communication plays a crucial role in ensuring transgender and gender diverse (TGD) populations have access to accurate, inclusive, and affirming information about their health needs, rights, and available resources. Transgender is a term used to describe individuals whose gender identity differs from the sex they were assigned at birth. Transgender individuals may undergo social, medical, or legal transition to align their gender expression with their gender identity. Gender diverse is a broader term that encompasses individuals whose gender identity or expression differs from societal expectations or norms associated with their assigned sex at birth. This includes transgender individuals as well as individuals who identify as non-binary, genderqueer, genderfluid, or any other non-conforming gender identity. The purpose of this research is to examine health information seeking and perceived source credibility among TGD populations.

Health disparities in TGD communities are largely attributed to structural and social barriers individuals face in accessing health information and resources (Augustaitis et al., 2021). Health information for TGD populations is scarce because of a systematic erasure of TGD health data (Nolan et al., 2019), avoidance of non-gender-transition-related medicine and health by TGD people due to the perception of discrimination (Kcomt et al., 2020), and broader institutional limitations of healthcare access for TGD people (Feldman et al., 2021). Extant research underscores that TGD populations often avoid visiting healthcare facilities citing reasons such as hostile environments (Kcomt et al., 2021), traumatic experiences at the medical facility (Jaffee et al., 2016), as well as structural barriers such as medical costs and insurance issues (Bakko & Kattari, 2020). Furthermore, social and institutional stigma against TGD individuals has led to the exclusion of TGD care in medical training, which contributes to limited knowledge and experience in the TGD health domain (Meyer et al., 2020), resulting in provider ambivalence and uncertainty when interacting with TGD patients (Dolan et al., 2020; Marshall-Paquin et al., 2023).

TGD individuals may face challenges in accessing comprehensive and accurate health information tailored to their specific needs. Much of the available health information may not address their unique healthcare requirements (Pohjanen & Kortelainen, 2016), leading to gaps in knowledge and understanding about TGD health issues (Korpaisarn & Safer, 2018). Health information resources often lack cultural competence, meaning they may not be sensitive to the needs, identities, and experiences of TGD individuals. This can result in misunderstandings, miscommunication, and ultimately, inadequate care. Without access to accurate health information, TGD individuals may be more vulnerable to misinformation and harmful practices (Billard, 2024; Lepore et al., 2022). Misinformation and a lack of accurate and affirming health information (Augustaitis et al., 2021) can contribute to mental health disparities within TGD communities (Scheim et al., 2020), and feelings of isolation, anxiety, and depression can arise when individuals feel that their health needs are not understood or supported (Hughto et al., 2021).

Addressing health disparities in TGD communities requires efforts to ensure that health messages are inclusive, accurate, and readily accessible. Health messages are conveyed through a variety of communication methods including traditional media (e.g., television,

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radio, print media), digital media (e.g., websites, social media, blogs and email newsletters), mobile applications, community outreach and events (e.g., health fairs, workshops, seminars), interpersonal communication (e.g., peer-to-peer communication, consultations with practitioners) and campaigns (e.g., public service announcements, pharmaceutical advertising). Research in health communication has generated evidence that demonstrates strategic health communication can reduce health risks and incidence of disease and improve quality of life (Kreps & Neuhauser, 2015). While health communication is an important component of addressing TGD health inequities, there is a dearth of research attending to the experiences and perspectives of TGD populations (Combs et al., 2018), and a lack of research on health information seeking and source credibility among priority populations (Jackson et al., 2019). Source credibility and health information seeking are vital to ensure TGD populations receive accurate, safe, empowering, and affirming healthcare that meets their unique needs and identities.Top of Form Therefore, through in-depth interviews with 30 TGD people, we examine health information seeking and source credibility pertaining among TGD populations.

Literature Review

Health Information Seeking—Health information seeking has been long studied among non-TGD populations, and research has examined health information needs (Chiet et al., 2020; Shi & Luo, 2020; Pian et al., 2020) and the influencers of health information seeking behavior (Chang & Huang, 2020; Rowley et al., 2017) and source selection process (Zhang, 2014; Song et al., 2021). Populations may seek health information online via search engines, provider websites, and online health communities, and by utilizing online networks through social media platforms (Wang et al., 2021) Online health communities can fill information gaps, which may be useful for individuals isolated from others. Among TGD populations, health information is frequently exchanged in online communities, and users post and/or consume health information on social media platforms and user-generated information sites (see Evans et al., 2017; Hawkins & Gieseking, 2017; Karami et al., 2018; Selkie et al., 2019). Importantly, despite the wealth of health information online for TGD people, individuals must vet content on social media channels for relevance and quality (Morse et al., 2023).

Health information seeking behavior is influenced by a variety of factors, many of which have been studied extensively among non-TGD populations. Demographics play a role in how individuals seek health information. For example, younger people may be more likely to use the internet for health information, while older adults may rely more on traditional sources like healthcare providers (Miller & Bell, 2012). Perceived health status may impact online health information seeking, whereby individuals who perceive themselves as being in poor health are more likely to seek health information to address their concerns (Alwi & Murad, 2018). Availability of resources such as internet access, libraries, healthcare providers, and health insurance can influence health information seeking behavior. Lack of access to these resources may limit an individual's ability to seek out information (Kang et al., 2022). Additionally, trust in the source of health information is critical (Rowley et al., 2017). Non-TGD individuals are more likely to seek information from sources they perceive as credible, such as healthcare providers, government agencies, and

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reputable websites. However, health information seeking and source credibility among TGD populations remains underexamined.

Source Credibility—Source credibility is crucial when seeking and evaluating health information, and several factors influence perceptions of credibility. Individuals are more likely to perceive information as credible if it comes from sources perceived as knowledgeable or expert in the field (Eastin, 2001). For health information, this often includes healthcare professionals, researchers, and reputable health organizations (Kivits, 2006). The reputation of the source significantly affects credibility and perceptions; therefore, established institutions, organizations, and well-known experts are generally considered more credible than unfamiliar or obscure sources (Metzger & Flanagin, 2015). Over time, consistency of information may enhance credibility with sources that provide accurate, evidence-based information may be perceived as more credible than those that frequently make errors or contradict themselves (Stella, 2003). Recommendations from healthcare professionals or reputable institutions lend credibility to health information sources (Zhao et al., 2024). While scholars have long been examining factors that influence source credibility of health information among non-TGD populations, sexual and gender minority populations have historically not been studied.

A growing body of research analyzes the factors influencing LGBTQ+ individuals' health information seeking. Certain demographic factors are associated with online health information seeking. For example, LGBTQ participants identifying as Hispanic/Latina were less likely to seek health information online than whites (Gerke et al., 2020). Psychological factors may influence health information seeking among LGBTQ+ individuals, including sexual self-efficacy, the perceived bias of health care providers, and perceived control, with sexual health information from significant others as the best predictor of one's sexual self-efficacy (Charest et al., 2016). LGBQ individuals who perceived provider bias were significantly more likely to seek health information on the internet and from friends and family members who were not medical professionals (Jabson et al., 2017). Physical and behavioral health information related to STDs was reported to be the most frequently sought information, with STI/STD-related topics as the principal focus of LGBTQ+ health information seeking literature (Jia et al., 2022), leading underexamined source credibility of preventive health information among this population. We understand preventive health information as knowledge intended to prevent illness, disease, or injury rather than treating them once they occur. This information contains proactive steps aimed at maintaining or improving health and well-being that can encompass a variety of activities, including screenings, vaccinations, and education about risk factors. Therefore, this study is guided by the following inquiry: How do TGD individuals perceive source credibility of health information pertaining to preventive health?

Method

Thirty semi-structured interviews were conducted online via Zoom meeting software with TGD individuals between February 21, 2023 and July 31, 2023. The interviews were conducted online to eliminate geographic barriers to participation. The inclusion criteria were that the participants had to be 19 years of age or older, identify as gender diverse

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(e.g., transgender, gender queer, non-binary), and live in the United States. Participants were recruited via convenience sampling. A distribution list of 32 community-based organizations and coalitions working with TGD populations was created using a Google search. Recruitment messages with attached flyers were sent through the established list. Additional recruitment was done via social media sites and publicly accessible interest groups with a TGD focus on WhatsApp, Instagram, and Facebook. Recruitment materials included a QR code and a link to a webpage with information about the study, including inclusion criteria. Interested individuals completed an online, self-administered screener survey. Eligible and interested participants provided an online informed consent form prior to continuing registration. After consent, participants completed a demographic form and selected an interview time through the online scheduling platform. Inclusion criteria were validated by self-report. Participants were provided a password-protected Zoom link upon scheduling.

Thirty (30) interviews were included in the analysis. The interviews were conducted by two interviewers trained in qualitative interviewing techniques. A short TGD-responsive resource guide for referral was created and available to interviewees as a resource during or after the interviews. Interviews lasted approximately sixty (60) minutes each (range: 41–94 minutes) and were recorded to a secure cloud online server. An interview guide was followed, including open-ended questions and probes. The script was piloted with two TGD individuals, and adjustments were made to the script based on feedback. Questions regarding source credibility included: "*When it comes to your health, tell me about your trusted sources of health information"* and *"Tell me about why you trust these sources of information*." Participants were provided with operational definitions of key concepts such as "health communications campaigns." Participants were given examples of health communications campaigns and clarified how these differed from direct patient communication, as needed to ensure understanding of the concepts.

Upon completion of the interview, recordings were transcribed using Otter.ai and then matched to audio recordings for quality control. Participants were provided a $100 electronic gift card as an incentive for participation. Study protocols were approved by the Institutional Review Board at The University of Texas at Austin.

Data Analysis

Audio recordings of the interviews were transcribed, and participants were de-identified. Interview transcripts were coded using NVivo software for Mac. Thematic analysis was done using inductive coding, allowing themes to emerge organically using open coding. Coding procedures and theme development were completed by two members of the research team (Creswell & Poth, 2016). The research team collectively reviewed and discussed coding and revised themes as needed. The research team developed a codebook that was used in thematic development and assessment, a process that ensured validity of the study and its analysis. The following section presents the findings of the analysis, starting with the demographic characteristics of participants.

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Findings

Participant Demographics

Of the sample, 27% (n = 8) were young adults ages 19 – 24, 43% (n = 13) were ages 25 – 34, 23% (n = 7) were ages 35 – 59, and 7% (n = 2) were over 60 years old. Participants' ages ranged from 19 to 75 years of age. Half of the sample identified as White (n = 15), 20% Native American (n = 6), 13% African American/Black (n = 4), 10% Latinx (n = 3), 3% Asian (n = 1), and 3% Multiracial (n = 1). Gender identity was relatively evenly distributed with 30% identifying as a transgender woman (n = 9), 37% identifying as a transgender man (n = 11), and 33% identifying as non-binary (n = 10). For sexual orientation, 47% of the sample identified as queer (n = 14), 13% as bisexual (n = 4), 13% as pansexual (n = 4), 10% as asexual (n = 3), 7% as gay (n = 2), 7% as lesbian (n = 2), and 3% as straight (n = 1).

Category	Sub-category	Percentage (%)	Number (n)
Age Group	19 – 24	27	8
	25 – 34	43	13
	35 – 59	23	7
	60+	7	2
Race/Ethnicity	White	50	15
	Native American	20	6
	African American/Black	13	4
	Latinx	10	3
	Asian	3	1
	Multiracial	3	1
Gender Identity	Transgender Woman	30	9
	Transgender Man	37	11
	Non-binary	33	10
Sexual Orientation	Queer	47	14
	Bisexual	13	4
	Pansexual	13	4
	Asexual	10	3
	Gay	7	2
	Lesbian	7	2
	Straight	3	1

The following themes emerged from the data: 1) perilous socio-political climate; 2) precarious mass media landscape; and 3) benevolent community-based organizations.

Perilous socio-political climate

Although participants are largely distrustful of government, when asked about general health information, federal institutions were commonly cited as sources of credible health information due to providing scientific, peer-reviewed information. Health information from

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federal institutions such as the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH), were most often referenced as being credible, due to their reliance on evidence-based research. However, data point to source credibility as influenced by the broader socio-political climate. Political parties in power, influence of interest groups, and elected officials in leadership play a crucial role in shaping participants' perceptions of source credibility of health information. Many participants expressed diminishing trust and credibility in health information coming from both federal and local health agencies because of the interplay between federal agencies and government, a sentiment encapsulated by one participant:

> I don't like the government. If I'm gonna be honest, I have a lot of mistrust of the government or any authoritative like figures in that way. I mean, like, I did look at like CDC guidelines, and I do in general, like, trust the CDC. But if the governor puts out something, especially during COVID, I would always go and double check those things because I just genuinely didn't like trust it.

Participants perceive federal institutions like the National Institutes of Health as empirically driven institutions that are like the engine driving medical breakthroughs and advancements, aiming to make life better for everyone by tackling health challenges head-on. Findings illuminate that TGD individuals do not trust state and local government officials, but they do have faith in federally funded institutions, like health research organizations and federal or state university hospitals. Several participants expressed a deep distrust of the government, uncertain about health information disseminated from state-level entities. One participant noted:

Lord, Texas is a hot mess right now. I'm just gonna be blunt. Our key officials like the Governor and the Attorney General tried having the Department of Family Services go after parents who are helping their trans youth access gender affirming services…There's a ton of bills right now targeting the trans community, but especially youth. So, right now, the state government [is] very firmly on my distrust list.

Participants like this individual chronicled the ways anti-TGD legislation by state government officials erodes trust in government sources of health information. Another participant noted that in their home state of North Dakota, the governor signed a bill into law that restricts transgender health care in the state, making it a crime to provide gender-affirming care to people younger than 18, a ruling that goes against international health guidelines pertaining to TGD health. The participant recounted an attempt by government officials to enact a law that would require any government entity in North Dakota to use an individual's pronouns based on their assigned sex at birth. Because of this proposed legislation, he stopped going to the government-funded public health clinic for his medication and was forced to find another provider that would use his correct pronouns and name. He expressed a complete lack of trust in health information grounded in the larger bureaucratic influence government has on health and medical institutions. Other participants noted a broader skepticism of government resources of health information, because of the historical disregard and erasure of queer people, indigenous populations, and communities of color. One participant noted:

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> A lot of people are very skeptical of government resources in terms of health information. I still exercise a healthy skepticism, even for government resources, because historically governments have not had the needs of queer people and indigenous people, people of color in mind.

Participants' feelings of skepticism are rooted in a deep historical violence and erasure of queer lives in health and medicine, as well as erasure and epistemological violence that has dominated mainstream media.

Precarious mass media landscape

News media were frequently referenced as lacking credibility, and journalists' coverage of issues pertaining to TGD people was gravely impacted by the tone of state and local level legislation on TGD communities. Journalists were referenced as not reliable, often changing their messages to gain advertising or ratings, and exhibiting bias and polarizing TGD people in their reporting. One participant shared his longstanding distrust of news media: "I've always been skeptical of the news, because there's always an angle. There's always a bias. So, I prefer unbiased sources." For participants like him, a biased source is an uncredible source. Amidst the backdrop of the COVID-19 pandemic, a climate of misinformation shapes participants perceived source credibility of health information. One participant noted:

> I'm looking at health stuff through the news. I'm finding it's better to look at a couple different newspapers or online newspapers and compare what they're saying. [For] example, Fox News is very right leaning. They were very much spreading misinformation about masking or vaccination at one point, or very dismissive of it. CNN can be I guess, a little more left leaning, or it's considered more left leaning. I find they sometimes sensationalize certain things… So, I like to hop around to see how much I trust that particular statistic or recommendation before just jumping with it. In terms of anything relating to being trans, I tend to be really cautious with the news.

Participants tend to filter through health information content, making sense of messages and sources based on attitudes and beliefs they hold about media outlets.

Benevolent community-based organizations

Most participants pointed to community-based organizations (CBOs) as the most trusted source of health information. Describing her local CBO, one participant noted, "I absolutely love community-based organizations. Specifically, things like the Transformation Project here in South Dakota is something that I really trust for health information, especially regarding transgender people and healthcare specifically targeted for us." Participants expressed a benevolence embodied by these agencies, and this perception was paired with perceived health information credibility attributable to geographic proximity and a hyper-local focus of a CBO to TGD communities served. Participants conveyed trust in the health communication information provided by these agencies, as they often employed people with TGD identities and lived experiences.

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Discussion

Data from this research illuminate the complexity of perceived source credibility of health information among TGD individuals. On the one hand, TGD populations may only trust empirical, peer-reviewed health information. On the other hand, TGD populations demonstrate a distrust of any non-TGD community-based organizations. Because of the current legislative landscape in the United States, feelings about the anti-TGD political landscape creep into state and local health information sources. Based on the anti-TGD legislation in their regions, TGD populations operate from a place of deep distrust of governmental entities. Participants' responses to questions about health information conveyed a sense of uncertainty amid the broader sociopolitical landscape and climate of health misinformation.

Misinformation refers to information sent to media consumers that subject experts have determined to be incorrect (Vraga & Bode, 2020) without an intent to deceive (Hameleers et al., 2021; Wardle, 2017). Conversely, disinformation involves the dissemination of deliberately false information, and it is thereby intentional manipulation, fabrication, or decontextualization of information to attain a particular political goal (Hameleers et al., 2021). Findings from this study point to political disinformation about TGD people that impacts source credibility of health information.

Health misinformation is a core element of contemporary public discourse on transgender rights that has been mobilized to advance state and federal policies that limit and/or prohibit transition-related health care (Billard, 2024). Findings from this study suggest health information is marred by anti-TGD legislation, a sociopolitical force that bleeds into health information spaces. While perceptions of health information sources are implicated in misinformation, a deeper understanding of the concept is needed. The concepts of misinformation and disinformation are often interconnected and conflated, but they have significant conceptual distinctions. These distinctions manifest in the findings from this study.

The relationship between source credibility and trust in health communication is pivotal in shaping TGD individuals' perceptions, decisions, and behaviors related to their health. Most importantly, addressing disinformation is essential for health communication practitioners to effectively convey accurate and evidence-based information and promote positive health outcomes among TGD populations. Importantly, health institutions and health communication practitioners may not be aware of and comprehend the feelings TGD people have about their lives and their health. When making sense of health information, TGD people may rely on various cognitive schemas that affect how individuals perceive, interpret, and respond to health information from various messengers and media outlets. Findings suggest TGD people may seek out and interpret information in ways that confirm their pre-existing beliefs and attitudes toward health information sources, suggesting a confirmation bias. They may be more inclined to trust and accept health information sources that align with their existing worldview. TGD individuals may categorize health information sources based on generalizations about the source's political affiliation, credibility, or biases. For example, someone might dismiss a campaign about colon cancer and colorectal screening

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from a local government because they perceive it as biased or untrustworthy. Health disinformation can have significant implications for TGD populations, exacerbating existing health disparities and posing risks to individual well-being. Disinformation about health can lead to confusion and distrust among TGD individuals, potentially delaying or preventing them from accessing healthcare services. Health disinformation may contribute to increased risk of adverse health outcomes, such as increased risk of gynecological cancers among TGD people with cervixes (World Health Organization, 2018) and increased risk of venous thromboembolism among TGD people who use estrogen and androgen-lowering hormone therapies (Van Bunderen et al., 2022). Future research is needed that empirically examines confirmation bias, stereotyping, and authority bias in health information seeking and source credibility among TGD populations.

Health disinformation can impede TGD individuals' ability to make informed decisions about their own healthcare and well-being. When disinformation is widespread or presented as credible, it can be difficult for individuals to discern accurate information from falsehoods, undermining their autonomy and agency in making decisions about their bodies and identities. Health communication practitioners need to center the safety and humanity of TGD people. To address the implications of health misinformation for TGD populations, health communication practitioners need to prioritize accurate, evidence-based information within TGD populations and communities. This includes providing accessible, affirming resources and support services, increasing cultural competency among healthcare providers, combating stigma and discrimination, and fostering critical thinking skills to evaluate health information critically. Additionally, efforts to regulate and counteract misinformation through media literacy initiatives (Bulger & Davison, 2018), community education campaigns, and advocacy for policies that protect transgender rights and access to affirming healthcare (Alstott et al., 2024) are crucial for promoting the health and well-being of TGD individuals. Most importantly, the onus should not be placed on TGD populations to combat health misinformation. Political leaders and government need to be held accountable for health misinformation and the violence enacted on TGD people. Scientific misinformation has been used to uphold legislative actions in the United States, resulting in laws that threaten the health and safety of TGD people but also require health workers to practice care that is against evidence-based guidelines or face career-ending retribution (Lepore et al., 2022). However, research suggests that political accountability in the contemporary informational environment is particularly difficult (Schiff et al., 2023).

The implications of this research will be useful to health communication practitioners who can adapt messages to better address the health information needs of TGD populations. Researchers and practitioners with funding and support from governmental agencies (e.g., NIH, CDC) shouldn't assume this affiliation is a source of credibility to their audiences. Rather, disseminating health information should begin with community-based partnerships in TGD communities. Additionally, practitioners need to translate and disseminate empirical research by way of white papers co-written with trusted TGD-affirming community health organizations.

The strong support for CBOs as credible sources of health information among participants has several implications for scholars and practitioners of health communication. Participants

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perceive CBOs as trustworthy sources of health information; therefore, scholars and practitioners should recognize the importance of trusted messengers within communities and the potential impact they can have on health communication efforts. Understanding who community members view as credible sources can inform the development of effective communication strategies and interventions. Scholars and practitioners should prioritize partnerships with CBOs and community leaders to ensure that health messages are culturally relevant, linguistically appropriate, and resonate with the target audience. Collaborating with CBOs can facilitate access to diverse communities, build rapport and trust, and enhance the reach and effectiveness of health communication efforts.

Our research is not without limitations. This research employed convenience sampling, and participants were recruited through social media of community-based organizations and coalitions, which could have introduced bias. These audiences may have already had interaction and rapport with social service organizations and may be more inclined to prefer online communication. The study may not have captured the responses from those with limited resources or limited access to computers and technology. The sample size was limited to only 30 individuals and is not representative of the diversity of TGD populations.

Additional research is needed that focuses on identifying, examining, and solving health inequities faced by TGD individuals by way of communication problems, specifically research that develops a deeper understanding of social media and social networks, exploring the effectiveness of partnerships with TGD content creators to lead message delivery. Additionally, a content analysis of health communications campaigns currently in rotation, including social media campaigns, is needed to confirm the communications gap in a systematic manner. Research is also needed related to the long-term effects of health communications campaigns. Additionally, while there is a growing corpus of research on health information seeking among TGD populations, this research points to the need to distinguish the experiences of non-binary populations.

Conclusion

TGD health communication involves the dissemination of accurate and understandable health information, aiming to promote health, prevent disease, and improve healthcare outcomes. In addition to policy implications, TGD health disinformation can undermine trust in health institutions, lead to harmful behaviors, and contribute to the spread of diseases among gender diverse populations. Health communication efforts can counteract TGD health disinformation by providing evidence-based, accurate, and easily understandable information to policy makers and federal institutional stakeholders. Health communication practitioners can monitor channels where disinformation spreads and address false claims with accurate information, engaging with communities, fact-checking organizations, and social media platforms to correct misinformation and prevent further dissemination.

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Weddle Declaration
Exhibit E

PLOS ONE

RESEARCH ARTICLE

The worldwide burden of HIV in transgender individuals: An updated systematic review and meta-analysis

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Abstract

Introduction

Transgender individuals are at risk for HIV. HIV risks are dynamic and there have been substantial changes in HIV prevention (e.g., pre-exposure prophylaxis [PrEP]). It is thus time to revisit HIV prevalence and burden among transgender individuals. The objective of this systematic review and meta-analysis was thus to examine worldwide prevalence and burden of HIV over the course of the epidemic among trans feminine and trans masculine individuals.

Methods

We conducted an updated systematic review by searching PsycINFO, PubMed, Web of Science, and Google Scholar, for studies of any research design published in in a peer-reviewed journal in any language that reported HIV prevalence among transgender individuals published between January 2000 and January 2019. Two independent reviewers extracted the data and assessed methodological quality. We then conducted a meta-analysis, using random-effects modelling, to ascertain standardized prevalence and the relative burden of HIV carried by transgender individuals by country and year of data collection, and then by geographic region. We additionally explored the impact of sampling methods and pre-exposure prophylaxis (PrEP).

Results

Based on 98 studies, overall standardized HIV prevalence over the course of the epidemic, based on weights from each country by year, was 19.9% (95% CI 14.7% - 25.1%) for trans feminine individuals (n = 48,604) and 2.56% (95% CI 0.0% - 5.9%) for trans masculine individuals (n = 6460). Overall OR for HIV infection, compared with individuals over age 15, was 66.0 (95% CI 51.4–84.8) for trans feminine individuals and 6.8 (95% CI 3.6–13.1) for trans masculine individuals. Prevalence varied by geographic region (13.5% - 29.9%) and sampling method (5.4% - 37.8%). Lastly, PrEP effects on prevalence could not be established.

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Competing interests: The authors have declared that no competing interests exist.

Conclusion

Trans feminine and trans masculine individuals are disproportionately burdened by HIV. Their unique prevention and care needs should be comprehensively addressed. Future research should further investigate the impact of sampling methods on HIV prevalence, and monitor the potential impact of PrEP.

Introduction

Transgender individuals, defined as individuals who experience a misalignment between the sex they were assigned at birth and their gender identity or whose gender identity is incongruent with gender norms, [1, 2] are at significant risk for an HIV infection [3]. Individual level risk factors include condomless sex, particularly receptive anal sex, coinfection with other sexually transmitted infections, transactional sex, and the shared use of needles for hormone and/or silicon injections [4–8]. Individual level risk factors do not stand alone; they result from, and intersect with, other factors such as mental health difficulties, substance use, and many forms of marginalization and stigmatization that limit, among other things, educational and work opportunities, as well as legal recognition of one's chosen gender [6, 9–14]. Given that HIV risk among transgender individuals is a dynamic phenomenon, it is important to regularly monitor and update our knowledge of HIV prevalence and burden, such that we can identify trends that can inform policy-making and interventions. Here, we present a comprehensive updated systematic review of HIV prevalence over the course of the epidemic and a meta-analyses of HIV burden among transgender individuals covering literature from 2000 until 2019.

Previous systematic reviews and meta-analyses

Since 2008, a series of systematic reviews and meta-analyses have been published [1, 4, 5, 11, 15–17]. The first, by Herbst and colleagues, [15] investigated HIV prevalence among trans individuals in the United States, covering literature from 1988 until early 2007, and included laboratory-confirmed and self-reported prevalence. Pooled HIV prevalence based upon studies reporting laboratory-confirmed HIV status was, for trans women, 27.7%. HIV prevalence among trans women based upon self-reported HIV status was 11.8%. Among trans men, only one study reported laboratory confirmed prevalence (2%) and self-reported prevalence rates ranged from 0% to 3%. The second systematic review and meta-analysis by Operario et al. [16] set out to assess whether transgender female sex workers (FSW) experienced higher HIV infection rates than cis-gender sex workers and transgender women who do not engage in sex work, using both laboratory-confirmed and self-reported HIV prevalence rates published between 1998 and 2006. HIV prevalence was 27.3% in transgender FSW and 14.7% in trans women who did not engage in sex work. Operario et al.'s meta-analysis further showed that transgender FSW are at significantly higher risk for HIV than cis-gender sex workers and trans women who do not engage in sex work [16]. In 2013, Baral and colleagues [4] published a systematic review and meta-analysis of HIV prevalence among transgender women, covering literature from 2000 to November 2011 and using only laboratory-confirmed HIV prevalence rates. Pooled prevalence was 19.1% and the meta-analytical findings showed that, compared to all adults of reproductive age, the odds ratio for HIV infection in trans women was 49 across the 15 countries included, thus demonstrating that transgender women carry a high burden of HIV [4]. Poteat and colleagues [5] followed up on Baral et al.'s work with a systematic review, but not a meta-analysis, of HIV

prevalence literature published between 2012 and 2015, looking now at both trans feminine and trans masculine populations. Prevalence rates varied substantially based on locale but Poteat et al. [5] concluded, in line with the previous reviews, that HIV prevalence was high in trans feminine populations. They also concluded that data on HIV among trans masculine individuals is still very limited. Almost simultaneously, Reisner and Murchison [1] published a global research synthesis of HIV and STI risks in adult trans men, but not trans women, using 25 studies. They found HIV prevalence rates for trans men ranging from 0% to 4.3% for laboratory-confirmed HIV status and 0% to 10% for self-reported HIV, suggesting that trans masculine individuals may also be more vulnerable to HIV than cis-gender adults. Additionally, in 2017, MacCarthy and colleagues [11] published a global systematic review of HIV and sexually transmitted infections among transgender individuals. They reported HIV prevalence rates ranging from 0% to 17.6% for self-reported HIV status and 0.6% to 34.1% for laboratory-confirmed HIV status. However, given their focus on HIV and STI co-infection, the HIV prevalence rates reported in that review were derived only from studies that also reported STI prevalence rates. The reported prevalence rates were thus based on a mere 6 studies for self-reported HIV status and 13 studies for laboratory-confirmed HIV status. Recently, Becasen et al. [17] published a systematic review and meta-analysis of HIV prevalence among transgender individuals in the United States only using literature published in the United States between 2006 and May 2017. They established that laboratory-confirmed HIV prevalence was 14.1% for trans women and 3.2% for trans men; self-reported prevalence was 16.1% and 1.2% for trans women and trans men, respectively.

Current concerns

Overall, the various systematic reviews and meta-analyses demonstrate that transgender individuals, particularly trans feminine individuals, are disproportionately burdened with HIV but none of the more recent systematic reviews have comprehensively updated Baral et al.'s worldwide systematic review and meta-analysis with both transfeminine and transmasculine individuals. Furthermore, from a methodological perspective, more fine-grained analyses (e.g. by country and year of data collection) are being called for, rather than only pooled analyses by country or region, as has been the methodological approach in previous meta-analyses. Additionally, critique about reported prevalence rates has been levied, with the claim that many studies have relied on convenience samples of, often, transgender women who engage in sex work, which may inflate prevalence rates [18, 19]. Also, previous meta-analyses have not differentiated between various sampling strategies and this may impact meta-analytical findings. Further, there have been substantial and fundamental changes in HIV prevention in recent years. One is the emergence of pre-exposure prophylaxis (PrEP) as a powerful tool for HIV prevention for at risk groups like transgender individuals [5, 8, 20–23]. With these considerations in mind, we feel it is time to revisit worldwide HIV prevalence and burden among transgender individuals. We therefore systematically reviewed literature published between 2000 and 2019 on HIV prevalence among transgender individuals and then conducted a meta-analysis 1) to establish prevalence rates for both trans feminine and trans masculine individuals; and 2) to compare the burden of HIV infection among transgender individuals to individuals over 15 years of age in the countries and regions from which samples were derived, taking year of data collection into account. We then explored the possible impact of sampling methods and of PrEP on prevalence rates and the burden of HIV infection.

Methods

Search strategies and eligibility

We searched, in November 2017 and again in January 2019, PsycINFO, PubMed, Web of Science, and Google Scholar®, for studies in all languages published between January 1st, 2000

and January 28th, 2019. We selected this timeframe in order to gain a complete, comprehensive, and nuanced understanding of worldwide prevalence over and burden of HIV among transgender individuals. We also reviewed the studies included in Baral et al. [4] and in Poteat et al. [5] to ensure that they were covered in our analysis as well. We explicitly overlapped the timeframe in our meta-analysis with those of previous meta-analyses in order to generate comprehensive and robust meta-analytical findings. It also allowed us to explore the impact of applying more refined methodology (standardized vs. pooled prevalence rates) in the meta-analysis, and compare findings delivered by the different meta-analytical approaches. Articles and citations were downloaded and managed in the reference software Mendeley®.

We searched for articles on (the treatment of) HIV and transgender individuals using the following search terms: HIV OR AIDS OR "PrEP" OR "Pre-Exposure Prophylaxis" OR "TasP" OR "treatment as prevention" AND *transgender* OR "MTF" or "male to female transgender" OR "FTM" OR "female to male transgender" OR *transsexual* OR "travesty" OR "cross dresser" OR "koti" OR "hijra" OR "mahuvahine" OR "mahu" OR "waria" OR "katoey" OR "bantut" OR "nadleehi" OR "berdache" OR "xanith". These terms are in line with the terms previously used by Baral et al. [4].

Studies of any research design published in peer-reviewed journals that reported laboratory- confirmed prevalence of HIV among transgender individuals were included. When prevalence rates were pooled across trans feminine and trans masculine individuals or when prevalence was pooled across trans feminine individuals and men who have sex with men (MSM), we contacted the authors and requested separate prevalence rates for the populations included.

Study selection and data extraction

Titles and abstracts were screened by two independent reviewers and articles that clearly did not include HIV prevalence data were excluded, as were duplicates. All articles that met the inclusion criteria and articles that needed further review to ascertain whether they met the criteria were subsequently downloaded. When one reviewer deemed the title and/or abstract potentially relevant and the other did not, the full-text for that article was nonetheless downloaded. Subsequently, the full texts were reviewed. When studies reported duplicate data, the study with the smallest sample size was excluded. If sample sizes were identical, the later publication was excluded. Any conflicts over study inclusion were resolved by project leads (KJ and SS) in conjunction with the researchers running the meta-analysis (MvD and HW). The PRISMA reporting checklist was used to guide the reporting of this study. No protocol was registered for this review.

Data were extracted by two trained coders using a standardized extraction form that included details about sample size, sampling method, sample description, recruitment location, time period of study, age range, transgender type (trans masculine/trans feminine/both), HIV measure (self-reported/laboratory testing), and HIV prevalence or incidence.

Methodological quality assessment

Given the lack of consensus on fitting quality assessment tools for epidemiological studies, [24] we developed criteria specifically for this systematic review and meta-analysis. In doing so, we used and adapted appropriate criteria from the JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data [25]. Studies were deemed of sufficient quality if: 1) biological testing (rather than self-reported HIV status) was used to establish HIV diagnoses, as was done in Baral et al. [4]; 2) study participants were described in sufficient detail, meaning that prevalence was reported, or subsequently obtained directly from the authors, specifically for

trans feminine and/or trans masculine individuals (rather than transgender individuals as a whole group); 3) if the study setting/location was sufficiently detailed; 4) if the data collection timeframe was reported; 5) if prevalence or frequency of HIV diagnosis within the total sample were reported; and 6) if sample size was at least 40 for trans feminine individuals. We did not apply a minimum sample size for studies reporting prevalence among trans masculine individuals as the majority of studies had small sample sizes, and a minimum sample size would have led to the exclusion of most studies reporting HIV prevalence among trans masculine individuals. Additionally, we did not exclude studies based on sampling method as investigating the impact of sampling methods was one of the objectives of this meta-analysis.

Data analyses

First, we used analogous methodology to prior meta-analyses [4, 26, 27]. We grouped studies by country, weighted by sample size. We calculated pooled HIV prevalence and 95% confidence intervals (CIs) per country. We did this separately for trans feminine and trans masculine samples. In line with previous meta-analyses, we then calculated odds ratios per country by dividing the HIV prevalence among transgender individuals (numerator) by the HIV prevalence rate among individuals over 15 years of age in the general population in the country from which the sample was derived (denominator), as reported by the 2017 UNAIDS reports (where prevalence estimates for adults are from 15 years of age onward) [28] and estimations of adult population size from the US Census Bureau International Division [29]. These results are reported in S1 Appendix.

Then, to achieve a more refined methodological analysis, we standardized rather than pooled prevalence rates, and ran the meta-analysis again, this time matching country-level prevalence rates to year(s) of data collection for the included studies. When data were collected over multiple years in the original studies, the median year of the year-span was chosen for the country by year analysis. If HIV prevalence in the sample was 0, we calculated confidence intervals using the Wilson interval [30]. Then, we grouped countries by geographic region (Africa, Latin America, Asia, and Global North) and calculated, per geographic region, the standardized HIV prevalence among trans feminine individuals as well as odds ratios based on weights from each country-year.

Subsequently, given recent discussions about the impact of sampling methods on findings pertaining to HIV prevalence among trans feminine individuals, [18] we grouped studies by sampling method, and calculated standardized HIV prevalence by sampling method. We delineated ten sampling methods, namely cluster sampling, convenience sampling, purposive sampling, respondent driven sampling, snowball sampling, sampling from database health plan, as well as sampling via STI clinic, via hospital, via NGO, and via surveillance. Overlap in categories may exist as some studies used multiple sampling methods. In such cases, we categorized the study under its primary sampling method.

Lastly, we explored possible effects of the introduction of PrEP on HIV prevalence among trans feminine individuals. We focused on US studies only as PrEP has been available in the US since 2012, which is longer than in any other country. We conducted subgroup analyses, with data being collected either prior to the introduction of PrEP (1997–2011), or after the introduction of PrEP (2012–2017).

The meta-analysis was conducted with the statistical software R [31] using the metafor package [32]. We used a random-effects model and the DerSimonian-Laird method to estimate the model. The DerSimonian-Laird Q test and I^2 values were used to assess heterogeneity, with low, moderate, and high heterogeneity corresponding to I^2 values of 25%, 50%, and 75%. [33] We investigated publication bias by inspecting funnel plots [34].

Results

The study selection process is presented in Fig 1. We included 98 studies from a total of 34 countries, of which 78 studies described HIV prevalence in trans feminine individuals, 4 described prevalence in trans masculine individuals, and 16 described both. In total, we included 48,604 trans feminine individuals from 34 countries and 6460 trans masculine individuals from 5 countries. The included studies and relevant characteristics of those studies are reflected in Table 1.

The overall standardized HIV prevalence over the course of the epidemic, based on weights from each country by year, was 19.9% (95% CI 14.7% - 25.1% Table 2) for trans feminine individuals and 2.56% (95% CI 0.0% - 5.9%; Table 3) for trans masculine individuals. The overall OR for HIV infection, compared with individuals over 15 years of age, was 66.0 (95% CI 51.4–84.8; Table 2 and Fig 2) for trans feminine individuals and 6.8 (95% CI 3.6–13.1, Table 3 and Fig 3) for trans masculine individuals. Tables 2 and 3 also show the overall standardized prevalence rates and overall odds ratios per country by year for trans feminine individuals and trans masculine individuals, respectively.

Standardized prevalence rates and overall odd ratios (based on weights from each country by year) according to geographic region are presented in Table 4. In sub-Saharan Africa (n = 1192), standardized HIV prevalence among trans feminine individuals was 29.9% (95% CI 22.5% - 37.3%) and the overall OR for HIV infection, compared to individuals over 15

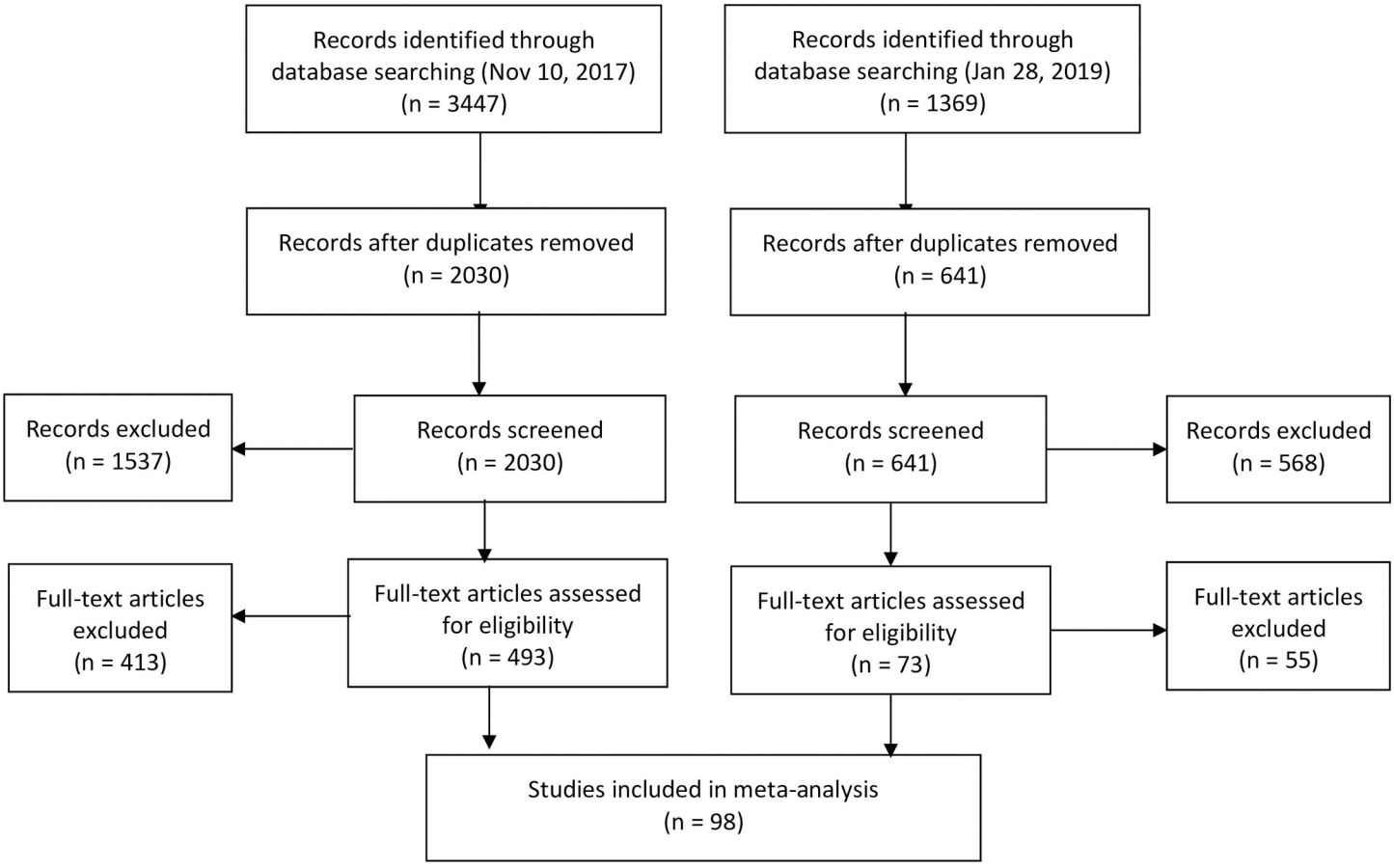


Fig 1. PRISMA flow chart describing the study selection process.

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Table 1. Studies included in review and meta-analysis.

Authors	Year of publication	Year of data collection	Transgender sample	HIV prevalence (%)	HIV frequency (n)	Sample size	Country	Geographic region	Sampling method
Aguayo, Munoz, & Aguilar [35]	2013	2011	TF	27.00%	64	237	Paraguay	Latin America	Cluster sampling
Akhtar, Badshah, Akhtar, et al. [36]	2012	2009–2010	TF (hijras)	21.60%	66	306	Pakistan	Asia	Respondent driven sampling
Altaf [37]	2009	2006–2007	TF (hijras)	4.70%	38	810	Pakistan	Asia	Surveillance
Altaf, Zahidie, & Agha [38]	2012	2008	TF (hijras)	6.40%	75	1181	Pakistan	Asia	Surveillance
Baqi, Shah, Baig et al. [39]	2006	1998	TF (hijras)	0.00%	0	208	Pakistan	Asia	Respondent driven sampling
Barrington, Weijnert, & Guardado et al. [40]	2012	2008	TF	19.00%	13	67	El Salvador	Latin America	Respondent driven sampling
Bastos, Bastos, Coutinho et al. [41]	2018	2016–2017	TF	29.62%	843	2846	Brazil	Latin America	Respondent driven sampling
Bellhouse, Walker, Fairley et al. [42]	2016	2011–2014	TM	3.57%	1	28	Australia	Global North	STI clinic visit
			TF	10.39%	8	77			
Brahmam, Kodavallaa, Rajkumar et al. [43]	2008	2006–2007	TF (hijras)	18.10%	104	575	India	Asia	Cluster sampling
Carballo-Dieguez, Balan, Dolezal et al. [44]	2012	2005–2006	TF	13.00%	12	84	Brazil	Latin America	Respondent driven sampling
Castel, Magnus, Peterson et al. [45]	2012	2006	TF & TM	10.59%	9	85	US	Global North	STI clinic visit
Castillo, Konda, Leon et al. [46]	2015	2008–2009	TF	16.82%	35	208	Peru	Latin America	Snowball
Chariyalersak, Kosachunhanan, Saokhieo et al. [47]	2011	2008–2009	TF	9.30%	13	140	Thailand	Asia	STI clinic visit
Chen, McFarland, Tompson et al. [48]	2011	2009	TM	0.00%	0	59	US	Global North	STI clinic visit
Chhim, Ngin, Chhoun et al. [49]	2017	2015–2016	TF	5.90%	81	1375	Cambodia	Asia	Respondent driven sampling
Clements-Noelle, Wilkenson, Kitano et al. [50]	2001	1997	TM	2.00%	2	123	US	Global North	Respondent driven sampling
			TF	35.00%	137	392			
Colby, Nguyen, Le et al. [51]	2016	2015	TF	18.00%	37	205	Vietnam	Asia	Snowball
Costa, Fontanari, Jacinto et al. [52]	2015	1998–2014	TM	25.00%	0	51	Brazil	Latin America	Hospital
			TF	25.00%	71	284			
Dasarathan & Kalaivani [53]	2017	2011–2014	TF	13.40%	11	82	India	Asia	STI clinic visit
Diez, Bleda, Varela et al. [54]	2014	2000–2009	TF	24.50%	129	529	Spain	Global North	STI clinic visit
Dos Ramos Farias, Garcia, Reynaga et al. [55]	2011	2006–2009	TF	34.10%	93	273	Argentina	Latin America	Respondent driven sampling
Fernandes, Zanini, Rezende et al. [56]	2015	2011–2013	TF	24.34%	37	152	Brazil	Latin America	Cluster sampling
Fernandez-Balbuena, Belza, Urdaneta et al. [57]	2015	2008–2012	TF & TM	45.54%	46	101	Spain	Global North	NGO
Fernandez-Lopez, Reyes-Uruena, Agusti et al. [58]	2018	2014–2016	TF	8.83%	40	453	Spain	Global North	STI clinic visit

(*Continued*)

Table 1. (Continued)

Authors	Year of publication	Year of data collection	Transgender sample	HIV prevalence (%)	HIV frequency (n)	Sample size	Country	Geographic region	Sampling method
Grandi, Goihman, Ueda et al. [59]	2000	1992–1998	TF	40.00%	174	434	Brazil	Latin America	Respondent driven sampling
Green, Hoenigl, Morris et al. [60]	2015	2008–2014	TM	3.00%	1	30	US	Global North	STI clinic visit
			TF	2.00%	3	151			
Grinsztejn, Jalil, Monteiro et al. [61]	2017	2015–2016	TF	31.20%/ 24.20%	141	345	Brazil	Latin America	Respondent driven sampling
Guadamuz, Wimonsate, Varangrat et al. [62]	2011	2005	TF	14.00%	64	474	Thailand	Asia	Convenience sampling
Gutierrez, Tajada, Alvarez et al. [63]	2004	1998–2003	TF	23.00%	14	60	Spain	Global North	Convenience sampling
Guy, Mustikawati, Wijaksono et al. [64]	2011	2006–2008	TF & TM	31.60%	151	477	Indonesia	Asia	STI clinic visit
Habarta, Wang, Mulatu et al. [65]	2015	2009–2011	TM	0.51%	12	2364	US	Global North	STI clinic visit
			TF	2.70%	355	13154			
Hadikusumo, Utsumi, Amin et al. [66]	2016	2012	TF	16.00%	16	100	Indonesia	Asia	STI clinic visit
Hakim, Coy, Patnaik et al. [67]	2018	2014–2015	TF	22.42%	37	165	Mali	Africa	Respondent driven sampling
Hawkes, Collumbien, Platt et al. [68]	2009	2007	TF (khusra)	2.00%	6	269	Pakistan	Asia	Respondent driven sampling
Hiransuthikul, Pattanachaiwit, Teeratakulpisarn et al. [69]	2018	2012–2013	TF	4.26%	2	47	Thailand	Asia	STI clinic visit
Januraga, Wulandari, Muliawan et al. [70]	2013	2009–2010	TF (waria)	36.87%	80	217	Indonesia	Asia	Respondent driven sampling
Jin, Restar, Biello et al. [71]	2019	2012–2015	TF	24.71%	65	263	US	Global North	Convenience sampling
Kaplan, McGowan, & Wagner [72]	2016	2012	TF	10.00%	4	40	Lebanon	Asia	Respondent driven sampling
Kellogg, Clements-Nolle, Dilley et al. [73]	2001	1997–2000	TF	15.00%	37	238	US	Global North	STI clinic visit
Keshinro, Crowell, Nowak et al. [74]	2016	2013–2016	TF	71.43%	75	105	Nigeria	Africa	Respondent driven sampling
Khan, Rehan, Qayyum et al. [75]	2008	2004	TF (hijras)	1.00%	5	409	Pakistan	Asia	Cluster sampling
Kojima, Park, Konda et al. [76]	2017	2013–2014	TF	30.10% / 27.60%	30	89	Peru	Latin America	STI clinic visit
Leinung, Urizar, Patel et al. [77]	2013	prior 2003	TM	0.00%	0	50	US	Global North	Hospital
			TF	8.33%	16	192			
Lipsitz, Segura, Castro et al. [78]	2014	2007–2009	TF	30.00%	64	214	Peru	Latin America	STI clinic visit
Lobato, Koff, Schestatsky et al. [79]	2008	1998–2005	TM	0.00%	0	16	Brazil	Latin America	Hospital
			TF	19.67%	24	122			

(*Continued*)

Table 1. (Continued)

Authors	Year of publication	Year of data collection	Transgender sample	HIV prevalence (%)	HIV frequency (n)	Sample size	Country	Geographic region	Sampling method
Logie, Lacombe-Duncan, Wang et al. [80]	2016	2015	TF	25.20%	26	103	Jamaica	Latin America	Respondent driven sampling
Long, Montano, Cabello et al. [81]	2017	2013–2015	TF	19.68%	61	310	Peru	Latin America	STI clinic visit
Luzzati, Zatta, Pavan et al. [82]	2016	2000–2014	TM	0.00%	0	20	Italy	Global North	Hospital
			TF	12.10%	21	173			
Manieri, Castellano, Crespi et al. [83]	2014	2005–2011	TM	0.00%	0	27	Italy	Global North	Hospital
			TF	5.36%	3	56			
McFarland, Wilson, Raymond et al. [84]	2017	2014	TM	0.00%	0	122	US	Global North	Convenience sampling
Mimiaga, Hughto, Biello et al. [85]	2019	2012–2015	TF	20.60%	48	233	US	Global North	Convenience sampling
Murrill, Liu, Guilin et al. [86]	2008	2004	TF & TM	13.00%	9	92	US	Global North	Convenience sampling
Nemoto, Bödeker, Iwamoto et al. [87]	2014	2000–2001	TF	29.93%	161	538	US	Global North	Purposive sampling
Nguyen, Nguyen, Le et al. [88]	2008	2004	TF ("male transvestites" "bong lo")	7.00%	5	75	Vietnam	Asia	Convenience sampling
Nuttbrock, Bockting, Rosenblum et al. [89]	2013	2004–2007	TF	2.80%	9	230	US	Global North	Convenience sampling
Nuttbrock, Hwahng, Bockting et al. [90]	2009	earlier than 2009	TF	35.98%	186	517	US	Global North	Convenience sampling
Ongwandee, Lertpiriyasuwat, Khawcharoenporn et al. [91]	2018	2015–2016	TF	900.00%	39	435	Thailand	Asia	STI clinic visit
Pando, Gomez-Carrillo, Vignoles et al. [92]	2011	2006–2008	TF	34.00%	38	112	Argentina	Latin America	NGO
Patrascioiu, Lopez, Porta et al. [93]	2013	2006–2010	TM	2.20%	2	92	Spain	Global North	Convenience sampling
			TF	12.60%	18	142			
Peitzmeier, Reisner, Harigopal et al. [94]	2014	2006–2012	TM	0.86%	2	233	US	Global North	Hospital
Pell, Prone, Vlahakis et al. [95]	2011	2004	TM	0.00%	0	17	Australia	Global North	STI clinic visit
			TF	4.26%	6	141			
Pisani, Girault, Gultom et al. [96]	2004	2002	TF (waria)	22.00%	53	241	Indonesia	Asia	Cluster sampling
Pitasi, Oraka, Clark et al. [97]	2019	2010–2013	TM	8.30%	10	120	US	Global North	STI clinic visit
			TF	14.20%	72	506			
Pizzicato, Vagenas, Gonzales et al. [98]	2017	2011	TF	14.59%	104	713	Peru	Latin America	Respondent driven sampling
Poteat, Ackerman, Diouf et al. [99]	2017	2011–2016	TF	2.78%	3	108	Burkina Faso	Africa	Respondent driven sampling
			TF	25.50%	76	298	Côte d'Ivoire		
			TF	59.15%	42	71	Lesotho		
			TF	16.00%	12	75	Malawi		
			TF	37.19%	74	199	Senegal		
			TF	14.17%	17	120	Swaziland		
			TF	17.65%	9	51	Togo		

(*Continued*)

Table 1. (Continued)

Authors	Year of publication	Year of data collection	Transgender sample	HIV prevalence (%)	HIV frequency (n)	Sample size	Country	Geographic region	Sampling method
Poteat, German, & Flynn [100]	2016	2004–2005	TF	43.00%	21	49	US	Global North	Surveillance
Prabawanti, Bollen, Palupy et al. [101]	2011	2007	TF (waria)	24.40%	183	748	Indonesia	Asia	Cluster sampling
Quinn, Nash, Hunkeler et al. [102]	2017	2006–2014	TM	0.31%	9	2892	US	Global North	Database health plan
			TF	5.35%	186	3475			
Rana, Reza, Alam et al. [103]	2016	2012	TF (hijras)	0.80%	7	889	Bangladesh	Asia	STI clinic visit
Raymond, Wilson, Packer et al. [104]	2019	2010	TF	39.17%	123	314	US	Global North	Respondent driven sampling
		2013	TF	36.05%	84	233			
		2016	TF	38.68%	123	318			
Reback, Lombardi, Simon et al. [105]	2005	1998–1999	TF	22.10%	54	244	US	Global North	STI clinic visit
Reisner, White, Mayer et al. [106]	2014	2007	TM	4.35%	1	23	US	Global North	STI clinic visit
Reisner, Vetters, White et al. [107]	2015	2001–2010	TF	7.93%	5	63	US	Global North	STI clinic visit
			TM	2.40%	2	82			
Rich, Scott, Johnston, et al. [108]	2017	2012–2014	TM	0.00%	0	11	Canada	Global North	Respondent driven sampling
Rowe, Santos, McFarland et al. [109]	2015	2012–2013	TF	4.00%	13	292	US	Global North	Snowball
Russi, Serra, Vinoles et al. [110]	2003	1999	TF ("male transvestites")	21.50%	49	200	Uruguay	Latin America	Convenience sampling
Sahastrabuddhe, Gupta, Stuart et al. [111]	2012	1993–2002	TF (hijras)	45.20%	38	84	India	Asia	STI clinic visit
Salas-Espinoza, Menchaca-Diaz, Patterson et al. [112]	2017	2012	TF	22.00%	22	100	Mexico	Latin America	Cluster sampling
Saravanamurthy, Rajendran, Ramakrishnan et al. [113]	2008	2007	TF	17.50%	23	125	India	Asia	Respondent driven sampling
Schulden, Song, Barros et al. [114]	2008	2005–2006	TM	0.00%	0	42	US	Global North	Convenience sampling
			TF	12.00%	67	559			
Seekaew, Pengnonyang, Jantarapakde et al. [115]	2018	2015–2016	TF	8.80%	69	786	Thailand	Asia	Respondent driven sampling
Shan, Yu, Yang et al. [116]	2018	2016	TF	7.60%	38	498	China	Asia	Snowball
Shaw, Lorway, Bhattacharjee et al. [117]	2016	2011	TF (kothi & hijras)	15.30%	27	176	India	Asia	Cluster sampling
Shaw, Emmanuel, Adrien et al. [118]	2011	2005–2006	TF (hijras)	1.00%	10	1162	Pakistan	Asia	Cluster sampling
Sherman, Park, Galai et al. [119]	2019	2016–2017	TF	40.30%	25	62	US	Global North	Convenience sampling
Shinde, Setia, Row-Kavi et al. [120]	2009	earlier than 2009	TF	41.00%	21	51	India	Asia	STI clinic visit
Silva-Santisteban, Raymond, Salazar et al. [121]	2012	2009	TF	30.00%	130	420	Peru	Latin America	Respondent driven sampling
Sotelo & Claudia [122]	2011	2009	TF	34.00%	152	441	Argentina	Latin America	Unknown
Stephens, Bernstein, Philip et al. [123]	2011	2006–2009	TM	2.90%	7	69	US	Global North	STI clinic visit
			TF	11.21%	25	223			

(*Continued*)

Table 1. (Continued)

Authors	Year of publication	Year of data collection	Transgender sample	HIV prevalence (%)	HIV frequency (n)	Sample size	Country	Geographic region	Sampling method
Subramanian, Ramakrishnan, Aridoss et al. [124]	2013	2005–2009	TF	12.00%	48	404	India	Asia	Cluster sampling
Toibaro, Ebensrtejin, Parlante et al. [125]	2009	2002–2006	TF	27.60%	29	105	Argentina	Latin America	STI clinic visit
Van Veen, Götz, van Leeuwen et al. [126]	2010	2002–2005	TF	19.00%	13	69	Netherlands	Global North	Cluster sampling
Waheed, Satti, Arshad et al. [127]	2017	2015–2016	TF	16.40%	22	134	Pakistan	Asia	Convenience sampling
Wasantioopapokakorn, Manopaiboon, Phoorisri et al. [128]	2018	2011–2016	TF	11.85%	82	692	Thailand	Asia	Convenience sampling
Weissman, Ngak, Srean et al. [129]	2016	2012	TF	4.00%	37	891	Cambodia	Asia	Respondent driven sampling
World Health Organization [130]	2016	2015–2016	TF	4.00%	11	299	Philippines	Asia	Surveillance
Wickersham, Gibson, Bazazi et al. [131]	2017	2014	TF	12.00%	24	193	Malaysia	Asia	Respondent driven sampling
Zaccarelli, Spizzichino, Venezia et al. [132]	2004	1993–2003	TF	31.50%	149	473	Italy	Global North	STI clinic visit
Zea, Reisen, del Rio-Gonzalez et al. [133]	2015	2011	TF	13.79%	8	58	Colombia	Latin America	Respondent driven sampling

TF = trans feminine; TM = trans masculine.

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years of age in the countries from which we had prevalence data for trans feminine individuals, matched to year of data collection, was 21.5 (95% CI 6.3–73.7). In Latin America (n = 7917), standardized prevalence was 25.9% (95% CI 20.0% - 31.8%) and the overall OR for HIV infection, compared to individuals over 15 years of age, was 95.6 (95% CI 73.7–122.7). In Asia (n = 14,798), the standardized HIV prevalence was 13.5% (95% CI 2.3% - 17.7%) and the overall OR was 68.0 (95% CI 42.9–107.8). Lastly, in the Global North, thus in Australia, Europe, and North America (n = 24,697), the standardized HIV prevalence was 17.1% (95% CI 13.1% - 21.1%) and the overall OR for HIV infection was 48.4 (95% CI 28.2–83.9).

The standardized HIV prevalence by sampling method is reported in Table 5. The standardized HIV prevalence among transgender individuals when respondent driven sampling was employed (33 studies) was 23.3% (95% CI 18.0% - 28.4%). When prevalence rates were ascertained via STI clinic visits (26 studies), standardized prevalence was 17.4% (95% CI 12.2% - 22.7%). When convenience sampling was employed (14 studies), standardized prevalence was 19.7% (95% CI 14.8% - 24.5%) and when cluster sampling was employed (11 studies), the standardized prevalence was 19.6% (95% CI 14.4% - 24.9%). The remaining sampling methods were relatively infrequently employed (i.e., employed in 5 or fewer studies).

Next, we looked at the potential role of PrEP in reducing HIV prevalence among trans feminine individuals. Prior to the introduction of PrEP (1997–2011), the standardized HIV prevalence in US-based studies was 18.4% (95% CI 14.8% - 22.0%; Table 6) and the overall OR for HIV infection, compared to individuals over 15 years of age in the USA, was 53.5 (95% CI 29.7–96.5). After the introduction of PrEP (2012–2017), the standardized HIV prevalence in

Table 2. Meta-analysis of HIV prevalence in trans feminine individuals compared to all adults (age 15+).

Country	Year of data collection	Number of samples	Sample size	Frequency of HIV among TF in the samples	Prevalence (95% CI)*	Odds Ratio (95%CI)	HIV prevalence in adults (95% CI)
Argentina	2004	1	105	29	27.6 (19.1–36.2)	147.2 (96.0–225.9)	0.258 (0.257–0.260)
Argentina	2007	2	385	131	34 (29.3–38.8)	176 (142.6–217.4)	0.292 (0.290–0.294)
Argentina	2009	1	441	152	34.5 (30–38.9)	168.3 (138.3–204.8)	0.312 (0.310–0.314)
Australia	2004	1	141	6	4.3 (0.9–7.6)	44 (19.4–99.7)	0.101 (0.099–0.102)
Australia	2012	1	77	8	10.4 (3.6–17.2)	92.1 (44.3–191.5)	0.126 (0.124–0.127)
Bangladesh	2012	1	889	7	0.8 (0.2–1.4)	74.7 (35.5–157.3)	0.011 (0.010–0.011)
Brazil	1995	1	434	174	40.1 (35.5–44.7)	304.8 (251.6–369.3)	0.219 (0.218–0.220)
Brazil	2002	1	122	24	19.7 (12.6–26.7)	78 (49.9–121.9)	0.313 (0.312–0.314)
Brazil	2005	1	84	12	14.3 (6.8–21.8)	46.7 (25.3–86.0)	0.356 (0.355–0.357)
Brazil	2006	1	284	71	25.0 (20.0–30.0)	89.3 (68.2–116.8)	0.372 (0.371–0.373)
Brazil	2012	1	152	37	24.3 (17.5–31.2)	69.7 (48.1–100.9)	0.460 (0.459–0.461)
Brazil	2015	1	345	141	40.9 (35.7–46.1)	136.4 (110.1–169.1)	0.504 (0.503–0.505)
Brazil	2016	1	2846	843	29.6 (27.9–31.3)	81.1 (74.9–87.9)	0.516 (0.515–0.517)
Burkina Faso	2013	1	108	3	2.8 (-0.3–5.9)	2.7 (0.9–8.5)	1.043 (1.036–1.049)
Cambodia	2012	1	891	37	4.2 (2.8–5.5)	5.7 (4.1–7.9)	0.756 (0.751–0.762)
Cambodia	2015	1	1375	81	5.9 (4.6–7.1)	9.2 (7.3–11.5)	0.678 (0.673–0.683)
China	2016	1	498	38	7.6 (5.3–10)	187.7 (134.8–261.3)	0.044 (0.044–0.044)
Colombia	2011	1	58	8	13.8 (4.9–22.7)	40.2 (19.1–84.8)	0.397 (0.394–0.399)
Côte d'Ivoire	2015	1	298	76	25.5 (20.6–30.5)	11.7 (9.1–15.2)	2.832 (2.823–2.841)
El Salvador	2008	1	67	13	19.4 (9.9–28.9)	37.9 (20.7–69.4)	0.631 (0.623–0.639)
India	1997	1	84	38	45.2 (34.6–55.9)	183.8 (119.6–282.4)	0.447 (0.447–0.448)
India	2006	1	575	104	18.1 (14.9–21.2)	66.7 (53.9–82.5)	0.330 (0.330–0.330)
India	2007	2	529	71	13.4 (10.5–16.3)	49.8 (38.8–63.9)	0.310 (0.310–0.311)
India	2011	1	176	27	15.3 (10.0–20.7)	65.7 (43.6–99.0)	0.275 (0.275–0.275)
India	2012	1	82	11	13.4 (6.0–20.8)	59.9 (31.7–113.0)	0.258 (0.258–0.258)
India	2009	1	51	21	41.2 (27.7–54.7)	255.3 (146.1–445.8)	0.273 (0.273–0.274)
Indonesia	2002	1	241	53	22 (16.8–27.2)	288.5 (212.7–391.4)	0.098 (0.097–0.098)
Indonesia	2007	2	1225	334	27.3 (24.8–29.8)	160.4 (141.5–181.9)	0.233 (0.232–0.234)
Indonesia	2009	1	217	80	36.9 (30.4–43.3)	214.1 (162.5–282.1)	0.272 (0.271–0.273)
Indonesia	2012	1	100	16	16.0 (8.8–23.2)	61.5 (36.0–105.0)	0.309 (0.308–0.310)
Italy	1998	1	473	149	31.5 (27.3–35.7)	390.4 (321.5–474.1)	0.118 (0.117–0.119)
Italy	2007	1	173	21	12.1 (7.3–17)	65.7 (41.7–103.8)	0.210 (0.208–0.211)
Italy	2009	1	56	3	5.4 (-0.5–11.3)	26.8 (8.4–85.6)	0.211 (0.210–0.212)
Jamaica	2015	1	103	26	25.2 (16.9–33.6)	22.7 (14.5–35.4)	1.468 (1.451–1.484)
Lebanon	2012	1	40	4	10.0 (0.7–19.3)	246.1 (87.5–692.4)	0.045 (0.043–0.047)
Lesotho	2013	1	71	42	59.2 (47.7–70.6)	4.6 (2.9–7.4)	23.950 (23.876–24.023)
Malawi	2013	1	75	12	16.0 (7.7–24.3)	1.8 (1.0–3.3)	9.683 (9.664–9.703)
Malaysia	2014	1	193	24	12.4 (7.8–17.1)	39.9 (26.0–61.1)	0.355 (0.352–0.357)
Mali	2014	1	165	37	22.4 (16.1–28.8)	220.9 (153.1–318.6)	0.131 (0.128–0.133)
Mexico	2012	1	100	22	22 (13.9–30.1)	123.9 (77.2–198.9)	0.227 (0.226–0.228)
Netherlands	2003	1	69	13	18.8 (9.6–28.1)	218.8 (119.7–400.2)	0.106 (0.104–0.108)
Nigeria	2014	1	105	75	71.4 (62.8–80.1)	183 (119.8–279.4)	1.348 (1.346–1.350)
Pakistan	1998	1	208	0	0 (0.0–0.0)	395.9 (24.6–6359.6)	0.001 (0.001–0.001)
Pakistan	2004	1	409	5	1.2 (0.2–2.3)	451.5 (186.8–1091.6)	0.003 (0.003–0.003)
Pakistan	2005	1	1162	10	0.9 (0.3–1.4)	73.0 (39.2–136.1)	0.012 (0.012–0.012)
Pakistan	2006	1	810	38	4.7 (3.2–6.1)	243.0 (175.4–336.6)	0.020 (0.020–0.021)

(*Continued*)

Table 2. (Continued)

Country	Year of data collection	Number of samples	Sample size	Frequency of HIV among TF in the samples	Prevalence (95% CI)*	Odds Ratio (95%CI)	HIV prevalence in adults (95% CI)
Pakistan	2007	1	269	6	2.2 (0.5–4)	78.4 (34.9–176.1)	0.029 (0.029–0.029)
Pakistan	2008	1	1181	75	6.4 (5–7.7)	172.4 (136.4–217.9)	0.039 (0.039–0.040)
Pakistan	2009	1	306	66	21.6 (17–26.2)	560.5 (426.8–736.1)	0.049 (0.049–0.049)
Pakistan	2015	1	134	22	16.4 (10.1–22.7)	214.8 (136.0–339.2)	0.091 (0.091–0.092)
Paraguay	2011	1	237	64	27 (21.4–32.7)	89.5 (67.2–119.3)	0.411 (0.406–0.417)
Peru	2007	1	214	64	29.9 (23.8–36)	158.9 (118.5–212.9)	0.268 (0.266–0.270)
Peru	2008	1	208	35	16.8 (11.7–21.9)	75.3 (52.4–108.3)	0.268 (0.266–0.270)
Peru	2009	1	420	130	31 (26.5–35.4)	166.9 (135.7–205.3)	0.268 (0.266–0.270)
Peru	2011	1	713	104	14.6 (12–17.2)	62.5 (50.7–76.9)	0.273 (0.270–0.275)
Peru	2013	1	89	30	33.7 (23.9–43.5)	176.6 (113.8–274.1)	0.287 (0.285–0.289)
Peru	2014	1	310	61	19.7 (15.3–24.1)	81.1 (61.3–107.4)	0.301 (0.299–0.303)
Philippines	2015	1	299	11	3.7 (1.5–5.8)	50.9 (27.9–92.9)	0.075 (0.074–0.076)
Senegal	2013	1	199	74	37.2 (30.5–43.9)	118.1 (88.6–157.4)	0.499 (0.494–0.504)
Spain	2000	1	60	14	23.3 (12.6–34)	115.6 (63.5–210.2)	0.263 (0.261–0.264)
Spain	2005	1	529	129	24.4 (20.7–28)	109.3 (89.6–133.3)	0.294 (0.293–0.296)
Spain	2008	1	142	18	12.7 (7.2–18.1)	43.6 (26.6–71.5)	0.332 (0.330–0.334)
Spain	2010	1	101	46	45.5 (35.8–55.3)	235.3 (159.1–348.1)	0.354 (0.352–0.356)
Spain	2015	1	453	40	8.8 (6.2–11.4)	28.1 (20.3–38.8)	0.344 (0.342–0.346)
Swaziland	2013	1	120	17	14.2 (7.9–20.4)	74.5 (44.6–124.4)	0.221 (0.218–0.225)
Thailand	2005	1	474	64	13.5 (10.4–16.6)	12.8 (9.9–16.7)	1.202 (1.199–1.205)
Thailand	2008	1	140	13	9.3 (4.5–14.1)	9 (5.1–16)	1.121 (1.119–1.124)
Thailand	2012	1	47	2	4.3 (-1.5–10)	4.4 (1.1–18.1)	1.002 (1.000–1.005)
Thailand	2013	1	692	82	11.8 (9.4–14.3)	13.7 (10.8–17.2)	0.975 (0.973–0.978)
Thailand	2015	2	1221	108	8.8 (7.3–10.4)	10.6 (8.7–12.9)	0.908 (0.906–0.911)
Togo	2013	1	51	9	17.6 (7.2–28.1)	8.9 (4.3–18.2)	2.359 (2.345–2.374)
Uruguay	1999	1	200	49	24.5 (18.5–30.5)	111.3 (80.6–153.8)	0.291 (0.284–0.297)
US	1997	1	392	137	34.9 (30.2–39.7)	190.7 (154.9–234.7)	0.281 (0.280–0.282)
US	1998	2	482	91	18.9 (15.4–22.4)	81.0 (64.5–101.7)	0.287 (0.286–0.287)
US	2000	1	538	161	29.9 (26.1–33.8)	138.9 (115.5–167.1)	0.306 (0.306–0.307)
US	2004	2	141	30	21.3 (14.5–28)	82.3 (55.0–123.2)	0.327 (0.327–0.328)
US	2005	3	852	81	9.5 (7.5–11.5)	31.1 (24.8–39.2)	0.336 (0.335–0.337)
US	2007	1	223	25	11.2 (7.1–15.4)	37.4 (24.7–56.7)	0.337 (0.336–0.337)
US	2009	2	602	195	32.4 (28.7–36.1)	134.8 (113.7–159.9)	0.354 (0.353–0.355)
US	2010	3	16943	664	3.9 (3.6–4.2)	10.8 (10–11.7)	0.375 (0.374–0.376)
US	2011	2	657	75	11.4 (9–13.8)	33.5 (26.3–42.6)	0.383 (0.383–0.384)
US	2012	1	292	13	4.5 (2.1–6.8)	11.8 (6.8–20.7)	0.392 (0.391–0.392)
US	2013	3	729	197	27 (23.8–30.2)	94.1 (79.9–110.8)	0.392 (0.391–0.393)
US	2016	2	380	148	38.9 (34–43.9)	166.6 (135.5–204.7)	0.382 (0.381–0.382)
US	2003	1	192	16	8.3 (4.4–12.2)	18.9 (11.3–31.5)	0.479 (0.478–0.480)
Vietnam	2004	1	75	5	6.7 (1–12.3)	24.7 (10–61.1)	0.289 (0.287–0.290)
Vietnam	2015	1	205	37	18 (12.8–23.3)	68.4 (47.9–97.6)	0.321 (0.320–0.322)
Overall	-	-	-	-	19.9 (14.7–25.1)*	66.0 (51.4–84.8)	-

Note. Heterogeneity: $Q = 6327.25$, $df = 86$, $p < .0001$, $I^2 = 98.63\%$.

*Overall prevalence was calculated by direct standardization based on country-year weights used in meta-analysis.

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Table 3. Meta-analysis of HIV prevalence in trans masculine individuals compared to all adults (age 15+).

Country	Year of data collection	Number of samples	Sample size	Frequency of HIV among TM in the samples	Prevalence (95% CI)*	Odds Ratio (95% CI)	HIV prevalence in adults (95% CI)
Australia	2004	1	17	0	0.0 (0.0–0.2)	28.3 (1.7–470.5)	0.101 (0.099–0.102)
Australia	2012	1	28	1	3.6 (-3.3–10.4)	29.4 (4–216.5)	0.126 (0.124–0.127)
Brazil	2002	1	16	0	0.0 (0.0–0.2)	9.7 (0.6–160.9)	0.313 (0.312–0.314)
Brazil	2006	1	51	0	0.0 (0.0–0.1)	2.6 (0.2–42.1)	0.372 (0.371–0.373)
Canada	2013	1	11	0	0.0 (0.0–0.3)	19.1 (1.1–323.8)	0.227 (0.226–0.229)
Italy	2007	1	20	0	0.0 (0.0–0.2)	11.6 (0.7–191.9)	0.210 (0.208–0.211)
Italy	2009	1	27	0	0.0 (0.0–0.1)	8.6 (0.5–140.9)	0.211 (0.210–0.212)
Spain	2008	1	92	2	2.2 (-0.8–5.2)	6.7 (1.6–27.1)	0.332 (0.330–0.334)
US	1997	1	123	2	1.6 (-0.6–3.9)	5.9 (1.5–23.7)	0.281 (0.280–0.282)
US	2003	1	50	0	0.0 (0.0–0.1)	3.0 (0.2–48.3)	0.331 (0.330–0.332)
US	2005	2	124	2	1.6 (-0.6–3.8)	4.7 (1.2–19.2)	0.345 (0.344–0.345)
US	2007	2	92	8	8.7 (2.9–14.5)	26.2 (12.7–54.2)	0.362 (0.361–0.362)
US	2009	2	292	2	0.7 (-0.3–1.6)	1.8 (0.5–7.3)	0.379 (0.378–0.379)
US	2010	2	5256	21	0.4 (0.2–0.6)	1.0 (0.7–1.6)	0.387 (0.386–0.388)
US	2011	1	120	10	8.3 (3.4–13.3)	22.9 (12–43.8)	0.395 (0.395–0.396)
US	2012	1	30	1	3.3 (-3.1–9.8)	8.7 (1.2–63.7)	0.396 (0.395–0.396)
US	2013	1	122	0	0.0 (0.0–2.8)	1.0 (0.1–16.7)	0.392 (0.391–0.393)
Overall	-	-	-	-	2.56 (0.0–5.9)*	6.8 (3.6–13.1)	-

Note. Heterogeneity: $Q = 13.06$, $df = 16$, $p<0.0001$, $I^2 = 70.62\%$.

*Overall prevalence was calculated by direct standardization based on country-year weights used in meta-analysis.

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US-based studies was 23.7% (95% CI 20.2% - 27.2%) and the OR for HIV infection, compared to individuals over 15 years of age, was 58.0 (95% CI 12.3–275.9). The forest plot of this analysis is presented in Fig 4.

Heterogeneity was high across the studies that included trans feminine individuals ($Q = 6327.25$, $df = 86$, $p < .0001$, $I^2 = 98.63\%$). This may be because the studies were conducted in different countries using different methodologies. Heterogeneity was moderate for the studies that included trans masculine individuals ($Q = 102.06$, $df = 15$, $p<0.0001$, $I^2 = 72.17\%$). The funnel plots showed an asymmetrical distribution of studies and may therefore indicate publication bias (S2 Appendix in Fig A2.1 and Fig A2.2).

Discussion

This systematic review and meta-analysis affirms that transgender individuals are disproportionately burdened by HIV, and that this is the case for not only trans feminine individuals, but also for trans masculine individuals. Using a larger pooled sample than ever compiled before, we ascertained that trans masculine individuals almost seven times more likely to have HIV, and trans feminine individuals are 66 times more likely to have HIV, than other individuals over 15 years of age. Additionally, based on data from 34 countries across major geographic regions, we found support for the contention that the disproportionate burden for HIV carried by transgender individuals is a worldwide phenomenon, and that some regions, such as Africa and Latin America, may be impacted more than others. Further, we established that sampling methods are likely to impact prevalence rates and that, to date, PrEP prevention effects on HIV prevalence cannot be established.

To our knowledge, no previous study has estimated the HIV burden carried by trans masculine individuals worldwide. Reisner and Murchinson [1] did conduct a research synthesis of

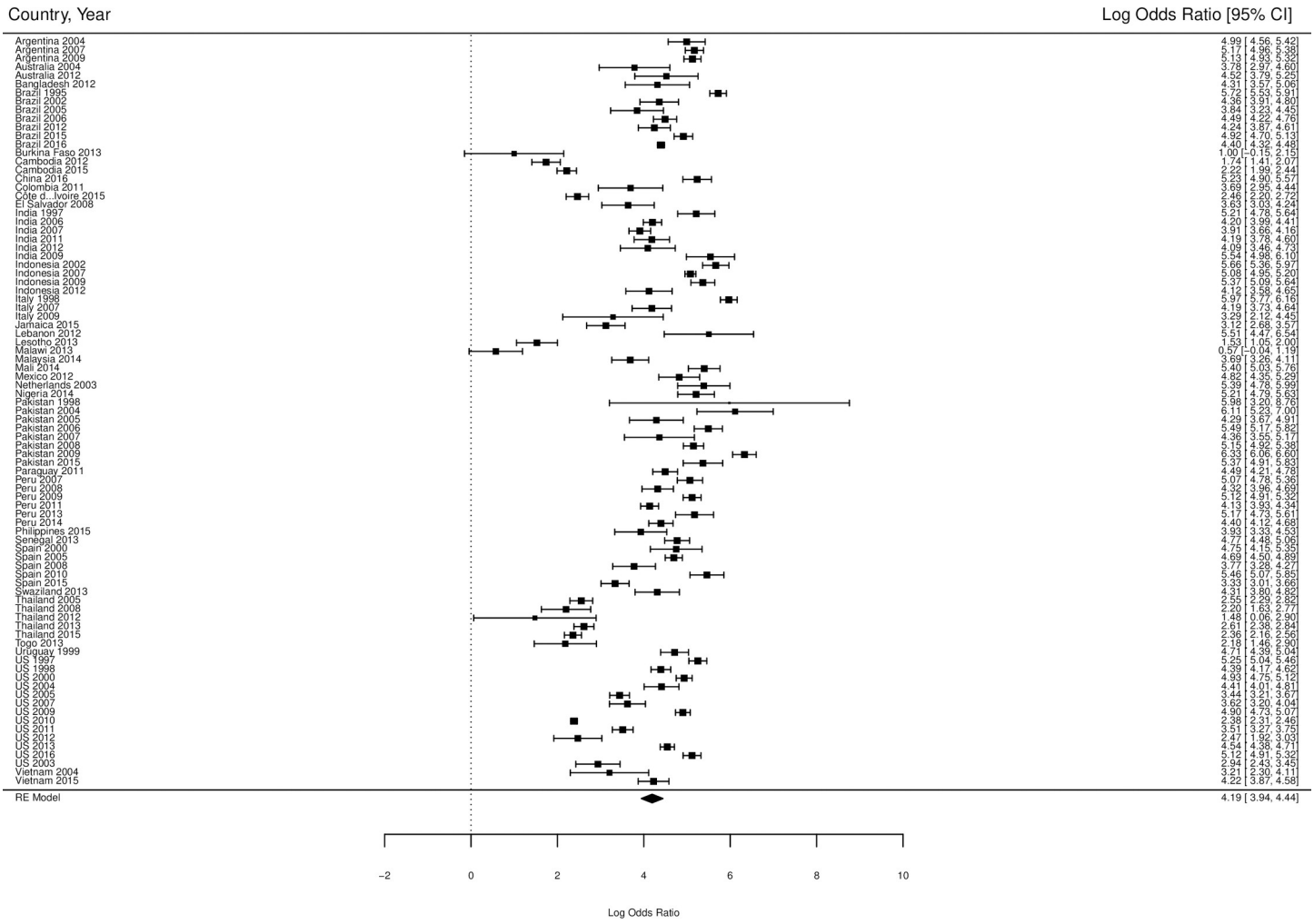


Fig 2. Forest plot of HIV prevalence in trans feminine individuals compared to all adults (age 15+). The scale on the x-axis is log odds ratio. The percentages indicate the weight of each country by year within the meta-analysis. The numbers in the right column are the log odds ratios including their confidence intervals. We converted these log odds ratios into odds ratios, as described in *Table 2*.

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HIV risks in trans masculine individuals where laboratory-confirmed prevalence ranged from 0% to 4.3% and Becasen and colleagues [17] established a laboratory-confirmed estimated prevalence rate of 3.2% but, in both studies, no odds ratios were calculated to ascertain the relative burden of HIV carried by trans masculine individuals. Our finding that trans masculine individuals are almost seven times more likely to have HIV than other individuals over 15 years of age indicates that many trans masculine individuals are indeed at risk for HIV. The presumption that trans masculine individuals almost exclusively have sex with cis-gender women and are therefore not at risk for HIV is thus incorrect [1]. As indicated by Reisner and Murchinson, there is a diverse range of bio-anatomies represented among trans masculine individuals and their partners in sexual encounters, and these should be considered in HIV prevention efforts [1].

Our finding that trans feminine individuals are 66 times more likely to have HIV than other individuals over 15 years of age is a higher estimate that the estimate generated in Baral and colleagues' meta-analysis, [4] where the odds ratio for HIV infection among transgender women was 49.1. We believe that the odds ratio and prevalence rates established in our

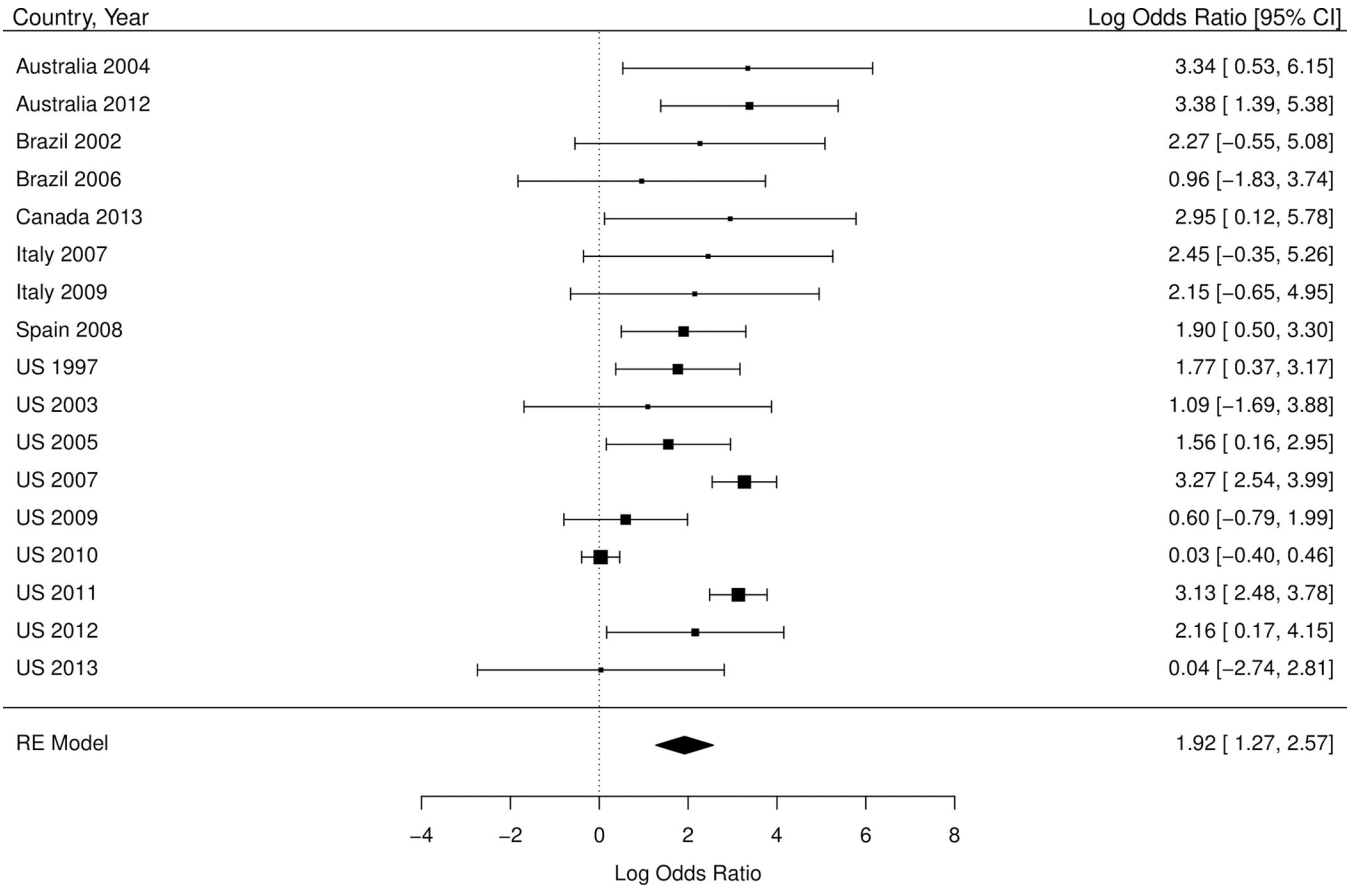


Fig 3. Forest plot of HIV prevalence in trans masculine individuals compared to all adults (age 15+). The scale on the x-axis is log odds ratio. The percentages indicate the weight of each country by year within the meta-analysis. The numbers in the right column are the log odds ratios including their confidence intervals. We converted these log odds ratios into odds ratios, as described in *Table 3*.

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systematic review and meta-analysis are likely more realistic estimations for two reasons. First, our methodological approach used standardized rather than pooled prevalence and took into account not only country but also year of data collection. In a pooled estimate, the total study population and total HIV cases are summed, and then a crude proportion is calculated. This does not take heterogeneity and variation among the included studies into account. Our standardization approach entailed taking the weights from each country-year into account. Without the weighted standardization, a country-year combination that contains large or small

Table 4. HIV prevalence and odds ratios for trans feminine individuals compared to all adults (age 15+), separated by geographic region.

Region	Number of countries	Number of Samples	Sample size	Prevalence (95% CI) *	Odds Ratio (95% CI) *	HIV prevalence in adults (95% CI)*
Africa	9	9	1192	29.9 (22.5–37.3)	21.5 (6.3–73.7)	4.69 (4.67–4.71)
Asia	11	35	14798	13.5 (2.3–17.7)	68.0 (42.9–107.8)	0.344 (0.343–0.345)
Global North	5	35	24697	17.1 (13.1–21.1)	48.4 (28.2–83.9)	0.297 (0.296–0.298)
Latin America	9	23	7917	25.9 (20.0–31.8)	95.6 (73.7–122.7)	0.391 (0.388–0.394)

Note. The HIV prevalence in adults of the population (last column) is the weighted prevalence of the countries included in this meta-analysis, not overall prevalence in the region.

* Results were calculated by direct standardisation of country-year sample size instead of pooling.

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Table 5. HIV prevalence in trans feminine individuals, separated by sampling method.

Sampling method	Number of samples	Sample size	HIV prevalence (95% CI)*
Respondent driven sampling	33	12202	23.3 (18.0–28.4)
STI clinic visit	26	19360	17.4 (12.2–22.7)
Convenience sampling	14	3733	19.7 (14.8–24.5)
Cluster sampling	11	4273	19.6 (14.4–24.9)
Hospital	5	827	15.0 (9.8–20.4)
Snowball	4	1203	11.8 (8.0–15.6)
Surveillance	4	2339	9.1 (6.1–12.0)
NGO	2	213	37.8 (31.5–44.2)
Database health plan	1	3475	5.4 (4.6–6.1)
Purposive sampling	1	538	29.9 (26.1–33.8)

Note. For one study, the sampling method was unknown and is not included in this table.

*: Results were calculated by direct standardisation of country-year sample size instead of pooling.

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study samples is likely to deliver misleading pooled results. The standardized approach thus delivers a more robust estimation than a pooled approach. Second, due to recent increases in the number of studies reporting HIV prevalence among transgender individuals, the total sample of transgender individuals in our meta-analysis was almost four and a half times larger than the pooled sample in Baral et al. [4] Third, the data reviewed in Baral et al. was derived from 15 countries, all of which have male-dominant epidemics, while the data in the meta-analysis reported here was derived from 34 countries, thus lending additional support to the contention that the high burden of HIV among transgender individuals is a worldwide phenomenon.

Our finding that HIV prevalence among transgender individuals appears to be, over the course of the epidemic, higher in African and Latin American regions may point to greater disapproval of gender fluidity and the accompanying marginalization that puts transgender individuals more at risk for HIV in these regions, although we recognize that overall prevalence rates for HIV are higher in Sub-Saharan Africa than in many other regions. Nonetheless, this was the first systematic review and meta-analysis to include samples from Sub-Saharan Africa, and the findings from Sub-Saharan Africa point to a significant burden of HIV among transgender individuals. However, given that, in our analyses, the sample sizes for African regions and Latin America were smaller than the sample sizes for other regions, more research is needed to confirm that transgender individuals in these regions do indeed have higher prevalence rates and carry an even greater burden of HIV. Additionally, future research should also seek to establish HIV prevalence rates and burdens in other understudied regions such as Eastern Europe.

This meta-analysis also demonstrated that sampling methods are likely to impact prevalence rates. This is in line with critiques of sampling methods that were levied in earlier

Table 6. HIV prevalence and odds ratios for trans feminine individuals compared to all adults (age 15+) in US-based studies, according to whether data was collected before or after the introduction of PrEP (2012).

	Number of studies	Sample size	Frequency of HIV among TF in the samples	Prevalence (95%CI)*	Odds Ratio (95%CI)
Before PrEP	18	21022	1475	18.4 (14.8–22.0)	53.5 (29.7–96.5)
After PrEP	6	1401	358	23.7 (20.2–27.2)	58.0 (12.3–275.9)

Note. *Overall prevalence was calculated by direct standardization based on country-year weights used in meta-analysis.

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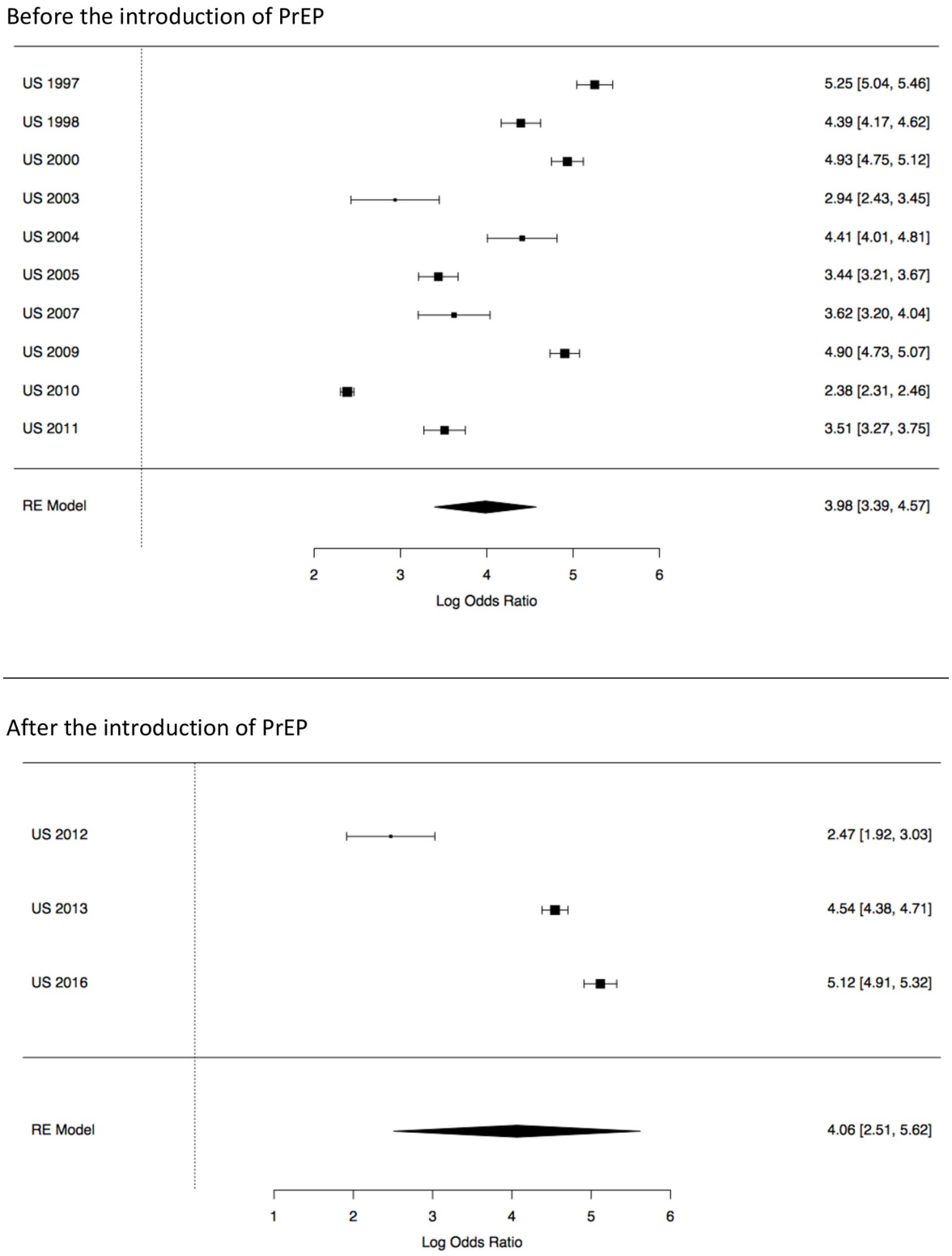


Fig 4. Forest plot of HIV prevalence in trans feminine individuals in the USA compared to all adults (age 15+) in the USA. The 10 country-year including 18 studies above the line are studies where data were collected prior to the introduction of PrEP (2012). The 3 country-year including 6 studies below the line are studies where data were collected after the introduction of PrEP. The scale on the x-axis is log odds ratio. The percentages indicate the weight of each sample within the meta-analysis. The numbers in the right column are the log odds ratios including their confidence intervals.

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commentaries on Baral et al. [4] and in other studies [11, 18, 134]. In our study, the various sampling methods generated very different prevalence rates for HIV in trans feminine individuals ranging from 5.4% to 37.8%. However, the four most frequently used sampling methods, namely respondent-driven sampling, sampling via STI clinics, convenience sampling, and cluster sampling had similar ranges (17.4% to 23.3%). We believe that the impact of sampling methods on prevalence rates is in need of further investigation. In our analyses, unambiguous classification was not always possible and the prevalence rates generated for less common sampling methods may be less reliable. We therefore recommend more comprehensive investigations of the impact of sampling methods in transgender studies.

In our meta-analyses, we also explored the potential role of PrEP availability by comparing studies conducted in the US where data was collected prior to and after the introduction of PrEP. No effect of PrEP could be established yet in our analyses. In fact, we found a higher HIV prevalence rate following the introduction of PrEP. This may be because there were only six studies done following the introduction of PrEP and the total sample after PrEP introduction was smaller and possibly less representative than the 18 studies conducted before PrEP was introduced. It is possible that no reduction in prevalence due to PrEP is the result of PrEP not yet reaching trans individuals. The inclusion of transgender individuals in PrEP trials has been low and access to PrEP for transgender individuals has been limited.[20, 21, 135] However, a qualitative study on PrEP acceptability among transgender women in San Francisco showed that interest was relatively high once participants were informed about the possibilities, thus suggesting that transgender individuals at high risk for HIV need to be informed about PrEP [20]. By the same bio-medical token, future meta-analytic studies should also include Treatment-as-prevention (TasP) effects in their analysis, once sufficiently robust primary data is available.

This systematic review and meta-analysis should be interpreted in light of possible limitations. One is potential sample size biases for studies originating from countries other than the USA, and those of trans masculine individuals. To be able to present a comprehensive, global picture, we set a lower bound for trans feminine individuals, excluding sample sizes of trans feminine individuals less than 40. Yet, we did not apply a minimum sample size for studies among trans masculine individuals as this would have resulted in the exclusion of most studies reporting HIV prevalence among trans masculine individuals. Further, we were not in a position to conduct city-level comparisons and thus acknowledge that our country-level analyses may provide a less precise estimation of the odds ratios, as these do not take into account that, in some countries, the HIV epidemic is more concentrated in certain areas. A third possible limitation is related to our classification of sampling methods. Unambiguous classification was not always feasible and it is possible that the prevalence rates generated for less common sampling methods were less reliable. Fourth, in our meta-analysis, the sample sizes for African regions and Latin America were smaller than the sample sizes for other regions, and this may have impacted the prevalence rates. Additionally, no prevalence rates from Eastern Europe were available. Fifth, our analysis did not account for sexual orientation or the presence or absence of gender reassignment surgery, both of which can impact HIV risk. It is also did not separately ascertain prevalence rates for trans feminine individuals who engage in sex work versus those who do not as primary level data on this is not available on a global scale. We recommend that future research take these potential shortcomings into consideration. Specifically, we recommend that future research explicitly investigate prevalence among subpopulations within the transgender community, and that new studies also take changes in HIV treatment (TasP) and sampling strategies, as well as their interactions, into account, as this will provide an even more comprehensive picture of HIV prevalence and burden among transgender individuals.

Summary and recommendations

That transgender individuals, both trans feminine and trans masculine, are, worldwide, disproportionately burdened by HIV points to the need to pay explicit attention to the unique HIV prevention and care needs of transgender individuals. HIV surveillance and research has traditionally grouped transgender individuals, particularly trans feminine individuals, with men who have sex with men (MSM), thus conflating gender with anatomy. This obscures the unique situation and vulnerabilities to HIV of transgender people [100]. It is therefore necessary to abandon the aggregation of data across MSM and trans feminine women [100, 136]. Additionally, and in line with MacCarthy et al., [11] we also propose disaggregating data across trans feminine and trans masculine individuals [106]. Although some individual and structural risk factors for HIV may be shared by transgender individuals, trans feminine and trans masculine individuals have unique needs [106].

Ascertaining that transgender individuals continue to be disproportionately burdened by HIV is important as it can serve as an impetus for efforts to change this burden. Although transgender individuals in certain regions may more affected by HIV and knowing that transgender processes are diverse across the world, we contend that it is important to, in all regions, target multiple levels of HIV risk, as well as their antecedents and their intersections, while being cognizant of the local context. Targeting individual level risk factors, such as unprotected sex, STI co-infection, and needle sharing, must occur alongside broader efforts to support transgender individuals and reduce stigmatization and marginalization [9, 137, 138].

Paramount to HIV risk reduction is gender affirmation, and in the context of HIV, gender affirmation is particularly important in health care [139–141]. Discrimination, judgment, insensitivity, and a lack of understanding from health care providers prevents many transgender individuals from accessing HIV prevention, testing, treatment, and care services [142]. Gender affirming care is not simply the provision of hormones and gender-affirming surgeries; it also includes using patients' preferred names and pronouns, respecting diversity in gender identities and expressions, employing inclusive intake forms, displaying images that are welcoming to transgender individuals, and creating safe spaces where transgender individuals can be themselves [135, 143]. We recommend integrating HIV prevention and care services in broader gender-affirming care services [6, 135, 142]. This includes actively making PrEP available to transgender individuals [141, 144, 145].

Conclusion

In sum, this systematic review and meta-analyses have served to update our understanding of HIV prevalence over the course of the epidemic as well as HIV burden in both trans feminine and trans masculine individuals using a larger sample than ever before, and has shown that, worldwide, both carry a substantially higher burden of HIV than other individuals over 15 years of age. It has further demonstrated that a by country and year analysis is recommended, that prevalence rates are higher in African and Latin American regions, that sampling methods may impact prevalence rates, and that, at this point in time, the evidence does not suggest that PrEP has played a role in reducing HIV among transgender individuals.

Supporting information

S1 Appendix. Initial meta-analyses.
(DOCX)

S2 Appendix. Fig A2.1. Funnel plot for the countries describing data from trans feminine individuals. Fig A2.2. Funnel plot for the countries describing data from trans masculine

individuals.
(ZIP)

S1 Checklist. PRISMA 2009 checklist.
(DOC)

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Weddle Declaration
Exhibit F

Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents With HIV

Developed by the HHS Panel on Antiretroviral Guidelines for Adults and Adolescents—A Working Group of the NIH Office of AIDS Research Advisory Council (OARAC)

How to Cite the Adult and Adolescent Antiretroviral Guidelines:

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It is emphasized that concepts relevant to HIV management evolve rapidly. The Panels have a mechanism to update recommendations on a regular basis, and the most recent information is available on the Clinicalinfo website (https://clinicalinfo.hiv.gov/).

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What's New in the Guidelines

Updated: September 12, 2024
Reviewed: September 12, 2024

These guidelines were updated by the U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) based on key new clinical evidence on the use of antiretroviral therapy (ART) for the treatment of people with HIV.

New Section Added to the Guidelines

Transplantation in People With HIV

This new section has been added to provide guidance on ART management in people with HIV who are candidates or recipients of solid organ and hematopoietic cell transplants. The Panel emphasizes the importance of maintaining HIV viral suppression before and after a transplant. The addition of immunosuppressive therapy and prophylaxis against opportunistic infections to ART increases pill burden and the potential for drug–drug interactions and adverse effects. Because of the complexities of medical management, the Panel recommends that people with HIV who require transplantation be managed by a multidisciplinary team before, during, and after transplant **(AIII).**

Key Revisions to the Guidelines

What to Start: Initial Combination Antiretroviral Regimens for People With HIV

Several changes have been made to the Panel's recommendations for initial ART regimens for people with HIV. The regimens recommended by the Panel as initial ART for people with HIV include those that have demonstrated clinical efficacy, have a high barrier to resistance, are well tolerated, and can be given as once-daily therapy. The Panel made the following changes to the recommended initial ART regimens:

- Dolutegravir (DTG)/abacavir/lamivudine (3TC) has been changed from one of the Recommended Initial Regimens for Most People With HIV (Table 6a) to a regimen recommended as part of Other Initial Antiretroviral Regimens for Certain Clinical Scenarios (Table 6b) due to the need for HLA-B*5701 testing before initiating therapy, the potential increase in the risk of cardiovascular events, and the availability of other options for initial therapy.
- Several antiretroviral (ARV) regimens are no longer recommended as initial therapy due to higher pill burdens, more adverse effects, or a lower barrier to resistance than other ART regimens recommended by the Panel. These regimens include the following:
  - Elvitegravir/cobicistat and raltegravir-based regimens
  - Boosted atazanavir-based regimens
  - Efavirenz-based regimens
  - Rilpivirine (RPV)/tenofovir disoproxil fumarate/emtricitabine (FTC) regimens

Virologic Failure

Updates made to the Virologic Failure section include the following:

- For people who experience virologic failure while on their first ARV regimen of a non-nucleoside reverse transcriptase inhibitor (NNRTI) plus two nucleoside reverse transcriptase inhibitors (NRTIs), a salvage regimen of DTG plus boosted darunavir can be used **(AI)**. This recommendation is based on data from the D^2EFT trial, a large randomized controlled trial comparing this regimen to a regimen of DTG plus two NRTIs.
- Some people with HIV cannot reach or maintain viral suppression on oral ART despite intensive adherence support. A complete regimen of long-acting injectable cabotegravir and rilpivirine (LA CAB/RPV) has been used in this population with some success, although long-term efficacy data are limited. Based on very limited data, the Panel recommends the use of LA CAB/RPV on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral ART, who have no evidence of resistance to CAB or RPV, and with shared decision-making between providers and people with HIV **(CIII).** The Panel notes that people with HIV and their providers must be aware of the significant risk of developing resistance to NNRTIs, and particularly integrase strand transfer inhibitors (INSTIs) if virologic failure occurs on LA CAB/RPV. Such resistance may limit future treatment options and may also lead to HIV transmission.

Optimizing Antiretroviral Therapy in the Setting of Viral Suppression

Updates made to the Optimizing Antiretroviral Therapy in the Setting of Viral Suppression section include the following:

- Because more people with HIV are switched to regimens that do not include NRTIs or only include 3TC, the Panel has expanded the guidance to emphasize the importance of keeping regimens that contain hepatitis B virus (HBV)–active drugs for people with HBV/HIV coinfection. For people with no known history of HBV infection, the Panel noted the need to screen for HBV before initiating NRTI-sparing (or limited) regimens.
- The discussion of LA CAB/RPV as a switch strategy with data from additional clinical trials and information on the use of this regimen in people who have challenges with adherence to oral ART.
- The Panel expanded on the discussion of clinical trial data on switch strategies in people with limited or extensive drug resistance.

HIV and the Older Person

Updates made to the HIV and the Older Person section include the following:

- A new subsection on HIV and Immunologic Aging.
- Expanded discussions on non-AIDS complications among older people with HIV.
- A discussion on atherosclerotic cardiovascular disease in older people with HIV and the recent recommendation for the use of statins in people with HIV (see Statin Therapy in People With HIV).

Substance Use Disorders and HIV

Updates made to the Substance Use Disorders and HIV section include the following:

- A new subsection on Substance Use and Unstable Housing that includes discussion of the impact of unstable housing on the HIV care continuum and adherence to ART.

- An expanded discussion on considerations when using LA CAB/RPV in people with HIV and substance use disorder.
- A new subsection that includes a discussion on xylazine, an adulterant that may be added to opioids, such as fentanyl. The Panel notes that xylazine is a cytochrome P450 (CYP) 3A4 substrate; thus, its half-life may be prolonged in the presence of CYP3A4 inhibitors, such as ritonavir or cobicistat, further increasing the risk of overdose.

Transgender People With HIV

Updates made to the Transgender People With HIV section include the following:

- An update on the epidemiology of transgender people with HIV based on recent data from national surveys and Centers for Disease Control and Prevention (CDC) surveillance reports.
- An expanded discussion on barriers that transgender adults and adolescents with HIV may face in accessing care and maintaining HIV suppression.
- A new table that lists the most commonly used gender-affirming hormone therapies (GAHT).
- Updates to the drug–drug interaction table for interactions between GAHT and ARV drugs to include newer ARV drugs used in clinical practice.
- The Panel expanded discussion on cardiovascular disease risk in transgender people with HIV who use GAHT.

Hepatitis B Virus/HIV Coinfection

Updates made to the Hepatitis B Virus/HIV Coinfection section include the following:

- The Panel no longer recommends pegylated interferon as a therapy for the treatment of HBV in people with HIV **(AIII).** Pegylated interferon should only be considered in rare cases and with consultation with an expert in HBV**.**
- The Panel noted that approximately 4% of people with HBV/HIV coinfection are also found to have hepatitis D virus (HDV) in serologic testing. Because HBV/HDV coinfection is associated with serious liver complications, experts recommend screening for HDV in people with HBV/HIV coinfection.
- The Panel emphasizes that for people with HBV/HIV coinfection who are planning to switch to an NRTI-sparing regimen, ARV drugs that are active against HIV should be continued **(AII)** or another anti-HBV drug (i.e., entecavir) should be initiated **(AII).**
- Due to increased interest in switching people to NRTI-sparing or NRTI-limiting ARV regimens, this section stresses the importance of screening for HBV before switching to NRTI-sparing or NRTI-limiting regimens in people who are not known to have HBV infection. The Panel recommends vaccination for those found to be nonimmune to HBV and provides guidance for monitoring and managing people with prior exposure to HBV.

Tuberculosis/HIV Coinfection

Updates made to the Tuberculosis/HIV Coinfection section include the following:

- The Panel previously did not recommend the use of a DTG-based regimen for people with HIV who use a once-daily isoniazid plus rifapentine regimen for the treatment of latent tuberculosis infection. Based on data from a recently published pharmacokinetics (PK) study, the Panel now recommends that—
    - For a person with virologic suppression while on a once-daily DTG 50 mg regimen, the DTG dose should be increased to 50 mg twice daily throughout the course of once-daily isoniazid plus rifapentine for 1 month (1HP), continuing DTG twice daily for 14 days after 1HP completion before switching back to once-daily DTG dosing **(AII).**
- The subsection on Drug Interaction Considerations has been updated to indicate that rifamycins are not recommended for use with the long-acting injectable drugs CAB, RPV, or lenacapavir.

Adherence to the Continuum of Care Section

Updates made to the Adherence to the Continuum of Care section include the following:

- The section emphasizes that addressing social determinants of health is essential for enhancing adherence throughout the HIV continuum of care.
- A new subsection has been added to discuss the importance of guiding individuals with HIV through transitions between different health care systems to ensure continuity of care.
- The subsection on the use of LA CAB/RPV in people with viremia and ongoing challenges to oral ART adherence or retention in care has been expanded to incorporate recommendations from the Virologic Failure section of the guidelines.

Drug–Drug Interactions

Tables 24a through 24g have been updated with new PK data on interactions between ARV drugs and other drugs, including drugs that were approved by the U.S. Food and Drug Administration in the past 3 years and that may have interactions with ARV drugs.

Other Updates

Minor updates have been made to the following sections of the guidelines:

- Drug-Resistance Testing
- Early (Acute and Recent) HIV Infection
- Women With HIV
- Cost Considerations and Antiretroviral Therapy
- Appendix B, Table 12

Sections Removed From the Guidelines

- Antiretroviral Components or Regimens Not Recommended as Initial Therapy
- What Not to Use

Panel Roster

Updated: September 12, 2024
Reviewed: September 12, 2024

Members and Consultants of the U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents

These guidelines were developed by the U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents (a working group of the National Institutes of Health Office of AIDS Research Advisory Council).

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Financial Disclosure

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U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents: Financial Disclosure for Companies Related to HIV Treatment or Diagnostics for the Period of April 1, 2023, to March 31, 2024

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Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents: Financial Disclosure for Companies Related to HIV Treatment or Diagnostics for the Period of April 1, 2023, to March 31, 2024 (continued)

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Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents: Financial Disclosure for Companies Related to HIV Treatment or Diagnostics for the Period of April 1, 2023, to March 31, 2024 (continued)

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Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents: Financial Disclosure for Companies Related to HIV Treatment or Diagnostics for the Period of April 1, 2023, to March 31, 2024 (continued)

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Key: C = Co-chair; CC = Cardiology Consultant; CTC = Consultant for Transgender Care; DSMB = Data Safety Monitoring Board; ES = Executive Secretary; HC = HIV-2 Consultant; M = Member; N/A = not applicable; PC = Pharmacology Consultant; TC = Transplant Consultant; UCSF = University of California, San Francisco

Introduction

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Antiretroviral therapy (ART) for the treatment of HIV infection has improved steadily since the advent of potent combination therapy in 1996. ART has dramatically reduced HIV-associated morbidity and mortality and has transformed HIV infection into a manageable chronic condition, with life expectancy approaching that for people without HIV.[1,2] ART is also highly effective at preventing sexual transmission of HIV in patients who have adequately suppressed viral loads.[3-5] Lack of viral load suppression is mostly due to undiagnosed HIV infection and failure to link or retain patients with HIV in care.

The U.S. Department of Health and Human Services (HHS) Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) is a working group of the Office of AIDS Research Advisory Council (OARAC). The Panel's primary goal is to provide HIV care practitioners with recommendations that are based on current knowledge of the antiretroviral (ARV) drugs that are used to treat adults and adolescents with HIV in the United States. The Panel reviews new evidence and updates recommendations when needed. These guidelines include recommendations on baseline laboratory evaluations, treatment goals, benefits of ART and considerations when initiating therapy, choice of the initial regimen for ART-naive people with HIV, ARV drugs or combinations to avoid, management of treatment failure, optimizing ARV regimens, management of adverse effects and drug interactions, and special ART-related considerations in specific populations. This Panel works closely with the HHS Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV to provide recommendations for adolescents at different stages of growth and development. Recommendations for ARV regimens in these guidelines are most appropriate for postpubertal adolescents (i.e., those with sexual maturity ratings [SMR] of 4 and 5). Clinicians should follow recommendations in the Pediatric Antiretroviral Guidelines when initiating ART in adolescents with an SMR of 3 or lower. For recommendations related to pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) for people who do not have HIV, clinicians should consult recommendations from the Centers for Disease Control and Prevention.[6]

These guidelines represent current knowledge regarding the use of ARV drugs. Because the science of HIV evolves rapidly, the availability of new agents and new clinical data may change therapeutic options and preferences. Information included in these guidelines may not always be consistent with approved labeling for the specific drugs or indications, and the use of the terms "safe" and "effective" may not be synonymous with the U.S. Food and Drug Administration–defined legal standards for drug approval. The Panel frequently updates the guidelines (current and archived versions of the guidelines are available on the Clinical Info website). However, updates to the guidelines may not keep pace with the release of new data, and the guidelines cannot offer guidance on care for all patients. Patient management decisions should be based on clinical judgement and attention to unique patient circumstances.

The Panel recognizes the importance of clinical research in generating evidence to address unanswered questions related to the optimal safety and efficacy of ART and encourages both the development of protocols and patient participation in well-designed Institutional Review Board–approved clinical trials.

HIV Expertise in Clinical Care

Several studies have demonstrated that overall outcomes in patients with HIV are better when care is delivered by clinicians with HIV expertise (e.g., those who have cared for a large group of patients with HIV),[7-11] reflecting the complexity of HIV transmission and its treatment. Appropriate training, continuing education, and clinical experience are all components of optimal care. Providers who do not have this requisite training and experience should consult HIV experts when needed.

Guidelines Development Process

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Goal of the guidelines	Provide guidance to HIV care practitioners on the optimal use of antiretroviral (ARV) agents for the treatment of HIV in adults and adolescents in the United States.
Panel members	The Panel is composed of approximately 50 voting members who have expertise in HIV care and research and includes at least one representative from each of the following U.S. Department of Health and Human Services (HHS) agencies: Centers for Disease Control and Prevention (CDC), U.S. Food and Drug Administration (FDA), Health Resource and Services Administration (HRSA), and National Institutes of Health (NIH). Approximately two-thirds of the Panel members are nongovernmental scientific members. The Panel also includes four to five community members with knowledge of HIV treatment and care. The U.S. government representatives are appointed by their respective agencies; other Panel members are selected after an open call for nominations. Each member serves on the Panel for a 4-year term, with an option for reappointment for an additional term. See the Panel Roster for a list of current Panel members.
Financial disclosure	All members of the Panel submit a written financial disclosure annually, reporting any association with manufacturers of ARV drugs or diagnostics used to manage HIV infection. The latest version of the Financial Disclosure list is available on the Clinical Info website.
Users of the guidelines	HIV treatment providers
Developer	Panel on Antiretroviral Guidelines for Adults and Adolescents—a working group of the Office of AIDS Research Advisory Council (OARAC)
Funding source	Office of AIDS Research, NIH
Evidence collection	The recommendations in the guidelines are based on studies published in peer-reviewed journals or data available in FDA drug labels. On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.
Recommendation grading	As described in Table 2 below
Method of synthesizing data	Each section of the guidelines is assigned to a working group of Panel members with expertise in the section's area of interest. The working groups synthesize available data and propose recommendations to the Panel. The Panel discusses all proposals during monthly teleconferences. Recommendations endorsed by the Panel are included in the guidelines.

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Other guidelines	These guidelines focus on antiretroviral therapy (ART) for adults and adolescents with HIV. For a more detailed discussion on the use of ART in children and prepubertal adolescents (those with sexual maturity ratings of 1 to 3), clinicians should refer to the Pediatric Antiretroviral Guidelines. These guidelines also include a brief discussion on the management of persons of childbearing potential and pregnant persons. For more details on the use of ARV drugs during pregnancy, see the Perinatal Guidelines.
Update plan	The Panel meets monthly by teleconference to review data that may warrant modification of the guidelines. Updates may be prompted by new drug approvals (or new indications, dosing formulations, or frequency of dosing), new safety or efficacy data, or other information relating to ARV drugs that may have an impact on the clinical care of people with HIV. In the event of new data of clinical importance, the Panel may post an interim announcement with recommendations on the Clinical Info website until the guidelines can be updated with the appropriate changes. Updated guidelines are available on the Clinical Info website.
Public comments	A 2-week public comment period follows the release of the updated guidelines on the Clinical Info website. The Panel reviews comments to determine whether additional revisions to the guidelines are indicated. The public also may submit comments to the Panel at any time at HIVinfo@NIH.gov.

Basis for Recommendations

Recommendations in these guidelines are based on scientific evidence and expert opinion. Each recommendation statement includes a letter **(A**, **B**, or **C)** that represents the strength of the recommendation and a Roman numeral **(I**, **II**, or **III)** that represents the quality of the evidence that supports the recommendation (see Table 2 below).

Table 2. Rating Scheme for Recommendations

Strength of Recommendation	Quality of Evidence for Recommendation
A: Strong recommendation for the statement **B:** Moderate recommendation for the statement **C:** Weak recommendation for the statement	**I:** One or more randomized trials with clinical outcomes and/or validated laboratory endpoints **II:** One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes **III:** Expert opinion

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Baseline Evaluation

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Every patient with HIV entering into care should have a complete medical history, physical examination, and laboratory evaluation and should be counseled regarding the implications of HIV infection. The goals of this initial evaluation are to confirm the diagnosis of HIV infection, obtain appropriate baseline historical and laboratory data, ensure patient understanding about HIV infection and its transmission, and initiate care as recommended in the HIV Medicine Association of the Infectious Diseases Society of America's (HIVMA/IDSA) Primary Care Guidance for Persons with HIV[1] and the Adult and Adolescent Opportunistic Infections Guidelines.[2] The initial evaluation also should include discussion of the benefits of antiretroviral therapy (ART) for the patient's health and to prevent HIV transmission, as well as strategies to optimize care engagement and treatment adherence **(AIII).** Information obtained in this baseline evaluation then can be used to define treatment management goals and plans. The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating ART at the time of diagnosis (when possible) or as soon as possible afterward to increase the uptake of ART, decrease the time required to achieve linkage to care and virologic suppression, improve the rate of virologic suppression, and reduce HIV transmission **(AII).**

The following laboratory tests performed during initial patient visits can be used to stage HIV progression and to assist in the selection of antiretroviral (ARV) drug regimens:

- HIV antigen/antibody testing (if prior documentation is not available or if HIV RNA is below the assay's limit of detection) **(AI)**
- CD4 T lymphocyte (CD4) cell count **(AI)**
- Plasma HIV RNA (viral load) **(AI)**
- Complete blood count; chemistry profile, including glucose, blood urea nitrogen and creatinine, liver enzymes and bilirubin, urinalysis, and serologies for hepatitis A, B, and C viruses **(AIII)**
  - If random blood glucose level is abnormal, repeat fasting
- Serum lipids (if random levels are abnormal, fasting lipids should be obtained)
- HLA-B*5701 test (if abacavir is being considered) **(AI)**
- Genotypic drug-resistance testing **(AII).** Based on current rates of transmitted drug resistance to different ARV medications, standard genotypic drug-resistance testing in ARV-naive people should focus on testing for mutations in the reverse transcriptase (RT) and protease (PR) genes. If transmitted integrase strand transfer inhibitor (INSTI) resistance is a concern in people with newly diagnosed HIV or in people who acquired HIV after receipt of long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP), testing for mutations in the integrase gene also should be performed.
- For patients who have HIV RNA levels <1,000 copies/mL, viral amplification for drug-resistance testing should still be performed; however, it may not always be successful **(BII)** (see Drug-Resistance Testing).

In addition, other tests (including screening tests for sexually transmitted infections, opportunistic infections, and cancer) should be performed as recommended in the HIVMA/IDSA's Primary Care Guidance for Persons with HIV[1] and the Adult and Adolescent Opportunistic Infections Guidelines.[2]

Many clinics have adopted a rapid start policy to initiate ART on the day of HIV diagnosis in order to increase ART uptake and engagement in care and to accelerate the time to viral suppression. Rapid ART initiation also reduces the time during which people with newly diagnosed HIV can transmit HIV. Prior to ART initiation, HIV infection should be confirmed. HIV RNA and CD4 count also should be obtained, but results need not be available before starting ART. CD4 count will determine the need for prophylaxis for certain opportunistic infections.

- If available, results of safety testing—such as complete blood count, renal function tests, and liver enzymes—should be reviewed. If safety test results are not available, ART can still be started, but a clinician should review the results as soon as possible.
- Genotypic resistance testing for RT and PR (and INSTI resistance testing if patient has a history of CAB PrEP use or if INSTI transmission is suspected) should be obtained before ART initiation. It is not necessary to delay ART until results are available, but results should be reviewed as soon as possible in order to make adjustments to the regimen, if needed.
- Screening for viral hepatitis should be done before starting ART, and if ART initiation occurs before results are available, a regimen that has activity against hepatitis B virus should be selected.
- In patients who do not have reliable methods of contact, rapid ART may be initiated, with a plan for a return clinic visit soon after ART initiation to review test results.
- Screening for sexually transmitted infections should, ideally, occur at the initial visit, but results do not need to be available before starting ART.

For previously treated patients who present for an initial evaluation with a new health care provider, it is critical to obtain a complete ARV history (including drug-resistance testing results, if available), preferably through the review of past medical records. A complete immunization history (including for SARS-CoV-2) also should be obtained. Newly diagnosed patients also should be asked about any prior use of ARV agents for prevention of HIV infection.

People with HIV often must cope with many social, psychiatric, and medical issues that are best addressed through a patient-centered, multidisciplinary approach. The baseline evaluation should include consideration of the patient's readiness for ART, including an assessment of substance use (including tobacco use), social support, mental health, medical comorbidities, economic factors (e.g., unstable housing, food instability), medical insurance status and adequacy of coverage, and other factors that are known to impair adherence to ART and increase the risk of HIV transmission. Once evaluated, these factors should be managed accordingly. The baseline evaluation also should include a discussion of risk reduction and disclosure to sexual and/or needle-sharing partners, especially with untreated patients who are still at high risk of HIV transmission. People with HIV should be informed that maintaining a plasma HIV RNA of <200 copies/mL, including any measurable value below this threshold, with ART prevents sexual transmission of HIV to their partners **(AII).** Patients may recognize this concept as Undetectable = Untransmittable or U=U.

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Laboratory Testing

Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy

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Several laboratory tests are important for initial evaluation of people with HIV upon entry into care. Some tests should be performed before and after initiation or modification of antiretroviral therapy (ART) to assess the virologic and immunologic efficacy of ART and to monitor for laboratory abnormalities that may be associated with antiretroviral (ARV) drugs. Table 3 below outlines recommendations from the Panel on Antiretroviral Guidelines for Adults and Adolescents on the frequency of testing. As noted in the table, some tests may be repeated more frequently if clinically indicated.

Two surrogate markers are used to monitor people with HIV: plasma HIV RNA (viral load) to assess level of HIV viremia and CD4+ T lymphocyte cell count (or CD4 count) to assess immune function. Standard (reverse transcriptase and protease) genotypic drug-resistance testing should be used to guide selection of an ARV regimen; if transmitted integrase strand transfer inhibitor (INSTI) resistance is a concern or for people who acquired HIV after taking long-acting cabotegravir as pre-exposure prophylaxis, testing also should include the integrase gene (see Drug-Resistance Testing). For guidance on the choice of ARV regimens before drug-resistance testing results become available, clinicians should consult the What to Start section. A viral tropism assay should be performed before initiation of a CCR5 antagonist or at the time of virologic failure that occurs while a patient is receiving a CCR5 antagonist. HLA-B*5701 testing should be performed before initiation of abacavir (ABC) to reduce the risk of hypersensitivity reaction, and HLA-B*5701-positive patients should not be prescribed ABC. Patients should be screened for hepatitis B and hepatitis C virus infections before initiating ART and, if indicated, periodically after ART initiation, because treatment of these coinfections may affect the choice of ART and likelihood of drug-induced hepatotoxicity. The rationale for and utility of some of these laboratory tests are discussed in the corresponding sections of the guidelines.

Table 3. Laboratory Testing Schedule for Monitoring People With HIV Before and After Initiation of Antiretroviral Therapy[a]

Laboratory Test	Timepoint or Frequency of Testing								
	Entry Into Care	ART Initiation[b] or Modification	4 to 8 Weeks After ART Initiation or Modification	Every 3 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation Is Delayed[c]
HIV Antigen/ Antibody Test	√ If HIV diagnosis has not been confirmed								
CD4 Count	√	√		√[d] If CD4 count is <300 cells/mm^3	√ During the first 2 years of ART, if CD4 count is ≥ 300 cells/mm^3	√ **After 2 Years on ART with Consistently Suppressed Viral Load** *CD4 Count 300–500 cells/mm^3* • Every 12 months *CD4 Count >500 cells/mm^3* • CD4 count monitoring is optional.	√	√	√ Every 3–6 months

Table 3. Laboratory Testing Schedule for Monitoring People With HIV Before and After Initiation of Antiretroviral Therapy[a]

Laboratory Test	Timepoint or Frequency of Testing								
	Entry Into Care	ART Initiation[b] or Modification	4 to 8 Weeks After ART Initiation or Modification	Every 3 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation Is Delayed[c]
HIV Viral Load	√	√	√[e]	√[f]	√[f]		√	√	Repeat testing is optional.
Genotypic Resistance Testing (PR/RT Genes)[g]	√	√					√	√	√
Genotypic Resistance Testing (Integrase Genes)[g]	√ If transmitted INSTI resistance is suspected or if there is a history of CAB-LA use for PrEP	√[f] If transmitted INSTI resistance is suspected or if there is a history of INSTI use					√ If there is a history of INSTI use	√ If there is a history of INSTI use	

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Laboratory Test	Timepoint or Frequency of Testing								
	Entry Into Care	ART Initiation[b] or Modification	4 to 8 Weeks After ART Initiation or Modification	Every 3 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation Is Delayed[c]
Tropism Testing		√ If considering a CCR5 antagonist					√ If considering a CCR5 antagonist, or for patients with virologic failure on a CCR5 antagonist	√	
HLA-B*5701 Testing		√ If considering ABC							
Hepatitis B Serology (HBsAb, HBsAg, HBcAb total)[h,i,j]	√	In patients not immune to HBV, consider retesting if switching to a regimen that does not contain TDF or TAF.						√ Including before starting HCV DAA	

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Hepatitis C Screening (HCV antibody or, if indicated, HCV RNA)[k]	√					√ Repeat HCV screening for at-risk patients[l]		√	
Basic Metabolic Panel[m,n]	√	√	√		√			√	√ Every 6–12 months
ALT, AST, Total Bilirubin	√	√	√		√			√	√ Every 6–12 months
CBC with Differential[o]	√	√		√ When monitoring CD4 count (if required by lab)	√ When monitoring CD4 count (if required by lab)	√ When no longer monitoring CD4 count		√	
Lipid Profile[p]	√		Consider 1–3 months after ARV initiation or modification			√ If normal at baseline but with CV risk		If normal at baseline, every 5 years or if clinically indicated	

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Laboratory Test	Timepoint or Frequency of Testing								
	Entry Into Care	ART Initiation[b] or Modification	4 to 8 Weeks After ART Initiation or Modification	Every 3 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated	If ART Initiation Is Delayed[c]
Random or Fasting Glucose[q]	√	√					√	√	
Urinalysis[n,r]	√							√ E.g., in patients with CKD or DM	
Pregnancy Test[s]	√	√						√	

[a] This table pertains to laboratory tests done to select an ARV regimen and monitor for treatment responses or ART toxicities. Please refer to the HIV Medicine Association of the Infectious Diseases Society of America's (HIVMA/IDSA) Primary Care Guidance for Persons with HIV for other laboratory tests generally recommended for primary health care maintenance of HIV patients.[1]

[b] If ART is initiated soon after HIV diagnosis and entry into care, repeat baseline laboratory testing is not necessary.

[c] ART is indicated for all people with HIV and should be started as soon as possible. However, if ART initiation is delayed, patients should be retained in care, with periodic monitoring as noted above.

[d] After 2 years of consistently suppressed HIV RNA, less frequent monitoring (e.g., every 6 months) may be considered.

[e] If HIV RNA is detectable at 4–8 weeks, repeat testing every 4–8 weeks until viral load is suppressed to <50 copies/mL. Thereafter, repeat testing every 3–6 months.

[f] For patients on ART, viral load typically is measured every 3–6 months. More frequent monitoring may be considered in individuals having difficulties with ART adherence or at risk for nonadherence. However, for adherent patients with consistently suppressed viral load and stable immunologic status for more than 1 year, monitoring can be extended to 6-month intervals.

[g] Standard genotypic drug-resistance testing in ARV-naive persons should focus on testing for mutations in the PR and RT genes. If transmitted INSTI resistance is a concern, or if a person has a history of INSTI use as PrEP or treatment, or a person presents with viremia while on an INSTI, providers also should test for resistance mutations in the IN gene. In ARV-naive patients who do not immediately begin ART, repeat testing before initiation of ART is optional if drug-resistance testing was performed at entry into care. In

Table 3. Laboratory Testing Schedule for Monitoring People With HIV Before and After Initiation of Antiretroviral Therapy[a]

patients with virologic suppression who are switching therapy because of toxicity or for convenience, viral amplification will not be possible; see the Drug-Resistance Testing section for a discussion of the potential limitations and benefits of proviral DNA assays in this situation. Results from prior drug-resistance testing should be considered because they can be helpful in constructing a new regimen.

[h] If a patient has HBV infection (as determined by a positive HBsAg or HBV DNA test result), TDF or TAF plus either FTC or 3TC should be used as part of the ARV regimen to treat both HBV and HIV infections (see the Hepatitis B Virus/HIV Coinfection section).

[i] If HBsAg, HBsAb, and HBcAb test results are negative, HBV vaccine series should be administered. Refer to the HIVMA/IDSA's Primary Care Guidance for Persons with HIV and the Adult and Adolescent Opportunistic Infection Guidelines for detailed recommendations.[1,2]

[j] Most patients with isolated HBcAb have resolved HBV infection with loss of HBsAb. Consider performing an HBV viral load test for confirmation. If the HBV viral load test is positive, the patient may be acutely infected (and will usually display other signs of acute hepatitis) or chronically infected. If the test is negative, the patient should be vaccinated. Refer to the HIVMA/IDSA's Primary Care Guidance for Persons with HIV and the Adult and Adolescent Opportunistic Infection Guidelines for more detailed recommendations.[2]

[k] The HCV antibody test may not be adequate for screening in the setting of recent HCV infection (acquisition within the past 6 months) or advanced immunodeficiency (CD4 count <100 cells/mm^3). HCV RNA screening is indicated in persons who have been successfully treated for HCV or who spontaneously cleared prior infection. HCV antibody-negative patients with elevated ALT may need HCV RNA testing.

[l] Injection drug users, people with a history of incarceration, men with HIV who have unprotected sex with men, and people with percutaneous/parenteral exposure to blood in unregulated settings are at risk of HCV infection.

[m] Serum Na, K, HCO_3, Cl, BUN, creatinine, glucose, and Cr-based eGFR. Serum P should be monitored in patients with CKD who are on TDF-containing regimens.[3]

[n] Consult the HIVMA/IDSA's Clinical Practice Guideline for the Management of Chronic Kidney Disease in Patients Infected with HIV for recommendations on managing patients with renal disease.[3] More frequent monitoring may be indicated for patients with evidence of kidney disease (e.g., proteinuria, decreased glomerular dysfunction) or increased risk of renal insufficiency (e.g., patients with diabetes, hypertension).

[o] CBC with differential should be done when a CD4 count is performed. When CD4 count is no longer being monitored, the recommended frequency of CBC with differential is once a year. More frequent monitoring may be indicated for people receiving medications that potentially cause cytopenia (e.g., TMP-SMX).

[p] If random lipids are abnormal, fasting lipids should be obtained. Consult the American College of Cardiology/American Heart Association's 2018 Guideline on the Management of Blood Cholesterol for diagnosis and management of patients with dyslipidemia.[4]

[q] If random glucose is abnormal, fasting glucose should be obtained. HbA1C is no longer recommended for diagnosis of diabetes in people with HIV on ART (see the American Diabetes Association Guidelines).[5]

[r] Urine glucose and protein should be assessed before initiating TAF- or TDF-containing regimens and monitored during treatment with these regimens.

[s] For persons of childbearing potential.

Key: 3TC = lamivudine; ABC = abacavir; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CAB-LA = cabotegravir long-acting; CBC = complete blood count; CD4 = CD4 T lymphocyte; CKD = chronic kidney disease; Cl = chloride; Cr = creatinine; CV = cardiovascular; DAA = direct-acting antiviral; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; FTC = emtricitabine; HbA1C = hemoglobin A1c; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCO_3 = bicarbonate; HCV = hepatitis C virus; IN = integrase; INSTI = integrase strand transfer inhibitor; K = potassium; Na = sodium; P = phosphorus; PR = protease; PrEP = pre-exposure prophylaxis; RT = reverse transcriptase; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TMP-SMX = trimethoprim-sulfamethoxazole

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Plasma HIV-1 RNA (Viral Load) and CD4 Count Monitoring

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HIV RNA (viral load) and CD4 T lymphocyte cell (CD4) count are the two surrogate markers of antiretroviral therapy (ART) responses and HIV disease progression that have been used for decades to manage and monitor HIV infection.

Viral load is a marker of response to ART. A patient's pre-ART viral load level and the magnitude of viral load decline after initiation of ART provide prognostic information about the probability of disease progression.[1] The key goal of ART is to achieve and maintain durable viral suppression. Thus, the most important use of the viral load is to monitor the effectiveness of therapy after initiation of ART.

CD4 count provides information on the overall immune function of a person with HIV. Measurement of CD4 count is particularly useful **before** initiation of ART to establish the need for the initiation of opportunistic infection (OI) prophylaxis and to assess the urgency to initiate ART; and **after** initiation of ART to assess immunologic response and to establish the need for discontinuation of OI prophylaxis.

The management of patients with HIV has changed substantially with the availability of newer, more potent, and less toxic antiretroviral (ARV) agents. ART is now recommended for all patients with HIV regardless of their viral load or CD4 count **(AI)** (see the Initiation of Antiretroviral Therapy section). In the past, the clinical practice supported by treatment guidelines was generally to monitor both CD4 count and viral load concurrently. However, because most patients with HIV in care now receive ART, the rationale for frequent CD4 count monitoring is weaker. The roles and usefulness of these two tests in clinical practice are discussed in the following sections.

Plasma HIV-1 RNA (Viral Load) Monitoring

Viral load is the most important indicator of initial and sustained response to ART and should be measured in all patients with HIV at entry into care **(AI),** at initiation of therapy **(AI),** and on a regular basis thereafter. For those patients who choose to delay therapy or remain untreated for whatever reason, repeat viral load testing while not on ART is optional **(CIII).** Pre-treatment viral load level is also an important factor in the selection of an initial ARV regimen, because several currently approved ARV drugs or regimens have been associated with poorer responses in patients with high baseline viral load (see the What to Start section). Commercially available HIV-1 RNA assays do not detect HIV-2 viral load. For further discussion on HIV-2 RNA monitoring in patients with HIV-1/HIV-2 coinfection or HIV-2 mono-infection, see the HIV-2 Infection section.

Several systematic reviews of data from clinical trials involving thousands of participants have established that decreases in viral load following initiation of ART are associated with reduced risk of progression to AIDS or death.[1-3] Thus, viral load testing is an established surrogate marker for treatment response.[4] The minimal change in viral load considered to be statistically significant (2 standard deviations) is a three-fold change (equivalent to a 0.5 $\log_{10}$ copies/mL change). Optimal viral suppression is defined as a confirmed HIV RNA level below the lower limit of detection of available assays (generally <20 copies/mL, depending on the assay used). After virologic suppression, an isolated detectable HIV RNA level that is followed by a return to virologic suppression, known as a "blip," may occur in successfully treated patients and is not usually predictive of virologic failure.[5] Furthermore, the data on the association between persistently low level but quantifiable viremia (HIV RNA <200 copies/mL) and virologic failure is conflicting. One study showed an increased risk of subsequent failure at this level of viremia; however, the association was not observed in other studies.[6-9] These guidelines and the AIDS Clinical Trials Group (ACTG) now define

virologic failure as the inability to achieve or maintain suppression of viral replication to HIV RNA level <200 copies/mL—a threshold that eliminates most cases of apparent viremia caused by viral load blips or assay variability[10] (see the Virologic Failure section).

Individuals who are adherent to their ARV regimens and do not harbor resistance mutations to the component drugs can generally achieve viral suppression 8 to 12 weeks after ART initiation or after modification due to virologic failure; rarely, it may take longer in some patients. Recommendations on the frequency of viral load monitoring are summarized below:

- **After initiation of ART.** Plasma viral load should be measured before initiation of ART and within 4 to 8 weeks after treatment initiation **(AIII).** The purpose of the measurements is to confirm an adequate virologic response to ART, indicating appropriate regimen selection and patient adherence to therapy. Repeat viral load measurement should be performed at 4- to 8-week intervals until the level falls below the assay's limit of detection **(BIII).**
- **In patients with viral suppression, with ART modification because of drug toxicity or for regimen simplification.** Viral load measurement should be performed within 4 to 8 weeks after changing therapy **(AIII).** The purpose of viral load monitoring at this point is to confirm the effectiveness of the new regimen.
- **In patients on a stable, suppressive ARV regimen.** Viral load measurement should be repeated every 3 to 4 months **(AIII)** or as clinically indicated to confirm continuous viral suppression. Clinicians may extend the interval to 6 months for adherent patients whose viral load has been suppressed for more than a year, whose clinical and immunologic status is stable, and who are not at risk for inadequate adherence **(AIII).**
- **In patients with virologic failure who require a change in ARV regimen.** Plasma viral load should be measured before ART change and within 4 to 8 weeks after treatment modification **(AIII).** The purpose of the measurements is to confirm an adequate virologic response to the new regimen. Repeat viral load measurement should be performed at 4- to 8-week intervals until the level falls below the assay's limit of detection **(BIII).** If viral suppression is not possible, repeat viral load measurement every 3 months or more frequently if indicated **(AIII).**
- **In patients with suboptimal response.** The frequency of viral load monitoring will depend on clinical circumstances, such as adherence and availability of further treatment options. In addition to viral load monitoring, several other factors—such as patient adherence to prescribed medications, suboptimal drug exposure, or drug interactions—should be assessed. Patients who fail to achieve viral suppression should undergo drug-resistance testing to aid in the selection of an alternative ARV regimen (see the Drug-Resistance Testing and Virologic Failure sections).

CD4 Count Monitoring

The CD4 count is the most important laboratory indicator of immune function in patients with HIV. It is also the strongest predictor of disease progression and survival according to findings from clinical trials and cohort studies.[11,12] CD4 counts are highly variable; a significant change (2 standard deviations) between two tests is approximately a 30% change in the absolute count, or an increase or decrease in CD4 percentage by 3 percentage points. Monitoring of lymphocyte subsets other than CD4 (e.g., CD8, CD19) has not proven clinically useful and is more expensive than monitoring CD4 count alone; therefore, it **is not recommended (BIII).**

Use of CD4 Count for Initial Assessment

CD4 count should be measured in all patients at entry into care **(AI).** It is the key factor in determining the need to initiate OI prophylaxis (see the Adult and Adolescent Opportunistic Infections Guidelines)[13] and the urgency to initiate ART **(AI)** (see the Initiation of Antiretroviral Therapy section). Although most OIs occur in patients with CD4 counts <200 cells/mm^3, some OIs can occur in patients with higher CD4 counts.[14]

Use of CD4 Count for Monitoring Therapeutic Response

The CD4 count is used to assess a patient's immunologic response to ART. It is also used to determine whether prophylaxis for OIs can be discontinued (see the Adult and Adolescent Opportunistic Infections Guidelines).[13] For most patients on therapy, an adequate response is defined as an increase in CD4 count in the range of 50 cells/mm^3 to 150 cells/mm^3 in the first year of ART, generally with an accelerated response in the first 3 months of treatment. Subsequent increases average approximately 50 cells/mm^3 to 100 cells/mm^3 per year until a steady state level is reached.[15] Patients who initiate therapy with a low CD4 count[16,17] or at an older age[18] may have a blunted increase in their counts despite virologic suppression.

Frequency of CD4 Count Monitoring

ART is now recommended for all patients with HIV. In patients who remain untreated for whatever reason, CD4 counts should be monitored every 3 to 6 months to assess the urgency of ART initiation and the need for OI prophylaxis **(AIII).**

A repeat CD4 count 3 months after ART initiation will provide information regarding the magnitude of immune reconstitution **(AIII).** This repeat measurement is most important in patients who initiate ART with more advanced disease and require OI prophylaxis or treatment. In these patients, the magnitude and duration of CD4 count increase can be used to determine whether to discontinue OI prophylaxis and/or treatment as recommended in the Adult and Adolescent Opportunistic Infections Guidelines.[13] For patients beginning ART, CD4 count should be repeated every 3 months for the first 2 years of suppressive ART for those with CD4 counts <300 cells/mm^3 and every 6 months if CD4 count is ≥300 cells/mm^3. After 2 years of suppressive ART, CD4 count monitoring can be reduced to every 6 months for patients whose CD4 counts remain at <300 cells/mm^3 and every year for patients with CD4 counts between 300 cells/mm^3 and 500 cells/mm^3, and is optional for those with CD4 counts >500 cells/mm^3 **(BII).**

The CD4 count response to ART varies widely, but a poor CD4 response in a patient with viral suppression is rarely an indication for modifying an ARV regimen. In patients with consistently suppressed viral loads who have already experienced ART-related immune reconstitution (i.e., CD4 count >500 cells/mm^3), the CD4 count provides limited information. Frequent testing is unnecessary, because the results rarely lead to a change in clinical management. One retrospective study found that declines in CD4 count to <200 cells/mm^3 are rare in patients with viral suppression and CD4 counts >300 cells/mm^3.[19] Similarly, the ARTEMIS trial found that CD4 count monitoring had no clinical benefit in patients who had suppressed viral loads and CD4 counts >200 cells/mm^3 after 48 weeks of therapy.[20] Furthermore, the risk of *Pneumocystis jirovecii* pneumonia is extremely low in patients on suppressive ART who have CD4 counts between 100 cells/mm^3 and 200 cells/mm^3.[21] Although uncommon, CD4 count declines can occur in a small percentage of virologically suppressed patients and may be associated with adverse clinical outcomes, such as cardiovascular disease, malignancy, and death.[22] An analysis of costs associated with CD4 count monitoring in the United States estimated that reducing CD4 count monitoring in treated patients from every 6 months to every 12 months could result in annual savings of approximately $10 million.[23]

For the patient on a suppressive ARV regimen whose CD4 count has consistently ranged between 300 cells/mm^3 and 500 cells/mm^3 for at least 2 years, the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends CD4 count monitoring on an annual basis **(BII).** Continued CD4 count monitoring for virologically suppressed patients whose CD4 counts have been consistently >500 cells/mm^3 for at least 2 years may be considered optional **(CIII).** The CD4 count should be monitored more frequently, as clinically indicated, when there are changes in a patient's clinical status that may decrease CD4 count and thus prompt OI prophylaxis. Examples of such changes include the appearance of new HIV-associated clinical symptoms or initiation of treatment known to reduce CD4 count (e.g., chronic corticosteroids, antineoplastic agents) **(AIII).** In patients who fail to maintain viral suppression while on ART, the Panel recommends CD4 count monitoring every 3 to 6 months **(AIII).**

Factors that Affect Absolute CD4 Count

The absolute CD4 count is a calculated value based on the total white blood cell (WBC) count and the percentages of total and CD4 T lymphocytes. This absolute number may fluctuate in individuals or may be influenced by factors that may affect the total WBC count and lymphocyte percentages, such as use of bone marrow-suppressive medications, chronic corticosteroids, or the presence of acute infections. Splenectomy[24,25] or coinfection with human T-lymphotropic virus type I (HTLV-1)[26] may cause misleadingly elevated CD4 counts. In all these settings, CD4 percentage remains stable and may be a more appropriate parameter to assess a patient's immune function.[27]

Table 4. Recommendations on the Indications and Frequency of Viral Load and CD4 Count Monitoring[a]

Clinical Scenario	Viral Load Monitoring	CD4 Count Monitoring
Before initiating ART	At entry into care **(AIII)** If ART initiation is deferred, repeat before initiating ART **(AIII).** In patients not initiating ART, repeat testing is optional **(CIII).**	At entry into care **(AI)** If ART is deferred, every 3 to 6 months[a] **(AIII)**
After initiating ART	Preferably within 4 to 8 weeks after initiation of ART **(AIII);** thereafter, every 4 to 8 weeks until viral load is suppressed **(BIII).**	3 months after initiation of ART **(AIII)**
After modifying ART because of drug toxicities or for regimen simplification in a patient with viral suppression	4 to 8 weeks after modification of ART to confirm effectiveness of new regimen **(AIII).**	Monitor according to prior CD4 count and duration on ART, as outlined below.
After modifying ART because of virologic failure	Preferably within 4 to 8 weeks after modification **(AIII);** thereafter, every 4 to 8 weeks until viral load is suppressed **(BIII).** If viral suppression is not possible, repeat viral load testing every 3 months or more frequently if indicated **(AIII).**	Every 3 to 6 months **(AI)**
During the first 2 years of ART	Every 3 months **(AIII)**	Every 3 months if CD4 <300 cells/mm^3 **(BII)** Every 6 months if CD4 ≥300 cells/mm^3 **(BII)**
After 2 years of ART (VL consistently suppressed, CD4 remains <300 cells/mm^3)	Can extend to every 6 months for patients with consistent viral suppression for ≥2 years **(AIII).**	Every 6 months **(BII)**
After 2 years of ART (VL consistently suppressed, CD4 consistently 300–500 cells/mm^3)	Can extend to every 6 months for patients with consistent viral suppression for ≥2 years **(AIII).**	Every 12 months **(BII)**
After 2 years of ART (VL consistently suppressed, CD4 consistently >500 cells/mm^3)	Can extend to every 6 months for patients with consistent viral suppression for ≥2 years **(AIII).**	Optional **(CIII)**
While on ART with detectable viremia (VL repeatedly >200 copies/mL)	Every 3 months **(AIII)** or more frequently if clinically indicated (see Virologic Failure).	Every 3 to 6 months **(AIII)**
Change in clinical status (e.g., new HIV clinical symptom or initiation of chronic systemic corticosteroids, or antineoplastic therapy)	Every 3 months **(AIII)**	Perform CD4 count and repeat as clinically indicated[b] **(AIII)**

[a] Some experts may repeat CD4 count measurement every 3 months in patients with low baseline CD4 counts (<200–300 cells/mm^3) before ART but every 6 months in those who initiated ART at higher CD4 counts (e.g., >300 cells/mm^3).

[b] The following are examples of clinically indicated scenarios: changes in a patient's clinical status that may decrease CD4 count and thus prompt initiation of prophylaxis for opportunistic infection, such as new HIV-associated symptoms, or initiation of treatment with medications that are known to reduce CD4 count.

Key: ART = antiretroviral therapy; CD4 = CD4 T lymphocyte; VL = viral load

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Drug-Resistance Testing

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Panel's Recommendations

For Initial Treatment of HIV

- HIV drug-resistance testing is recommended at entry into care for people with HIV to guide the selection of the initial antiretroviral (ARV) regimen **(AII).** If antiretroviral therapy (ART) is deferred, repeat testing may be considered at the time of ART initiation **(CIII).**
- The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends genotypic, rather than phenotypic, testing as the preferred resistance testing to guide therapy in ARV-naive people **(AIII).**
- In people with early (acute and recent) HIV infection, in pregnant people with HIV, or in people who will initiate ART on the day of or soon after HIV diagnosis, ART initiation should not be delayed while awaiting resistance testing results; the regimen can be modified once results are reported **(AIII).**
- Standard genotypic drug-resistance testing in ARV-naive people involves testing for mutations in the reverse transcriptase and protease genes. If transmitted integrase strand transfer inhibitor (INSTI) resistance is suspected, if the person has ever used long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis, or if the person has ever received an INSTI-based regimen for post-exposure prophylaxis, providers should ensure that genotypic resistance testing also includes the integrase gene **(AIII).**

For Antiretroviral Therapy–Experienced People

- HIV drug-resistance testing should be performed to assist the selection of active drugs when changing ARV regimens in—
  - People with virologic failure and HIV RNA levels >200 copies/mL (**AI** for >1,000 copies/mL**, AIII** for 501–1,000 copies/mL**, CIII** for confirmed HIV RNA 201–500 copies/mL). For people with confirmed HIV RNA levels >200 copies/mL but <500 copies/mL, drug-resistance testing may be unsuccessful but should still be considered.
  - People with suboptimal viral load reduction **(AII).**
- Reverse transcriptase and protease genotypic resistance testing should be performed on people with virologic failure. Integrase resistance testing should be performed on individuals who have virologic failure and have a history of prior use of an INSTI (for prevention or treatment) or are currently receiving an INSTI-based regimen **(AII).**
- For people taking a non–long-acting ARV regimen, drug-resistance testing in the setting of virologic failure should be performed while the person is still taking their ARV regimen or, if that is not possible, within 4 weeks after discontinuing their ARV regimen **(AII).** If more than 4 weeks have elapsed since the non–long-acting agents have been discontinued, resistance testing may still provide useful information to guide therapy; however, it is important to recognize that previously selected resistance mutations can be missed due to lack of drug-selective pressure **(CIII).**
- For people who previously received long-acting cabotegravir and rilpivirine (LA CAB/RPV) and present with virologic failure, resistance testing (including INSTI genotypic testing) should be performed regardless of the time since the last dose of LA CAB/RPV **(AIII).**
- Genotypic testing is preferred over phenotypic-resistance testing to guide therapy in people with suboptimal virologic response or virologic failure while on first- or second-line regimens and in people in whom resistance mutation patterns are known or not expected to be complex **(AII).**
- The addition of phenotypic to genotypic resistance testing is recommended for people with known or suspected complex drug-resistance mutation patterns **(BIII).**
- All prior and current drug-resistance test results, when available, should be reviewed and considered when constructing a new regimen **(AIII).**

• When the use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed **(AI).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Genotypic and Phenotypic-Resistance Assays

Genotypic and phenotypic-resistance assays are used to assess viral strains and select treatment strategies. These assays provide information on resistance to nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and integrase strand transfer inhibitors (INSTIs). In some circumstances, INSTI-resistance tests may need to be ordered separately, and clinicians should check this with the testing laboratory. INSTI-resistance testing is particularly important in people who experience virologic failure while taking an INSTI-containing regimen or in those with prior use of injectable long-acting cabotegravir (CAB-LA) (either for treatment of HIV or as pre-exposure prophylaxis [PrEP]). Testing for fusion inhibitor resistance can be ordered separately when needed. There is currently no commercially available resistance test for the CD4 T lymphocyte post-attachment inhibitor ibalizumab, the gp120 attachment inhibitor fostemsavir, or the capsid inhibitor lenacapavir. For a description of co-receptor tropism testing, see Co-Receptor Tropism Assays.

Genotypic Assays

Genotypic assays detect drug-resistance mutations in relevant viral genes; in general, these assays require a plasma viral load of at least 500 to 1,000 copies/mL. Most genotypic assays involve conventional Sanger sequencing of the reverse transcriptase (RT), protease (PR), and integrase (IN) genes of circulating RNA in plasma to detect mutations that are known to confer drug resistance. A genotypic assay that assesses mutations in the gp41 (envelope) gene associated with resistance to the fusion inhibitor enfuvirtide is also commercially available. Genotypic assays can be performed rapidly, and results are available within 1 to 2 weeks of sample collection. Interpreting these test results requires knowledge of the mutations selected by different antiretroviral (ARV) drugs and of the potential for cross-resistance to other drugs conferred by certain mutations. The International AIDS Society–USA maintains an updated list of significant resistance-associated mutations in the RT, PR, IN, and envelope genes. The Stanford University HIV Drug Resistance Database also provides helpful guidance for interpreting genotypic resistance test results.[1] Various additional tools are available to assist providers in interpreting genotypic test results.[2-5] Clinical trials have demonstrated that consulting with specialists in HIV drug resistance improves virologic outcomes.[6] Clinicians are thus encouraged to consult a specialist to interpret genotypic test results and design new, optimal ARV regimens.

A next-generation sequencing genotypic resistance assay that analyzes HIV-1 proviral DNA in host cells is now commercially available. This test aims to detect archived resistance mutations in people with HIV RNA below the limit of detection or with low-level viremia.

Phenotypic Assays

Phenotypic assays measure the ability of a virus to grow in different concentrations of ARV drugs. RT, PR, and, more recently, IN and envelope gene sequences derived from a person's plasma HIV

RNA are inserted into the backbone of a laboratory clone of HIV or used to generate pseudotyped viruses that express that person's HIV genes of interest. Replication of these viruses at different drug concentrations is monitored by expression of a reporter gene and is compared with the replication of a reference HIV strain. The drug concentration that inhibits viral replication by 50% (i.e., the median inhibitory concentration [IC_{50}]) is calculated, and the ratio of the IC_{50} of test and reference viruses is reported as the fold increase in IC_{50} (i.e., fold resistance).

Automated phenotypic assays that can produce results in 2 to 3 weeks are commercially available, but they cost more to perform than genotypic assays. In addition, interpreting phenotypic assay results can be complicated by incomplete information regarding the specific resistance level (i.e., fold increase in IC_{50}) associated with drug failure, although clinically significant fold increase cutoffs have been described for some drugs.[7-11] Again, consulting with a specialist to interpret test results can be helpful.

Limitations of Genotypic and Phenotypic Assays

Limitations of both genotypic and phenotypic assays include lack of uniform quality assurance testing for all available assays, relatively high cost, and insensitivity to minor viral species. Drug-resistant viruses that constitute <10% to 20% of the circulating virus population will probably not be detected by commercially available assays. This limitation is important to note because a wild-type virus often re-emerges as the predominant population in the plasma after discontinuation of drugs that exert selective pressure on drug-resistant populations. As a consequence, the proportion of virus with resistance mutations can decrease to below the 10% to 20% threshold.[12-14] In the case of some oral ARV drugs, this reversion to predominantly wild-type virus can occur in the first 4 to 6 weeks after the drugs are discontinued. However, with injectable agents that have prolonged half-lives (e.g., long-acting cabotegravir and rilpivirine [LA CAB/RPV]), drug pressure may persist for prolonged periods. Prospective studies have demonstrated that despite plasma reversion, reinitiating the same ARV agents (or those with similar resistance pathways) often leads to early treatment failure; the virus responsible for this failure is derived from a previously archived resistant virus.[15] Therefore, for people taking a non–long-acting ARV regimen, drug-resistance testing in the setting of virologic failure should be performed while the person is still taking their ARV regimen or, if that is not possible, within 4 weeks after discontinuing their ARV regimen **(AII).** If more than 4 weeks have elapsed since the non–long-acting agents were discontinued, resistance testing may still provide useful information to guide therapy; however, it is important to recognize that previously selected resistance mutations can be missed due to lack of drug-selective pressure **(CIII).** Given the long half-lives of the long-acting injectable ARV drugs, resistance testing (including testing for resistance to INSTIs) should be performed in all people who have experienced virologic failure on a regimen of LA CAB/RPV or acquired HIV after receiving CAB-LA as PrEP, regardless of the amount of time since drug discontinuation **(AIII).** However, the absence of detectable resistance in people not currently on antiretroviral therapy (ART) must be interpreted with caution when designing subsequent ARV regimens. Importantly, in addition to considering prior ART history, prior genotypic- or phenotypic-resistance test results should be obtained from old records when possible. Because the most current drug-resistance test may not be able to detect resistance mutations that were previously detected, these prior test results are clinically important and should be reviewed and considered when designing a new ARV regimen **(AIII).**

A next-generation sequencing genotypic assay that analyzes HIV-1 proviral DNA may provide additional information on drug resistance in people with low levels of plasma HIV RNA or in people whose levels are below the limit of detection **(CIII).** However, these assays might miss some or all

previous drug-resistance mutations, and they should be interpreted with caution. The usefulness of these assays in the clinic is still under investigation and has yet to be fully determined.

Use of Resistance Assays in Clinical Practice

Note: See Table 5 below for recommendations for the use of drug resistance assays.

Use of Resistance Assays in Determining Initial Treatment

Transmission of drug-resistant HIV strains is well documented and associated with suboptimal virologic response to initial ART.[16-19] The risk of acquiring drug-resistant virus is related to the prevalence of drug resistance in people with HIV who engage in activities that may result in HIV transmission within a given community. The prevalence of resistance and mutations by ARV drug class depends upon the population being studied (e.g., people with previous ARV exposure versus ARV-naive people), geography, and ARV class available in the region.[20] Pre-existing HIV drug resistance before initiation of ART is recognized as an issue for both high- and low-income countries. The prevalence of transmitted drug resistance (TDR) in high-income countries ranges from 9% to 14% and varies by country.[21-23] Pre-treatment drug resistance—which includes people exposed to ARVs prior to initiating first-line therapy (e.g., for PrEP or for the prevention of perinatal transmission), as defined by the World Health Organization—exceeds 10% in many countries.[20] In most TDR surveys, NNRTI resistance and NRTI resistance are the most common mutation class types detected, followed by PI- and INSTI-resistance mutations, respectively.[21-23]

Resistance testing is recommended to guide therapy selection to optimize virologic response in all people starting ART **(AII).** A genotypic assay is preferred for this purpose **(AIII).** In early (acute and recent) HIV infection, in pregnant people with HIV, or in people willing and able to initiate ART on the day or soon after HIV diagnosis, treatment initiation should not be delayed pending resistance testing results. Once results are reported, the regimen can be modified if warranted (see Early [Acute and Recent] HIV Infection) **(AIII).** In the absence of ART, resistant viruses may decline over time to less than the detection limit of standard resistance tests. However, when ART is eventually initiated, even low levels of resistant viruses may still increase the risk of treatment failure.[24-26] Therefore, if ART is deferred, resistance testing should still be performed at the time of entry into care to optimize the chance of capturing transmitted resistance **(AIII).** In this situation, the genotypic resistance test result should be used for regimen selection in the future when the person begins ART. If a person received CAB-LA as part of ART or PrEP, genotypic resistance testing should include the IN gene.

The rate at which transmitted resistance-associated mutations revert to wild-type virus has not been completely delineated, but mutations present at the time of HIV transmission are more stable than those selected under drug pressure. It is often possible to detect resistance-associated mutations in viruses that were transmitted several years earlier.[27-29] Though no prospective trial has directly addressed whether drug-resistance testing before initiation of therapy confers benefit in this population, data from several studies, including one prospective clinical trial, suggest that virologic responses in people with baseline resistance mutations are suboptimal.[16-19,30-34] In addition, an analysis of early RT and PR genotypic resistance testing in ARV-naive people suggests that baseline testing in this population is cost-effective and should be performed.[35] Therefore, resistance testing in people with chronic HIV is recommended at the time of entry into HIV care **(AII).**

Although no definitive prospective data exist to support the choice of one type of resistance testing over another, genotypic testing is generally preferred over phenotypic testing because of lower cost,

faster turnaround time, greater sensitivity for detecting mixtures of wild-type and resistant virus, and easier interpretation of test results **(AIII).** If therapy is deferred, repeat testing shortly before initiating ART may be considered, because the person may have acquired drug-resistant virus (i.e., superinfection) **(CIII).**[36] Standard genotypic drug-resistance testing in ARV-naive people involves testing for mutations in the RT and PR genes. Although reports of transmission of INSTI-resistant virus are rare, as use of INSTIs increases, the potential for transmission of INSTI-resistant virus also may increase. The prior use of CAB-LA for PrEP also may increase the risk of INSTI resistance at the time of HIV diagnosis. When INSTI resistance is possible, providers should supplement standard, baseline, genotypic resistance testing with genotypic testing of the IN gene, which may need to be ordered separately **(AIII).**

The next-generation sequencing genotypic resistance assay that analyzes proviral DNA in host cells can be considered in people with baseline HIV RNA <1,000 copies/mL or when conventional HIV RNA drug-resistance testing is unsuccessful **(CIII).** As outlined above, the results should be interpreted with caution, as this assay might miss some or all previously existing drug-resistance mutations.

Use of Resistance Assays in the Event of Virologic Failure

Resistance assays are important tools to inform treatment decisions for people who experience virologic failure while on ART. Several prospective studies have assessed the utility of resistance testing to guide ARV drug selection in people who experience virologic failure. These studies have involved genotypic assays, phenotypic assays, or both.[6,37-43] In general, these studies have found that changes in therapy based on resistance test results produce better early virologic response to salvage regimens than regimen changes guided only by clinical judgment.

In addition, one observational cohort study found that the use of genotypic drug-resistance testing in ART-experienced people with detectable plasma HIV RNA was independently associated with improved survival.[44] Thus, resistance testing is recommended as a tool for selecting active drugs when changing ARV regimens because of virologic failure in people with HIV RNA >200 copies/mL (**AI** for >1,000 copies/mL, **AIII** for 501 to 1,000 copies/mL, **CIII** for confirmed HIV RNA 201 to 500 copies/mL) (see Virologic Failure). In people with HIV RNA >200 copies/mL but <500 copies/mL, testing may be difficult to obtain outside of a research setting but still should be considered. Conventional drug-resistance testing in people with plasma viral loads ≤200 copies/mL **is not recommended** because there are unclear benefits and drug-resistance assays cannot be consistently performed at very low HIV RNA levels **(AIII).**

Resistance testing can also help to guide treatment decisions for people with HIV who have suboptimal viral load reduction **(AII).** Virologic failure in the setting of ART is, for certain people with HIV, associated with resistance to only one component of the regimen.[45-47] In this situation, substituting individual drugs in a failing regimen may be an option, but this concept will require clinical validation (see Virologic Failure).

Genotyping is preferred for resistance testing in people with HIV who experience virologic failure or suboptimal viral load reduction while on a first or second ARV drug regimen and in people for whom resistance mutation patterns are known or not expected to be complex (i.e., mutations that are straightforward, usually limited in number, or those that have clear significance) **(AII).** Often in these situations, the mutation patterns detected can be interpreted by algorithms used to predict the impact of subsequent regimens on virologic response. For people with HIV who have extensive treatment

history, complex mutational patterns may occur. In such situations, the interpretation of complex genotypes and the impact of the mutation pattern on subsequent treatment regimens can be challenging. For these individuals, phenotypic-resistance testing may provide additional helpful information **(BIII).** Rather than only predicting the impact of the detected mutations, these assays can measure *in vitro* the actual fold change in drug susceptibility, as well as the actual impact of mutation combinations and interactions on each drug under consideration.

When compared with phenotypic testing, genotypic testing costs less to perform and has a faster turnaround time and greater sensitivity for detecting mixtures of wild-type and resistant virus. In addition, observations show that genotypic and phenotypic assays are comparable predictors of virologic response to subsequent ARV regimens.[48] In people with HIV who experience virologic failure while on INSTI-based regimens or in those with prior INSTI exposure, including to CAB-LA for HIV treatment or prevention, testing for INSTI resistance should be performed to determine whether to include drugs from this class in subsequent regimens **(AII).** In this circumstance, clinicians should confirm that, when they order a resistance test, their laboratory is testing for INSTI resistance in addition to NNRTI, NRTI, and PI resistance. If INSTI-resistance testing needs to be ordered separately (as is the case in some laboratories), clinicians should request this assay in addition to standard drug-resistance testing. The addition of phenotypic to genotypic testing is generally indicated for people with known or suspected complex drug-resistance mutation patterns **(BIII).**

The next-generation sequencing genotypic resistance assay that analyzes proviral DNA can be considered for people with HIV who are experiencing treatment failure and for whom conventional HIV RNA genotypic drug-resistance testing is unsuccessful or unavailable due to low HIV RNA levels **(CIII).** As outlined above, results should be interpreted with caution, as these assays might miss some or all previously existing drug-resistance mutations.

When the use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed **(AI)** (see Co-Receptor Tropism Assays).

Use of HIV Proviral DNA Resistance Assays for Optimizing Antiretroviral Regimen in People With Viral Suppression

In the past decade, simpler, more potent, and better-tolerated ARV drugs have become available, and new ARV drugs will likely continue to emerge. Switching individual or multiple ARV drugs in a regimen is sometimes considered for people with HIV with suppressed viral load to simplify a regimen, avoid drug interactions or toxicity, or for other reasons. If a person's viral load is suppressed, standard drug-resistance testing will not be successful.

The next-generation sequencing genotypic resistance assay that analyzes proviral DNA can be considered for people with viral suppression, particularly if complex or semi-complex pre-existing resistance is suspected. In individuals who have experienced no prior virologic failures and who are on their first or second regimen, or who have genotypic testing results from when they had prior virologic failures, the use of the proviral DNA genotypic test is unlikely to provide additional useful information. However, in individuals who have experienced multiple prior failures, have a prolonged history of prior ARV regimens, or for whom prior genotypic resistance test results are not available, it may be appropriate to utilize proviral DNA genotypic testing **(CIII).** When such testing is obtained, results should be combined with all prior genotypic and phenotypic test results to construct a cumulative genotype, which incorporates all current and previously detected drug-resistance

mutations. Results from proviral DNA genotypes should be interpreted with caution, as these assays might miss some or all previously existing drug-resistance mutations.[49,50] The usefulness of these assays in the clinic is still under investigation and has yet to be fully determined.

Use of Resistance Assays in Pregnancy

In pregnancy, the goal of ART is to rapidly and maximally reduce plasma HIV RNA in order to provide optimal therapy for the pregnant person and to prevent perinatal transmission of HIV. Genotypic resistance testing is recommended for all pregnant people with HIV before initiation of therapy **(AIII)** and for those entering pregnancy with detectable HIV RNA levels while on therapy **(AI).** Phenotypic testing in those found to have complex drug-resistance mutation patterns may provide additional information **(BIII).** Optimal prevention of perinatal transmission requires prompt initiation of ART pending resistance testing results. Once the results are available, the ARV regimen can be changed as needed.

Table 5. Recommendations for the Use of Drug-Resistance Assays

Clinical Setting and Recommendation	Rationale
In Early (Acute and Recent) HIV Drug-resistance testing is recommended **(AII).** A genotypic assay is generally preferred **(AIII).** Treatment should not be delayed while awaiting resistance testing results **(AIII).** See Early (Acute and Recent) HIV Infection for discussion on ART selection.	Drug-resistance testing can determine whether drug-resistant virus was transmitted or acquired while using PrEP. The initial ARV regimen can be modified, if necessary, once resistance test results are available. Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
If ART is deferred, repeat genotypic resistance testing may be considered when therapy is initiated **(CIII).** A genotypic assay is preferred **(AIII).**	Repeat testing when ART is initiated may be considered because the person may have acquired a drug-resistant virus (i.e., superinfection).
Before ART Initiation in People With Chronic HIV Drug-resistance testing is recommended at entry into HIV care to guide the selection of initial ART **(AII).** A genotypic assay is generally preferred **(AIII).** Treatment should not be delayed while awaiting resistance testing results **(AIII).**	Transmitted HIV with baseline resistance to at least one drug has been reported, and suboptimal virologic responses may be seen in people with baseline resistance mutations to ARVs in the prescribed regimen. Some drug-resistance mutations can remain detectable for years in untreated people with chronic HIV.
If transmitted or acquired INSTI resistance (including among people who had received INSTI for post-exposure prophylaxis) is a concern, providers should supplement standard resistance testing with a specific INSTI genotypic resistance assay, which may need to be ordered separately **(AIII).** Given the prolonged half-life of CAB-LA, INSTI-resistance testing should be considered in all people with HIV who previously received CAB-LA for PrEP, regardless of the time since drug discontinuation **(AIII).** See What to Start for discussion on ART selection.	Genotypic assays provide information on resistance to NRTIs, NNRTIs, PIs, and INSTIs. In some circumstances, INSTI-resistance tests need to be ordered separately (clinicians should check with the testing laboratory). Currently, transmitted INSTI resistance is infrequent, but the risk of people acquiring INSTI-resistant strains may be greater in certain known exposure settings. INSTI-resistance testing should be ordered for all people with prior exposure to CAB-LA for PrEP or an INSTI-based regimen for post-exposure prophylaxis.

Table 5. Recommendations for the Use of Drug-Resistance Assays

Clinical Setting and Recommendation	Rationale
For pregnant people or people who will initiate ART on the day of or soon after HIV diagnosis, treatment can be initiated prior to receiving resistance testing results.	If necessary, the ARV regimen can be modified once resistance test results are available.
If therapy is deferred, repeat genotypic resistance testing may be considered before initiation of ART **(CIII).** A genotypic assay is generally preferred **(AIII).**	Repeat testing before initiation of ART may be considered, because the person may have acquired a drug-resistant virus (i.e., a superinfection). Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
In People With Virologic Failure Drug-resistance testing is recommended in people on ART with HIV RNA >200 copies/mL (**AI** for >1,000 copies/mL**, AIII** for 501–1,000 copies/mL) and a confirmed HIV RNA 201–500 copies/mL **(CIII).** In people with confirmed HIV RNA levels between 201–500 copies/mL, testing may not be successful but should still be considered.	Drug-resistance testing can help determine the role of resistance in virologic failure and maximize the ability to select active drugs for the new regimen. Resistance testing for HIV RNA levels 201–500 copies/mL may need to be conducted within a research setting.
Resistance testing should be done while the person is taking ART or, if that is not possible, within 4 weeks after discontinuation of non–long-acting ARV drugs **(AII).** If >4 weeks have elapsed, resistance testing may still be useful to guide therapy; however, previously selected mutations can be missed due to lack of drug-selective pressure **(CIII).**	The absence of detectable resistance in such people with HIV must be interpreted with caution when designing subsequent ARV regimens, as mutations may decay with time.
For people who previously received LA CAB/RPV and present with virologic failure, resistance testing (including INSTI genotypic testing) should be performed regardless of the time since the last dose of LA CAB/RPV **(AIII).**	Because of the long half-lives of LA CAB and RPV, resistance mutations to INSTI and NNRTI may emerge even months after the last doses of these drugs.
Reverse transcriptase and protease genotypic resistance testing should be performed on people with virologic failure. Integrase resistance testing should be performed on individuals who have virologic failure and have a history of prior use of an INSTI (for prevention or treatment) or are currently receiving an INSTI-based regimen **(AII).**	Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant HIV. INSTI-resistance tests may need to be ordered separately. (Clinicians should check with the testing laboratory.)
All prior and current drug-resistance testing results should be reviewed and considered when designing a new ARV regimen for a person experiencing virologic failure **(AIII).**	Drug-resistance mutations may decay with time, and mutations detected in prior resistance tests may not be detected in current tests, though they remain clinically relevant.
Adding phenotypic testing to genotypic testing is generally preferred in people with known or suspected complex drug-resistance patterns **(BIII).**	Phenotypic testing can provide additional useful information in people with complex drug-resistance mutation patterns.
If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed **(AI).**	See Co-Receptor Tropism Assays section.

Table 5. Recommendations for the Use of Drug-Resistance Assays

Clinical Setting and Recommendation	Rationale
In People With Suboptimal Suppression of Viral Load Drug-resistance testing is recommended in people with suboptimal viral load suppression after initiation of ART **(AII).**	Testing can determine the role of resistance in suboptimal viral suppression, and it can help the clinician identify the number of active drugs available in the current ARV regimen and assess the need for a new regimen.
In Pregnant People With HIV Genotypic resistance testing is recommended for all pregnant people before initial ART **(AIII)** and for those entering pregnancy with detectable HIV RNA levels while on therapy **(AI).**	The goals of ART in pregnant people with HIV are to achieve maximal viral suppression for treatment of HIV in the pregnant person and to prevent perinatal transmission of HIV. Genotypic resistance testing will assist the clinician in selecting the optimal ARV regimen. However, treatment should not be delayed while awaiting resistance testing results. The initial regimen can be modified once resistance test results are available, if needed.
In People With Undetectable Viral Load or Low-Level Viremia Who Are Planning to Change Their ARV Regimen HIV-1 proviral DNA resistance assays may be useful if HIV RNA is below the limit of detection or with low-level viremia, where a HIV RNA genotypic assay is unlikely to be successful **(CIII).**	HIV-1 proviral DNA resistance assays may provide information about previously circulating resistant viral variants that are archived within proviral DNA. These assays may miss some or all prior resistance mutations that have occurred within the viral quasi-species and, therefore, they should be interpreted with caution. The clinical utility of HIV-1 proviral DNA assays has not been fully determined.

Key: ART = antiretroviral therapy; ARV = antiretroviral; CAB-LA = long-acting cabotegravir; CCR5 = cysteine-cysteine chemokine receptor 5; INSTI = integrase strand transfer inhibitor; LA = long-acting; LA CAB/RPV = long-acting cabotegravir/rilpivirine; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PrEP = pre-exposure prophylaxis; RPV = rilpivirine

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Co-Receptor Tropism Assays

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Panel's Recommendations
• A co-receptor tropism assay should be performed whenever the use of a CCR5 co-receptor antagonist is being considered **(AI).** • Co-receptor tropism testing is recommended for patients who exhibit virologic failure on a CCR5 antagonist **(BIII).** • A phenotypic tropism assay is preferred to determine HIV-1 co-receptor usage **(AI).** • A genotypic tropism assay should be considered as an alternative test to predict HIV-1 co-receptor usage **(BII).** • A proviral DNA tropism assay can be utilized for patients with undetectable HIV-1 RNA when a CCR5 antagonist is considered for use in a new regimen (e.g., as part of a regimen switch or simplification) **(BII).**
***Rating of Recommendations**: A = Strong; B = Moderate; C = Weak* ***Rating of Evidence**: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

HIV enters cells by a complex process that involves sequential attachment to the CD4 T lymphocyte (CD4) receptor followed by binding to either the CCR5 or CXCR4 molecules and fusion of the viral and cellular membranes.[1] CCR5 co-receptor antagonists prevent HIV entry into target cells by binding to the CCR5 receptors.[2] Phenotypic and genotypic assays have been developed that can determine or predict the co-receptor tropism (i.e., use of CCR5, CXCR4, or both as either dual-tropic virus or a mixed population of viruses referred to for purposes of assay results as dual/mixed [D/M]) of the patient's dominant virus population. An older generation assay (Trofile,® Monogram Biosciences, Inc., South San Francisco, CA) was used to screen patients who were participating in clinical trials that led to the approval of maraviroc (MVC), the only CCR5 antagonist currently available. The assay has been improved and is now available with enhanced sensitivity. In addition, genotypic assays to predict co-receptor usage are commercially available.

During acute/recent infection, the vast majority of patients harbor a CCR5-utilizing virus (R5 virus), which suggests that the R5 variant is preferentially transmitted; however, up to 19% of individuals with acute/recent infection can harbor CXCR4-tropic virus.[3-5] Viruses in many untreated patients eventually exhibit a shift in co-receptor tropism from CCR5 usage to either CXCR4 usage or D/M tropism. This shift is temporally associated with a more rapid decline in CD4 counts,[6,7] but whether this tropism shift is a cause or a consequence of progressive immunodeficiency remains undetermined.[1] Antiretroviral-treated patients with extensive drug resistance or persistently high-level viremia are more likely to harbor CXCR4- or D/M-tropic variants than untreated patients with comparable CD4 counts.[8,9] The prevalence of CXCR4- or D/M-tropic variants increases to more than 50% in treated patients who have CD4 counts <100 cells/mm^3.[8,10] Since CXCR4-tropic viruses may be present at initial presentation or a patient may shift to CXCR4-tropism over the course of infection, co-receptor tropism should always be assessed prior to the use of CCR5 antagonists for treatment. Once a patient has ever been documented with detectable CXCR4- or D/M-tropic virus, it is assumed that such viruses will always be present. CCR5 co-receptor antagonists will no longer be active for that patient and should not be used.

Phenotypic Assays

Phenotypic assays characterize the co-receptor usage of plasma-derived virus. These assays involve the generation of laboratory viruses that express patient-derived envelope proteins (i.e., gp120 and gp41). These pseudoviruses, which are replication-defective, are used to infect target cell lines that express either CCR5 or CXCR4.[11,12] Using the Trofile® assay, the co-receptor tropism of the patient-derived virus is confirmed by testing the susceptibility of the virus to specific CCR5 or CXCR4 inhibitors *in vitro*. This assay takes about 2 weeks to perform and requires a plasma HIV RNA level ≥1,000 copies/mL.

The performance characteristics of these assays have evolved. Most, if not all, patients enrolled in premarketing clinical trials of MVC and other CCR5 antagonists were screened with an earlier, less sensitive version of the Trofile® assay.[12] This earlier assay failed to routinely detect low levels of CXCR4-utilizing variants. As a consequence, some patients enrolled in these clinical trials harbored low levels of such variants at baseline, which were below the assay limit of detection, and these patients exhibited rapid virologic failure after initiation of a CCR5 antagonist.[13] The assay has been improved and is now able to detect lower levels of CXCR4-utlizing viruses. *In vitro*, the assay can detect CXCR4-utilizing clones with 100% sensitivity when those clones represent 0.3% or more of the virus population.[14] Although this more sensitive assay has had limited use in prospective clinical trials, it is now the only assay that is commercially available. For unclear reasons, a minority of samples cannot be successfully phenotyped with either generation of the Trofile® assay.

In patients with an undetectable viral load or detectable plasma HIV RNA <1,000 copies/mL, phenotypic co-receptor usage can be determined using proviral DNA obtained from peripheral blood mononuclear cells (e.g., Trofile® DNA, Monogram Sciences); however, the clinical utility of this assay remains to be determined.[15]

Genotypic Assays

Genotypic determination of HIV-1 co-receptor usage is based on sequencing of the V3-coding region of HIV-1 *env*, the principal determinant of co-receptor usage. A variety of algorithms and bioinformatics programs can be used to predict co-receptor usage from the V3 sequence.[16] When compared to the phenotypic assay, genotypic methods show high specificity (~90%) but only modest sensitivity (~50% to 75%) for the presence of a CXCR4-utilizing virus. Studies in which V3 genotyping was performed on samples from patients screened for clinical trials of MVC suggest that genotyping performed as well as phenotyping in predicting the response to MVC.[17-19] An important caveat is that the majority of patients who received MVC were first shown to have R5 virus by a phenotypic assay (Trofile®). Consequently, the opportunity to assess treatment response to MVC in patients whose virus was considered R5 by genotype but D/M or X4 by phenotype was limited to a relatively small number of patients. Other studies have also demonstrated relatively high concordance between genotypic- and phenotypic-assessed tropism;[20,21] however, there is variability between different genotypic platforms.[22]

Given these performance characteristics, genotypic tropism assays may not be sufficiently robust to completely rule out the presence of an X4 or D/M variant;[23] therefore, the Panel preferentially recommends phenotypic testing. Based on accessibility, capacity, logistics, and cost, European guidelines currently include genotypic testing as an equivalent option to phenotypic testing when determining co-receptor usage among patients with HIV RNA >1,000 copies/mL and preferentially for those with HIV RNA ≤1,000 copies/mL.[24]

HIV-1 proviral DNA genotypic tropism testing is available for patients with HIV RNA <1,000 copies/mL. These assays evaluate the HIV-1 proviral DNA integrated within infected cells for CXCR4-utilizing viral strains.[25] As discussed above, caution is advised when using such assays, as their detection limit, concordance with plasma HIV RNA tropism, and clinical utility are not yet fully determined.

Use of Assays to Determine Co-receptor Usage in Clinical Practice

An assay for HIV-1 co-receptor usage should be performed whenever the use of a CCR5 antagonist is being considered (**AI**). This is true even in the setting of prior tropism testing showing CCR5 usage, as viral evolution may occur over the course of infection. In addition, because virologic failure may occur due to a shift from CCR5-using to CXCR4-using virus, testing for co-receptor usage is recommended in patients who exhibit virologic failure on a CCR5 antagonist **(BIII).** Virologic failure may also be caused by resistance of a CCR5-using virus to a CCR5 antagonist, but such resistance is uncommon. Compared to genotypic testing, phenotypic testing has more evidence supporting its utility. Therefore, a phenotypic test for co-receptor usage is generally preferred **(AI).** However, because phenotypic testing is more expensive, requires more time to perform, and may have logistic challenges, a genotypic test to predict HIV-1 co-receptor usage should be considered as an alternative test **(BII).**

As with HIV resistance testing, the results of all prior tropism tests should be obtained. If CXCR4-utlizing or D/M-tropic viruses have ever been detected previously, then repeat testing is not necessary and a CCR5 co-receptor antagonist **should not be used.**

If a CCR5 co-receptor antagonist is being considered in a patient with an undetectable HIV RNA (e.g., in cases of regimen simplification or a toxicity-related switch), a proviral DNA tropism assay can be utilized **(BII).**[26-28] If CXCR4-utlizing or D/M-tropic viruses are detected, then the CCR5 co-receptor antagonist **should not be used.**

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HLA-B*5701 Screening

Updated: December 1, 2007
Reviewed: January 10, 2011

Panel's Recommendations
• The Panel recommends screening for HLA-B*5701 before starting patients on an abacavir (ABC)-containing regimen to reduce the risk of hypersensitivity reaction (HSR) **(AI).** • HLA-B*5701-positive patients should not be prescribed ABC **(AI).** • The positive status should be recorded as an ABC allergy in the patient's medical record **(AII).** • When HLA-B*5701 screening is not readily available, it remains reasonable to initiate ABC with appropriate clinical counseling and monitoring for any signs of HSR **(CIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = data from randomized controlled trials; II = data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = expert opinion*

The abacavir (ABC) hypersensitivity reaction (HSR) is a multiorgan clinical syndrome typically seen within the initial 6 weeks of ABC treatment. This reaction has been reported in 5% to 8% of patients participating in clinical trials when using clinical criteria for the diagnosis, and it is the major reason for early discontinuation of ABC. Discontinuing ABC usually promptly reverses HSR, whereas subsequent rechallenge can cause a rapid, severe, and even life-threatening recurrence.[1]

Studies that evaluated demographic risk factors for ABC HSR have shown racial background as a risk factor, with white patients generally having a higher risk (5%–8%) than black patients (2%–3%). Several groups reported a highly significant association between ABC HSR and the presence of the major histocompatibility complex (MHC) class I allele HLA-B*5701.[2,3] Because the clinical criteria used for ABC HSR are overly sensitive and may lead to false-positive ABC HSR diagnoses, an ABC skin patch test (SPT) was developed as a research tool to immunologically confirm ABC HSR.[4] A positive ABC SPT is an ABC-specific delayed HSR that results in redness and swelling at the skin site of application. All ABC SPT–positive patients studied were also positive for the HLA-B*5701 allele.[5] The ABC SPT could be falsely negative for some patients with ABC HSR and, at this point, is not recommended for use as a clinical tool. The PREDICT-1 study randomized participants with HIV before starting ABC either to be prospectively screened for HLA-B*5701 (with HLA-B*5701–positive patients not offered ABC) or to standard of care at the time of the study (i.e., no HLA screening, with all patients receiving ABC).[6] The overall HLA-B*5701 prevalence in this predominately white population was 5.6%. In this cohort, screening for HLA-B*5701 eliminated immunologic ABC HSR (defined as ABC SPT positive) compared with standard of care (0% vs. 2.7%), yielding a 100% negative predictive value with respect to SPT and significantly decreasing the rate of clinically suspected ABC HSR (3.4% vs. 7.8%). The SHAPE study corroborated the low rate of immunologically validated ABC HSR in black patients and confirmed the utility of HLA-B*5701 screening for the risk of ABC HSR (100% sensitivity in black and white populations).[7]

On the basis of the results of these studies, the Panel recommends screening for HLA-B*5701 before starting an ABC-containing regimen in a person with HIV **(AI).** HLA-B*5701–positive patients should not be prescribed ABC **(AI),** and the positive status should be recorded as an ABC allergy in the patient's medical record **(AII).** HLA-B*5701 testing is needed only once in a patient's lifetime;

thus, efforts to carefully record and maintain the test result and to educate the patient about its implications are important. The specificity of the HLA-B*5701 test in predicting ABC HSR is lower than the sensitivity (i.e., 33%–50% of HLA-B*5701–positive patients would likely not develop confirmed ABC HSR if exposed to ABC). HLA-B*5701 should not be used as a substitute for clinical judgment or pharmacovigilance, because a negative HLA-B*5701 result does not absolutely rule out the possibility of some form of ABC HSR. When HLA-B*5701 screening is not readily available, it remains reasonable to initiate ABC with appropriate clinical counseling and monitoring for any signs of ABC HSR **(CIII).**

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Treatment Goals

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Reviewed: January 28, 2016

Antiretroviral therapy (ART) has reduced HIV-related morbidity and mortality at all stages of HIV infection[1-4] and has reduced HIV transmission.[5-8] Maximal and durable suppression of plasma viremia delays or prevents the selection of drug-resistance mutations, preserves or improves CD4 T lymphocyte (CD4) cell numbers, and confers substantial clinical benefits, all of which are important treatment goals.[9, 10] HIV suppression with ART may also decrease inflammation and immune activation thought to contribute to higher rates of cardiovascular and other end-organ damage reported in cohorts with HIV (see Initiating Antiretroviral Therapy). Despite these benefits, eradication of HIV infection cannot be achieved with available antiretrovirals (ARVs). Treatment interruption has been associated with rebound viremia, worsening of immune function, and increased morbidity and mortality.[11] Thus, once initiated, ART should be continued, with the following key treatment goals:

- Maximally and durably suppress plasma HIV RNA;
- Restore and preserve immunologic function;
- Reduce HIV-associated morbidity and prolong the duration and quality of survival; and
- Prevent HIV transmission.

Achieving viral suppression currently requires the use of combination ARV regimens that generally include three active drugs from two or more drug classes. Baseline patient characteristics and results from drug resistance testing should guide design of the specific regimen (see What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient). When initial HIV suppression is not achieved or not maintained, changing to a new regimen with at least two active drugs is often required (see Virologic Failure).The increasing number of ARV drugs and drug classes makes viral suppression below detection limits an achievable goal in most patients.

After initiation of effective ART, viral load reduction to below limits of assay detection usually occurs within the first 12 to 24 weeks of therapy. Predictors of virologic success include the following:

- Low baseline viremia;
- High potency of the ARV regimen;
- Tolerability of the regimen;
- Convenience of the regimen; and
- Excellent adherence to the regimen.

Strategies to Achieve Treatment Goals

Selection of Initial Combination Regimen

Several ARV regimens are recommended for use in ART-naive patients (see What to Start). Most of the recommended regimens have comparable efficacy but vary in pill burden, potential for drug interactions and/or side effects, and propensity to select for resistance mutations if ART adherence is suboptimal. Regimens should be tailored for the individual patient to enhance adherence and support long-term treatment success. Considerations when selecting an ARV regimen for an individual patient include potential side effects, patient comorbidities, possible interactions with conconcomitant medications, results of pretreatment genotypic drug-resistance testing, and regimen convenience (see Table 7).

Improving Adherence

Suboptimal adherence may result in reduced treatment response. Incomplete adherence can result from complex medication regimens; patient-related factors, such as active substance abuse, depression, or the experience of adverse effects; and health system issues, including interruptions in patient access to medication and inadequate treatment education and support. Conditions that promote adherence should be maximized before and after initiation of ART (see Adherence to Antiretroviral Therapy).

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Initiation of Antiretroviral Therapy

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Reviewed: December 18, 2019

Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all persons with HIV to reduce morbidity and mortality **(AI)** and to prevent the transmission of HIV to others **(AI).** • The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating ART immediately (or as soon as possible) after HIV diagnosis in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients, and improve the rate of virologic suppression among persons with HIV **(AII).** • When initiating ART, it is important to educate patients regarding the benefits of ART and to deploy strategies to optimize care engagement and treatment adherence **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

The primary goal of antiretroviral therapy (ART) is to prevent HIV-associated morbidity and mortality. This goal is accomplished by using effective ART to achieve and maintain a plasma HIV-1 RNA (viral load) below the quantification limits of commercially available assays. Durable viral suppression improves immune function and overall quality of life, lowers the risk of both AIDS-defining and non-AIDS–defining complications, and allows persons with HIV to live a lifespan approaching that of persons without HIV.[1]

Another goal of ART is to reduce the risk of HIV transmission to sexual partners and to infants born to persons with HIV. High plasma HIV RNA levels are a major risk factor for HIV transmission; effective ART can reduce both viremia and the risk of transmission of HIV to sexual partners[2-6] and prevent perinatal transmission.[7, 8] Modelling studies and ecological studies of populations with high ART uptake and high viral suppression rates suggest that expanded use of ART may lower the incidence of HIV and, eventually, the prevalence of HIV on a community or population level.[9-11]

Two large, randomized controlled trials addressed the optimal time to initiate ART—START[12] and TEMPRANO.[13] Both studies demonstrated reductions in morbidity and mortality among individuals with HIV who had CD4 T lymphocyte (CD4) cell counts >500 cells/mm^3 and who were randomized to receive ART immediately when compared to individuals who delayed initiation of ART.

Deferring ART until CD4 counts decline puts individuals with HIV at risk of both AIDS-defining conditions and certain serious non-AIDS–defining conditions. Furthermore, the magnitude of CD4 recovery is directly correlated with CD4 count at ART initiation. Consequently, many individuals who start treatment with CD4 counts <350 cells/mm^3 do not achieve CD4 counts >500 cells/mm^3 after up to 10 years on ART,[14, 15] and they have a shorter life expectancy than those who initiated therapy at higher CD4 count thresholds.[14-16]

Fundamental to the recommendation for earlier initiation of ART in these guidelines is the assumption that HIV will be diagnosed early in the course of the disease. Unfortunately, in some individuals, the diagnosis of HIV is not made until the later stages of the disease. In a survey conducted between 2016 and 2017, it was noted that fewer than 40% of American adults had ever had an HIV test.[17] Evidence shows that many people with HIV access health care years before their HIV diagnosis but are not offered HIV testing despite recommendations from the Centers for Disease Control and Prevention (CDC) for routine testing for everyone aged 13 to 64 years.[18, 19] There are also economic benefits to early diagnosis, including prolonging life, improving the quality of life, and decreasing the costs related to the management of AIDS and its co-morbidities.[20, 21] Additionally, HIV screening is a key step in the Ending the HIV Epidemic initiative to prevent the transmission of HIV to others.[22]

Diagnosis of HIV is delayed more often in nonwhite individuals, those who inject drugs, those who live in rural communities, and older adults, and many individuals in these groups develop AIDS-defining illnesses within 1 year of diagnosis.[23-25] Therefore, to ensure that the current treatment guidelines have maximum impact, routine HIV screening per current CDC recommendations is essential. The U.S. Preventative Services Task Force recommends HIV testing for persons aged 15 to 65 years and for all pregnant individuals. HIV testing should also be performed for younger and older persons when indicated. This recommendation has been designated a Grade A recommendation by the U.S. Preventative Services Task Force, meaning that third-party payers should cover this service without cost to patients.[26] It is critical that everyone who receives an HIV diagnosis be educated about HIV disease and linked to care for full evaluation, follow-up, and management as soon as possible. In order for both individuals with HIV and their sexual partners to fully benefit from early diagnosis, clinicians should initiate ART as soon as possible and provide support to enhance retention in care and ART adherence (see Adherence to the Continuum of Care).

Initiating Antiretroviral Therapy

ART is recommended for all individuals with HIV to reduce the morbidity and mortality associated with HIV infection **(AI)** and to prevent HIV transmission to sexual partners and infants **(AI).** ART should be initiated as soon as possible after HIV diagnosis **(AII).** When initiating ART, it is important to educate patients about the goals and benefits of ART and to identify and address barriers to care engagement and treatment adherence **(AIII).** Patients should also understand that currently available ART does not cure HIV. To improve and maintain immunologic function and maintain viral suppression, ART should be continued indefinitely without interruption. Initiating ART early is particularly important for patients with AIDS-defining conditions, those with acute or recent HIV infection, and individuals who are pregnant; delaying therapy in these subpopulations has been associated with high risks of morbidity, mortality, and HIV transmission.

Immediate Antiretroviral Therapy Initiation on the Day of HIV Diagnosis

Since individuals may fail to engage in care between the initial HIV diagnosis (or first clinic visit) and the time ART is prescribed, some groups have proposed rapid ART initiation on the same day of HIV diagnosis as a strategy to increase ART uptake and engagement in care and to accelerate the time to ART-mediated viral suppression. Rapid ART initiation also has the potential to reduce the time during which people with newly diagnosed HIV can transmit HIV. The rapid ART initiation strategy is supported by randomized controlled trials that were performed in resource-limited settings outside of the United States[27-29] and observational trials in the United States that included both

immediate initiation of ART (on the day of diagnosis)[30-32] and rapid ART initiation (within days or weeks of diagnosis).[32, 33] The results from some of these studies are discussed below.

A randomized controlled trial conducted in South Africa enrolled 377 individuals who had recently received HIV diagnoses (median CD4 count was 210 cells/mm^3). Participants were randomized to receive ART on the day of diagnosis or to receive the usual care (three to five additional visits over 2–4 weeks before ART initiation). Those who received immediate ART were significantly more likely to be virally suppressed at 10 months (64% vs. 51% of patients achieved viral suppression, respectively).[27] In another randomized controlled trial conducted in Haiti, a higher proportion of participants who were randomized to receive same-day ART initiation were retained in care and had viral suppression at the end of 1 year than those who initiated ART at the standard time (3 weeks after HIV testing); survival was also higher in the same-day ART initiation group.[28] A novel randomized controlled trial in Lesotho compared same-day, home-based ART to usual care and standard clinic referral (which involved a minimum of two counseling sessions prior to ART initiation). Participants randomized to receive same-day ART initiation were significantly more likely to achieve linkage to care within 90 days after enrollment (68.6% vs. 43.1%) and virologic suppression at approximately 12 months (50.4% vs. 34.3%).[29]

There are many differences between health care in southern Africa and Haiti and in the United States—including differences in the health care systems, structural barriers to engagement in care, underlying HIV and tuberculosis (TB) epidemics, and ART regimens used—that limit the generalizability of the findings of the results from the studies described above. These studies, however, suggest that same-day initiation of ART is feasible and could potentially improve clinical outcomes.

While no randomized controlled trials have been conducted in the United States, several prospective observational studies have demonstrated the feasibility of same-day ART initiation. City-wide implementation of the San Francisco RAPID program among 225 patients who were newly diagnosed with HIV showed a median time from HIV diagnosis to ART start of 0 days (with a range of 0–56 days) and a median time from ART initiation to viral suppression (defined as <200 copies/mL) of 41 days. Over a median follow-up of 1.09 years (range 0–3.92 years), 92.1% of patients achieved virologic suppression. The RAPID study included a diverse and traditionally marginalized population, with a substantial proportion of participants having a major substance use disorder (51.4%), a major mental health disorder (48.1%), or unstable housing (30.6%).[31]

Whether rapid ART initiation improves long-term care engagement and virologic suppression is not yet known. One cohort study from France, however, found that earlier initiation of ART was negatively associated with care engagement at 1 year.[34] It should be emphasized that ART initiation on the same day of HIV diagnosis is resource intensive, and this strategy may require additional staff, multidisciplinary coordination, provision of ART starter packs, and consolidation of "usual care" patient services (e.g., clinical evaluation, education, counseling, initiation or optimization of insurance coverage, intake laboratory testing) into a 2- or 3-hour visit.[31] While the infrastructure and resources necessary to implement an immediate ART program may not be available in all health care settings, removing structural barriers in order to facilitate rapid ART initiation may improve outcomes in the United States. The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends initiating ART at the time of diagnosis (when possible) or soon afterwards to increase the uptake of ART, decrease the time required to achieve linkage to care and virologic suppression, and improve the rate of virologic suppression among individuals who have recently received HIV diagnoses **(AII).** This rating for this recommendation reflects the fact that only

observational trials have been conducted in the United States or other highly resourced countries, where health systems and socioeconomic contexts differ substantially from those in the countries where randomized trials were conducted.

Antiretroviral Therapy for Persons with Acute Opportunistic Infections and Malignancies

Initiation of ART in the setting of an acute, AIDS-associated opportunistic infection (OI) or malignancy can improve immune function and potentially enhance treatment success for the OI. Clinicians should refer to the Adult and Adolescent Opportunistic Infection Guidelines for a more in-depth discussion on specific OIs. Below is a list of important factors to consider when initiating ART in these situations.

- When no effective therapy exists for the OI (e.g., cryptosporidiosis, microsporidiosis, progressive multifocal leukoencephalopathy): In these situations, ART may be the only treatment that can improve immune function and clinical outcomes. ART should be initiated without delay in these patients (see the Adult and Adolescent Opportunistic Infection Guidelines for more information).
- Concerns regarding immune reconstitution inflammatory syndrome (IRIS): For some OIs, such as cryptococcal and TB meningitis, immediate ART initiation may increase the risk of serious IRIS. A short delay before initiating ART may be warranted.[35-38] After ART initation, the patient should be closely monitored for signs and symptoms associated with IRIS.
- Non-meningeal TB: In these patients, initiating ART during treatment for TB confers a significant survival advantage;[39-43] therefore, ART should be initiated as recommended in Tuberculosis/HIV Coinfection.
- For patients with mild to moderate cutaneous Kaposi sarcoma: Prompt initiation of ART alone without chemotherapy has been associated with improvement of cutaneous Kaposi sarcoma lesions, even though initial transient progression of Kaposi sarcoma lesions as a manifestation of IRIS can also occur.[44]
- For patients with malignancies that require chemotherapy:
    - A diagnosis of malignancy should not delay initiation of ART, nor should initiation of ART delay treatment for the malignancy.
    - Although an IRIS-like presentation of non-Hodgkin's lymphoma after initiation of ART has been described,[45] ART-mediated viral suppression is associated with longer survival among individuals undergoing treatment for AIDS-related lymphoma.[46]
    - Drug interactions should be considered when selecting ART, as there is the potential for significant interactions between chemotherapeutic agents and some antiretroviral drugs (particularly some ritonavir-boosted or cobicistat-boosted regimens).

Evidence Supporting the Benefits of Antiretroviral Therapy in Preventing Morbidity and Mortality

Randomized Controlled Trials of Early vs. Deferred Antiretroviral Therapy

Two large randomized controlled trials, START and TEMPRANO, provide the evidence for the Panel's recommendation to initiate ART in all patients regardless of CD4 count **(AI).** The results of these two studies are summarized below.

START was a large, multi-national, randomized controlled clinical trial designed to evaluate the role of early ART initiation in asymptomatic patients with HIV in reducing a composite clinical endpoint of AIDS-defining illnesses, serious non-AIDS events, or death. The study began at a time when initiating ART was not recommended until an individual's CD4 count fell below 350 cells/mm^3. In this study, ART-naive adults (aged >18 years) with CD4 counts >500 cells/mm^3 were randomized to initiate ART at randomization (early initiation arm) or to wait to initiate ART until their CD4 counts declined to <350 cells/mm^3 or until they developed a clinical indication for therapy (deferred initiation arm).

The study enrolled 4,685 participants, with a mean follow-up of 3 years. The primary endpoint of serious AIDS or non-AIDS events was reported in 42 participants (1.8%, or 0.60 events per 100 person-years) who were randomized to initiate ART early, and 96 participants (4.1%, or 1.38 events per 100 person-years) in the deferred ART arm (hazard ratio [HR] 0.43, favoring early ART; 95% confidence interval [CI], 0.30–0.62, $P < 0.001$). The most common clinical events reported were TB and malignancies (including both AIDS and non-AIDS malignancies). The majority of clinical events (59%) in the deferred ART arm occurred in participants whose CD4 counts were still above 500 cells/mm^3, evidence for a benefit of initiating ART even before CD4 count declines below this threshold. Furthermore, the benefit of early ART was consistent across all participant subgroups, including gender, age, plasma HIV RNA levels, and income level of country. Although START was not sufficiently powered to compare the benefits of early ART initiation and deferred ART initiation for each category of clinical events, the benefit appeared to be particularly strong for AIDS events (HR 0.28), TB (HR 0.29), malignancies (HR 0.36), and severe bacterial infections (HR 0.39). The benefit at lower CD4 counts was primarily a reduction in the number of AIDS events, while the benefit at higher CD4 counts was primarily a reduction in the number of serious non-AIDS events. Importantly, early ART initiation also significantly reduced the rate of pooled serious non-AIDS events (HR 0.61).[12, 47]

The TEMPRANO ANRS 12136 study was a randomized controlled trial conducted in Cote d'Ivoire. Using a two-by-two factorial design, participants with HIV who had CD4 counts <800 cells/mm3 and who did not meet the criteria for starting ART according to World Health Organization guidelines at that time were randomized to start ART early (upon enrollment) or defer ART based on the national guidelines criteria for starting treatment. Half of the participants in each group received isoniazid for prevention of TB for 6 months and half did not. The primary study endpoint was a combination of all-cause deaths, AIDS diseases, non-AIDS malignancies, and non-AIDS invasive bacterial diseases.

More than 2,000 participants enrolled in the trial, with a median follow-up of 30 months. Among the 849 participants who had baseline CD4 counts >500 cells/mm^3, 68 primary outcome events were reported in 61 patients. The risk of primary events was lower among those who were randomized to start ART early than among those in the deferred arm, with an HR of 0.56 in favor of early ART

(95% CI, 0.33–0.94). On the basis of these results, the study team concluded that early ART initiation is beneficial in reducing the rate of these clinical events.[13]

The TEMPRANO and START trials had very similar estimates for the protective effect of ART among individuals with HIV who had CD4 counts >500 cells/mm^3, further supporting the Panel's recommendation that ART be initiated in all patients regardless of CD4 count.

Use of Antiretroviral Therapy to Prevent HIV Transmission

Prevention of Sexual Transmission

A randomized clinical trial[3] and several large observational cohort studies[4-6] have provided strong evidence that achieving sustained viral suppression prevents sexual transmission of HIV. Thus, a key goal of ART is to prevent transmission of HIV to seronegative sexual partners **(AI).** All persons with HIV should be informed that maintaining a plasma HIV RNA (viral load) of <200 copies/mL, including any measurable value below this threshold value, with ART prevents sexual transmission of HIV to their partners **(AII).** Patients may recognize this concept as Undetectable = Untransmittable, or U=U. The results of these studies are summarized in Antiretroviral Therapy to Prevent Sexual Transmission of HIV.

Prevention of Perinatal Transmission

The first well-established example of ART reducing the risk of HIV transmission is the use of ART during pregnancy to prevent perinatal transmission of HIV. Effective suppression of HIV replication is a key determinant in reducing the risk of perinatal transmission. In the setting of maternal viral load suppressed to <50 copies/mL near delivery, the use of combination ART during pregnancy has reduced the rate of perinatal HIV transmission from approximately 20% to 30% to 0.1% to 0.5%.[7, 8] ART is thus recommended for all pregnant individuals with HIV, for both maternal health and for the prevention of HIV transmission to the newborn. In ART-naive pregnant individuals, ART should be initiated as soon as possible, with the goal of suppressing plasma viremia throughout pregnancy. All pregnant individuals should be tested for HIV upon confirmation of pregnancy, with testing repeated throughout pregnancy as needed for those at risk of HIV acquisition (see Maternal HIV Testing and Identification of Perinatal HIV Exposure in the Perinatal Guidelines).

Considerations When Initiating Antiretroviral Therapy

The ART regimens that are currently recommended as initial therapy in these guidelines (see What to Start) can suppress and maintain viral loads below the level of quantification in most patients who adhere to their regimens. Most of the recommended regimens have a low pill burden and are well tolerated. Once started on treatment, patients must continue ART indefinitely.

Optimizing Adherence, Antiretroviral Therapy Access, and Care Engagement

The key to successfully maintaining viral suppression is continuous access to ART and adherence to the prescribed regimen. Lack of adherence or intermittent access to ART can result in treatment failure and the emergence of drug resistance mutations that may compromise future treatment options. While optimizing adherence and linkage to care and ensuring continuous access are critical regardless of the timing of ART initiation, the evidence thus far indicates that drug resistance occurs more frequently in individuals who initiate therapy later in the course of infection than in those who

initiate ART earlier.[48] It is important to discuss strategies to optimize adherence, care engagement, and ART access with all patients.

Several clinical, behavioral, and social factors have been associated with poor adherence. These factors include untreated major psychiatric disorders, neurocognitive impairment, substance use disorder, unstable housing, unfavorable social circumstances, patient concerns about side effects, and poor adherence to clinic visits. Clinicians should identify areas where additional intervention is needed to improve adherence both before and after initiation of therapy. Some strategies to improve adherence are discussed in Adherence to the Continuum of Care. However, mental illness, substance use disorder, and psychosocial challenges are not reasons to withhold ART from a patient. Rather, these issues indicate the need for additional interventions to support adherence, and they may influence the ART regimen that is recommended (see What to Start).

Considerations for Special Populations

Elite HIV Controllers

A small subset of individuals with HIV maintains plasma HIV-1 RNA levels below level of quantification for years without ART. These individuals are often referred to as elite HIV controllers.[49, 50] There are limited data on the benefits of initiating ART in these individuals. The START and TEMPRANO studies demonstrated that initiating ART is clearly beneficial for the patient regardless of CD4 count; therefore, delaying ART to see if a patient becomes an elite controller is **strongly discouraged**. Nevertheless, significant uncertainty remains about the optimal management of elite controllers who have maintained undetectable viremia in the absence of ART for years.

Given that ongoing HIV replication occurs even in elite controllers, ART is strongly recommended for controllers with evidence of HIV disease progression, which is defined by declining CD4 counts or the development of HIV-related complications **(AIII).** Nonetheless, even elite controllers with normal CD4 counts show evidence of abnormally high immune activation and surrogate markers of atherosclerosis, which may contribute to an increased risk of non-AIDS–related diseases.[49, 51-53] One observational study suggested that elite controllers are hospitalized more often for cardiovascular and respiratory disease than patients from the general population and ART-treated patients.[54] Moreover, elite controllers with preserved CD4 counts appear to experience a decline in immune activation after ART initiation, suggesting that treatment may be beneficial.[55] Whether this potential immunologic benefit of ART in elite controllers outweighs the potential risks of ART toxicity and results in clinical benefit is unclear. Unfortunately, it is unlikely that randomized controlled trials will be able to address this question, given the very low prevalence of elite controllers. Although the START study included a number of participants with very low viral loads and demonstrated the benefit of immediate ART initiation regardless of the extent of viremia, the study did not include a sufficient number of controllers to definitively determine the clinical impact of ART in this specific population.[56] Nevertheless, there is a clear rationale for prescribing ART to elite controllers even in the absence of detectable plasma HIV RNA levels. If ART is withheld, elite controllers should be followed closely, as some may experience CD4 cell decline, loss of viral control, or complications related to HIV infection.

Adolescents with HIV

Neither the START trial nor the TEMPRANO trial included adolescents. The Panel's recommendation to initiate ART in all patients is extrapolated to adolescents based on the expectation that they will derive benefits from early ART initiation that are similar to those observed in adults. Compared to adults, youth have demonstrated significantly lower levels of ART adherence and viral suppression, and higher rates of viral rebound following initial viral suppression.[57] In recent years, more adolescents have been prescribed once-daily regimens, which has increased the rate of viral suppression in this population, even though there has been no significant difference in treatment adherence.[58] Because youth often face psychosocial and other barriers to adherence, their ability to adhere to therapy should be carefully considered when making decisions about ART initiation. Although some adolescents may not be ready to initiate therapy, clinicians should offer ART while providing effective interventions to assess and address barriers to receiving care and to adherence. To optimize the benefits of ART for youth, a multidisciplinary care team should provide psychosocial and adherence support to adolescent patients (see Adolescents and Young Adults with HIV).[59]

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Antiretroviral Therapy to Prevent Sexual Transmission of HIV (Treatment as Prevention)

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Panel's Recommendations
• All persons with HIV should be informed that maintaining a plasma HIV RNA (viral load) of <200 copies/mL, including any measurable value below this threshold value, with antiretroviral therapy (ART) prevents sexual transmission of HIV to their partners. Patients may recognize this concept as Undetectable = Untransmittable or U=U **(AII).**
• Persons with HIV who are starting ART should use another form of prevention with sexual partners (e.g., condoms, pre-exposure prophylaxis [PrEP] for the HIV-negative sexual partner, sexual abstinence) for at least the first 6 months of treatment and until a viral load of <200 copies/mL has been documented **(AII).** Many experts would recommend confirming sustained suppression before assuming that there is no further risk of sexual HIV transmission **(AIII).**
• When the viral load is ≥200 copies/mL, additional methods are needed to prevent transmission of HIV to sexual partners until resuppression to <200 copies/mL has been confirmed **(AIII).**
• Persons with HIV who intend to rely upon ART for prevention need to maintain high levels of ART adherence **(AIII).** They should be informed that transmission is possible during periods of poor adherence or treatment interruption **(AIII).**
• At each visit for HIV care, clinicians should assess adherence to ART and counsel patients regarding the importance of ART to their own health as well as its role in preventing sexual HIV transmission **(AIII).**
• Providers should inform patients that maintaining a viral load of <200 copies/mL does not prevent acquisition or transmission of other sexually transmitted infections (STIs) **(AII).**
• Providers should also routinely screen all sexually active persons with HIV for STIs, both for their own health and to prevent transmission of STIs to others **(AIII).**
***Rating of Recommendations**: A = Strong; B = Moderate; C = Weak*
***Rating of Evidence**: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Antiretroviral therapy (ART) not only reduces morbidity and mortality for persons with HIV but has now been definitively shown to prevent sexual transmission of the virus when the plasma HIV RNA (viral load) is consistently suppressed to <200 copies/mL, which includes any measurable viral load that is lower than this threshold value. Providers who manage patients with HIV need to be aware of the data supporting treatment as prevention (TasP, which persons with HIV may recognize as Undetectable = Untransmittable or U=U), its implications, and how to operationalize this prevention strategy in clinical practice. For persons with HIV who intend to rely on TasP for HIV prevention, providers should make an individualized assessment of the person's risk tolerance, personal health, history of maintaining viral suppression on treatment, and access to health care services and ART, as well as other factors that may affect their ability to maintain a high level of adherence to ART.

Evidence That Viral Load Suppression Prevents Sexual HIV Transmission

Suppressing the HIV viral load to <200 copies/mL with ART prevents sexual transmission of HIV. Observational data collected in the early 1990s from heterosexual couples demonstrated that sexual transmission from untreated persons with HIV was rare at viral loads of <1,000 copies/mL to 1,500 copies/mL and that the risk of transmission increased in dose-response fashion with increasing viral

load.[1, 2] Additional reports[3-7] and a meta-analysis[8] supported the observation that sexual HIV transmission risk in heterosexual persons was correlated with plasma viral load, and transmission was infrequent below the lowest limits of quantification for the viral load assays used at the time.

The first prospective clinical trial designed specifically to address this question was HPTN 052, which randomized people with HIV who were in mixed HIV status couples (previously referred to as serodiscordant couples) to initiate ART early or to delay initiation. Initial results from this study were reported in 2011,[9] with final results reported in 2016.[10] The 2016 analysis reported that no phylogenetically linked sexual transmissions of HIV occurred among 1,763 couples who were followed a median of 5.5 years while the person with HIV was on ART and had a viral load <400 copies/mL for at least 6 months. Notably, four phylogenetically linked infections occurred within the 90 days after the partner with HIV had started ART and was presumably not yet virally suppressed, and four others occurred after the partner with HIV had experienced virologic failure. There were also a number of transmission events that were not phylogenetically linked, indicating acquisition from someone other than the enrolled study index partner.[11] HPTN 052 was conducted almost exclusively among heterosexual couples that lived in Africa and Asia and did not track the number or type of sexual exposures. In addition, ART was used as an adjunct to a comprehensive prevention package that provided condoms and encouraged condom use, as well as frequent testing for HIV and other sexually transmitted infections (STIs).

Three prospective observational studies—PARTNER 1,[12] PARTNER 2,[13] and Opposites Attract[14]—provided data from more diverse populations of mixed HIV status couples in which condomless sex was common. Clinical follow-up in these studies closely mimicked that of routine clinical care. Conducted in 14 European countries (PARTNER 1 and PARTNER 2) as well as Australia, Thailand, and Brazil (Opposites Attract), the investigators followed 548 heterosexual and 1,481 male-male mixed HIV status couples that engaged in 144,631 episodes of condomless vaginal or anal sex while the partner with HIV had a suppressed viral load on ART, defined as <200 copies/mL. In these studies, no phylogenetically linked transmissions were observed; however, as in HPTN 052, there were numerous non-phylogenetically linked transmissions attributed to partners outside the enrolled study couple relationship.

Integrating the Principles of Treatment as Prevention into Clinical Care

The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends that providers inform all persons with HIV that maintaining an HIV viral load <200 copies/mL with ART prevents sexual transmission of HIV **(AII).** This information may help motivate patients and help relieve stigma that can be a barrier to getting tested and entering into care, starting and remaining adherent to ART, and ultimately achieving and maintaining a viral load <200 copies/mL.[15] Although PARTNER 1, PARTNER 2, and Opposites Attract were designed to follow patients in the study as they would be typically be followed in clinical care for HIV, the participants reported high levels of ART adherence at study entry and many reported at least 1 year of condomless sex with an established sexual partner without transmission. As the principles of TasP are integrated into the clinical management of people with HIV who are on ART, implementation research will be critical to maximize the effectiveness of TasP in practice.

Frequency of Viral Load Assessment

The Panel has issued recommendations for viral load monitoring to manage the health of persons with HIV (see Plasma HIV-1 RNA (Viral Load) and CD4 Count Monitoring). However, current data

are insufficient to determine whether these recommendations represent the optimal monitoring schedule for the purpose of preventing sexual transmission of HIV. In the PARTNER studies and Opposites Attract, viral loads were generally assessed every 3 to 6 months during study follow-up, usually during the course of regular HIV care. Pending further data, the Panel recommends no change to the existing recommendations for monitoring viral load (see Plasma HIV-1 RNA (Viral Load) and CD4 Count Monitoring) **(BII).**

Time to Adequate Suppression after Starting Antiretroviral Therapy

A subgroup analysis from the Partners PrEP Study provided data regarding the risk of HIV transmission during and after the first 6 months on ART for the partner with HIV.[16] This analysis included 1,573 heterosexual East African couples in which the partners without HIV were randomized to the placebo arm of the Partners PrEP Study and were tested monthly for HIV while the viral load of the partner with HIV was assessed every 6 months. Three phylogenetically linked infections were diagnosed in the 6 months prior to the first follow-up visit for the partners with HIV. The observed incidence rate of 1.79 per 100 person-years during this initial 6-month period after the partner with HIV started ART was slightly less than the 2.08 per person-years incidence rate observed in couples in which the person with HIV was not receiving ART. Viral suppression in this study was defined as <40 copies/mL, and the three infections were diagnosed at 0 days, 56 days, and 149 days after the partner with HIV started ART. After the partners with HIV had been taking ART for ≥6 months, no further transmissions were observed.

At this time, the Panel recommends that persons with HIV who are starting ART use another form of prevention with sexual partners for at least the first 6 months of treatment and until a viral load of <200 copies/mL has been documented **(AII).** Many experts would recommend confirming sustained suppression before assuming that there is no further risk of sexual transmission of HIV **(AIII).**

Adherence to Antiretroviral Therapy

Adherence to ART is paramount for persons who intend to prevent HIV transmission by achieving and maintaining a suppressed viral load. Viral rebound typically occurs within days to weeks after ART cessation and has been observed as early as 3 to 6 days after stopping treatment.[17-29] The minimum level of adherence that is required to prevent sexual transmission has not been determined and may vary depending on the ART regimen. In the key studies that defined the efficacy of TasP, adherence levels prior to study entry and during follow-up were very high. In clinical practice, most people who start ART will achieve a viral load <200 copies/mL within 6 months, but once this viral load is achieved, maintaining viral suppression can be a challenge, especially for those who have difficulty accessing ART and other HIV care. The Centers for Disease Control and Prevention (CDC) estimates that during 2015, 60% of persons with HIV and 78% of persons engaged in clinical care had viral loads <200 copies/mL at their most recent assessment.[30] Observational cohort data have demonstrated that within the first year of starting ART, up to 10% of persons with HIV can experience loss of viral suppression; however, the likelihood of maintaining a suppressed viral load generally improves over time. After a few years, 5% or fewer of persons on ART may experience loss of viral suppression.[31, 32]

The Panel recommends that persons with HIV who intend to rely upon TasP be made aware of the need for high levels of ART adherence **(AIII).** The Panel further recommends that adherence be assessed and counseling be provided at each visit for HIV care to reinforce the importance of adherence for the individual's health as well as its role in preventing HIV transmission **(AIII).**

Patients should be informed that transmission is possible during periods of poor adherence or treatment interruption **(AIII).**

Adherence can be especially challenging for certain groups of patients, such as adolescents and young adults, homeless persons, persons with active substance use disorder, and persons who are involved with the criminal justice system. Recommendations to help manage and maximize ART adherence can be found in Adherence to the Continuum of Care. Persons for whom there is concern about adherence also merit counseling on how to properly use other prevention methods, especially barrier methods that prevent STIs.

Managing Transient Viremia, or "Blips"

Highly adherent patients may experience intermittent or transient viremia, commonly termed "viral blips." Blips are defined in the context of effective treatment as a single, measurable HIV RNA level, typically <200 copies/mL, that is followed by a return to a viral load below the limit of detection or quantification. With contemporary ART regimens, about 10% of persons per year who are adherent to ART may experience a blip.[33-35] Most blips likely represent normal biological fluctuation (i.e., variation around a mean undetectable viral load) or laboratory artifact and not inadequate adherence.[36-38] Persistent viremia ≥200 copies/mL has been associated with increasing risk of virologic failure[33, 39] that, in the context of TasP, can lead to increased risk of sexual transmission.[10] The PARTNER studies and Opposites Attract excluded observation time when the viral load of the participant with HIV was ≥200 copies/mL. The frequency of blips <200 copies/mL was not reported in Opposites Attract; however, in PARTNER 1 and PARTNER 2, transient elevations in viral loads above the limit of detection (50 copies/mL in these studies) but <200 copies/ml were observed for 6% and 4% of the total follow-up time, respectively, during which time no phylogenetically linked infections were observed.

One of the clinical challenges with blips is that they can only be defined retrospectively once the viral load has returned to a suppressed value. The Panel recommends that when the viral load is ≥200 copies/mL, persons with HIV and their sexual partners should use another form of prevention (e.g., condoms, pre-exposure prophylaxis for sexual partners without HIV, sexual abstinence) to protect against HIV transmission until a viral load <200 copies/mL is achieved (AII). This recommendation applies both to persons who are starting ART (as noted earlier) and to those who have been taking ART and have achieved viral suppression but develop viral loads ≥200 copies/mL.

In cases where a patient achieves resuppression to <200 copies/mL after a detectable viral load ≥200 copies/mL, or when a patient with a viral load <200 copies/mL switches regimens (e.g., for regimen simplification or to avoid certain side effects), providers should check the viral load per recommendations in Plasma HIV-1 RNA (Viral Load) and CD4 Count Monitoring and Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression, respectively **(AIII).** There are presently no data to guide how long, if at all, a person might need to continue to use another form of prevention in these two circumstances. Individualized assessment is recommended based on the length and quality of adherence and time with viral load <200 copies/mL preceding the viral load ≥200 copies/mL.

Effect of Sexually Transmitted Infections on Treatment as Prevention

The presence of STIs in a person with HIV does not appear to meaningfully alter the risk of sexual transmission when the person's viral load is <200 copies/mL. The PARTNER studies and the

Opposites Attract study regularly assessed participants for STIs, which were diagnosed in 6% of heterosexual participants and 13% to 27% of men who have sex with men. Although the authors of the studies noted that their findings could not rule out the possibility that STIs in participants with viral loads <200 copies/mL might affect the risk of HIV transmission, when viewed collectively, these data suggest that any effect is very small, since STIs were common and no linked infections were observed. The Panel recommends that patients using TasP be informed that maintaining a viral load of <200 copies/mL does not prevent acquisition or transmission of other STIs, and that it is not substitute for condoms or behavioral modifications **(AII).** Providers should also routinely screen all sexually active persons with HIV for STIs, both for their own health and to prevent transmission of STIs to others **(AIII).** Refer to CDC's Sexually Transmitted Diseases Treatment Guidelines for details.

Treatment as Prevention Applies Only to Sexual Transmission of HIV

Available clinical data only support the use of TasP to prevent sexual HIV transmission in patients with viral loads <200 copies/mL. The effectiveness of this strategy to prevent transmission from blood exposure (e.g., through nonsterile drug injection) has not been determined. In addition, while suppression of maternal viral load substantially reduces the risk of perinatal transmission and transmission through breastfeeding, it does not eliminate these risks, and transmission has occurred via breastfeeding despite continuous viral suppression (refer to the Perinatal Guidelines for details).

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What to Start: Initial Combination Antiretroviral Regimens for People With HIV

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Introduction

More than 30 antiretroviral (ARV) drugs in nine mechanistic classes are U.S. Food and Drug Administration (FDA)–approved for treatment of HIV infection. These nine classes include nucleos(t)ide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase strand transfer inhibitors (INSTIs), a fusion inhibitor, a CCR5 antagonist, a CD4 T lymphocyte (CD4) cell post-attachment inhibitor, a gp120 attachment inhibitor, and a capsid inhibitor. In addition, two drugs—ritonavir (RTV) and cobicistat (COBI)—are used as pharmacokinetic (PK) enhancers (or boosters) to improve the PK profiles of PIs and the INSTI elvitegravir (EVG).

Over time, incremental improvements in potency, tolerability, safety, convenience, drug interactions and genetic barriers to the emergence of drug resistance have led to streamlined recommendations for initial ARV regimens for most people with HIV. The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) now recommends initial ARV regimens based on an oral second-generation INSTI plus two NRTIs—bictegravir (BIC)/tenofovir alafenamide (TAF)/emtricitabine (FTC) **(AI)** or dolutegravir (DTG) plus TAF/FTC or tenofovir disoproxil fumarate (TDF)/ FTC or TDF/lamivudine (3TC) **(AI)**—for most people with HIV. In some people with HIV, the two-drug regimen DTG/3TC can be used **(AI).** When INSTI resistance is possible, such as after exposure to long-acting injectable cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP) and/or if INSTI genotype results are not yet available, a boosted PI (boosted darunavir [DRV]) in combination with two NRTIs (TAF or TDF with FTC or 3TC) is recommended **(AIII).** The Panel's recommendations are summarized in Tables 6a and 6b.

Table 6a. Recommended Initial Regimens for Most People With HIV

Selection of antiretroviral therapy (ART) should be based on the regimen's virologic efficacy, potential adverse effects, pill burden, dosing frequency, drug–drug interaction potential, cost, access, resistance test results, and the comorbid condition of the person with HIV. A pregnancy test should be performed in people of childbearing potential, and choice of ART for pregnant individuals should be guided by recommendations from the Perinatal Guidelines. Drug classes and regimens within each class are arranged first by evidence rating and, when ratings are equal, in alphabetical order. Additional initial ARV regimen options for certain clinical scenarios are listed in Table 6b below.

Table 6a. Recommended Initial Regimens for Most People With HIV Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. Choice of ART during pregnancy should be guided by recommendations from the Perinatal Guidelines.
For people who do not have a history of using CAB-LA as PrEP, one of the following regimens is recommended[a]: • BIC/TAF/FTC **(AI)**

Table 6a. Recommended Initial Regimens for Most People With HIV

- DTG plus (TAF or TDF)[b] plus (FTC or 3TC) **(AI)**
- DTG/3TC **(AI),** except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.

For people who have a history of CAB-LA use as PrEP, INSTI genotype resistance testing should be performed before starting ART. If ART is to be started before results of genotypic testing results, the following regimen is recommended:

- DRV/c[c] or DRV/r with (TAF or TDF)[b] plus (FTC or 3TC)—pending the results of the genotype test **(AIII)**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion*

[a] Because of the current low rates of transmitted INSTI resistance in the United States, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started pending the results of the INSTI genotype.

[b] TAF and TDF are two forms of TFV approved by the U.S. Food and Drug Administration. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

[c] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters. For further information, refer to the Perinatal Guidelines.

Note: The following are available as coformulated drugs: BIC/TAF/FTC, DRV/c/TAF/FTC, DTG/3TC, TAF/FTC, TDF/3TC, and TDF/FTC.

Key: 3TC = lamivudine; ART = antiretroviral therapy; BIC = bictegravir; CAB-LA = long-acting cabotegravir; COBI = cobicistat; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; HBV = hepatitis B virus; INSTI = integrase strand transfer inhibitor; PrEP = pre-exposure prophylaxis; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Table 6b. Other Initial Antiretroviral Regimens for Certain Clinical Scenarios

Several antiretroviral regimens are found to be effective and tolerable as initial regimens but have some disadvantages or have fewer supporting data from randomized clinical trials compared with the recommended regimens listed in Table 6a. However, one of these regimens may be preferred for an individual with HIV in certain clinical situations (also see Table 7). These regimens are listed below.

Type of Regimen	ARV Regimen	For Certain Clinical Scenarios	Other Considerations
INSTI Plus Two NRTIs	DTG/ABC/3TC **(BI)** (if HLA-B*5701-negative)	When concern about renal- or bone-associated AEs precludes the use of TDF or TAF	Test for HLA-B*5701 before prescribing ABC; do not prescribe if HLA-B*5701-positive. Consider avoiding ABC for people with multiple CV risk factors or known CV disease.

Table 6b. Other Initial Antiretroviral Regimens for Certain Clinical Scenarios

Type of Regimen	ARV Regimen	For Certain Clinical Scenarios	Other Considerations
			Do not use in people with HBV coinfection unless an HBV-active drug, such as entecavir, TAF, or TDF is also used. Do not use following exposure to CAB-LA unless INSTI genotype shows sensitivity.
Boosted PI Plus Two NRTIs	(DRV/c[a] or DRV/r) plus (TAFor TDF[b]) plus (FTC or 3TC) **(BI)**	To avoid an INSTI-based regimen (e.g., documented INSTI resistance).	Assess for potential RTV- or COBI-related DDIs.
	(DRV/c[a] or DRV/r) plus ABC/3TC **(BII)** (if HLA-B*5701-negative)	To avoid an INSTI-based regimen (e.g., with suspected or documented INSTI resistance), *and* When concern about renal or bone-associated AEs precludes the use of TDF or TAF	Test for HLA-B*5701 before prescribing ABC; do not prescribe if HLA-B*5701-positive. Consider avoiding ABC for people with multiple CV risk factors or known CV disease. Do not use in people with HBV coinfection unless used with an HBV-active drug other than 3TC. Assess for potential RTV- or COBI-related DDIs.
NNRTI Plus Two NRTIs	DOR/TDF/3TC[b] **(BI)** or DOR plus TAF/FTC[b] **(BIII)**	To avoid an INSTI-based regimen (e.g., with suspected or documented INSTI resistance), *and* To avoid a PI-based regimen (e.g., with significant DDIs with concomitant medications)	
	RPV/TAF/FTC **(BII)** Only if HIV RNA <100,000 copies/mL **and** CD4 count >200 cells/mm^3	To avoid an INSTI-based regimen (e.g., with suspected or documented INSTI resistance), *and* To avoid a PI-based regimen (e.g., with significant DDIs with concomitant medications), *and* When a single-tablet regimen containing an NNRTI and TAF is desired	Cannot take with PPI; space apart from H2 antagonist. Needs to be taken with a meal.

Table 6b. Other Initial Antiretroviral Regimens for Certain Clinical Scenarios

Type of Regimen	ARV Regimen	For Certain Clinical Scenarios	Other Considerations
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*			
Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion*			

[a] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been observed during the second and third trimesters. For further information, refer to the Perinatal Guidelines.

[b] TAF and TDF are two forms of TFV approved by the U.S. Food and Drug Administration. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

Note: The following are available as coformulated drugs: ABC/3TC, DOR/TDF/3TC, DRV/c, DRV/c/TAF/FTC, DTG/ABC/3TC, RPV/TAF/FTC, TAF/FTC, TDF/3TC, and TDF/FTC.

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse event; ARV = antiretroviral; CD4 = CD4 T lymphocyte; COBI = cobicistat; CV = cardiovascular; DDI = drug–drug interaction; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; H2 = histamine type 2; HBV = hepatitis B virus; HLA = human leukocyte antigen; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Supporting Evidence and Rationale Used for the Panel's Recommendations

The Panel's recommendations are primarily based on clinical trial data published in peer-reviewed journals and on data prepared by drug manufacturers for FDA review. In select cases, the Panel considers data from abstracts presented at major scientific meetings. The Panel considers published information from randomized prospective clinical trials with adequate sample size that demonstrate that an ARV regimen produces high rates of viral suppression, increases CD4 count, and has a favorable safety profile to be the strongest evidence on which to base recommendations. Comparative clinical trials of initial treatments generally are not designed to show significant differences in HIV-related clinical endpoints (such as progression to AIDS-defining conditions) or survival. Thus, the assessment of regimen efficacy and safety is primarily based on surrogate marker endpoints (i.e., rates of HIV RNA suppression) and the incidence and severity of adverse events.

In some instances, the Panel recommends regimens that include ARV drugs approved by the FDA based on bioequivalence or relative bioavailability studies that demonstrate that the exposure of the drug(s) in the new formulation or combination is comparable to the exposure of a reference drug(s) that has demonstrated safety and efficacy in randomized clinical trials. When developing recommendations, the Panel may also consider data from randomized switch studies in which a drug in an ARV initial regimen that suppressed patients' viral loads is replaced by a new drug from the same class. Switch trials do not evaluate the ability of a drug or regimen to induce viral suppression; they only examine the drug or regimen's ability to maintain suppression. Therefore, results from switch trials may not be directly applicable to the selection of an initial regimen and should be considered in conjunction with other data, including data from bioavailability/bioequivalence studies and from trials conducted in people taking their first ARV treatment regimen. In this section of the guidelines, the definition of an evidence rating of **II** is expanded to include supporting data from bioavailability/bioequivalence studies or randomized switch studies.

When developing recommendations, the Panel also considers tolerability and toxicity profiles, pill burden and dosing frequency, drug interaction potential, cost and access, postmarketing safety data, observational cohort data published in peer-reviewed publications, the experience of clinicians who are actively engaged in patient care, and the views of community members.

The Panel reviewed the available data to arrive at two classifications for initial ARV treatment regimens: (1) *Recommended Initial Regimens for Most People With HIV* (Table 6a) and (2) *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b). *Recommended Initial Regimens for Most People With HIV* are those regimens with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. The Panel also recognizes that in certain clinical situations, other regimens may be preferred; these options are included in Table 6b. See Table 7 for examples of clinical scenarios in which certain drugs in these regimens may be particularly advantageous.

Many other ARV regimens are effective for initial therapy but have disadvantages when compared with the regimens listed in Tables 6a and 6b. These disadvantages include greater toxicity, higher pill burden, less supporting data from large comparative clinical trials, and limitations for use in certain populations. These regimens are no longer included in Tables 6a and 6b. For people with HIV who have a suppressed viral load and are not experiencing any adverse effects while on a regimen that is not listed, changing to a regimen listed in Table 6a or 6b is not necessary. Clinicians should refer to Optimizing Antiretroviral Therapy in the Setting of Viral Suppression for further guidance if switching to a new regimen is desired.

Several tables in these guidelines provide clinicians with guidance on selecting and prescribing an optimal regimen for a person with HIV. Table 7 provides information on considerations based on specific clinical scenarios and ARV drug characteristics. Table 9 lists the potential advantages and disadvantages of the different ARV drug components. Appendix B, Tables 3–11, lists characteristics of individual ARV agents for initial therapy (e.g., formulations, dosing recommendations, PK, common adverse effects). Appendix B, Table 12 provides ARV dosing recommendations for people who have renal or hepatic insufficiency.

Changes Since the Last Revision of the Guidelines

Since the last revision of these guidelines, the Panel has made several important changes to the recommendations for initial therapy in people with HIV. Among these changes, the following deserve emphasis:

Changes in the Panel's Recommendations for Initial Regimens in Most People With HIV:

- The single-tablet regimen (STR) DTG/abacavir (ABC)/3TC has moved from *Recommended Initial Regimens for Most People With HIV* (Table 6a) to *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b) due to the necessity of obtaining an HLA-B*5701 assay to avoid ABC-associated hypersensitivity, data suggesting increased risk for cardiovascular events associated with ABC, and the availability of several other options for initial therapy (see the Nucleoside Reverse Transcriptase Inhibitor Options as Part of Initial Therapy section for more information).
- Because of the current low rates of transmitted INSTI resistance in the United States, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started pending the results of the INSTI genotype test.

No Longer Recommended as Initial Antiretroviral Regimens:

- Raltegravir (RAL)-, elvitegravir/cobicistat (EVG/c)-, boosted atazanavir (ATV)-, and efavirenz (EFV)-based regimens and rilpivirine (RPV)/TDF/FTC are no longer recommended as initial therapy due to the following disadvantages compared with other regimens:
  - RAL: Low genetic barrier to resistance and higher pill burden
  - EVG/c: Drug–drug interactions with COBI and low genetic barrier to resistance of EVG
  - Boosted ATV: Toxicities, including hyperbilirubinemia, and drug–drug interactions
  - EFV: Toxicities, including neuropsychiatric effects and suicidality; low barrier to resistance; and drug–drug interactions
  - RPV/TDF/FTC: Availability of doravirine (DOR)/TDF/3TC as an STR, more drug–drug interactions than DOR, food restrictions, and HIV RNA and CD4 restrictions. RPV/TAF/3TC remains an option for those who wish to use an STR containing RPV and TAF
- The two-drug regimens darunavir/ritonavir (DRV/r) plus RAL and DRV/r plus 3TC are no longer recommended for initial therapy.
  - DRV/r plus RAL is not recommended due to the higher rate of virologic failure in people with HIV RNA >100,000 copies/mL, the low genetic barrier to resistance, and the high pill burden of RAL.[1-3]
  - DRV/r plus 3TC is not recommended because it requires a PK booster with accompanying drug interactions, and published clinical trial data are lacking.[4] For further information, see Other Antiretroviral Regimens for Initial Therapy.

Selecting an Initial Antiretroviral Regimen

The goal of ART is to improve health and prolong life for people with HIV and to prevent the transmission of HIV to others by maximizing virologic suppression. This is achieved by initiating therapy with a potent, safe, tolerable, and easy-to-adhere-to ARV regimen as soon as possible after diagnosis. Table 6a provides a list of Panel-recommended ARV regimens for most people with HIV. Some factors listed below may influence the selection of a regimen. See Table 6b and Table 7 for additional regimen recommendations to use in specific clinical scenarios.

Initial Characteristics to Consider in All People With HIV

- Pre-treatment HIV RNA level (viral load)
- Pre-treatment CD4 count
- History of prior exposure to CAB-LA or oral TDF/FTC or TAF/FTC as PrEP, or use of INSTI-based post-exposure prophylaxis (PEP)
- Suspected drug resistance (prior to availability of genotypic testing results)
- HIV genotypic drug resistance test results
  - Genotypic drug resistance testing in people without prior ARV exposure should focus on testing for mutations in the reverse transcriptase and protease genes.

  - If transmitted INSTI resistance is a concern, providers should also test for resistance mutations to this class of drugs.
- Individual preferences
- Anticipated adherence to the regimen

Presence of Specific Conditions

- Comorbid conditions: Cardiovascular disease; hyperlipidemia; renal disease; liver disease; osteopenia, osteoporosis, or other conditions associated with bone mineral density loss; psychiatric illness; neurologic disease; substance use disorder requiring narcotic replacement therapy
- Coinfections: Hepatitis B virus (HBV), hepatitis C virus, tuberculosis
- Pregnancy and potential for pregnancy: See below in General Considerations for Persons of Childbearing Potential Initiating Antiretroviral Therapy

Regimen-Specific Considerations

- Regimen's barrier to resistance
- HLA-B*5701 status (only for those considering initiation of ABC). Those who are HLA-B*5701 positive should not receive ABC. See Table 7 for regimens to initiate.
- Potential adverse effects and drug toxicities, including risk for the development of comorbid diseases
- Known or potential drug interactions with other medications (see Drug–Drug Interactions)
- Convenience (e.g., pill burden, dosing frequency, availability of a fixed-dose combination or of STR formulations, food requirements)
- Cost and access (see Cost Considerations and Antiretroviral Therapy)

Considerations for People With Prior Use of Pre- or Post-Exposure Prophylaxis

- For people who acquired HIV after taking oral PrEP with TAF/FTC or TDF/FTC, there is concern for transmitted resistance, especially related to FTC or 3TC with the M184V/I mutation. In a cohort of people in New York City with newly diagnosed HIV, 2% had the M184V/I mutation. People who had used prior oral PrEP were four to seven times more likely to harbor resistance than people who had never used oral PrEP.[5] This reinforces the Panel's recommendation not to initiate DTG/3TC without the results of genotypic resistance testing.
- For people who acquired HIV after exposure to CAB-LA as PrEP, there is concern for INSTI resistance. CAB-LA may remain detectable after treatment discontinuation for up to 3 years in men and 4 years in women.[6] This long PK tail may contribute to the selection of drug-resistant variants in the setting of incident infection. In the HPTN 083 trial of CAB-LA as PrEP in cisgender men and transgender women, 10 of 32 people who acquired HIV after exposure to CAB-LA were found to harbor major INSTI resistance mutations.[7] This is the basis for the Panel's recommendation to obtain INSTI genotypic drug resistance testing in people with prior CAB-LA exposure and not to initiate INSTIs before these results are available and show INSTI

sensitivity. If therapy is initiated before INSTI sensitivity is confirmed, the Panel recommends initiating a boosted DRV regimen with TAF/FTC or TDF/FTC while awaiting INSTI genotype results; once INSTI sensitivity is confirmed by genotypic resistance testing, a switch to an INSTI-based regimen can occur **(AIII).**

- For people with no history of using CAB-LA for PrEP and who acquire HIV despite INSTI-based PEP use, an INSTI genotype should be obtained prior to beginning an INSTI-based regimen. However, because selection of INSTI-resistant virus is likely to be uncommon in this setting, an INSTI-based regimen could be started prior to the return of genotype results **(CIII).** This recommendation is based largely on theoretical concerns that INSTI resistance could occur in the setting of INSTI-based PEP failure, but it is likely to be uncommon. In addition, transmitted INSTI resistance remains low in the United States. For these reasons, the Panel supports using INSTI-based regimens in this setting.

General Considerations for Persons of Childbearing Potential Initiating Antiretroviral Therapy

- A pregnancy test should be performed before initiating ART.
- Clinicians should discuss intentions regarding pregnancy with all persons of childbearing potential.
- People with HIV should attain maximum viral suppression before attempting conception in order to protect their own health, prevent sexual HIV transmission to partners without HIV, and minimize the risk of perinatal HIV transmission to the infant.
- For individuals who are trying to conceive, the Panel recommends initiating a regimen designated as a *Preferred* regimen during pregnancy, as detailed in the Perinatal Guidelines.

General Considerations for INSTI-, PI-, or NNRTI-Based Regimens

Except when HIV is acquired after exposure to CAB-LA as PrEP and results from INSTI genotypic resistance testing are not available, INSTIs (specifically BIC and DTG) are recommended for initial therapy in most people because of their demonstrated efficacy, high barrier to resistance, tolerability, low potential for drug–drug interactions, convenience, and better adverse effects profile compared with NNRTIs and boosted PIs (see Tables 7 and 9).

INSTI-Based Regimens

The Panel's *Recommended Initial Regimens for Most People With HIV*, as listed in Table 6a, include one of two INSTIs: BIC coformulated with TAF/FTC **(AI);** or DTG plus TAF or TDF plus FTC or 3TC **(AI);** or coformulated DTG/3TC **(AI)** for people who have not had exposure to CAB-LA as PrEP. In those with prior exposure to CAB-LA as PrEP, these regimens should not be initiated unless a recent genotype test result showing no INSTI resistance mutations is available. If an INSTI-based regimen is initiated and viral suppression is not achieved in 8 to 12 weeks, genotypic resistance testing should be repeated, including for INSTIs.

For most people, these INSTI-containing regimens will be highly effective and have relatively infrequent treatment-limiting adverse effects and few drug interactions. In several head-to-head comparisons between boosted PI- and INSTI-containing regimens, the INSTI-based regimens were better tolerated and caused fewer treatment discontinuations.[8-10]

The Panel recommends a two-drug regimen of DTG/3TC for initial therapy if certain criteria are met. Data from two randomized trials showed that, in terms of virologic efficacy, DTG plus 3TC was non-inferior to a three-drug regimen of DTG plus TDF/FTC. No treatment-emergent resistance was seen in either the two-drug or the three-drug group.[11] Based on these data, DTG/3TC is not currently recommended for rapid ARV initiation as initial therapy before the availability of HBV serology, HIV RNA level, and an HIV genotypic test demonstrating sensitivity to 3TC.

Among the INSTI-based regimens, BIC- and DTG-containing regimens have a higher barrier to resistance than the first-generation INSTI-based regimens containing EVG or RAL and do not require a PK booster. Transmitted resistance to BIC or DTG is rare. Treatment-emergent resistance has been reported in individuals who failed three-drug DTG-based therapy[12-15] and BIC-based regimens.[16-19] Because of this high barrier to resistance and tolerability, BIC- and DTG-containing regimens may be used in people who have not previously used CAB-LA for PrEP and plan to start ART before resistance testing results are available (e.g., with rapid initiation of ART after diagnosis). BIC-based regimens have been shown to be non-inferior to DTG-based regimens in clinical trials.[20-22]

There are data suggesting greater weight gain after initiating therapy with certain INSTI-based regimens and TAF than with other ARV drugs. The reasons for differences in weight gain are unclear and should not be a reason to withhold an INSTI- or TAF-based regimen.[23-30]

EVG- and RAL-based regimens have the disadvantage of having lower barriers to resistance than DTG- or BIC-containing regimens and therefore are no longer recommended as initial therapy. Additionally, the pill burden with RAL is higher than for other INSTI-based regimens whereas EVG-based regimens have a greater potential for drug interactions because EVG is combined with COBI, a strong cytochrome P3A4 inhibitor (see Table 7).

PI-Based Regimens

In the setting of HIV acquisition following CAB-LA exposure, an RTV- or COBI-boosted DRV regimen containing TAF or TDF plus FTC or 3TC is recommended as initial therapy if a genotypic drug resistance test indicating INSTI sensitivity is not available at the time of ART initiation **(AIII),** if resistance to INSTI is confirmed **(BI),** or in certain clinical situations, such as when INSTIs must be avoided **(BI).** DRV/c/TAF/FTC is available as an STR. Large observational cohorts found an association between some PIs, including DRV/r, and an increased risk of cardiovascular events; however, further study is needed.[31-36] COBI-boosted regimens should not be initiated during pregnancy because of inadequate drug levels. Boosted ATV is no longer recommended as initial therapy due to frequent adverse events (e.g., hyperbilirubinemia) and high rates of drug–drug interactions, including with tenofovir and acid-suppressive therapy.

Boosted ATV is no longer recommended as initial therapy due to frequent adverse events, such as hyperbilirubinemia and higher rates of drug–drug interactions (including with tenofovir and acid-suppressive therapy) compared to boosted DRV.

NNRTI-Based Regimens

NNRTI-based regimens are not recommended for initial therapy in most people with HIV, but selected regimens may be useful in some circumstances. The NNRTI-based regimens that are currently recommended by the Panel to be used in certain clinical scenarios include DOR/TDF/3TC **(BI),** DOR plus TAF/FTC **(BIII),** and RPV/TAF/FTC **(BII).** The emergence of drug resistance at the time of virologic failure has been reported with all NNRTIs, which generally have a lower barrier to resistance than INSTIs or boosted PIs.

DOR is available both as a single-drug tablet to be used with two NRTIs and as part of an STR with TDF/3TC. In randomized trials, DOR was non-inferior to both EFV and DRV/r when either of these drugs was taken in combination with two NRTIs,[37,38] but DOR has not yet been compared against INSTIs. DOR has fewer central nervous system (CNS) side effects than EFV and more favorable lipid effects than both DRV/r and EFV. DOR also has fewer potential drug interactions than EFV or RPV, and unlike RPV, the virologic efficacy of DOR is not compromised in people with high HIV RNA levels and low CD4 counts.

RPV has fewer adverse effects than EFV, and RPV/TAF/FTC is available as one of the smallest tablet sizes among STRs. However, RPV has lower virologic efficacy in people with baseline HIV RNA levels >100,000 copies/mL and CD4 counts <200 cells/mm^3 and is subject to numerous drug–drug interactions.[39] EFV is no longer recommended for initial therapy due to a relatively high rate of CNS-related side effects, reported suicidality, high rates of drug discontinuation, and numerous drug–drug interactions.

Regimens When Abacavir, Tenofovir Alafenamide, and Tenofovir Disoproxil Fumarate Cannot Be Used or Are Not Optimal

In people in whom ABC, TDF, or TAF cannot be used or are not optimal, only DTG/3TC is recommended by the Panel **(AI).** Several other NRTI-sparing/limiting two-drug regimens have been evaluated in clinical trials but are not currently recommended for initial therapy due to insufficient data. For more information on these regimens, see Other Antiretroviral Regimens for Initial Therapy. Two-drug ARV options **should not be used** in pregnancy due to insufficient data, or in those with known pre-existing resistance to any of the ARVs in the combination. Tenofovir-sparing regimens **should not be used** in individuals with HBV coinfection unless a drug with HBV activity (i.e., entecavir) is also used.

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Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

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This table guides clinicians in choosing an initial antiretroviral (ARV) regimen according to various patient and regimen characteristics and specific clinical scenarios. ARV drugs/regimens that are listed in Table 6a as *Recommended Initial Regimens for Most People With HIV* and in Table 6b as *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* are included in this table (see Initial Combination Antiretroviral Regimens for People With HIV). When more than one scenario applies to a person with HIV, clinicians should review considerations for each relevant scenario and use their clinical judgment to select the most appropriate regimen. Please see Table 9 for additional information regarding the advantages and disadvantages of particular ARV medications recommended to be used as initiation therapy.

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Pre-ART Characteristics	CD4 count <200 cells/mm^3	**Do not use** RPV-based regimens.	Higher rates of virologic failure have been observed in those with low pre-treatment CD4 counts.
	HIV RNA >100,000 copies/mL (also see next row if HIV RNA >500,000 copies/mL)	**Do not use** RPV-based regimens.	Higher rates of virologic failure have been observed in those with high pre-treatment HIV RNA levels.
	HIV RNA >500,000 copies/mL	**Do Not Use** the Following Regimens: • RPV/TAF/FTC • DTG/3TC	For DTG/3TC, limited data are available in patients with viral loads above this threshold.
	HLA-B*5701 positive or result unknown	**Do not use** ABC-containing regimens.	ABC hypersensitivity is a potentially fatal reaction that is highly associated with the HLA-B*5701 allele.
	Prior exposure to oral TDF/(3TC or FTC) or TAF/3TC PrEP	Use DTG or BIC plus two NRTIs. DTG/3TC could be considered if testing confirms no 3TC resistance mutations.	DTG/3TC should be avoided if resistance testing results are not available, as presence of 3TC resistance mutations may lead to use of DTG monotherapy.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	Prior exposure to CAB-LA for PrEP	INSTI genotype resistance testing should be performed. **If INSTI Resistance Is Present or If ART Needs to Be Started Before Genotype Test Results** • (DRV/r or DRV/c) plus (TAF or TDF)[a] plus (3TC or FTC) **If No INSTI Resistance Is Identified** • BIC/TAF/FTC, *or* • DTG plus (TAF or TDF)[a] plus (3TC or FTC)	Mutations conferring resistance to INSTIs have been seen in association with CAB-LA PrEP. CAB-LA has a very long half-life, and drug exposure may persist at levels suboptimal to prevent infection and may select for INSTI-resistant virus.

	People with **no prior exposure** to CAB-LA for PrEP and ARV regimen should be started rapidly and before HIV drug resistance results are available.	**Avoid** ABC, DTG/3TC, and NNRTI-based regimens.
		
		Use
		• BIC/TAF/FTC, *or*
		• DTG plus (TAF or TDF)[a] plus (3TC or FTC)
		
		In People Who Used INSTI-Based ART for PEP Post-exposure Prophylaxis or Who Are Suspected to Have Acquired HIV From Someone Failing an INSTI-Based Regimen
		• Obtain INSTI genotypic resistance test and start one of the following regimens:
		  ○ BIC/TAF/FTC, *or*
		  ○ DTG plus (TAF or TDF)[a] plus (3TC or FTC)
			Transmitted mutations conferring NNRTI and NRTI resistance are more likely than mutations associated with PI or INSTI resistance.
			
			HLA-B*5701 results may not be available rapidly; thus, ABC is not recommended.
			
			Because of the current low rates of transmitted INSTI resistance in the United States, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started, pending the results of the INSTI genotype.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
ART-Specific Characteristics	A one-pill, once-daily regimen is desired.	**STR Options as Initial ART Include the Following:** • BIC/TAF/FTC • DOR/TDF/3TC • DRV/c/TAF/FTC • DTG/ABC/3TC • DTG/3TC • RPV/TAF/FTC	**Do not use** DTG/ABC/3TC if the patient is HLA-B*5701 positive. DTG/3TC **is not recommended** if HIV RNA is >500,000 copies/mL. **Do not use** DTG/ABC/3TC or DTG/3TC in the setting of HBV coinfection without another HBV agent. **Do not use** RPV/TAF/FTC if HIV RNA is >100,000 copies/mL and CD4 count is <200 cells/mm^3.
	Food effects	**Regimens That Can Be Taken Without Regard to Food** • BIC-, DOR-, or DTG-based regimens	Oral bioavailability of these regimens is not significantly affected by food.
		Regimens That Should Be Taken With Food • DRV/r- or DRV/c-based regimens • RPV/TAF/FTC	Food improves absorption of these regimens. RPV-containing regimens should be taken with ≥390 calories of food.
Presence of Other Conditions	Chronic kidney disease (defined as CrCl <60 mL/min)	In general, **avoid TDF.** For patients with progressively declining renal function, consider avoiding all TFV-containing (TAF or TDF) regimens. Refer to Appendix B, Table 12 for specific ARV drug dosing recommendations in patients with renal impairment.	TDF has been associated with proximal renal tubulopathy. Higher rates of renal dysfunction have been reported in patients using TDF in conjunction with RTV-containing regimens. TAF has less impact on renal dysfunction than TDF. Avoid the use of TDF- or TAF-sparing regimens in the setting of HBV coinfection or unknown HBV status unless also receiving a fully active HBV regimen (see Hepatitis B Virus/HIV Coinfection).
	Liver disease with cirrhosis	Some ARVs are contraindicated or may require dosage modification in patients with Child-Pugh class B or C disease.	Refer to Appendix B, Table 12 for specific dosing recommendations. Patients with cirrhosis should be carefully evaluated by an expert in advanced liver disease.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	Concern for weight gain	For many people with HIV, gaining weight after starting ART is part of a "return to health." However, some ARV regimens are associated with greater weight increase than others.	Reasons for differences in weight gain among ART regimens are unknown. **Note:** Weight gain should not be a reason to avoid taking an INSTI-based regimen.
	Osteoporosis	**Avoid TDF.**[a]	TDF is associated with decreases in BMD, along with renal tubulopathy, urine phosphate wasting, and resultant osteomalacia. TAF[a] and ABC are associated with smaller declines in BMD than TDF.
	Psychiatric illnesses	**Consider avoiding** RPV-based regimens. Patients on INSTI-based regimens who have preexisting psychiatric conditions should be closely monitored. Some ARVs are contraindicated, and some psychiatric medications need dose adjustments when coadministered with certain ARVs.	RPV can exacerbate psychiatric symptoms and may be associated with suicidality. Some INSTIs have been associated with adverse neuropsychiatric effects in some retrospective cohort studies and case series. See the drug–drug interaction tables (Tables 24a, 24b, 24d, and 24g) for dosing recommendations when drugs used for psychiatric illnesses are used with certain ARVs.
	Cardiac QTc interval prolongation	Consider avoiding RPV-based regimens if the patient is taking other medications with known risk of Torsades de Pointes or in patients at higher risk of Torsades de Pointes.	High RPV concentrations may cause QTc prolongation.
	High risk for CV events	Consider avoiding ABC-based regimens. Refer to Hyperlipidemia, below, for regimens associated with more favorable lipid profiles.	An increased risk of CV events with ABC has been observed in some, but not all, studies. Certain ARV regimens are associated with more favorable lipid profiles than other regimens.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	Hyperlipidemia	PI/c and PI/r have been associated with hyperlipidemia. BIC, DOR, DTG, and RPV have fewer lipid effects.	TDF has been associated with lower lipid levels than ABC or TAF.
	Patients with history of poor adherence to non-ARV medications or inconsistent engagement in care	Consider using regimens with a boosted PI or BIC or DTG.	These regimens have a high genetic barrier to resistance.
	Pregnancy	Refer to the Perinatal Guidelines for further guidance on ARV use during pregnancy.	
Presence of Coinfections	HBV infection	**Avoid regimens** that do not contain NRTIs. Use (TDF or TAF) with (FTC or 3TC) as part of the ARV regimen. **If TDF and TAF Are Contraindicated** • For treatment of HBV, use FTC or 3TC with entecavir and a suppressive ARV regimen (see Hepatitis B Virus/HIV Coinfection).	TDF, TAF, FTC, and 3TC are active against both HIV and HBV. 3TC- or FTC-associated HBV resistance mutations can emerge when these drugs are used without another drug that is active against HBV.
	HCV treatment required	Refer to recommendations in Hepatitis C Virus/HIV Coinfection, with special attention to potential interactions between ARV drugs and HCV drugs.	
	Concomitant use with rifamycin antibiotics (e.g., rifabutin, rifampin, and rifapentine)	Recommended regimens may require dose adjustment. See the drug–drug interaction tables (Tables 24a, 24b, 24c, 24d, 24e, 24f, 24g, 25a, and 25b) and Tuberculosis/HIV Coinfection for information on ARV use with rifamycin antibiotics.	Rifamycin antibiotics are inducers of CYP3A4 and UGT1A1 enzymes, causing significant decreases in concentrations of PIs, INSTIs, and RPV.

[a] TAF and TDF are two U.S. Food and Drug Administration–approved forms of TFV. TAF has fewer bone and kidney toxicities than TDF, whereas TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BMD = bone mineral density; CAB-LA = long-acting cabotegravir; CD4 = CD4 T lymphocyte; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; HBV = hepatitis B virus; HCV = hepatitis C virus; HLA = human leukocyte antigen;

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PEP = post-exposure prophylaxis; PrEP = pre-exposure prophylaxis; QTc = QT corrected for heart rate; RPV = rilpivirine; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; UGT = uridine diphosphate glucuronosyltransferase

Nucleoside Reverse Transcriptase Inhibitor Options as Part of Initial Therapy

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Reviewed: September 12, 2024

The following sections provide detailed information on antiretroviral (ARV) drugs that the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends for initial therapy for most people with HIV and for initial therapy in certain clinical scenarios (see Tables 6a and 6b in the Initial Combination Antiretroviral Regimens for People With HIV section), including ARV drug characteristics, adverse effects, clinical trial results, and Panel recommendations on their use.

Table 8a. Characteristics of Nucleoside Reverse Transcriptase Inhibitor Options for People Without Prior Antiretroviral Treatment

Note: Listed in order of the Panel's recommendations in Tables 6a and 6b.

Characteristics	TAF/FTC	TDF/FTC	TDF/3TC	3TC	ABC/3TC
Dosing Frequency	Once daily	Once daily	Once daily	Once daily	Once daily
Available Coformulations for People Without Prior ARV Treatment	• TAF 25 mg/FTC • BIC/TAF 25 mg/FTC • DRV/c/TAF 10 mg/FTC • RPV/TAF 25 mg/FTC	• TDF/FTC	• TDF/3TC • DOR/TDF/3TC	• DTG/3TC	• ABC/3TC • DTG/ABC/3TC
Adverse Effects	**TAF** • Renal insufficiency, proximal renal tubulopathy (less frequent than with TDF) • Decrease in BMD (less than with TDF)	**TDF** • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters.	**TDF** • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters.	**3TC** • No notable adverse effects	**ABC** • HSR to ABC is associated with the presence of HLA-B*5701 allele.[b] • Increase in CV events is associated with ABC use in some but not all cohort studies.
Other Considerations	• Also used for HBV treatment. Discontinuation may precipitate HBV flare. • See Appendix B, Table 11 for dosing recommendations in people with renal insufficiency.			• 3TC or ABC/3TC **should not be used** as treatment for HBV without adding another HBV-active drug.	

Table 8a. Characteristics of Nucleoside Reverse Transcriptase Inhibitor Options for People Without Prior Antiretroviral Treatment

Characteristics	TAF/FTC	TDF/FTC	TDF/3TC	3TC	ABC/3TC
	• Some studies reported less weight gain and lower LDL, HDL, TC, and triglycerides with TDF than with TAF.				

[a] 3TC is recommended for use with DTG in some people as initial ART. See Table 6a and the discussion below for more information. Otherwise, dual-NRTI backbones are recommended.

[b] Perform HLA-B*5701 testing before initiating ABC; if result is positive, do not start ABC and add ABC to patient's allergy list. See the HLA-B*5701 Screening section for more information.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BMD = bone mineral density; CV = cardiovascular; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; FTC = emtricitabine; HBV = hepatitis B virus; HDL = high-density lipoprotein; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; LDL = low-density lipoprotein; NRTI = nucleoside reverse transcriptase inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate

Summary

The U.S. Food and Drug Administration (FDA)–approved nucleos(t)ide reverse transcriptase inhibitors (NRTIs) include zidovudine (ZDV), stavudine (d4T), didanosine (ddI), abacavir (ABC), tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF), lamivudine (3TC), and emtricitabine (FTC). Older NRTIs (ZDV, d4T, ddI) are no longer recommended for use in clinical practice in the United States because of high rates of serious toxicities. All of these drugs can cause mitochondrial toxicity that may lead to myopathy, hepatic steatosis, lactic acidosis, or lipoatrophy; ZDV may cause bone marrow suppression, whereas peripheral neuropathy is commonly seen with ddI or d4T use. The incidence of these complications is substantially lower with 3TC, FTC, ABC, TDF, and TAF than with older NRTIs.[1,2]

TAF/FTC, TDF/3TC, and TDF/FTC are NRTI combinations that are part of *Recommended Initial Regimens for Most People With HIV* (see Table 6a in Initial Combination Antiretroviral Regimens for People With HIV). In addition, 3TC may be used as a single NRTI with dolutegravir (DTG), except in individuals with HIV RNA >500,000 copies/mL or in whom antiretroviral therapy (ART) is to be started before the results of HIV RNA and HIV genotypic resistance tests are available. If used in those with hepatitis B virus (HBV) coinfection, another HBV-active drug should be added. Tables 6a and 6b in the Initial Combination Antiretroviral Regimens for People With HIV section provide recommendations and ratings for the individual regimens. These recommendations are based on the virologic potency and durability, short- and long-term toxicity, and dosing convenience of these drugs. TDF has been associated with bone and kidney toxicities, especially when used with a pharmacologic booster.[3] TAF is less likely to cause kidney and bone toxicities than TDF, whereas TDF is associated with lower lipid levels than TAF. Like TDF, TAF is a recommended option in pregnancy because of reassuring data from a multinational trial in pregnant women with HIV[4] and data from the Antiretroviral Pregnancy Registry that show no evidence of teratogenicity. Please refer to the Perinatal Guidelines for more information on the use of ARVs during pregnancy.

ABC/3TC, including DTG/ABC/3TC, is no longer recommended for initial therapy in most people with HIV but may be considered in circumstances in which tenofovir (TFV)-containing regimens or DTG/3TC cannot be used. Before starting any regimen with ABC, screening for the HLA-B*5701 allele is necessary because there is a strong link with a potentially life-threatening hypersensitivity reaction in people who test positive for this allele. In addition, some data continue to support an association between ABC and an increased risk for serious cardiovascular events.[5,6]

Along with safety and efficacy, cost and access are among the factors to consider when choosing among available options. ABC/3TC, TDF/3TC, TDF/FTC, and 3TC are available as generic formulations.

Clinical Trials Comparing Nucleoside Reverse Transcriptase Inhibitors

Tenofovir Alafenamide Compared to Tenofovir Disoproxil Fumarate

Safety and HIV Efficacy

Two randomized double-blind Phase 3 clinical trials compared the safety and efficacy of elvitegravir/cobicistat (EVG/c)/TDF/FTC and EVG/c/TAF/FTC in 1,733 ART-naive adults with estimated glomerular filtration rate (eGFR) ≥50 mL/min.

- TAF/FTC was virologically non-inferior to TDF/FTC at Week 48 (92% vs. 90% of participants had plasma HIV RNA <50 copies/mL, respectively),[7] but TAF/FTC was superior to TDF/FTC at Week 144 (84.2% vs. 80% of participants with plasma HIV RNA <50 copies/mL), largely driven by a higher rate of treatment discontinuation in the TDF arm.[8]
- Participants in the TAF arm had significantly smaller reductions in bone mineral density (BMD) at the spine and hip than those in the TDF arm through 144 weeks.[8] Those receiving TAF also had less pronounced changes in eGFR and renal biomarkers and fewer clinically significant renal events through Week 96.[9] Conversely, levels of fasting low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides increased more in the TAF group than in the TDF group at Week 96, with no change in total cholesterol to HDL ratio.[10]

Two randomized studies have compared the safety and efficacy of TAF/FTC to TDF/FTC, with each combination administered with boosted darunavir (DRV) in ART-naive participants:

- A Phase 2 study of coformulated darunavir/cobicistat (DRV/c) plus TAF/FTC versus DRV/c plus TDF/FTC in treatment-naive participants demonstrated similar virologic suppression rates in both arms (75% vs. 74%).[11] In the TAF arm, fewer participants developed proteinuria. Changes in BMD were also less pronounced among participants in the TAF group.
- The AMBER study randomized ART-naive participants to receive either coformulated DRV/c/TAF/FTC or DRV/c plus TDF/FTC. At Week 48, HIV RNA <50 copies/mL was achieved in 91% of the DRV/c/TAF/FTC participants versus 88% of the DRV/c plus TDF/FTC participants. Participants in the TAF/FTC arm showed less decline in hip and spine BMD and eGFR than participants in the TDF/FTC arm.[12]

One analysis evaluated data from 14 randomized trials that compared the virologic efficacy, frequency of renal events, and bone density changes associated with the use of TDF and TAF when either drug was taken with or without pharmacokinetic (PK) boosters (ritonavir [RTV] or cobicistat [COBI]). No significant differences appeared between unboosted regimens with TDF and TAF in terms of virologic efficacy. When used with PK boosters, TAF resulted in a clinically small but statistically significant greater virologic efficacy than TDF (94% vs. 92%; $P = 0.0004$). No difference was seen in bone-related toxicities and clinical or laboratory adverse events between TAF and TDF, regardless of whether used with a boosting agent. The rate of discontinuation due to renal adverse events was higher for those on boosted regimens containing TDF compared with those containing TAF, with a small but statistically significant difference ($P = 0.03$).[13]

Although conducted in people without HIV for pre-exposure prophylaxis (PrEP), the DISCOVER trial, with 5,387 treated participants, was the largest trial to directly compare the adverse effects of TAF/FTC with those of TDF/FTC.[14] The following findings were observed after 48 weeks of follow-up:

- Adverse events did not significantly vary between the two groups, including Grade 3 and 4 events, serious adverse events, discontinuations due to adverse events, and overall.
- Changes in renal biomarkers and bone density significantly favored the TAF arm over TDF. One case of proximal tubular disease occurred in the TDF arm.
- LDL, HDL, and total cholesterol were significantly lower in the TDF arm than in the TAF arm, with no significant difference in the total cholesterol to HDL ratio.
- Participants in the TAF arm gained an average of 1.1 kg whereas those in the TDF arm had a mean loss of 0.1 kg.

Efficacy in People With HIV and HBV

To assess the ability of TAF to maintain HIV and HBV suppression, 72 people with HIV/HBV coinfection who had HIV RNA <50 copies/mL and HBV DNA <9 $\log_{10}$ IU/mL on a stable regimen were switched to EVG/c/TAF/FTC.[15] In this study, 96% of participants were on a TDF/FTC-containing regimen before the switch. Key results of the study showed the following:

- Among those who switched to EVG/c/TAF/FTC, HIV suppression was maintained in 91.7% of participants at Week 48, and 91.7% of participants had HBV DNA <29 IU/mL.
- Markers of proximal tubular proteinuria and biomarkers of bone turnover decreased in those who switched to EVG/c/TAF/FTC.[15]

Lamivudine Compared to Tenofovir Disoproxil Fumarate/Emtricitabine

A single-tablet regimen (STR) of DTG/3TC has now been approved as an initial ARV regimen. Please refer to the Integrase Strand Transfer Inhibitor-Based Regimens section for a full discussion.

GEMINI 1 and GEMINI 2 were identically designed randomized, double-blind clinical trials that found DTG plus 3TC non-inferior to DTG plus TDF/FTC in ART-naive adults with HIV RNA <500,000 copies/mL and eGFR ≥50 mL/min.[16,17]

Abacavir/Lamivudine Compared to Tenofovir Disoproxil Fumarate/Emtricitabine

Several randomized controlled trials in ART-naive participants compared ABC/3TC to TDF/FTC, each administered in combination with a third ARV drug[18-20] (see the Integrase Strand Transfer Inhibitor-Based Regimen section).[21]

- The ACTG 5202 study, a randomized controlled trial in >1,800 participants, evaluated the efficacy and safety of ABC/3TC and TDF/FTC when each combination was used with either efavirenz (EFV) or atazanavir/ritonavir (ATV/r). In people with baseline HIV RNA ≥100,000 copies/mL, the time to virologic failure was significantly shorter with ABC/3TC than with TDF/FTC, regardless of whether the third active drug was EFV or ATV/r. In addition, time to first adverse event was also shorter in the ABC/3TC groups.[18]

- In the HEAT study, 688 participants received ABC/3TC or TDF/FTC with once-daily lopinavir/ritonavir. Virologic efficacy was similar in the two study arms, including in a subgroup of participants with HIV RNA ≥100,000 copies/mL.[20]
- The ASSERT study compared open-label ABC/3TC with TDF/FTC in 385 HLA-B*5701-negative people with HIV who were ART-naive; all participants also received EFV. The primary study endpoint was renal safety of the regimens. Although eGFR did not differ significantly between the regimens, biomarkers associated with tubular dysfunction (retinol-binding protein and beta-2 microglobulin) increased significantly, to a greater extent in the TDF/FTC arm than the ABC/3TC arm (+50% vs. +24% and no change vs. −47%, respectively). At Week 48, the proportion of participants with HIV RNA <50 copies/mL was lower among ABC/3TC-treated participants (59%) than among TDF/FTC-treated participants (71%).[19]

Nucleoside Reverse Transcriptase Inhibitor Options for Initial Therapy

Tenofovir Alafenamide/Emtricitabine

TAF, an oral prodrug of TFV, is hydrolyzed to TFV in plasma and then converted to TFV-diphosphate (TFV-DP) intracellularly, where it exerts its activity as an NRTI. Unlike TDF, which readily converts to TFV in plasma after oral absorption, TAF remains relatively stable in plasma, resulting in lower plasma and higher intracellular TFV concentrations. After oral administration, TAF 25 mg resulted in plasma TFV concentrations that were 90% lower than those seen with TDF 300 mg. Intracellular TFV-DP concentrations, however, were substantially higher with TAF.

Adverse Effects

Renal and Bone Effects

- In randomized controlled trials that compared TAF and TDF in people without prior ARV treatment experience or those with virologic suppression, TAF had more favorable effects on renal biomarkers and bone density than TDF.

Lipid Effects

- In randomized controlled trials in ART-naive participants, in switch studies, and in a large study of PrEP, levels of LDL and HDL cholesterol and triglycerides were lower in participants who received TDF than those who received TAF. However, total cholesterol to HDL ratios did not differ between participants receiving TAF and those receiving TDF. The clinical significance of this finding is not clear.[7,22,23]

Weight Gain

- Initiation of TAF in previously untreated individuals and in people without HIV has been associated with greater weight gain than initiation of TDF[24-26] and ABC.[25] In ADVANCE, an open-label trial conducted in South Africa that compared EFV/TDF/FTC versus DTG plus TDF/FTC versus DTG plus TAF/FTC in ART-naive participants, a greater increase in body weight was reported with initiation of TAF than with TDF.[24] This area is under intense investigation, and the reason for the difference in weight gain between regimens is still uncertain. It is also unclear whether change of ART results in reversal of weight gain.

Other Factors and Considerations

- TAF/FTC is available in fixed-dose combinations (FDCs) with bictegravir (BIC), DRV/c, EVG/c, and rilpivirine (RPV), allowing the regimens to be administered as a single pill taken once daily.
- TAF-containing regimens are approved for people with eGFR ≥30 mL/min. Renal function, urine glucose, and urine protein should be assessed before initiating treatment with TAF, and these assessments should be repeated periodically during treatment. EVG/c/FTC/TAF was safe and effective in a single-arm switch study that was conducted in people on hemodialysis.[27] Based on the results from this study, TAF/FTC can be used without dosage adjustment in people with HIV who require hemodialysis.
- Both TAF and FTC are active against HBV. In people with HIV/HBV coinfection, TAF/FTC may be used as the NRTI pair in an ARV regimen because these drugs have activity against both viruses (see Hepatitis B Virus/HIV Coinfection).[15]
- TAF is recommended as a preferred drug in pregnancy because of reassuring data from a multinational trial of pregnant women and data from the Antiretroviral Pregnancy Registry that show no evidence of teratogenicity.[4]

The Panel's Recommendation

- On the basis of clinical trial safety and efficacy data, and its availability as a component of various FDCs, the Panel considers TAF/FTC a recommended NRTI combination for initial ART in most people with HIV when prescribed with BIC or DTG **(AI),** and as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (see Table 6b in the Initial Combination Antiretroviral Regimens in People With HIV section) when given with RPV, DOR, RTV-boosted DRV (DRV/r), or DRV/c.

Tenofovir Disoproxil Fumarate/Emtricitabine and Tenofovir Disoproxil Fumarate/Lamivudine

TDF, with either 3TC or FTC, has been studied in combination with DOR, EFV, RPV, several boosted protease inhibitors (PIs), EVG/c, RAL, and DTG in randomized clinical trials.[28-37]

Adverse Effects

Renal Effects

- New onset or worsening renal impairment has been associated with TDF use.[38,39] Risk factors may include advanced HIV disease, longer treatment history, low body weight (especially in women),[40] and preexisting renal impairment.[41] Adverse effects on renal biomarkers, such as proteinuria, especially tubular proteinuria, were more frequent with TDF than with TAF.[42]
- Adverse renal outcomes are more likely when TDF/FTC is coadministered with PK boosters (RTV or COBI). A meta-analysis of randomized trials found that discontinuation due to renal adverse events is more frequent in people who take TDF/FTC than TAF/FTC with PK boosters.[13]

Bone Effects

- Although initiation of all NRTI-containing regimens has been associated with a decrease in BMD, the loss of BMD is greater with TDF-containing regimens. For example, in two randomized studies that compared TDF/FTC with ABC/3TC, participants who received TDF/FTC experienced a significantly greater decline in BMD than ABC/3TC-treated participants.[43,44] BMD generally stabilizes following an early decline after ART initiation. Loss of BMD is also greater with TDF than with TAF.
- Cases of osteomalacia associated with proximal renal tubulopathy have been reported with the use of TDF.[45] Adverse bone outcomes have been found to be more likely when TDF/FTC is coadministered with PK boosters. However, a meta-analysis found no difference in bone-related toxicities between TAF and TDF, regardless of boosting.[13]

Other Factors and Considerations

- TDF/3TC is available as a coformulated generic drug.
- TDF/3TC is available in an FDC with DOR 100 mg.
- Renal function, urine glucose, and urine protein should be assessed before initiating treatment with TDF and periodically during treatment (see Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy). In people who have preexisting renal insufficiency (CrCl <60 mL/min),[46] use of TDF generally should be avoided. If TDF is used, a dose adjustment is required if the person's CrCl falls below 50 mL/min (see Appendix B, Table 12 for dose recommendations).
- TDF, FTC, and 3TC are active against HBV. In people with HBV/HIV coinfection, TDF/FTC or TDF/3TC may be used as the NRTI pair of the ARV regimen because these drugs have activity against both viruses (see Hepatitis B Virus/HIV Coinfection).

The Panel's Recommendations

- On the basis of clinical trial safety and efficacy data, long-term experience in clinical practice, and the combination's availability as a component of FDC drugs, the Panel considers TDF/FTC and TDF/3TC as recommended NRTI combinations for initial ART in most people with HIV when combined with DTG, and as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b in the Initial Combination Antiretroviral Regimens for People With HIV section).
- TDF should be used with caution or avoided in people with renal disease and/or osteopenia/osteoporosis.
- When TDF is used, especially in conjunction with a PK booster, clinicians should monitor for renal and bone safety during therapy. Boosters should be avoided when possible in people taking TDF.

Emtricitabine Versus Lamivudine

FTC and 3TC generally are used interchangeably in combination with other ARVs, based on the results of randomized clinical trials and a meta-analysis of 12 trials that compared virologic efficacy and safety.[47,48] In the ATHENA cohort, virologic efficacy of TDF/FTC was compared to TDF/3TC

when either was combined with a non-nucleoside reverse transcriptase inhibitor (NNRTI)—EFV or nevirapine[49]—or with a boosted PI.[50] No difference was reported in the rates of virologic failure in people who were taking TDF/FTC and people who were taking TDF/3TC when these drug combinations were used with a boosted PI. TDF/3TC was associated with higher rates of virologic failure than TDF/FTC in the NNRTI analysis; however, participants in the NNRTI cohort who were taking 3TC generally had higher viral loads and lower CD4 T lymphocyte cell counts and were more likely to be using injection drugs at the start of the study than those taking FTC.

Adverse Effects

- Both FTC and 3TC have been well tolerated with no significant treatment-limiting adverse effects.
- In early clinical trials, FTC was infrequently associated with mild hyperpigmentation of palms and soles.

Other Factors and Considerations

- 3TC is now generic in the United States and is coformulated with other drugs, such as DOR/TDF/3TC and DTG/ABC/3TC.
- Both 3TC and FTC have activity against hepatitis B but are insufficient for HBV treatment when used alone due to the emergence of resistance. Discontinuation of FTC or 3TC can precipitate a flare in HBV if no other HBV-active drugs are in the regimen.
- See Appendix B, Table 12 for dosing recommendations in people with renal impairment.
- No significant drug interactions have been identified with FTC. Sorbitol-containing drugs can decrease 3TC concentration, and coadministration should be avoided.
- Both FTC and 3TC select for the M184V mutation when viral suppression is suboptimal.

The Panel's Recommendation

- FTC and 3TC are considered interchangeable in combination with other ARV drugs.

Lamivudine as a Single Nucleoside Reverse Transcriptase Inhibitor

Based on the GEMINI-1 and GEMINI-2 studies[17] that found DTG plus 3TC non-inferior to DTG plus TDF/FTC in ART-naive people with HIV RNA <500,000 copies/mL, 3TC may be used as a single NRTI with DTG (see Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs for more information).

Other Factors and Considerations

- 3TC with DTG is available as a STR.
- 3TC is active against HBV but is insufficient for HBV treatment when used alone due to the emergence of resistance. Discontinuation of 3TC can precipitate a flare in HBV if no other HBV-active drugs are in the regimen.
- 3TC is available in two brand-name formulations (one for HIV and the other for HBV), but the doses are different. The dose for HIV treatment is 3TC 300 mg daily.

- See Appendix B, Table 12 for dosing recommendations in people with renal impairment.
- Sorbitol-containing drugs can decrease 3TC concentration, and coadministration should be avoided.

The Panel's Recommendations

The Panel recommends the use of DTG/3TC **(AI)** as a *Recommended Initial Regimen for Most People With HIV,* with four exceptions. DTG/3TC **is not recommended** for:

- Individuals with HIV RNA >500,000 copies/mL.
- Individuals with HBV coinfection unless receiving another HBV-active drug.
- Individuals who have received long-acting injectable cabotegravir as PrEP and do not have integrase strand transfer inhibitor (INSTI) genotype resistance testing results available demonstrating INSTI sensitivity.
- Individuals starting ART before the results of genotypic resistance testing for reverse transcriptase are available.

Abacavir/Lamivudine

ABC plus 3TC has been studied in combination with EFV, several PIs, and DTG in people who are ART-naive.[21,51-53]

Adverse Effects

Hypersensitivity Reactions

- Clinically suspected hypersensitivity reactions (HSRs) were observed in 5% to 8% of individuals who started ABC in clinical trials conducted before the use of HLA-B*5701 testing. The risk of HSRs is highly associated with the presence of the HLA-B*5701 allele; approximately 50% of people who are HLA-B*5701-positive and are given ABC will have a related HSR.[54,55] HLA-B*5701 testing should be done if the use of ABC is being considered. A person who tests positive for HLA-B*5701 should not be given ABC, and ABC hypersensitivity should be noted on the person's allergy list. People who are HLA-B*5701 negative are far less likely to experience an HSR, but they should be counseled about the symptoms of the reaction. People who discontinue ABC because of a suspected HSR **should never be rechallenged,** regardless of their HLA-B*5701 status.

Cardiovascular Risk

- An association between ABC use and myocardial infarction (MI) was first reported in the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study. This large, multinational, observational study group found that recent (i.e., within 6 months) or current use of ABC was associated with an increased risk of an MI, particularly in participants with preexisting cardiac risk factors.[5,6]
- Since the D:A:D report, several studies have evaluated the relationship between ABC therapy and cardiovascular events. Some studies have found an association.[56-63] Others, including an FDA meta-analysis of 26 randomized clinical trials that evaluated ABC, have not.[64-68]

- No consensus has been reached on the association between ABC use and MI risk or the mechanism for such an association.

Other Factors and Considerations

- ABC/3TC is available as a coformulated tablet and as a coformulated STR with DTG.
- ABC and 3TC are available separately and as a coformulated tablet in generic tablet formulations.
- ABC does not cause renal dysfunction and can be used instead of TDF in people with underlying renal dysfunction or in those who are at high risk for renal effects. No dose adjustment is required in people with renal dysfunction.

The Panel's Recommendations

- ABC should be prescribed only for people who are HLA-B*5701 negative.
- Due to the need for HLA-B*5701 testing before use, ongoing concerns about increased risk of cardiovascular events seen in association with ABC (observed in some but not all studies), and the availability of other effective and well-tolerated options, the Panel no longer recommends DTG/ABC/3TC for most individuals initiating ART and now classifies DTG/ABC/3TC as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (see Table 6b in the Initial Combination Antiretroviral Regimens in People With HIV section) **(BI)** (see Characteristics of Integrase Strand Transfer Inhibitors for discussion regarding the clinical efficacy data for ABC/3TC plus DTG).
- ABC/3TC use with DRV/r or DRV/c is also recommended as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b in the Initial Combination Antiretroviral Regimens in People With HIV section) **(BII).**
- ABC should be used with caution or avoided in people with cardiovascular disease or known high cardiovascular risk.

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Integrase Strand Transfer Inhibitor–Based Regimens as Initial Antiretroviral Therapy

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Table 8b. Characteristics of Integrase Strand Transfer Inhibitors That Are Recommended as Part of Initial Antiretroviral Therapy

	BIC	DTG
Dosing Frequency	Once daily	**Once Daily** • As initial ART or in people with no INSTI-resistance mutations **Twice Daily** • If used with certain CYP3A4 and UGT1A1 inducers; *or* • In people with certain INSTI drug resistance mutations
STR Available as Initial ART	BIC/TAF/FTC	• DTG/ABC/3TC • DTG/3TC
Available as a Single Drug Tablet	No	Yes
Virologic Efficacy Against EVG- or RAL-Resistant HIV	*In vitro* data indicate activity, but clinical trial data are not available.	Yes, for some isolates; effective with DTG 50 mg twice-daily dose
Adverse Reactions	• ↑ CPK 4% • CNS side effects were rarely reported in clinical trials. • Diarrhea, nausea, and headache may occur in some cases.	• ↑ CPK, myositis • CNS side effects such as insomnia and headache have been reported; depression and suicidality are rare, occurring primarily in people with preexisting conditions. • Hypersensitivity, hepatotoxicity
CYP3A4 Drug–Drug Interactions	CYP3A4 substrate	CYP3A4 substrate (minor)
Chelation With Polyvalent Cation Supplements and Antacids	Oral absorption may be reduced by polyvalent cations. See Table 24d for recommendations regarding dosing separations and these drugs.	
Other Key Potential Drug Interaction Mechanisms	P-gp substrate, UGT1A1 substrate, OCT2 and MATE1 inhibitor	P-gp substrate, UGT1A1 substrate
Other Factors	Both BIC and DTG decrease tubular secretion of creatinine without affecting glomerular function. This may result in an increase in serum creatinine of approximately 0.1–0.2 mg/dL.	

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC = bictegravir; CNS = central nervous system; CPK = creatine phosphokinase; CYP = cytochrome P450; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; MATE1 = multidrug and toxic compound extrusion 1; OCT2 = organic cation transporter 2; P-gp = p-glycoprotein; RAL = raltegravir; STR = single-tablet regimen; TAF = tenofovir alafenamide; UGT = uridine diphosphate glucuronosyltransferase

Four oral integrase strand transfer inhibitors (INSTIs)—bictegravir (BIC), dolutegravir (DTG), elvitegravir (EVG), and raltegravir (RAL)—are approved for use in people with HIV as their initial ARV treatment. Intramuscular cabotegravir (CAB) is approved for use with rilpivirine (RPV) (with or without an oral CAB + RPV lead-in) as part of a long-acting injectable complete antiretroviral (ARV) regimen to replace a stable oral regimen in people with HIV and viral suppression. The role of this combination is discussed in the Optimizing Antiretroviral Therapy in the Setting of Viral Suppression section. Long-acting injectable cabotegravir (CAB-LA) is also approved for pre-exposure prophylaxis (PrEP). The first-generation INSTIs EVG and RAL have some disadvantages, which include a low barrier to resistance. In addition, because EVG has to be given with cobicistat (COBI), a pharmacokinetic (PK) booster, it has a high potential for drug–drug interactions, whereas RAL-based regimens have a higher pill burden than other INSTI regimens. Because of these disadvantages, elvitegravir/cobicistat (EVG/c) and RAL are no longer recommended by the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) as initial ART. Because the second-generation INSTIs BIC and DTG have high barriers to resistance, BIC/tenofovir alafenamide (TAF)/emtricitabine (FTC) and DTG plus TAF/FTC or tenofovir disoproxil fumarate (TDF)/FTC are recommended for most people with HIV (see Appendix B, Table 6 for more information on the INSTIs BIC and DTG).

This section of the guidelines will focus on BIC and DTG, the two INSTIs recommended by the Panel as part of the *Recommended Initial Regimens for Most People With HIV* (Table 6a) and *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b) (see Tables 6a and 6b and Table 7).

Panel's Recommendations for Integrase Strand Transfer Inhibitor–Based Regimens as Initial Therapy

The Panel recommends one of the following INSTI-based regimens as initial ART for people with HIV who do not have a history of using CAB-LA as PrEP (see Table 6a in Initial Combination Antiretroviral Regimens for People With HIV):

- BIC/TAF/FTC **(AI)**
- DTG plus (TAF or TDF) with (FTC or lamivudine [3TC]) **(AI)**
- DTG/3TC **(AI),** except for those with HIV RNA >500,000 copies/mL, with hepatitis B virus (HBV) coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.

INSTI resistance has been reported in people who acquired HIV following exposure to CAB-LA as PrEP.[1] For a person who has had exposure to CAB-LA as PrEP, an INSTI-containing regimen should not be initiated unless an INSTI genotypic resistance test result is available and shows no INSTI-resistance mutations **(AIII).** If treatment is initiated before genotypic test results are available, boosted darunavir (DRV) plus (TAF or TDF) plus (FTC or 3TC) should be used, pending INSTI resistance results **(AIII).** See Table 6a in Initial Combination Antiretroviral Regimens for People With HIV for more details.

Because of the low rates of transmitted INSTI resistance in the United States at present, when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started pending the results of the INSTI genotype test.

For people who have never used CAB-LA for PrEP and who acquired HIV despite using INSTI-based post-exposure prophylaxis, an INSTI genotype should be obtained prior to beginning an INSTI-based regimen. However, because selection of INSTI-resistant virus is likely to be uncommon in this setting, an INSTI-based regimen could be started prior to the return of genotype results **(CIII).**

The Panel also recommends using DTG/abacavir (ABC)/3TC **(BI)** when concerns about renal or bone-associated adverse events preclude the use of TAF or TDF. However, ABC should only be given to people who are documented to be HLA-B*5701-negative.

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Adverse Effects

BIC and DTG are generally well tolerated, although there are reports of insomnia in some people. Depression and suicidal ideation, primarily in people with a history of psychiatric illnesses, have been reported rarely in those receiving INSTI-based regimens.[2-5]

Among people with HIV who have not yet received ART, initiation of INSTI-containing regimens has been associated with greater weight increases compared to non-nucleoside reverse transcriptase inhibitor (NNRTI) or boosted protease inhibitor (PI) regimens.[6-11] In randomized trials of ARV-naive individuals, the mean increase in weight from baseline associated with BIC and DTG was similar and greater than with EVG/c or with efavirenz (EFV).[8,12-14] Weight gain was also greater in those initiating TAF than other nucleoside reverse transcriptase inhibitors (NRTIs).[7,8,15] These weight increases appear to disproportionately affect women and Black and Hispanic people,[6-8,16] yet predictors and mechanisms for the weight gain are still unclear. In general, concerns for weight gain should not be a reason to avoid an INSTI- or TAF-based regimen.

Integrase Strand Transfer Inhibitor Use in People of Childbearing Potential

Clinicians should refer to the Perinatal Guidelines for detailed recommendations on ARV regimens in treatment-naive people, including recommendations on the use of INSTI-based regimens during conception and throughout pregnancy.

- Earlier data from a birth outcomes surveillance study in Botswana raised concern about an increased risk of neural tube defects (NTDs) (0.9%) in infants born to women who were receiving DTG at the time of conception.[17,18] Updated data from the same study showed that the prevalence of NTDs in infants born to women on DTG at the time of conception is not significantly different from those on non-DTG regimens at the time of conception.[19] Based on these data, DTG is now the preferred INSTI for pregnant individuals with HIV. See the Perinatal Guidelines for further discussion.
- BIC is recommended as an alternative INSTI during pregnancy because data about safety, PK, and efficacy in pregnancy are available but are more limited than data about drugs classified as *Preferred* by the Perinatal Guidelines. See the Perinatal Guidelines for more details.

Bictegravir

BIC is approved by the U.S. Food and Drug Administration for initial therapy in adults with HIV as a component of a once-daily single-tablet regimen with TAF and FTC.

Efficacy in Clinical Trials

- The efficacy of BIC in ART-naive adults has been evaluated in two large Phase 3 randomized double-blind clinical trials that compared BIC to DTG administered in combination with two NRTIs. The primary efficacy endpoint was the proportion of participants with plasma HIV RNA <50 copies/mL at Week 48.
  - The GS-US-380-1490 trial randomized participants 1:1 to receive either BIC/TAF/FTC or DTG with coformulated TAF/FTC. Both regimens were given once daily. At Week 96, 84% of participants in the BIC arm and 86% of those in the DTG arm achieved HIV RNA <50 copies/mL.[15]
  - The GS-US-380-1489 trial randomized participants 1:1 to receive BIC/TAF/FTC or coformulated DTG/ABC/3TC once daily. At Week 96, 88% of participants in the BIC/TAF/FTC arm and 90% of those in the DTG/ABC/3TC arm achieved HIV RNA <50 copies/mL.[20]
  - Week 144 follow-up from both trials demonstrated noninferiority of the BIC/TAF/FTC regimen to both DTG-containing regimens, with high levels of virologic suppression and no treatment-emergent resistance.

Adverse Effects

- BIC is generally well tolerated.
- Neuropsychiatric adverse events have been reported with INSTIs. BIC-associated serious neuropsychiatric effects were uncommon (<1%) in clinical trials and mainly occurred in the setting of preexisting depression, other psychiatric illness, or prior suicide attempt.[21]

Drug–Drug Interactions

Note: See Table 24d for a comprehensive list of potential INSTI-related drug–drug interactions.

- BIC is a cytochrome P450 (CYP) 3A4 substrate and a uridine diphosphate glucuronosyltransferase (UGT) 1A1 substrate; therefore, its metabolism may be affected by concomitant use of CYP3A4 and UGT1A1 inducers or inhibitors. Rifampin or other rifamycins may decrease BIC or TAF concentrations, which may result in loss of therapeutic effect of the ART. For people who require rifamycins, BIC/FTC/TAF should not be used. Use of certain anti-seizure medications and St. John's wort should also be avoided.[21]
- BIC is an inhibitor of the drug transporters OCT2 (organic cation transporter 2) and MATE1 (multidrug and toxic compound extrusion 1); therefore, BIC may increase concentrations of drugs that are substrates of these transporters. For this reason, dofetilide is **contraindicated** with BIC/TAF/FTC.

- Like other INSTIs, oral absorption of BIC may be reduced when BIC is coadministered with polyvalent cations (e.g., aluminum-, magnesium-, or calcium-containing antacids; calcium or iron supplements).

Other Factors and Considerations

- BIC decreases tubular secretion of creatinine without affecting glomerular function. Increases in serum creatinine are observed typically within the first 4 weeks of BIC therapy (with a median increase of 0.10 mg/dL after 48 weeks). This increase is comparable to that seen with other ARV drugs that have a similar effect on creatinine secretion, including DTG, RPV, and COBI.
- Treatment-emergent mutations that confer BIC resistance have rarely been reported in people receiving BIC for initial therapy.[22] BIC has not been studied in prospective trials for people with prior INSTI failure or INSTI-related resistance mutations. One analysis of 20 individuals with preexisting INSTI-related resistance mutations showed maintenance of virologic suppression in 19 people after switch to BIC, and viral suppression after beginning BIC in one person without prior ARV treatment. There are, however, insufficient data at present to recommend BIC use in such cases.

The Panel's Recommendation

The Panel recommends the use of BIC/TAF/FTC as a *Recommended Initial Regimen for Most People With HIV* **(AI)** (see Table 6a and Table 7 for more detailed recommendations).

Dolutegravir

As initial ARV regimens, both DTG plus two NRTIs and DTG/3TC demonstrated high efficacy in achieving HIV suppression in clinical trials. DTG is given once daily, with or without food.

Efficacy in Clinical Trials

The efficacy of DTG in ART-naive individuals has been evaluated in several fully powered randomized controlled clinical trials. In these trials, DTG-based regimens were noninferior or superior to a comparator INSTI-, NNRTI-, or PI-based regimen. The primary efficacy endpoint in these clinical trials was the proportion of participants with plasma HIV RNA <50 copies/mL.[13,23,24]

DTG Plus Two NRTIs Versus Other INSTIs Plus Two NRTIs

- DTG-based regimens (with TAF/FTC or ABC/3TC) have been compared to BIC/TAF/FTC in two randomized controlled trials. These regimens have virologic efficacy that is similar to BIC/TAF/FTC (see discussion in the BIC section above).[15,20,23,25]

DTG Plus Two NRTIs Versus EFV Plus Two NRTIs

- The SINGLE trial compared DTG 50 mg once daily plus ABC/3TC to EFV/TDF/FTC in 833 participants. At Week 48, DTG plus ABC/3TC was superior to EFV/TDF/FTC, primarily because the study treatment discontinuation rate was higher in the EFV arm than in the DTG arm.[26] At Week 144, DTG plus ABC/3TC remained superior to EFV/TDF/FTC.[27]
- The ADVANCE trial, an open-label, noninferiority trial conducted in South Africa, compared DTG with either TDF/FTC or TAF/FTC to EFV/TDF/FTC. At Week 96, the DTG-based

regimens were noninferior to the EFV regimen based on the proportion of participants with HIV RNA levels <50 copies/mL (79% in DTG/TAF/FTC vs. 78% in DTG/TDF/FTC vs. 74% in EFV/TDF/FTC arms). More participants discontinued the trial regimen in the EFV group than in the DTG group. Mean weight gain was 7.1 kg in the DTG/TAF/FTC group, 4.3 kg in the DTG/TDF/FTC group, and 2.3 kg in the EFV/TDF/FTC group and was greater among women than men.[14]

DTG Plus Two NRTIs Versus Ritonavir-Boosted Darunavir Plus Two NRTIs

- The FLAMINGO study, a randomized open-label clinical trial, compared DTG 50 mg once daily to the boosted PI—darunavir/ritonavir (DRV/r) 800 mg/100 mg once daily—each administered in combination with investigator-selected ABC/3TC or TDF/FTC. At Week 48, DTG was superior to DRV/r, with 90% and 83% of participants achieving HIV RNA <50 copies/mL, respectively. More participants discontinued their assigned regimen in the DRV/r arm.[28] The difference in efficacy between the DTG and DRV/r regimens was more pronounced in people with pre-treatment HIV RNA levels >100,000 copies/mL. At Week 96, DTG remained superior to DRV/r.[29]

DTG/3TC

- In the GEMINI-1 and GEMINI-2 trials, 1,433 ART-naive participants with baseline HIV RNA <500,000 copies/mL and no evidence of HBV infection were randomized to receive DTG plus 3TC or DTG plus TDF/FTC. At Week 96, DTG plus 3TC was noninferior to DTG plus TDF/FTC with 86% of participants in the DTG plus 3TC group and 89.5% in the DTG plus TDF/FTC group with viral load <50 copies/mL.[30] Virologic nonresponse was uncommon, occurring in 3.1% of participants who received DTG plus 3TC and 2% of participants who received DTG plus TDF/FTC. No treatment-emergent NRTI or INSTI resistance occurred in either treatment group. Among participants who started the study with CD4 counts <200 cells/mm^3, the rate of HIV RNA <50 copies/mL at Week 96 was lower in the DTG plus 3TC group than in the DTG plus TDF/FTC group; however, the difference was not related to a higher rate of virologic failure in the two-drug group. Overall mean change in weight from baseline was 3.1 kg in the DTG plus 3TC group and 2.1 kg in the DTG plus TDF/FTC group. At Week 144, DTG plus 3TC maintained noninferiority to DTG plus TDF/FTC with 82% versus 84% of participants maintaining viral load <50 copies/mL, respectively. The proportion of participants with viral load ≥50 copies/mL was 3% in both treatment groups. A lower risk of drug-related adverse events was found with DTG plus 3TC versus DTG plus TDF/FTC (20% vs. 27%; relative risk, 0.76 [95% confidence interval, 0.63–0.92]).[30]
- Two other small, nonrandomized single-arm studies showed similar rates of viral suppression with DTG plus 3TC.[31,32]

Adverse Effects

- DTG is generally well tolerated. The most reported adverse reactions of moderate-to-severe intensity were insomnia and headache.
- Some studies have shown greater weight increase among people initiating INSTI-based regimens, including regimens with DTG.[7,8,33,34] In a pooled analysis of eight randomized controlled trials in ART-naive individuals, the weight gain at 96 weeks with BIC- and

DTG-based regimens was similar (approximately 3.5 kg). The clinical significance of weight gain in this setting is unclear.[8]

- Neuropsychiatric adverse events (e.g., sleep disturbances, depression, anxiety, suicidal ideation) associated with the initiation of DTG and other INSTIs have been reported.[2,3,35,36] However, analyses of data from large randomized controlled trials and a health care database demonstrated similar rates of neuropsychiatric adverse events between DTG-based regimens and regimens that included RAL, EFV, DRV, and ATV.[37] Neuropsychiatric events rarely led to DTG discontinuation.

Drug–Drug Interactions

Note: See Table 24d for a comprehensive list of potential INSTI-related drug–drug interactions.

- DTG has fewer drug interactions than BIC.
- DTG oral absorption may be reduced when the ARV is coadministered with polyvalent cations. DTG should be taken at least 2 hours before or 6 hours after cation-containing antacids or laxatives are taken. Alternatively, DTG and supplements containing calcium or iron can be taken simultaneously with food.

Other Factors and Considerations

- DTG decreases tubular secretion of creatinine without affecting glomerular function, with increases in serum creatinine observed within the first 4 weeks of treatment.
- Treatment-emergent mutations that confer DTG resistance have been rarely reported in people receiving DTG as part of a three-drug regimen for initial therapy.[38-40] The incidence of resistance with DTG is much lower than with EVG or RAL, which suggests that DTG, like BIC, has a higher barrier to resistance than EVG or RAL.

The Panel's Recommendations

- The Panel classifies the following as *Recommended Initial Regimens for Most People With HIV* (see Table 6a and Table 7 for more detailed recommendations):
  - DTG plus (TAF or TDF) plus (FTC or 3TC) **(AI)**
  - DTG/3TC **(AI)—not recommended** for those with HIV RNA >500,000 copies/mL, with HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.
- The Panel recommends DTG/ABC/3TC **(BI)** in certain clinical scenarios for people with HIV who are documented to be HLA-B*5701-negative and who have concerns about renal or bone toxicities associated with TAF or TDF. This regimen should not be used in people with HBV coinfection unless an HBV-active drug (i.e., entecavir) other than 3TC is used.

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Non-Nucleoside Reverse Transcriptase Inhibitor–Based Regimens as Initial Antiretroviral Therapy

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Table 8c. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors That Are Recommended as Initial Antiretroviral Therapy in Certain Clinical Scenarios

Characteristics	DOR	RPV[a]
Dosing Frequency	Once daily	Once daily
Food Requirement	With or without food	With a meal
STR Available as Initial ART Recommended in Table 6b	DOR/TDF/3TC	RPV/TAF/FTC
Available as a Single-Drug Tablet	Yes	Yes
Adverse Effects	Generally well tolerated	• Depression • Headache • Skin rash • QTc prolongation
CYP3A4 Drug–Drug Interactions	CYP3A4 substrate	CYP3A4 substrate
Other Significant Drug Interactions	None	RPV oral absorption is reduced with increased gastric pH. Use of RPV with PPIs is not recommended; see Drug–Drug Interactions for dosing recommendations when RPV is coadministered with an H2 blocker or antacids.

[a] See Optimizing Antiretroviral Therapy section and Appendix B, Table 4 for information regarding injectable RPV.

Key: 3TC = lamivudine; ART = antiretroviral therapy; CYP = cytochrome P; DOR = doravirine; FTC = emtricitabine; H2 = histamine 2; PPI = proton pump inhibitor; QTc = QT corrected for heart rate; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Summary

Four non-nucleoside reverse transcriptase inhibitors (NNRTIs)—doravirine (DOR), efavirenz (EFV), nevirapine (NVP), and rilpivirine (RPV)—are currently approved by the U.S. Food and Drug Administration (FDA) for the initial treatment of HIV when used in combination with other antiretroviral (ARV) drugs. A fifth NNRTI, etravirine (ETR), is approved only for people who are ART-experienced.

NNRTI-based regimens have demonstrated virologic potency and durability. The major disadvantages of currently available NNRTIs (especially EFV and RPV) include the prevalence of NNRTI-resistant viral strains in people without prior antiretroviral therapy (ART),[1] a low barrier for

the development of resistance, and potential for drug–drug interactions, although drug–drug interactions are less common with DOR. Resistance testing should be performed before initiation of an NNRTI-based regimen in people without prior ART. High-level resistance to all NNRTIs (except ETR or DOR) may occur with a single mutation. In people treated with RPV, the presence of RPV resistance mutations at virologic failure may confer cross-resistance to other NNRTIs, including ETR.[2,3] DOR-based regimens and one of the RPV-based regimens are now categorized as recommended *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios*. More details about these NNRTIs are provided below.

This section of the guidelines focuses on DOR and RPV, the two NNRTIs recommended by the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) as part of an initial ART regimen for people with HIV in certain clinical scenarios (see Table 6b in the Initial Combination Antiretroviral Regimens for People With HIV section and Table 7). There is no clinical trial comparing the efficacy of these two NNRTIs as initial ARV regimens. The Panel no longer recommends EFV as initial therapy because of the high incidence of serious toxicities, including neuropsychiatric effects and suicidality. NVP is no longer commonly used in clinical practice in the United States due to a relatively high potential for adverse effects compared to other NNRTIs.

Doravirine

Efficacy in Clinical Trials

The efficacy of DOR-based therapy as initial ART was demonstrated in two randomized, double-blind, placebo-controlled trials.

Doravirine-Based Regimen Versus Efavirenz-Based Regimen

- In the DRIVE-AHEAD trial, 734 participants received either DOR/tenofovir disoproxil fumarate (TDF)/lamivudine (3TC) or EFV/TDF/emtricitabine (FTC), both as a daily fixed-dose combination (FDC) tablet.[4]
  - At 96 weeks, DOR/TDF/3TC was noninferior to EFV/TDF/FTC, with 77.5% of participants who received DOR/TDF/3TC and 73.6% of those who received EFV/TDF/FTC achieving HIV RNA <50 copies/mL. Although virologic responses to ART overall were lower in participants with pre-treatment HIV RNA >100,000 copies/mL or pre-treatment CD4 T lymphocyte (CD4) cell counts of ≤200 cells/mm^3, there was no difference between the DOR-treated and EFV-treated participants.
  - Virologic rebound and virologic nonresponse were similar in the DOR/TDF/3TC (9.3%) and EFV/TDF/FTC (7.7%) treatment groups. At 96 weeks, genotype resistance results were reported for 21 participants with protocol-defined virologic failure in the DOR arm and 15 participants in the EFV arm. For the DOR arm, 7 of 21 (33.3%) participants had NNRTI resistance and 6 of 21 (28.6%) had NRTI resistance. For EFV, 10 of 15 (66.7%) participants had NNRTI resistance and 5 of 15 (33.3%) had NRTI resistance.
  - More participants in the EFV arm discontinued their assigned ART due to adverse events than in the DOR arm (6.6% vs. 3.0%). Neuropsychiatric side effects and rash were more common in the EFV arm.

Doravirine-Based Regimen Versus Darunavir/Ritonavir-Based Regimen

- In the DRIVE-FORWARD trial, 769 participants received DOR or darunavir/ritonavir (DRV/r) once daily along with two investigator-selected nucleoside reverse transcriptase inhibitors (NRTIs), either abacavir (ABC)/3TC or TDF/FTC.[5]
  - At 48 weeks, DOR was noninferior to DRV/r with 84% of study participants who received DOR versus 80% of those who received DRV/r achieving HIV RNA <50 copies/mL. Participants who received DOR plus ABC/3TC (n = 48) and those who received DOR plus TDF/FTC (n = 316) had similar virologic responses.
  - At 96 weeks, DOR was superior to DRV/r in terms of virologic suppression (73% vs. 66%).[5]
  - Protocol-defined virologic failure was similar in the DOR and DRV/r groups (9% vs. 11%) by Week 96. Genotype resistance results were reported for 11 and 14 participants with virologic failure in the DOR and DRV/r arms, respectively. Treatment-emergent resistance to any study drug occurred in 2 of 11 participants in the DOR group and 1 of 14 participants in the DRV/r group.
  - Treatment-related diarrhea was more frequently reported in the DRV/r arm. Greater increases in fasting low-density lipoprotein cholesterol, triglycerides, non–high-density lipoprotein cholesterol, and total cholesterol were seen in the participants who received DRV/r than in those who received DOR.
- In a pooled analysis of DRIVE-AHEAD and DRIVE-FORWARD participants who entered an open-label extension phase following the initial 96 weeks of randomized treatment, 550 participants continued their DOR-based regimen and 502 participants switched to a DOR-based regimen from the control arms. At 192 weeks, 83% percent of participants who continued on DOR and 81% of participants in the switch arm maintained viral suppression. Discontinuation due to drug-related adverse events was <1% overall and similar between the two arms, with no discontinuations due to renal adverse events.[6]

Other Factors and Considerations

- DOR is available as a single-drug 100-mg tablet[7] and as part of a single-tablet regimen (STR) that contains DOR/TDF/3TC 100 mg/300 mg/300 mg[8] and is dosed once daily, with or without food.
- DOR-based regimens have not been directly compared to integrase strand transfer inhibitor (INSTI)–based regimens in clinical trials and have not been studied with tenofovir alafenamide (TAF) in clinical trials.
- A post hoc analysis of three randomized controlled trials examined weight gain among ART-naive participants receiving DOR versus DRV/r or EFV. At week 96, mean weight gain was similar in the DOR group (2.4 kg), DRV/r group (1.8 kg), and EFV group (1.6 kg). No significant differences between treatment groups were found in the proportion of participants whose body mass index classification increased to overweight or obese at Week 48 or Week 96.[9]
- DOR is primarily metabolized by the CYP3A4 enzyme and should not be coadministered with strong CYP3A4 inducers. DOR concentration may increase in the presence of a CYP3A4 inhibitor (see Table 24b). DOR is not a CYP3A4 inducer or inhibitor; thus, it is not expected to affect the concentrations of concomitant CYP3A4 substrates.

- Treatment-emergent resistance mutations to DOR may confer cross-resistance to certain other NNRTIs. Most isolates with DOR mutations remain susceptible to ETR.[10]
- There are currently no data on the safety of DOR use during pregnancy.
- There are limited clinical trial data with the combination of DOR + ABC/3TC, so the Panel is less certain about the efficacy of this regimen.

The Panel's Recommendations

- Based on the clinical trial data discussed above, the Panel classifies DOR/TDF/3TC **(BI)** and DOR plus two NRTIs (**BI** for TDF/FTC and **BIII** for TAF/FTC) as *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios*.

Rilpivirine

Oral RPV is approved for use in combination with two NRTIs as initial ART for people with HIV who have pre-treatment viral loads <100,000 copies/mL. RPV is also approved as an extended-release injectable suspension as part of a long-acting (LA) injectable complete ARV regimen when used with cabotegravir (CAB), an INSTI. This regimen is approved to replace oral ART in people with virologic suppression and no history of resistance to RPV or INSTIs (see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression for discussion of LA CAB/RPV).

Efficacy in Clinical Trials

- Two Phase 3 randomized, double-blind clinical trials—ECHO and THRIVE—compared RPV and EFV, each combined with two NRTIs.[11] At 96 weeks, the following findings were reported:
  - RPV was noninferior to EFV overall.
  - Among participants with pre-ART viral loads >100,000 copies/mL, more RPV-treated participants experienced virologic failure than EFV-treated participants. NNRTI and NRTI resistance were more frequently found in RPV-treated participants with virologic failure.
  - Among the RPV-treated participants, the rate of virologic failure was greater in those with pre-treatment CD4 counts <200 cells/mm^3 than in those with CD4 counts ≥200 cells/mm^3.
- STaR, a Phase 3b, open-label study, compared two STRs—RPV/TDF/FTC and EFV/TDF/FTC—as initial ART in 786 people with HIV. The results at 96 weeks[12] were similar to those reported at 48 weeks.[13]
  - RPV was noninferior to EFV overall.
  - RPV was superior to EFV in participants with pre-ART viral loads ≤100,000 copies/mL and noninferior in those with pre-ART viral loads >100,000 copies/mL. Among participants with pre-ART viral loads >500,000 copies/mL, virologic failure was more common in RPV-treated than in EFV-treated participants.
  - At Week 96, there were more participants with emergent resistance in the RPV/FTC/TDF arm than in the EFV/FTC/TDF arm (5.3% vs. 1.0%, respectively).
- The STR of RPV/TAF/FTC was approved by the FDA based on results from a bioequivalence study. In this study, plasma concentrations of RPV, FTC, and TAF 25 mg in participants taking

the coformulated drug were similar to those seen in participants who received RPV as the single-drug tablet and TAF/FTC as part of the STR of EVG/c/TAF 10 mg/FTC.[14]

Adverse Effects

- RPV is generally well tolerated. In the ECHO, THRIVE, and STaR trials, fewer instances of CNS adverse events (e.g., abnormal dreams, dizziness, psychiatric side effects), skin rash, and dyslipidemia were reported in the RPV arms than in the EFV arms, and fewer people in the RPV arms discontinued therapy due to adverse events. However, up to 9% of clinical trial participants experienced depressive disorders, including approximately 1% of participants who had suicidal thoughts or who attempted suicide. People receiving RPV who have severe depressive symptoms should be evaluated to assess whether the symptoms may be due to RPV and if the risks of continuing the same regimen outweigh the benefits.

Other Factors and Considerations

- Oral RPV is formulated both as a single-drug tablet and in STRs with TAF/FTC, with TDF/FTC, and with DTG. Among available STRs, RPV/TDF/FTC is no longer recommended by the Panel for initial therapy.
- RPV is also available as part of an LA injectable ARV regimen for use in combination with LA CAB in people with HIV who are virologically suppressed and do not have resistance to these drugs (see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression).
- The STR of RPV/TAF/FTC is given once daily and must be administered with a meal (containing at least 390 kcal).
- RPV is also coformulated as a once-daily FDC tablet with DTG that is used as continuation therapy for people with HIV who have achieved viral suppression.[15] However, this combination has not been studied in people with HIV and no prior ART, and it **is not recommended** for initial therapy (see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression).
- The oral drug absorption of RPV can be significantly reduced in the presence of acid-reducing agents. RPV is **contraindicated** in people who are receiving proton pump inhibitors and should be used with caution in those receiving H2 antagonists or antacids (see Drug–Drug Interactions for dosing recommendations).
- RPV is primarily metabolized in the liver by the CYP3A enzyme; its plasma concentration may be affected in the presence of CYP3A inhibitors or inducers (see Drug–Drug Interactions).
- At doses above the approved dose of 25 mg, RPV may cause QTc interval prolongation. RPV should be used with caution when coadministered with a drug known to increase the risk of Torsades de Pointes.

The Panel's Recommendations

- Given the availability of other effective regimens that do not have virologic and immunologic prerequisites to initiate treatment, substantial drug–drug interactions, and a low genetic barrier to resistance, RPV is **not recommended** for initial therapy in most persons with HIV. RPV/TDF/FTC is no longer recommended as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios*, largely due to the limitations of RPV and the availability of

DOR/TDF/3TC, which has fewer drug–drug interactions and no virologic and immunologic prerequisites. The Panel continues to recommend RPV/TAF/FTC as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (see Table 6b in the Initial Combination Antiretroviral Regimens for People With HIV section), largely to retain an STR option containing an NNRTI and TAF.

- Use of RPV with TAF/FTC **(BII)** should be limited to persons with pre-treatment viral loads <100,000 copies/mL and CD4 counts >200 cells/mm^3.
- Data on RPV plus ABC/3TC are insufficient to consider recommending this regimen.

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Protease Inhibitor–Based Regimens

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Table 8d. Characteristics of Protease Inhibitor Options as Initial Antiretroviral Therapy in Certain Clinical Scenarios

Characteristic	DRV
Dosing Frequency	Once daily for persons with no prior PI experience.
PK Boosting	DRV should only be used with a PK booster (i.e., RTV or COBI).
Fixed-Dose Formulation	• DRV/c • DRV/c/TAF/FTC
Available as a Single-Drug Tablet	Yes
Adverse Effects	• Skin rash • Increase in serum transaminase • Hyperlipidemia • Diarrhea, nausea
CYP3A4 Drug–Drug Interactions	CYP34A substrate, inhibitor
Other Significant Drug Interactions	N/A

Key: COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; FTC = emtricitabine; N/A = not applicable; PI = protease inhibitor; PK = pharmacokinetic; RTV = ritonavir; TAF = tenofovir alafenamide

Summary

The U.S. Food and Drug Administration (FDA)–approved protease inhibitors (PIs) include atazanavir (ATV), atazanavirATV/cobicistat (ATV/c), darunavir (DRV), darunavir/cobicistat (DRV/c), fosamprenavir (FPV), indinavir (IDV), lopinavir/ritonavir (LPV/r), nelfinavir (NFV), ritonavir (RTV), saquinavir (SQV), and tipranavir (TPV). PI-based regimens using pharmacokinetic (PK) enhancement with either cobicistat (COBI) or RTV (also called PK boosting) increase concentration and prolong the half-lives of the PI. These regimens have demonstrated virologic potency, durability in people who are ART-naive, and a high barrier to resistance. Because LPV/r, fosamprenavir/ritonavir (FPV/r), ATV (with or without a PK enhancer), and saquinavir/ritonavir (SQV/r) have disadvantages—such as greater pill burden, lower efficacy, or increased toxicity—only boosted DRV in combination with two nucleoside reverse transcriptase inhibitors (NRTIs) is recommended as initial therapy in certain clinical situations (see Table 6b in Initial Combination Antiretroviral Regimens for People With HIV).

Because transmitted PI resistance is uncommon, boosted DRV-based regimens are preferred over a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen as an option for treatment initiation before resistance test results are available. In addition, a boosted DRV-based regimen can be used for rapid antiretroviral therapy (ART) initiation, in the setting of acute HIV infection, and as the preferred option while awaiting resistance test results for people with a history of long-acting cabotegravir (CAB-LA) use as pre-exposure prophylaxis (PrEP). Few or no PI mutations are

detected when a patient's first PI-based regimen fails, which is not the case with non-nucleoside reverse transcriptase inhibitor (NNRTI)–based regimens and regimens with a first-generation integrase strand transfer inhibitor (INSTI) (e.g., raltegravir or elvitegravir).[1] Because of their high barrier to resistance, PI-based regimens may be useful for people at risk for intermittent therapy because of poor adherence.

DRV requires PK boosting with either RTV or COBI to inhibit the cytochrome P3A4 (CYP3A4) isoenzyme, which may lead to significant drug–drug interactions (see Drug–Drug Interactions). The specific characteristics of DRV are listed in Appendix B, Table 5.

Darunavir/Ritonavir

Efficacy in Clinical Trials

Darunavir/ritonavir (DRV/r) has been studied in several large, randomized controlled trials in people with HIV without prior antiretroviral (ARV) experience. These trials compared DRV/r-based regimens to PI-, INSTI-, or NNRTI-based regimens. Summaries of the results from some key trials are listed below.

- The FLAMINGO study compared DRV/r with dolutegravir (DTG), each administered in combination with two NRTIs—either tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) or abacavir (ABC)/lamivudine (3TC)—in 488 participants who were ART-naive. The rate of virologic suppression at Week 96 was significantly higher among those who received DTG than in those who received DRV/r. The higher rate of virologic failure observed in the DRV/r group was related primarily to the number of failures among those with a viral load >100,000 copies/mL and secondarily to more drug discontinuations in the DRV/r group.[2]
- The AIDS Clinical Trial Group (ACTG) study A5257 (ARDENT), a large, randomized, open-label trial, compared atazanavir/ritonavir (ATV/r) to DRV/r or raltegravir (RAL) over 96 weeks, each given with TDF/FTC. The trial showed similar virologic efficacy for DRV/r, ATV/r, and RAL, but more participants in the ATV/r group discontinued randomized treatment because of adverse events.[3]
- The DRIVE-FORWARD study compared DRV/r to doravirine (DOR), both administered with two investigator-selected NRTIs, in 769 ART-naive participants. At 48 weeks, DOR was found to be non-inferior to DRV/r, with 80% and 84% of participants achieving HIV RNA levels <50 copies/mL, respectively.[4] At Week 96, DOR was superior to DRV/r in terms of virologic suppression (73% vs. 66%).[4] Rates of virologic failure were low and similar in the DOR and DRV/r groups (9% vs. 11%). Treatment-emergent resistance to any study drug was infrequent, occurring in <1% of participants in both the DOR group (2 of 383) and the DRV/r group (1 of 383).

Adverse Effects

- People with HIV who take DRV/r may develop a skin rash, which is usually mild-to-moderate in severity and self-limited. Treatment discontinuation is necessary on rare occasions when severe rash occurs with fever or elevated transaminases.
- ACTG A5257 showed similar lipid changes in participants in the ATV/r and DRV/r arms. Bone mineral density decreased to a greater extent in participants in the ATV/r and DRV/r arms

compared to participants in the RAL arm.[3] The likelihood of developing metabolic syndrome was equivalent among the three arms, although a larger increase in waist circumference was observed at 96 weeks in participants assigned to the RAL arm than in those assigned to the DRV/r arm ($P = 0.023$).[5]

- In the DRIVE-FORWARD study, treatment-related diarrhea was more frequently reported in the DRV/r arm, and greater increases were observed in fasting low-density lipoprotein cholesterol, triglycerides, non–high-density lipoprotein cholesterol, and total cholesterol compared to the DOR arm.[4]

Other Factors and Considerations

- DRV/r is administered once daily with food in people who are ART-naive.
- DRV has a sulfonamide moiety and should be used with caution in people with severe sulfonamide allergies. In clinical trials, the incidence and severity of rash were similar in participants with and without a history of sulfonamide allergy. Most people with sulfonamide allergy can tolerate DRV.
- DRV/r is a potent CYP3A4 inhibitor, which may lead to significant interactions with other medications metabolized through this same pathway (see Drug–Drug Interactions).
- Unlike DRV/c, DRV/r may be used in pregnancy.

The Panel's Recommendations

- Based on efficacy and safety data from clinical trials and clinical experience, the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) classifies DRV/r with (tenofovir alafenamide [TAF] or TDF) plus (FTC or 3TC) as a *Recommended Initial Regimen for Most People With HIV* who have a history of CAB-LA use as PrEP, pending the results of INSTI genotype testing **(AIII)** (see Table 6a). DRV/r plus (TAF or TDF) plus (FTC or 3TC) **(BI)** and DRV/r plus ABC/3TC **(BII)** are also part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (see Table 6b and Table 7).

Darunavir/Cobicistat

Efficacy in Clinical Trials

- The AMBER trial enrolled 725 ART-naive participants in a Phase 3 randomized controlled trial that compared the single-tablet regimen (STR) DRV/c/TAF/FTC with DRV/c plus TDF/FTC. At 48 weeks, similar virologic suppression rates among participants were achieved in both arms of the study (91% and 88% had HIV RNA <50 copies/mL, respectively). No treatment-emergent mutations associated with DRV or TAF/TDF resistance were observed in either group.[6] At 96 weeks, 85% of participants on the STR maintained HIV RNA levels <50 copies/mL compared to 84% in the DRV/c plus TDF/FTC arm.[7]
- The DIAMOND study evaluated DRV/c/TAF/FTC as an STR in 109 participants in a rapid-initiation model of care. At Week 48, 97 (89%) participants completed the study and 92 (84%) achieved HIV-1 RNA <50 copies/mL by the FDA snapshot analysis. No protocol-defined virologic failures occurred, and incidences of adverse events at least possibly related to study

drugs (33%) were low. No study drug-related serious adverse events occurred, and only one (<1%) participant discontinued because of a study drug-related adverse event.[8]

Adverse Effects

- The most common drug-related adverse events were diarrhea, nausea, fatigue, flatulence, rash, and headache.

Other Factors and Considerations

- DRV/c 800 mg/150 mg is available as a coformulated boosted PI or as an STR with TAF/FTC 10 mg/200 mg.
- Both DRV and COBI exposures are reduced markedly during the second and third trimesters of pregnancy, and should be avoided if possible.[9] However, if pregnant women with viral suppression while on DRV/c elect to continue on the drug, frequent viral load monitoring is recommended. For further information, please refer to the Perinatal Guidelines.

The Panel's Recommendations

- The Panel recommends DRV/c plus (TAF or TDF) plus (FTC or 3TC) **(BI)** and DRV/c plus ABC/3TC **(BII)** as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios*.
- Per product label recommendation, DRV/c plus TDF/FTC **is not recommended** for people with creatinine clearance (CrCl) <70 mL/min, whereas DRV/c plus TAF/FTC **is not recommended** for people with CrCl <30 mL/min.
- For people who have a history of CAB-LA use as PrEP, INSTI genotype resistance testing should be performed before starting ART. If ART is to be started before genotypic testing results are available, DRV/c with (TAF or TDF) plus (FTC or 3TC) can be started **(AIII).**

Rating of Recommendations: A = Strong; B = Moderate; C = Weak

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

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Antiretroviral Regimens for Initial Therapy When Abacavir, Tenofovir Alafenamide, and Tenofovir Disoproxil Fumarate Cannot Be Used or Are Not Optimal

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Most of the currently recommended antiretroviral (ARV) regimens for initial therapy consist of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a third active drug. In addition, dolutegravir (DTG)/lamivudine (3TC) is a two-drug, NRTI-limiting regimen that is a recommended option for people with HIV (see Table 6a in Initial Combination Antiretroviral Regimens for People With HIV) and would be preferred over others in situations where it is desirable to avoid abacavir (ABC), tenofovir alafenamide (TAF), and tenofovir disoproxil fumarate (TDF). Several other NRTI-limiting/sparing two-drug regimens have been evaluated in clinical studies, but are not yet recommended by the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) due to insufficient evidence. Note that two-drug regimens **are not currently recommended** during pregnancy and tenofovir-sparing regimens **are not recommended** in people with hepatitis B virus (HBV)/HIV coinfection unless another HBV-active drug (i.e., entecavir) is added. Clinicians should refer to HBV/HIV Coinfection for guidance on treatment of people with HBV infection when TAF or TDF cannot be used as part of the ARV regimen.

Strategies Supported by Evidence From Clinical Trials

Dolutegravir/Lamivudine

- In the GEMINI-1 and GEMINI-2 trials, 1,433 antiretroviral therapy (ART)–naive participants with baseline HIV RNA <500,000 copies/mL and no evidence of HBV infection were randomized to receive a two-drug regimen of DTG plus 3TC or a three-drug regimen of DTG plus TDF/emtricitabine (FTC). At Week 96, DTG plus 3TC was non-inferior to DTG plus TDF/FTC based on the proportion of participants with viral loads <50 copies/mL (86% in DTG plus 3TC group and 89.5% in DTG plus TDF/FTC group).[1] Virologic nonresponse was uncommon, occurring in 3.1% of participants who received DTG plus 3TC and 2% of participants who received DTG plus TDF/FTC. No instances of treatment-emergent NRTI or integrase strand transfer inhibitor (INSTI) resistance occurred in either treatment group. Among participants who started the study with CD4 counts <200 cells/mm^3, the proportion of participants with HIV RNA <50 copies/mL at Week 96 was lower in the DTG plus 3TC group than in the DTG plus TDF/FTC group; however, the difference was not related to a higher rate of virologic failures in the two-drug group. At Week 144, DTG plus 3TC maintained noninferiority to DTG plus TDF/FTC with 82% versus 84% of participants maintaining viral load <50 copies/mL, respectively. The proportion of participants with viral load ≥50 copies/mL was similar between both treatment groups at 3%. There was a lower risk of drug-related adverse events with DTG plus 3TC versus DTG plus TDF/FTC (19.6% vs. 25.0%; relative risk ratio, 0.78; 95% confidence interval, 0.64–0.95).[1]

The Panel's Recommendation

When ABC, TAF, or TDF cannot be used or are not optimal, the Panel recommends DTG/3TC as an initial regimen for people with HIV **(AI)** who—

- Have a viral load ≤500,000 copies/mL,

- Have a genotype available that demonstrates sensitivity to 3TC,
- Do not have a history of long-acting cabotegravir (CAB-LA) use as pre-exposure prophylaxis, *or*
- Have CAB-LA exposure but with documented INSTI sensitivity on genotypic resistance testing.

HBV status must be determined, and if HBV/HIV coinfection is present, another HBV-active drug should be added (see HBV/HIV Coinfection).

Nucleoside-Limiting Regimens With Some Supporting Data but Not Recommended as Initial Therapy

The Panel **does not recommend** the following nucleoside-limiting or nucleoside-sparing regimens for initial therapy due to insufficient clinical trial data.

Darunavir/Ritonavir Plus Lamivudine

- In the ANDES trial, 336 participants were randomized 1:1 to receive open-label, once-daily dual therapy with darunavir/ritonavir (DRV/r) plus 3TC or triple therapy with DRV/r plus TDF/3TC. This study was conducted in Argentina, and the researchers used an FDC of DRV/r 800 mg/100 mg that is available in that country. The median baseline HIV RNA was 4.5 $\log_{10}$ copies, and 23% of participants had HIV RNA >100,000 copies/mL. At Week 48, 91% of the participants in the dual-therapy group and 93% of the participants in the triple-therapy group achieved an HIV RNA <50 copies/mL, demonstrating that dual therapy was non-inferior to triple therapy.[2] The rates of virologic suppression among study participants who had pre-therapy HIV RNA levels >100,000 copies/mL were similar in the dual- and triple-therapy groups (87% and 90%, respectively). The Panel **does not recommend** this regimen as initial therapy as the results from this study have not yet been published.

Darunavir/Ritonavir Plus Raltegravir

- In the NEAT/ANRS 143 study, 805 treatment-naive participants were randomized to receive twice-daily raltegravir (RAL) or once-daily TDF/FTC, each with DRV/r (800 mg/100 mg once daily). At Week 96, DRV/r plus RAL was non-inferior to DRV/r plus TDF/FTC based on the primary endpoint, the proportion of people with virologic or clinical failure. Among those with baseline CD4 counts <200 cells/mm^3; however, there were more virologic failures in the RAL plus DRV/r arm. A trend towards more failure was also observed among those with pre-treatment HIV RNA ≥100,000 copies/mL.[3] High rates of virologic failure in participants with HIV RNA >100,000 copies/mL were also seen in two smaller studies of DRV/r plus RAL.[4,5] The Panel **does not recommend** DRV/r plus RAL as initial ART because of the higher rate of virologic failure in participants with HIV RNA ≥100,000 copies/mL and the higher pill burden of this regimen compared to other Panel-recommended initial ARV regimens.

Darunavir/Ritonavir Plus Rilpivirine

- In a single-arm, open-label pilot study, 36 ART-naive participants without genotypic evidence of resistance to DRV or rilpivirine (RPV) received DRV/r plus RPV for 48 weeks. Half of the participants (18 of 36) had baseline HIV viral loads >100,000 copies/mL. By Week 36, 97% of participants (35 of 36) achieved HIV RNA <50 copies/mL, and by Week 48, all achieved viral

suppression (HIV RNA < 50 copies/mL).[6] The Panel **does not recommend** this regimen as initial ART given the small sample size of the study described above and the lack of comparative data evaluating DRV/r plus RPV as initial therapy for people with HIV.

Long-Acting Injectable Cabotegravir With Rilpivirine

- The long-acting injectable combination of CAB plus RPV (LA CAB/RPV) has not been studied in ART-naive participants. In the Phase 3 trial FLAIR and Phase IIb trial LATTE-2,[7,8] ART-naive participants were first treated with 20 weeks of DTG/ABC/3TC or oral CAB+ABC/3TC, respectively. Study participants who achieved virologic suppression were eligible for randomization to receive LA CAB/RPV every month or to continue oral daily ART. The Panel **does not recommend** the LA CAB/RPV as initial therapy for people with HIV because of the lack of data supporting the efficacy of this combination in people who are ART-naive **(AIII).** People desiring to use LA CAB/RPV early in their treatment history should first attain viral suppression on a recommended regimen before transitioning to LA CAB/RPV. See Optimizing Antiretroviral Therapy in the Setting of Viral Suppression for more discussion.

Rating of Recommendations: A = Strong; B = Moderate; C = Weak

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

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Table 9. Advantages and Disadvantages of Antiretroviral Components of Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

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Note: All drugs within an ARV class are listed in alphabetical order. Information based on Table 6a and Table 6b in the Initial Combination Antiretroviral Regimens for People With HIV section.

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
Dual-NRTI	**ABC/3TC**	• Coformulated with DTG • Generic formulations are available for ABC/3TC, ABC, and 3TC.	• May cause life-threatening HSRs in people who test positive for the HLA-B*5701 allele. As a result, HLA-B*5701 testing is required before use. • ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies.
	TAF/FTC	• Coformulated with BIC, DRV/c, or RPV • Active against HBV; a recommended dual-NRTI option for people with HBV/HIV coinfection • Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than TDF/FTC • Approved for people with eGFR ≥30 mL/min • Can be used in people on chronic hemodialysis	• See text in the NRTI section regarding weight gain with TAF.
	TDF/3TC	• Coformulated with DOR • Generic formulations are available for TDF, 3TC, or TDF/3TC. • Long-term clinical experience • Active against HBV	• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters • Osteomalacia has been reported as a consequence of proximal tubulopathy. • Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.
	TDF/FTC	• Active against HBV; a recommended dual-NRTI option for people with HIV/HBV coinfection • TDF is associated with lower lipid levels than TAF.	• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters • Osteomalacia has been reported as a consequence of proximal tubulopathy.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
			• Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.
Single NRTI	**3TC**	• Coformulated with DTG as STR • Avoids potential toxicities associated with TDF, TAF, ABC	• DTG/3TC **is not recommended** for individuals with HIV RNA >500,000 copies/mL, HBV coinfection unless on another HBV active drug, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.
INSTI	**BIC**	• Coformulated with TAF/FTC • Higher barrier to resistance than EVG and RAL • No food requirement	• Oral absorption of BIC can be reduced by simultaneous administration with drugs or supplements containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements or multivitamin tablets with minerals). See dosing recommendations in Table 24d. • CYP3A4 and UGT1A1 substrate (but not a CYP3A4 inducer or inhibitor); potential for drug–drug interactions. • See text in the INSTI section regarding weight gain and INSTI use.
	DTG	• Higher barrier to resistance than EVG or RAL • Coformulated with ABC/3TC and 3TC as STR • No food requirement • Minimal CYP3A4 interactions • Favorable lipid profile	• Oral absorption of DTG can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements or multivitamin tablets with minerals). See dosing recommendations in Table 24d. • UGT1A1 substrate; potential for drug interactions (see Table 24d) • Depression and suicidal ideation (rare; usually in people with preexisting psychiatric conditions) • See text in the INSTI section regarding weight gain and INSTI use.
NNRTI	**DOR**	• Coformulated with TDF/3TC • Fewer CNS side effects compared to EFV and RPV • No food requirement	• Shorter-term clinical experience than with RPV • Potential for CYP450 drug interactions (see Tables 24b, 25a, and 25b) • Treatment-emergent DOR resistance mutations may confer resistance to certain NNRTIs.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)

	RPV	• Coformulated with TAF/FTC	• **Not recommended** in people with pre-ART HIV RNA >100,000 copies/mL or CD4 counts <200 cells/mm^3 because of higher rate of virologic failure in these people.
			• Depression and suicidality
			• QTc interval prolongation; consider using an alternative to RPV in people taking medications with known risk of causing Torsades de Pointes or in those at higher risk of Torsades de Pointes.
			• Rash
			• Transmitted resistance is more common than with PIs and INSTIs.
			• More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimens that contain EFV and two NRTIs
			• Potential for CYP450 drug interactions (see Tables 24b and 25a)
			• Meal requirement (>390 kcal)
			• Requires acid for adequate absorption
			  ○ Contraindicated with PPIs.
			  ○ Use with H2 antagonists or antacids with caution (see Table 24a for detailed dosing information).

PI	**DRV/c** or **DRV/r**	• Higher barrier to resistance than NNRTIs • PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs.	• Skin rash • Food requirement • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 24a) • Increased CV risk reported in one observational cohort study[a] • Hepatotoxicity has been reported, especially in those with preexisting liver disease.
	DRV/c Specific considerations	• Coformulated as DRV/c and DRV/c/TAF/FTC	• COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function. • Coadministration with TDF **is not recommended** in people with CrCl <70 mL/min.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
			• COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates. • COBI should be avoided in pregnancy because levels of COBI and its boosted drugs are lower in the second and third trimesters. If women who are pregnant with suppressed virus on DRV/c elect to continue on the drug, frequent viral load monitoring is recommended.

[a] D:A:D international prospective multicohort study[1]

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BMD = bone mineral density; Ca = calcium; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; Cr = creatinine; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; eGFR = estimated glomerular filtration rate; FTC = emtricitabine; GI = gastrointestinal; H2 = histamine 2; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; INSTI = integrase strand transfer inhibitor; Mg = magnesium; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT = uridine diphosphate glucuronosyltransferase

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Management of People With HIV and Antiretroviral Therapy Experience

Virologic Failure

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Key Considerations and Recommendations
• Assessing and managing a person with HIV who is experiencing antiretroviral therapy (ART) failure can be complex. Expert advice can be critical and should be sought in many instances. • Evaluation of virologic failure should include an assessment of ART adherence, drug–drug and drug–food interactions, drug tolerability, HIV RNA level and CD4 T lymphocyte (CD4) cell count trends over time, ART history, and prior and current drug-resistance test results. • Drug-resistance testing should be performed while the person is taking the failing antiretroviral (ARV) regimen **(AI)** or within 4 weeks of discontinuing a non–long-acting ARV regimen **(AII).** If more than 4 weeks have elapsed since non–long-acting ARV regimens were discontinued, resistance testing still can provide useful information to guide therapy, although it may not detect previously selected resistance mutations **(CIII).** • For people who previously received long-acting (LA) cabotegravir (CAB) plus rilpivirine (RPV), or LA CAB/RPV, and present with virologic failure, resistance testing (including integrase strand transfer inhibitor [INSTI] genotypic testing) should be performed regardless of the time since the last dose of LA CAB/RPV **(AIII).** • The goal of treatment for people with HIV with drug resistance who are experiencing virologic failure is to establish virologic suppression (i.e., HIV RNA levels below the lower limits of detection of currently used assays) **(AI).** • A new ARV regimen should preferably include two fully active drugs if at least one has a high resistance barrier, such as a second-generation INSTI or a boosted protease inhibitor (PI) **(AI).** • A new ARV regimen can also include a second-generation INSTI (i.e., dolutegravir [DTG]) plus a boosted PI (preferably boosted darunavir) without nucleoside reverse transcriptase inhibitors (NRTIs) if both are fully active **(AI)**. • If the above two options are not feasible, a new ARV regimen that includes at least one drug with a high resistance barrier plus two partially active NRTIs—particularly tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF) with lamivudine (3TC) or emtricitabine (FTC)—can also be considered, although this is a less well-defined strategy and is based on an extrapolation of existing data. Caution with close monitoring of virologic response is advised **(BII),** as discussed below. • If no fully active drug with a high resistance barrier is available, every effort should be made to include three fully active drugs in the new ARV regimen **(AI).** • In general, adding a single ARV drug to a virologically failing regimen **is not recommended,** because this would rarely result in full virologic suppression and may risk the development of resistance to all drugs in the regimen **(BII).** • In some rare instances, it might not be possible to achieve maximal virologic suppression in people with HIV who are highly ART-experienced and have extensive drug resistance. In this case, ART should be continued **(AI)** with regimens that are designed to maintain CD4 counts, preserve treatment options, delay clinical progression, and minimize toxicity. • When it is not possible to construct a viable suppressive regimen for a person with multidrug-resistant HIV, the clinician should consider enrolling the person in a clinical trial of investigational agents or contacting pharmaceutical companies that may have investigational agents available.

- In people with HIV and virologic failure, it is crucial to provide continuous adherence support before and after ARV regimen changes.
- When switching an ARV regimen in a person with hepatitis B virus (HBV)/HIV coinfection, the person should remain on an ARV agent that is active against HBV and has a high resistance barrier to HBV (i.e., TAF, TDF, or entecavir) to avoid HBV rebound and hepatocellular damage **(AII)** (see Hepatitis B Virus/HIV Coinfection for more information).
- Discontinuing or briefly interrupting therapy may lead to a rapid increase in HIV RNA, a decrease in CD4 count, and an increase in the risk of clinical progression. Therefore, discontinuing or interrupting ART **is not recommended** in the setting of virologic failure **(AI).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Antiretroviral (ARV) regimens that are currently recommended for initial therapy in people with HIV have a high likelihood of achieving and maintaining plasma HIV RNA levels that are below the lower limits of detection (LLOD) of currently used assays (see Initial Combination Antiretroviral Regimens for People With HIV). People on antiretroviral therapy (ART) who do not achieve this treatment goal or who experience virologic rebound can develop resistance mutations to one or more components of their ARV regimen with possible cross-resistance to other ARVs. Adherence to ARV regimens can be challenging for some people with HIV, and poor adherence can result in detectable HIV RNA levels. The extent of drug resistance varies based on ARV treatment history, with some people having minimal or no resistance and others with extensive resistance. Managing people with extensive resistance is complex and usually requires consultation with an HIV expert. This section of the guidelines defines virologic failure in people on ART and discusses strategies to manage ART in these individuals.

Virologic Response Definitions

The following definitions are used in this section to describe the different levels of virologic response to ART.

- **Virologic suppression:** A confirmed HIV RNA level below the LLOD of available assays.
- **Virologic failure:** The inability to achieve or maintain suppression of viral replication to HIV RNA level <200 copies/mL.
- **Incomplete virologic response:** Two consecutive plasma HIV RNA levels ≥200 copies/mL after 24 weeks on an ARV regimen in a person who has not yet had documented virologic suppression on that regimen. A person's baseline HIV RNA level may affect the time course of response, and some regimens may take longer than others to suppress HIV RNA levels.
- **Virologic rebound:** After virologic suppression, confirmed HIV RNA level ≥200 copies/mL.
- **Virologic blip:** After virologic suppression, an isolated detectable HIV RNA level that is followed by a return to virologic suppression.
- **Low-level viremia:** Confirmed HIV RNA level above the LLOD but <200 copies/mL.

Antiretroviral Therapy Goals and Presence of Viremia While on Antiretroviral Therapy

The goal of ART is to suppress HIV replication to a level below which drug-resistance mutations cannot emerge. Although not conclusive, the evidence suggests that selection of drug-resistance mutations does not occur in people with HIV RNA levels that are persistently suppressed below the LLOD of current assays.[1]

Virologic blips are not usually associated with subsequent virologic failure.[2] In contrast, there is controversy regarding the clinical implications of low-level viremia, i.e., persistent HIV RNA levels between the LLOD and <200 copies/mL in people on ART. Viremia at this threshold is detected with some frequency by commonly used real-time polymerase chain reaction (PCR) assays, which are more sensitive than the PCR-based HIV RNA platforms used in the past.[3-5] Several retrospective studies support the supposition that virologic failure is more likely to occur in people with HIV RNA levels ≥200 copies/mL than in those with low-level viremia between 50 copies/mL and 199 copies/mL.[6-8] However, other studies have suggested that detectable viremia at <200 copies/mL can be predictive of virologic failure[9] and can be associated with the evolution of drug resistance[10] and non-AIDS morbidities.[11]

Persistent HIV RNA levels ≥200 copies/mL are often associated with evidence of viral evolution and accumulation of drug-resistance mutations.[12] This association is particularly common with HIV RNA levels >500 copies/mL.[13] Therefore, people who have persistent HIV RNA levels ≥200 copies/mL are considered to be experiencing virologic failure.

Causes of Virologic Failure

Virologic failure can occur for many reasons. Data from cohorts in the earlier era of combination ART suggested that suboptimal adherence and drug intolerance/toxicity are key contributors to virologic failure and regimen discontinuations.[14,15] Current ARVs are easier to tolerate and have less pill burden, which may improve adherence.[16-18] Virologic failure may be associated with a variety of factors, including the following:

HIV-Related Factors

- Presence of transmitted or acquired drug-resistant virus that may or may not be documented by current or past drug-resistance test results
- Prior ARV treatment failure
- Innate drug resistance to prescribed ARV drugs
- Higher pre-treatment HIV RNA levels (e.g., HIV RNA >100,000 copies/mL; some regimens may be less effective at higher levels)

Antiretroviral Regimen–Related Factors

- Suboptimal pharmacokinetics (PK) (e.g., variable absorption, metabolism, penetration into reservoirs)
- Suboptimal virologic potency

- Low barrier to resistance
- Reduced efficacy due to prior exposure to suboptimal regimens (e.g., monotherapy, dual–nucleoside reverse transcriptase inhibitor [NRTI] therapy, or the sequential introduction of drugs)
- Food requirements
- Drug–drug interactions with concomitant medications, which may reduce concentrations of the ARV drugs
- Adverse drug effects
- High pill burden and/or dosing frequency
- Prescription (prescribing or dispensing) errors

Social and Adherence-Related Factors

Note: Each of the social and adherence-related factors listed below are discussed in the Adherence to the Continuum of Care section.

- Active substance use, mental health disorders, or neurocognitive impairment
- Unstable housing and other psychosocial factors
- Missed clinic appointments
- Interruption of or intermittent access to ART
- Cost and affordability of ARV drugs, which may affect the ability to access or continue therapy (see the Cost Considerations and Antiretroviral Therapy section)

Managing People With HIV and Virologic Failure

If virologic failure is suspected or confirmed, a thorough assessment of whether one or more of the above factors could have been the cause(s) of failure is indicated. The causes of virologic failure can usually be identified but may not be obvious in some cases. Distinguishing among the causes of virologic failure is important, because the approaches to subsequent therapy may differ, depending on the cause. Potential causes of virologic failure should be explored in depth. Once virologic failure is confirmed, steps should be taken to improve virologic outcomes. If a new ARV regimen is needed, approaches to designing a new regimen are discussed below.

Key Factors to Consider When Designing a New Antiretroviral Regimen After Virologic Failure

General Principles on Antiretroviral Use in Virologic Failure

- When designing a new ARV regimen for a person with virologic failure, it is important to consider the factors outlined above on causes of virologic failure and, if possible, consider better tolerated and adherence-friendly regimens.
- A new ARV regimen should be selected based on ART history, current and previous drug-resistance test results, and whether a fully susceptible ARV drug with a high barrier to resistance and other fully active drugs are available.[9,19-31]

- ARV drugs with a high barrier to resistance are those in which emergent resistance is uncommon in people experiencing virologic failure. These include boosted darunavir (DRV), dolutegravir (DTG), and bictegravir (BIC).
- Fully active drugs may include—
  - Drugs in classes for which the person has not previously selected for drug-resistant virus.
  - Newer drugs in existing drug classes that are predicted to be fully active against HIV isolates despite the presence of resistance mutations for some drugs in the same drug class. For example, the non-nucleoside reverse transcriptase inhibitors (NNRTIs) etravirine and possibly doravirine (DOR), the protease inhibitor DRV, and the integrase strand transfer inhibitors (INSTIs) DTG and BIC. However, clinical data supporting the use of DOR or BIC in the setting of virologic failure are limited.
  - Drugs with novel mechanisms of action that the person with HIV has not received before, such as the post-attachment inhibitor ibalizumab (IBA), the gp120 attachment inhibitor fostemsavir (FTR), the capsid inhibitor lenacapavir (LEN), the fusion inhibitor enfuvirtide (T-20), or the CCR5 antagonist maraviroc (MVC) in people with no detectable CXCR4-using virus.
- ARV drugs with partial activity are those predicted to have antiviral activity but to a lesser extent than when there is no underlying drug resistance.
- Administering a drug that a person has never used does not ensure that the drug will be fully or partially active; the potential exists for cross-resistance among drugs from the same class.
- Discontinuing or briefly interrupting therapy in a person with viremia **is not recommended** because it may increase HIV RNA levels, decrease CD4 T lymphocyte (CD4) cell count, and increase the risk of clinical progression **(AI)**[32,33] (see Discontinuation or Interruption of Antiretroviral Therapy).
- The presence of preexisting (transmitted) drug resistance also may lead to virologic failure.[34,35]

Drug-Resistance Testing to Guide New Antiretroviral Regimens

- The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends that drug-resistance testing should be used to guide ARV regimen design and should be performed while the person with HIV is still taking the failing regimen **(AI)** or within 4 weeks of discontinuation of a non–long-acting regimen **(AII).** If more than 4 weeks have elapsed since discontinuation of a non–long-acting regimen, drug-resistance testing still may provide useful information to guide therapy, although it may not detect previously selected resistance mutations **(CIII).**
- Drug-resistance testing is recommended in persons with confirmed virologic failure, i.e., HIV RNA repeatedly >200 copies/mL (**AI** for >1,000 copies/mL, **AIII** for 501–1,000 copies/mL, **CIII** for confirmed 201–500 copies/mL), although at low HIV RNA levels, testing may be difficult to obtain outside of a research setting. In persons with HIV RNA >200 copies/mL but <500 copies/mL, testing may be unsuccessful, but it still should be considered.
- Drug resistance is cumulative, meaning that once a mutation is detected in a resistance assay, it should be considered present in that person's HIV thereafter (this is sometimes referred to as "archived" resistance), regardless of whether it appears on subsequent drug-resistance assays.

Thus, clinicians should evaluate the extent of drug resistance, taking into account all of the person's ART history and, importantly, prior genotypic- or phenotypic-resistance test results.

- Activity of ART based on current and cumulative genotypic mutations can be estimated by tools and interpretation algorithms, such as the Stanford University HIV Drug-Resistance Database. Also see Drug-Resistance Testing.
- Some drug-resistance assays only detect resistance to NRTIs, NNRTIs, or protease inhibitors (PIs); INSTI-resistance testing may need to be ordered separately. INSTI-resistance testing should be ordered in people who experience virologic failure on an INSTI-based regimen. Additional drug-resistance tests for people who experience failure on a fusion inhibitor **(AII),** and viral tropism tests for people who experience failure on a CCR5 antagonist **(BIII)** are also available. There is currently no commercially available resistance test for IBA, FTR, or LEN (see Drug-Resistance Testing).

Strategies for New Antiretroviral Regimen Design

- A new ARV regimen should preferably include two fully active drugs if at least one has a high resistance barrier, such as a second-generation INSTI or a boosted PI **(AI).**[36]
- A new ARV regimen can also include a second-generation INSTI (e.g., DTG) plus a boosted PI (preferably boosted DRV) without NRTIs if both are fully active **(AI);**[37-41] see more detailed discussion in *Managing Virologic Failure in Different Clinical Scenarios* below. If this regimen is used in people with hepatitis B virus (HBV)/HIV coinfection, an HBV-active drug with a high barrier to resistance (e.g., tenofovir alafenamide [TAF], tenofovir disoproxil fumarate [TDF], or entecavir) should be continued or started to avoid HBV rebound and hepatocellular damage.
- If the above two options are not feasible, a new ARV regimen can also include a fully active drug with a high resistance barrier plus two partially active NRTIs—particularly TAF or TDF with lamivudine (3TC) or emtricitabine (FTC)—though this is less well-defined and close monitoring is advised **(BII);** this is discussed in more detail in *Managing Virologic Failure in Different Clinical Scenarios* below.[36,37,42,43]
- If no fully active drug with a high resistance barrier is available, every effort should be made to include three fully active drugs in the regimen **(AI).** See the clinical scenarios below for further guidance on the number of fully active drugs a regimen should contain.
- Despite the presence of drug-resistance mutations, some ARV drugs in the regimen may still have partial activity against the person's HIV and may be retained as part of a salvage regimen. These drugs may include NRTIs, PIs, and second-generation INSTIs, although dosing of some drugs (e.g., DRV and DTG) may need to be increased when treating people with relevant resistance mutations to achieve drug concentrations necessary to be at least partially active against a less sensitive virus.[44-46]
- In contrast, other agents in which resistance may be expected should be discontinued, because their continued use is unlikely to contribute to virologic suppression. These drugs include NNRTIs (especially efavirenz, nevirapine, and rilpivirine [RPV]), the first-generation INSTIs raltegravir (RAL) and elvitegravir (EVG), and T-20.[47-49]
- Long-acting (LA) cabotegravir (CAB)/rilpivirine (RPV) is currently approved as a complete ART regimen for individuals engaged in care who have good adherence to an oral regimen, sustained undetectable HIV RNA levels for >3 months, no known or suspected resistance to

either drug, and no active HBV infection. To date, no large or randomized clinical trials have been published using any INSTI plus NNRTI, including LA CAB/RPV, as a complete regimen for people without viral suppression. However, a few small observational studies have shown that people with viremia despite intensive efforts on oral ART, without resistance to CAB or RPV, can achieve viral suppression with LA CAB/RPV when intensive supportive services are available.[50-53] If considering LA CAB/RPV in this population, it is important to note that data are limited, and this is not an approved indication of the regimen. If the regimen is used in people with inconsistent adherence and virologic failure, there is a high likelihood of developing acquired resistance to CAB and/or RPV, which might limit future treatment options. The approaches and considerations for the use of LA CAB/RPV in people with viremia is further outlined below.

- When changing an ARV regimen in a person with HBV/HIV coinfection, ARV drugs that are active against HBV (especially TAF or TDF) should be continued as part of the new regimen or, if not possible, entecavir should be initiated **(AII).** Using 3TC or FTC as the only drug with HBV activity in a regimen **is not recommended (AII)** because HBV resistance to these drugs can emerge. Discontinuation of these drugs may lead to the reactivation of HBV, which may result in serious hepatocellular damage (see Hepatitis B Virus/HIV Coinfection).
- Virologic responses should be closely monitored after regimen switch (e.g., HIV RNA level testing performed within 4 to 8 weeks), with prompt drug-resistance testing if virologic response is inadequate.

Managing Virologic Failure in Individuals With Different Levels of Viremia

People with HIV and detectable HIV RNA levels while on ART comprise a heterogeneous group of individuals with different ART exposure histories, degrees of drug resistance, durations of virologic failure, and levels of plasma viremia. Management strategies should be individualized. The first steps are to confirm the level of HIV viremia and to assess and address adherence and potential drug–drug interactions (including interactions with over-the-counter products and supplements) and drug–food interactions. Some general approaches based on the level of viremia are addressed below.

- **Low-level viremia (HIV RNA above the LLOD and <200 copies/mL):** People who have these HIV RNA levels do not typically require a change in treatment **(AII).**[4] Although there is no consensus on how to manage these individuals, the risk that drug resistance will emerge is believed to be relatively low. Therefore, these individuals should continue their current regimens and have their HIV RNA levels monitored at least every 3 months to assess the need for changes to ART in the future **(AIII).**
- **HIV RNA ≥200 copies/mL and <1,000 copies/mL:** In contrast to people with detectable HIV RNA levels that are persistently <200 copies/mL, people with levels that are persistently ≥200 copies/mL often develop drug resistance, particularly when HIV RNA levels are >500 copies/mL.[6,7] People who have persistent plasma HIV RNA levels in the range of 200 copies/mL to 1,000 copies/mL are considered to be experiencing virologic failure, and drug-resistance testing should be attempted, particularly in people with HIV RNA levels >500 copies/mL (at <500 copies/mL, testing may not be possible for technical reasons). Management approaches should be the same as for people with HIV RNA >1,000 copies/mL (as outlined below). When drug-resistance testing cannot be performed because of low HIV RNA levels, the decision of whether to empirically change ARV drugs should be made on a case-by-case basis, taking into account whether a new regimen that is expected to fully suppress viremia

can be constructed. If genotypic-resistance test results cannot be obtained because of low HIV RNA levels, proviral DNA genotypic testing may be considered. Results from this test should be interpreted with caution because these assays might miss some or all previously existing drug-resistance mutations. However, mutations that are detected using proviral DNA genotypic testing may be significant and can affect the effectiveness of future regimens (see Drug-Resistance Testing).

- **HIV RNA ≥1,000 copies/mL and no drug-resistance mutations identified using current or previous genotypic-resistance test results:** This scenario is almost always associated with suboptimal adherence. A thorough assessment should be conducted to evaluate the level of adherence, identify and address the underlying cause(s) for incomplete adherence and, if possible, simplify the regimen (e.g., decrease pill count, simplify food requirement or dosing frequency; see Adherence to the Continuum of Care). Assessment includes the following:
    - Assessing the person's access to ART, including access to pharmacy, refills, and copays or patient assistance programs, and seeking assistance to overcome any barriers to consistent access to ART.
    - Assessing social determinants that may impact adherence (e.g., substance use, unstable housing, mental health challenges, etc.).
    - Assessing the person's tolerance of the current ARV regimen and the severity and duration of side effects if intolerance is a concern, while considering that even minor side effects can affect adherence.
    - Addressing intolerance by treating symptoms (e.g., with antiemetics or antidiarrheals), switching one ARV agent in a regimen to another agent in the same drug class, or switching from one drug class to another class (e.g., from an NNRTI to a PI or an INSTI; see Adverse Effects of Antiretroviral Agents).
    - Reviewing food requirements for each medication and assessing whether the person adheres to the requirements.
    - Assessing whether a recent history of gastrointestinal symptoms (e.g., vomiting, diarrhea) may result in short-term malabsorption.
    - Reviewing concomitant medications (including over-the-counter medications and dietary supplements) for possible adverse drug–drug interactions (consult Drug–Drug Interactions and Tables 24a through 25b for common interactions) and, if possible, making appropriate substitutions for ARV agents and/or concomitant medications.
    - Considering therapeutic drug monitoring if PK drug–drug interactions (e.g., when used with rifamycin) or impaired drug absorption (e.g., using polyvalent cations with an INSTI) leading to decreased ARV drug exposure is suspected.
    - Considering the timing of the drug-resistance test (e.g., was the person mostly or completely nonadherent to oral ART for >4 weeks before testing?) (see Drug-Resistance Testing).
    - After a thorough assessment, the following approaches may be considered:
        - If the current regimen is well tolerated, with no significant drug–drug or drug–food interactions, it is reasonable to continue the same regimen while focusing on improving adherence.

  - If the agents are poorly tolerated or have important drug–drug or drug–food interactions, changing the regimen to an equally effective but more tolerable regimen should be considered.
  - HIV RNA level testing should be repeated 4 to 8 weeks after treatment adherence is encouraged or treatment is modified **(AII);** if RNA levels remain >200 copies/mL, genotypic drug-resistance testing should be performed to determine whether a resistant viral strain has emerged (**AI** for >1,000 copies/mL, **AIII** for 501–1,000 copies/mL, **CIII** for 201–500 copies/mL), though at low RNA levels, testing may be difficult to obtain outside of a research setting.

- **HIV RNA >1,000 copies/mL and drug resistance identified:** If new or previously detected resistance mutations compromise the regimen, the regimen should be modified as soon as possible to avoid progressive accumulation of resistance mutations.[54] In addition, several studies have shown that virologic responses to new and fully active regimens are greater in individuals with lower HIV RNA levels and/or higher CD4 counts at the time of regimen changes; thus, the change is best done before viremia worsens or before CD4 count declines.[9,55] The availability of newer ARV drugs, including some with new mechanisms of action, makes it possible to suppress HIV RNA levels to below the LLOD in most people with HIV. The options in this setting depend on the extent of drug resistance and are addressed in the clinical scenarios outlined below.

Managing Virologic Failure in Different Clinical Scenarios

Note: See Table 10 below for a summary of these recommendations.

Virologic Failure on the First Antiretroviral Regimen

The Panel recommends that drug-resistance testing should be performed upon treatment failure to inform regimen design **(AI).**

NNRTI plus NRTI regimen failure: Although an NNRTI plus NRTI regimen is no longer considered a preferred first-line ART option in treatment guidelines, data from clinical trials comparing different ARV regimens after NNRTI plus NRTI failure provide the most robust evidence to inform second-line treatment strategies and, therefore, are included here.

In this setting, people with HIV often have viral resistance to the NNRTI, with or without the M184V/I mutation, which confers high-level resistance to 3TC and FTC. Additional NRTI mutations also may be present. Below are some treatment options.

- **Second-generation INSTI (BIC or DTG) plus NRTIs:** The Panel recommends that fully active DTG plus two NRTIs, at least one of which is fully active, can be a treatment option after failure of a first-line NNRTI-based therapy **(AI).** BIC, which is available only in a combination pill with FTC/TAF, also has a high resistance barrier and may have similar activity to that of DTG in this setting, and is also an option **(AIII);** however, no clinical trial data for this strategy with BIC is available. If at least one fully active NRTI cannot be assured and a clinician wants to avoid using a boosted PI or a drug from other classes, a regimen that includes fully active DTG plus two NRTIs that are estimated to be only partially active (particularly TAF or TDF with 3TC or FTC) can be considered, with caution and close monitoring of viral response, as further discussed below **(BII).**

In the DAWNING trial, participants from 13 countries who experienced virologic failure while on a first-line NNRTI-based regimen were randomized to receive either lopinavir/ritonavir(LPV/r) or DTG, each with two NRTIs, one of which had to be fully active based on real-time drug-resistance testing. The study was stopped early after an interim analysis showed that the DTG arm was superior to the LPV/r arm. The superiority of DTG was somewhat counterbalanced by the finding that 2 of 11 participants in the DTG arm who met virologic withdrawal criteria selected for INSTI resistance, with no PI resistance selected for in the LPV/r arm.[36]

In the NADIA trial, participants in Uganda, Kenya, and Zimbabwe who experienced virologic failure while on a first-line NNRTI plus TDF and 3TC or FTC were randomized to receive either darunavir/ritonavir (DRV/r) or DTG, each with 3TC; participants were assigned by a second randomization to receive a third ARV, either TDF or zidovudine (ZDV). Unlike the DAWNING study, full activity of the NRTIs based on genotype testing at the time of switch was not required.[42,43] The primary study outcome was virologic suppression <400 copies/mL; at 48 and 96 weeks, >85% of participants had HIV RNA levels <400 copies/mL in all arms, and the DTG-based regimens were non-inferior to the DRV/r-based regimens. However, at 96 weeks, 9 of 235 (4%) participants in the DTG group developed DTG resistance. This represented 45% of participants in the DTG group with HIV RNA levels >400 copies/mL, six of whom were assigned to ZDV. In contrast, no PI resistance was selected for in the DRV/r group. When comparing TDF with ZDV, the two NRTIs demonstrated virologic suppression noninferiority at 48 weeks, but TDF was superior to ZDV at 96 weeks. These results included 84 of 92 (91%) participants in the DTG group who had virologic suppression <400 copies/mL despite no predicted active NRTIs at the time of failure of first-line NNRTI-based regimens, and a large proportion of this group had the K65R and M184V/I mutations. Individual-level drug-resistance data would have enabled further examination of specific mutation patterns and their association with patient characteristics and treatment outcomes. Although such data are not available, these results suggest that ZDV should not be used over TDF in a public health approach. The decision to use DTG or DRV/r without another fully active drug should balance the overall efficacy data of these regimens, with considerations for potential emergent drug resistance, drug–drug interactions, convenience, and tolerability. The results from these studies should be interpreted with caution, as individual-level drug-resistance data and their linkage to patient characteristics and outcomes were not available, thus preventing full interpretation of these results. Additionally, these results may not be generalizable to settings and populations outside of the trials due to differences in geography, HIV-1 subtype, study population, ART availability, and treatment monitoring practice.

- **Boosted PI plus NRTIs:** The Panel recommends that a boosted PI (preferably boosted DRV) plus two NRTIs, at least one of which is fully active, can be an option after failure of a first-line NNRTI-based therapy **(AI).** However, if full activity of at least one NRTI in the regimen cannot be assured, fully active boosted DRV plus two NRTIs estimated to be only partially active (particularly TAF or TDF with 3TC or FTC) can be considered, with close monitoring **(BII).** Notably, boosted PIs as monotherapy **are not recommended (AI).**[37,39,40,42,43,56]

  Several large, randomized controlled trials (primarily conducted in resource-limited settings where NNRTI-based regimens have been used as first-line therapy) have explored different second-line regimen options. The studies found that regimens that contained LPV/r or DRV/r plus at least two NRTIs were as effective as regimens that contained LPV/r plus RAL or DTG plus two NRTIs. Participants in some of these studies did not undergo drug-resistance testing before randomization. In the NADIA trial (summarized above), virologic efficacy of DTG and DRV/r-based regimens were non-inferior at 48 and 96 weeks, with TDF being non-inferior at

48 weeks and superior at 96 weeks compared with ZDV. Although there were nine participants in the DTG group who developed DTG resistance (six on ZDV and three on TDF), no participant in the DRV/r group developed PI resistance. Additionally, 74 of 80 (93%) participants in the DRV/r group had virologic suppression <400 copies/mL at 96 weeks despite no predicted active NRTIs at the time of failure of first-line NNRTI-based regimens. As outlined above in the discussion about second-generation INSTI plus no estimated fully active NRTIs based on current drug-resistance algorithms, these results should be interpreted with caution within, and particularly beyond, the study populations and settings.

- **Boosted PI plus an INSTI:** The Panel recommends that boosted DRV plus DTG, both with high barriers to resistance, should be the preferred boosted PI plus INSTI option **(AI).** In a setting where a two-drug boosted PI and INSTI combination are being considered and both boosted DRV and DTG cannot be used, LPV/r plus RAL can be a treatment option for those who experienced virologic failure on an NNRTI-based regimen **(CI).**

  D^2EFT is an open-label multinational randomized controlled trial that assessed the efficacies of DRV/r plus DTG versus DTG plus two NRTIs versus standard of care (DRV/r plus two NRTIs) for participants with first-line failure of an NNRTI-based regimen.[41] In D^2EFT, TDF plus 3TC or FTC were the NRTIs used. At 48 weeks, the proportion of participants who achieved HIV RNA <50 copies/mL was 84% for the DRV/r + DTG arm, 75% for the DRV/r plus two NRTI arm, and 78% for the DTG plus two NRTI arm, showing that the DRV/r + DTG arm was non-inferior to the other two regimens, with more participants achieving viral suppression. Several other small retrospective studies have found that a regimen of boosted DRV plus DTG is effective in achieving viral suppression in people with documented resistance to multiple drug classes.[57-59] Three randomized controlled trials have found that a regimen that consisted of LPV/r plus RAL can be as effective as LPV/r plus at least two NRTIs as second-line therapy for people who failed first-line ART (mostly with an NNRTI-based regimen).[37,39,40]

  If this regimen is used in people with HBV coinfection, an HBV-active drug with a high barrier to resistance (i.e., TAF, TDF, or entecavir) should be continued or started to avoid HBV rebound and hepatocellular damage.

Boosted PI plus NRTI regimen failure: In this scenario, because boosted PI has a high barrier to resistance, most people will have either no resistance or resistance that is limited to 3TC and FTC, though additional NRTI mutations also may be present.[60,61] Failure in this setting is often attributed to poor adherence, drug–drug interactions, or drug–food interactions. Below are some management options.

- **Switch to a second-generation INSTI plus NRTIs regimen:** Second-generation INSTIs have increasingly become preferred options over boosted PIs due to lower drug–drug interaction potential, improved tolerability, comparable efficacy, and a high barrier to resistance. Therefore, consideration should be given to switching to DTG or possibly BIC plus two NRTIs (if at least one of them is fully active) **(AIII).** If only one of the NRTIs is fully active or if adherence is a concern, DTG is currently preferred over BIC **(AIII).** If full activity of at least one NRTI in the regimen cannot be assured, DTG plus two NRTIs estimated to be only partially active based on current drug-resistance algorithms (particularly TAF or TDF with 3TC or FTC) can be considered **(CIII).** As outlined above, results from studies that may suggest such extrapolations should be interpreted with caution, as they did not involve failure of first-line boosted PI plus NRTIs regimens and as individual-level drug-resistance data and their linkage to patient characteristics and outcomes were not available, thus preventing full interpretation of these results. Additionally, these results may not be generalizable to settings and populations

outside of the trials due to differences in geography, HIV-1 subtype, patient population, ART availability, and treatment monitoring practice.

- **Maintain the same regimen:** A systematic review of multiple randomized trials that investigated the failures of first-line ritonavir-boosted PI-based regimens showed that taking actions to improve adherence to the original regimen is as effective as changing to new regimens with or without drugs from new classes **(AII).**[62] If the regimen is well tolerated with no concerns about drug–drug or drug–food interactions or drug resistance, then the regimen can be continued with adherence support and viral monitoring.
- **Switch to another PI-based regimen:** If a regimen with an INSTI plus two NRTIs is not an option and poor tolerability is contributing to virologic failure, the regimen can be modified with a different boosted PI that has no evidence for cross-resistance, plus a second-generation INSTI **(AIII),** or plus two NRTIs (at least one of which is fully active) **(AIII).** If full activity of at least one NRTI in the regimen cannot be assured, another fully active boosted PI plus two NRTIs estimated to be only partially active (particularly TAF or TDF with 3TC or FTC) can be considered, with close monitoring of viral response **(BIII).**

INSTI plus NRTI regimen failure: Virologic failure in people on a regimen that consists of RAL or EVG plus two NRTIs may be associated with emergent resistance to 3TC or FTC (with/without additional NRTI mutations) and, possibly, the INSTI.[63] Viruses with EVG or RAL resistance often remain susceptible to DTG and BIC.[55] However, in the presence of certain INSTI mutations, DTG dose should be increased from once daily to twice daily.[44] The effective dose of BIC in these situations is unknown. In contrast, in clinical trials, people who experienced virologic failure while receiving DTG or BIC plus two NRTIs as first-line therapy were unlikely to develop resistance to DTG or BIC.[63-65] No existing clinical trial data guide therapy for first-line INSTI failures; therefore, treatment strategy should be based on drug-resistance test results and the potential potency of the next regimen. Below are some treatment options, based on drug-resistance pattern considerations.

- **Virologic failure without any resistance mutations:** The person with HIV should be managed as outlined above in the section on virologic failure without drug resistance.
- **Virologic failure without INSTI resistance:** The regimen can be modified to one of the following:
  - A boosted PI plus two NRTIs (preferably at least one of which is fully active) **(AIII);** *or*
  - DTG, or likely BIC, plus two NRTIs (preferably at least one of which is fully active) **(AIII);** *or*
  - A boosted PI plus DTG **(AIII).**
- **Virologic failure with resistance to RAL and/or EVG but susceptibility to DTG:** The regimen can be modified to one of the following:
  - A boosted PI plus two NRTIs (preferably at least one of which is fully active) **(AIII);** *or*
  - DTG (twice daily) plus two NRTIs (at least one of which is fully active) **(BIII);** *or*
  - DTG (twice daily) plus a boosted PI **(AIII).**

Although BIC has a high resistance barrier, there are no data on whether the current BIC dose is efficacious in settings with RAL or EVG resistance and, therefore, it **is not currently recommended (BIII).**

INSTI plus NNRTI regimen failure: Virologic failure in people on a regimen that consists of an INSTI (e.g., DTG or CAB) plus an NNRTI (e.g., RPV) may be associated with resistance to one or both of the medications in the regimen.[66,67] Experience to guide therapy upon failure of these regimens is limited. Therefore, treatment strategies should be based on past treatment history, drug-resistance test results, and the potential potency of the next regimen, based on the guidance provided above.

Second-Line Regimen Failure and Beyond

Drug resistance with fully active commonly used ARV drug options: Using a person's complete ARV treatment history and drug-resistance data, a clinician can decide whether to include a fully active boosted PI or INSTI in future regimens. For example, those who have no documented PI resistance and who have never been treated with an unboosted PI likely harbor virus that is fully susceptible to PIs. Similarly, people who have no documented INSTI resistance and who have never been treated with an INSTI are likely to have virus susceptible to DTG or BIC. In this setting, virologic suppression should be achievable using a boosted PI plus either two NRTIs (preferably at least one of which is fully active), a boosted PI plus an active INSTI, or DTG or BIC plus two NRTIs (preferably at least one of which is fully active). Drugs should be selected based on the likelihood that they will be fully active, as determined by the person's treatment history, past and present drug-resistance testing, and tropism testing if a CCR5 antagonist is being considered.

Multidrug resistance without fully active commonly used ARV drug options: Use of currently available ARV drugs has resulted in a dramatic decline in the number of people with HIV who have few treatment options because of multiclass drug resistance.[68,69] Despite this progress, some people have experienced toxicities with and/or developed resistance to most currently available commonly used ARV drugs. Maximal virologic suppression should remain the goal; however, if it cannot be achieved, the goals of ART will be to preserve immunologic function, prevent clinical progression, and minimize the development of further resistance that may compromise future regimens.

Consensus on the optimal management of people with multidrug-resistant HIV is lacking. If neither a fully active boosted PI nor a second-generation INSTI (e.g., DTG or BIC) is available, the new regimen should include at least two, and preferably three, fully active agents. If less than three fully active drugs are available, the regimen should include as many fully active drugs as possible, along with potentially partially active agents **(BII).** If resistance to NNRTIs, T-20, MVC, BIC, DTG, CAB, EVG, or RAL are identified, there is rarely a reason to continue using these drugs, because there is little evidence that keeping them in the regimen helps delay disease progression **(BII).** Moreover, continuing these drugs (in particular, early-generation INSTIs) may allow selection of additional resistance mutations and development of within-class cross-resistance that may limit future treatment options. It should be noted that even partial virologic suppression of HIV RNA to >0.5 $\log_{10}$ copies/mL from baseline correlates with clinical benefit.[68,70] Cohort studies provide evidence that even in the presence of viremia and no improvement in CD4 count, continuing ART reduces the risk of disease progression.[71] Other cohort studies suggest that even modest reductions in HIV RNA levels continue to confer immunologic and clinical benefits.[72,73] However, these potential benefits must be balanced with the ongoing risk of accumulating additional resistance mutations. In general, adding a single, fully active ARV drug to the regimen **is not recommended** because of the risk of rapid development of resistance **(BII).**

People with HIV and ongoing detectable viremia who lack sufficient treatment options due to an inability to construct a fully suppressive regimen with common ARVs may be candidates for the

first-in-class CD4 post-attachment inhibitor IBA,[74] the gp120-directed attachment inhibitor FTR,[75] and/or the capsid inhibitor LEN.[76]

- **Ibalizumab (IBA)** is a long-acting CD4 post-attachment inhibitor that is given intravenously every 2 weeks. A single-arm, multicenter clinical trial enrolled 40 heavily ART-experienced participants who had multidrug-resistant HIV-1 and who were experiencing virologic failure on an ARV regimen. Subjects received intravenous IBA infusions every 2 weeks, in addition to an optimized background regimen (OBR) that included at least one additional agent to which the subject's virus was susceptible. At Week 24, 43% of participants achieved HIV RNA <50 copies/mL, and 50% achieved HIV RNA <200 copies/mL.[77] Of the 27 participants who continued to the 48-week follow-up study, 59% and 63% had HIV RNA <50 copies/mL and <200 copies/mL, respectively. All 15 participants who had HIV RNA <50 copies/mL at Week 24 maintained virologic suppression up to Week 48.[78]
- **Fostemsavir (FTR)** is a gp120 attachment inhibitor that is given orally twice daily. A Phase 3 multicenter trial enrolled 371 heavily ART-experienced participants who had multidrug-resistant HIV-1 and who were experiencing virologic failure. Participants were enrolled into two cohorts, according to their remaining treatment options. The randomized cohort (n = 272) included those with at least one fully active approved ARV drug in at least one but no more than two classes. These individuals were randomized to FTR (oral 600 mg twice daily) or placebo for 8 days, followed by open-label FTR plus OBR. In the nonrandomized cohort (n = 99), participants with no remaining ARV options were started on open-label FTR (oral 600 mg twice daily) plus OBR on Day 1. The primary endpoint for the randomized cohort was a change in HIV RNA level from baseline at Day 8. In the FTR group, the mean RNA level decrease was 0.79 $\log_{10}$ copies/mL compared to 0.17 $\log_{10}$ copies/mL in the placebo group ($P < 0.001$). At Week 96, 60% of participants in the randomized cohort and 37% of those in the nonrandomized cohort had HIV RNA levels <40 copies/mL, with mean CD4 increases of 205 cells/mm^3 and 119 cells/mm^3, respectively.[79,80] In this study, 15 individuals in the nonrandomized cohort used the CD4 post-attachment inhibitor IBA in combination with FTR and other ARVs. The virological response rate for these participants by snapshot analysis was 53% at Week 48 and 33% at Week 96.
- **Lenacapavir (LEN)** is a LA HIV capsid inhibitor that can be given by one of two initiation schemes (oral plus subcutaneous [SQ] dosing), followed by SQ injections every 6 months (see Appendix B, Table 11 for dosing details).

  A Phase 3 multicenter trial (CAPELLA) enrolled 72 heavily ART-experienced participants who had multidrug-resistant HIV-1 and experienced virologic failure into two cohorts.[81] Cohort 1 (n = 36) included participants who had a <0.5 $\log_{10}$ HIV-1 RNA decline between screening and baseline (i.e., stable viremia at ≥400 copies/mL, confirming lack of response to the failing therapy). The participants were randomized 2:1 to either oral LEN or placebo (on Days 1, 2, and 8) and continued to receive the failing ARV regimen for 14 days to evaluate the virologic effect of LEN functional monotherapy. Starting on Day 15, all participants began on an OBR; those randomized to oral LEN began SQ LEN every 6 months, whereas participants in the placebo arm received oral LEN on Days 15, 16, and 22 followed by SQ LEN on Day 29 (14 days after the first oral LEN dose) and then every 6 months. On Day 15, 88% of participants in the LEN arm and 17% in the placebo arm had HIV RNA level reduction of ≥0.5 $\log_{10}$ copies/mL, with least-squares mean change in HIV RNA level of −2.1 $\log_{10}$ copies/mL versus −0.07 $\log_{10}$ copies/mL for the LEN and placebo arms, respectively ($P < 0.001$). At the end of 26 weeks (i.e., after one dose of SQ LEN), 81% of participants had RNA levels <50 copies/mL, and 89% had RNA levels <200 copies/mL, with a mean change in RNA level of −2.58 ± 1.04 $\log_{10}$ copies/mL.[81] At the end

of 52 weeks (i.e., after two doses of SQ LEN), 83% of participants had RNA levels <50 copies/mL, with 94% of those with at least two active OBR drugs and 67% with no active OBR drugs. The mean CD4 cell count change at 52 weeks[76] was +82 cells/mm^3.

Cohort 2 (n = 36) was a nonrandomized cohort that included participants who either had a ≥0.5 $\log_{10}$ HIV-1 RNA decline from screening to baseline visit or were enrolled after Cohort 1 reached its planned sample size. All participants were started on an OBR and received oral LEN on Days 1, 2, and 8; on Day 15, SQ LEN was started and given every 6 months. After 26 weeks, 83% of the participants had HIV RNA levels <50 copies/mL, and 86% had HIV RNA levels <200 copies/mL. At Week 52, 72% had RNA levels <50 copies/mL, and the mean CD4 cell count change was +113 cells/mm^3.

Oral lead-in therapy was well tolerated overall, with nausea reported in 13% of participants who received LEN. Injection site reactions, which were generally mild and transient, were reported in 63% of the participants.[81]

Twenty-two of 72 (31%) participants met the criteria for resistance testing at confirmed virologic failure through Week 52.[76] LEN-associated capsid resistance mutations were found in 9 of the 22 (41%) participants with confirmed virologic failure. The M66I mutation was the most common mutation, reported in six participants. Four of the nine participants with LEN-associated capsid resistance mutations had no active agent in the OBR. Four others had low plasma concentrations of the OBR drugs at Week 26, suggesting poor adherence of the self-administered OBR, resulting in an unfavorable LEN functional monotherapy.[82]

Taken together, these data[76,82,83] highlight the importance of selecting a robust OBR to support LEN and counseling about adherence to the OBR. Additionally, LEN is a moderate CYP3A4 inhibitor and may increase concentrations of some coadministered drugs, whereas LEN concentration may be significantly decreased in the presence of a strong CYP3A4 inducer (see Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs for further details). Therefore, people with HIV should be routinely counseled to inform all their health care providers of all medications they are taking, including LEN, even though it is not taken daily. Potential drug–drug interactions should be discussed, particularly before a new drug is started, to minimize the risk of toxicities, nonadherence, and drug resistance.

People with HIV who continue to have detectable viremia and who lack sufficient treatment options to construct a fully suppressive regimen also may be candidates for research studies or expanded access programs, or they may qualify for single-person access to an investigational new drug, as specified in the U.S. Food and Drug Administration's Physician Request for a Single Patient Investigational New Drug for Compassionate or Emergency Use. Information about ARV agents that are in clinical studies can be found in the drug database available on the Clinicalinfo website.

People With HIV on ART With Suspected Drug Resistance Who Present With Limited Information (Incomplete or No Self-Reported ARV History, Medical Records, or Drug-Resistance Test Results)

Every effort should be made to obtain the person's ARV history and prior drug-resistance test results; however, this may not always be possible. One strategy is to restart the most recent ARV regimen and assess drug resistance in 2 to 4 weeks to guide the selection of the next regimen. Another strategy is to start two or three drugs that are predicted to be fully active based on the person's treatment history. If no ARV history is available, a clinician may consider using agents with a high barrier to resistance—such as twice-daily DTG, BIC (which is available only in a combination pill

with FTC/TAF and for which dosage in this setting is unclear), and/or twice-daily boosted DRV—as part of the regimen. Regardless of which strategy is employed, people should be closely monitored for virologic response (e.g., HIV RNA level testing approximately 4 to 8 weeks after reinitiation of therapy), with prompt drug-resistance testing performed if virologic response is inadequate.

People With HIV Who Are Unable to Achieve Viral Suppression Due to Poor Adherence to Oral ART and Who Do Not Have Resistance to Cabotegravir and Rilpivirine

Based on very limited data discussed below, the Panel recommends the use of LA CAB/RPV on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral ART, who have no evidence of resistance to RPV or CAB, and with shared decision-making between providers and people with HIV **(CIII).**

Some people with HIV cannot reach or maintain viral suppression on oral ART despite intensive adherence support. Although a complete LA injectable regimen may overcome some adherence obstacles for people with viremia, long-term clinical efficacy data are limited in these circumstances and the regimen is only approved for people who are virologically suppressed for at least 3 months. No large, published randomized controlled trial has demonstrated the efficacy of a complete regimen of any INSTI plus NNRTI, including LA CAB/RPV, in people with viremia. However, cohort data are emerging, resulting in two possible approaches to use LA CAB/RPV in this population. If achieving viral suppression with oral ART is possible with intensive adherence support to oral ART, switching to LA CAB/RPV after viral suppression can serve as a goal to incentivize the person to adhere to the oral regimen. Data from the Long-Acting Therapy to Improve Treatment Success in Daily Life (LATITUDE) AIDS Clinical Trial Group (ACTG) A5359 study using this strategy is discussed in Approach #1 below.[84] If achieving viral suppression with oral ART is not possible despite intensive adherence support to oral ART, switching to LA CAB/RPV without viral suppression may be an option in certain circumstances, as discussed in Approach #2 below.

Approach #1: Intensive efforts to achieve viral suppression prior to switching to LA CAB/RPV

Because all of the large LA CAB/RPV studies enrolled participants who were adherent to ART with sustained viral suppression, every effort should be made to achieve viral suppression before considering a switch to LA CAB/RPV, even in people with poor adherence. The Phase 3 prospective, randomized, open-label LATITUDE study was designed to assess this strategy in people who faced challenges with ART adherence. Preliminary data have been presented from this study that enrolled individuals without resistance to CAB or RPV from 33 sites in the United States and Puerto Rico.[84] Participants received adherence support and conditional economic incentives to assist in achieving viral suppression on oral ART. Study participants who experienced viral suppression were randomized to continue oral ART or switch to LA CAB/RPV every 4 weeks. At a planned data safety monitoring board (DSMB) interim efficacy analysis, only 294 (68%) of the 434 participants enrolled achieved viral suppression and were eligible for randomization, with 146 assigned LA CAB/RPV and 148 continuing standard of care (SOC) oral ART. At randomization, it was noted that despite the intensive adherence support, 17% in the LA CAB/RPV arm and 7% in the SOC arm had HIV RNA >200 copies/mL. At Week 48 of the randomized phase, 24% in the LA CAB/RPV arm and 39% in the SOC arm met the primary endpoint of earliest confirmed virologic failure or treatment discontinuation, which did not meet the predefined stringent stopping criteria. However,

two secondary endpoints—virologic failure alone (7% in LA CAB/RPV vs. 25% in SOC) and treatment-related failure (defined as first virologic failure or discontinuation due to adverse events) (10% in LA CAB/RPV vs. 26% in SOC)—met the predefined stopping criteria and were statistically significant. Based upon the totality of the data, in February 2024, the DSMB recommended halting randomization and offering all eligible participants LA CAB/RPV. Of the six participants with virologic failure on LA CAB/RPV, two had new drug-resistance mutations (one conferring high-level resistance to CAB and one conferring high-level resistance to both CAB and RPV). The available data suggest that an intensive effort to achieve viral suppression followed by a switch to LA CAB/RPV may be a viable option for individuals who cannot adhere to an oral ARV regimen. Further analyses and formal publication of LATITUDE study results are pending.

Approach #2: Administer LA CAB/RPV in people with viremia who are unable to achieve viral suppression despite intensive adherence support

Emerging data show that select people with HIV who are unable to achieve viral suppression on an oral ARV regimen despite intensive support might benefit from use of LA CAB/RPV, which is currently not approved for use in this population. Available data with this strategy include an initial case report,[85] followed by outcome data from a compassionate use program,[86] showing that 16 of 28 (57%) people with viremia achieved virologic suppression after a median of 5 months with LA CAB/RPV. Among those with virologic failure and for whom resistance data were available, all had new NNRTI mutations conferring RPV resistance and 50% had new integrase mutations, two of which conferred CAB resistance. Since then, three small observational studies have suggested that LA CAB/RPV may achieve viral suppression in select people with viremia and poor adherence to oral ART.[50-52] In these studies, select people with viremia who were unable to adhere to daily oral ART were initiated on monthly or twice-monthly LA CAB/RPV with or without oral lead-in therapy. At up to 10 months of follow-up, 95% achieved HIV RNA <50 copies/mL. Of those with virologic failure for whom genotypes were available, new reverse transcriptase (e.g., L100I, E138K, Y181I) and/or integrase (e.g., G140S, Q148R, R263K) mutations were detected, conferring intermediate to high resistance to RPV and/or CAB, respectively. Various levels of multidisciplinary support and intensive case management were utilized throughout these studies (e.g., provision of injections in field sites, financial incentives, appointment reminders, and transportation assistance). Despite the intensive support, not all injections were given on time.

In the multisite U.S. Observational Pharmacoepidemiology Research and Analysis (OPERA) cohort,[87] clinical data on the use of LA CAB/RPV were prospectively captured from electronic health records from 84 clinics in 18 U.S. states and territories. Among the 36 individuals who had HIV RNA >200 copies/mL before starting LA CAB/RPV and had at least one follow-up HIV RNA test, 94% had an HIV RNA <200 copies/mL at their last follow-up visit.

Taken together, until additional data are available, these approaches may provide alternatives for individuals with viremia and difficulties with adherence to oral ART, especially for those at the highest risk for disease progression or death. If either of the above approaches are employed, close monitoring is recommended with drug-resistance testing performed if virologic response is inadequate. Importantly, beyond conventional and intensive multidisciplinary team involvement, case management and outreach support are needed to ensure adherence and adequate monitoring while on LA CAB/RPV (see the Adherence to the Continuum of Care section for discussion on strategies to improve adherence in these situations). Caution with close monitoring is advised, as data are unavailable for detailed guidance regarding the need for specific adherence or intensive case management services or whether every 4- or every 8-week LA CAB/RPV will yield similar virologic

outcomes in people with viremia before switching. Every 4-week dosing was used in the LATITUDE study. In the published case series to date in people with viremia, every 4-week dosing was prescribed for most, with the option of switching to every 8 weeks after achieving viral suppression. Until further data are available, it may be prudent to use similar strategies when LA CAB/RPV is being considered. People with HIV and providers need to be aware of the significant risk of developing resistance to NNRTIs, and particularly INSTIs if virologic failure occurs on LA CAB/RPV. Such resistance may limit future treatment options and may also lead to its transmission, which should be balanced with the individual's HIV-related risk for disease progression and death.[88] Closely monitoring for viral responses is advised if LA CAB/RPV is used in people with viremia and who have challenges with adherence.

Summary

The goal of treatment for people with HIV and virologic failure is to establish virologic suppression. The management of people with virologic failure often requires expert advice to construct virologically suppressive regimens. Before modifying a regimen, it is critical to carefully evaluate the potential cause(s) of virologic failure, including incomplete adherence, poor tolerability, and drug–drug and drug–food interactions, as well as review HIV RNA and CD4 count changes over time, complete treatment history, and current and previous drug-resistance test results. If HIV RNA suppression is not possible with currently approved agents, consider the use of investigational agents through participation in clinical trials or expanded/single-patient access programs. If virologic suppression is still not achievable, the choice of regimens should focus on minimizing toxicity and preserving treatment options while maintaining CD4 counts to delay clinical progression.

Table 10. Antiretroviral Options for People With HIV and Virologic Failure

Designing a new regimen for people with HIV who are experiencing treatment failure should always be guided by ARV history and results from current and past resistance testing. This table summarizes the text above and displays the most common or likely clinical scenarios seen in people with virologic failure. For more detailed descriptions, please refer to the texts above and/or consult an expert in HIV drug resistance to assist in the design of a new regimen. It is also crucial to provide continuous adherence support before and after regimen changes.

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a]	Goal
First Regimen Failure	NNRTI plus two NRTIs	Most likely resistant to NNRTI +/– 3TC or FTC (i.e., NNRTI mutations +/– M184V/I).[b] Additional NRTI mutations also may be present.	DTG (or possibly BIC) plus two NRTIs (preferably at least one fully active[c]) **(AI);** *or* Boosted PI plus two NRTIs (preferably at least one fully active) **(AI);** *or* Boosted PI plus INSTI (boosted DRV plus DTG **[AI]**; LPV/r plus RAL **[CI]**)	Resuppression
	Boosted PI plus two NRTIs	Most likely no resistance or resistance only to 3TC or FTC (i.e., M184V/I, without resistance to other NRTIs)[b]	DTG, or possibly BIC, plus two NRTIs (preferably at least one fully active; if only one of the NRTIs is fully active[c] or if adherence is a concern, DTG is currently preferred over other INSTIs) **(AIII);** *or* Continue same regimen **(AII);** *or* Boosted PI plus INSTI (boosted DRV plus DTG **[AIII]**; LPV/r plus RAL **[CI]**); *or* Another boosted PI plus two NRTIs (at least one fully active[c]) **(AIII).**	Resuppression
	INSTI plus two NRTIs	If failure with no INSTI resistance	Boosted PI plus two NRTIs (preferably at least one fully active[c]) **(AIII);** *or* DTG, or likely BIC, plus two NRTIs (preferably at least one fully active[c]) **(AIII);** *or* DRV/r plus DTG **(AIII)**	Resuppression
		If failure on EVG or RAL, often have INSTI resistance, but potentially susceptible to DTG	Boosted PI plus two NRTIs (preferably at least one fully active[c]) **(AIII);** *or*	Resuppression

Table 10. Antiretroviral Options for People with HIV and Virologic Failure

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a]	Goal
		Can have 3TC or FTC resistance.	DTG[d] twice daily or possibly BIC (if HIV is sensitive) plus two fully active NRTIs **(BIII);** *or* DTG[d] twice daily or possibly BIC (if HIV is sensitive) plus a boosted PI (preferably DRV/r) **(AIII).**	
	INSTI plus NNRTI (DTG/RPV or LA CAB/RPV)	INSTI and/or NNRTI resistance possible	Use ART history and past and current resistance testing to design a new regimen. Consult an expert in drug resistance as needed.	Resuppression
Second Regimen Failure and Beyond	Drug resistance with fully active treatment options—	Use past and current genotypic- +/– phenotypic-resistance testing and ART history when designing new regimen.	New regimen according to original treatment type—	Resuppression
	(i) Boosted PI, but not second-generation INSTI, fully active		(i) Boosted PI with two NRTIs (preferably at least one fully active)	
	(ii) Second-generation INSTI, but not boosted PI, fully active		(ii) DTG or BIC with two NRTIs (preferably at least one fully active)	
	(iii) Both PI and INSTI fully active		(iii) The two options above or boosted PI with INSTI	
	Multiple or extensive drug resistance with few treatment options (e.g., fully active boosted PI or second-generation INSTI unavailable)	Use past and current genotypic- and phenotypic-resistance testing to guide therapy. Confirm with a viral tropism assay when use of MVC is considered. Consult an expert in drug resistance if needed.	New regimen should include at least two, and preferably three, fully active agents, including those with novel mechanisms of action (e.g., IBA, FTR, LEN). If fewer than three fully active drugs, include as many fully active drugs as possible, along with potentially partially active drugs **(BII).** Consider enrollment into clinical trials or expanded access programs for investigational agents if available. Discontinuation of all ARV drugs **is not recommended (AI).**	Resuppression if possible; otherwise, keep viral RNA levels as low as possible and CD4 count as high as possible.

Table 10. Antiretroviral Options for People with HIV and Virologic Failure

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a]	Goal
People With Suspected Drug Resistance and Limited or Incomplete ARV and Resistance History	Unknown	Obtain medical records if possible. Resistance testing may be helpful in identifying drug-resistance mutations, even if the person has been off ART. Keep in mind that resistance mutations may not be detected in the absence of drug pressure.	Consider restarting the old regimen with careful monitoring of virologic response and early resistance testing if inadequate virologic suppression. If no ARV history is available, consider initiating a regimen with drugs with high genetic barriers to resistance (e.g., DTG, BIC, and/or boosted DRV) with careful monitoring of virologic response and early resistance testing, if inadequate virologic suppression.	Resuppression

[a] When switching an ARV regimen in a person with HBV/HIV coinfection, ARV drugs that are active against HBV and have a high resistance barrier to HBV (i.e., tenofovir) should be continued as part of the new regimen, or another HBV drug (i.e., entecavir) should be started. Discontinuation of these drugs may lead to the reactivation of HBV, which may result in serious hepatocellular damage.

[b] If other NRTI-resistance mutations are present, use resistance test results to guide NRTI usage in the new regimen.

[c] See text for details and additional options in special settings.

[d] Response to DTG depends on the type and number of INSTI mutations.

Key: 3TC = lamivudine; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CD4 = CD4 T lymphocyte; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; FTR = fostemsavir; HBV = hepatitis B virus; IBA = ibalizumab; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RAL = raltegravir

Isolated Central Nervous System Virologic Failure and Neurologic Symptoms

Cerebrospinal Fluid Viral Escape

Presentation with new-onset central nervous system (CNS) signs and symptoms has been reported as a rare form of "compartmentalized" virologic failure. People experiencing this present with new, usually subacute, neurological symptoms that are associated with a breakthrough of HIV replication within the CNS compartment, despite relative plasma HIV RNA suppression. In this case, cerebrospinal fluid (CSF) HIV RNA shows higher concentrations than in plasma.[89-91] Clinical evaluation frequently shows abnormalities on magnetic resonance imaging (MRI) and abnormal CSF findings with characteristic lymphocytic pleocytosis.[92] In most (though not all) people, drug-resistant CSF virus is evident.[93] Consensus among experts is that this "neurosymptomatic" form of CNS viral escape should be treated through optimization of ARV regimens based on drug-resistance testing results if available **(CIII).**[94] Although drug-resistance testing of HIV in CSF can be used to guide changes in the ARV regimen, according to the principles outlined above for plasma HIV RNA resistance, such testing typically needs to be conducted in a research setting. If CSF HIV drug-resistance testing is not available, the regimen may be changed based on the person's treatment history or on predicted drug penetration into the CNS **(CIII).**[95-98]

This "neurosymptomatic" CNS viral escape should be distinguished from "neuroasymptomatic" escape, defined as—

- The incidental detection of asymptomatic and mild CSF HIV RNA elevation, which is similar to plasma viral blips in that it is usually transient with low levels of CSF HIV RNA and has been associated with PI-based regimens[99-101]; *or*
- A transient increase in CSF HIV RNA that is related to other CNS infections that can induce a brief increase in CSF HIV RNA (e.g., herpes zoster).[102]

There is not clear evidence to support a change in an ARV regimen for incidentally detected "neuroasymptomatic" escape, although careful clinical review and follow-up of each person with this condition are recommended to monitor for the emergence of neurologic symptoms or systemic viremia.[94] There does not appear to be an association between these asymptomatic CSF HIV RNA elevations and the relatively common chronic, usually mild, neurocognitive impairment in people with HIV who show no evidence of CNS viral breakthrough.[103]

Neurological Symptoms in People With HIV on Antiretroviral Therapy

Evidence is currently not available to support empiric intensification or switch of ARV regimens in people on systemically suppressive ART with mild neurological and/or cognitive symptoms who do not have documented CSF escape. Such individuals should be referred for neurological evaluation to determine if further evaluation is indicated. This may include blood laboratory testing, lumbar puncture, neuropsychological testing, and MRI to evaluate for CSF escape, as well as other causes of neurological symptoms. A recent multinational randomized, double-blinded, placebo-controlled trial randomized 191 ART-experienced participants—with cognitive impairment and suppressed plasma HIV RNA level and not taking an INSTI—to one of three arms: dual placebo, addition of DTG plus placebo, or DTG plus MVC. Compared with placebo, ART intensification with DTG or DTG plus MVC did not alter neuropsychological performance or depressive symptoms over time in participants with cognitive impairment.[104]

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Poor CD4 Cell Recovery and Persistent Inflammation Despite Viral Suppression

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Key Considerations and Recommendations
• Persistently low CD4 T lymphocyte (CD4) cell counts and immune activation are each associated with increased AIDS- and non-AIDS-related morbidity and mortality among individuals with antiretroviral therapy (ART)-mediated viral suppression. • Adding antiretroviral (ARV) drugs to a suppressive ARV regimen (ART intensification) does not improve CD4 cell recovery or reduce immune activation and, therefore, **is not recommended (AI).** • In individuals with viral suppression, switching ARV drug classes does not consistently improve CD4 cell recovery or reduce all relevant markers of immune activation and **is not recommended (BIII).** • Interleukin-2 **is not recommended (AI)** to increase CD4 cell counts and/or decrease immune activation, because clinical trial data demonstrated no clinical benefit. • Other interventions designed to increase CD4 cell counts and/or decrease immune activation **are not recommended** outside of a clinical trial, because no current interventions have been proven to decrease morbidity or mortality during ART-mediated viral suppression **(AII).** • Efforts to decrease morbidity and mortality during ART-mediated viral suppression should focus on addressing modifiable risk factors for chronic disease (e.g., encouraging smoking cessation, a healthy diet, and regular exercise; treating hypertension and hyperlipidemia). • Monitoring markers of immune activation and inflammation is not recommended, because no intervention targeting immune pathways has proven to improve the health of individuals with HIV, and many blood markers that predict morbidity and mortality fluctuate within individuals **(AII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Despite marked improvements in antiretroviral treatment (ART), morbidity and mortality in individuals with HIV continue to be greater than in the general population, particularly when ART is delayed until advanced disease stages. These morbidities include cardiovascular disease, many non-AIDS cancers, non-AIDS infections, chronic obstructive pulmonary disease, osteoporosis, type 2 diabetes, thromboembolic disease, liver disease, renal disease, neurocognitive dysfunction, and the frailty phenotype.[1] Although health-related behaviors and toxicities of antiretroviral (ARV) drugs are important factors, immune characteristics, such as a poor CD4 T lymphocyte (CD4) cell recovery and persistent immune activation and inflammation, likely also contribute to the disease risk among persons with HIV.

Poor CD4 Cell Recovery

As long as ART-mediated viral suppression is maintained, peripheral blood CD4 cell counts in most individuals with HIV will continue to increase for at least a decade. The rate of CD4 cell recovery is typically most rapid in the first 3 months of suppressive ART, followed by more gradual increases over time.[2-4] If ART-mediated viral suppression is maintained, most individuals will eventually recover CD4 counts in the normal range (>500 cells/mm^3); however, approximately 15% to 20% of individuals who initiate ART at very low CD4 counts (<200 cells/mm^3) may plateau at abnormally

low CD4 cell counts.[3-5] Early initiation of ART in individuals with recent HIV diagnoses likely provides the best opportunity for maximal CD4 cell recovery.[6]

Persistently low CD4 cell counts despite ART-mediated viral suppression are associated with increased risk of morbidity and mortality. For example, individuals with HIV who have CD4 counts <200 cells/mm^3, despite at least 3 years of suppressive ART, had a 2.6-fold greater risk of mortality than those with higher CD4 cell counts.[7] Lower CD4 cell counts during ART-mediated viral suppression are associated with an increased risk of non-AIDS morbidity and mortality,[8-11] including cardiovascular disease,[12] osteoporosis and fractures,[13] liver disease,[14] and infection-related cancers.[15] The prognostic importance of higher CD4 cell counts likely spans all ranges of CD4 cell counts, though incremental benefits are harder to discern once CD4 counts increase[16] to >500 cells/mm^3.

Individuals with poor CD4 cell recovery should be evaluated for modifiable causes of CD4 cell lymphopenia. Concomitant medications should be reviewed, with a focus on those known to decrease white blood cells or, specifically, CD4 cells. If possible, these drugs should be substituted for or discontinued. Untreated coinfections (e.g., hepatitis C virus, HIV-2) and serious medical conditions (e.g., malignancy) also should be considered as possible causes of CD4 lymphopenia, particularly in individuals with consistently declining CD4 cell counts (and percentages) and in those with CD4 counts consistently below 100 cells/mm^3.

In rare cases, CD4 cell counts actually decline, despite suppressive ART in the absence of an obvious clinical cause. Severe derangements in interleukin (IL)-7-**mediated** naive T cell homeostasis have been reported in these individuals, although the pathophysiology is likely to be multifactorial.[17-19]

Despite strong evidence linking low CD4 cell counts and increased morbidity during ART-mediated viral suppression, no adjunctive therapies that increase CD4 cell count beyond levels achievable with ART alone have been proven to decrease morbidity or mortality. Adding ARV drugs to an already suppressive ARV regimen does not improve CD4 cell recovery,[20-25] and does not reduce morbidity or mortality. Therefore, ART intensification is not recommended as a strategy to improve CD4 cell recovery **(AI).** Similarly, for individuals who are already maintaining viral suppression, switching ARV drug classes also does not consistently improve CD4 cell recovery and is not recommended **(BIII).**[26]

Immune-based therapies also have been investigated as a strategy to increase CD4 cell counts (e.g., IL-2, IL-7, growth hormone). Two large clinical outcome trials, powered to assess impact on clinical endpoints (AIDS and death), evaluated the role of interleukin-2 for improving CD4 cell recovery. IL-2 adjunctive therapy resulted in substantial CD4 cell count increases but with no observable clinical benefit.[27] Therefore, IL-2 is **not recommended (AI).** Given the lack of established clinical benefit to date, other immune-based therapies should not be used except in the context of a clinical trial.

Persistent Immune Activation and Inflammation

HIV infection results in heightened systemic immune activation and inflammation, which predict more rapid CD4 cell decline and progression to AIDS and death, independent of plasma HIV RNA levels.[28] Although immune activation declines with suppressive ART, it often persists at abnormal levels in many individuals with HIV maintaining long-term ART-mediated viral suppression—even in those with CD4 cell recovery to normal levels.[29, 30] Immune activation and inflammatory markers (e.g., IL-6, D-dimer, high sensitivity C-reactive protein (hs-CRP) also predict mortality and non-

AIDS morbidity during ART-mediated viral suppression, including cardiovascular and thromboembolic events, cancer, neurocognitive dysfunction, and frailty.[28] A low CD4/CD8 ratio also might reflect this inflammatory state to some degree,[31] although it predicts AIDS events far more strongly than non-AIDS morbidity.[32] Although individuals with poor CD4 cell recovery (i.e., counts persistently <350 cells/mm^3) tend to have greater immune activation and inflammation than those with greater recovery,[29] the relationship between innate immune activation and inflammation and morbidity/mortality is largely independent of CD4 cell count.[33, 34] Even in individuals with CD4 counts >500 cells/mm^3, immune activation and inflammation are associated with increased morbidity and mortality.[35, 36]

ART as a Strategy to Reduce Inflammation

Early diagnosis and treatment of HIV is, potentially, an effective strategy to achieve a lower level of persistent immune activation with ART. Most inflammatory markers decline during the first several months of ART and achieve a stable "setpoint" within 1 to 2 years.[37, 38] In observational studies, people with HIV who initiated ART during acute HIV infection appeared to achieve a lower immune activation setpoint during ART-mediated viral suppression than those who started ART at later disease stages.[39, 40] Indeed, those randomized to the immediate treatment arm of the START trial appeared to achieve a lower early inflammatory setpoint than those who were randomized to delayed therapy.[41] Longer-term follow-up of START participants is needed to determine whether such a reduced inflammatory setpoint persists and translates into reduced morbidity and mortality. Collectively, these data reinforce the recommendation to start ART as soon as possible after HIV diagnosis (see Initiation of Antiretroviral Therapy).

Although earlier initiation of ART appears to consistently reduce the inflammatory setpoint during ART, intensifying or modifying ART after viral suppression is already achieved does not appear to consistently reduce immune activation. For example, adding ARV drugs to an already suppressive ARV regimen (or ART intensification) does not consistently improve immune activation.[20-23, 25] Although some studies have suggested that switching an ARV regimen to one with a more favorable lipid profile may improve some markers of immune activation and inflammation,[42-44] these studies have limitations and results are not consistent across markers and among studies. Thus, at this time, ART modification cannot be recommended as a strategy to reduce immune activation **(BIII).**

Other Immune-Based Strategies

Because persistent immune activation is associated with morbidity and mortality among people with HIV who are virologically suppressed with ART, strategies targeting immune-mediators of inflammation are under investigation. Although the efficacy of canakimumab is not yet proven in people with HIV, the CANTOS trial provided important proof of concept for the causal role of inflammation in the risk of multi-morbidity in people without HIV but with cardiovascular disease. The study demonstrated that treatment with canakimumab, a human monoclonal antibody targeting cytokine IL-1β, a driver of the IL-6 signaling pathway, reduced cardiovascular events and cancer death.[45] In people with HIV, canakinumab and the IL-6 inhibitor tocilizumab have been shown to reduce blood levels of markers of inflammation and immune activation.[46, 47] Nevertheless, it remains unclear whether the potential risks of these therapies, such as the increased risk of death from sepsis observed in the CANTOS trial, might outweigh any benefits in people with HIV. Therefore, interventions targeting immune mediators of inflammation are not currently recommended for clinical use for the treatment of immune activation in people with HIV **(AII).**

Treatments Targeting Traditional Risk Factors and Inflammation

Beyond the well-established clinical benefit for reducing cardiovascular events, HMG-CoA reductase inhibitors (or statins) have been shown to improve biomarker levels of inflammation (e.g., hsCRP) and immune activation in the general population.[48-50] This premise, and the data suggesting similar benefit among people with HIV, motivated the design of a large clinical trial (REPRIEVE), now fully enrolled, to determine whether pitavastatin reduces cardiovascular events in people with HIV who do not already have a clinical indication for cholesterol-lowering therapy. [51] Although the results will not be known for several years, in addition to identifying the primary cardiovascular outcomes, assessing the impact of pivitastatin on non-cardiovascular events (such as cancer, osteoporotic fractures, and frailty phenotypes) that may be linked to the inflammatory state also will be valuable. Similarly, it remains unclear whether statins might further increase type 2 diabetes risk, which is increased in people with HIV.[52] Other commonly used medications with anti-inflammatory properties—like aspirin, angiotensin-converting enzyme inhibitors, methotrexate, and angiotensin receptor blockers[53]—have failed to consistently reduce biomarkers of immune activation and/or inflammation in people with HIV in randomized controlled trials and,[54-57] as a result, clinical outcome trials specific to this population are not anticipated.

Treatments Targeting Putative Drivers of the Inflammatory State

Other investigational approaches to reduce the inflammatory state in patients with viral suppression on ART have focused on the presumed root drivers of inflammation, including HIV reactivation from latently infected cells, microbial translocation, and chronic co-infections, particularly cytomegalovirus (CMV).[28] Thus far, the only approach targeting these root drivers that has broadly reduced systemic immune activation is treating asymptomatic CMV co-infection,[58] an approach that is being pursued further in a prospective larger trial (ACTG A5383). Presently, none of these strategies have been proven to be effective in clinical endpoint trials, so these interventions should be pursued only in the context of clinical trials.

Monitoring Inflammation

In the absence of proven interventions, there is no clear rationale to routinely monitor levels of immune activation and inflammation in treated HIV infection. Furthermore, many of the inflammatory markers that predict morbidity and mortality fluctuate significantly in individuals with HIV. Thus, clinical monitoring with immune activation or inflammatory markers **is not currently recommended (AII).** The focus of care to reduce chronic non-AIDS morbidity and mortality should be on maintaining ART-mediated viral suppression and addressing strategies to reduce risk factors (e.g., smoking cessation, healthy diet, and exercise) and managing chronic comorbidities, such as hypertension, hyperlipidemia, and diabetes **(AII).**

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Optimizing Antiretroviral Therapy in the Setting of Viral Suppression

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Key Considerations and Recommendations
• Advances in antiretroviral (ARV) treatment and a better understanding of HIV drug resistance have made it possible to consider switching a person with HIV from an effective ARV regimen to an alternative ARV regimen in some situations. • The fundamental principle of ARV regimen optimization is to maintain viral suppression without jeopardizing future treatment options. • Adverse events, drug–drug or drug–food interactions, pill burden, pregnancy, cost, stigma, inconvenience from taking oral medications, or the desire to simplify a regimen may prompt regimen optimization. • It is critical to review a person's full ARV history, including virologic responses, past ARV-associated toxicities and intolerances, and cumulative resistance test results before selecting a new ARV regimen **(AI).** • People with HIV who have no history of drug-resistance mutations or virologic failure can likely switch to any regimen that has been shown to be highly effective in people who are ARV-naive **(AI)** or to NRTI-sparing options extensively researched in switch studies, such as dolutegravir (DTG) plus rilpivirine (RPV) **(AI)** or long-acting cabotegravir plus rilpivirine (LA CAB/RPV) **(AI).** • For regimen optimization in the setting of existing nucleoside reverse transcriptase inhibitor (NRTI) resistance, if an NRTI is to be included in the new regimen, two NRTIs (tenofovir alafenamide [TAF] or tenofovir disoproxil fumarate [TDF] plus emtricitabine [FTC] or lamivudine [3TC]) should be included, along with a fully active drug with a high resistance barrier, such as DTG **(AII),** bictegravir (BIC) **(BIII),** or boosted darunavir **(BIII).** Alternatively, as noted above, an NRTI-sparing regimen (such as DTG/RPV **[AI]** or LA CAB/RPV **[AI]**) is possible if there is no evidence of prior integrase strand transfer inhibitor (INSTI) or RPV resistance. • Monotherapy with either a boosted protease inhibitor or an INSTI has been associated with unacceptable rates of virologic failure and the development of resistance; therefore, monotherapy as a switch strategy **is not recommended (AI).** • When switching an ARV regimen in a person with chronic hepatitis B virus (HBV)/HIV coinfection, HBV-active drugs that are potent and have a high barrier to resistance (i.e., TAF, TDF, or entecavir) should be used **(AII).** Discontinuation of HBV drugs may lead to reactivation of HBV, which may result in serious hepatocellular damage. • Consultation with an HIV specialist is recommended when planning a regimen switch for a person with a history of resistance to two or more drug classes **(AIII).** • Close monitoring to assess tolerability, viral suppression, adherence, and safety is recommended during the first 3 months after a regimen switch **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

With currently available antiretroviral therapy (ART), most people with HIV can achieve and maintain HIV viral suppression. Furthermore, advances in antiretroviral (ARV) treatment and a better understanding of drug resistance have made it possible to consider switching a person with HIV from one effective regimen to another in some situations. When considering optimization—a switch in therapy to improve certain aspects of therapy—clinicians must keep several key principles in mind to maintain viral suppression while addressing the concerns with the current regimen.

Reasons to Consider Regimen Optimization in the Setting of Viral Suppression

- To simplify a regimen by reducing pill burden and/or dosing frequency
- To enhance tolerability and/or decrease short- or long-term toxicity (see Table 20 and Table 21 in the Adverse Effects of Antiretroviral Agents section for a more in-depth discussion of toxicities)
- To prevent or mitigate drug–drug interactions (see Drug–Drug Interactions)
- To eliminate food requirements
- To switch to a long-acting (LA) injectable regimen for convenience, to relieve pill fatigue, or to decrease potential stigma or disclosure concerns associated with taking daily oral medications
- To allow optimal use of ART during pregnancy or when pregnancy is desired or may occur (see Perinatal Guidelines)
- To reduce costs (see Cost Considerations and Antiretroviral Therapy)

General Principles of Regimen Optimization

Maintain Viral Suppression

The fundamental principle of ARV regimen optimization is to maintain viral suppression without jeopardizing future treatment options. If a regimen switch results in virologic failure with the emergence of new resistance mutations, the person may require a more complex and/or a less tolerated regimen.

Careful Review of Antiretroviral Treatment and Drug-Resistance History Before Optimization

Before switching treatments, it is critical to thoroughly assess a person's full ARV history, including virologic responses, inferred resistance (as discussed below), cumulative resistance test results, and any past ARV-related intolerances, toxicities, or adverse reactions **(AI).**

If a person with pre-ART wild-type HIV achieves and maintains viral suppression after ART initiation, one can safely assume that no new drug-resistance mutations emerged while the person was on the suppressive regimen. In people with a history of virologic failure or pre-treatment drug resistance, a review of cumulative resistance test results and clinical and virologic response to prior regimens is essential when designing a new regimen. Cumulative resistance test results refer to all previous and currently available results from standard genotype, proviral DNA genotype (if available), phenotype, and tropism assays that can be used to guide the selection of a new regimen. Once selected, a drug-resistance mutation—even when it is not detected in the person's most recent drug-resistance test—can be archived in the HIV reservoir and reemerge under the appropriate selective drug pressure. Resistance often can be inferred from the ARV history. For people with documented failure on a regimen that includes drugs with relatively low barriers to resistance—such as a non-nucleoside reverse transcriptase inhibitor (NNRTI), elvitegravir (EVG), raltegravir (RAL), lamivudine (3TC), or emtricitabine (FTC)—a clinician should assume that there is resistance to these drugs, so-called *inferred resistance*. When uncertain about prior resistance, it is generally not advisable to switch from a suppressive ARV regimen, unless the new regimen is likely to be at least as active against potential resistant virus as the current suppressive regimen. This principle is particularly applicable when switching ARV-experienced individuals from a regimen with a

relatively high barrier to resistance—such as those that include pharmacologically boosted protease inhibitors (PIs), dolutegravir (DTG), or bictegravir (BIC)—to one with a lower barrier to resistance.[1] The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends that clinicians consult an HIV specialist when contemplating optimization for a person with a history of resistance to two or more drug classes **(AIII).**

If optimization is considered in people with suppressed viral loads who do not have prior drug resistance data, proviral DNA genotypic resistance testing can be considered. For those who have no prior virologic failures and who are on their first or second regimen, or who have genotypic test results from prior virologic failures, the use of the proviral DNA genotypic test is unlikely to provide valuable information. In individuals with a history of multiple prior failures or multiple prior ARV regimens, the use of proviral DNA genotypic testing may be useful. However, whenever proviral DNA genotypic testing is used, the results must be interpreted with caution because these assays may not detect any or all drug-resistance mutations, especially those that were selected by a previous ARV regimen.[2] In addition, these assays may identify mutations that appear inconsistent with a person's response to treatment, making the clinical relevance of the assay results questionable. Overall, the clinical utility of these assays remains an area of active investigation (see Drug-Resistance Testing).

For People With HBV/HIV Coinfection

When switching an ARV regimen in a person with active hepatitis B virus (HBV)/HIV coinfection (hepatitis B surface antigen [HBsAg] positive), tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) (generally given with 3TC or FTC) should be continued as part of the new regimen. Both TDF and TAF are active against HBV and can be used as HBV monotherapy. Although 3TC and FTC are active against HBV, their use as monotherapy against HBV infection **is not recommended (AII)** because emergent HBV resistance to these drugs is highly likely. If TAF or TDF cannot be used, entecavir—a potent antiviral with a high HBV resistance barrier—should be used to treat HBV alongside a fully suppressive ARV regimen **(AII).** Entecavir should not be used without an active ARV regimen to prevent the development of the HIV M184V resistance mutation. Discontinuation of HBV antivirals may lead to reactivation of HBV, which can result in serious hepatocellular damage and death. Refer to the Hepatitis B Virus/HIV Coinfection section for specific recommendations.

Screening for HBV for People With No History of HBV/HIV Coinfection

People with HIV and unknown or nonimmune HBV status should be screened for HBV infection before switching an ARV regimen to one that does not include TAF or TDF plus 3TC or FTC (e.g., DTG/rilpivirine [RPV], DTG/3TC, LA cabotegravir [CAB]/RPV). If a person with HIV shows no evidence of chronic HBV infection (i.e., negative for hepatitis B surface antibody [HBsAg]) and is not immune to HBV (i.e., negative for HBsAb), vaccination should be initiated while considering the ARV switch (including in those with isolated hepatitis B core antibody [HBcAb]).

People with HIV and prior exposure to HBV infection without evidence of chronic infection (i.e., negative HBsAg, positive HBcAb, and either positive or negative HBsAb) are likely at low risk (<1%) of HBV reactivation and even lower risk of HBV reactivation-associated hepatitis, despite the discontinuation of NRTIs. However, there are no published studies to confidently estimate risk in this population. Within this group, those with positive HBsAb are at the lowest risk for HBV reactivation, although HBV reactivation has been described when HBV active therapy is withdrawn as part of an

ART regimen in this situation.[3] See more information in the Hepatitis B Virus Infection section in the Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV.

For people previously exposed to HBV, alanine aminotransferase (ALT) should be monitored for 6 months (e.g., at the time of HIV viral load follow-up visits) after switching from ART that includes tenofovir (TDF or TAF) to one that does not include either of these drugs. An increase in ALT levels should prompt HBV DNA testing to assess for the reactivation of HBV. The presence of HBV reactivation would require the immediate addition of TAF, TDF, or entecavir to the ARV regimen.

Assessment for Potential Drug Interactions

Before switching a regimen, it is important to review each ARV drug in the new regimen and concomitant medications to assess whether any potential drug–drug interactions exist. For example, oral rilpivirine (RPV) and atazanavir (ATV) interact with acid-lowering agents, and many ARV drugs may interact with drug transporters or drugs that are inhibitors, inducers, or substrates of cytochrome P450 (CYP) enzymes (see Drug–Drug Interactions). In addition to new drug interactions, the discontinuation of some ARV drugs also may necessitate adjusting the dosage of concomitant medications. For example, discontinuation of pharmacokinetic (PK) boosters (ritonavir or cobicistat) may reduce the concentrations of some concomitant medications. Concomitant medications, which may have been previously managed with dose adjustments, will need to be reevaluated in the context of the new ARV regimen.

Assessment for Pregnancy or Pregnancy Potential

People of childbearing potential should have a pregnancy test before switching ART. If a person with HIV is found to be pregnant or desires pregnancy, clinicians should refer to the Perinatal Guidelines for recommendations on the safety and efficacy of ARV use at the time of conception or during pregnancy. All pregnancies that occur while an individual is receiving ART should be reported to the Antiretroviral Pregnancy Registry.

Monitoring After Switching Antiretroviral Therapy

After a treatment switch, people with HIV should be evaluated closely for 3 months (e.g., a clinic visit or telephone call 1 to 2 weeks after the change and a viral load test to check for rebound viremia 4 to 12 weeks after the switch) **(AIII).** The purpose of this close monitoring is to ensure the person clearly understands their prescribed ART regimen, assess medication tolerance, and conduct targeted laboratory testing when there are preexisting laboratory abnormalities or if there are potential concerns with the new regimen. For example, if lipid abnormality prompted the ARV change or is a concern with the new regimen, fasting cholesterol subsets and triglycerides should be assessed within 3 months after the ART change. In the absence of any new complaints, laboratory abnormalities, or evidence of viral rebound over the first 2 to 3 months, clinical and laboratory monitoring may resume on a regularly scheduled basis (see Laboratory Testing for Initial Assessment and Monitoring).

Specific Regimen Optimization Considerations

As with the recommendation for people who are starting ART, the use of a 2- or 3-drug ARV regimen (as discussed below) is generally recommended when switching ART in people with suppressed viral loads **(AI).** People who have no history of resistance mutations or virologic failure

can likely switch to any regimen that has been shown to be highly effective in people who have not been on ART **(AI).** People with prior drug resistance can be switched to a new regimen based on their ARV history and cumulative resistance testing results. Monotherapy with either a boosted PI or an integrase strand transfer inhibitor (INSTI) has been explored in several trials or cohort studies.[4-7] Both INSTI[8] and boosted PI[9] monotherapy have been associated with higher rates of virologic failure than combination regimens. In addition, INSTI monotherapy has been associated with the development of resistance;[10,11] therefore, ARV monotherapy as a maintenance strategy is **not recommended (AI).**

Optimization Strategies With Good Supporting Evidence for People Without Known Drug Resistance

Many clinical trials have enrolled participants with stable, suppressed viral loads without known underlying drug resistance and switched them to another regimen. Most of these studies demonstrated maintenance of viral suppression, some of which are referenced below. However, some regimen switches have had limited success in clinical trials but have informed optimization strategies. The SWITCHMRK 1 and 2 studies illustrated the importance of considering the possibility of underlying drug resistance before switching therapy in those with virologic suppression, particularly when the switch is to a drug with a low barrier to resistance.[1] In the two SWITCHMRK studies, those with viral suppression on two NRTIs plus lopinavir/ritonavir (LPV/r) were switched to two NRTIs plus RAL. The studies found that individuals with a history of previous virologic failure had a higher risk of failure after switching to the RAL-based regimen. This finding is likely explained by underlying NRTI resistance, a setting where viral suppression can generally be maintained by drugs with a high barrier to resistance, such as boosted PIs, but is less likely to maintain viral suppression when switched to a drug with a low barrier to resistance, such as RAL. The strategies listed below support these observations and principles of optimizing therapy and include a discussion about switching ART regimens in those with underlying resistance.

Three-Drug Regimens

Within-Class Switches

Within-class switches (e.g., switching from one INSTI to another INSTI) may be prompted by adverse events or the availability of ARVs in the same class that offer a better safety profile, reduced dosing frequency, higher barrier to resistance, lower pill burden, or do not require PK boosting. Within-class switches usually maintain viral suppression, provided there is no drug resistance to the new ARV. Below are examples of within-class switch strategies that are proven to be effective in clinical trials or are likely to be effective in those without underlying drug resistance:

- From TDF[12,13] or abacavir (ABC)[14] to TAF
- From RAL or elvitegravir/cobicistat (EVC/c)[15] to BIC or DTG
- From DTG[16-18] to BIC or BIC to DTG
- From efavirenz to RPV,[13,19] doravirine (DOR),[20] or RPV to DOR

Between-Class Switches

Between-class switches (e.g., switching from a boosted PI to an INSTI) generally maintain viral suppression, provided there is no resistance to the other components of the regimen. In general, such switches should be avoided if any doubt exists about the activity of the other agents in the regimen. As noted earlier, prior resistance test results will be very informative in guiding this switch. The following are examples of between-class switches that have been proven to be effective in clinical trials or are likely to be effective in those without underlying drug resistance:

- From a boosted PI to a second-generation INSTI (e.g., DTG,[21] BIC[22])
- From a boosted PI to RPV[23] or DOR[20]
- From an NNRTI to a second-generation INSTI[24,25] or a boosted PI

Two-Drug Regimens

Some two-drug ARV regimens are effective in maintaining HIV virologic control in people who initiated therapy with three-drug regimens and achieved sustained virologic suppression for at least 3 months. However, none of the two-drug regimens are effective as treatment for HBV and are therefore not recommended for people with HBV coinfection. In people with HBV who cannot take TAF or TDF, these regimens can be considered if used with a potent, high barrier-to-resistance anti-HBV active medication (i.e., entecavir) **(AII).** See the section above on HBV considerations during optimization. The following are examples of successful strategies studied in clinical trials for switching from 3- to 2-drug regimens in people with suppressed HIV.

Dolutegravir Plus Rilpivirine

Two Phase 3 trials, SWORD-1 and SWORD-2, demonstrated noninferior efficacy of switching to a 2-drug regimen of DTG with RPV compared to continuing a first or second ARV regimen in individuals with suppressed HIV-RNA without prior virologic failure.[26] Individuals were excluded from the study if they had active HBV infection (unless the person was also on a specific HBV active regimen), resistance to DTG or RPV, or significant drug interactions. DTG/RPV is suitable for use in people with an isolated K103N resistance mutation and in those with NRTI resistance. Individuals with active HBV infection need to be on a potent HBV drug with a high barrier to resistance (i.e., TAF, TDF, or entecavir).

Dolutegravir Plus Lamivudine or Emtricitabine

A switch from a stable 3-drug ARV regimen to DTG plus 3TC or FTC as a maintenance strategy in people with ongoing virologic suppression and no history of prior virologic failure or resistance to these agents was noninferior to continuing a 3-drug therapy in a large randomized clinical trial (TANGO),[27] in smaller clinical trials,[28-30] and in observational studies[31-33] **(AI).** Individuals with active HBV infection need to be on a potent HBV drug with a high barrier to resistance (i.e., TAF, TDF, or entecavir). 3TC or FTC monotherapy is not considered standard of care for HBV treatment because of a high risk of emerging resistance.[34]

Boosted Protease Inhibitor Plus Lamivudine

A boosted PI plus 3TC is a reasonable 2-drug optimization option in individuals without resistance who are suppressed on a current regimen and who do not have active HBV infection. Pill burden and potential drug interactions are limitations compared to the above 2-drug regimens. Several regimens using a boosted PI plus 3TC have been shown to be effective in clinical trials, including darunavir/ritonavir (DRV/r) **(BI),**[35] darunavir/cobicistat (DRV/c) **(BIII),** atazanavir/ritonavir (ATV/r) **(CI),**[36,37] and LPV/r **(CI).**[38] Individuals with active HBV infection need to be on a potent HBV drug with a high barrier to resistance (i.e., TAF, TDF, or entecavir). 3TC or FTC monotherapy is not considered the standard of care for HBV treatment because of a high risk of emerging resistance.[34]

Boosted Darunavir Plus Dolutegravir

An open-label, Phase 3b, noninferiority clinical trial evaluated the continuation of DRV/r plus two NRTIs versus a switch to DRV/r plus DTG; the switched regimen was noninferior.[39] Because of the small sample size of this study, the regimen of DRV/r plus DTG is recommended only in the absence of other alternative options but can be considered in particular for individuals with resistance and/or intolerance to 3TC (or FTC), ABC, and TDF (or TAF) **(CI).** Similar results were observed in two small observational studies.[40,41] Individuals with active HBV infection need to be on a potent HBV drug with a high barrier to resistance (i.e., TAF, TDF, or entecavir).

Long-Acting Intramuscular Cabotegravir Plus Rilpivirine

Long-acting ARV medications provide the convenience of reduced dosing frequency and may improve quality of life for individuals with pill fatigue or concerns about disclosure of HIV status or stigma associated with daily oral medication. Long-acting (LA) intramuscular (IM) injectable formulations of the INSTI cabotegravir (CAB) and the NNRTI RPV are approved by the U.S. Food and Drug Administration (FDA) to be given once monthly or every 2 months as a complete regimen for individuals ≥12 years old with sustained (e.g., ≥3 months) virologic suppression (HIV-1 RNA <50 copies/mL) on a stable ARV regimen, with no history of treatment failure, and with no known or suspected resistance to either CAB or RPV.[42-44]

Panel's Recommendation

The Panel recommends that monthly or every 2-month LA CAB/RPV can be used to replace an existing oral ARV regimen in people with HIV who fulfill all of the following criteria **(AI)**:

- Sustained viral suppression for at least 3 months
- No history of documented or suspected resistance to either CAB or RPV
- No active HBV infection (unless also receiving TAF, TDF, or entecavir)
- Not pregnant or actively planning pregnancy
- Not receiving medications with significant drug interactions with oral (during lead-in or bridging therapy) or injectable CAB or RPV (see Tables 24b and Table 24d)

Oral lead-in therapy with CAB and RPV is optional and can be done based on provider–patient discussion.

Clinical Trial Data

Two Phase 3 clinical trials (ATLAS and FLAIR) randomized almost 1,200 participants with HIV-1 and viral suppression on oral ART to receive once-monthly LA CAB/RPV or to continue their oral ARV regimens.[45,46] Participants could not have prior resistance to INSTIs or NNRTIs (except the K103N mutation), previous virologic failure (ATLAS trial), or active or occult HBV infection. Both studies used a 1-month oral lead-in of once-daily CAB 30 mg with RPV followed by injectable LA CAB/RPV monthly (loading dose x 1 followed by maintenance dosing). In the intention to treat the exposed population, HIV RNA >50 copies/mL at Week 48 occurred in 11 (1.9%) participants in the IM arms and 10 (1.7%) participants in the oral therapy arms (combining data from both studies) demonstrating that long-acting therapy was noninferior to continued oral therapy.[47] Virologic failure was rare; however, when it occurred, resistance to INSTIs, NNRTIs, or both was common.

The ATLAS-2M study compared LA CAB 600 mg/RPV 900 mg every 8 weeks (n = 522) versus LA CAB 400 mg/RPV 600 mg every 4 weeks (n = 523) in ART-experienced adults.[48] At 48 and 96 weeks, every 8-week dosing was noninferior to every 4-week dosing (HIV RNA ≥50 copies/mL; 2% vs. 1% at 48 weeks).[49,50]

In the SOLAR study, 687 individuals who were virologically suppressed on BIC/FTC/TAF were randomized 2:1 to either switch to LA CAB/RPV every 2 months or remain on BIC/FTC/TAF.[51] At 48 weeks LA CAB/RPV was virologically noninferior to continued BIC/FTC/TAF with 1% versus <1% virologic failure, respectively. There was also no difference in viral suppression with or without oral lead-in when initiating LA CAB/RPV therapy. Based on these data and other existing data, oral lead-in therapy is now considered optional (see the CABENUVA FDA drug label).

Lastly, the Cabotegravir and Rilpivirine Efficacy and Safety (CARES) trial, an open-label trial conducted in Africa, randomized people with HIV and viral suppression to receive LA CAB/RPV every 8 weeks or to continue with their oral ARV regimen. At 48 weeks, 246 of 255 (96%) in the LA CAB/RPV arm and 250 of 257 (97%) in the oral ARV arm maintained HIV RNA <50 copies/mL. Two LA CAB/RPV participants had virologic failure at Week 48 and developed high-level resistance to both CAB and RPV.[52]

Adverse Effects

The most common adverse events associated with LA CAB/RPV are injection site reactions (ISRs) which occurred in more than 80% of participants at least once. ISRs reduce in frequency over time, occurring in about 10% to 30% of participants after the first year. ISRs were generally mild to moderate, with 99% being Grade 1 or 2 and the median duration of symptoms being 3 days. Hypersensitivity reactions, post-injection reactions, hepatotoxicity, and depressive disorders have also been reported.[49,53]

Practical Considerations When Using Long-Acting Injectable Cabotegravir and Rilpivirine

When prescribing LA CAB/RPV, clinicians should refer to the FDA product label[42] for guidance with the following practical considerations:

- Injection techniques, including injection sites and needle length in people with body mass index >30 kg/m^2

- Several drugs, particularly those interacting with CYP3A or uridine diphosphate glucuronosyltransferase 1A1, are contraindicated with CAB and RPV (oral and/or IM) due to significant drug interactions (Drug–Drug Interaction Tables 24b and 24d).
- Management strategies for missed doses of IM injections and use of oral bridging therapy

HIV Viral Load and Drug-Resistance Testing Monitoring

HIV viral load monitoring should be performed 4 to 8 weeks after a switch to LA CAB/RPV. HIV viral load also should be checked in people with unplanned missed visits and delayed dosing of LA CAB/RPV. When viremia develops during LA therapy, resistance testing, including integrase resistance testing, should be performed. Follow-up dosing in people with missed doses should not be delayed while awaiting viral load and resistance test results. In a pooled analysis from FLAIR, ATLAS, and ATLAS-2M, confirmed virologic failure was more common in the setting of baseline, proviral, RPV resistance-associated mutations; HIV-1 subtype A6 (rare in the United States); higher baseline body mass index; and lower week-8 trough RPV concentration.[54] However, some recent studies did not observe worse outcomes in people with a high body mass index (Opera Cohort and CARES Study).[55,56] In the setting of confirmed virologic failure on LA CAB/RPV, resistance to NNRTIs and INSTIs is common.[57-59]

Pregnancy Considerations

Initiation of LA CAB/RPV is not recommended during pregnancy. Clinicians should refer to the Perinatal Guidelines for recommendations in managing people who become pregnant or are planning pregnancy while receiving LA CAB/RPV. Health care providers are strongly encouraged to register people with HIV who become pregnant while receiving LA CAB/RPV in the Antiretroviral Pregnancy Registry.

Considerations Regarding Long-Acting Cabotegravir Plus Rilpivirine Use in People With a History of Adherence Challenges

There are emerging data on the use of LA CAB/RPV in people with a history of adherence challenges. The open-label Long-Acting Therapy to Improve Treatment Success in Daily Life (LATITUDE [ACTG A5359]) Study enrolled people who had HIV viremia, challenges in taking daily oral ART, and no evidence of CAB or RPV resistance.[60] After adherence support and conditional financial incentive, participants who were able to achieve viral suppression were randomized to monthly LA CAB/RPV or to continue on the oral regimen. Study randomization was stopped early by the Data Safety Monitoring Board because of lower rates of virologic failure in individuals randomized to LA CAB/RPV than those staying on oral therapy (see the Virologic Failure section for more discussion).

Optimization Strategies for People With Viral Suppression and a History of NRTI and/or NNRTI Resistance

Some existing data demonstrate the safety and efficacy of select within-class and between-class switches for individuals with underlying drug resistance who are on a stable ARV regimen with suppressed HIV RNA (e.g., for 6 months or longer). These findings are further supported by data extrapolated from those experiencing virologic failure.

Within-Class Switch From Dolutegravir to Bictegravir in the Setting of Limited Resistance

The GS-US-380-4030 study enrolled 565 participants who were stably suppressed on DTG plus two NRTIs. The participants were randomized to either remain on their current regimen or switch to BIC/FTC/TAF. After 48 weeks, the groups had similar rates of sustained suppression. The rates of viral suppression were similar for those with a documented history of NRTI resistance (approximately 25% of participants) and those without a history of NRTI resistance.[61] Results from this trial lend theoretical support to other optimization strategies that include a switch from one high-barrier drug to another in the setting of underlying NRTI genotypic resistance. This study also supports using drugs with a high barrier to resistance when only one, and possibly no NRTIs in the background regimen, need to be fully active. This is further supported by other lines of evidence, some of which are discussed below.

Data of Within and Between Class Switches to Bictegravir in the Setting of Limited Drug Resistance

The BRAAVE study was an open-label, optimization study for Black people with HIV and viral suppression for ≥12 months on a standard regimen of two NRTIs plus a third agent (INSTI, NNRTI, or PI). Individuals were randomized to switch to BIC/FTC/TAF or to remain on current therapy (although individuals on TDF were switched to TAF). Switching to BIC-based therapy was noninferior for maintaining viral suppression compared with continuing current oral therapy. Baseline regimens included 61% INSTI, 31% NNRTI, and 9% PI. Baseline resistance did not affect the outcomes of therapy. In particular, NRTI resistance was present in 14% of participants, with 10% harboring the M184V/I mutation.[62]

Switch From a Boosted Protease Inhibitor to Dolutegravir in Individuals With Viral Suppression and Prior First-Line NNRTI Plus NRTI Failure

The second-line switch to DTG (2SD) study was conducted at four sites in Kenya in a population of people with HIV who had prior first-line NNRTI plus NRTI regimen failure and achieved viral suppression on a current ritonavir-boosted PI-based regimen without undergoing genotypic resistance testing.[63] In this prospective, open-label trial, 795 participants with HIV were randomized 1:1 to switch the boosted PI to DTG or continue the current regimen. NRTIs were not switched, although a switch was allowed if clinically indicated. At Week 48, switching to DTG was noninferior to continuing a boosted PI with about 5% of participants in each arm having viral rebound >50 copies/mL. In the 40 people with virologic rebound, 20 in each arm, no resistance to DTG or PIs was found. Grade 3 or 4 adverse events were similar in the two groups. This study was limited by the absence of genotypic resistance data demonstrating the amount of NRTI resistance present at the time of first-line NNRTI plus NRTI failure. Nevertheless, several related studies in similar settings have demonstrated that extensive NRTI and NNRTI resistance is expected in this situation, often including resistance to tenofovir and 3TC or FTC.[64-66] Accepting that substantial NRTI resistance was likely to be present in this study population, 2SD provided evidence that a person who is suppressed on a boosted PI-based regimen is likely to remain suppressed on a second-generation INSTI-based regimen in the setting of NRTI resistance. This is further supported by data showing that people with virologic failure and NRTI resistance can be successfully treated with second-generation INSTIs plus TAF or TDF and FTC or 3TC.[64]

Data From Virologic Failure Studies Inform Optimization With NRTI Resistance in Clinical Practice

Several studies conducted in resource-limited countries where people with first-line NNRTI-based virologic failure and who have NRTI-resistance support treatment recommendations for optimizing ART in these settings (details in the Virologic Failure section). In the DAWNING study,[67] for individuals who failed first-line NNRTI-based ART, DTG (84%) outperformed LPV/r (70%) for 48-week viral suppression <50 copies/mL. Participants who had one active NRTI in their study regimen had similar virologic responses as those with two active NRTIs. In the NADIA study, participants failing first-line NNRTI-based therapy were randomized to either DTG or DRV/r combined with randomized NRTIs. At enrollment, resistance to NRTIs was common with 86% of participants having an M184V mutation and 50% having a K65R mutation. At 48 weeks, DTG was noninferior to DRV/r, with both groups achieving viral suppression to <400 copies/mL in about 90% of participants. There were no differences in rates of viral suppression between participants with resistance to one or both NRTIs in their regimen compared to those with no NRTI resistance.[64] At Week 96, TDF was superior to zidovudine when combined with 3TC.[68]

Although these were studies of ART use in the setting of initial NNRTI-based virologic failure, we expect that regimens that are effective during viremia would also be effective in the setting of viral suppression in people with similar ARV resistance patterns (NRTI resistance, but no known or suspected PI or INSTI resistance). These studies support that for optimization in the setting of NRTI resistance, two NRTIs (TAF or TDF plus 3TC or FTC) should be included in the regimen with a fully active drug with a high resistance barrier, such as DTG **(AII),** BIC **(BIII),** or boosted DRV (DRV/c or DRV/r) **(BIII).** The use of regimens without any fully active NRTIs **is not routinely recommended** when there are other viable treatment options. However, in some clinical situations—such as when prior resistance testing is not fully available, to avoid major drug–drug interactions, to keep regimens simpler, or for other reasons—a regimen with a fully active drug with a high resistance barrier plus two partially active NRTIs can be considered. Both tenofovir and cytidine analogs may retain partial activity even when resistance is present.

Optimization Strategies for People With Viral Suppression and a History of Complex Underlying Resistance

Before optimizing an ARV regimen of a person with viral suppression who has a history of treatment failure and complex drug resistance, a careful review of the individual's full ARV history and cumulative drug resistance profile should be undertaken. Consultation with a clinician with expertise in HIV drug resistance is recommended **(AIII).**

As described in the Optimization Strategies for People With Viral Suppression and a History of NRTI and/or NNRTI Resistance section above, any regimen that includes a fully active drug with a high barrier to resistance (e.g., DTG, BIC, or boosted DRV) plus two NRTIs (even if resistance is present), is likely to achieve suppression in those experiencing virologic failure and maintain suppression in the setting of optimization.[63,64] Reliably maintaining suppression when there is not a fully active drug with a high resistance barrier is more complicated and requires careful consideration before any switch is made. In people with prior virologic failure(s) and/or limited prior resistance testing, proviral DNA genotypes can be considered. Clinicians should keep in mind that proviral DNA resistance mutations found will be useful, but some archived resistance mutations may not be found with this testing. Previous studies demonstrated that it is best to include at least 2 (preferably 3) fully active drugs in the setting of virologic failure if a fully active drug with a high resistance

barrier is not included in the regimen due to resistance and/or intolerance.[69] In this setting, it will often require incorporating active drugs in classes other than NRTIs, NNRTIs, PIs, and INSTIs, such as entry inhibitors (i.e., CCR5 antagonists, post-attachment inhibitors, attachment inhibitors, and fusion inhibitors) or capsid inhibitors (e.g., lenacapavir), recognizing that entry and capsid inhibitors have primarily been studied and are indicated for those with virologic failure.

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Discontinuation or Interruption of Antiretroviral Therapy

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Discontinuation or interruption of antiretroviral therapy (ART) may result in viral rebound, immune decompensation, and/or clinical progression.[1-5] Thus, discontinuation or planned interruption of ART is not recommended outside the context of a clinical trial **(AI).** However, unplanned interruption of ART may occur under certain circumstances as discussed below.

Unanticipated Interruptions of Oral Antiretroviral Drugs

Reasons for short-term interruption (days to weeks) of ART vary and may include intercurrent illnesses that preclude oral intake (e.g., gastroenteritis, pancreatitis), surgical procedures, drug toxicity, or interrupted access to antiretroviral (ARV) drugs. Stopping ART for a short time (i.e., less than 1 day to 2 days) usually can be done by holding all drugs in the regimen. Whether unplanned interruptions occur by accident or by necessity (e.g., because of drug toxicities), all efforts should be made to minimize their duration. Recommendations for some specific scenarios are listed below.

When a Patient Experiences Unexpected Inability to Take Solid Oral Medications

For patients who require tube feeding, some ARV drugs are available in liquid formulations, and some pills may be crushed. The Oral Antiretroviral/HCV DAA Administration[6] provides information on crushing pills and formulating liquid ARV drugs. Additional information also may be available in drug product labels. Clinicians should consult an HIV specialist and/or pharmacist to assess the best way for a patient with a feeding tube to continue an effective ARV regimen.

For patients unable to take medications by any enteral route (e.g., in the context of severe gastrointestinal disease), all components of the oral drug regimen should be stopped simultaneously, regardless of half-lives of the drugs. After resolution, all components of the ARV regimen should be restarted simultaneously.

Several ARV drugs are available as parenteral formulations; these include zidovudine, enfuvirtide, ibalizumab (IBA), and the long-acting (LA) injectable formulations of cabotegravir (CAB LA) and rilpivirine (RPV LA). The combination of CAB LA and RPV LA is approved as a complete regimen for the treatment of HIV. However, this regimen has not been studied as an alternative for patients who cannot take oral medications. Clinicians should consult with an HIV specialist before prescribing any of these agents.

When a Patient Experiences a Severe or Life-Threatening Toxicity to an Antiretroviral Agent

All components of the ARV drug regimen should be stopped simultaneously, regardless of drug half-life. After resolution, a different complete regimen that does not include the offending agent should be started.

Interruption of Long-Acting Antiretroviral Drugs

The combination of CAB LA and RPV LA is approved as a complete regimen for the treatment of HIV. CAB LA and RPV LA are given as intramuscular (IM) injections and have extended half-lives. Therefore, patients who miss doses or discontinue therapy without bridging with an oral ARV regimen are at increased risk of virologic failure with development of drug resistance. Clinicians should refer to prescribing information for CAB LA and RPV LA for the management of missed doses or discontinuations.[7] For planned missed injection doses of CAB LA and RPV LA, oral formulations of CAB and RPV should be made available to patients as a bridging therapy for up to 2 months. Oral formulation of RPV is available by prescription in community pharmacies, but oral formulation of CAB is available only through the manufacturer. When stopping long-acting injectable ART, transition to a suppressive oral ARV regimen should occur within 4 weeks of the last planned IM doses. Patients who have missed or delayed clinic visits repeatedly should be reassessed to determine if resumption of injections is appropriate or if they may need to be transitioned back to an oral regimen. Plasma viral load testing should be performed before the transition, and drug-resistance testing should be considered if plasma viremia is present.

Patients with drug-resistant HIV may receive IBA as part of a salvage regimen. IBA is initiated with a 2,000-mg loading dose given as an intravenous (IV) infusion, then followed by 800 mg given as an IV infusion every 14 days as maintenance therapy. If a dose is missed by ≥3 days, a repeat loading dose of 2,000 mg IV infusion is recommended before resumption of maintenance therapy.

Analytical Treatment Interruption

Several research studies are evaluating approaches to achieve sustained ART-free viral remission or a functional cure for HIV.[8] Viral eradication (i.e., elimination of HIV entirely from an individual) remains a more challenging, longer-term goal. Currently, the only way to reliably test the effectiveness of these strategies is to interrupt ART and closely monitor for viral rebound in the setting of a clinical trial, an approach referred to as "analytical treatment interruption" or ATI.[9] The duration of treatment interruption, the dynamics of viral rebound, and the criteria for restarting ART are part of ATI clinical trial designs with the goal to conduct these clinical trials safely.

Before ART is interrupted, participants of ATI trials should be made aware of and understand the risks of viral rebound,[10] acute retroviral syndrome, increased risk of HIV transmission, decline of CD4 count, HIV disease progression, development of minor HIV-associated manifestations (e.g., oral thrush) or serious non-AIDS complications (e.g., renal, cardiac, hepatic, or neurologic complications), and the development of drug resistance. Patients should be counseled about the need for close clinical and laboratory monitoring during ART interruptions and provided counseling and linkage to pre-exposure prophylaxis services should they wish to refer sexual partners at risk for acquiring HIV.

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Considerations for Antiretroviral Use in Special Populations

Adolescents and Young Adults With HIV

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Key Considerations and Recommendations
• Adolescents and young adults (AYA) with HIV largely belong to two distinct groups: those who acquired HIV in the first decade of life and who may be heavily antiretroviral therapy (ART)–experienced (early-acquired HIV); and those who acquired HIV in or after the second decade of life who may be mostly ART-naive. • ART is recommended for **all** AYA with HIV **(AI)** to reduce HIV-related morbidity, mortality, and transmission. • For AYA with HIV who are at risk for poor clinical outcomes, it is critically important to assess the behavioral and psychosocial context, and their ability to adhere to ART. Efforts should be made to provide youth-friendly support and infrastructure to reduce barriers to adherence and maximize success in achieving sustained viral suppression **(AIII).** • Pediatric and adolescent care providers should prepare AYA with HIV for the transition into adult care settings. Adult providers should be knowledgeable about this unique patient population and the challenges that frequently accompany the transition into the adult care setting. Consulting and collaborating with pediatric and adolescent HIV care providers is critical to ensure the successful transition of AYA with HIV to adult providers and continued engagement in care **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

Adolescents (13–19 years old) and young adults (20–24 years old) (AYA) with HIV consistently account for about one-fifth of new infections in the United States.[1] AYA with HIV have lower rates of testing, diagnosis, treatment engagement, and viral suppression than adults with HIV. Importantly, unique developmental, psychosocial, behavioral, and infrastructural factors affect this vulnerable population. Without having their specific challenges and needs addressed, AYA with HIV remain at risk for poorer HIV-related outcomes, including persistent viremia, drug resistance, morbidity, mortality, and secondary transmission.

Epidemiology

Globally, approximately 5 million young people aged 15 to 25 years live with HIV.[2] AYA with HIV are mostly individuals who acquired HIV in the first decade of life, mainly perinatally and rarely via blood transfusion or from sexual abuse. During adolescence and young adulthood, most individuals acquire HIV through sexual activity. Among the latter group, the Centers for Disease Control and Prevention (CDC) estimates that consistently one-fifth of the approximately 40,000 individuals newly diagnosed with HIV in the United States annually are adolescents and young adults.[1] The majority of new infections in this age group are among Black/African Americans and Hispanic/Latino males who identify as men who have sex with men (MSM). For example, in 2018, more than 50% of the infections in this age group were among young Blacks and African Americans,

and 27% were among Hispanics and Latinos. Most (87%) were male, with 92% identifying as MSM. Compared to adults with HIV, AYA with HIV are less likely to have acquired HIV from injection drug use, and trends in HIV and AIDS prevalence indicate that the disproportionate burden of HIV among racial and ethnic minorities is even greater among youths 13 to 24 years of age than among those older than 24. Together, AYAWH account for approximately 34,000 of the individuals being followed at pediatric and adult clinics in the United States.[3]

Heterogeneity of Adolescents and Young Adults With HIV

AYA with HIV represent a diverse population in terms of socio-demographics, mode of HIV acquisition, sexual and substance use history, clinical and immunologic status, psychosocial development, and ability to adhere to medications. These distinctions have implications for HIV treatment, including the best ways to support AYA with HIV to optimize outcomes. AYA with HIV largely belong to two distinct groups:

- ***Adolescents and Young Adults With Early-Acquired HIV:*** These individuals, who acquired HIV in the first decade of life, are more likely to be treatment-experienced and have antiretroviral (ARV) drug resistance that may limit their options for ART regimens. This may be even more relevant for AYA with HIV who emigrated from parts of the world where routine viral load and genotypic resistance testing are not as readily available so that recognition of virologic failure and drug resistance may be delayed or missed. Also, individuals in this group generally have undergone a longer duration of disease chronicity and may have greater disease burden and more complications, less functional autonomy, and higher mortality risks.[4]
- ***Adolescents and Young Adults With HIV Acquired Later in Life:*** Individuals in this group are a more heterogeneous group of mostly young men (especially MSM) and young cisgender and transgender women with HIV acquired primarily through sexual activities. A minority in this group have acquired HIV through injecting drugs or were victims of sexual abuse. The intersection of adolescence and young adulthood with other key risk populations (e.g., MSM, people who use drugs, transgender individuals) magnifies the risk of poor clinical outcomes in this younger population. A statistically higher percentage of individuals in this group reported experiencing an even more extensive number of negative life experiences compared to those who acquired HIV early in life (38.8% versus 16.3%, $P<.012$).[5]

Unique Characteristics and Considerations for Adolescents and Young Adults With HIV

Although a diverse group, many AYA with HIV share unique characteristics that distinguish them from adults with HIV. Furthermore, AYA with HIV have certain commonalities that, while not necessarily unique to youth, disproportionately affect their chances of successful HIV treatment. Compared to adults 25 years old and older, AYA with HIV have poorer outcomes on each step of the HIV care continuum[6] (i.e., HIV diagnosis, linkage to HIV care, receipt of care, retention in care, achievement of viral suppression, maintenance of viral suppression). Most notably, only 40% of AYA with HIV are aware of their diagnosis and only 6% to 30% are virally suppressed.[7] These numbers are significantly worse than documented in older adults with HIV.[8] In one study of MSM of all ages, the percentage of those linked to HIV care within one month of diagnosis was lowest among AYA with HIV aged 13 to 19 (69%) and 20 to 24 (70%) years.[9] This group also had the lowest rates of retention in care and viral suppression. Older young adults (through age 29), who currently have

the highest incidence of HIV infection among all age groups, have similar challenges, with 30% unaware of their infection status. They, too, require focused attention.

There are myriad reasons AYA with HIV do not perform as well on the HIV care continuum and are at greater risk of poorer clinical outcomes than adults with HIV. Perhaps most important, AYA with HIV often do not have the same developmental capacity or ability to secure resources as their adult counterparts. These key features, discussed below, should be considered carefully because they can negatively affect HIV treatment and may alter clinical decision-making.

Adolescents and Young Adults With HIV as a Developmentally Distinct Patient Population

Developmental maturity in AYA with HIV generally can be grouped into several, often overlapping, areas, including physical, cognitive, communication and language, and social and emotional, combined with an emerging recognition of sexual identity. Several overarching factors—especially HIV-related stigma, discrimination, and a fear of familial and/or social rejection—can contribute to impaired development in all areas and adversely affect HIV treatment and clinical outcomes for many AYA with HIV. Additional important psychosocial factors discussed below commonly are seen in this population and also can affect development and successful HIV treatment.

Key developmental factors that may impact HIV treatment are highlighted below:

- ***Cognitive development:*** Evolving cognitive processes, which normally continue well into the third decade of life, are particularly relevant to HIV treatment in AYA with HIV. Their developing decision-making capacity often is driven by concrete thinking processes, risk-taking behaviors, preoccupation with self-image, and the need to fit in with their peers, all of which can affect HIV treatment negatively, including medication adherence and long-term clinical outcomes.[4,10,11] Likewise, AYA with HIV are at risk for neurocognitive impairment and mental health comorbidities,[12-15] including psychiatric, behavioral, and substance use disorders, which can further affect cognitive development and compromise effective HIV treatment.
- ***Physical development:*** The rapid physiologic changes (e.g., puberty, rapid growth) that occur in adolescence may result in altered ARV pharmacokinetics, underscoring the importance of adolescent-specific studies.[4] AYA with HIV, particularly those with infection acquired early in life and/or while sexually immature, also are at risk for impaired physical development, especially delayed sexual maturation and impaired normal bone development, which may have long-term consequences like reduced final height and peak bone mass, the latter being a key risk factor for developing osteoporosis.[16] Both delayed maturation and short stature may increase anxiety, depression, and stigma, which may, in turn, affect treatment adherence.[17] AYA with HIV who acquire HIV later in life still may be affected because peak bone mass is not achieved until around age 30. A small study showed lower bone mass in Tanner Stage 5 young men aged 20 to 25 years who acquired HIV during adolescence than in HIV-uninfected age-matched controls.[18]

Thus, developmental maturity should be considered in AYA with HIV, because associated clinical implications may alter HIV treatment decisions, including ARV selection and dosing.

Psychosocial and Related Risk Factors Affecting Adolescents and Young Adults With HIV

Several psychosocial, behavioral, and environmental risk factors affect many AYA with HIV and can undermine successful HIV treatment disproportionately in this population. Common key risk factors are summarized here:

- ***Mental and behavioral health:*** The percentage of AYA with HIV with behavioral and mental health conditions is very high and can undermine engagement in care and medication adherence. The most common conditions include anxiety and behavioral disorders, mood disorders (including depression), and attention deficit hyperactivity disorder. Among adolescents with early-acquired HIV, nearly 70% meet criteria for a psychiatric disorder at some point in their lives.[13,19-21] Similarly, depression and anxiety were identified by symptom inventory 43% and 31% of the time, respectively, among AYA with HIV presenting for care at treatment sites in the Adolescent Trials Network.[22]
- ***Substance use:*** Substance use is prevalent among AYA with HIV. Among more than 2,000 AYA with HIV (72% acquiring HIV later in life) surveyed by the Adolescent Trials Network, weekly or more frequent use of tobacco (33%), marijuana (28%), alcohol (21%), and other illicit drugs (23%) was reported.[23,24] Young MSM had higher odds of each substance use behavior, whereas transgender women had increased odds of marijuana and other illicit drugs. Suboptimal ART was associated with increased risk of substance use behaviors,[24] underscoring the need to screen for and address substance use to improve treatment outcomes.
- ***Transgender AYA with HIV:*** About 1 in 3 new HIV diagnoses among transgender individuals are among those aged 13 to 24 years.[25,26] Transgender AYA with HIV report high rates of stigma and other structural and logistical barriers that affect their access to gender-affirming care, as well as HIV prevention and treatment services, which are known to be associated with retention in care and adherence to treatment (see Transgender People with HIV).
- ***Homelessness and unstable housing:*** Among the 4.2 million homeless adolescents and young adults in the United States (of whom 700,000 are unaccompanied minors)[27] , the estimated HIV prevalence ranges from 3% to 16%. Youth who identify as lesbian, gay, bisexual, transgender, or queer (LGBTQ); those with mental health concerns; and those who engage in substance use are disproportionately represented among homeless youth.[28] Homeless and unstably housed AYA with HIV have greater difficulties securing and sustaining resources and engaging in and being retained in care and treatment.[29]
- ***Additional social and environmental factors:*** A number of social and environmental factors commonly found among AYA with HIV negatively affect their HIV treatment, including limited familial and/or social support, lack of health insurance and/or experience with health care systems, unstructured and chaotic lifestyles, transportation barriers, food insecurity, limited educational opportunities, limited employment opportunities and/or unstable employment, and a history of trauma and/or sexual abuse.[30]

Optimizing Treatment Effectiveness and Supporting Adherence in Adolescents and Young Adults With HIV

Given the unique physiologic, developmental, and psychosocial characteristics discussed above, AYA with HIV require comprehensive systems of care with culturally competent providers and tailored treatment to serve all their specific medical and psychosocial needs. To maximize their chances of success, it is also imperative to routinely assess each AYA with HIV for individual factors that may need to be addressed or considered in treatment decisions or that may affect adherence.

Table 13 summarizes common adherence barriers among AYA with HIV, along with recommended support strategies. Refer to the Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection and the Adherence to Antiretroviral Therapy in Children and Adolescents with HIV

additional approaches. Targeted interventions to improve treatment effectiveness and adherence related to a few key psychosocial factors among AYA with HIV also are highlighted here:

- ***Mental health care:*** Strategies to improve the provision of mental health care for AYA with HIV are critically important for optimizing treatment for co-occurring HIV and mental health problems.[31] These strategies include improving provider education, integrating trauma-informed care practices, increasing access to mental health professionals through colocated services for HIV care, expanding care delivery paradigms like telemedicine, and optimizing treatment approaches. An example of the latter is a combination of tailored psychotherapy and pharmacotherapy.[26,32] Further guidance for providing appropriate mental health care for AYA with HIV can be found in the Pediatric Guidelines.
- ***Substance use disorders:*** Providers should assess and recommend treatment for substance use disorders, with consideration of emerging substance use trends, such as the use of electronic vapor products. Further guidance for providing appropriate substance use screening and treatment for AYA with HIV can be found in the Pediatric Guidelines and in the Substance Use Disorders and HIV section.
- ***Transgender AYA with HIV:*** Providers must increase their understanding of this population to minimize barriers and optimize testing, engagement, and outcomes for transgender AYA with HIV. Drug-drug interactions between hormonal therapy and ART can occur but are less common with newer ART regimens. Further information can be found in the Transgender People with HIV section and Adolescent Trials Network Transgender Youth Resources.[33]
- ***Psychosocial and environmental stressors:*** Multimodal interventions that enhance social support and teach adaptive coping skills may help AYA with HIV manage environmental stressors and improve clinical outcomes.

Specific Antiretroviral Therapy Considerations in Adolescents and Young Adults With HIV

All AYA with HIV should initiate ART as soon as possible and stay on ART indefinitely to maximize viral suppression, reduce morbidity and mortality, and prevent secondary HIV transmission **(AI)**. As described below, clinicians should consider simplifying ART regimens and using antiretrovirals with high barriers to resistance whenever possible to support adherence.

Strategies to Improve Medication Adherence

Clinicians selecting ART for AYA with HIV must balance the goal of prescribing a maximally potent regimen with a patient-by-patient assessment of existing and potential adherence barriers and available youth-friendly support strategies to facilitate adherence.[34] Additional considerations and strategies that may affect adherence among AYA with HIV are highlighted below in **Table 11.**

Table 11. Antiretroviral Therapy–Specific Strategies to Improve Medication Adherence

Antiretroviral Therapy-Specific Strategies to Improve Medication Adherence	
Regimen selection	• Simple ART regimens (e.g., fixed-dose, once daily combinations) with high barriers to resistance are preferable, if possible.[35] • Minimal side effects (e.g., gastrointestinal)
Treatment plan	• Develop the plan in partnership with AYA with HIV, considering daily schedule; tolerance of pill number, size, and frequency; issues affecting absorption; and potential adverse effects and interactions with other medications.[34,36] • Design adolescent-friendly reminder systems[37] (e.g., apps, cell phone reminders, pill boxes) for adherence support.[38]
Motivators	• Emphasize personal benefits (e.g., viral suppression, improved health). • Undetectable equals untransmittable (U=U) status disclosure to sexual partners without HIV may act as a particularly strong motivator for reducing stigma and improving adherence among AYA with HIV.

Antiretroviral Therapy Regimens for Adolescents and Young Adults With HIV Without Drug Resistance

The boosted protease inhibitor (PI) darunavir (DRV) and the integrase strand transfer inhibitors (INSTIs) dolutegravir (DTG) and bictegravir (BIC) offer once-daily dosing. When coformulated with a dual nucleoside backbone, they also provide single-tablet regimens with high genetic barriers to resistance.

Clinical trials have demonstrated the superiority of DTG over boosted PI-based regimens. BIC coformulated with tenofovir (TAF) and emtricitabine (FTC) also appears to have a low risk of treatment-emergent resistance and is available as a single-tablet regimen with a small pill size and no food requirements. BIC is currently licensed for use in children or adolescents ≥25kg. Adolescent studies are ongoing with an adult fixed-dose combination of BIC/FTC/TAF from 12 years of age and 35 kg with a favorable interim analysis in a stable adolescent switch study.[39]

A two-drug once-daily single-tablet regimen of DTG/lamivudine is recommended as an initial ART regimen except for individuals with HIV RNA >500,000 copies/mL, hepatitis B virus (HBV) coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.

Long-acting formulation regimens, the first of which (cabotegravir/rilpivirine) was recently FDA-approved in the United States, are considered a viable option for patients who are engaged in care, virologically suppressed on oral therapy, and agreeable to the administration schedule. These agents are being studied for AYA with HIV[40] ages 12 to 17 without relevant antiretroviral drug resistance. Case reports of viral suppression with the use of long-acting rilpivirine (RPV) and cabotegravir (CAB)[41] in AYA with HIV with a history of poor adherence are encouraging (see Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression). Studies to evaluate these modalities among nonadherent AYA with HIV are under development.[42]

Antiretroviral Therapy–Experienced Adolescents and Young Adults With HIV with Drug Resistance

AYA with HIV who acquired HIV early in life often have treatment challenges associated with the long-term use of ART that mirrors those of ART-experienced adults, such as extensive resistance, complex regimens, and adverse drug effects. In ART-experienced adolescents, DTG was safe and well tolerated, and it achieved viral suppression rates of 44% to 66% when combined with an optimized background regimen. Acquired treatment-emergent INSTI resistance may occur.[43] For adolescents with dual-class resistance, the introduction of DRV/cobicistat/FTC/TAF in combination with DTG offers the potential of a potent triple-class regimen with a high genetic barrier to resistance with only two pills once daily[44] (see Virologic Failure and Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression).

Antiretroviral Therapy Considerations in Sexually Immature Adolescents and Young Adults With HIV

The physiologic changes (e.g., puberty, rapid growth) that occur in adolescence may result in altered pharmacokinetics. Therefore, although generally it is appropriate for postpubertal adolescents to be dosed with ARV drugs according to adult guidelines, adolescents in early puberty should be dosed according to the Pediatric Guidelines, which factor in dosages by weight and sexual maturity ratings.

Additional Antiretroviral Therapy Considerations in Adolescents and Young Adults With HIV

Additional considerations include an increased risk of side effects, such as bone and renal toxicity with tenofovir-based drugs in the rapidly growing adolescent. These concerns are magnified in low-weight adolescents for whom appropriate lower-dose formulations are not available. Because AYA with HIV have not yet reached peak bone mass, TAF generally should be used instead of TDF, because of a greater bone loss with the latter ARV.

For a more detailed discussion on ART therapy in AYA with HIV, please see the What to Start section and the Pediatric Guidelines. For additional information on treatment adherence in AYA with HIV, please see Table 18, Adherence to the Continuum of Care, and the Pediatric Guidelines.

Preventive Measures and Supporting Long-Term Health in Adolescents and Young Adults With HIV

People with HIV are at an increased risk of HIV- and ART-related comorbidities, including cardiovascular disease, diabetes, metabolic syndrome, osteoporosis, and neurocognitive impairment. When HIV is acquired at birth or early in life, an individual can live for many decades with the condition. However, engagement in health-risk behaviors (e.g., tobacco smoking, alcohol and drug use, unhealthy diet, physical inactivity) may have greater long-term implications for clinical outcomes in this population.

Preventive health care and promotion of positive health behavior during the critical time of adolescence and young adulthood can shape future habits and clinical outcomes over a lifetime. Incorporating regular screening, preventive health care, and health education is critical for optimizing short- and long-term physical and mental well-being and should be considered part of routine HIV treatment. Careful attention should be paid to modifiable risk factors in these early decades, such as weight gain and obesity, dyslipidemia, vitamin D deficiency, and tobacco use. Aggressive screening

and risk factor mitigation early in the life of AYA with HIV not only improves current health but also can decrease their risk of developing comorbidities later in life. See HIV Medicine Association of the Infectious Diseases Society of America HIV primary care guidance for more details.

Transitioning to Adult HIV Care

Given lifelong infection with HIV and the need for treatment throughout the life course, HIV care programs and providers need flexibility to transition care appropriately for AYA with HIV. A successful transition requires an awareness of fundamental differences between many adolescent and adult HIV care models.

In most adolescent HIV clinics, care is more teen-centered and multidisciplinary, with primary care highly integrated into HIV care.[45] Often there is anonymity, with clinics not being devoted specifically to HIV or infectious diseases. Moreover, such services as sexual and reproductive health and mental health care are often found in one clinic setting (i.e., the medical home). Additionally, these clinics are more likely to be "youth-friendly" by including such aspects as waiting areas where AYA with HIV can access computers and other items that may facilitate engagement; flexible schedules that include evening hours or walk-ins; technology like social media and texting to engage patients; staff who are trained specifically in the unique cognitive, developmental, and other psychosocial aspects of AYA with HIV; and lower patient-to-provider ratios. In contrast, some adult HIV clinics may be more HIV-specific and rely more on referral of the patient to separate subspecialty care settings, such as gynecology.[46] Furthermore, adult clinic settings tend to be larger and can easily intimidate younger, less motivated patients.

Transitioning the care of an AYA with HIV must consider such factors as medical insurance; degree of independence, autonomy, and decision-making capacity; patient confidentiality; and informed consent. Nonetheless, given the structural limitations (adolescent clinics not being able to see patients over a certain age), care transitions must occur, usually between the ages of 21 and 25. The period of transition is a highly vulnerable time for attrition from HIV care. Data on transition outcomes are emerging, showing variable rates of successful transition to adult care ranging between 50% and 85%.[47-50]

It is important to recognize that the transition for AYA with HIV with early-acquired HIV versus those who acquired HIV later in life may pose distinct challenges. AYA with HIV who acquired HIV early in life—who often have experienced significant instability and prior loss—may experience the transition to adult HIV care as yet another traumatizing event. Alternatively, those who acquired HIV later in life, given their more recent engagement in the medical system, may be less likely to be effectively engaged in pediatric and adolescent care, which may affect their ability to transition successfully. Factors to date that have been associated with successful transition for those with early-acquired HIV include high self-management and perceived emotional and social support.[51]

To maximize the likelihood of a successful transition, interventions to facilitate transition are best implemented early on.[49,52-54] Strategies and approaches for both the adult and pediatric and adolescent programs are discussed below:

Table 12: Approaches to Optimize Care Transition for AYA With HIV

Pediatric/Adolescent	Adult
Personnel	
• Engage a multidisciplinary team knowledgeable about medical and psychosocial issues of AYA with HIV, including the challenges of transitioning youth to adult care settings. • Utilize combined internal medicine and pediatrics-trained providers if available. • Assign a transition point person and have their contact information readily available. • Educate HIV care teams and staff about transitioning AYA with HIV and their needs.	• Engage a multidisciplinary adult care team knowledgeable about medical and psychosocial issues of AYA with HIV, including the challenges of transitioning youth to adult care settings. • Utilize combined internal medicine and pediatrics providers if available. • Assign a transition point person and have their contact information readily available. • Identify outreach specialists, navigators, social workers, case managers, and providers with a youth-friendly approach. • Educate clinic personnel about AYA with HIV and their challenges to enhance sensitivity and understanding and minimize stigma.
Education and Preparation of AYA with HIV	
• Enhance AYA with HIV health literacy, including understanding of HIV and their medical history. • Address patient and family resistance to transition of care caused by lack of information, concerns about stigma or risk of disclosure, and differences in practice styles. • Help youth develop life skills, including, but not limited to, counseling on appropriate use of a primary care provider and how to manage appointments; the importance of prompt symptom recognition and reporting; and self-efficacy in managing medications, insurance, and assistance benefits.	• Meet AYA with HIV before transition, if possible. • Clearly outline policies and expectations before and during the first visit. • Have an orientation plan to acquaint newly transitioned AYA with HIV to the clinic environment and adult clinical care program. • Implement interventions that may improve outcomes, such as patient navigators, peer support groups, mental health assessment, and inclusion of parents and guardians where available. • Address health literacy and ensure AYA with HIV understand HIV, goals of care, etc. • Continue to work with AYA with HIV toward developing life skills, etc.

Table 12: Approaches to Optimize Care Transition for AYA With HIV

Pediatric/Adolescent	Adult
Strategies and Approaches	
• Identify adult care providers able to provide youth-friendly care for adolescents and young adults. • Develop a formal, purposeful individualized transition plan to address comprehensive care needs, including medical, psychosocial, and financial aspects of transitioning to adult HIV care. • Optimize provider communication between adolescent and adult clinics, including a warm multidisciplinary, comprehensive medical history hand-off that includes prior regimens and outcomes (e.g., adherence, virologic failure and resistance).	• Develop a realistic clinic model based on specific needs (e.g., simultaneous transition of mental health and/or case management versus a gradual phase-in) and staffing. • Engage in a warm handoff from the pediatric team, which allows the accepting adult team to learn about and understand the multidisciplinary challenges and goals for the patient. Devise a plan for how to continue building the skills on the adult side. • Build in flexibility (e.g., permissive grace period for appointments, leniency for missed appointments, particularly when first transitioning). • Incorporate other aspects of care beyond HIV management, if possible (e.g., family planning, sexually transmitted infection testing and treatment, mental health, substance use).
Communication	
• Foster regular dialogue between pediatric and adolescent and adult teams before and after transition through regular meetings, case conferences, etc. • Solicit feedback from the AYA with HIV • Use technology (e.g., texting, HIPAA-compliant messaging apps, telemedicine).	
Evaluation	
• Implement ongoing evaluation to measure the success of the selected model (retention in adult care).	

Discussions regarding transition should begin early and before the actual transition process.[55] Attention to the key interventions noted above will be likely to improve adherence to appointments and avoid the potential for youth to fall through the cracks, as this concept is referred to commonly in adolescent medicine. For a more detailed discussion on specific topics related to transitioning care for adolescents and young adults, see Transitioning into Adult HIV Care. Please also refer to the Pediatric Guidelines.

Table 13: AYA With HIV ARV Adherence Barriers and Strategies to Support Adherence

ART Adherence Barrier	Adherence Support Strategy	Rationale for Adherence Support Strategy
Prioritization of short-term goals and socialization with peers over daily HIV treatment adherence	Youth-friendly reminder systems (e.g., text, phone, apps)	• Daily adherence to ARV regimens may not take priority in the lives of AYA with HIV. • AYA with HIV benefit from reminder systems to facilitate adherence.
	Novel ART delivery strategies (e.g., long-acting oral or injectable ARVs)	• AYA with HIV show interest in long-acting alternatives for ART delivery. • Long-acting ARVs are a promising tool to facilitate adherence, once approved for AYA with HIV.
Social concerns related to loss of confidentiality	Simple ARV regimens	• Adolescents do not want to be different from peers; adherence to complex regimens is particularly challenging. • Simple ARV regimens are preferable for AYA with HIV.
	User-friendly and discreet regimens	• Avoidance of HIV-related stigma and of unintentional disclosure of HIV status is a priority for AYA with HIV. • Protect confidentiality with user-friendly and discreet adherence supports (e.g., discreet pill bottles, reminder systems, etc.).
Side effects/fear of side effects	ARV regimens that minimize side effects	• Side effects are associated with nonadherence to ARVs. • Regimens with minimal side effects and medications that manage side effects have utility for AYA with HIV.
Denial or dismissal of HIV diagnosis	Motivational interviewing (MI) and motivational enhancement therapy (MET)	• MI and MET acknowledge AYA with HIV's autonomy and potential ambivalence about treatment adherence. • MI and MET have shown promise for improving adherence to chronic disease treatment, including HIV.
	Positive affirmation messages (e.g., text, app)	• Electronically delivered positive affirmation messages can improve self-esteem and ARV adherence among AYA with HIV.
Lack of health literacy regarding the benefits of ART	Health literacy support and U=U education	• AYA with HIV may not fully understand the importance of taking ARVs daily, particularly when they are asymptomatic. • Increased health literacy is associated with better adherence to ARV regimens. • U=U education holds promise for AYA with HIV.

Table 13: AYA With HIV ARV Adherence Barriers and Strategies to Support Adherence

ART Adherence Barrier	Adherence Support Strategy	Rationale for Adherence Support Strategy
Mistrust of providers and the medical establishment	Empathetic and patient-centered communication	• Communication exploring the needs of AYA with HIV patients can build trust, including exploring needs not directly related to HIV treatment (e.g., school, employment, relationships, etc.).
Mental health and/or substance use	Individualized mental health and substance use services	• Comprehensive mental health and substance use services have shown promise for improving viral suppression among AYA with HIV. • Service should be delivered based on individualized needs assessments.
	Directly observed therapy may be considered	• For some AYA with HIV with difficult adherence problems, directly observed therapy may be considered.
Lack of familial and social support	Family and peer support groups	• Family members and peers are a defense against stigma and social isolation, source of emotional support, and partners in medication management. • Family and peer support groups have utility for AYA with HIV living with HIV.
Provider views of AYA with HIV as "risky" and/or not ready for ART	Promote development of a positive rather than risk-centered identity among AYA with HIV	• Adolescence and young adulthood are periods of identity development where HIV stigma is particularly problematic. • Providers should not conceptualize AYA with HIV as "high risk" to reduce stigma and improve ARV adherence.
Provider implicit biases of AYA with HIV	Implicit bias training	• Consciously changing biased associations and repeated bias self-regulation training can reduce providers' implicit biases.
	Gender-affirming care	• Transgender individuals are more likely to achieve viral suppression when HIV care providers affirm their gender (e.g., use chosen name and pronoun). • For a more detailed discussion, see guidelines for Transgender People with HIV.

Table 13: AYA With HIV ARV Adherence Barriers and Strategies to Support Adherence

ART Adherence Barrier	Adherence Support Strategy	Rationale for Adherence Support Strategy
Lack of youth-friendly services	Dedicated youth HIV clinic	• Clinic days or hours dedicated to AYA with HIV patients better address unique adherence needs; youth-friendly services include the following: ○ flexible hours, easy scheduling, telephone/telehealth appointments; ○ providers trained in working with AYA with HIV; ○ youth-friendly waiting rooms and physical spaces; ○ supplemental services that comprehensively address psychosocial and health needs of AYA with HIV; and ○ incentives for AYA with HIV care engagement.
	Youth-friendly hours, staff, and physical space	• Where dedicated hours and services are not possible, youth-friendly service elements can be integrated into existing clinic structures, e.g.: ○ offering evening hours; ○ staff training on service delivery to AYA with HIV; and ○ youth-friendly waiting rooms and physical spaces.
	Referrals to more youth-friendly HIV providers	• Where youth-friendly services are not possible, referrals to more youth-friendly HIV care providers should be considered. • Referral decisions should be made collaboratively with the patient.
Lack of comprehensive services that address common psychosocial stressors	Supplemental health, behavioral health, and psychosocial support services	• Individualized delivery of comprehensive supplemental services helps address unique needs of AYA with HIV, including the following: ○ primary care and sexual and reproductive health services; ○ behavioral health services; and ○ psychosocial support services (e.g., school support, transportation, support groups, housing and food assistance).
	Collaboration with and referrals to outside support services	• Where delivery of comprehensive supplemental services is not possible, collaborations with and referrals to outside support services should be considered.

Key: ART = antiretroviral treatment; ARV = antiretroviral; AYA = adolescent and young adult; U=U = undetectable equals untransmittable

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Early (Acute and Recent) HIV Infection

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Panel's Recommendations

• Antiretroviral therapy (ART) is recommended for all people with HIV, including those with early[a] HIV infection **(AI).** ART should be initiated as soon as possible after HIV diagnosis **(AII).**
• The goals of ART are to suppress plasma HIV RNA to undetectable levels **(AI),** prevent transmission of HIV **(AI),** and preserve immune function **(AIII).** Monitoring of plasma HIV RNA levels, CD4 T lymphocyte cell counts, and antiretroviral (ARV) drug-related adverse effects should be done as recommended for people with chronic HIV infection **(AII).**
• A blood sample for genotypic resistance testing should be sent to the laboratory before initiating ART **(AIII).**
  ○ Standard genotypic drug-resistance testing should be performed for mutations in the reverse transcriptase and protease genes **(AIII)** for all people with early HIV**.**
  ○ Genotype testing for integrase strand transfer inhibitor (INSTI) resistance should be performed for those who acquire HIV during or after the use of long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP), if transmitted integrase stand transfer inhibitor (INSTI) resistance is suspected, or if HIV diagnosis occurs after receiving an INSTI-based regimen for post-exposure prophylaxis (PEP) **(AIII).**
• ART can be initiated before drug-resistance test results are available.
  ○ For those without a history of using CAB-LA as PrEP, one of the following ARV regimens is recommended[b] **(AIII):**
  ▪ Bictegravir (BIC)/tenofovir alafenamide (TAF)/emtricitabine (FTC)
  ▪ Dolutegravir (DTG) with (TAF or tenofovir disoproxil fumarate [TDF])[c] plus (FTC or lamivudine [3TC])
  ○ For those with a history of CAB-LA use as PrEP, genotype testing before starting ART should include screening for INSTI-resistance mutations **(AIII).**
  ▪ A regimen of cobicistat- (COBI)[d] or ritonavir-boosted darunavir (DRV) with (TAF or TDF)[b] plus (FTC or 3TC) is recommended while awaiting the results of the genotype testing **(AIII).**
  ▪ Use of an empiric INSTI-containing regimen **is not recommended** unless genotype testing shows no evidence of INSTI resistance **(AIII).** This is because INSTI resistance may be present in those who acquire HIV during and possibly after the use of CAB-LA as PrEP.
• In people with HIV RNA levels ≥200 copies/mL and who are taking PrEP, immediate initiation of an effective HIV treatment regimen is recommended while awaiting confirmation of HIV diagnosis **(AIII).**
• Pregnancy testing should be performed in people of childbearing potential before initiating ART **(AIII).**
• When the results of drug-resistance tests are available, the treatment regimen can be modified if needed **(AII).**
• Providers should inform individuals starting ART of the importance of adherence in achieving and maintaining viral suppression **(AIII).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed non-randomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

[a] Early infection represents either acute or recent (≤6 months) infection.

[b] Because of the low rates of transmitted INSTI resistance in the United States at present, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started while awaiting the results of the INSTI genotype.

[c] TAF and TDF are two forms of tenofovir that are approved in the United States. TAF has fewer bone and kidney toxicities than TDF, whereas TDF is associated with lower lipid levels. Safety, cost, and accessibility are among the factors to consider when choosing between these drugs.

[d] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters.

Introduction

Acute HIV infection occurs soon after transmission and is typically characterized by the lack of anti-HIV antibodies and the presence of viremia, which can be detected by an HIV RNA test or p24 antigen test. Recent HIV infection is considered the period of ≤6 months after infection during which anti-HIV antibodies become detectable. Throughout this section, the term "early HIV infection" is used to refer to either acute or recent HIV infection. People with acute HIV infection may experience fever, lymphadenopathy, pharyngitis, skin rash, myalgia, arthralgia, and other symptoms; however, illness is generally nonspecific, and people can be asymptomatic or experience relatively mild symptoms.[1-6] Clinicians may fail to recognize acute HIV infection because its manifestations are similar to those of many other viral infections, such as COVID-19, influenza, and infectious mononucleosis. Table 14 below provides clinicians with guidance to recognize, diagnose, and manage acute HIV infection.

Diagnosing Acute HIV Infection

Health care providers should consider a diagnosis of acute HIV infection in a person who has a suggestive clinical syndrome or in asymptomatic individuals who report recent engagement in activities that may put them at high risk of HIV acquisition (see Table 14 below).[7] Individuals may not always disclose high-risk activities or perceive that such activities put them at risk for HIV acquisition. Thus, even in the absence of reported high-risk activities, health care providers should have a low threshold for considering a diagnosis of acute HIV infection. Health care visits to emergency departments provide an opportunity for health care providers to screen for acute or established HIV infection, as well as other sexually transmitted infections. Since 2019, the United States Preventive Services Task Force has recommended routine screening for HIV in adolescents and adults aged 15 to 65 years (Grade A recommendation). Testing of remnant blood specimens from an emergency department identified acute HIV infection in approximately 5 of 499 (1%) people presenting with flu-like symptoms.[8] Acute HIV infection was also diagnosed in 7 of 563 (1.2%) people presenting for evaluation of possible mononucleosis with negative heterophile antibody tests.[9] A study of HIV screening in nine emergency departments in six U.S. cities found that a new HIV diagnosis was made in 0.4% of 214,524 adolescents and adults, of whom 14.5% had acute HIV infection.[10] Current statistics on the prevalence of HIV in geographical areas in the United States can be found on the AIDSVu and Centers for Disease Control and Prevention (CDC) AtlasPlus websites.

The recommended initial laboratory HIV testing algorithm includes combination immunoassays that detect HIV-1 and HIV-2 antibodies, as well as HIV p24 antigen (Ag/Ab assays),[11] primarily due to their enhanced ability to detect acute HIV infection. Specimens that are reactive on an initial Ag/Ab assay should be tested with an immunoassay that differentiates HIV-1 from HIV-2 antibodies. Specimens that are reactive on the initial assay and have either a negative or indeterminate antibody differentiation test result should be tested for quantitative or qualitative HIV RNA; an undetectable HIV RNA test result indicates that the original Ag/Ab test result was a false positive. Detection of HIV RNA in this setting indicates that acute HIV infection is highly likely.[11] People presenting to care during the earliest days following HIV infection may have yet to develop a positive p24 Ag

response, which typically occurs with viral load levels of >20,000 to 30,000 copies/mL. In clinical settings with a high probability of infection, quantitative or qualitative HIV RNA testing should be considered even if the HIV Ag/Ab test result is negative. HIV infection should be confirmed by repeat quantitative HIV RNA testing or subsequent testing to document HIV antibody seroconversion. People who receive antiretroviral therapy (ART) during acute or very early HIV infection may demonstrate weaker reactivity to screening antibody assays or incomplete HIV antibody evolution; may remain non-reactive to confirmatory antibody assays; and in the setting of sustained virologic suppression, may have complete or partial seroreversion.[12-16]

Providers should be aware that even a low-positive quantitative HIV RNA level (e.g., <200 copies/mL but detectable) in the setting of a negative or indeterminate antibody test result is consistent with acute HIV infection. When a low-positive quantitative HIV RNA test result is present at this level, the HIV RNA test should be repeated on a new blood specimen to confirm the diagnosis. Repeated false-positive HIV RNA test results are unlikely.[2] HIV RNA levels in acute infection are generally very high (e.g., >100,000 copies/mL)[1,2,4]; however, levels may be <200 copies/mL in the earliest weeks following infection as viral load continues to rise. In rare cases, however, such low HIV RNA levels also may represent a false-positive result. The previously proposed threshold of <3,000 copies/mL is based on historical data, which used laboratory methods that are now considered obsolete.[17] Improvements in plasma viral load methodology suggest that any positive result on a quantitative plasma HIV RNA test in the setting of a negative or indeterminate antibody test result may be consistent with acute HIV infection. Some health care facilities may still be using HIV testing algorithms that test only for anti-HIV antibodies. In such settings, when acute HIV infection is suspected in a person with a negative or indeterminate HIV antibody test result, a quantitative or qualitative HIV RNA test should be performed. A negative or indeterminate HIV antibody test result and a positive HIV RNA test result (<200 copies/mL)[18] indicate that acute HIV infection is highly likely.

Diagnosing Acute HIV Infection in People Taking Pre-Exposure Prophylaxis

Three antiretroviral (ARV) options—oral emtricitabine (FTC) with either tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF) and intramuscular long-acting cabotegravir (CAB-LA)—are now available for HIV pre-exposure prophylaxis (PrEP). People who acquire HIV while taking PrEP may sometimes have ambiguous HIV test results. A positive HIV Ag/Ab test result or a positive HIV RNA test result in the setting of a negative HIV antibody test result should prompt immediate confirmation of HIV diagnosis. It is important to collect a new blood specimen to verify the HIV diagnosis before initiating ART. Important considerations include the following:

- In people with HIV RNA level ≥200 copies/mL who are taking PrEP, immediate initiation of an effective HIV treatment regimen[18] is recommended while awaiting confirmation of HIV diagnosis **(AIII).**

- In people taking PrEP who have a negative HIV antibody test result and a low-positive quantitative HIV RNA test result (<200 copies/mL), a confirmatory HIV antibody test and repeat quantitative plasma HIV RNA test should be performed, and results should be available before initiating ART.

- In rare cases, particularly when PrEP is transitioned to an ARV regimen and HIV RNA and antibody diagnostic testing are inconclusive, HIV DNA testing may be of value.[19] Options for

confirming HIV infection and managing such cases are areas of evolving science summarized by the CDC.[19] Clinicians seeking urgent advice can contact the Clinical Consultation Center's PrEP Service at 1-855-HIV-PREP (or 1-855-448-7737).

Acute HIV Infection in People Taking Long-Acting Cabotegravir for Pre-Exposure Prophylaxis

In the HPTN 083 trial, a pivotal trial of CAB-LA versus TDF/FTC for HIV PrEP with more than 2,000 participants enrolled in each arm, 25 incident cases of HIV were identified in the CAB-LA arm compared to 72 cases in the TDF/FTC arm.[20,21] Selection of a potent ARV regimen in people who develop acute HIV infection while taking CAB-LA for PrEP should consider that injectable cabotegravir (CAB) may remain detectable after treatment discontinuation, for up to 3 years in men and 4 years in women.[22] This long pharmacokinetic tail may contribute to the selection of drug-resistant variants in the setting of incident infection. In an extended analysis of HPTN 083, 34 cases of HIV infection were reported in the CAB-LA arm, with 6 of these cases occurring despite on-time CAB-LA injections.[23,24] Detection of HIV infection was delayed in 15 of 32 cases and was associated with waxing and waning HIV Ag/Ab, HIV antibody, and qualitative and quantitative HIV RNA test results (i.e., fluctuating between reactive/non-reactive, detectable/non-detectable).[23] Major resistance to an integrase strand transfer inhibitor (INSTI) occurred in 10 of the 32 cases evaluated. All 10 participants with INSTI resistance in the CAB-LA arm received their last CAB dose within 6 months of their initial HIV-positive site visit. While the risk of acquired INSTI resistance appears to wane after 6 months, this trend is based on few observations. These data reinforce the importance of screening for INSTI-resistance mutations when acute HIV infection is diagnosed in people taking CAB-LA or with a history of prior CAB-LA PrEP use **(AIII).**

Treating Early HIV Infection

The goals of ART during early HIV infection are to suppress plasma HIV RNA to undetectable levels **(AI),** prevent the transmission of HIV **(AI),** and preserve immune function **(AIII).**[25-27] Importantly, as with chronic HIV infection, an individual's barriers to ART adherence and appointments should be assessed at the time of ART initiation (see Adherence to the Continuum of Care). ART should be initiated as soon as possible after a positive qualitative or quantitative HIV RNA test result **(AII).** Same-day or rapid ART initiation in people with acute HIV has been shown to be safe, acceptable, and effective.[28] It is important to collect a new blood specimen for a confirmatory HIV antibody test and quantitative plasma HIV RNA test to verify the HIV diagnosis. Given the sensitivity of current HIV RNA assays,[29] a positive result by quantitative or qualitative plasma HIV RNA testing in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. HIV treatment does not need to be delayed while awaiting confirmation of HIV diagnosis. Some individuals may not accept their diagnosis or may decline ART initially for other reasons. Individuals who do not begin ART immediately should be maintained in care, and every effort should be made to initiate therapy as soon as they are ready.

Clinical trial data indicate that individuals who are treated during early HIV infection may experience immunologic and virologic benefits.[26,30-41] In addition, early HIV infection is considered a period of high infectivity,[42] and early ART substantially reduces the risk of HIV transmission.[43-46]

Drug-Resistance Testing in the Setting of Early HIV Infection

Prior to the widespread use of INSTIs, data from the United States and Europe demonstrated that transmitted virus strains with resistance to at least one ARV drug were present in up to 16% of people with HIV.[47,48] In one study, 21% of isolates from people with acute HIV infection demonstrated resistance to at least one ARV drug, most commonly non-nucleoside reverse transcriptase inhibitors (NNRTIs).[49-51] The rate of transmitted INSTI resistance was reported to be ≤2.5% of the samples tested, and <0.5% with second-generation INSTIs.[52-55] Before initiating ART in a person with early HIV infection, a blood specimen should be sent for standard genotypic drug-resistance testing for mutations in the reverse transcriptase and protease genes **(AIII).** Genotype testing for INSTI resistance should be performed for those who acquire HIV during or after the use of CAB-LA as PrEP, if transmitted INSTI resistance is suspected, or if HIV diagnosis occurs after receiving an INSTI-based regimen for post-exposure prophylaxis (PEP) **(AIII).**[22]

Treatment should not be delayed pending resistance-test results. The test results should be used to modify the ARV regimen if necessary **(AII).** In people with no history of CAB-LA use or use of an INSTI-based regimen for PEP, the Panel on Antiretroviral Guidelines for Adults and Adolescents does not currently recommend genotype testing for INSTI resistance given the low rate of transmitted INSTI resistance and the high barrier to resistance of bictegravir (BIC) and dolutegravir (DTG), unless transmitted INSTI resistance is a concern **(AIII).**

Considerations for Preventing HIV Transmission During Early HIV Infection

People with early HIV infection have a higher likelihood of sexual transmission of HIV to others. Prompt initiation of ART and sustained viral suppression to <200 copies/mL can prevent transmission of HIV to sexual partners. Individuals starting ART should use another form of prevention (e.g., condoms, PrEP for partners who are HIV negative, sexual abstinence) for at least the first 6 months of treatment and until they have a documented viral load of <200 copies/mL **(AII).** Many experts would recommend confirming sustained viral suppression before assuming no risk of sexual transmission of HIV **(AIII)** (see Antiretroviral Therapy to Prevent Sexual Transmission of HIV).

Antiretroviral Regimens for Early HIV Infection

ART should be initiated with one of the combination regimens recommended for people with chronic HIV infection **(AIII)** (see What to Start). Providers should inform individuals starting ART of the importance of adherence in achieving and maintaining viral suppression **(AIII).** If available, the results of ARV drug-resistance testing or the resistance pattern of the source person's virus should be used to guide selection of the regimen. All people of childbearing potential should undergo a pregnancy test before initiating ART **(AIII).**

For individuals who have not received CAB-LA as PrEP prior to diagnosis of acute HIV, one of the following INSTI-based regimens is recommended **(AIII):**

- BIC/TAF/FTC
- DTG with (TDF or TAF) plus (3TC or FTC)

DTG and BIC are good treatment options because transmitted resistance to second-generation INSTIs in the United States is rare at present and both BIC and DTG have a high barrier to resistance.

For individuals who acquire HIV during and after the use of CAB-LA as PrEP:

- While awaiting integrase genotype results, the use of an INSTI-based regimen **is not recommended (AIII).** The recommended regimen, until resistance testing confirms the absence of INSTI-resistance mutations, is a cobicistat (COBI)- or ritonavir (RTV)-boosted darunavir (DRV) with (TAF or TDF) plus (FTC or 3TC) **(AIII).**

A pharmacologically boosted protease inhibitor (PI)–based regimen (e.g., boosted DRV) is an option because resistance to PIs emerges slowly, and clinically significant transmitted resistance to PIs is uncommon. Therefore, boosted DRV plus (TAF or TDF) plus (FTC or 3TC) is generally recommended in this setting. Baseline laboratory testing recommended for individuals with chronic HIV infection should be performed (see Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy). Individuals with hepatitis B virus/HIV coinfection should receive TDF/FTC or TAF/FTC as part of their ARV regimen.

Given the increasing use of TDF/FTC[56-58] and TAF/FTC as PrEP,[59,60] early HIV infection may be diagnosed in some people while they are taking TDF/FTC or TAF/FTC. In this setting, drug-resistance test results are particularly important; however, these regimens remain reasonable treatment options pending drug-resistance test results.

Abacavir/3TC **is not recommended** for treatment of acute HIV infection unless the person is known to be HLA-B*5701-negative, and this information is rarely available in people with acute HIV infection. Additionally, due to relatively high rates of transmitted drug resistance for NNRTIs, agents in this drug class **are not recommended** as a component in the regimen of people initiating ART before the results of drug-resistance tests are available.

Treatment Regimens for Early HIV Infection During Pregnancy

All people of childbearing potential who receive a diagnosis of early HIV infection should have a pregnancy test **(AIII).** Because early HIV infection, especially in the setting of high-level viremia, is associated with a high risk of perinatal transmission, all pregnant people with HIV should start combination ART as soon as possible to prevent perinatal transmission **(AI).** COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters. For more information on the safety and efficacy of ARV use in pregnancy, refer to the Perinatal Guidelines.

Follow-Up After Antiretroviral Therapy Initiation

After ART initiation, monitoring of plasma HIV RNA levels, CD4 T lymphocyte cell counts, and adverse effects should be performed as described in Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy (i.e., HIV RNA testing 2–8 weeks after ART initiation, then every 4–8 weeks until viral suppression and every 3–4 months thereafter) **(AII).**

Table 14. Identifying, Diagnosing, and Treating Acute and Recent HIV Infection

Suspicion of Acute HIV Infection

- Health care providers should consider the possibility of acute HIV infection in people with the signs, symptoms, or laboratory findings described below and in asymptomatic people with a possible acute (within 2–6 weeks) exposure to HIV.[a]
  - Signs, symptoms, or laboratory findings of acute HIV infection may include but are not limited to, one or more of the following: fever, lymphadenopathy, skin rash, myalgia, arthralgia, headache, diarrhea, pharyngitis, oral ulcers, leucopenia, thrombocytopenia, and transaminase elevation.
  - High-risk exposures include sexual contact with someone who has HIV or is at risk of HIV infection, sharing needles, syringes, or equipment for drug preparation or injection, or any situation where a person's mucous membranes or broken skin come into contact with bodily fluids that may carry HIV.

Differential Diagnosis

- The differential diagnosis of acute HIV infection may include but is not limited to, viral illnesses such as COVID-19, EBV and non-EBV (e.g., CMV) infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, or syphilis. Diagnosis of any STI should prompt HIV testing and consideration of acute HIV infection.

Testing to Diagnose or Confirm Acute HIV Infection

- Acute HIV infection is defined as detectable HIV RNA or p24 antigen (the specific antigen used in currently available HIV-1/2 Ag/Ab combination assays) in the setting of a negative or indeterminate HIV antibody test result.
- A reactive HIV antibody test result or Ag/Ab combination test result must be followed by supplemental confirmatory testing.
- A negative or indeterminate HIV antibody test result in a person with a reactive Ag/Ab test result or in whom acute HIV infection is suspected requires plasma HIV RNA testing to diagnose acute HIV infection.
- A positive result on a quantitative or qualitative plasma HIV RNA test in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. In this case, the diagnosis of HIV infection should be confirmed by subsequent documentation of HIV antibody seroconversion.
- A positive HIV Ag/Ab test result or a positive HIV RNA test result in the setting of a negative HIV antibody test result in a person taking PrEP should prompt immediate confirmation of HIV diagnosis. It is important to collect a new blood specimen to verify the HIV diagnosis before initiating HIV treatment.

Antiretroviral Therapy After Diagnosis of Early HIV Infection

- ART is recommended for all people with HIV, including those with early HIV infection **(AI).** ART should be initiated as soon as possible after HIV diagnosis **(AII).**
- Once initiated, the goals of ART are to achieve sustained plasma virologic suppression, prevent HIV transmission **(AII),** and preserve immune function **(AIII).**
- All people of childbearing potential who receive a diagnosis of early HIV infection should have a pregnancy test **(AIII).**
- Pregnant people with early HIV infection should begin ART as soon as possible for their own health and to prevent perinatal transmission of HIV **(AI).**
- A blood sample for genotypic drug-resistance testing should be obtained before initiating ART to guide the selection of the regimen **(AIII),** but ART should be initiated as soon as possible, often before resistance-test results are available. If resistance is subsequently identified, treatment should be modified as needed.

Table 14. Identifying, Diagnosing, and Treating Acute and Recent HIV Infection

- Standard genotypic drug-resistance testing should be performed for mutations in the reverse transcriptase and protease genes **(AIII)** for all people with early HIV**.** Genotype testing for INSTI resistance should be performed for those who acquire HIV during or after the use of CAB-LA as PrEP, if transmitted INSTI resistance is suspected, or if HIV diagnosis is made after receiving an INSTI-based regimen for PEP **(AIII).**
- ART can be initiated before the results of drug-resistance testing are known. For individuals who do not have a history of using CAB-LA as PrEP, one of the following ARV regimens is recommended **(AIII):**
  - BIC/TAF/FTC **(AIII**); or
  - DTG with (TAF or TDF)[b] plus (FTC or 3TC) **(AIII)**
- For individuals with a history of using CAB-LA as PrEP, genotypic resistance testing performed before starting ART should include screening for INSTI-resistance mutations **(AIII).** Recommended regimens include the following:
  - (DRV/c[c] or DRV/r) with (TAF or TDF)[b] plus (FTC or 3TC)—pending the results of the genotype **(AIII).** Empiric INSTI-containing regimens **are not recommended (AIII),** because INSTI resistance may be present in those who acquire HIV during the use of CAB-LA and possibly up to 4 years after.

[a] In some settings, activities that increase the risk of HIV infection may not be recognized or perceived as risky by the health care provider, the person at risk, or both. Thus, even in the absence of reported high-risk activities, symptoms and signs consistent with acute retroviral syndrome should motivate health care providers to consider a diagnosis of acute HIV infection.

[b] TAF and TDF are two forms of tenofovir that are approved in the United States. TAF has fewer bone and kidney toxicities than TDF, whereas TDF is associated with lower lipid levels. Safety, cost, and accessibility are among the factors to consider when choosing between these drugs.

[c] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters.

Key: 3TC = lamivudine; Ag/Ab = antigen/antibody; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CAB-LA = long-acting cabotegravir; CMV = cytomegalovirus; COBI = cobicistat; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EBV = Epstein-Barr virus; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; PEP = post-exposure prophylaxis; PrEP = pre-exposure prophylaxis; STI = sexually transmitted infection; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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HIV-2 Infection

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Key Considerations and Recommendations
• The clinical course of HIV-2 infection is generally characterized by a longer asymptomatic stage, lower plasma viral loads, and lower mortality rate than HIV-1 infection. However, without treatment, the majority of individuals with HIV-2 will progress to AIDS and death.
• No randomized controlled trials have addressed when a person with HIV-2 should start antiretroviral therapy (ART) or which regimens are most effective for initial or second-line ART when treating HIV-2; thus, the optimal treatment strategy is not well defined.
• Existing data on the treatment of HIV-2, and extrapolation from data on the treatment of HIV-1, suggest that ART should be started at or soon after HIV-2 diagnosis to prevent disease progression and transmission of HIV-2 to others **(AIII).**
• Quantitative plasma HIV-2 RNA viral load testing for clinical care is available and should be performed before initiating ART **(AIII).**
• For ART-naive patients who have HIV-2 mono-infection or HIV-1/HIV-2 coinfection, antiretroviral (ARV) regimens should include an integrase strand transfer inhibitor (INSTI) plus two nucleoside reverse transcriptase inhibitors (NRTIs) **(AII).** A recommended alternative regimen is a boosted protease inhibitor (PI) that is active against HIV-2 (darunavir or lopinavir) plus two NRTIs **(BII).**
• HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors (NNRTIs); therefore, NNRTI-based regimens, including long-acting injectable rilpivirine (given with the INSTI cabotegravir), **are not recommended** for treatment of HIV-2 **(AIII).**
• Patients with hepatitis B virus (HBV)/HIV-2 coinfection should be prescribed ART that contains drugs with activity against both HIV-2 and HBV **(AIII).**
• HIV-2 RNA, CD4 T lymphocyte (CD4) cell counts, and clinical status should be used to assess treatment response **(AII).** Unlike people with HIV-1, people with HIV-2 should continue to undergo periodic CD4 testing even if their viral loads are persistently suppressed, because disease progression can occur despite an undetectable viral load **(AIII).**
• Resistance-associated viral mutations to INSTIs, PIs, or NRTIs may develop in people with HIV-2 while they are on ART. However, no validated HIV-2 genotypic or phenotypic antiretroviral resistance assays are approved for clinical use.
• In the event of virologic, immunologic, or clinical failure, a new ARV regimen should be constructed in consultation with an expert in HIV-2 management.
• *In vitro* studies demonstrate that HIV-2 is intrinsically resistant to the fusion inhibitor enfuvirtide, and limited data also show that HIV-2 is intrinsically resistant to fostemsavir); therefore, these drugs **are not recommended** for treatment of people with HIV-2 **(AIII).**
• For patients with multidrug-resistant virus, ibalizumab and lenacapavir demonstrate *in vitro* potency against HIV-2 and may be considered **(BIII).**
***Rating of Recommendations**: A = Strong; B = Moderate; C = Weak*
***Rating of Evidence**: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Overview

HIV-2 infection is endemic in West Africa, with certain countries experiencing a population prevalence of >1%. The possibility of HIV-2 infection should be considered when treating people of

West African origin, people who have had sexual contact with or shared needles with people of West African origin, and people who reside in countries with strong socioeconomic ties to West Africa (e.g., France, Spain, Portugal, and former Portuguese colonies, such as Brazil, Angola, Mozambique, and parts of India). Globally, it has been estimated that 1 million to 2 million people have HIV-2—a number that includes people with HIV-1/HIV-2 dual infection. However, current and accurate prevalence data are scarce, and neither the Joint United Nations Programme on HIV and AIDS nor the World Health Organization has formal surveillance systems for HIV-2.[1]

Clinical Course of HIV-2 Infection

The clinical course of HIV-2 infection is generally characterized by a longer asymptomatic stage, lower plasma viral loads, and a lower mortality rate than HIV-1 infection.[2,3] However, without effective antiretroviral therapy (ART), HIV-2 infection will progress to AIDS and death in the majority of individuals.[4] Concomitant infection with HIV-1 and HIV-2 may occur, and the possibility of this coinfection should be considered when treating people from areas with a high prevalence of HIV-2.

Diagnostic and Monitoring Assays for HIV-2 Infection

In the appropriate epidemiologic setting, HIV-2 infection should be suspected in people who have clinical conditions that suggest HIV infection but who have atypical serologic results (e.g., a positive screening assay with an indeterminate HIV-1 Western blot).[5] The possibility of HIV-2 infection should also be considered in the appropriate epidemiologic setting in people who have serologically confirmed HIV infection but low or undetectable HIV-1 RNA levels, or in those who have declining CD4 T lymphocyte (CD4) cell counts despite apparent virologic suppression on ART.

The 2014 Centers for Disease Control and Prevention guidelines for HIV diagnostic testing[6] recommend using an HIV-1/HIV-2 antigen/antibody combination immunoassay for initial testing and using an HIV-1/HIV-2 antibody differentiation immunoassay for subsequent testing. The Geenius HIV 1/2 Supplemental Assay (Bio-Rad Laboratories) is approved by the U.S. Food and Drug Administration (FDA) to differentiate HIV-1 infection from HIV-2 infection. The Multispot HIV-1/HIV-2 Rapid Test is no longer available. Commercially available HIV-1 RNA assays do not reliably detect or quantify HIV-2 RNA.[7] Quantitative HIV-2 RNA testing is available at the University of Washington (UW)[8] and the New York State Department of Health (NYSDOH).[9] HIV-2 nucleic acid amplification test–based (total DNA/RNA) diagnostic testing is available for clinical care at UW.[10] However, it is important to note that up to one-third of people with untreated HIV-2 will have HIV-2 RNA levels below the limits of detection (10 copies/mL for UW testing and 7 IU/mL for NYSDOH testing); some of these people will have clinical progression and CD4 count decline. No validated HIV-2 genotypic or phenotypic antiretroviral (ARV) resistance assays are approved by the FDA for clinical use. HIV-2 genotypic ARV resistance assays are available at UW for research use only.

Treatment of HIV-2 Infection

To date, no randomized controlled trials that address when to start ART or the choice of initial or subsequent ART for HIV-2 have been reported[11]; thus, the optimal treatment strategy has not been defined. Existing data on the treatment of HIV-2 and extrapolation from data on the treatment of HIV-1 suggest that ART should be started at or soon after HIV-2 diagnosis to prevent disease

progression and transmission of HIV-2 to others **(AIII).** However, CD4 cell recovery in people with HIV-2 who are on ART is generally poorer than that observed in people with HIV-1.[12,13]

Data from *in vitro* studies suggest that HIV-2 is sensitive to the currently available nucleoside reverse transcriptase inhibitors (NRTIs); however, HIV-2 is more likely to develop resistance to NRTIs than HIV-1.[14] HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors (NNRTIs)[15]; thus, NNRTI-based regimens, including the long-acting injectable rilpivirine (RPV) (given with the integrase strand transfer inhibitor [INSTI] cabotegravir [CAB]), **are not recommended** for treatment of HIV-2 **(AIII).** Several small studies in individuals with HIV-2 have reported poor responses to dual-NRTI regimens[16,17] or regimens that contain an NNRTI plus two NRTIs.[18,19] Clinical data on the effectiveness of triple-NRTI regimens are conflicting.[20,21]

INSTI-based regimens or protease inhibitor (PI)–based regimens are treatment options for people with HIV-2. As discussed below, three single-arm clinical trials showed favorable outcomes in patients who received INSTI-based regimens. Data regarding the efficacy of PI-based regimens primarily come from observational reports. A randomized controlled trial comparing raltegravir (RAL) plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) to lopinavir/ritonavir (LPV/r) plus TDF/FTC is completed, but the results have not been reported (FIT-2; NCT02150993).

Integrase Strand Transfer Inhibitor–Based Regimens

All FDA-approved INSTIs—RAL, elvitegravir (EVG), dolutegravir (DTG), bictegravir, and CAB—have potent activity against HIV-2 *in vitro*.[22-27] INSTI-based regimens have shown favorable treatment responses in observational studies.[28-30] Three small, single-arm, open-label clinical trials have assessed the effectiveness of INSTI-based regimens in ART-naive individuals with HIV-2. These studies evaluated RAL plus TDF/FTC, EVG/cobicistat/TDF/FTC, and DTG plus either abacavir/lamivudine or TDF/FTC. All the studies demonstrated favorable clinical and immuno-virologic results at 48 weeks, providing the best evidence to date for HIV-2 treatment recommendations.[31-33]

Protease Inhibitor–Based Regimens

In general, regimens that contain boosted PIs that are active against HIV-2 (and that also include two NRTIs) have resulted in more favorable virologic and immunologic responses than regimens that consist of only two or three NRTIs.[12,13,21,34] Darunavir (DRV), lopinavir (LPV), and saquinavir are more active against HIV-2 than other approved PIs.[35-37] While LPV/r is more active against HIV-2 than DRV *in vitro*, it is less well tolerated. Some clinicians may use boosted DRV (where available) to enhance adherence. Older unboosted PI-based regimens, including nelfinavir or indinavir plus zidovudine and lamivudine, and atazanavir-based regimens have shown poor clinical success rates.[11,16,17,38,39]

Other Antiretroviral Drugs

Among the entry inhibitors, HIV-2 is intrinsically resistant to enfuvirtide.[40] The CCR5 antagonist maraviroc appears to be active against some HIV-2 isolates[41]; however, there are no FDA-approved assays that can determine HIV-2 co-receptor tropism, and HIV-2 is known to use many other minor co-receptors in addition to CCR5 and CXCR4.[42] The post-attachment inhibitor ibalizumab (IBA) has

potent *in vitro* activity against HIV-2 isolates.[43] Limited data suggest HIV-2 is intrinsically resistant to the attachment inhibitor fostemsavir (FTR).[44,45]

The capsid inhibitor lenacapavir (LEN) demonstrates nanomolar potency against HIV-2 *in vitro* but is 11- to 25-fold less active against HIV-2 than HIV-1.[46,47]

Some national and international guidelines have recommended specific preferred and alternative drug regimens for initial and second-line ART for HIV-2 infection[48-51]; however, there are currently no comparative randomized controlled clinical trial data that support the effectiveness of a specific recommended regimen.

The Panel's Recommendations

Until more definitive data on outcomes are available, the Panel on Antiretroviral Guidelines for Adults and Adolescents provides the following recommendations for the management of individuals with HIV-2 mono-infection or HIV-1/HIV-2 dual infection:

- A regimen that contains one INSTI plus two NRTIs is the recommended initial ART for most individuals with HIV-2 **(AII).**
- An alternative regimen is a boosted PI (DRV or LPV) that is active against HIV-2 plus two NRTIs **(BII).**
- HIV-2 is intrinsically resistant to NNRTIs; therefore, NNRTI-based regimens, including long-acting injectable RPV (given with the INSTI CAB), **are not recommended** for treatment of HIV-2 **(AIII).**
- HIV-2 demonstrates intrinsic resistance to the fusion inhibitor enfuvirtide *in vitro*, and limited data show intrinsic resistance to FTR; therefore, these drugs **are not recommended** for treatment of people with HIV-2 **(AIII).**
- For people with multidrug-resistant HIV-2, IBA and LEN may be considered based on *in vitro* data **(BIII).**
- Patients with hepatitis B virus (HBV)/HIV-2 coinfection require ART that contains drugs with activity against both HIV-2 and HBV **(AIII).** See Hepatitis B Virus/HIV Coinfection for more information.
- HIV-2 plasma RNA levels, CD4 counts, and clinical status should be monitored to assess treatment response, as is recommended for HIV-1 **(AII).**
- People who have HIV-2 RNA levels that are below the limits of detection before they initiate ART should still undergo routine HIV-2 plasma RNA monitoring in addition to CD4 count and clinical monitoring. Unlike HIV-1, people with HIV-2 require continued CD4 count monitoring, as disease progression can occur in the setting of undetectable HIV-2 viral load **(AIII).**

People with HIV-2 who are of childbearing potential require similar considerations when choosing a regimen as people of childbearing potential with HIV-1 (see What to Start). There are no data on HIV-2 treatment as prevention; however, both data from studies of people with HIV-1 and data on the natural history of HIV-2 transmission suggest that effective ART likely provides a reduced risk of transmission to sexual partners.[52-54]

Viral mutations that are associated with resistance to NRTIs, PIs, and/or INSTIs may develop in people with HIV-2 while they are on ART.[37,55,56] Currently, transmitted drug resistance appears to be rare among people with HIV-2.[57,58] In several small studies, twice-daily dosing of DTG was found to have some residual activity as a second-line INSTI in some people with HIV-2 who had extensive ART experience and RAL resistance.[59-62] Genotypic algorithms that are used to predict drug resistance in HIV-1 may not be applicable to HIV-2 because the pathways and mutational patterns that lead to resistance may differ between the HIV types (see the HIV2EU Algorithm and the Stanford University HIV Drug Resistance Database).[63] In the event of virologic, immunologic, or clinical failure, a new ART regimen should be constructed in consultation with an expert in HIV-2 management.

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HIV and the Older Person

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Key Considerations and Recommendations When Caring for Older People With HIV
• Diagnosis of HIV at a later stage of disease is more common among older people. Early diagnosis and treatment of HIV and counseling to prevent secondary HIV transmission remain important in the clinical care of older people with HIV.
• Antiretroviral therapy (ART) is recommended for all people with HIV **(AI).** ART is especially important for older individuals because they have a greater risk of serious non-AIDS complications and potentially a blunted immunologic response to ART.
• Compared to people without HIV, people with HIV have a twofold higher risk of developing atherosclerotic cardiovascular disease (ASCVD), and their age at incident ASCVD diagnosis is about a decade younger. In addition to current American Heart Association (AHA)/American College of Cardiology (ACC)/Multisociety Guidelines, the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends initiating at least a moderate-intensity statin in people with HIV aged 40 to 75 years who have 10-year ASCVD risk estimates of 5% to <20% **(AI).** See Statin Therapy in People With HIV for the Panel's additional recommendations on the use of statin therapy as primary prevention for people with HIV.
• Polypharmacy is common in older people with HIV, and all drugs, supplements, and herbal treatments should be assessed regularly for appropriateness, potential for adverse effects, proper dosing, and drug interactions **(AIII).**
• Potential for drug–drug interactions between antiretroviral drugs and concomitant medications (including statins, supplements, and herbal medicines) should be assessed regularly, especially before a new ART regimen or concomitant medication is started. In this context, it is also important to inquire and counsel about the use of non-daily medications, including long-acting injectables and as-needed medications**.**
• Adverse drug events from ART and concomitant drugs may occur more frequently in older people with HIV than in younger individuals with HIV. Therefore, the bone, kidney, metabolic, cardiovascular, cognitive, and liver health of older individuals with HIV should be monitored closely.
• HIV infection is associated with immunologic aging and systemic inflammation, which may contribute to the development of comorbidities across multiple organ systems as well as aging phenotypes like frailty. HIV experts, primary care providers, and other specialists should work together to optimize the medical care of older people with HIV, including adhering to treatment and prevention guidelines for different medical comorbidities.
• Age-related decline in neurocognitive function is faster in people with HIV compared to those without. Cognitive impairment in people with HIV—with manifestations including problems with memory, attention, and executive function—is associated with reduced adherence to therapy and poorer health outcomes, including increased risk of death. For people with progressive cognitive impairment, referral to a specialist (e.g., neurologist, neuropsychologist, geriatrician) for evaluation, testing, and management may be warranted **(BIII).**
• Mental health disorders, including an increased risk of anxiety and depression, are a concern among aging people with HIV. Screening for depression and management of mental health issues are important when caring for older people with HIV.
• Given that the burden of aging-related diseases is significantly higher among people with HIV than in the general population, additional medical and social services may be required to effectively manage both HIV and comorbid conditions.
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*
Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

Effective antiretroviral therapy (ART) has increased survival in people with HIV[1-4], resulting in an increasing number of older people with HIV. In the United States in 2022, the proportion of people newly diagnosed with HIV aged ≥55 years was 9%, according to the Centers for Disease Control and Prevention (CDC). Among people with HIV in 2022, 38% were aged ≥55 years, 13.2% were aged ≥65 years, and these proportions are expected to increase steadily.[5] The difference in life expectancy between people with HIV and the general population has significantly narrowed since the use of effective ART and is now estimated to be 5 years or fewer for those with CD4 T lymphocyte (CD4) cell count >500/μL after initiating ART.[3] However, the difference in mortality rates increases significantly with advancing age. While there has been a large reduction in AIDS-related mortality with effective ART, noninfectious comorbidities and complications, including atherosclerotic cardiovascular diseases (ASCVD) and non-AIDS malignancies, now account for a growing proportion of the causes of death among people with HIV.[2,3,6,7]

The discussion in this section of the guidelines refers to individuals aged ≥50 years as older people with HIV. Many older people with HIV have had HIV for years or decades; therefore, accumulating disease risk associated with longstanding HIV disease itself and/or exposure to antiretroviral (ARV) medications (including prior use of older ART regimens with greater toxicity in some cases) should be considered. Specifically, HIV may affect the biology of aging, possibly resulting in earlier manifestations of morbidities generally associated with more advanced age. As a result, older people with HIV may suffer from aging-related illnesses earlier and at higher rates than those without HIV, and will require more non-ART medications than younger people, which may complicate HIV clinical care.[8,9,10]

It is also important to consider distinct issues for people who are diagnosed with and/or acquire HIV at older ages. For example, older adults may have an increased risk of acquisition and transmission of HIV, in part as a consequence of reduced mucosal and immunologic defenses and changes in risk related-behaviors (e.g., decrease in condom use because of less concern about pregnancy or more high-risk sexual activity with increased use of erectile dysfunction drugs).[11,12] In addition, HIV screening among older adults remains low because they are generally perceived to be at low risk of acquiring HIV. The sections below review important considerations for the diagnosis and treatment of HIV among older people, as well as the potential clinical implications for people now living to older ages with longstanding HIV disease.

HIV Screening and Diagnosis in the Older Person

Older people with HIV (aged ≥55 years) are significantly more likely to meet the case definition of AIDS at HIV diagnosis than people aged <55 years (threshold defined by CDC surveillance data).[13] Also, older adults appear to have lower CD4 counts at seroconversion and steeper CD4 count decline over time[14] and tend to present to care with significantly lower CD4 counts.[15,16] Therefore, education, preventive measures (including pre-exposure prophylaxis or PrEP), and routine screening of asymptomatic older adults for HIV should be emphasized,[17] as well as considering HIV infection in the medical evaluation of older adults.

Antiretroviral Therapy in the Older Person With HIV

Importance of Prompt Initiation of Antiretroviral Therapy After HIV Diagnosis

ART is recommended for all individuals with HIV (**AI;** see Initiation of Antiretroviral Therapy). Early treatment may be particularly important in older adults because of blunted immune recovery and increased risk of serious non-AIDS events in this population.[18,19] However, ART-associated CD4 cell recovery in older adults is generally slower and lower in magnitude than in younger people,[20-23] suggesting that early diagnosis and treatment may result in better immunologic response and possibly improved clinical outcomes. In a modeling study based on data from an observational cohort, the beneficial effects of early ART were projected to be greatest in the oldest age group (people aged 45 to 65 years).[24] The benefits of early ART initiation were further demonstrated in an analysis of HIV cohorts from Europe and the Americas showing a lower all-cause and non-AIDS mortality with immediate ART initiation in people aged 50 to 70 years.[25] More definitive information was provided by the START study, which randomized ARV treatment–naive participants with CD4 counts >500 cells/mm^3 to either immediate ART or deferred ART until CD4 count dropped below 350 cells/mm^3. The highest absolute risk reduction of serious AIDS and non-AIDS events associated with immediate ART was found in participants aged 50 years or older.[26] All older people with HIV should be informed that maintaining a plasma HIV RNA (viral load) at <200 copies/mL with ART improves overall health and prevents sexual transmission of HIV (see the Treatment as Prevention section).

Choice of Antiretroviral Regimens in the Older Person With HIV

The choice of ARV regimen for an older person with HIV should be informed by a comprehensive review of the person's other medical conditions and medications (including non-prescription drugs, supplements, and herbal treatments), and results from cumulative genotypic resistance testing. The What to Start section (Table 7) of these guidelines provides guidance on selecting an ARV regimen based on a person's characteristics and specific clinical conditions (e.g., kidney disease, elevated risk for cardiovascular disease [CVD], osteoporosis). In older people with HIV and reduced renal function, dosage adjustment of nucleoside reverse transcriptase inhibitors (NRTIs) may be necessary (see Appendix B, Table 12). In addition, ARV regimen selection may be influenced by potential interactions between ARV medications and drugs used concomitantly to manage comorbidities (see Tables 24a through 25b). Adults aged >50 years should be monitored for ART effectiveness and safety as similarly recommended for other populations with HIV (see Table 3); however, in older people, special attention should be paid to the greater potential for adverse effects of ART on renal, liver, cardiovascular, central nervous system, metabolic, and bone health (see Table 20). A meta-analysis confirmed that people with HIV have a 1.5-fold higher risk of fragility-related fracture and a fourfold higher risk of hip fracture. The increased risk is not completely explained by differences in bone mineral density (BMD) alone, indicating there may be differences due to bone microarchitecture or other HIV-related factors contributing to the marked fracture risk. ART regimens that contain tenofovir disoproxil fumarate (TDF),[27] boosted protease inhibitors (PIs), or both are associated with a significantly greater loss of BMD, with or without osteoporosis, compared to regimens containing other NRTIs and integrase strand transfer inhibitors (INSTIs).[28-31] Abacavir (ABC), NRTI-sparing regimens, and tenofovir alafenamide (TAF) may be considered as alternatives to the use of TDF in older individuals who may be at risk of nephrotoxicity, osteopenia, or osteoporosis; however, with ABC, the benefit should be balanced with its potential for increasing the risk of CVD (see What to Start). The long-acting (LA) injectable combination of cabotegravir (CAB) and rilpivirine (RPV) is also an option for ART among older people with HIV, with the same

considerations as for all people with HIV (see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression).

Antiretroviral Efficacy and Safety Considerations in the Older Person With HIV

The efficacy, pharmacokinetics (PK), adverse effects, and drug interaction potentials of ART in older adults have not been studied systematically. Data from clinical trials of second-generation INSTIs (dolutegravir [DTG] and bictegravir),[32] two-drug regimens (DTG/lamivudine),[33] and LA CAB/RPV have shown similar virologic efficacy, safety, and tolerability between participants >50 years of age and those aged 50 and younger.[34]

Hepatic metabolism and renal elimination are the major routes of drug clearance, including the clearance of ARV drugs. Both liver and kidney functions decrease with age and may result in impaired drug elimination and increased drug exposure.[35] Most clinical trials have included only a small proportion of participants aged >50 years, and current ARV dosing recommendations are based on PK and pharmacodynamic data derived from participants with normal organ function. Because it is not known whether drug accumulation in older people may lead to greater incidence and severity of adverse effects than in younger people, therapy in older people requires close monitoring and heightened awareness of drug-related adverse effects, especially in those with hepatic or renal impairment.

Adherence Concerns

Suboptimal adherence to ART is the most common cause of treatment failure. Although most older people with HIV are able to achieve viral suppression with a single-tablet regimen, some people who have a long history of ART may have acquired drug resistance, thus requiring more complex multiple-pill regimens. Complex dosing requirements, high pill burden, polypharmacy, inability to access medications because of cost or availability, limited health literacy (including misunderstanding of instructions), depression, substance use, frailty, and neurocognitive impairment are among the key reasons for nonadherence and should be regularly assessed and managed (see Adherence to the Continuum of Care).[36-38] Although some of the factors associated with nonadherence may be more prevalent in older people with HIV, older people have demonstrated better adherence to ART than younger people in some studies.[39-41] Severe menopausal symptoms are also associated with reduced adherence to ART, which increases the risk of drug resistance and adverse HIV-related health outcomes in menopausal cisgender women, highlighting the importance of managing these symptoms among women with HIV.[42,43] To facilitate ART adherence, it may be useful to discontinue unnecessary non-HIV medications, simplify ART regimens, and apply evidence-based behavioral approaches including the use of adherence aids such as pillboxes or daily calendars, and support from family members and friends (see Adherence to the Continuum of Care). LA dosing options, such as LA CAB/RPV, may ease pill burden and adherence concerns for some older adults (see Optimizing Antiretroviral Therapy).

Optimizing Antiretroviral Therapy in Older People With HIV

Given the greater incidence of comorbidities, non-AIDS complications, and frailty among older people with HIV, switching one or more ARVs in an HIV regimen may be necessary to minimize toxicities, drug–drug interactions, or to reduce pill burden.[38] Expert guidance now recommends bone density monitoring in men aged ≥50 years and postmenopausal cisgender women and suggests switching from TDF or boosted PIs to other ARVs (such as TAF or INSTIs, respectively) in older

people at high risk for fragility fractures.[44] Given the high prevalence and faster progression of chronic kidney disease (CKD) in aging people with HIV—likely from a combination of HIV, ART, and non-HIV risk factors—development of CKD must be closely monitored in an older person on ART.[45,46] Table 7 provides guidance for ARV drugs to use based on selected clinical scenarios, including comorbidities.

Polypharmacy in Older People With HIV

People with HIV and aging-associated comorbidities may require additional pharmacologic interventions that can complicate therapeutic management.[8] In addition to taking medications to manage HIV and comorbid conditions, many older people with HIV are also taking medications to relieve discomfort (e.g., pain medications, sedatives) or to manage adverse effects of medications (e.g., anti-emetics). Older individuals may also self-medicate with over-the-counter medicines or supplements.

Polypharmacy is more common in older people with HIV than similarly aged people in the general population.[8,47,48] Among people with HIV aged ≥65 years, it is predicted that the prevalence of comorbidities and polypharmacy rose with increasing age and duration of HIV infection.[49,50] In the Swiss HIV Cohort Study, the prevalence of polypharmacy and inappropriate prescribing in people aged ≥75 was 66% and 67%, respectively.[51]

In people aging with HIV, the effects of polypharmacy, including the use of drugs that affect neurocognitive function, can contribute to serious adverse outcomes, such as serious falls and fractures, delirium, hospitalization (including intensive care unit admissions), and death.[52-57] Polypharmacy may also increase the likelihood of adverse consequences such as medication errors (by prescribers or prescription recipients), medication nonadherence, additive drug toxicities, and drug–drug interactions. Older people with HIV are probably at an even greater risk of polypharmacy-related adverse consequences than younger or similarly aged people without HIV. When evaluating any new clinical concern or laboratory abnormality in people with HIV, especially in older people, clinicians should always consider the possible role of adverse drug reactions from both ARV drugs and other concomitantly administered medications.

Drug–Drug Interaction Concerns

Interactions between ARV drugs and concomitant medications, supplements, and herbal treatments can occur and can be easily overlooked by prescribers.[58] Potential drug–drug interactions can occur between ARV and non-ARV medications, as well as between non-ARV medications.[48,59] The available drug interaction information on ARV agents is derived primarily from PK studies performed in small numbers of relatively young participants with normal organ function who do not have HIV (see Tables 24a–25b). Data from these studies provide clinicians with a basis to assess whether a significant interaction may exist. However, the magnitude of an interaction may be greater in older than in younger people with HIV; therefore, it is important for clinicians to remain vigilant to assess for potential drug–drug interactions given the high prevalence of polypharmacy in older people with HIV. The risk of significant drug–drug interactions appears to be higher with PI-based or non-nucleoside reverse transcriptase inhibitors-based ART than with INSTI-based ART, although there are some important interactions with INSTIs that should be recognized and managed (including with polyvalent cations that are frequently taken as supplements).[60-62]

Hormonal therapies may be taken to alleviate symptoms of menopause among cisgender women or to facilitate gender affirmation among transgender individuals. Although data on drug–drug interactions between hormonal therapies and ART are limited, existing data suggest little to no impact of hormonal therapies on the efficacy of some ART.[63-65]

HIV and Immunologic Aging

Chronic HIV infection is associated with elevated soluble markers of immune activation and inflammation, as well as cellular phenotypes indicative of T cell and myeloid cell activation, even after HIV RNA levels are suppressed with ART.[66] The levels of inflammation and immune activation also increase with age and age-associated diseases.[67] In this context, the combined effects of HIV and advancing age on chronic inflammation have implications for risk from a broad spectrum of diseases.[68,69]

A contributing factor to the early development of aging-related diseases among people with HIV has been posited to be the effect of HIV on immunologic aging. In addition to higher levels of immune activation, aging is associated with a higher frequency of cellular senescence as well as impaired immune responses and surveillance.[70] HIV infection is associated with higher frequencies of T cell phenotypes characteristic of immunosenescence, as well as phenotypes reflective of highly differentiated or activated states.[71-74] Higher frequencies of senescent T cells are then associated with a greater risk for such comorbidities as CVD. In addition, the degree of CD4 T cell recovery after ART initiation is diminished among people ≥50 years old versus younger people with HIV.[75,76] This impaired T cell recovery with advancing age may then have functional consequences, as people with HIV demonstrate reduced immune responses to vaccination, as well as impaired control of copathogens such as cytomegalovirus (CMV).[77-79] The persistence of impaired or ineffective immune response toward copathogens then contributes to ongoing chronic immune activation (e.g., CMV-specific responses),[78] as well as the increased risk of both AIDS and non-AIDS–defining cancers that are driven by pro-oncogenic viruses (e.g., human papillomavirus [HPV]-and Epstein-Barr virus [EBV]-related cancers).[80]

Immunologic aging in the context of HIV also entails chromosomal and genetic changes. Whether a consequence of untreated HIV viremia, direct toxicity from ARV drugs, or both, people with HIV have been shown to have shorter leukocyte chromosome telomere length, itself a marker of poor health and mortality.[81-83] DNA methylation is an epigenetic alteration that occurs at a predictable rate with advancing age, predicts lifespan, and increases in the setting of chronic HIV disease.[84-87] Finally, a genetic mechanism that may more directly link immunologic aging to comorbid disease risk is clonal hematopoiesis, which entails an age-related expansion of somatic gene mutations among leukocytes (also referred to as age-related clonal hematopoiesis or ARCH). Clonal hematopoiesis is more common among people with HIV, and the degree of difference with people without HIV may be more pronounced with advancing age[88,89] and in people with low nadir CD4 counts.[90,91] Several of the leukocyte gene mutations characteristic of clonal hematopoiesis lead to dysregulation of inflammatory pathways, which is then associated with higher levels of inflammatory markers and ASCVD.[92-94] In summary, clonal hematopoiesis is an example of HIV disease influencing age-related genetic somatic mutations that may contribute to ongoing systemic inflammation and associated disease risk among older people with HIV.

Disease-modifying pharmacologic interventions targeting immunologic aging are an area of active study within geroscience, but none are currently recommended specifically for older people with

HIV with the exception of statin therapy as primary prevention of ASCVD risk (see Atherosclerotic Cardiovascular Disease in the Older Person With HIV below and Statin Therapy in People With HIV).

Morbidity, Mortality, and Non-AIDS Complications Among Older People With HIV

The clinical implications of greater immunologic aging and persistent inflammation can manifest in any organ system, diminishing the health span of older people with HIV. The frailty phenotype—defined clinically as a decrease in muscle mass, weight, physical strength, energy, and physical activity—represents an important example of an age-related syndrome that occurs with greater frequency and at earlier ages among people with HIV and is associated with a broad spectrum of adverse effects and disease risk. Specifically, frailty among people with HIV has been associated with incident CVD, diabetes mellitus, recurrent falls and fractures, lower quality of life, cognitive impairment, hospitalization, and mortality.[95-104] The frailty phenotype remains incompletely characterized among older people with HIV and identifying effective treatment strategies is an important priority for clinical management. However, pharmacologic and non-pharmacologic interventions addressing frailty among people with HIV have been proposed and have the potential to significantly impact their quality of life and survival.[105,106]

Although the life expectancy of people with HIV is approaching that of people without HIV, the incidence and prevalence of age-associated comorbidities in people with HIV are increasing.[107,108] The age-related comorbidity burden is significantly higher in people with HIV compared to the age-matched general population.[8] These predictions differ by comorbidity and by demographic factors—including race, ethnicity, age, gender identity, and HIV transmission mode—displaying substantial disparities for some populations.

Data from insured adults suggest that people with HIV spend approximately 15 years more of their lifespan with one or more major comorbidities when compared to people without HIV; this difference is reduced but persists (at approximately 10 years) for people who initiate ART at a CD4 count of >500 cells/mm^3.[109] A simulation modeling study projected that by 2030, 45% of people with HIV on ART would be living with two or more physical comorbidities and 64% with at least one mental health comorbidity.[110]

Non-AIDS–Defining Complications and Comorbidities in the Older Person With HIV

Non-AIDS comorbid conditions constitute an increasing proportion of morbidity and mortality among people with HIV.[3,111] Heart disease and cancer are the leading causes of death in older people with HIV in the United States. Similarly, other non-AIDS events, such as cognitive impairment and liver disease, have also emerged as major causes of morbidity and mortality in people with HIV receiving effective ART. The prevalence of multimorbidity among people with HIV has increased in the past decade,[112] with hypertension and hypercholesterolemia being the most common comorbidities.[113]

Three groups of factors likely contribute to this burden of noncommunicable diseases among people with HIV: (1) an over-representation of traditional risk factors in this population, especially higher rates of smoking, diabetes, and dyslipidemia; (2) HIV-associated chronic inflammation and immune activation, which are not completely abated by suppressive ART; and (3) possible cardiometabolic complications of some ARV drugs.[114-122]

As the life expectancy of people with HIV increases with ART, more cisgender women with HIV are experiencing menopause. Although menopause may occur earlier in cisgender women with HIV than in cisgender women in the general population,[123] early menopause may also be a consequence of smoking, depression, substance use disorder, and other psychosocial factors that are disproportionately present in cisgender women with HIV.[124] Also, HIV might compound menopause-related metabolic changes. For instance, HIV infection and menopausal stage were independent predictors of lower BMD and had an additive effect on lumbar spine and total hip BMD.[125]

HIV-specific primary care guidelines have been developed and are available for clinicians caring for people with HIV, especially for older people with HIV.[126,127] Additional specific guidelines have also been developed for the evaluation and management of the following specific comorbidities in people with HIV: bone health,[44] kidney disease,[128] and secondary prevention for ASCVD.[129] In addition, the following guidelines recently developed for the general population can be applied to older people with HIV: management of hypertension[130], hyperglycemia[131], and hyperlipidemia.[132] However, it is important to note that the recommendations in many of these guidelines have not all been validated in the context of HIV disease. For instance, cardiovascular risk prediction functions developed for the general population likely underestimate the risk in people with HIV.[129,133] Findings of the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) study have provided significant insight into the potential role of statins in the prevention of major adverse cardiovascular events in people with HIV. See Statin Therapy in People With HIV for recommendations from the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) on statin therapy as primary prevention of ASCVD among people with HIV. Further analyses of the REPRIEVE data will likely yield additional insights into their benefits (and potential risks) in people with HIV, as well as differences in the predictive value of risk equation scores in demographic subsets of study participants.

Atherosclerotic Cardiovascular Disease in the Older Person With HIV

When compared to people without HIV, data from several studies have shown that people with HIV have about a twofold higher risk of developing ASCVD, and their age at incident ASCVD diagnosis is about a decade younger.[108,109,134,135] ASCVD risk prediction tools used for the general population tend to underestimate risk among people with HIV.[133,136] Data also suggest that the relative increase in ASCVD risk is greater among women with HIV than among age-matched men with HIV when compared to people without HIV.[137,138] Factors influencing ASCVD risk among people with HIV include both higher prevalence of traditional cardiometabolic risk factors and ongoing systemic inflammation associated with HIV,[114,137] even in individuals with viral suppression while on ART. In addition, structural barriers and health disparities in screening and treatment of ASCVD risk factors likely also contribute to excess ASCVD risk among people with HIV in the United States.[139,140]

The 2018 American Heart Association (AHA)/American College of Cardiology (ACC)/Multisociety Guidelines provide recommendations on the use of statins as primary prevention based on risk stratification using estimates of 10-year ASCVD risk from the pooled cohort equations.[141,142] In the general population, statin therapy is recommended for all people at high 10-year ASCVD risk (defined as ≥20%). Recent findings from the REPRIEVE trial have provided evidence for the use of statin therapy as primary prevention for people with HIV at low-to-intermediate ASCVD risk (i.e., <20%). REPRIEVE, a large randomized controlled trial among people with HIV aged 40 to 75 years who were receiving ART, showed that when compared to placebo, pitavastatin 4 mg daily was associated with a 35% reduction in major adverse cardiovascular events over a median follow-up duration of 5 years.[143] Results from REPRIEVE informed the Panel's recommendation on the use of

at least moderate-intensity statin therapy as primary prevention among people with HIV of age 40 to 75 years, with a stronger recommendation for those with ASCVD risk score ≥5% who will have a higher absolute benefit from statin therapy. See Statin Therapy in People With HIV for the Panel's full recommendations on statin therapy.

Neurocognitive Impairment in the Older Person With HIV

Cognitive impairment in people with HIV can manifest as difficulty with memory, attention, speed of information processing, and executive and motor functions. Studies that use neuropsychological testing to define categories of impaired cognition—termed HIV-associated neurocognitive disorder (HAND)—find that up to 30% of people with HIV on virally suppressive ART meet these research-based criteria[144], although these categories have not been validated for use in clinical practice. Research studies also demonstrate a steeper decline in performance on neuropsychological tests with advancing age in individuals with HIV compared to those without HIV over the same age range.[145] Although viral persistence and chronic brain inflammation can contribute, cognitive impairment is multifactorial in people with HIV. It is not solely HIV-associated, but also influenced by factors related to comorbidities, including polypharmacy, mood disorders, vascular disease, social isolation, stress, and independent neurodegenerative conditions.[146-151] Hormonal shifts that occur with aging may contribute to neurocognitive impairment, and these changes may manifest as unique differences in clinical manifestations by sex assigned at birth.[152] Finally, the risk of neurodegenerative disease rises with increasing age independent of HIV, and diagnosis of Alzheimer's disease or other forms of progressive dementia in older people with HIV is now an important clinical concern.[153]

Cognitive impairment carries potentially detrimental clinical consequences for aging people with HIV. In a prospective observational study, cognitive impairment was predictive of a lower likelihood of retention in care among older people.[154] Cognitive impairment is also associated with reduced adherence to therapy[155] and poorer health outcomes including increased mortality.[156] Given the importance of cognitive health, screening for neurocognitive impairment is important, though optimal primary care-based screening methods remain unclear. Initial screening with questions about symptoms of memory loss, slowness, and poor attention can help to guide the need for referral to a specialist (e.g., neurologist, neuropsychologist, or geriatrician).[157,158] Though such questions can be useful in identifying cognitive impairment, a positive response to these questions is not necessarily specific to impairment related to HIV.[159] Of note, people with substantial impairment may not have enough insight into their condition to answer the questions, and input from a partner or family member corroborating the impaired person's cognitive history may enhance the validity of the assessment. No brief cognitive screening test has been clearly shown to be sensitive or specific for cognitive impairment in HIV; the frequently used Mini-Mental State Exam does not typically capture executive function impairment, which is the main manifestation of subtle cognitive impairment in people with HIV.[160] The Montreal Cognitive Assessment may be more sensitive but is not specific. A lower threshold than the original cut-off score of 26 on the Montreal Cognitive Assessment is likely more optimal for HAND screening, as it lowers false positive rates and improves diagnostic accuracy.[161] If a person has persistent concerns over time, has symptoms corroborated by an acquaintance, or has progressively worsening symptoms, referral to a neurologist for evaluation and management or to a neuropsychologist for formal neuropsychological testing may be warranted **(BIII).**[160]

Beyond screening and referral to specialists in neurology, neuropsychology, or geriatrics, an approach to cognitive impairment in aging people with HIV should involve assessing and correcting

reversible and treatable factors that contribute to cognitive symptoms, as well as directly addressing modifiable risk factors. Reversible and treatable factors that may contribute to cognitive symptoms include hypothyroidism, low vitamin B12 levels, syphilis, sleep apnea, and cerebrovascular disease.[162] Hearing impairment, diabetes, obesity, hypertension, depression, smoking, alcohol or substance use, and limited physical and social activity have been identified as significant modifiable risk factors for dementia in people without HIV.[163] Given the prevalence of many of these risk factors in older people with HIV, careful attention to their prevention or amelioration is an important component of primary care and cognitive care in aging people with HIV. Finally, the U.S. Preventive Service Task Force now recommends screening older adults (>65 years) for depression.[164]

Mental Health Concerns in the Older Person With HIV

Mental health-related problems are a growing concern in aging people with HIV, though little is known about their prevalence and consequences in this population specifically. In a study that compared a cohort of individuals aged >60 years with HIV to a historical control group of healthy older people, a heightened risk of mood disorders including anxiety and depression was noted among people with HIV.[165] Social isolation combined with depression is particularly common among older adults with HIV and, in addition to its direct effects on morbidity and mortality, it may contribute to poor medication adherence and retention in care.[166,167] The risk of suicide remains greater in people with HIV than in the general population, though increasing age might not further heighten the risk.[168] In one analysis of a multicenter observational study in France, suicide emerged as the second-highest cause of death among virologically suppressed people with HIV on ART.[169] Screening for depression and management of mental health issues are critical aspects of HIV primary care; guidelines for people with HIV, as well as for aging individuals without HIV, recommend behavioral approaches including individual psychotherapy, cognitive behavioral therapy, group therapy, and often pharmacological treatment.[169] When resources are available, integrated care models with routine screening by health care support staff, review by primary providers, and referral to on-site mental health specialists are likely to be the most effective approaches in vulnerable aging populations.

Health Care Utilization and Cost Sharing

The substantially increased burden of age-related comorbidities among people aging with HIV, including CVD, CKD, neurocognitive disease, and fractures, can lead to increased healthcare utilization and higher costs.[170] Out-of-pocket health care expenses (e.g., copayments, deductibles), loss of employment, and other financial-related factors can cause temporary interruptions in treatment, including ART, which should be avoided whenever possible (see Cost Considerations and Antiretroviral Therapy for more information). The increased life expectancy and higher prevalence of chronic complications in aging populations with HIV can place greater demands upon HIV services[171] and require a focused approach to prioritize modifiable health-related problems. Facilitating continued access to health care, including access to insurance-covered care and medications, is essential to minimize treatment interruptions; clinical outcomes can improve with additional multidisciplinary services to manage concomitant chronic disorders and assist with overcoming structural barriers to care. See the Ryan White HIV/AIDS Program's Available Care & Services page for additional information.

End-of-Life Issues, Including Palliative Care and Interruption of ART

As with all aging people, it is important to discuss living wills, advance directives, and long-term care planning. Palliative care and hospice should be discussed with a person-centered approach that

incorporates the person's family situation and cultural, religious, and personal values, among other factors.[172,173]

Few data exist on the use of ART in people with debilitating chronic, severe, or non-AIDS terminal conditions.[174,175] Discontinuation of ART usually results in rebound viremia and a decline in CD4 count; an acute retroviral syndrome has also been reported after abrupt ART discontinuation. For these reasons, most clinicians would continue ART if there are no significant adverse reactions to the ARV drugs. In cases where ART negatively affects quality of life, the decision to continue therapy should be made together with the affected person and/or family members after a discussion of the risks and benefits of continuing or stopping ART.

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Substance Use Disorders and HIV

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Key Considerations and Recommendations
• Substance use disorders (SUDs) are prevalent among people with HIV and contribute to poor health outcomes; therefore, screening for SUDs should be a routine part of clinical care **(AII).**
• The most commonly used substances among people with HIV include the following (listed in alphabetical order): alcohol, benzodiazepines, cannabinoids, club drugs, opioids, stimulants (cocaine and methamphetamines), and tobacco.
• Health care providers should be nonjudgmental when addressing substance use with people with HIV **(AIII).**
• People with HIV and SUDs should be screened for additional mental health disorders **(AII).**
• People with HIV and SUDs should be offered evidence-based pharmacotherapy (e.g., opioid agonist therapy, tobacco cessation treatment, alcohol use disorder treatment; see Table 15 below) as part of comprehensive HIV care in clinical settings **(AI).**
• Ongoing substance use is not a contraindication to antiretroviral therapy (ART). People who use substances can achieve and maintain viral suppression with ART.
• Substance use may increase the likelihood of HIV transmission risk behaviors, the potential for drug–drug interactions, and the risk or severity of substance-associated adverse events (e.g., increased hepatotoxicity or an increased risk of overdose).
• Selection of antiretroviral (ARV) regimens for individuals who practice unhealthy substance and alcohol use should take into account potential adherence barriers, comorbidities that could impact care (e.g., advanced liver disease from alcohol or hepatitis viruses), potential drug–drug interactions, and possible adverse events associated with the medications **(AII).**
• For people with SUDs, ARV regimens with once-daily formulations (ideally as a single-tablet regimen), high barriers to resistance, low hepatotoxicity, and low potential for drug–drug interactions are preferred **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*
Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Background on Substance Use Disorders Among People With HIV

Ending the HIV epidemic requires addressing substance use among people with HIV, which poses a barrier to optimal engagement in the HIV care continuum. Ongoing substance use may prevent an individual from being tested for HIV, initiating antiretroviral therapy (ART), or adhering to ART. Substance use may also increase the likelihood of risk-taking behaviors (e.g., sexual transmission risk behaviors, needle sharing, injection of substances), the potential for drug–drug interactions, and the risk or severity of substance-related adverse events (e.g., increased hepatotoxicity and increased risk of overdose). In the United States, the death toll for drug overdose (102,123 deaths as of February 2024)[1] far exceeds the death toll for HIV (4,941 deaths in 2022).[2] As the drug overdose epidemic continues to expand, health care providers need a basic understanding of how to screen for and treat substance use disorders (SUDs) in people with HIV in clinical settings.[3]

Substance use exists on a continuum, from episodic use to an SUD with its concomitant negative consequences. Research on alcohol consumption has defined a threshold at which consumption does not reach a diagnosis of SUD, but where the level of consumption is nonetheless hazardous to the

person. This level of consumption has been defined as at-risk or hazardous use. A comparable category does not exist for other substances. The prevalence of substance use and SUDs is higher among people with HIV than among the general public,[4] and polysubstance use is common. This section will focus on the most commonly used substances among people with HIV (listed in alphabetical order): alcohol, benzodiazepines, cannabinoids, club drugs,[5] opioids, stimulants (cocaine and methamphetamines), and tobacco. Additionally, xylazine, a non-opioid veterinary analgesic that is a common substance adulterant—a substance added to another substance that may lead to negative health consequences—is also discussed.

People with HIV may use more than one substance and may not be ready to consider reducing the use of substances or seeking treatment for SUDs. Polysubstance use occurs for multiple reasons, including to improve the euphoria associated with use (e.g., use of cocaine and heroin mixtures called "speedballs") and to reduce the adverse effects of a particular substance (e.g., the use of alcohol or benzodiazepines to reduce the anxiety caused by cocaine use).

Substance Use and Sexual Risk-Taking

A growing body of literature describes the intersection of substance use and sexual risk-taking, in which drugs are intentionally used to enhance sexual activity ("chemsex"). This research highlights the impact of substance use on sexual transmission risk behaviors; although no precise definition of "chemsex" exists, studies have investigated various substances used to enhance sexual pleasure, decrease inhibitions related to particular sexual acts, and combat low self-esteem. In a retrospective study in a London sexual health clinic, individuals who disclosed substance use (463 of 1,734 participants) had higher odds of acquiring new HIV infection, bacterial sexually transmitted infections (STIs), and/or hepatitis C virus (HCV).[6] A much larger analysis using the European Men Who Have Sex With Men (MSM) Internet Survey, which collected data from 16,065 United Kingdom-based respondents, found that MSM who reported using methamphetamines or gamma-hydroxybutyrate (GHB) during the previous year were more likely to have gonorrhea infection than MSM who did not use these drugs, with odds ratios of 1.92 and 2.23, respectively.[7] Between 2017 and 2020, the American Men's Internet Survey collected data on chemsex drug use among MSM in the United States over the preceding 12 months. Of 30,294 MSM respondents, 3,113 (10.3%) self-reported chemsex in the past 12 months, with 3,4-methylenedioxymethamphetamine (MDMA or "ecstasy") (65.1%), methamphetamine (42.5%), and GHB (21.7%) being the top drugs reported for use.[8] A recent study in Spain using an online, self-administered questionnaire found that 81.4% of 2,919 MSM attending four HIV/STI testing sites in Madrid and Barcelona had ever used any drug, and 50% had engaged in chemsex in the past 12 months. Of those engaging in chemsex, half engaged in condomless anal sex.[9] These data emphasize the need to screen people with HIV for substance use and STIs in clinical settings and to discuss strategies with these individuals to reduce potential harm.[10]

Substance Use and Unstable Housing

People with HIV who inject drugs are more likely to be unhoused.[11] Houselessness among people who inject drugs is associated with an increased risk of HIV acquisition.[12]

Among people with HIV and SUD, houselessness confers an increased risk for disruptions in the HIV care continuum independent of ongoing substance use. In a longitudinal study of people with HIV who used drugs, lack of housing was associated with a 44% decrease in the odds of progression through the HIV care continuum.[13] After adjusting for multiple intersecting risks, including

unhealthy alcohol use, other substance use, incarceration, unemployment, education, age, sex, and race/ethnicity, unhoused people with HIV and SUD had significantly decreased odds of ART initiation and, adherence, and of viral suppression.

Interventions supporting housing among people with HIV and SUD can result in improved HIV treatment outcomes. A randomized controlled trial of a rapid rehousing intervention for people with HIV who were houseless (n = 236, 81% with substance use) found that clients in the Enhanced Housing Placement Assistance arm were more likely to be placed and, placed faster, and were twice as likely as the control group to reach or maintain viral suppression (95% confidence interval [CI], 1.1–4.0).[14,15] An observational study of applicants to a supportive housing program for low-income people with HIV and a mental health condition or SUD (n = 958; 86% with SUD) found that people who achieved stable housing were more likely to engage in HIV care and to achieve viral suppression.[16] These data reflect the importance of not only addressing SUD among people with HIV, but also understanding the co-occurring structural determinants that contribute to poorer outcomes among people with HIV and SUD.

Screening for Substance Use Disorders

Screening for SUDs should be incorporated into the routine clinical care of all people with HIV. The following questions can be used to screen for drug or alcohol use: "How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?" and "How many times in the past year have you had X or more drinks in a day?" (X is five for men and four for women).[17] Data are lacking on the appropriate threshold for alcohol use among transgender individuals with HIV, although a study among transgender individuals without HIV recommends a threshold of five standard drinks on a drinking day or a score of ≥3 on the Alcohol Use Disorders Identification Test (AUDIT-C).[18] Individuals with liver disease, including active HCV infection, should not consume alcohol.

A positive response to either of the two questions above should prompt additional screening with other short screening tools (see the Screening and Assessment Tools Chart from the National Institute on Drug Abuse). These tools can identify substance use and guide decisions on appropriate treatment interventions. Currently, there are not enough data to determine how often people with HIV should be screened for SUDs; however, given the potential negative impact that SUDs may have on people with HIV, it is advisable to ask these questions during every clinical visit.

Health care providers should be nonjudgmental when discussing substance use with people who have HIV **(AIII).** People with HIV who experience stigma or judgment may lose trust in their health care provider's advice, avoid future visits, and consequently experience poorer health outcomes.[19] Language is one way in which stigma is communicated, and words such as "addict" and "dirty urine" convey a negative connotation. The Office of National Drug Control Policy (ONDCP), American Medical Association, American Society of Addiction Medicine, International Society of Addiction Journal Editors, and others have recommended the adoption of clinical, nonstigmatizing language for substance use, as described in the *Changing the Language of Addiction* report from ONDCP.

Co-occurring Mental Illness

Many people who use substances have co-occurring mental health disorders, including a history of trauma that may drive or exacerbate their substance use. Conversely, ongoing use of substances can place individuals at risk for trauma, such as sexual assault and sexual exploitation, which may further

exacerbate their substance use.[6,20] People with SUDs should undergo evaluation and treatment for concurrent mental health disorders using standardized screening instruments (e.g., the Patient Health Questionnaire-2, or PHQ-2, for depression). Where applicable, clinicians should use available behavioral and pharmacological interventions to address mental health concerns, because recommending that people stop their substance use without providing treatment for underlying mental health conditions has very limited efficacy.[21]

Selecting, Initiating, and Maintaining Antiretroviral Therapy

Ongoing substance use is **not** a contraindication for prescribing ART. ART is recommended for all people with HIV to improve their health and to prevent transmission of HIV to others **(AI),** including sexual partners and individuals who share drug paraphernalia. These clinical, community, and individual benefits should encourage health care providers to initiate ART in all people with HIV who use substances. Although effective ART prevents sexual transmission of HIV, its effectiveness in preventing transmission through shared needles and shared use of other drug paraphernalia remains unknown.

For people actively injecting drugs, engagement in a syringe service program (SSP) can facilitate access and adherence to ART. SSPs primarily provide clean drug preparation and injection supplies to reduce transmission of HIV, HCV, and other bloodborne, skin, and soft tissue pathogens. As a regular point of contact for people with complex health and social challenges, SSPs also provide opportunities to offer other integrated health-related and social support services,[22] including those for treating SUDs.[23] For people with HIV, SSPs can be adapted to provide or link to rapid initiation[24,25] and maintenance of effective ART.[25]

When selecting ART regimens for individuals who use substances, clinicians should consider potential barriers to adherence (see Adherence to the Continuum of Care), comorbidities that could impact care (e.g., advanced liver disease from alcohol or HCV), potential drug–drug interactions, and possible adverse events that are associated with the medications. Providers and people with HIV should discuss adherence during multiple, nonjudgmental evaluations. In general, the use of simplified ART regimens should be considered to aid adherence. Regimens for people with SUDs should be easy to take, such as once-daily formulations, ideally as a single-tablet regimen,[26] and should have a high barrier to resistance and a low risk of hepatotoxicity **(AIII).** Adherence counseling should highlight the benefits of ART use, irrespective of concurrent substance use. While a reduction in substance use may improve adherence to ART,[27,28] ongoing use is not a contraindication to ART.

Long-Acting Antiretroviral Therapy

The development of long-acting (LA) injectable ART provides additional options for treatment. The combination of injectable cabotegravir (CAB) and rilpivirine (RPV) is an optimization option for people with HIV who demonstrate retention in HIV care and who are virologically suppressed on oral therapy (see Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression). Current U.S. Food and Drug Administration (FDA) approval for LA CAB/RPV is limited to individuals with expected good adherence and an ability to achieve virologic suppression on oral therapy prior to starting LA ART. Limited data from a small, ongoing observational study found that LA CAB/RPV leads to high levels of viral suppression in people with HIV who have struggled with adherence to oral ART and those who are viremic at treatment initiation, including people who use stimulants.[29] Of note, the clinic in this study provided a significant amount of social support to ensure adherence

to the LA CAB/RPV regimen (see Virologic Failure for additional details). It is not known if similar responses can be seen in clinics without the resources to provide a similar level of adherence support. Missing LA CAB/RPV doses or a delay in receiving scheduled injections may result in emergence of HIV drug resistance.[29]

The following factors should be considered when contemplating the use of LA CAB/RPV in people with HIV and SUDs:

- As with all treatment conversations, providers should discuss adherence with their patients during multiple, nonjudgmental evaluations.
- Providers and people with HIV should consider the impact of using LA CAB/RPV in the context of current or past substance use behaviors. Although some people may welcome or even prefer LA CAB/RPV,[30] one qualitative study highlighted that using a needle for administering LA CAB/RPV could be a trigger for people with a history of injecting illicit substances.[31]
- Studies utilizing LA CAB/RPV have included individuals with good adherence before starting the LA ART, but this should not exclude people with SUDs who are struggling with adherence from being considered for LA CAB/RPV. Rather, the clinical team should consider what additional support may be needed to help people with SUDs be successful with LA CAB/RPV and whether using LA ART without established viral suppression is warranted based on preliminary data (see Virologic Failure and Adherence to the Continuum of Care for additional details). Case management, patient navigators, and/or peer navigators should be considered to help people with HIV return for follow-up injections.
- Given the often unpredictable lifestyles of people with SUDs, clinical care teams should be flexible in scheduling injections or accommodating walk-ins for injections. However, it should be stressed, however, that the doses should be given within the mandatory 7 days before or after the scheduled LA CAB/RPV injection date.
- As for all people with HIV, hepatitis B virus (HBV) status should be evaluated before the initiation of LA CAB/RPV (see HBV/HIV Coinfection and Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression for additional details). If not already immune or infected, HBV vaccination should be initiated while considering LA CAB/RPV, including in those with isolated hepatitis B core antibody (HBcAb).
- LA CAB/RPV is not recommended for people with HBV/HIV coinfection unless HBV-active drugs (i.e., tenofovir, entecavir) are included in the regimen.
- As depressive disorders have been associated with LA CAB/RPV in all populations, people with SUD also should be screened for depressive disorders and treated for depression if indicated.[32] If depressive disorders worsen while on LA CAB/RPV, reevaluation should occur to determine whether continued therapy with this regimen is advisable.

Importantly, despite emerging observational data, multiple knowledge gaps exist regarding the use of LA ARVs among people with HIV and SUDs. The results from the ongoing Long-Acting Therapy to Improve Treatment Success in Daily LifE (LATITUDE) Study (NCT 03635788) will provide clinical trial results to help inform the use of LA CAB/RPV among people with HIV and SUDs who have struggled with ART adherence.[33] Additional research is also needed to determine optimal methods for supporting ART adherence (including to LA ARVs) among people with HIV and SUDs. These research studies will need to take into consideration the combination of various interventions

(e.g., peer support, case management, pharmacotherapy for SUDs, housing) and the appropriate individual interventions needed to support overall ART adherence.

Commonly Used Substances and Their Impact on HIV and Antiretroviral Therapy

Health care providers should have a basic understanding of evidence-based pharmacologic and behavioral (e.g., cognitive behavioral therapy, motivational interviewing, motivational enhancement therapy, contingency management) treatments for different substances, including alcohol, benzodiazepines, cannabinoids, club drugs, opioids, stimulants (cocaine and methamphetamines), and tobacco. The sections below discuss the impact of these substances on people with HIV and how these substances affect ART use.

Alcohol

Epidemiology

Alcohol consumption is common among people with HIV. Recent estimates indicate that >50% of people with HIV in the United States consume any amount of alcohol (range, 54% to 67%).[34,35] Among a sample of people with HIV across seven university-based HIV clinics in the United States, 27% of people screened positive for unhealthy alcohol use as determined by the AUDIT-C.[35] Unhealthy alcohol use includes a spectrum of consumption, including at-risk or hazardous use, heavy episodic use (binge drinking), and alcohol use disorder (AUD).[36]

Risk-Taking Behaviors, the HIV Care Continuum, and Comorbidities

Unhealthy alcohol use has been linked to HIV acquisition because it can increase the frequency of behaviors that put a person at risk for sexual transmission of HIV.[37-39] In a meta-analysis of 27 studies, any alcohol use, unhealthy alcohol use, and alcohol use in sexual contexts all were associated with condomless sex among people with HIV.[38]

In addition, unhealthy alcohol use has been associated with interruptions in all steps of the HIV care continuum, including lower adherence to ART.[40,41] Studies have demonstrated both temporal and dose-related relationships between alcohol use and adherence, where ART is more likely to be missed on a given drinking day and the day after drinking, with a stronger association on heavy (binge) drinking days.[42-44] The negative impact of unhealthy alcohol use on ART adherence is likely multifactorial and driven by the effects of intoxication, ARV regimen complexity, and patient perceptions of adverse interactions between alcohol and ARV drugs.[45-47] Studies also have demonstrated an association between unhealthy alcohol use and the loss of durable viral suppression,[48-50] greater time spent with a viral load >1,500 copies/mL after ART initiation,[51] increased risk of viral rebound, lower retention in care,[52,53] and increased mortality.[54-56] Unhealthy alcohol use alone (hazardous or AUD) and in combination with other common comorbidities, including viral hepatitis coinfection, can hasten liver fibrosis progression in people with HIV.[57,58] Finally, in general medical populations, unhealthy alcohol use complicates the management of diabetes mellitus, hypertension, mental health disorders, other substance use, and other chronic diseases, and it increases the risk for pneumonia, osteoporosis, a number of cancers (e.g., liver, head and neck, and breast cancers), and tuberculosis.

Management of Unhealthy Alcohol Use

Ongoing alcohol use is not a contraindication for a person to receive ART. However, treatment for unhealthy alcohol use may improve HIV treatment outcomes. Behavioral treatments for unhealthy alcohol use among people with HIV demonstrate a small but significant reduction in alcohol use[59,60] (see additional resources for alcohol management from the National Institute on Alcohol Abuse and Alcoholism and the Substance Abuse and Mental Health Services Administration [SAMHSA]). Pharmacotherapy also can reduce alcohol use among people with HIV. The FDA has approved three pharmacotherapies for AUD: naltrexone, disulfiram, and acamprosate (see Table 15 below).

Clinical trials have demonstrated the efficacy of naltrexone in reducing the number of heavy drinking days among those with HIV and among the general population. Naltrexone appears to be safe to use in people with HIV,[61,62] and it is not associated with significant drug–drug interactions or irreversible hepatotoxicity. However, it is not recommended for individuals with decompensated liver disease and should be used with caution in individuals with elevated transaminase levels. Use of naltrexone in people with HIV and AUD can improve HIV treatment outcomes.[63] In a randomized placebo-controlled trial of 100 prisoners with HIV who met the criteria for AUD, individuals who were provided depot naltrexone upon release from prison were more likely to achieve viral suppression at 6 months than the placebo group (56.7% vs. 30.3%).[62]

Data on the use of disulfiram and acamprosate among people with HIV are lacking. Notably, integrating treatment for AUD with treatment for HIV has been shown to increase the number of people who receive alcohol treatment medication, counseling, and formal outpatient alcohol treatment services. Integrating these treatments also may improve the likelihood that a person with HIV will achieve viral suppression on ART. A randomized controlled trial of 128 individuals with HIV and AUD compared an integrated stepped-care model of alcohol treatment in Veterans Administration HIV clinics to treatment as usual. At the end of treatment (24 weeks), integrated stepped-care resulted in more participants receiving pharmacotherapy for AUD and participating in counseling. Although differences in alcohol use and viral suppression were not seen at 24 weeks, at 52 weeks, integrated stepped-care was associated significantly with an increased number of alcohol-abstinent days, a decrease in the number of drinks per drinking day, and a decreased number of heavy drinking episodes. In addition, the participants in the stepped-care group had increased odds of achieving viral suppression (odds ratio [OR] 5.58; 95% CI, 1.11–27.99).[64]

Liver cirrhosis—whether related to chronic heavy alcohol use, viral hepatitis, or metabolic dysfunction–associated steatotic liver disease—can result in altered metabolism of ARV drugs. For those who have hepatic impairment due to alcohol-related liver disease, ART dosing should follow the recommendations in Appendix B, Table 10, which are based on Child-Pugh classifications.

Benzodiazepines

Epidemiology

While the specific epidemiologic data on the prevalence of benzodiazepine use among people with HIV are limited, benzodiazepine misuse is a growing public health concern due to its impact on both morbidity and mortality.[65] Benzodiazepines cause anterograde amnesia, defined as difficulty recalling events after taking the medication. Individuals do not develop tolerance to this neurocognitive effect, and long-term use of benzodiazepines may result in impairment of neurocognitive functioning.[66]

Risk-Taking Behaviors and the HIV Care Continuum

People who inject drugs and who also use benzodiazepines engage in riskier behaviors than people who inject drugs but do not use benzodiazepines; these behaviors may include paying for sex, sharing injection equipment with more people, and performing more frequent injections.[67] A cohort of 2,802 people who injected drugs was followed from 1996 to 2013. During that time, benzodiazepines were the substances with the greatest association with mortality.[68] In a study of opioid and benzodiazepine use and all-cause mortality among 64,602 veterans (16,989 with HIV and 47,613 without) from the Veterans Aging Cohort Study (VACS) cohort (October 2008 to September 2009), long-term benzodiazepine receipt was associated with increased mortality regardless of long-term opioid receipt.[69] The long-term neurocognitive impact of benzodiazepines on ART adherence among people with HIV is unclear, but prescribing a memory-impairing medication to people with HIV who are prone to neurocognitive impairments from other causes may increase the risk of poor ART adherence.[70] Benzodiazepines also are used illicitly to counteract the negative side effects of stimulants, such as cocaine and methamphetamine.[71]

Management of Benzodiazepine Use

Repeated use of benzodiazepines can result in physiologic dependence and life-threatening withdrawal in some people. When feasible, individuals who chronically use benzodiazepines should be slowly tapered off the benzodiazepines under the supervision of an experienced clinician. Different benzodiazepines have different potencies (e.g., alprazolam is more potent than diazepam) and, therefore, require different tapers in terms of length and graduated decrease in dosage.

Benzodiazepine and Antiretroviral Drug Interactions

Several pharmacological interactions between benzodiazepines and ARV drugs have also been described. For example, some benzodiazepines are cytochrome P450 (CYP) 3A4 substrates; thus, when these benzodiazepines are used with a ritonavir (RTV)-boosted or cobicistat (COBI)-boosted ARV drug, their half-lives and concentrations can increase significantly, leading to enhanced and prolonged sedating effects. See Drug–Drug Interactions for available data on benzodiazepine-related interactions.[72]

Cannabis and Cannabinoids

Epidemiology

Both medical and recreational cannabis (marijuana) use are prevalent among people with HIV.[73] Cannabis belongs to a class of compounds that activate cannabinoid receptors. This class, known as cannabinoids, also includes synthetic compounds, such as K2. In recent years, cannabinoids have become more popular. In 2009, two cannabinoids were reported to the National Forensic Laboratory Information System. By 2015, 84 compounds had been reported.[74] These compounds most commonly cause tachycardia, agitation, and nausea, but they have a wide range of psychiatric effects, including psychosis and paranoia.[75]

Risk-Taking Behaviors and the HIV Care Continuum

Cannabis has not been shown to negatively impact adherence to ART or a person's ability to achieve viral suppression. In one study, among 874 people with HIV, daily cannabis use did not predict lower

odds of ART use or achieving an undetectable HIV RNA level, except when combined with binge drinking.[76] Data from the Multicenter AIDS Cohort Study have supported the idea that marijuana use does not predict problems with adherence to ART or achieving viral suppression.[77] In some cases, however, cannabinoids have been listed as the cause of death in overdoses. While data are lacking among adults with HIV, the nationally representative 2015 Youth Risk Behavior Survey (which includes data from 15,624 adolescent students in Grades 9 to 12) found that students who had ever used synthetic cannabinoids engaged in riskier activities, including sex, than students who only used marijuana.[78] While the available data suggest that the use of marijuana is not associated with decreased adherence to ART,[79] data are lacking on the impact of synthetic cannabinoids on ART adherence. Finally, with the growing use of synthetic cannabinoids, there is concern that fentanyl could be added to these products, which may increase the risk of opioid overdose.

Management of Cannabis and Cannabinoid Use

Because of the aforementioned concerns regarding cannabinoid use, particularly the variety of compounds and neuropsychiatric effects, people with HIV should be discouraged from using cannabinoids until more data are available. No pharmacological treatment exists for cannabinoid use disorder; however, behavioral health treatment may be effective for some people.[80-82]

Club Drugs

Epidemiology

Club drugs are recreational substances that have euphoric or hallucinogenic effects or that are used to enhance sexual experiences.[5] The use of multiple club drugs or other drugs simultaneously is common. Although these substances are used by many different people with HIV, the majority of data come from MSM with HIV. The use of club drugs in this population has been shown to negatively impact HIV treatment.[83] Club drugs include MDMA, GHB, ketamine, benzodiazepines (see the benzodiazepine section above), and other drugs that are used to enhance sexual experiences (e.g., mephedrone, inhaled nitrates [poppers], and phosphodiesterase-5 inhibitors [PDE5] for erectile dysfunction). Survey data from users of club drugs also have revealed that efavirenz is purchased by people without HIV for its intoxicating effects.[84]

Risk-Taking Behaviors and the HIV Care Continuum

Club drugs have disinhibitory effects. Using club drugs increases the likelihood that a person will engage in high-risk sexual practices, which can increase the risk of HIV transmission. In addition, these disinhibitory effects can lead to poor ART adherence.[72,83,85]

Management of Club Drug Use

Treatment strategies for club drug use have not been well studied in controlled trials.[86] No recommended pharmacotherapies exist at this time, and the most common strategy for treating people who use club drugs is to employ the behavioral interventions that are used for other drug use disorders.

Club Drug and Antiretroviral Drug Interactions

MDMA, GHB, ketamine, and methamphetamine all have the potential to interact with ARV drugs because they are metabolized, at least in part, by the CYP450 system.[72,85] Overdoses secondary to interactions between club drugs (i.e., MDMA or GHB) and protease inhibitor–based ART have been reported.[72,87] For instance, using PDE5 or ketamine concurrently with potent CYP3A4 inhibitors, such as RTV or COBI, can potentiate the effects of these substances.[83]

Cocaine

See the discussion in the section on stimulants below.

Opioids

Epidemiology

Opioids remain a significant concern for people with HIV, both for the acquisition of HIV and as major contributors to morbidity and mortality. Overdose involving opioids is the leading cause of accidental death in the United States.[88] The appropriate use of opioids while caring for people with HIV and chronic pain is an important component of combating the opioid epidemic, but this subject is beyond the scope of this section. Please refer to additional resources, such as those from the Centers for Disease Control and Prevention (CDC) and the Infectious Diseases Society of America.[89] To combat the opioid overdose epidemic, health care providers should prescribe naloxone for opioid overdose prevention for all people who are using opioids beyond the short-term treatment of acute pain.[3]

Risk-Taking Behaviors and the HIV Care Continuum

Many people who use opioids start by using opioid tablets (e.g., oxycodone) that are ingested orally or crushed and sniffed. Once tolerance develops, some individuals move from sniffing the crushed tablets to injecting heroin purchased on the streets. This transition from sniffing to injecting dramatically increases the risk of HIV and HCV infection.

Low-cost heroin is often a mix of heroin and higher-potency synthetic opioids, such as fentanyl.[88] Methamphetamines and cocaine also have been combined with fentanyl but at a lower rate than heroin.[90,91] With the growing use of synthetic cannabinoids, there is concern that fentanyl could be added to these as well. In all instances where fentanyl or other high-potency opioids are added to other drugs, the risk of overdose increases.

Although treatment for an opioid use disorder (OUD) can improve HIV treatment outcomes, it is not a prerequisite for treating HIV, as some people with HIV are able to adhere successfully to ART despite ongoing opioid use. Although ART coverage among people with HIV who injected drugs increased from 58% to 71% between 2009 and 2015, additional work is needed to improve ART coverage in this population.[92] Data from the Johns Hopkins HIV Clinical Cohort (2001–2012) demonstrated that in the early years of the cohort, people who injected drugs were less likely to be retained in care; however, this gap in retention had closed by 2012, and people who injected drugs and noninjectors had similar probabilities of being on ART and having a suppressed viral load during the later years of the cohort.[93]

Management of Opioid Use

FDA has approved three medications for the treatment of OUD that can help decrease or eliminate opioid use, reduce the risks of morbidity and mortality that are associated with opioid use, and improve HIV treatment success. These medications—collectively termed medications for opioid use disorder (MOUD)—include buprenorphine, methadone, and naltrexone (see Table 15 below). Buprenorphine and methadone are opioid agonists (the use of these drugs is termed opioid agonist therapy), whereas naltrexone is an opioid antagonist or "blocker." Both buprenorphine and naltrexone can be prescribed in the setting of routine HIV clinical care.[94] Prescribing buprenorphine requires specific training but no longer requires an X waiver (see the SAMHSA website for more information). Methadone must be prescribed through a licensed opioid treatment program (OTP). An OTP directory also can be found on the SAMHSA website.[95]

Use of buprenorphine or methadone can lead to reductions in risky behaviors associated with HIV transmission, psychosocial and medical morbidity related to OUD, and criminal behaviors. People who are receiving treatment for opioid use are already engaging with the health care system; therefore, they are more likely to initiate treatment for HIV and to be adherent to their ARV regimens. Both buprenorphine and methadone are cost-effective interventions at the societal level.[96] Methadone has better retention in SUD treatment than either buprenorphine or naltrexone, and it should be considered for individuals who do not achieve successful outcomes with buprenorphine or naltrexone.[97] Buprenorphine has a lower risk of overdose than methadone. In addition, it can be prescribed in primary care offices. People who are taking buprenorphine have significantly better retention in treatment than those who are taking daily oral naltrexone.[98] Although several randomized, controlled clinical trials have demonstrated efficacy for naltrexone when treating OUD, subsequent study results have been disappointing; one meta-analysis revealed that oral naltrexone was equivalent to placebo.[99] To address the adherence challenges with naltrexone, a depot formulation was created for monthly administration. This preparation has the potential to improve adherence; however, studies that compare opioid agonists (i.e., buprenorphine and methadone) to depot naltrexone as treatments for OUD have not been conducted. In a randomized, placebo-controlled trial in people with both HIV and OUD, participants who received at least three doses of depot naltrexone before discharge from prison achieved longer periods of continuous abstinence after transitioning from prison to the community than those who received either placebo or two or less doses of depot naltrexone.[62] On the basis of these data, methadone or buprenorphine generally are used as first-line agents for the treatment of OUD. Depot naltrexone is used as an alternative treatment for people who have been released recently from correctional facilities when other options are not available.

Important pharmacokinetic interactions between these medications (particularly methadone) and certain ARV drugs are listed in Drug–Drug Interactions.

Although medications remain the backbone of treatment for OUD, there is growing recognition of the critical importance of the social drivers of health and how they impact the willingness of people to engage in treatment with the medications discussed above. A recent randomized study of 114 people with HIV compared the effectiveness of different medications for the treatment of OUD to achieve viral suppression, finding that stable housing, high school–level education or greater, and income stability were associated with a greater reduction in opioid use.[95]

Xylazine and Opioids

Xylazine—a non-opioid analgesic utilized in veterinary medicine that is a commonly used adulterant in opioids and other substances—has become an emerging drug threat associated with the opioid epidemic.[100] The CDC has documented a 276% increase in the monthly percentage of illicitly manufactured fentanyl (IMF)–involved deaths where xylazine was detected.[101] Between 2020 and 2021, the Drug Enforcement Agency reported that xylazine-associated deaths increased by over 100% in all regions of the United States and over 1,000% in the South.[102] This growing body of data led the ONDCP to formally designate fentanyl adulterated with xylazine as an emerging drug threat.[103]

Xylazine is a substrate of CYP3A4 and, as such, when used with an ARV regimen including a CYP3A4 inhibitor, such as RTV or COBI, may lead to elevated levels and prolonged half-lives of xylazine.[104] For people with HIV who continuously use opioids in areas with high rates of xylazine-adulterated IMF, providers should weigh the risks and benefits of using ARV drugs with CYP3A4 inhibitors, given potential interactions and the increase in xylazine-associated adverse effects.

Opioid adulterants, such as xylazine, increase the risk of overdose. Although naloxone only reverses opioid effects, that alone may be sufficient to reverse the overdose. This highlights the need for universal access to naloxone and the active prescribing of naloxone by health care providers. The CDC maintains information about xylazine and how to reduce its harm on its website.[105]

Stimulants

Epidemiology

Cocaine and methamphetamine are powerful stimulants that have been associated with multiple detrimental effects among people with HIV, including accelerated disease progression, poor ART adherence, and lack of viral suppression. Cocaine powder is snorted or injected, whereas the free-base form (crack) is smoked. Methamphetamines can be taken orally or rectally, injected, or smoked. Cocaine and methamphetamine are commonly used with other substances, including alcohol, and can be combined with fentanyl, which increases the risk of overdose.[90,91] Individuals who use stimulants experience a sense of euphoria and may have heightened sexual desire and arousal. This can lead to disinhibited sexual behaviors, increasing the risk of HIV transmission.

The prevalence of stimulant use among people with HIV has been estimated to be 5% to 15% across multiple studies.[106-108] Methamphetamine use is more common among MSM,[109] and increased rates of cocaine use have been observed among ethnic and racial minorities and persons with a history of incarceration.[110]

Risk-Taking Behaviors and the HIV Care Continuum

People with HIV who use stimulants may experience multiple negative health consequences, including rapid development of dependence and adverse effects on multiple organ systems, particularly the central nervous and cardiovascular systems. Stimulant use is associated with neurocognitive impairment,[111] delirium, seizures, hemorrhagic strokes, and mental health disturbances, including anxiety, psychosis, and paranoia.

Stimulant use may independently lead to HIV disease progression even among people who are taking ART and have achieved viral suppression. Research to identify the cellular mechanisms responsible

for this is ongoing, but increased viral replication, direct effects on the immune system that lead to declines in CD4 T lymphocyte cell count, enhanced immune activation, and disruption of the blood-brain barrier, facilitating HIV entry into the brain, have been implicated.[112-116] Stimulant use has been associated with poor HIV continuum of care outcomes, including suboptimal rates of ART adherence,[117] retention in care, and viral suppression.[118-120] Lack of viral suppression, combined with the increased likelihood of risky sexual behaviors that occur under the influence of stimulants, poses a threat to the HIV treatment-as-prevention paradigm.[121]

Management of Stimulant Use

Several pharmacologic and behavioral interventions for stimulant dependence have been investigated, and some trials have included people with HIV. The results of pharmacologic interventions generally have been disappointing. No FDA-approved pharmacotherapy for cocaine use disorder currently exists, despite research on multiple drug classes, including antidepressants, antipsychotics, anticonvulsants, and dopaminergic medications (e.g., disulfiram).[122,123] Among people with HIV who use crack and opioids, medication-assisted treatment for OUD may improve ART adherence and viral suppression.[124,125] Limited evidence indicates that some pharmacologic interventions (e.g., methylphenidate, modafinil, bupropion, naltrexone)[126] can reduce methamphetamine use or cravings. A double-blind, placebo-controlled trial of extended-release injectable naltrexone plus oral extended-release bupropion in adults with moderate or severe methamphetamine use disorder demonstrated a higher response of methamphetamine-free urine samples compared to placebo; however, the overall response rate was low.[127] A double-blind randomized clinical trial on people with methamphetamine use disorder evaluated daily mirtazapine versus placebo in cisgender men and transgender women who have sex with men. Over 36 weeks of follow-up, daily mirtazapine use led to reduced methamphetamine-positive urine drug tests and concurrent reductions in sexual risk behaviors.[128] No specific recommended pharmacotherapy exists to treat stimulant use disorder in people with HIV.

Several behavioral interventions have shown promise in randomized trials. People with HIV who received motivational interviewing sessions, cognitive behavioral therapy, or a combination of the two experienced decreased stimulant use, improved ART adherence, and were less likely to engage in sexual transmission risk behaviors.[129] Contingency management has been shown to be effective in decreasing stimulant use among people with HIV, but the sustained effects on the reduction of stimulant use and improvements in ART adherence are less clear.[107,130,131] The addition of a positive affect intervention to contingency management, compared with an attention control condition, decreased HIV viral load among sexual minority men with HIV.[132] Technology-based interventions, such as text messaging, may have a role in supporting ART adherence and decreasing methamphetamine use among people with HIV, but further research is needed.[133] People with HIV who use stimulants benefit most from multidimensional interventions that target substance use, ART adherence, and risky sexual behaviors.[129]

Despite the challenges discussed above, people with HIV who use stimulants can achieve viral suppression with ART[120] and should be prescribed ART even if stimulant use is ongoing.

Tobacco

Epidemiology

The prevalence of tobacco smoking among people with HIV in the United States is approximately twice that of the general population (33.6% vs. 16.8%).[134] Prevalence is even higher among specific subgroups, including those who use alcohol and/or other drugs, those who have concurrent mental health disorders, and those of a lower socioeconomic status. Although smoking rates are declining overall in the United States, people with HIV are less likely to quit smoking than people in the general population.[134]

Associated Risks of Tobacco Use and HIV Infection

With respect to substance use and HIV, tobacco smoking is the biggest threat to health-related gains achieved through ART. Among individuals with viral suppression on ART, more years of life may be lost from continued smoking than from HIV infection itself.[135,136] Tobacco smoking among people with HIV is associated with an increased risk of numerous health conditions, including lung cancer and other smoking-related cancers, cardiovascular disease, and pulmonary disease. In a sample of 17,995 people with HIV on ART in Europe and North America, individuals who smoked had nearly twice the mortality of those who did not (mortality rate ratio 1.94; 95% CI, 1.56–2.41) with significant mortality attributed to cardiovascular disease and non-AIDS-related malignancy.[135] Importantly, tobacco cessation reduces the incidence of cardiovascular disease and smoking-related cancers (although definitive data on lung cancer are not available) and improves quality of life.[137-139]

Managing Tobacco Use

To maximize the survival benefits of ART, clinicians should consider using evidence-based behavioral and pharmacological[140-142] cessation strategies when treating people with HIV who smoke tobacco (see the tools and recommendations provided by the CDC and the U.S. Preventive Services Task Force and recent review).[143] These include (but are not limited to) advising the individual to quit smoking, using the five A's, employing motivational interviewing, and referring them to a tobacco quitline. Pharmacotherapies for smoking cessation (nicotine replacement therapy, bupropion, and varenicline) have few clinically significant interactions with ARV drugs and can lead to enormous reductions in morbidity and mortality if the person is able to stop smoking. Nicotine replacement is efficacious[144]; however, bupropion doubles rates of smoking cessation compared with nicotine replacement therapy.[145] Varenicline is a partial nicotine receptor agonist. In comparative studies, varenicline was more effective than bupropion in smoking cessation.[145,146] Clinical trials among people with HIV have found varenicline to be both effective and safe.[140,142] In a randomized controlled trial among 179 individuals with HIV who were assigned to receive 12 weeks of behavioral counseling and either varenicline or placebo, varenicline use led to an increase in the percentage of participants who achieved a 7-day abstinence period at 12 weeks (28.1% vs. 12.1%, OR 4.5; 95% CI, 1.83–11.2) and produced higher continuous abstinence between Weeks 9 and 12 (23.6% vs. 10%, OR 4.65; 95% CI, 1.71–12.67) compared to placebo.[142] Although significant between-group differences were not observed after 24 weeks, these data support the use of varenicline among people with HIV. Varenicline should be used in combination with relapse prevention strategies and other measures for long-term tobacco cessation.

Table 15. Medications for Treatment of Substance Use Disorders

Medication	Dose and Recommendations	Potential Interaction With ARV Drugs	Comments
Alcohol Use Disorder			
Acamprosate	666 mg PO three times a day *or* 333 mg PO three times a day for people with CrCl 30–50 mL/min	No significant interaction with ARV drugs expected.	**Contraindicated** in people with CrCl <30 mL/min
Disulfiram	250 mg PO once daily	Use with caution when prescribing an ARV oral solution that contains ethanol and/or propylene glycol (e.g., FPV, LPV/r, RTV).	Counsel people regarding disulfiram reaction when taken with alcohol; symptoms for the reaction may include flushing, tachycardia, nausea, vomiting, or hypotension.
Naltrexone	50–100 mg PO once daily Depot formulation is a fixed-dose monthly injection.	No significant interaction with ARV drugs expected.	Has the greatest efficacy of all FDA-approved medications for AUD.
Opioid Use Disorder			
Buprenorphine	Individualize buprenorphine dosing based on the person's opioid use. The dose range is 4–24 mg sublingually. Dosing is once daily or twice daily.	Potential interaction with ARV drugs that are CYP inhibitors or inducers. See Drug–Drug Interactions for further recommendations.	Buprenorphine has 90% first-pass hepatic metabolism. Verify that the person is using the appropriate technique for sublingual administration before adjusting the dose, because improper administration will result in poor absorption and low drug levels.
Methadone	Individualize the dose. People who receive higher doses (>100 mg) are more likely to remain in treatment.	Potential interaction with ARV drugs that are CYP inhibitors or inducers. See Drug–Drug Interactions for further recommendations.	QTc prolongation is a concern at higher doses. Methadone can be prescribed for OUD only by a licensed OTP.
Naltrexone	50–100 mg PO once daily Depot formulation is a fixed-dose monthly injection.	No significant interaction with ARV drugs expected.	Longer time of continuous abstinence in those who received depot formulation naltrexone compared with placebo after transition from prison to community.
Nicotine Use Disorder			
Nicotine Replacement Therapy	The FDA has approved a wide variety of nicotine replacement products. All formulations are effective.	No significant interaction with ARV drugs expected.	Work with the person to identify the route of delivery that they will use and find most helpful.

Table 15. Medications for Treatment of Substance Use Disorders

Medication	Dose and Recommendations	Potential Interaction With ARV Drugs	Comments
Bupropion	Start at 150 mg PO daily for 3 days, then increase to either 150 mg twice daily or 300 mg once daily (use only formulations that are approved for once-daily dosing).	Concentration may be reduced when used with ARV drugs that are CYP2D6 inducers. See Drug–Drug Interactions for further recommendations.	For optimal results, tobacco quit date should occur 1 week after starting therapy.
Varenicline	Titrate the dose based on tolerability until the desired effect is achieved. The goal is to reach a dose of 1 mg PO twice daily. Requires dose adjustment in people with CrCl <30 mL/min.	No significant interaction with ARV drugs expected.	For optimal results, tobacco quit date should occur 1 week after starting therapy.

Key: ARV = antiretroviral; AUD = alcohol use disorder; CrCl = creatinine clearance; CYP = cytochrome P450; FDA = U.S. Food and Drug Administration; FPV = fosamprenavir; LPV/r = lopinavir/ritonavir; OTP = opioid treatment program; OUD = opioid use disorder; PO = orally; QTc = QT corrected for heart rate; RTV = ritonavir

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Transgender People With HIV

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Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all transgender people with HIV to improve their health and reduce the risk of HIV transmission to sexual partners **(AI).** • HIV care services should be provided within a gender-affirmative care model to reduce potential barriers to ART adherence and to maximize the likelihood of achieving sustained viral suppression **(AII).** • Prior to ART initiation, a pregnancy test should be performed for transgender individuals of childbearing potential **(AIII).** • Some antiretroviral drugs may have pharmacokinetic interactions with gender-affirming hormone therapy. Clinical effects and hormone levels should be routinely monitored with appropriate titrations of estradiol, testosterone, or androgen blockers, as needed **(AIII).** • Some gender-affirming hormone therapies are associated with hyperlipidemia, elevated cardiovascular risk, and osteopenia; therefore, clinicians should choose an ART regimen that will not increase the risk of these adverse effects **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

Because transgender and nonbinary people bear a disproportionate burden of HIV, it is important for HIV care providers to be knowledgeable about the specific HIV care needs of these individuals.

Terminology

Transgender people are broadly defined as those whose gender identity differs from their assigned sex at birth.[1-3] The terminology used to describe transgender identities continues to evolve over time and across geographical and cultural contexts.[3,4] The terms cisgender, cis man, and cis woman are used to describe people who identify with their assigned sex at birth. The terms used to describe women who were assigned male at birth include transgender women, trans women, transfeminine individuals, and women of transgender experience. The terms for men who were assigned female at birth include transgender men, trans men, transmasculine individuals, and men of transgender experience. Some individuals identify outside the gender binary of man or woman, describing themselves as gender diverse, gender nonbinary, genderqueer, or gender nonconforming. Other individuals may not have a fixed sense of their gender and may move back and forth among different gender identities; these individuals are described as gender fluid. Gender fluidity refers to the nonfixed, adaptable nature of gender identity and expression that can occur and is commonly seen during adolescence.[5] Agender people do not identify with having any gender and can use other terms, such as null gender or neutrois.

Gender affirmation describes processes whereby a person receives social recognition, value, and support for their gender identity and expression.[6] Gender affirmation is often described across several dimensions, including social (e.g., social support and acceptance, use of pronouns, names, or clothing

that align with their gender identity), medical (e.g., use of hormones or surgery), legal (e.g., legal name change or changing gender markers on identity documents), and psychological (e.g., the degree of self-acceptance and comfort with their gender identity).[7] Medical gender affirmation has been shown to improve mental health outcomes and measures of well-being in transgender individuals.[8,9]

Epidemiology

National surveys indicate that 1.14% of the U.S. adult population, representing 3 million people, identify as transgender.[10] Data from the Pew Research Center suggests that gender diversity is more commonly reported among adolescents and young adults, with approximately 5% of young adults (aged 18 to 29) expressing a gender that is different from the sex on their original birth certificate, compared to 0.3% of older adults (aged 50 or older).[11] Meta-regression modeling suggests that the number of people who are willing to report that they are transgender and/or gender nonbinary is likely to increase in the future.[12]

The most recent estimate of global HIV prevalence among transgender people is 19.9% among transgender women and 2.6% among transgender men.[13] In the United States, the highest prevalence was found among Black and Latina transgender women[14], although data among transgender men are more limited.[15] Data on HIV prevalence among nonbinary individuals is scant. Of 164 nonbinary adults who completed nationally representative LGBTQ surveys between 2016 and 2018, 3% self-reported having HIV; however, results should be interpreted with caution due to the small sample size.[16] In 2022, HIV diagnoses among transgender people accounted for approximately 2% of all diagnoses. Of transgender and nonbinary people diagnosed in 2022, 31% were aged 13 to 24 years.[17] HIV diagnoses increased among transgender and nonbinary people while remaining stable among other gender groups, and transgender women were the only gender group to experience an increase (20%) in HIV-related deaths since 2018.[17]

The Centers for Disease Control and Prevention (CDC) surveillance reports indicate that 83% of transgender and nonbinary people with HIV diagnosed at year-end 2022 had received some aspect of HIV medical care, and 67% were virologically suppressed, which is well below the National HIV Strategy goal of 95% viral suppression for all people with HIV. Transgender women were the gender group with the lowest percentage of receipt of care and viral suppression.[18] In 2022, the Ryan White HIV/AIDS Program (RWHAP) provided services for 11,085 transgender people, representing 2.8% of RWHAP clients.[19] Of these transgender clients, 2.3% were transgender women, 0.3% transgender men, and 0.2% with another gender identity (e.g., nonbinary). Among RWHAP participants, retention in care (73.5%) and viral suppression (86.4%) for transgender adults and adolescents were lower than the national averages (77.5% and 89.6%, respectively). Overall, existing data are limited and likely underrepresent the proportion of transgender people due to a lack of systematic collection of gender identity and possible reluctance to disclose transgender identities because of social stigma.[20]

HIV Care Continuum

Some studies have reported that transgender women with HIV are less likely than cisgender men to receive antiretroviral therapy (ART), be adherent to ART, and achieve viral suppression.[21-27] However, data from a large multisite cohort study suggest that transgender women who are effectively engaged in care may have similar, if not better, HIV outcomes than cisgender people in HIV care.[28] Another retrospective study of Medicare beneficiaries with HIV found that transgender beneficiaries had greater care engagement than cisgender beneficiaries.[29] These results suggest that

once transgender people are linked to care, they are as likely to achieve positive HIV outcomes as cisgender people.

However, transgender people may experience numerous barriers to health care access and viral suppression.[30-32] The CDC Medical Monitoring Project found that transgender women diagnosed with HIV were more likely than cisgender men with HIV to have unmet subsistence needs (e.g., housing, transportation).[33] Unmet needs for services were negatively associated with higher levels of ART nonadherence (adjusted prevalence ratio [aPR]: 1.39; 95% confidence interval [CI], 1.13–1.70) and detectable viral loads (aPR: 1.47; 95% CI, 1.09–1.98). Among transgender and nonbinary participants in RWHAP, retention in care was lowest among those with temporary (68.3%) or unstable (67.5%) housing, and viral suppression was lowest among people with unstable housing (73.6%).[19] For a more detailed discussion on social determinants of health and adherence to HIV health care appointments and medications, clinicians should refer to Adherence to the Continuum of Care.

Barriers to HIV Care and Treatment

Transgender people may avoid the health care system due to stigma and past negative experiences (e.g., being called the wrong name or pronoun, being verbally harassed, being asked invasive questions about being transgender, or having to educate their providers about transgender people).[14,31,34-37] For many transgender people, gender-affirming therapy (e.g., feminizing hormones) is a greater priority than HIV treatment and care.[38,39]

Concerns about adverse interactions between antiretroviral (ARV) drugs and gender-affirming hormone therapy are common among transgender people.[38] One study found that 40% of transgender women with HIV did not take their ARV drugs as directed due to concerns about drug–drug interactions, yet less than half had discussed this concern with their providers.[40]

Facilitating HIV Care Engagement

Gender Affirmation

Individuals are more likely to engage in HIV care when gender affirmation needs are met.[6,35] A national study of transgender people with HIV found that participants who work with HIV care providers who affirm their gender (e.g., providers who use their chosen name and pronoun) were more likely to be virologically suppressed.[39] Adherence to hormone therapy correlates with adherence to ART.[41,42] However, making access to hormone therapy contingent upon ART adherence is associated with a lower likelihood of viral suppression.[39]

Integration of HIV Care With Gender Care

According to research on transgender youth[35] and adults,[38] integrating HIV care with gender care facilitates treatment and is associated with higher rates of viral suppression. In addition to minimizing the number of provider visits and potentially stressful clinical interactions, care integration makes it easier to discuss concerns about drug–drug interactions between HIV treatment and gender-affirming medications. In instances where integrated care is not feasible, the ART prescriber should refer the individual to an appropriate hormone therapy prescriber. Collaboration between these two care providers may enhance the quality of care.

Peer Navigation

Peer navigation has been found to improve the likelihood of sustained viral suppression among key populations, including among transgender women.[43] Research including youth and adults suggests that having visible transgender staff in the clinical environment also facilitates engagement in care.[35]

Gender-Affirming Clinical Settings

HIV care services should be provided within a gender-affirmative care model to reduce potential barriers to ART adherence and to maximize the likelihood of achieving sustained viral suppression **(AII).** Concrete steps that clinicians can take include ensuring that registration forms and electronic medical records are inclusive of transgender and gender nonbinary identities, preferably using a two-step method that records both gender and sex assigned at birth.[44,45] A self-reported, electronic approach may facilitate the disclosure of gender identity. Clinicians should also ask people with HIV about their gender identity, chosen names, and pronouns, using developmentally appropriate language. However, before including these items in the electronic health record, clinicians should discuss with people with HIV the possibility of inadvertent disclosure to others, such as parents or guardians.[46]

> *Example of an affirming way to ask about chosen names and pronouns:*
>
> *"My name is Dr. Smith. I use she/her pronouns. What name would you like me to use for you? What pronouns do you use?"*

Clinicians and staff should avail themselves of resource lists, brochures, and other materials that meet the specific needs of transgender people with HIV.

Integrating hormone therapy with HIV services is the recommended practice; this requires HIV providers to become knowledgeable about hormone therapy and other aspects of gender-affirming services. When integration of HIV and transgender services is not possible, the individuals should be referred to clinicians who are knowledgeable in the field of transgender medicine. Both the World Professional Association for Transgender Health (WPATH) and GLMA: Health Professionals Advancing LGBTQ+ Equality (previously known as the Gay & Lesbian Medical Association) have provider directories that list endocrinologists, primary care providers, and psychiatrists who have expertise working with transgender populations.

Pharmacological Considerations

Hormone Therapy

Hormone therapy is an important aspect of gender-affirming care for many transgender individuals. Hormones facilitate the acquisition of the secondary sex characteristics that are associated with the affirmed gender. Several guidelines for hormonal treatment of transgender people have been published, including guidelines from the Endocrine Society[47] and WPATH.[3] Clinical outcomes, potential adverse effects, treatment goals, and the person's current hormone levels should be taken into account when determining the appropriate doses of hormone and androgen blockers. A clinician should be aware of the typical doses and routes of administration for all the hormones and androgen blockers that the person is taking, whether these medications are prescribed or not. All additional interventions (such as gonadectomy) should be documented. These interventions could potentially

increase the risk of ART-related adverse effects on cardiovascular and bone health. Table 16a provides a list of gender-affirming hormone therapies (GAHT) that are commonly used in practice.

Feminizing regimens that are used by transgender women and others who were assigned male at birth usually include estrogens and androgen blockers. Feminizing regimens result in breast growth, redistribution of body fat, softening of the skin, and a decrease in muscle mass.[3] These regimens do not reduce facial (beard) hair or change the voice. In the United States, oral, parenteral, or transdermal preparations of 17-beta estradiol, or, less often, conjugated estrogens, are the mainstay of gender-affirming medical care for transgender women. Spironolactone, a mineralocorticoid receptor antagonist with anti-androgen properties, is normally used for androgen blockade; alternatives include gonadotropin-releasing hormone (GnRH) agonists (e.g., goserelin acetate and leuprolide acetate). Cyproterone acetate is a steroidal anti-androgen that is frequently used outside of the United States. 5-alpha reductase inhibitors that decrease the production of dihydrotestosterone (e.g., finasteride or dutasteride) may be used to reverse scalp hair loss. Some people may request progesterone to assist with breast growth; however, this has not been proven to be effective.[44] When using feminizing regimens, the goal is to suppress the testosterone level to <50 ng/dL and reach a serum estradiol level in the physiologic cisgender female range of 100 pg/mL to 200 pg/mL.[47]

Masculinizing regimens for transgender men and others who were assigned female at birth involve parenteral or transdermal testosterone preparations. These regimens are designed to stimulate the growth of facial and body hair, increase muscle mass, and deepen the voice; use of these regimens also results in clitoral enlargement, vaginal atrophy, and amenorrhea.[47] When using masculinizing therapy, the target testosterone levels are recommended to be 400 ng/dL to 700 ng/dL.[47]

Table 16a. Common Gender-Affirming Hormone Therapies

Feminizing Drugs		Physical Effects
Estrogens	Estradiol, PO 17 β-Estradiol, transdermal (patch) Estradiol valerate, IM Estradiol cypionate, IM	Redistribution of body fat Breast growth Decrease in muscle mass and strength Softening of skin Decrease in spontaneous erection
Androgen Blockers	**Mineralocorticoid Receptor Antagonist** • Spironolactone, PO **5α-Reductase Inhibitors** • Dutasteride, PO • Finasteride, PO • Cyproterone acetate, PO* **GnRH Agonists** • Leuprolide, IM • Triptorelin, IM or SQ • Goserelin, SQ	

Table 16a Common Gender-Affirming Hormone Therapies

Masculinizing Drugs		Physical Effects
Testosterones	Testosterone enanthate, IM or SQ Testosterone cypionate, IM or SQ Testosterone undecanoate, IM Testosterone gel, transdermal	Fat redistribution Facial/body hair growth Deepening of voice Increased muscle mass Amenorrhea Vaginal atrophy Clitoral enlargement

* Not available in the United States

Key: GnRH = gonadotropic hormone-releasing hormone; IM = intramuscular; PO = oral; SQ = subcutaneous

Hormones and Antiretroviral Therapy

Studies that have examined interactions between exogenous estrogens and ART have predominantly focused on combined oral contraceptive use in cisgender women.[48] The data from these studies have been used to make predictions about the direction and extent of drug–drug interactions (see Table 16b). However, there are known differences between the pharmacologic characteristics of ethinyl estradiol, which is used in contraceptives, and 17-beta estradiol, which is used for gender affirmation. These differences may influence the accuracy of the predictions about the interactions between feminizing hormonal regimens and ART.[49]

Table 16b. Potential Interactions Between Common Gender-Affirming Hormone Therapies and Antiretroviral Drugs*

Potential Effect on GAHT Drugs	ARV Drugs	GAHT Drugs That May Be Affected by ARV Drugs	Clinical Recommendations and Other Considerations for GAHT or ARV Drugs
ARV Drugs With the Least Potential to Impact GAHT Drugs	All NRTIs **Entry Inhibitors** • IBA, MVC, T-20 **INSTIs (Unboosted)** • BIC, CAB (IM or PO), DTG, RAL **NNRTIs** • DOR, RPV (IM or PO)	None	No dose adjustments necessary. Titrate dose based on desired clinical effects and hormone concentrations. **Note:** Avoid IM buttock injections into sites with gluteal implants and/or soft tissue fillers.

Table 16b. Potential Interactions Between Common Gender-Affirming Hormone Therapies and Antiretroviral Drugs*

ARV Drugs That May Increase Concentrations of Some GAHT Drugs	• EVG/c • PI/c, PI/r • LEN	Dutasteride Finasteride Testosterone	Monitor for associated adverse effects; decrease the doses of GAHT drugs as needed to achieve the desired clinical effects and hormone concentrations.
ARV Drugs That May Decrease Concentrations of Some GAHT Drugs	PI/r **NNRTIs** • EFV, ETR	Estradiol	Increase the dose of estradiol as needed to achieve the desired clinical effects and hormone concentrations.
	NNRTIs • EFV, ETR	Dutasteride Finasteride Testosterone	Increase the doses of GAHT drugs as needed to achieve the desired clinical effects and hormone concentrations.
ARV Drugs With an Unclear Effect on Some GAHT Drugs	EVG/c PI/c	Estradiol	There is the potential for increased or decreased estradiol concentrations. Adjust the dose of estradiol to achieve the desired clinical effects and hormone concentrations.

Note: See Tables 24a, 24b, 24c, 24d, 24e, 24f, and 24g for additional information regarding drug–drug interactions between ARV drugs and gender-affirming medications.

* Only ARV drugs commonly used in clinical practice in the United States are included in this table.

Key: ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; GAHT = gender-affirming hormone therapy; IBA = ibalizumab; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PO = oral; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; T-20 = enfuvirtide

Other Hormonal Therapy Considerations

Bone Health

Bone metabolism is influenced by sex hormones. Current recommendations for osteoporosis screening are based on age and sex and have not been studied in transgender populations, which include people who have used hormone therapy and/or undergone removal of their gonads. Studies investigating bone mineral density (BMD) changes in transgender women have shown inconsistent results, with the use of estrogens being associated with both elevations and declines in BMD.[50-52] In one study, transgender women had high rates of osteopenia even before initiating hormones, possibly due to low levels of physical activity and low vitamin D levels.[50] Transgender men receiving testosterone appear to maintain adequate BMD.[53] The risk for osteoporosis increases after gonadectomy for both transgender men and transgender women, especially if hormone regimens are stopped. Consequently, clinicians should consider early BMD screening in this setting. The use of GnRH agonists to delay puberty is associated with a reduction in BMD. Although BMD has been shown to improve after these agents are stopped and/or gender-affirming hormones are initiated, peak bone mass attainment may be reduced.[54,55]

When using the FRAX® tool, which requires a sex designation, expert consensus is that assigned birth sex should be used, because transgender people who initiate hormones in early adulthood have generally already achieved peak bone mass.[47,56] Transgender people with HIV should be screened for

osteoporosis by age 50 using dual-energy X-ray absorptiometry, in accordance with current primary care recommendations.[57]

Since the use of tenofovir disoproxil fumarate (TDF) has been associated with reductions in BMD in people with HIV, TDF should be used with caution in transgender people with risk factors for osteoporosis, or in those with established osteoporosis.

Interpretation of Laboratory Values

Interpretation of laboratory results requires special attention when reference ranges vary by sex. The sex listed on laboratory requisition forms typically corresponds with the gender listed on the insurance forms and may not reflect the person's current anatomical or hormonal configuration. Reference ranges have not been established for transgender individuals who are receiving gender-affirming hormonal or surgical interventions. Interpretation of laboratory results is dependent on the person's physiology, dose and duration of hormone therapy, and the specific test being performed.[58]

Renal Concerns

Gender-affirming hormones can affect estimates of glomerular filtration rates (eGFR) that rely on serum creatinine due to changes in muscle mass. In a systematic review assessing the impact of gender-affirming hormones on kidney function, transgender men showed a mean increase in serum creatinine levels of 0.15 mg/dL (95% CI, 0.00 to 0.29) at 12 months after GAHT initiation, compared to a decrease of -0.05 mg/dL (95% CI, -0.16 to 0.05) among transgender women.[59] Creatinine-based eGFR calculations may therefore overestimate glomerular filtration rates (GFR) in transgender women and underestimate it in transgender men using GAHT. Obtaining a measured GFR or using cystatin C–based eGFR calculations may be considered for people with marginal renal function who are taking gender-affirming hormones.

Cardiovascular Disease Risk

Transgender individuals may have elevated cardiovascular disease (CVD) risk due to both traditional risk factors and cardiometabolic effects associated with hormone use.[60] Rates of tobacco use are higher among transgender people than in the general population,[61] and exogenous testosterone has been associated with increased levels of low-density lipoprotein (LDL) and decreased levels of high-density lipoprotein (HDL) among transgender men.[62] Transgender women have a higher risk of venous thromboembolism and ischemic stroke, primarily associated with the duration of estrogen use.[63] Transgender women on estrogens may show an increase in serum levels of triglycerides and HDL and a decrease in levels of LDL.[62] The implications of these differences are unclear. For example, one small study found transgender women with HIV have altered biomarkers associated with systemic inflammation and CVD when compared to matched cisgender men with HIV.[64] Yet, another small study of people with HIV found that subclinical CVD pathophysiology was not elevated in transgender women taking estrogen when compared with matched cisgender controls.[65]

Assessment of cardiometabolic risk among transgender people with HIV can be complicated by hormone-induced changes in lipid levels, as well as sex-specific variations in levels of homocysteine and high-sensitivity C-reactive protein.[66] American Heart Association (AHA) guidelines recommend using sex-specific calculators to determine cardiovascular risk and guide interventions;[67,68] however, AHA guidelines do not provide guidance for transgender people whose assigned sex at birth may differ from their hormonal and/or anatomical sex.[69] The WPATH Standards of Care, Version 8,

recommends clinicians use their professional judgment to tailor such calculators to the needs of transgender and gender-diverse people, taking into consideration the duration of hormone use, dosing, serum hormone levels, current age, and the age at which hormone therapy was initiated.[3]

Providers should take CVD risk into consideration when selecting both ART regimens and GAHT regimens. For transgender people with an elevated CVD risk or a history of CVD events, ARV drugs that are associated with CVD should be avoided whenever possible. See Table 20 for a list of ARV drugs that are associated with an increased risk of CVD. See Table 21 for alternative ARV agents to use in individuals with CVD. In transgender women who have an elevated risk for CVD or who have experienced a CVD event, transdermal estradiol may be the safest option for hormone therapy, because it carries a lower risk of thromboembolism than other routes of administration.[70] Of the 7,769 people with HIV in the recent Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE), 127 (1.6%) were identified as transgender.[71,72] However, sub-analyses by gender identity have not been published. For guidance on the use of statins in people with HIV based on the REPRIEVE results, please see Recommendations for the Use of Statin Therapy as Primary Prevention of Atherosclerotic Cardiovascular Disease in People With HIV.

Pregnancy Potential

Important information on contraception, drug–drug interactions between ARV drugs and hormone therapy drugs, and pregnancy is provided in Women With HIV and in the Drug–Drug Interactions tables of the guidelines. Much of this information also applies to transgender and nonbinary individuals. Below are specific ART considerations for transgender and nonbinary people of childbearing potential. Clinicians who care for pregnant people should also consult the current Perinatal Guidelines for a more in-depth discussion and guidance.

Some transgender individuals use exogenous hormones and/or undergo gonadectomy for gender affirmation. Understanding exactly what interventions someone has undergone and the timeline for these interventions will clarify the person's potential for pregnancy. Transgender individuals without a uterus (by birth or by hysterectomy) do not have pregnancy potential. Ovulation may continue in the presence of hormone therapy in transgender people with a uterus and ovaries, and these individuals may retain their fertility.[1] Gender-affirming surgeries do not impair fertility unless the uterus, ovaries, and vagina are removed.[73,74]

All transgender people who have a uterus and ovaries and engage in sexual activity that could result in pregnancy should receive a pregnancy test prior to initiating ART **(AIII).** All ART-naive persons who are pregnant should be started on ART for their health and to prevent perinatal transmission. Transgender people of childbearing potential should be counseled about ARV drug use during pregnancy, and clinicians should consult the Perinatal Guidelines when designing a regimen **(AIII).**

Testosterone Exposure in Transgender Persons With Ovaries

Testosterone alone is not a reliable form of contraception, and pregnancies have been reported in transgender men following prolonged testosterone treatment. Testosterone is a teratogen and it is contraindicated in pregnancy. Clinicians should assess the reproductive desires and fertility potential of their transgender clients and provide accurate information on contraceptive and reproductive options.[75]

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Transplantation in People With HIV

Updated: September 12, 2024
Reviewed: September 12, 2024

Panel's Recommendations and Key Considerations
• People with HIV who are eligible for solid organ transplant (SOT) or hematopoietic cell transplant (HCT) should have equitable access to transplant **(AII).**
• People with HIV should be managed by a multidisciplinary team before, during, and after transplant **(AIII).**
• Transplant candidates with HIV should be up-to-date on their vaccination schedule **(AIII).**
Antiretroviral Drug Considerations Before Transplant
• In preparation for transplant, HIV providers should review the transplant candidate's antiretroviral (ARV) history, efficacy of the current ARV regimen, prior HIV drug resistance results, ARV adherence, and the potential for drug–drug interactions **(AIII).**
• All ARV regimen changes should be guided by ARV history, along with current and prior HIV drug resistance testing results **(AIII).**
• If switching to an alternative ARV regimen is necessary, changes should be completed several weeks before the transplant whenever possible to minimize drug–drug interactions in the post-transplant period and to assure tolerability and efficacy of the new regimen before transplant **(BIII).**
• Tenofovir alafenamide (TAF) is preferred over tenofovir disoproxil fumarate (TDF) in transplant candidates and recipients due to the lower risk of affecting renal function and bone mineral density **(AII).**
• To avoid significant drug–drug interactions between ARV drugs and anticipated immunosuppressive therapies, chemotherapies (for HCT), and prophylactic regimens for opportunistic infections, the following should be considered: ○ Unboosted second-generation oral integrase strand transfer inhibitor (INSTI)–based regimens (i.e., with bictegravir or dolutegravir) are preferred in most people with HIV needing transplant **(AII).** ○ In general, potent cytochrome P450 (CYP) 3A4 inhibitors—including pharmacokinetic boosters, such as ritonavir (RTV) or cobicistat (COBI), and protease inhibitor (PI)-containing regimens—should be avoided **(AII).** ○ In general, non-nucleoside reverse transcriptase inhibitors (NNRTIs) such as nevirapine (NVP), efavirenz (EFV), and etravirine (ETR), which are CYP3A4 inducers, should be avoided **(AII).**
Maintenance of Viral Suppression
• HIV viral suppression should be maintained before and after transplant **(AIII).***
• HIV providers with appropriate expertise should design alternative ARV regimen(s) that are likely to achieve viral suppression if post-transplant regimen changes are necessary **(AIII).**
Immediately Post-Transplant
• Immediately post-transplant, renal or hepatic function may fluctuate; close monitoring of these organ functions is recommended to ensure appropriate dosing of ARV drugs and other concomitant medications to avoid potential drug toxicities **(AIII).**
• Interruption of antiretroviral therapy (ART) post-transplant should be avoided **(AIII).**
• If interruption is necessary, all components of an oral ART regimen should be stopped simultaneously to avoid exposure to an incomplete regimen. The period of interruption should be kept to a minimal duration **(AIII).**
• If a person cannot swallow pills, providers should consider using oral liquid formulation if available; alternatively, some pills can be crushed or dissolved for administration orally or via an enteral tube **(AIII).**

Post-Transplant
• Therapeutic drug monitoring for immunosuppressive drugs should be performed to guide dosing adjustments, especially before, during, and after the start or switch of ARV drugs that may interact with immunosuppressive drugs **(AII).** • The burden of medication increases significantly post-transplant. Providers should continue to evaluate for potential drug–drug interactions and overlapping toxicities with the addition of new medications **(AIII).**   ○ When feasible, providers should consider consolidating ART using fixed-dose combination tablets and/or single-tablet regimens to minimize pill burden and bolster adherence **(AIII).**
Hepatitis B Virus or Hepatitis C Virus Coinfection
• All donors and recipients should be screened for hepatitis B virus (HBV) and hepatitis C virus (HCV) with a serological and/or nucleic acid amplification test, according to transplant guidelines **(AIII).** • Transplant candidates and recipients who are nonimmune to HBV (as measured by HBV surface antibody [HBsAb]) should be vaccinated, ideally before transplant **(AIII).** • HBV serology should be monitored after transplant for loss of HBsAb in order to guide the need for revaccination per professional society and transplant center guidelines **(AIII).** • Transplant recipients with active HBV infection should be treated with ARV regimens with anti-HBV activity before transplant and indefinitely after transplant **(AIII).** Use of nucleos(t)ide reverse transcriptase inhibitors (NRTIs) with activities against both HIV and HBV is strongly recommended unless contraindicated or not tolerated **(AIII).** • For management of recipients with HIV without HBV who receive an organ from a donor with markers of HBV infection, see guidance in the HBV-Positive and HCV-Positive Donors section below and follow appropriate institutional protocols. • All transplant candidates and/or recipients with HCV infection should be treated with direct-acting antivirals against HCV **(AII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*
* In some cases, it may be necessary to interrupt ART due to intolerance of or inability to administer ARV drugs pre-transplant, such as in end-stage liver disease or when enteral access is limited. In these situations, the HIV provider should design a regimen that will result in viral suppression after transplant and resume therapy as soon as feasible.

General Principles When Managing People With HIV Before and After Transplant

Below are some key principles to follow when caring for people with HIV before and after transplant.

- Ensure that people with HIV have equitable access to transplant.
- Utilize a multidisciplinary approach.
- Maintain HIV viral suppression.
- Select or maintain an antiretroviral (ARV) regimen to minimize drug–drug interactions.
- Be aware of changes in renal or liver function.
- Perform therapeutic drug monitoring (TDM) of immunosuppressants for all transplant recipients.
- Consider pill burden.
- Consider and address hepatitis B virus (HBV) and hepatitis C virus (HCV) coinfection.

- Prevent infectious complications post-transplant with updated vaccination and antimicrobial prophylaxis.

Outcomes of Transplant in People With HIV and the Importance of Equitable Access to Transplant

Before the introduction of potent antiretroviral therapy (ART), people with HIV were systematically denied solid organ transplantation (SOT).[1] When performed, SOT was linked to unfavorable outcomes,[2] partly attributed to the use of older antiretroviral (ARV) regimens that included protease inhibitors (PI), which interact with immunosuppressive medications, such as calcineurin inhibitors or mTOR inhibitors.[3] SOT also had unfavorable outcomes in people with HIV and HCV coinfection before the era of direct-acting antivirals (DAAs) for HCV treatment.[4] The use of PIs also affects the choice of DAAs for HCV treatment. In the era of integrase strand transfer inhibitors (INSTIs) with fewer drug–drug interactions and the widespread availability of DAAs for HCV, recent cohorts have shown a reduction in the disparity of transplant outcomes between people with and without HIV.[5-7]

In people with end-stage renal disease (ESRD), those with HIV are less likely to be referred for kidney transplant than those without HIV. With the use of potent ART, kidney transplant in people with HIV is associated with a survival benefit over chronic hemodialysis, with high rates of recipient and graft survival at both 1 and 3 years post-transplant.[8] Lower but acceptable rates of recipient and graft survival have been reported with long-term (between 5 and 15 years) follow-up when comparing kidney and liver transplantation outcomes in people with HIV compared with recipients without HIV. This difference was primarily driven by lower rates of survival in people with HIV/HCV coinfection before the use of DAAs for HCV treatment.[6,9] In retrospective studies conducted in the post-DAA era, rates of recipient and graft survival in liver transplant recipients with HIV/HCV appear to be similar to people with HIV without HCV.[5,6] Acute rejection rates for kidney transplant recipients are higher in people with HIV than in recipients without HIV.[10]

Hematopoietic cell transplants (HCTs) in people with HIV are now the standard of care in people with hematologic malignancies for which HCT is indicated.[11] In most reported prospective and retrospective studies in the combination ART era, HIV status does not appear to impact the outcome of autologous or allogeneic HCT with respect to nonrelapse mortality. Allogeneic HCT is particularly intriguing due to its potential to significantly reduce HIV reservoirs or even achieve a cure, particularly when complete chimerism is achieved and the donor is CCR5delta32 homozygous. It is important to note that acute and even life-threatening viral rebound can occur if ART is discontinued after HCT. Planned ARV interruptions should only be attempted in the setting of a clinical trial.[11-16]

Given the improved outcomes and benefits to quality of life and other measures associated with transplantation, transplant eligibility should be equitable between people with and people without HIV **(AII).** Infectious complications and malignancy risk remain a concern post-transplant. For discussion of transplantation from donors with HIV to recipients with HIV, see Solid Organ Transplant Considerations From Donors With HIV below.

Multidisciplinary Approach

With the complexity of care required before, during, and after transplant in people with HIV, a multidisciplinary team approach is recommended, including transplant-specific specialists such as nephrologists, hepatologists, hematologists, infectious disease and HIV specialists, transplant

surgeons, pharmacists, nurses, and social workers **(AIII).** This approach is to ensure favorable outcomes and to effectively prevent and manage adverse events.

Antiretroviral Therapy Before, During, and After Transplant

This section of the guidelines will focus on special considerations for ART use before, during, and after SOT or HCT in people with HIV.

Maintain HIV Viral Suppression

Before and after a transplant, it is crucial to ensure that HIV suppression is maintained **(AIII).** This involves continuing ART as prescribed and closely monitoring viral load. Consistent adherence to ART is essential to prevent HIV viral rebound and maintain overall immune health. However, interruption of ART may be necessary in certain situations, such as intolerance of or inability to take oral ARV drugs pre-transplant, which may occur in some people with end-stage liver disease or when enteral access is limited post-transplant. In these situations, an ART regimen that will result in viral suppression after transplant should be resumed as soon as feasible**.**

Antiretroviral History and Review of Drug Resistance Testing Results

Before transplant and before starting, stopping, or changing any ARV drug, it is essential to review the person's ART history and any current and previous drug resistance testing results. This review guides the selection of an appropriate ARV regimen that will maintain or result in viral suppression.

If a person with wild-type HIV achieves and maintains viral suppression after starting ART, it is generally safe to assume that no drug resistance mutations have developed during that time. However, for people who have experienced virologic failure in the past, it is important to thoroughly review their resistance test results and their clinical and virologic responses to previous regimens when designing a new treatment plan.

Cumulative resistance test results encompass all previous and current test results, including genotypic, proviral DNA genotypic (if available), phenotypic, and tropism assays. Proviral DNA genotypic resistance testing can be considered in people with HIV who have suppressed viral loads and no prior drug resistance or unknown ART history information. In individuals with multiple treatment failures, proviral DNA genotypic testing may be useful but should be interpreted with caution. For additional information on proviral DNA assays, refer to the Drug Resistance Testing section.

Using the ART history and resistance results, one should be able to design at least one future suppressive regimen if changes are necessary.

Minimize Drug–Drug Interactions

Transplant recipients require multiple medications to prevent organ rejection, graft versus host disease (GVHD), and opportunistic infections, and to manage post-transplant complications. Polypharmacy can result in a complex array of drug–drug interactions. Consultation with a pharmacist with expertise in transplant, oncology, and/or HIV is recommended to aid with assessing and managing these challenging drug interactions.

Transplant-related drug interactions are commonly mediated by the cytochrome P450 (CYP) enzyme system. Below are some key principles for managing these drug–drug interactions.

- Use an ARV regimen with the lowest potential for drug interactions with medications used post-transplant, such as immunosuppressants, certain chemotherapeutic agents (for HCT recipients), azoles, corticosteroids, and acid-reducing drugs.
- Unboosted, oral, second-generation INSTI-based regimens (i.e., bictegravir or dolutegravir [DTG]) are preferred for most people with HIV needing transplantation **(AII).**
- In general, potent CYP3A4 inhibitors, including pharmacokinetic (PK) boosters such as ritonavir or cobicistat and PI-containing regimens, should be avoided **(AII).**
- In general, non-nucleoside reverse transcriptase inhibitors (NNRTIs) (e.g., efavirenz, etravirine, nevirapine), which are CYP3A inducers, should be avoided **(AII).** Among NNRTIs, doravirine (DOR) has fewer drug–drug interactions; however, experience with DOR in the transplant setting is limited.
- To minimize interactions in the post-transplant period and to assure tolerability and efficacy of the new regimen before transplant, whenever possible, any necessary ARV switches should be completed several weeks before the transplant **(BIII).**
- Therapeutic drug monitoring (TDM) of immunosuppressants is recommended for all transplant recipients; this is particularly important when drug–drug interactions with ARVs are expected **(AII).** Consultation with a pharmacist is recommended.

Drug Interactions Between Antiretroviral Drugs and Immunosuppressants

Immunosuppressants such as cyclosporine, sirolimus, and tacrolimus are mainstays of therapy post-transplant to prevent organ rejection or GVHD and are metabolized by CYP3A4.[17] These immunosuppressants have a narrow therapeutic window for efficacy and toxicity, and their drug concentrations may be impacted by ARV drugs that are CYP3A4 inhibitors or inducers because significant changes in their exposure may occur. There are limited data and experience evaluating interactions between newer ARV drugs and immunosuppressants, including a lack of published studies or case reports.[18-20] Immunosuppressant dose and target drug levels depend on the type of transplant, time since transplant, transplant center-specific protocols, transplant recipients' medical conditions, and other factors. Table 17a provides information regarding expected interactions based on available data and theoretical estimates. Safe and effective use of immunosuppressants should be guided by TDM.

Table 17a. Drug Interactions Between Antiretroviral Drugs and Immunosuppressants Used Post-Transplant

	Overview of Interaction Potential	Tacrolimus	Sirolimus	Cyclosporine
NRTI	↔ NRTI ↔ Immunosuppressant	Initiate standard doses. Monitor renal function if used with TDF.	Initiate standard doses. Monitor renal function if used with TDF.	Initiate standard doses. Monitor renal function if used with TDF.

Table 17a. Drug Interactions Between Antiretroviral Drugs and Immunosuppressants Used Post-Transplant

	Overview of Interaction Potential	Tacrolimus	Sirolimus	Cyclosporine
NNRTI	↔ NNRTI **With EFV, ETR, and NVP** • ↓ Immunosuppressant expected **With DOR (A Weak Inducer)** • ↓ Immunosuppressant possible **With RPV** • ↔ Immunosuppressant	Initiate standard doses and adjust based on TDM. **With EFV, ETR, and NVP** • May need higher doses **With RPV** • Monitor QTc with RPV.	Initiate standard doses and adjust based on TDM. **With EFV, ETR, and NVP** • May need higher doses **With RPV** • Monitor QTc with RPV.	Initiate standard doses and adjust based on TDM. **With EFV, ETR, and NVP** • May need higher doses. **With RPV** • Monitor QTc with RPV.
PI (With COBI or RTV as PK Booster)	↔ PI ↑ Immunosuppressant requiring dose reduction and/or extending dosing interval	↑ ↑ Tacrolimus Switch to a non-PI/c or PI/r-based regimen. If not possible, consider initiating tacrolimus 0.5 mg PO every 5–7 days. Adjust based on TDM.	↑ ↑ Sirolimus Switch to a non-PI/c or PI/r-based regimen. If not possible, consider initiating sirolimus 1–1.5 mg PO once weekly. Adjust based on TDM.	↑ CsA Consider initiating reduced dose of CsA at 5% to 20% of standard daily dose. Adjust based on TDM.
INSTI	↔ INSTI **For BIC, CAB, DTG, or RAL** • ↔ Immunosuppressant **With EVG/c** • ↑ Immunosuppressant with EVG/c	**For BIC, CAB, DTG, or RAL** • Initiate standard doses and adjust based on TDM. **With EVG/c** • ↑ ↑ Tacrolimus expected • Switch to a non–EVG/c-based regimen. If not possible, consider initiating tacrolimus 0.5 mg PO every 5–7 days. Adjust based on TDM.	**For BIC, CAB, DTG, or RAL** • Initiate standard doses and adjust based on TDM. **With EVG/c** • ↑ ↑ Sirolimus expected • Switch to a non–EVG/c-based regimen. If not possible, consider initiating sirolimus 1–1.5 mg PO once weekly. Adjust based on TDM.	**For BIC, CAB, DTG, or RAL** • Initiate standard doses and adjust based on TDM. **With EVG/c** • ↑ CsA expected • Consider initiating reduced CsA at 10% to 20% of total standard daily dose. Adjust based on TDM.
Capsid Inhibitors	↔ LEN expected ↑ Immunosuppressant expected	No data to guide dosing Adjust based on TDM.	No data to guide dosing Adjust based on TDM.	No data to guide dosing Adjust based on TDM.

Table 17a. Drug Interactions Between Antiretroviral Drugs and Immunosuppressants Used Post-Transplant

	Overview of Interaction Potential	Tacrolimus	Sirolimus	Cyclosporine
CCR5 Antagonist, Fusion, Attachment, and Post-Attachment Inhibitors	↔ ARV drugs expected ↔ Immunosuppressant expected	Initiate standard doses. Adjust based on TDM.	Initiate standard doses. Adjust based on TDM.	Initiate standard doses. Adjust based on TDM.

Key: ↔ = No clinically significant change; ↓ = decreased; ↑ = increased; ↑ ↑ = greatly increased; ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; CCR5 = chemokine co-receptor 5; COBI = cobicistat; CsA = cyclosporine; DOR = doravirine; DTG = dolutegravir; EFV= efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; NRTI = nucleos(t)ide reverse transcriptase inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PO = orally; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring

Drug Interactions Between Antiretroviral Drugs and Other Transplant-Related Medications

Transplant recipients often require other medications that may interact with ARV drugs via the CYP450 system or through decreased oral absorption due to altered gastric pH. These include azole antifungals, chemotherapy drugs, corticosteroids, and acid-reducing agents. A summary of these commonly encountered interactions can be found in Tables 24a to 24g. The table below is not comprehensive and is meant to highlight commonly used drug classes in transplant recipients with HIV.

Table 17b. Drug Interactions Between Antiretroviral Drugs and Medications Commonly Used in Transplant Recipients

Drug Class	Examples	Effects of Interactions
Azole Antifungals	Isavuconazole Itraconazole Posaconazole Voriconazole	**CYP Inhibition (e.g., With RTV or COBI as PK Booster, Azoles)[a]** • ↑ Azole concentration, ↑ toxicities • ↑ ARV concentration possible, ↑ toxicities **CYP or Glucuronidation Induction (e.g., EFV, NVP)** • ↓ Azole concentration, ↓ efficacy
Chemotherapy	Busulfan Cyclophosphamide Etoposide[b]	**CYP Inhibition or Induction (e.g., With RTV or COBI as PK Booster)** • ↑ or ↓ Chemotherapy concentration with RTV, ↑ toxicities, or ↓ efficacy • ↑ Chemotherapy concentration with COBI, ↑ toxicities **CYP Induction (e.g., EFV, ETR, NVP)** • ↓ Chemotherapy concentration, ↓ efficacy

Table 17b. Drug Interactions Between Antiretroviral Drugs and Medications Commonly Used in Transplant Recipients

Corticosteroids	Dexamethasone	**Dose-Dependent CYP3A4 Induction** • ↓ ARVs that are metabolized by CYP3A4
	High-dose Prolonged Use Prednisone/Prednisolone	**CYP3A4 Inhibition (e.g., With RTV or COBI as PK booster)** • ↑ Steroid concentration, ↑ toxicities
Acid-Reducing Medications	PPI, H2 Antagonists	**Increase in Gastric pH** • ↓ Absorption of certain ARVs, including ATV or RPV. See Table 24a and 24b for recommended timing of administration if concomitant therapy is needed.

Key: ARV = antiretroviral, ATV = atazanavir; COBI = cobicistat; CYP = cytochrome P450; CYP3A4 = cytochrome P3A4; EFV = efavirenz; ETR = etravirine; H2 = histamine 2; NVP = nevirapine; PK = pharmacokinetic; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir

[a] CYP inhibition by azoles can ↑ concentrations of immunosuppressants and certain cancer chemotherapy drugs.

[b] The listed are frequently used conditioning therapy pre-hematopoietic transplants that have potential interactions with ART. For other chemotherapeutic agents, consult a clinical pharmacist with expertise in transplant-related drug–drug interactions.

Considerations When Switching Antiretroviral Drugs Due to Drug–Drug Interactions

To minimize immediate interactions in the post-transplant period, whenever possible, any necessary ARV drug switches should be completed several weeks before the transplant **(BIII).** Waiting at least five half-lives would allow for adequate elimination of any interacting ARV drugs and/or PK booster prior to transplant. Switching ART by at least several weeks before transplant also allows clinicians to assess the tolerability and efficacy of the new regimen. Clinicians should be aware that discontinuation of certain ARV drugs may reverse previously stable drug interactions, therefore other comedications may need to be adjusted. For example, a person's immunosuppressant dose may need to be increased if the clinician is discontinuing a PI-based ARV regimen or the dose may need to be decreased if the clinician is discontinuing certain NNRTI-based regimens.

Changes in Renal or Hepatic Function

Following a kidney or liver transplant or after HCT, there may be abrupt changes in renal or hepatic function that may require dose adjustments of one or more drugs, including certain ARV drugs. All NRTIs except for abacavir (ABC) primarily undergo renal elimination and should be adjusted for dynamic changes in renal function. During the post-transplant period, it may be necessary to use individual components of ARV drugs instead of single-tablet regimens or fixed-dose combinations to allow for appropriate dose adjustments. Tenofovir alafenamide (TAF) is preferred over tenofovir disoproxil fumarate (TDF) because it has a lower risk of affecting renal function **(AII).** Because the rate of renal or hepatic function recovery can differ among recipients and immediate fluctuations may occur post-transplant, regular monitoring of organ function is important to ensure appropriate dosing of ARV drugs and minimize adverse effects or reduced efficacy (refer to Appendix B, Table 12 for ARV dosing in renal and hepatic insufficiency).

Alternative Methods for Antiretroviral Drug Delivery Post-Transplant

Interruption of ART post-transplant should be avoided **(AIII)**. If interruption is necessary, all components in an oral ART regimen should be stopped simultaneously to avoid exposure to an

incomplete regimen. The period of interruption should be kept to a minimal duration **(AIII).** If an ARV regimen includes both oral and long-acting injectable drugs (e.g., lenacapavir [LEN] or ibalizumab [IBA]) and interruption of the oral drugs is necessary, the oral ARV drugs should be resumed as soon as feasible to avoid monotherapy with the injectable agent.

If a transplant recipient cannot swallow pills immediately post-transplant, providers should consider using oral liquid formulation if available, or crushing and administering ARV drugs (if possible) to administer orally or via an enteral tube **(AIII).** Only a few ARV drugs are available in liquid formulations (Appendix B, Tables 1–12). Although PK data are limited, some ARVs can be temporarily crushed or dissolved and immediately administered orally or via an enteral tube until the recipients are able to swallow whole tablets (see more on Crushing and Liquid Antiretroviral Formulations). For people who require administration of crushed ARVs over an extended period of time, more frequent HIV viral load monitoring is recommended. If adequate oral absorption is a concern, TDM of certain ARV drugs may be considered.

Pill Burden and Post-Transplant Medication Management

Medications required for preventing graft rejection or opportunistic infections following SOT or HCT add significant pill burden and potential cost through medication copays. The complex medication schedule may also lead to medication errors and increased risk for suboptimal adherence. When renal and liver function are more stable, switching to single-tablet regimens or a fixed-dose combination ARV regimen (e.g., TAF or TDF with lamivudine [3TC] or emtricitabine [FTC]), dosed separately pre-transplant, can help reduce pill burden. Assisting transplant recipients with medication coordination, such as using a single pharmacy for dispensing all medications; attempting to synchronize refills to minimize trips to the pharmacy; and utilizing services such as adherence packaging, medication delivery, and refill reminders can also facilitate adherence. Medication and adherence counseling for transplant recipients and caregivers at each medical encounter is essential to ensure safe and effective therapy.

Impact of Medications on Adverse Effects and Comorbid Conditions

Close monitoring and prompt management of drug-associated adverse events is critical for all transplant recipients. Transplant medications, ARV drugs, and other medications may have some overlapping effects that can increase the risk or severity of toxicity. This overlap may have both short-term and long-term effects. Electrolyte disturbances may occur with sirolimus, tacrolimus, and cyclosporine. Of note, TDF may cause Fanconi syndrome, which could exacerbate the electrolyte disturbances. Similarly, nephrotoxicity associated with tacrolimus may also increase with concomitant TDF use.[21] All immunosuppressants are associated with side effects, such as nausea, vomiting, and diarrhea. These gastrointestinal side effects may be worsened when combined with ARV drugs, particularly PIs. While some of these adverse effects may be mitigated with symptomatic treatment, risk can be lowered pre-emptively by avoiding PIs and using TAF over TDF whenever possible.

In the long-term, people undergoing transplant are at high risk of developing new cardiovascular disease, diabetes, or osteoporosis.[22-24] If those conditions were present before transplant, they may worsen post-transplant. ARVs and/or transplant medications may play a role in the worsening of these conditions. Dyslipidemias associated with sirolimus or tacrolimus may be compounded by lipid disturbances associated with PIs or NNRTIs, such as efavirenz.[25,26] Cardiovascular events have been associated with ABC in some studies.[27] Fracture risk may be increased if corticosteroids are used in

combination with TDF.[28] Since TDF may negatively impact bone mineral density,[28] TAF is preferred over TDF **(AII).** Management of comorbid conditions in transplant recipients is highly individualized. Clinicians must consider the risks and benefits of adjusting stable ARV regimens versus using other medications to manage complications. If ARV regimens are adjusted post-transplant, selecting agents that have minimal impact on transplant-related comorbidities is helpful in optimizing therapy. (For more information, see Table 21. Antiretroviral Therapy-Associated Adverse Effects That Can Be Managed With Substitution of Alternative Antiretroviral Agents)

Considerations for Long-Acting Antiretroviral Drugs

Several important factors should be considered when making decisions to initiate or continue transplant candidates on long-acting (LA) injectable ARV drugs, including cabotegravir (CAB) and rilpivirine (RPV) (typically used together as a complete ART regimen), IBA, and LEN. Experience with these LA ARV drugs in transplant candidates is limited, and these agents have not been studied in the setting of severe hepatic disease, ESRD, or post-transplant. The impact of fluctuations in renal function, hepatic function, and fluid shifts that may occur around the time of transplant on the PK of these LA ARVs is largely unknown. Additionally, it should be noted that because LA ARVs may be difficult to obtain in the hospital, administration must be carefully timed to avoid any medication access issues and treatment interruptions.

The benefits of initiating LA CAB/RPV pre-transplant should be weighed against potential risks. People who are stable on LA CAB/RPV prior to transplant may be maintained on their regimen and monitored closely. For individuals with very low platelet counts or who require anticoagulation, intramuscular (IM) injections of LA CAB/RPV may need to be postponed. In these cases, initiation of a bridging regimen with oral CAB and oral RPV until IM injections can be resumed may need to be considered. If oral CAB is not available, DTG may be used in its place.

Although there are occasions when a transplant recipient may not be able to take oral medications immediately post-transplant, in general, this should be resolved within a few days. There are no data on temporarily switching to LA CAB/RPV as a bridging strategy in this instance and, therefore, this strategy is not advised.

IBA and LEN are two LA ARV drugs approved for use in people with multiple drug-resistant HIV. IBA is given as an intravenous infusion every 2 weeks, whereas LEN is given as a subcutaneous injection every 6 months. These drugs should not be started post-transplant just to reduce pill burden without other indications for their use. Transplant candidates on ARV regimens containing LEN or IBA likely have very limited alternative treatment options and should continue these LA ARV drugs as scheduled, in combination with any oral ARVs that are part of their complete regimen.

Because LA ARV drugs have very long half-lives, abruptly stopping any oral ARVs can lead to functional monotherapy with the LA ARV drugs, which may result in viral rebound and resistance. Therefore, the oral background regimen should be continued. People undergoing transplant who are maintained on these medications should be monitored closely for adverse events, drug interactions, and HIV viral load suppression. Drug interactions are an especially important consideration with LEN, which is a moderate CYP3A4 inhibitor (see Table 17a). There is a prolonged period of drug interaction risk due to the extended presence of LEN in the body. Clinicians may inadvertently miss these interactions if they are unaware that LEN is part of the ARV regimen, as clinic-administered

injectable LA ARV drugs are often listed separately from other ambulatory prescription medications in electronic health records.

Prevention of Infectious Complications Post-Transplant

Vaccination

Vaccination is a critical tool for preventing infections in all transplant recipients; however, the timing and some aspects of the approach to vaccination differ between SOT and allogeneic bone marrow transplant (BMT) candidates.

Timing of Vaccination

After registering as a transplant candidate and before SOT, there is typically a waiting period that provides an opportunity to assess vaccination status and update the vaccination record. It is important to consult the Centers for Disease Control and Prevention for up-to-date and specific vaccination recommendations, which include those for individuals with end-stage organ disease or immunocompromising conditions. Following an allogeneic BMT, vaccination plays a crucial role in restoring immune function and protecting against infectious diseases. Notably, the goal of vaccination in allogeneic BMT is to induce immune responses by the new engrafted donor immune system, not the pre-existing (recipient) one. However, vaccination strategies can vary based on the recipient's specific condition, transplant protocols, and recommendations from the transplant center. After allogeneic BMT, vaccination schedules are typically planned in phases, starting after the initial recovery period. Following that, vaccines are usually administered sequentially based on the transplant recipient's immune reconstitution status.

General principles for both SOT and allogenic BMT include the following:

- Vaccine recommendations for both SOT and BMT candidates and recipients should follow the same guidance as those recommended for those without HIV.
- In addition to reviewing standard pre- and post-transplant vaccine strategies described by the American Society of Transplantation Infectious Diseases Community of Practice, the need for additional vaccines based on HIV status (e.g., meningococcus) and/or exposure-related risk factors (e.g., mpox) should be assessed (see Immunization section of the *Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV*).
- For people without HBV infection, HBV vaccination is important to maximize options for ARV simplification strategies that may involve tenofovir-sparing regimens.
- Inactivated vaccines, which do not contain live pathogens, are generally considered safe after BMT. These include vaccines such as influenza, COVID-19, pneumococcal, HBV, tetanus, and diphtheria, as well as the new recombinant zoster vaccine.
- Live vaccines—including the varicella-zoster virus (VZV) and measles, mumps, and rubella (MMR) vaccines—should be avoided in SOT recipients while on immunosuppressants and may not be recommended immediately after BMT due to the recipient's weakened immune system. The decision to administer live vaccines is based on the individual's clinical condition and time since transplantation.

Pre-transplant Screening for Infection Risk and Antimicrobial Prophylaxis

Prior to transplant, transplant candidates should undergo a detailed assessment for infection risk, including history of prior infections, travel history, and environmental exposures. Due to the increased risk of reactivation of latent infections (e.g., tuberculosis, Strongyloides), transplant candidates with HIV who are at risk for these latent infections should undergo screening to guide pre-transplant treatment to prevent reactivation and disease post-transplant. Active opportunistic infections are a contraindication for transplantation. Additionally, both HIV and the immunosuppression associated with transplant are risk factors for anogenital or cervical human papillomavirus-related malignancies.[29] Prophylaxis against bacterial, fungal, and viral diseases is a standard of care at transplant centers and is tailored to factors such as serostatus (e.g., cytomegalovirus) or geographic risk (e.g., coccidioidomycosis). Clinicians should also be aware of the risk for donor-derived infections, especially in the early transplant period.

For more information regarding the prevention and treatment of opportunistic infections and donor-derived infections, refer to the *Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV* and center-specific protocols.

Recipient Considerations

HBV and HCV Coinfection

Due to overlapping risk factors, HBV and HCV coinfection is common in people with HIV. Both HBV and HCV are causes of cirrhosis that may lead to the need for liver transplant, and are also associated with extrahepatic manifestations such as diabetes mellitus, polyarteritis nodosa, membranoproliferative glomerulonephritis, and cryoglobulinemic vasculitis, which may contribute to ESRD.[30,31] Immunosuppression and chemotherapy (in cases of HCT) associated with transplant may result in loss of control of either HBV or HCV. Flares of active HBV or HCV following liver transplant begin with rises in HBV or HCV viral load, often followed by elevations in liver transaminases,[32,33] and can result in shortened graft survival. In those with only markers of prior HBV infection (core antibody [HBcAb] positive) and without evidence of active replication, HBV may reactivate from a latent state. Rarely, fibrosing cholestatic hepatitis results in rapidly progressive liver disease in transplant recipients.[34-38]

Assessment for HBV and HCV coinfection should occur at entry into HIV care and periodically for those at risk; status should be updated during the pre-transplant period. Transplant candidates or recipients who lack immunity to HBV (as indicated by negative HBV surface antibody [HBsAb]), including those with HBsAb loss, should receive vaccination regardless of HBcAb status and ideally before SOT.[39] Despite repeated attempts at vaccination, some people with end-stage organ disease or immunosuppression do not respond serologically and thus may be at risk for flares. Those undergoing allogeneic HCT generally undergo vaccination after the procedure.[40] For additional information regarding ARV drugs for people with HIV/HBV coinfection, refer to the Hepatitis B Virus/HIV Coinfection section.

Candidate/Recipient Considerations

Candidate/recipient is HBsAg positive. In people with active HBV (HBV surface antigen [HBsAg]–positive) coinfection, it is important to include either TAF or TDF as part of the ARV regimen, with the goal of suppressing both viruses. Both TAF and TDF are active against HBV, and

either can serve as the only active agent for HBV, although they are often used in combination with 3TC or FTC in people with both HIV and HBV. If TAF or TDF cannot be included, another potent anti-HBV drug—entecavir—should be initiated. Entecavir has weak anti-HIV activity and is not considered part of the ARV regimen but can induce nucleoside resistance mutation (M184V) and thus should never be used without a fully active ARV regimen.[41] Due to the low barrier to resistance and high likelihood for viral rebound, the use of 3TC or FTC as the only anti-HBV drug in individuals with HBV/HIV coinfection **is not recommended.**

Maintaining regimens with anti-HBV activity before transplant and indefinitely after transplant is recommended for transplant recipients with HIV and active HBV infection due to the risk of HBV reactivation and the potential for severe liver damage, including fulminant liver failure.

Candidate/recipient is HBcAb positive, HBsAg negative, and HBsAb negative or positive. The risk of HBV reactivation in the transplant recipient depends on the type of transplant, the depth of immunosuppression, and the presence of HBsAb. For liver transplant recipients who are HBcAb positive without evidence of active HBV (negative serum HBsAg and HBV DNA), reactivation risks are considered negligible due to removal of the potential liver reservoir. By contrast, in non-hepatic transplant recipients with markers of past infection, reactivation may occur in up to approximately 5%, usually during the first year, when immunosuppression is most intense and in the absence of protective levels of HBsAb.[42] This risk can be further abrogated if anti-HBV agents are already part of the ART regimen and by boosting HBsAb levels with vaccination. For non-hepatic transplant recipients not already on agents with anti-HBV activity, periodic prophylaxis or monitoring (regular measurements of transaminases and if newly elevated, rapid HBV DNA) strategies may be deployed to the highest-risk recipients per institutional protocol.[43,44]

Candidate/recipient is HCV RNA positive. All transplant candidates and/or recipients with HCV infection should be treated with DAAs against HCV **(AII),** preferably prior to transplant. Exceptions to this principle might include select candidates awaiting liver transplant, with a short waiting time for transplant (e.g., high Model for End-Stage Liver Disease, or MELD, score),[45] or select candidates for non-liver transplants who elect to defer treatment to remain eligible for donor organs from HCV viremic donors,[46-48] per discretion of the transplant providers. For those deferring treatment for HCV before transplant, treatment should be initiated early in the post-transplant period.[49-51] Additional considerations for the care of people with HIV and HCV, including fibrosis assessment, are found in the Hepatitis C Virus/HIV Coinfection section.

Donor-Related Considerations

HBV-Positive and HCV-Positive Donors

Organs from donors with serologic or virologic markers of HBV or HCV infection may be considered when recipients have given informed consent and providers have determined that benefits outweigh potential risks.[52,53] Antiviral treatment for recipients prior to transplantation can help prevent or manage post-transplant infection. Additionally, monitoring for donor-derived transmission and close follow-up of the recipient post-transplantation are necessary to detect and manage any potential infection.

Donor is HBcAb and/or HBsAg positive. To expand the size of the donor pool, use of HBcAb positive/HBsAg negative organs has become common practice.[54] More rarely, donors who are HBsAg positive are also utilized.[55] Without prophylaxis or recipient immunity (presence of surface

antibody), the risk of HBV transmission from such donors is present for non-hepatic organs and is extraordinarily high for liver transplants. Strategies to mitigate the risk of donor-derived HBV include pre-transplant vaccination, nucleos(t)ide therapy, and—particularly for liver transplant recipients who receive HBsAg-positive organs—hepatitis B immunoglobulin.[56] Anti-HBV agent prophylaxis may be deployed for moderate to high-risk recipients, with the highest risk (liver transplant recipients) receiving lifelong nucleos(t)ide analogues. Organ recipients with HIV may continue on regimens that already include tenofovir; those on tenofovir-sparing regimens pre-transplant may require the addition of anti-HBV agents such as tenofovir or entecavir. 3TC or FTC alone is not preferred for this indication.

Donor is HCV antibody or HCV RNA positive. The safety of using organs from HCV antibody-positive donors in both HCV viremic and aviremic recipients has been established, especially with early initiation of antivirals in the post-transplant setting.[45-48,51,57-62] Although untreated chronic HCV infection may have an accelerated course in people with HIV and SOT, early and effective treatment abrogates this risk substantially. Transplant candidates with HIV without current HCV infection should consider accepting HCV viremic organs if prompt DAA therapy is available at their center (see the Hepatitis C Virus section for more information).

Solid Organ Transplant Considerations From Donors With HIV

Kidney transplantation demonstrates survival benefit compared to dialysis for people with HIV and ESRD.[63] Previously, the use of organs from donors with HIV was banned. After a successful study of transplanting kidneys from donors with HIV into recipients with HIV in South Africa, the U.S. HIV Organ Policy Equity (HOPE) Act was approved in 2013, amending the law to allow transplantation of organs from donors with HIV into recipients with HIV (HIV D+/R+) under research protocols.[64]

For transplant candidates, eligibility criteria for HIV D+/R+ transplantation are the same as standard transplant criteria. For donors, federally mandated research criteria require that donors do not have active opportunistic infections.[65] Organs from donors with any CD4 lymphocyte cell count or viral load are allowed; however, transplant teams need to consider the likelihood of any ART resistance in the donors and justify whether an ART regimen in the recipient will be effective and tolerated.[65] To date, INSTI resistance has been rare in deceased donors with HIV.[66]

Early studies have shown excellent outcomes of HIV D+/R+ kidney and liver transplantation.[64,67] Based on this, the federal Advisory Committee on Blood and Tissue Safety and Availability has recommended to the U.S. Department of Health and Human Services that HIV D+/R+ kidney and liver transplantation be moved outside of research and into clinical care.[68] Due to the paucity of outcome data, HIV D+/R+ heart or lung transplantation remains under research protocols for now.[68] HIV D+/R+ kidney transplantation has been shown to decrease wait times for transplant.[69] SOT candidates with HIV may therefore consider being listed at a center currently offering organs from donors with HIV, if feasible.

As organ allocation in the United States occurs at a national level, all people with HIV may register as organ donors regardless of their distance from these centers, as their organs would only be directed to transplant candidates with HIV.[70] In addition, people with HIV may be living organ donors under HOPE Act research protocols.[68,71]

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Women With HIV

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Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all people with HIV to improve their health and to reduce the risk of HIV transmission to sexual partners without HIV **(AI).**
• When prescribing antiretroviral (ARV) drugs for women with HIV, clinicians should consider that some ARV drugs have significant pharmacokinetic (PK) interactions with hormonal contraceptives **(AII)** and hormone replacement therapy **(BIII).** Consult Tables 24a, 24b, 24d, 24e, 24f, and 24g for detailed recommendations and a summary of available data when selecting ARV and hormone combination therapy **(AIII).**
• Clinicians should discuss with women the possibility of weight gain after initiating or changing ART. Some women in general, and Black women in particular, experience greater weight gain with ART over time than men. Concerns for weight gain should not be a reason for deferring ART.
• A pregnancy test should be performed for women of childbearing potential before initiation of ART **(AIII).**
• When selecting or evaluating an ARV regimen for women with HIV of childbearing potential, clinicians should consider the regimen's effectiveness, the woman's hepatitis B status, the teratogenic potential of the drugs in the ARV regimen, and the possible adverse outcomes for the mother and the fetus if the woman becomes pregnant while receiving the regimen **(AII).**
• During pregnancy, an additional goal of ART is to maintain a viral load below the limit of detection throughout pregnancy in order to reduce the risk of HIV transmission to the fetus and newborn **(AI).**
• When selecting an ARV regimen for a pregnant woman, clinicians should consider the available safety, efficacy, and PK data on the use of each agent during pregnancy. The risks and benefits of ARV use during pregnancy should be discussed with all pregnant women **(AIII),** and clinicians should consult the Perinatal Guidelines when designing a regimen **(AIII).**
• Achieving and maintaining viral suppression with ART while breastfeeding does not completely eliminate HIV transmission risk but does reduce it to less than 1% **(AI).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*
Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

This section focuses on some unique clinical and therapeutic issues to consider and basic principles to follow when caring for cisgender women with HIV. Cisgender women are defined as individuals who were assigned female at birth and who identify themselves as women. In this section, cisgender women will be referred to as "women." Some topics discussed in this section—such as contraception, drug–drug interactions between antiretroviral (ARV) drugs and hormonal therapy, and pregnancy—also apply to transgender men (men assigned female at birth) and individuals assigned female at birth who identify as nonbinary (gender identities that are not exclusively feminine or masculine) or gender fluid (gender identity is not fixed). See Transgender People With HIV for more information on the specific HIV care needs of these individuals. Clinicians who care for pregnant people with HIV should consult the Perinatal Guidelines for a more in-depth discussion.

Sex Difference Considerations in Antiretroviral Therapy

In general, studies to date have not shown sex differences in virologic responses to antiretroviral therapy (ART).[1-6] However, limited data show that pharmacokinetics (PK) for some ARV drugs may differ between men and women, possibly because of variations in factors such as body weight,

plasma volume, gastric emptying time, plasma protein levels, cytochrome P450 activity, drug transporter function, and excretion activity.[6-10]

Adverse Effects

Several studies with older ARV drugs have suggested that sex may influence the frequency, presentation, and severity of some ARV-related adverse events.[11-13] In the ICONA cohort, people with HIV treated with dolutegravir (DTG)-based regimens were followed for up to 4 years. There was a higher risk of DTG discontinuation due to toxicity in both ART-naive and ART-experienced women compared with men.[14]

Some studies have investigated how metabolic complications that are associated with the use of ARV drugs differ between women and men. Women have an increased risk of osteopenia, osteoporosis, and fractures, particularly after menopause, and this risk is exacerbated by HIV and some ARV drugs.[15-18] ARV regimens that contain tenofovir disoproxil fumarate (TDF), ritonavir-boosted protease inhibitors (PI/r), or both are associated with a significantly greater loss of bone mineral density (BMD) than regimens that contain other nucleoside reverse transcriptase inhibitors (NRTIs) and raltegravir (RAL).[19-22] Abacavir (ABC), NRTI-sparing regimens, and tenofovir alafenamide (TAF) may be considered as alternatives to TDF for patients who are at risk of osteopenia or osteoporosis. Recommendations for the management of bone disease in people with HIV have been published.[23]

Weight Gain and Antiretroviral Therapy

Weight gain after initiation of ART, especially in people with advanced HIV, can be a sign of a return to better health. However, data from clinical trials and longitudinal cohort studies suggest sex differences in ARV-associated weight gain across all classes of ART among treatment-naive individuals, particularly with the use of certain integrase strand transfer inhibitor (INSTI)–based regimens (DTG and bictegravir [BIC]). In a pooled analysis of eight randomized controlled trials with ARV-naive people initiating HIV treatment, female sex was associated with 1.5 times the odds of a ≥10% weight gain compared with male sex (17.4% vs. 12.2%), with Black females significantly more likely to experience a ≥10% weight gain than non-Black females (19.7% vs. 12.4%).[24] At 144 weeks of follow-up in the ADVANCE study, a 12.3-kg weight gain was recorded among women receiving TAF/emtricitabine (FTC)/DTG compared with 7.4 kg and 5.5 kg among women receiving TDF/FTC/DTG and TDF/FTC/efavirenz (EFV), respectively.[25] In addition to women being more likely to experience weight gain with ARV initiation, the pattern of weight gain differs between men and women. In the ADVANCE study, at 96 weeks of follow-up, women gained more fat than lean body mass than men, with weight gain concentrated in the limbs and trunk. ARV-associated weight gain similarly has been observed among virologically suppressed women switching to an INSTI-based regimen.[26-28] In the Women's Interagency HIV Study, virologically suppressed women who switched to INSTI-based ART or had an INSTI added to their regimen (n = 234) gained an average of 4.2 kg in body weight at the 2-year follow-up compared with 0.2 kg in women remaining on non-INSTI ART (n = 884).[27] Mean change in percent body fat (1.7% vs. 0.3%) and body circumference measures were also greater in the INSTI group than in the non-INSTI group. Investigators did not detect a difference in weight gain by individual INSTI.

It should be noted that, although randomized controlled trials and observational studies suggest that individuals receiving INSTI-based regimens experience greater weight gain than those receiving comparator regimens, significant uncertainty continues as to whether INSTIs are causing weight gain

or whether the comparator drugs are suppressing weight gain. For example, an analysis in the ADVANCE trial demonstrated that the greater weight gain observed in DTG- versus EFV-treated participants was dependent primarily on CYP2B6 polymorphisms, which are associated with slow EFV metabolism (and presumably higher EFV levels). Among those with rapid EFV metabolism genotypes, no evidence was found for a weight difference between DTG- and EFV-treated participants.[29] The underlying mechanisms for weight gain in people receiving an INSTI-based regimen, and their impact on cardiovascular diseases, diabetes, pregnancy-related outcomes, and age-related comorbidities among women with HIV are currently unknown.

Switching from TDF to TAF, regardless of whether participants took INSTI, non-nucleoside reverse transcriptase inhibitor (NNRTI), or PI combinations, was found to be associated with weight gain, particularly in women and people of African descent.[30] The extent of TAF-associated weight gain may be affected by baseline body mass index (BMI). Among participants of the Women's Interagency HIV Study (WIHS) cohort, weight and BMI rose among women with baseline BMI below 30kg/m^3 when transitioning to INSTI, TAF, or INSTI and TAF together.[31]

All these data indicate that ARV-associated weight gain should be a factor to consider when initiating or changing ART, particularly in Black women. Because some ART regimens are more likely to cause weight gain in women, clinicians should weigh the benefits and risks of a particular regimen when initiating or changing ART. However, concerns about weight gain should not be a reason for deferring ART.

Adherence to Antiretroviral Therapy

Some observational studies have found that women are more likely than men to have suboptimal adherence to ART. Defining adherence as missing no dose of ART in the prior 3 days, the Centers for Disease Control and Prevention analyzed data from the nationally representative Medical Monitoring Project (n = 12,394) by race and gender.[32] Race comparisons by gender indicated that women had consistently lower ART adherence than men of the same race. Adherence rates were 94% for White men compared with 88% for White women, 93% for Latino men compared with 88% for Latina women, and 89% for Black men compared with 87% for Black women. A Canadian study followed 4,534 individuals (including 904 women) for a median of 65.9 months and found that a significantly lower proportion of women relative to men were optimally adherent (57.0% vs. 77.1%).[33] In the analysis adjusted for ethnicity and injection drug use, female sex remained associated independently with suboptimal adherence. Women with HIV face multifactorial barriers to adherence. Increasing access to social services—such as food, housing, and transportation—has been associated with improved ART adherence, as have social support and good patient–provider relationships.[34,35] Another analysis of 6,186 women from the Medical Monitoring Project found that women aged 50 and older were more likely to be adherent to ART than women younger than 50.[36] However, menopausal symptoms have been associated significantly with suboptimal ART adherence in cross-sectional[37] and longitudinal studies[38] of older women with HIV. It also was noted that 68.8% of older women with HIV experienced symptoms of menopause, but only 17% received treatment for these symptoms. It is plausible that treating menopausal symptoms may improve ART adherence among older women with HIV.[38,39]

Antiretroviral Therapy Considerations in Adults and Adolescents With HIV Who Are of Childbearing Potential

All adults and adolescents with HIV who are of childbearing potential should be offered comprehensive reproductive and sexual health counseling and care as part of routine primary medical care. Topics for discussion should include safe sex practices, reproductive desires and options for conception, the HIV status of sexual partner(s), the use of effective contraception to prevent unplanned pregnancy, and maintaining viral suppression to optimize health in preparation for pregnancy. Counseling also should include discussion of special considerations pertaining to ARV use when using hormonal contraceptives, when trying to conceive, and during pregnancy (see the Perinatal Guidelines). Clinicians should discuss intentions regarding pregnancy with all people of childbearing potential, and a pregnancy test should be performed before initiating ART **(AIII).**

Antiretroviral Regimen Considerations for Individuals Who Are Trying to Conceive

ART should be initiated and viral suppression achieved prior to pregnancy whenever possible. People should be given information about the benefits and risks of initiating specific ARV regimens when trying to conceive so they can make informed decisions about their care (see Appendix C: Antiretroviral Counseling Guide for Health Care Providers).

Earlier data from the birth outcomes surveillance study in Botswana raised concern about an increased risk of neural tube defects (NTDs) (0.9%) in infants born to women who were receiving DTG at the time of conception.[40,41] At the time of the study, folate fortification of grains in Botswana was uncommon. Folate prescribed before conception was low (0.1% to 0.2%) among the study participants.[42] Updated results from the same study showed that the prevalence of NTDs in infants born to women on DTG at the time of conception was not significantly different from those on non-DTG regimens at the time of conception.[43] Because folic acid is known to prevent NTDs in the general population, all pregnant women and women who might conceive should take at least 400 mcg of folic acid daily **(AI).** In a small cohort of 69 U.S. women who had periconceptional or early-pregnancy DTG exposure and access to folic acid fortification of food and/or received folate supplementation, there was no increased risk of NTDs in exposed infants.[44]

EFV is teratogenic in nonhuman primates.[45] However, in humans, no increase in teratogenicity has been reported with the use of EFV. Based on drug-specific risk assessments by the Antiretroviral Pregnancy Registry, sufficient numbers of first-trimester exposures to EFV have been monitored with no detected increase in the risk of overall birth defects, including in cardiovascular and genitourinary systems. Individuals who become pregnant while on EFV-containing regimens should continue their current regimens **(BIII).**

Before initiating ART in a person of childbearing potential, clinicians should review the What to Start: Initial Combination Regimens for People With HIV section and the Perinatal Guidelines for information to consider when choosing an ARV regimen. The key recommendations are listed below:

For individuals who are trying to conceive, the Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating one of the following regimens, which are designated as *Preferred* regimens during pregnancy in the Perinatal Guidelines: DTG or darunavir/ritonavir (DRV/r) plus a dual NRTI combination (ABC/lamivudine [3TC], TAF/FTC, TDF/FTC, or TDF/3TC). DTG-based

regimens are associated with rapid, durable viral load suppression, which is important for maternal health and the prevention of perinatal HIV transmission. BIC/TAF/FTC is an alternative INSTI-based regimen. The use of long-acting injectable cabotegravir (CAB) with rilpivirine (RPV) has not been studied in pregnancy.

For individuals who are not planning to conceive but who are at risk for pregnancy, consider a regimen's effectiveness and tolerability the available data on potential teratogenicity, and the person's preferences (e.g., pill burden) when choosing between regimens that are recommended for initial therapy (see Tables 6a and 6b in the Initial Combination Antiretroviral Regimens for People With HIV section). Clinicians should refer to the Perinatal Guidelines for recommendations.

Reproductive Options for Couples With Differing HIV Status

Couples with differing HIV status should be informed of options to prevent sexual transmission of HIV while attempting conception. If the partner with HIV is on ART and has achieved sustained viral suppression, sexual intercourse without a condom allows conception with effectively no risk of sexual HIV transmission to the partner without HIV (see Antiretroviral Therapy to Prevent Sexual Transmission of HIV).[46-48] People with HIV who intend to prevent transmission by using ART need to maintain high levels of ART adherence and should be informed that transmission is possible during periods of poor adherence, treatment interruption, and viremia. Both partners should be screened for sexually transmitted infections (STIs) and receive appropriate treatment if STIs are diagnosed.

Hormonal Contraception

Safe and effective reproductive health and family planning services to prevent unplanned pregnancies and perinatal transmission of HIV are essential components of care for individuals with HIV of childbearing potential. These individuals should receive ongoing counseling on reproductive issues. Individuals who do not desire pregnancy currently but are sexually active or considering initiating sexual activity should be offered effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy. Individuals with HIV can use all available contraceptive methods (e.g., pill, patch, ring, injection, implant) and intrauterine devices (IUDs),[49] after consideration of potential drug–drug interactions as discussed in the next section (also see the Perinatal Guidelines).

Drug–Drug Interactions Between Hormonal Contraceptives and ARV Drugs

Interactions between some ARV drugs and hormonal contraceptives may reduce contraceptive efficacy. However, most data are generated from healthy-volunteer, short-duration PK studies, and clinical data regarding interactions between ARV drugs and hormonal contraceptives in women with HIV are limited. The magnitude of change in drug concentrations that may reduce contraceptive efficacy or increase the risk of adverse effects is not known for all forms of contraceptives, making the clinical implications of some ARV-hormone drug interactions challenging to predict.

Concerns about PK interactions between hormonal contraceptives and ARV drugs should not prevent clinicians from prescribing hormonal contraceptives for individuals on ART. However, an alternative or additional effective contraceptive method is recommended if significant interactions may occur between hormonal contraceptives and ARV drugs (see Tables 24a, 24b, 24d, 24e, 24f, and 24g). A summary of ARVs with known interactions with hormonal contraceptives is described below:

Combination contraceptives containing ethinyl estradiol and progestins, including combined oral contraceptives (COCs), transdermal patches, and intravaginal rings:[50,51]

- EFV significantly decreases progestin concentrations from both COCs and intravaginal rings, which may increase the risk of contraceptive failure. EFV did not reduce oral ethinyl estradiol exposure in one small study, but it reduced exposure when combined with an intravaginal ring, which may increase the risk of intermenstrual bleeding (spotting), particularly with ultra-low and low-dose estrogen-containing contraceptives.
- Elvitegravir boosted with cobicistat (EVG/c), and cobicistat-boosted PIs or PI/r decrease ethinyl estradiol levels, which may increase the risk of spotting, particularly with ultra-low and low-dose estrogen-containing contraceptives. However, these ARV regimens also increase progestin exposure, which preserves contraceptive effectiveness.
- Cobicistat- and ritonavir-containing regimens should be avoided with drosperinone-containing products because of an increased risk of hyperkalemia.
- Fostemsavir (FTR) increases ethinyl estradiol exposure, which may increase risk of thromboembolic events. Product labeling recommends a maximum dose of ethinyl estradiol of 30 mcg per day when combined with FTR.[52]

Progestin-only pills:[50,51]

- EFV significantly decreases concentrations of oral progestin pills, including emergency contraception, which may increase the risk of contraceptive failure.
- Cobicistat- or ritonavir-boosted ARV regimens may increase progestin exposure. The combination may be used without dose adjustment; monitor for progestin-related adverse effects.

Injectable contraceptives (depot-medroxyprogesterone):

- One study of EFV-based ART plus depo-medroxyprogesterone acetate (DMPA) did not find a significant reduction in medroxyprogesterone acetate (MPA) exposure. No change in DMPA dose or frequency is necessary.[53]
- For women receiving both rifampin and EFV for the treatment of tuberculosis and HIV, some experts suggest administering DMPA every 8 to 10 weeks instead of every 12 weeks.[54]

Progestin-releasing contraceptive implants:[50,51]

- EFV significantly decreases progestin concentrations released from a contraceptive implant. Cohort studies have found that women receiving EFV-based ART and contraceptive implants have a higher rate of unintended pregnancies than women receiving other ART combinations.[55,56]
- Cobicistat- or ritonavir-boosted ARV regimens may increase progestin exposure, but the combination may be used without dose adjustment.

Pregnancy

All women with HIV should receive ART early in pregnancy, regardless of their viral load or CD4 T lymphocyte (CD4) cell count, for their own health and for the prevention of perinatal HIV transmission and transmission of HIV to sexual partners **(AI).** ARV drugs reduce the risk of perinatal

HIV transmission by decreasing maternal viral load in blood and genital secretions.[57-59] Clinicians who are caring for pregnant adults and adolescents with HIV should review the Perinatal Guidelines.

Antiretroviral Regimen Considerations

In general, the recommendations for the use of ART in pregnant women are the same as those for women who are not pregnant. As in nonpregnant individuals, genotypic drug-resistance testing is recommended for all people who are pregnant before initiating ARV drugs **(AIII)** and for those with detectable HIV viral load while on ART **(AI).** However, if not yet on ART, ART initiation should not be delayed pending genotypic drug-resistance test results. The ARV regimen can be modified, if necessary, once the resistance test results are available **(BIII).** Unique considerations that influence recommendations on the ARV drugs to use during pregnancy include the following:

- Potential ARV-associated adverse effects for pregnant women, fetuses, and infants
- Need for strict adherence to the prescribed ARV regimen to avoid viremia and drug resistance, optimize health outcomes, and minimize the risk of perinatal transmission
- Limited long-term outcome data for infants who were exposed to ARV drugs *in utero*, especially for newer ARV drugs

Clinicians should review the Perinatal Guidelines for ARV drug recommendations for individuals who recently have received an HIV diagnosis or those who become pregnant while on ART. Selection of ARV drugs for women who are pregnant should be individualized according to specific ARV history, the results of drug-resistance assays, and the presence of comorbidities, as well as the individual's preferences for balancing known and unknown risks and benefits of an ARV regimen.

Because of data suggesting decreased drug levels during pregnancy and associated loss of virologic suppression, cobicistat-containing regimens, including EVG/c, ATV/c, or DRV/c, are not recommended for initiation during pregnancy.[60] A pregnant woman who has a suppressed plasma viral load on one of these regimens could continue the regimen with frequent (e.g., monthly) viral load monitoring. Alternatively, another regimen that is predicted to maintain viral suppression can be used for the duration of the pregnancy.

The use of long-acting (LA) CAB with RPV has not been studied in pregnancy. In clinical trials, participants who became pregnant were switched from LA CAB and RPV to an alternative oral ARV regimen throughout the remainder of their pregnancies. Based on the pharmaceutical company's clinical trials and compassionate program through March 2021, 25 pregnancies were reported (20 LA CAB/RPV and 5 during oral lead-in phase); in 4 cases, conception occurred during the washout period after treatment discontinuation. There were 8 elective abortions, 6 miscarriages, and 1 ectopic pregnancy. Among the 10 livebirths (9 LA CAB/RPV and 1 oral), 1 infant had congenital ptosis.[61] Individuals who become pregnant while on ART will need close monitoring, and their pregnancy outcomes should be reported to the Antiretroviral Pregnancy Registry.

If maternal HIV viral load is ≥1,000 copies/mL (or unknown) near delivery, intravenous infusion of zidovudine during labor is recommended, regardless of the mother's antepartum regimen and resistance profile and the mode of infant delivery **(AI).** Administration of combination ART should continue during labor and before a cesarean delivery (oral medications can be administered with sips of water during this time).

Clinicians who are treating pregnant individuals with HIV are strongly encouraged to report cases of prenatal exposure to ARV drugs (either administered alone or in combination) to the Antiretroviral Pregnancy Registry.

Postpartum Management

Following delivery, clinical, immunologic, and virologic follow-up should continue as recommended for nonpregnant adults and adolescents. Maternal ART should be continued after delivery. For more information regarding postpartum management of HIV, refer to the Perinatal Guidelines.

Some studies have demonstrated that adherence to ART may decline during the postpartum period.[62-64] Clinicians should address ART adherence at each postpartum clinic visit, including an evaluation of specific factors that facilitate adherence or present as a barrier to adherence. Clinicians may recommend an intervention to improve adherence (see Adherence to the Continuum of Care).

Clinicians should discuss future reproductive plans and timing, the risks and benefits of conceiving on specific ARV medications, and the use of appropriate contraceptive options to prevent unintended pregnancy. If an LA reversible contraceptive—such as an implant or IUD—is desired by the person, it should be inserted before hospital discharge or during the postpartum visit if possible.

Infant Feeding

Clinicians should refer to the Perinatal Guidelines for detailed recommendations regarding initiation or modification of infant feeding. People with HIV should receive evidence-based, patient-centered counseling to support shared decision-making about their desire for infant feeding. Replacement feeding with properly prepared formula or pasteurized donor human milk eliminates the risk of postnatal HIV transmission to the infant.

Breastfeeding is **not recommended** for women who are not virally suppressed or for those who develop a detectable viral load while breastfeeding because of concern for increased risk of HIV transmission through breast milk.[65] If viremia occurs during breastfeeding, the woman should be advised to replace breastfeeding with another mode of feeding. Viral load testing should be repeated and plasma genotypic resistance testing should be performed if the level of viremia allows for a test to be done.

HIV and Menopause

The population of people with HIV is aging; thus, the number of women with HIV who are experiencing menopause is increasing. The median age of menopause in the general U.S. population is 52.5 years.[66] Evidence suggests that women with HIV are reaching menopause at earlier ages than those who do not have HIV.[67,68] The WIHS, which included 3,059 participants, demonstrated that approximately 1% (n = 35) experienced premature menopause before age 41, 3% (n = 101) between ages 41 and 45, and 21% (n = 442) between ages 46 and 50. These participants self-reported low ranges of hormone replacement therapy (14%, 16%, and 7%, respectively).[39] However, other confounding factors may affect age of menopause in women with HIV, such as sociodemographic factors, illicit drug use, hepatitis C coinfection, smoking, and possibly ART.

A Canadian study of 229 women with HIV reported that the average age of menopause was 48 years, which was 3 years younger than the general Canadian population. Lower level of education and

hepatitis C coinfection were associated independently with menopause at <45 years of age.[69] In another study of 667 women with HIV in Rio de Janeiro, Brazil, 24% reached menopause during the observational period and 27% had early menopause (<45 years of age). The median age of menopause was 48 years of age. Age at menarche <11 years, cigarette smoking, chronic hepatitis C, and CD4 count <50 cell/mm^3 were associated significantly with an earlier age of natural menopause.[70]

Menopause is a high-risk period for osteoporosis, which may be exacerbated by HIV and/or ART. A small, randomized international multicenter study demonstrated a trend of increased BMD at the lumbar spine after a switch from TDF to TAF in peri- and early postmenopausal women with HIV.[71]

Defining the relationship between HIV and menopausal symptoms, mental health, and depression is complicated because of overlapping symptoms from HIV itself, effects of ART, other comorbidities, and substance use. Some studies suggest that women with HIV experience a greater burden of menopausal symptoms, including vasomotor symptoms, sexual dysfunction, and mood changes.[67,68,72] Other studies did not find differences between women with HIV and those without HIV.[73,74] Menopausal symptoms also have been associated with reduced adherence to ART and poor cognitive performance.[37,38,75,76]

No studies have shown evidence of estrogen deficiency (i.e., menopause) affecting CD4 count, plasma HIV viral loads, or response to ART.[77,78] Two small studies showed no difference in plasma levels of tenofovir and RAL between pre- and postmenopausal women.[79,80]

The use of hormone replacement therapy (HRT) is low among women with HIV.[38] Data are limited on drug–drug interactions between ART and estradiol as part of HRT, and drug interaction data with ethinyl estradiol cannot be extrapolated to the estrogens used for HRT because of differences in metabolism. Drug interactions between HRT and ART are possible, particularly regimens containing cobicistat, ritonavir, PIs, or some NNRTIs. See the drug–drug interaction Tables 24a, 24b, 24c, 24d, 24e, 24f, and 24g for predicted interactions and clinical recommendations.

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Considerations for Antiretroviral Use in People With Coinfections

Hepatitis B Virus/HIV Coinfection

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Panel's Recommendations
• Hepatitis A, B, and C virus serologies should be performed for all people with HIV **(AIII).** • Before initiating or switching antiretroviral therapy (ART), all people who test positive for hepatitis B surface antigen (HBsAg) should be tested for hepatitis B virus (HBV) DNA using a quantitative assay to determine the level of HBV replication **(AIII).** • Because tenofovir alafenamide (TAF), tenofovir disoproxil fumarate (TDF), emtricitabine (FTC), and lamivudine (3TC) are active against both HIV and HBV, an antiretroviral (ARV) regimen for people with both HIV and HBV should include (TAF or TDF) plus (3TC or FTC) as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of a fully suppressive ARV regimen **(AI).** • In people with HBV/HIV coinfection, using 3TC or FTC as the only drug in a regimen with HBV activity **is not recommended (AII),** because HBV resistance to these drugs can emerge. • If TAF or TDF cannot be safely used, or if there is a desire to use a tenofovir-sparing ART regimen, entecavir should be used as the alternative HBV therapy **(BI).** Entecavir has weak activity against HIV. Using entecavir for HBV treatment without ART may result in selection of the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, entecavir must be used in addition to a fully suppressive ARV regimen when given to people with HBV/HIV coinfection **(AII).** • Adefovir **(AI)** or pegylated interferon alfa **(AIII) are not recommended** for people with HBV/HIV coinfection. • In people with HBV/HIV coinfection, the discontinuation of agents with anti-HBV activity may cause serious hepatocellular injury resulting from HBV reactivation hepatitis; people with HBV/HIV coinfection should be advised against stopping these medications and should be carefully monitored during interruptions of HBV-active treatment **(AII).** • When switching or modifying an ARV regimen in a person with HBV/HIV coinfection, including switching to long-acting injectables, ARV drugs that are active against HBV should be continued **(AII)** or specific anti-HBV drugs, such as entecavir, should be initiated **(AII).** • HBV reactivation has been reported in people with HIV and prior exposure to HBV (positive hepatitis B core antibody, negative HBsAg) when HBV-active agents are withdrawn as part of an ART regimen. Regardless of hepatitis B surface antibody level, people with HIV and prior HBV exposure are at low risk for reactivation and the associated hepatitis, which can result in serious hepatocellular injury. A monitoring strategy is considered a safe and effective way to assess HBV reactivation in low-risk people **(BIII).** • HBV reactivation has been observed in people with HBV/hepatitis C virus (HCV) coinfection while receiving interferon-free HCV treatment. For this reason, all people initiating HCV therapy should be tested for HBV. People with HCV/HIV coinfection and active HBV infection (determined by a positive HBsAg test) should receive ART that includes two agents with anti-HBV activity before initiating HCV therapy **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Approximately 5% to 15% of people with HIV in the United States also have chronic hepatitis B virus (HBV) infection, defined as positive HBV surface antigen (HBsAg).[1-3] The progression of chronic HBV to cirrhosis, end-stage liver disease, or hepatocellular carcinoma is more rapid in people with HBV/HIV coinfection than in people with chronic HBV mono-infection.[4] Conversely, chronic HBV does not substantially alter the progression of HIV infection and does not influence HIV suppression or CD4 T lymphocyte cell responses following the initiation of antiretroviral therapy (ART).[5,6] Liver-associated complications may occur due to immune reconstitution after initiation,[7,8] or HBV reactivation after discontinuation of antiretroviral (ARV) drugs that are active against both HIV and HBV.[9-14]

Recommendations for People With HBV/HIV

- All people with HIV should be tested for viral hepatitis, including hepatitis A virus (HAV), HBV, and hepatitis C virus (HCV). People without immunity to HAV or HBV should receive a full vaccination series **(AIII).**
- A survey of people with HIV/HBV coinfection in the United States revealed that 4.0% had a positive hepatitis D virus (HDV) serologic test, of which 41.7% had detectable HDV RNA.[15] Because HBV/HDV coinfection has been associated with serious liver complications, many experts recommend that people with HIV and chronic HBV be tested for HDV infection.[16,17] The recommended initial serologic test is an HDV antibody test, which, if positive, should be followed by HDV RNA testing. People with HIV and HBV/HDV coinfection should be referred to an expert in the management of viral hepatitis.
- All people with chronic HBV should be evaluated to assess the severity of HBV infection (see Hepatitis B Virus in the Adult and Adolescent Opportunistic Infections Guidelines). In addition, people with chronic HBV should be advised to abstain from alcohol, be screened for alcohol use disorder,[18] and be counseled on prevention methods that protect against both HBV and HIV transmission.[19]
- Before ART is initiated, all persons who test positive for HBsAg should be tested for HBV DNA by using a quantitative assay to determine the level of HBV DNA **(AIII),** and the test should be repeated every 3 to 6 months to ensure effective HBV suppression. The goal of HBV therapy with nucleos(t)ide reverse transcriptase inhibitors (NRTIs) is to prevent liver disease complications by sustaining the suppression of HBV replication. A large cohort study found that persistent HBV viremia while taking ART and high HBV DNA levels were associated with a higher risk of hepatocellular carcinoma (HCC), even if HIV was suppressed; whereas sustained HBV DNA suppression for ≥1 year was associated with a 58% reduction in HCC risk.[20] The most common reason for persistent HBV viremia in people with HBV/HIV coinfection on tenofovir alafenamide (TAF)– or tenofovir disoproxil fumarate (TDF)–containing ART is suboptimal adherence; thus, the primary focus in this setting should be on improving adherence.[21]
- Because HBV reactivation has been observed in people with HBV infection during interferon-free HCV treatment,[22,23] people with HCV/HIV coinfection and chronic HBV infection should receive ART that includes two agents with anti-HBV activity (such as TAF or TDF plus emtricitabine [FTC] or lamivudine [3TC]) prior to initiating HCV therapy **(AIII).** The diagnosis of HBV reactivation should be considered in people with current HBV infection who experience elevated liver transaminases during or immediately after HCV therapy.

Antiretroviral Drugs With Dual Activities Against HBV and HIV

The NRTIs TAF, TDF, FTC, and 3TC are active against HBV. Entecavir is an HBV nucleoside analog that has weak HIV activity. TAF is a tenofovir prodrug with HBV activity and potentially less renal and bone toxicity than TDF,[24,25] although weight gain has been observed more frequently with TAF than TDF.[26,27]

The efficacy of TAF versus TDF in hepatitis B e antigen (HBeAg)–negative patients with HBV mono-infection was evaluated through a randomized controlled trial, involving both treatment-naive and treatment-experienced participants. In this study, TAF was non-inferior to TDF, based on the percentage of participants with HBV DNA levels <29 IU/mL at 48 weeks of therapy (94% for TAF vs. 93% for TDF; $P = 0.47$).[28] In another study, TAF was also non-inferior to TDF in HBeAg-positive people with chronic HBV mono-infection, with a similar percentage of participants achieving HBV DNA levels <29 IU/mL at 48 weeks of therapy (64% for TAF vs. 67% for TDF; $P = 0.25$).[29] In both studies, people on TAF experienced significantly smaller mean percentage decreases from baseline in hip and spine bone mineral density at 48 weeks than participants receiving TDF. The median change in estimated glomerular filtration rate (eGFR) from baseline to 48 weeks also favored TAF.[28,29]

In people with HBV/HIV coinfection, (TAF or TDF) plus (3TC or FTC) can be considered part of the ARV regimen; entecavir has weak anti-HIV activity and must not be considered part of an ARV regimen. In addition, TDF is fully active for the treatment of people with known or suspected 3TC-resistant HBV infection, whereas 3TC resistance compromises the activity of entecavir against HBV.

Recommended Therapy

The combination of (TAF or TDF) plus (3TC or FTC) should be used as the NRTI backbone of an ARV regimen and for the treatment of both HIV and HBV infection **(AI).**[30-32] The decision whether to use a TAF- or TDF-containing regimen should be based on an assessment of risk for nephrotoxicity and the acceleration of bone loss. In a switch study in people with HBV/HIV coinfection, study participants who switched from a primarily TDF-based ARV regimen to the fixed-dose combination elvitegravir/cobicistat (EVG/c)/TAF/FTC maintained or achieved HBV suppression with improved eGFR and bone turnover markers.[33] See Appendix B, Table 12 for guidance on renal dosing of NRTIs. Although data on switching from a TDF-based to a TAF-based ARV regimen are limited, the data from the EVG/c/TAF/FTC switch study suggest that people with HBV/HIV coinfection can switch to TAF/FTC-containing regimens with a potential reduction in renal and bone toxicity while maintaining HBV suppression.

Alternative Therapy

If TDF or TAF cannot be safely used or if there is a desire to use a TAF- or TDF-sparing ART regimen**,** entecavir can be used as an alternative HBV therapy in addition to a fully suppressive ARV regimen **(BI).** Entecavir has weak activity against HIV; its use for HBV treatment without ART may result in the selection of the M184V mutation that confers HIV resistance to 3TC and FTC.[34,35] Therefore, entecavir must be used in addition to a fully suppressive ARV regimen when given to people with HBV/HIV coinfection **(AII).** Because entecavir and 3TC share a partially overlapping pathway to HBV resistance, it is unknown whether the combination of entecavir plus 3TC or FTC will provide greater virologic or clinical benefit than entecavir alone. In people with known or suspected 3TC-resistant HBV infection, the entecavir dose should be increased from 0.5 mg/day to 1 mg/day.[36] However, entecavir resistance may emerge rapidly in people with 3TC-resistant HBV

infection. Therefore, entecavir should be used with caution in such people, with frequent monitoring (approximately every 3 months) of the HBV DNA level to detect viral breakthroughs.[35]

Important Considerations

- Discontinuation of HBV-active NRTI drugs may potentially cause serious hepatocellular injury resulting from the reactivation of HBV.[37]
- Entecavir has activity against HIV. However, when entecavir is used to treat HBV in people with HBV/HIV coinfection who are not on ART, the drug may select for the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, when used in people with HBV/HIV coinfection, entecavir must be used in addition to a fully suppressive ARV regimen **(AII).**[38]
- When 3TC is the only active drug used to treat chronic HBV in people with HBV/HIV coinfection, 3TC-resistant HBV emerges in approximately 40% and 90% of people after 2 years and 4 years on 3TC, respectively. Given the similarities between FTC and 3TC, these drugs should only be used in combination with other anti-HBV drugs **(AII).**[39]
- In people with HBV/HIV coinfection, immune reconstitution following the initiation of treatment for HIV and HBV can be associated with elevated liver transaminase levels, possibly because HBV-induced liver injury is primarily an immune-mediated disease.[40]
- Some ARV agents (especially older drugs, such as nevirapine, tipranavir, and high-dose ritonavir) can increase liver transaminase levels. The incidence and magnitude of these increases were higher with HBV/HIV coinfection than with HIV mono-infection.[41-43] The etiology and consequences of these changes in transaminases are unclear because the changes may resolve with continued ART. Nevertheless, some experts suspend the suspected agent(s) when the serum alanine transferase (ALT) level increases to 5 to 10 times the upper limit of normal, or at a lower threshold if the person has symptoms of hepatitis and/or new elevations in bilirubin. However, increased transaminase levels in people with HBV/HIV coinfection may indicate HBeAg seroconversion due to immune reconstitution; thus, the cause of the elevations should be investigated before medications are discontinued. In people with increases in transaminase, HBeAg seroconversion should be evaluated by testing for HBeAg and anti-HBe, as well as HBV DNA levels, which should decrease in the setting of immune reconstitution. Other causes of ALT elevation—such as HCV or HDV infection, alcohol use, metabolic dysfunction-associated steatotic liver disease, and hepatotoxicity from non-ARV agents—should also be considered.

HBV Drugs Not Recommended

Adefovir in combination with 3TC or FTC with a fully suppressive ARV regimen was studied in people with HIV/HBV coinfection.[30,44,45] Adefovir was associated with high rates of HBV treatment failure and a high incidence of renal toxicity. Therefore, the Panel **does not recommend** adefovir for people with HBV/HIV coinfection **(AI).** Pegylated interferon alfa monotherapy is a potential therapy for the treatment of HBV mono-infection; however, data on its use in people with HBV/HIV coinfection are limited, and tolerance of the therapy in people with HIV is a significant limitation to its use. As a result, the Panel **does not recommend** pegylated interferon alfa for people with HBV/HIV coinfection **(AIII).** Pegylated interferon alfa can remain a treatment option in rare cases and with the consultation of an expert.

Changing Antiretroviral Therapy

- **When switching or modifying an ARV regimen in a person with HBV/HIV coinfection:** ARV drugs that are active against HBV (TDF or TAF in combination with 3TC or FTC) should be continued **(AII)** or a specific anti-HBV drug such as entecavir should be initiated **(AII).**
- **When ARV medications that are active against HBV in people with HBV/HIV coinfection must be discontinued:** Withdrawal of HBV-active treatment in a person with chronic HBV infection **is not recommended (AII).** If TAF or TDF cannot be continued due to concern for safety or if there is a desire to use a TAF- or TDF-sparing regimen and entecavir cannot be used or if there is concern for entecavir resistance, the person's clinical course should be monitored with monthly testing of liver transaminases. The risk of HBV flare in this setting is highest in people with positive HBeAg and those with active HBV. If no anti-HBV ARV drug can be used, entecavir should be added to a fully suppressive ARV regimen to prevent HBV flare **(AII)**, especially in people with marginal hepatic reserve, such as those with compensated or decompensated cirrhosis.[37]

Screening for HBV Before Initiating NRTI-Sparing or NRTI-Limited Antiretroviral Regimens

HBV status should be evaluated in all people with HIV who are not known to have chronic HBV before the initiation of an NRTI-sparing or NRTI-limited ARV regimen (such as long-acting cabotegravir plus rilpivirine [LA CAB/RPV], dolutegravir [DTG]/rilpivirine [RPV], or DTG/3TC). Considerations for screening include the following:

- People with HIV should be screened for HBV infection, and if not already immune or infected (including those with isolated hepatitis B core antibody [HBcAb]), vaccination should be initiated while considering these new ARV regimens (see Hepatitis B Virus Infection in the Adult and Adolescent Opportunistic Infections Guidelines).

- People with HBV/HIV coinfection were not included in clinical trials that evaluated NRTI-sparing or NRTI-limited regimens. If LA CAB/RPV, DTG/RPV, or DTG/3TC are used in people with HBV coinfection, TAF, TDF, or entecavir should also be prescribed **(AII).** In people with prior exposure to 3TC monotherapy, TAF or TDF is preferred due to the risk of HBV resistance to 3TC; thus, there is a lower barrier of resistance for entecavir.

- People with HIV and prior exposure to HBV infection (negative HBsAg, positive HBcAb, and either positive or negative hepatitis B surface antibody [HBsAb]) are likely at low risk (<1%) of HBV reactivation and even lower risk of HBV reactivation hepatitis,[14] although there are insufficient studies to confidently estimate the risk in this population. Of people with HIV and prior exposure to HBV infection, those with positive HBsAb are at the lowest risk for HBV reactivation, although HBV reactivation has been described when HBV-active therapy is withdrawn as part of an ART regimen.[14]

- For individuals with prior HBV exposure, it is reasonable and feasible to incorporate ALT monitoring into the frequent laboratory testing already recommended after switching from ART with HBV NRTI therapy (TDF, TAF, or entecavir) to LA CAB/RPV, DTG/RPV, or DTG/3TC. An increase in ALT would warrant HBV DNA testing to assess for HBV reactivation hepatitis and immediate initiation of HBV therapy once reactivation is confirmed. A monitoring strategy is

considered a safe and effective way to assess for HBV reactivation in low-risk people **(BIII).**[46,47] The timeline for reactivation is not clear in this population. Monitoring every 1 to 3 months for 6 months after switching from HBV-active ART is consistent with current recommendations for low-risk people without HIV.

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Hepatitis C Virus/HIV Coinfection

Updated: March 23, 2023
Reviewed: March 23, 2023

Panel's Recommendations
• All people with HIV should be screened for hepatitis C virus (HCV) infection **(AIII).** Patients at high risk of HCV infection should be screened annually and whenever incident HCV infection is suspected **(AIII).**
• Antiretroviral therapy (ART) may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation. For most patients with HCV/HIV coinfection, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury. Therefore, ART should be initiated in all patients with HCV/HIV coinfection, regardless of CD4 T lymphocyte cell count **(AI).**
• Initial antiretroviral (ARV) regimens that are recommended for most patients with HCV/HIV coinfection are the same as those recommended for people with HIV who do not have HCV infection. However, when treatment for both HIV and HCV is indicated, the ARV and HCV treatment regimens should be selected with special consideration for potential drug–drug interactions and overlapping toxicities **(AIII)** (see discussion in the text below and in Table 18).
• All patients with HCV/HIV coinfection should be evaluated for HCV therapy, which includes assessing their liver fibrosis stage to guide the duration of therapy and to predict subsequent risk of hepatocellular carcinoma and liver disease complications **(AIII).**
• Patients with chronic HCV/HIV coinfection should be screened for active and prior hepatitis B virus (HBV) infection by testing for the presence of hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B surface (HBsAb) and hepatitis B core (HBcAb; total or Immunoglobulin G). Persons who are not immune to HBV infection (HBsAb negative) should receive anti-HBV vaccination **(AIII).**
• HBV reactivation has been observed in people with HBV infection during HCV treatment with direct-acting antivirals. Accordingly, before initiating HCV therapy, patients with HCV/HIV coinfection and active HBV infection (HBsAg positive) should receive ART that includes two agents with anti-HBV activity **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*
Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

The treatment of hepatitis C virus (HCV) infection is rapidly evolving. Patients with HCV/HIV coinfection treated with all-oral, direct-acting antiviral (DAA) HCV regimens can achieve sustained virologic response (HCV cure) at rates comparable to those in patients with HCV mono-infection.[1-3] This section of the guidelines focuses on hepatic safety and drug–drug interaction issues related to HCV/HIV coinfection and the concomitant use of antiretroviral (ARV) agents and HCV drugs. For specific guidance on HCV treatment, clinicians should refer to the HCV Guidance from the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America.

Approximately one-third of patients with chronic HCV infection progress to cirrhosis at a median time of <20 years.[4,5] The rate of progression increases with older age, alcoholism, male sex, and HIV infection.[6-9] A meta-analysis found that patients with HCV/HIV coinfection had a threefold greater risk of progression to cirrhosis or decompensated liver disease than patients with HCV mono-infection.[8] The risk of progression is even greater in patients with HCV/HIV coinfection who have low CD4 T lymphocyte cell counts. Although antiretroviral therapy (ART) appears to slow the rate of HCV disease progression in patients with HCV/HIV coinfection, several studies have demonstrated that the rate of disease progression continues to exceed that observed in patients

without HIV.[10,11] Whether HCV infection accelerates HIV progression, as measured by the occurrence of AIDS-related opportunistic infections or death,[12] is unclear. With older ARV drugs, people with HIV and HCV coinfection experienced higher rates of hepatotoxicity than those seen in people with HIV but not HCV.[13,14] These higher rates have not been observed with the newer ARV agents that are currently in use.

Assessment of HCV/HIV Coinfection

All people with HIV should be screened for HCV infection using sensitive immunoassays licensed for the detection of antibodies to HCV in blood.[15] Patients who are HCV-seronegative but at risk for HCV infection should undergo repeat testing annually or as clinically indicated. Patients who are HCV-seropositive should be tested for HCV RNA using a sensitive quantitative assay to confirm the presence of active infection. Patients who test HCV RNA positive should undergo HCV genotyping and liver disease staging as recommended by the HCV Guidance.

- Patients with HCV/HIV coinfection should be counseled to avoid consuming alcohol.
- Patients with HCV/HIV coinfection also should be counseled about appropriate precautions to prevent transmission of HIV and/or HCV to others.
- Patients with chronic HCV/HIV coinfection should be screened for active and prior hepatitis B virus (HBV) infection by testing for the presence of hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B surface (HBsAb) and hepatitis B core (HBcAb; total or Immunoglobulin G).
    - Patients with evidence of active HBV infection (HBsAg positive) should be further evaluated and treated with ART that includes agents with anti-HIV and anti-HBV activities **(AIII).**
    - Those who are not immune to HBV infection (HBsAb negative) should receive anti-HBV vaccination.
- Patients with HCV/HIV coinfection who are susceptible to hepatitis A virus (HAV) should be vaccinated against HAV.
- All patients with HCV/HIV coinfection are candidates for curative HCV treatment.

Antiretroviral Therapy in HCV/HIV Coinfection

When to Start Antiretroviral Therapy

Initiation of ART for patients with HCV/HIV coinfection should follow the recommendations for all persons with HIV infection, considering the need for concurrent HCV treatment with oral DAA regimens, the potential for drug–drug interactions, and the individual's HBV status.

Considerations When Starting Antiretroviral Therapy

The same regimens that are recommended for initial treatment of HIV in most ART-naive persons also are recommended for patients with HCV/HIV coinfection. Special considerations for ARV selection in patients with HCV/HIV coinfection include the following:

- When both HIV and HCV treatments are indicated, the ARV regimen should be selected with careful consideration of potential drug–drug interactions with the HCV treatment regimen (see Table 18 below).
- In patients with HCV/HBV coinfection, HBV reactivation has been observed during HCV treatment with DAAs.[16,17] Therefore, before initiating HCV therapy, patients with HCV/HIV coinfection and active HBV infection (HBsAg positive) should receive ART that includes agents with anti-HBV activity (such as tenofovir disoproxil fumarate [TDF] or tenofovir alafenamide plus emtricitabine or lamivudine) **(AIII).**
- Patients with cirrhosis should be evaluated for signs of liver decompensation according to the Child-Turcotte-Pugh classification system. All patients with Child-Pugh class B or C disease should be evaluated by an expert in advanced liver disease and considered for liver transplantation. Furthermore, hepatically metabolized ARV and HCV DAA drugs may be contraindicated or require dose modification in patients with Child-Pugh class B and C disease (see Appendix B, Table 12).

Hepatotoxicity

Drug-induced liver injury (DILI) following the initiation of ART is more common in patients with HCV/HIV coinfection than in those with HIV mono-infection. Individuals with HCV/HIV coinfection who have advanced liver disease (e.g., cirrhosis, end-stage liver disease) are at greatest risk for DILI.[18] Eradicating HCV infection with treatment may decrease the likelihood of ARV-associated DILI.[19] Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels should be monitored 4 to 8 weeks after initiation of ART and at least every 6 to 12 months thereafter, and more often if clinically indicated. Mild to moderate fluctuations in ALT and/or AST levels (<5 times upper limit of normal [ULN]) are typical in individuals with chronic HCV infection. In the absence of signs or symptoms of liver disease or increases in bilirubin, these fluctuations do not warrant interruption of ART, but they do warrant monitoring to ensure a return to baseline. Patients with significant elevations in ALT or AST levels (>5 times ULN), concomitant increase in total bilirubin, or concomitant symptoms (weakness, nausea, vomiting) should be evaluated carefully for signs and symptoms of liver insufficiency and for alternative causes of liver injury (e.g., acute HAV or HBV infection, hepatobiliary disease, alcoholic hepatitis). If these signs and symptoms do not resolve, ART should be discontinued.

Concurrent Treatment of HIV and HCV Infections

Guidance on the treatment and management of HCV in adults with and without HIV can be found in the HCV Guidance. Several ARV drugs and HCV DAAs have the potential for clinically significant pharmacokinetic drug–drug interactions when used in combination. Before starting HCV therapy, the ART regimen may need to be modified to reduce the drug–drug interaction potential. Table 18 below provides recommendations on the concomitant use of selected drugs for the treatment of HCV and HIV infection. In patients receiving ART that has been modified to accommodate HCV treatment, HIV RNA should be measured within 2 to 8 weeks after changing HIV therapy to confirm the effectiveness of the new regimen. After ART modification, initiation of an HCV DAA regimen should be delayed for ≥2 weeks. Resumption of the original ARV regimen also should be delayed until ≥2 weeks after the HCV DAA regimen is completed. The prolonged half-life of some HIV and HCV drugs poses a potential risk of drug–drug interactions if a regimen is resumed soon after ART modification or HCV treatment completion.

Table 18. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

The recommendations in this table for concomitant use of select HIV drugs with U.S. Food and Drug Administration (FDA)–approved HCV DAA drugs are based on available pharmacokinetic (PK) interaction data or are predictions based on the known metabolic pathways of the agents. (Instances where PK interaction data are limited or not available are indicated in the table.) Whenever HIV and HCV drugs are used concomitantly, patients should be closely monitored for HIV and HCV virologic efficacy and potential toxicities. Because the field of HCV therapy is rapidly evolving, readers also should refer to the latest drug product labels and the HCV Guidance for updated information.

Note: Interactions with fosamprenavir (FPV) and nelfinavir (NFV) are **not** included in this table. Please refer to the FDA product labels for information regarding drug interactions with these HIV protease inhibitors (PIs).

ARV Drugs	Individual Drug	Coformulated				
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-Pugh class B or C)		
	Sofosbuvir	**Ledipasvir/ Sofosbuvir**	**Sofosbuvir/ Velpatasvir**	**Sofosbuvir/ Velpatasvir/ Voxilaprevir**	**Glecaprevir/ Pibrentasvir**	**Elbasvir/ Grazoprevir**
3TC	✓	✓	✓	✓	✓	✓
ABC	✓	✓	✓	✓	✓	✓
FTC	✓	✓	✓	✓	✓	✓
TAF	✓	✓	✓	✓	✓	✓
TDF	✓	✓ Monitor for TDF-associated adverse events.	✓ Monitor for TDF-associated adverse events.	✓ Monitor for TDF-associated adverse events.	✓	✓
Unboosted ATV	✓	✓	✓	✖	✖	✖
ATV/r or ATV/c	✓	✓	✓	✖	✖	✖

Table 18. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

ARV Drugs	Individual Drug	Coformulated				
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-Pugh class B or C)		
	Sofosbuvir	**Ledipasvir/ Sofosbuvir**	**Sofosbuvir/ Velpatasvir**	**Sofosbuvir/ Velpatasvir/ Voxilaprevir**	**Glecaprevir/ Pibrentasvir**	**Elbasvir/ Grazoprevir**
DRV/r or DRV/c	✓	If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated adverse events.[a]	If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated adverse events.[a]	✓ If a PI/r is used with TDF, ↑ TDF concentrations are expected. Monitor for TDF-associated adverse events.[a] Consider monitoring for hepatotoxicity.[b]	✖	✖
LPV/r	✓			✖	✖	✖
TPV/r	✖	✖	✖	✖	✖	✖
DOR	✓	✓ If used with TDF, monitor for TDF-associated adverse events.	✓	✓	✓	✓
EFV	✓		✖	✖	✖	✖
ETR	✓		✖	✖	✖	✖
NVP	✓		✖	✖	✖	✖
RPV PO and IM	✓		✓	✓	✓	✓
BIC/TAF/FTC	✓	✓	✓	✓	✓	✓
CAB PO and IM	✓	✓	✓	✓	✓	✓

Table 18. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

ARV Drugs	Individual Drug	Coformulated				
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-Pugh class B or C)		
	Sofosbuvir	**Ledipasvir/ Sofosbuvir**	**Sofosbuvir/ Velpatasvir**	**Sofosbuvir/ Velpatasvir/ Voxilaprevir**	**Glecaprevir/ Pibrentasvir**	**Elbasvir/ Grazoprevir**
DTG	✓	✓ If used with TDF, monitor for TDF-associated adverse events.	✓	✓	✓	✓
EVG/c/TDF/FTC	✓	✖	✓ If used with TDF, monitor for TDF-associated adverse events.	✓ If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity.[b]	✓ If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity.[c]	✖
EVG/c/TAF/FTC	✓	✓	✓	✓ Consider monitoring for hepatotoxicity.[e]	✓ Consider monitoring for hepatotoxicity.[f]	✖
RAL	✓	✓	✓	✓	✓	✓
MVC	✓	✓	✓	✓	✓	✓
FTR	✓	✓	✓	✖ Use alternative HCV regimen if possible.	✓	✖ Use alternative HCV regimen if possible.
LEN	✓	✓	✓	✓	✓	✓

[a] Consider using an alternative HCV treatment or ARV regimen to avoid increases in TDF exposure. If coadministration is necessary, monitor patient for TDF-associated adverse events.

[b] Voxilaprevir exposures can increase when it is coadministered with pharmacologically boosted DRV or EVG. Until more safety data in clinical settings become available, patients who are receiving voxilaprevir and pharmacologically boosted DRV or EVG should be monitored for hepatotoxicity.

Table 18. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

[c] Glecaprevir exposures can increase when it is coadministered with EVG/c. Until more safety data in clinical settings become available, patients who are receiving glecaprevir and EVG/c should be monitored for hepatotoxicity.

Key to Symbols:

✓ = ARV agents that can be used concomitantly
✖ = ARV agents not recommended
? = Data on PK interactions with ARV drug are limited or not available
↑ = Increase
↓ = Decrease

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; DAA = direct-acting antiviral; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; FTR = fostemsavir; HCV = hepatitis C virus; IM = intramuscular; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PO = oral; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir

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Tuberculosis/HIV Coinfection

Updated: September 12, 2024
Reviewed: September 12, 2024

Key Considerations and Recommendations

• Treatment for latent tuberculosis infection (LTBI) in people with HIV should take into consideration the individual's antiretroviral (ARV) regimen as noted below.
  ○ General recommendations for **once-weekly** isoniazid plus rifapentine for 3 months (3HP) and **once-daily** isoniazid plus rifapentine for 1 month (1HP):
  ▪ These regimens **are not recommended** for people who require twice-daily dolutegravir (DTG) therapy (e.g., those with certain integrase strand transfer inhibitor [INSTI]–associated resistance substitutions or clinically suspected INSTI resistance) **(AIII).**
  ▪ Tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) **(AIII),** tenofovir alafenamide (TAF)/FTC **(BIII),** or abacavir (ABC)/lamivudine (3TC) **(BIII)** can be used as the nucleoside reverse transcriptase inhibitor (NRTI) backbone. Rifapentine may lower concentrations of TAF. If used, monitor for virologic response.
  ○ For 3HP
  ▪ Efavirenz (EFV) 600 mg once daily or raltegravir 400 mg twice daily can be used **(AII).**
  ▪ DTG 50 mg once daily may be used for those in whom once-daily DTG is appropriate **(BII).**
  ○ For 1HP
  ▪ EFV 600 mg once daily can be used without dose adjustment **(AI).**
  ▪ For a person with virologic suppression while on a DTG 50 mg once-daily regimen, the DTG dose should be increased to 50 mg twice daily throughout the course of 1HP, continuing DTG 50 mg twice daily for 14 days after 1HP completion before switching back to once-daily DTG dosing **(AII).**
  ○ With daily isoniazid alone for 6 or 9 months, any ARV regimen can be used **(AIII).**
  ○ If rifampin is used to treat LTBI, clinicians should review Tables 24a through 24g to assess the potential for drug–drug interactions between rifampin and different ARV drugs **(AII).**
• All people with HIV and active tuberculosis (TB) who are not on antiretroviral therapy (ART) should be started on ART **(AI)** as described below.
  ○ **CD4 T lymphocyte (CD4) cell counts <50 cells/mm³:** Initiate ART as soon as possible, but within 2 weeks of starting TB treatment **(AI).**
  ○ **CD4 counts ≥50 cells/mm³:** Initiate ART within 2 to 8 weeks of starting TB treatment **(AI).**
  ○ **During pregnancy, regardless of CD4 count:** Initiate ART as early as feasible for treatment of the person with HIV and prevention of HIV transmission to the infant **(AIII).**
  ○ **With TB meningitis:** Initiate ART after TB meningitis is under control and after at least 2 weeks of anti-TB treatment to reduce the risk of life-threatening inflammation in a closed space as a result of immune reconstitution **(AIII).**
• For people with active TB who are receiving ART, the ARV regimen should be assessed with particular attention to potential drug–drug interactions between ARVs and TB drugs. Rifamycin antibiotics (rifabutin, rifampin, and rifapentine), in particular, have considerable potential for drug–drug interactions. The ARV regimen may need to be modified to permit use of the optimal TB treatment regimen (see Tables 24a through 24g for drug interaction data and dosing recommendations) **(AII).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Managing Latent Tuberculosis Infection in People With HIV

Approximately one-quarter of the world's population has tuberculosis (TB) infection, with a 5% to 10% lifetime risk of progressing to active disease.[1] Among individuals with latent TB infection (LTBI), the risk of developing active TB is much higher among those who also have HIV, and this risk increases as immune deficiency worsens.[2]

Tuberculosis Preventive Treatment

After active TB has been excluded, the Centers for Disease Control and Prevention preferentially recommends one of the following short-course regimens for LTBI treatment (see Treatment Regimens for Latent TB Infection):

- 3 months of once-weekly isoniazid plus rifapentine (3HP)
- 4 months of daily rifampin (4R)
- 3 months of daily isoniazid plus rifampin (3HR)

The World Health Organization (WHO)[3] and the Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV also recommend 1 month of daily isoniazid with rifapentine (1HP) as an alternative short-course regimen.

For more than 30 years, isoniazid had been the cornerstone of treatment for LTBI to prevent active TB. Randomized controlled clinical trials have demonstrated that treatment with isoniazid for 6 or 9 months for LTBI in people with HIV reduces the risk of active TB, especially in those with a positive tuberculin skin test.[4] Isoniazid given daily or twice weekly for 6 or 9 months can be coadministered with any antiretroviral (ARV) regimen and remains an alternative option, especially for people in whom rifamycin antibiotics cannot be used **(AIII).**

In the PREVENT TB study, the combination of isoniazid and rifapentine administered once a week for 3 months (3HP), as directly observed therapy, was as safe and effective as 9 months of isoniazid in preventing TB in people with HIV who were not on antiretroviral therapy (ART).[5] Another study randomized 1,148 South African adults with HIV who were not on ART to one of four treatment groups: 3 months of isoniazid and rifapentine, 3 months of isoniazid and rifampin, 6 months of isoniazid, or isoniazid continued for the duration of the trial. TB incidence did not differ among the groups.[6] The Panel for the Use of Antiretroviral Agents in Adults and Adolescents With HIV (the Panel) recommends dolutegravir (DTG) 50 mg once daily with 3 months of once-weekly isoniazid and rifapentine in people with virologic suppression and for whom once-daily DTG is appropriate **(BII).** More importantly, this 3-month regimen **is not recommended** for people who require twice-daily DTG therapy (e.g., those with certain integrase strand transfer inhibitors [INSTI]–associated resistance substitutions or clinically suspected INSTI resistance) **(AIII).** Isoniazid given daily for 6 or 9 months should be used in this setting.

A study of 6,000 people that compared completion rates, safety, and effectiveness of 4 months of daily rifampin (4R) versus 9 months of isoniazid found that 4R was non-inferior to isoniazid for 9 months for the prevention of TB disease, and that safety and completion rates were superior for 4R.[7] However, this trial included only 242 (4%) participants with HIV. While 4R may also be considered for TB-preventive treatment, clinicians should pay careful attention to potential drug–drug interactions with specific ARV drugs (see Tables 24a through 24g).

In 3,000 people with HIV infection in the BRIEF TB study, no difference was observed in TB incidence between those who received 1HP and those who received 9 months of isoniazid.[8] Approximately half of the participants were on ART (either efavirenz [EFV] or nevirapine-based regimens) while receiving the 1-month regimen. Fewer adverse events and a higher treatment completion rate occurred with the 1HP regimen than with 9 months of isoniazid.

Although rifapentine induces cytochrome P450 (CYP) isoenzymes and can potentially cause significant drug–drug interactions with ARVs, pharmacokinetic (PK) data support its use daily **(AI)** or once weekly **(AII)** with EFV 600 mg daily,[9,10] and once weekly with raltegravir (RAL) 400 mg twice daily **(AII).**[11] In a Phase 1/2 study of 60 adults with HIV and virologic suppression on once-daily dolutegravir (DTG)-based ART and weekly rifapentine with isoniazid,[12] DTG trough concentrations were reduced by 50% to 60%; all but one participant's trough concentration remained above the DTG protein-adjusted 90% inhibitory concentration (IC_{90}), and all HIV viral loads remained suppressed. In a multicenter PK study (A5372), 32 adults with HIV and virologic suppression on DTG-containing ART received DTG 50 mg twice daily throughout the course of 1HP and for 14 days after.[13] DTG trough concentrations were comparable with standard-dose DTG once daily without 1HP, and 31 (96.9%) of 32 participants maintained virologic suppression. One participant had an HIV RNA of 160 copies/mL at Day 28, with HIV RNA <50 copies/mL upon repeat testing on Day 42. Based on these data, the Panel recommends DTG 50 mg twice daily when given with 1HP in people with virologic suppression, continuing DTG 50 mg twice daily for 14 days after 1HP completion before switching back to once-daily DTG dosing **(AII).**

When prescribing either 1HP or 3HP, tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) **(AIII),** tenofovir alafenamide (TAF)/FTC **(BIII),** or abacavir (ABC)/lamivudine (3TC) **(BIII)** can be used as the nucleoside reverse transcriptase inhibitor (NRTI) backbone. The drug concentrations for ABC, TDF, 3TC, and FTC are not expected to be affected by rifapentine. Rifapentine may lower concentrations of TAF; if TAF is used, monitor for virologic response.

If a person with HIV has been in close contact with a person with drug-resistant TB, the options for LTBI treatment should be modified, taking into consideration drug-susceptibility test results from the source patient. In this setting, consultation with a TB expert is advised.

Isoniazid Preventive Therapy Plus Antiretroviral Therapy in Pregnant People With HIV

A randomized trial of isoniazid preventive therapy (IPT) compared isoniazid initiated during pregnancy (immediate IPT) to isoniazid delayed until 12 weeks postpartum (deferred IPT) in 956 women with HIV on ART. A greater number of adverse pregnancy outcomes were seen in women on immediate IPT, suggesting that IPT should be delayed until after delivery.[14] Treatment-related maternal adverse events were higher than expected in both arms. In the BRIEF TB study, first-trimester IPT exposure was associated with a nearly twofold increased risk of fetal demise—mostly spontaneous abortion—though the association was attenuated when adjusted for covariates proximal to pregnancy outcome, including ART use.[15] However, two observational studies from South Africa showed better pregnancy outcomes and no increase in hepatotoxicity in pregnant women on ART receiving antenatal IPT.[16,17] The WHO continues to recommend IPT for individuals with HIV.[3]

Impact of Antiretroviral Therapy in Preventing Active Tuberculosis

Effective ART can prevent active TB in areas with high TB prevalence. The TEMPRANO study conducted in Côte d'Ivoire randomized 2,056 participants with HIV to one of four study arms: deferred ART, deferred ART plus IPT, early ART, or early ART plus IPT. The initial results

demonstrated that IPT and early ART each independently reduced the risk of a serious HIV-related event, many of which were TB, and that IPT with early ART provided the best protection from serious HIV events and death.[18] Data from longer follow-up (median 4.9 years) showed that 6 months of IPT given early in the course of HIV infection provided a durable survival benefit, with a 37% reduction in the risk of death that was independent of ART.[19] In the START study, 4,685 participants with CD4 T lymphocyte (CD4) cell counts >500 cells/mm^3 were randomized to receive immediate ART or deferred ART. For participants in the deferred ART arm, ART was started when their CD4 count dropped to 350 cells/mm^3 or if they developed a clinical condition that required ART. TB was one of the three most common clinical events, occurring in 14% of participants in the immediate ART group and 20% of participants in the deferred ART group.[20] Collectively, these two large randomized studies showed that early initiation of ART (with or without IPT) reduced active TB, particularly in countries with a high prevalence of TB/HIV coinfection.

Antiretroviral Therapy for People With HIV and Active Tuberculosis

All people with HIV/TB disease should be treated with ART **(AI)**, although the timing of ART initiation may vary as discussed below. Important considerations related to the use of ART in people with active TB disease include the following:

- When to start ART in the setting of drug-resistant TB and in people with TB meningitis,
- Significant PK drug–drug interactions between anti-TB and ARV drugs, *and*
- The development of TB-associated immune reconstitution inflammatory syndrome (IRIS) after ART initiation.

Active pulmonary or extrapulmonary TB disease requires prompt initiation of TB treatment. The treatment of active TB disease in people with HIV should follow the general principles guiding treatment for people without HIV. The Adult and Adolescent Opportunistic Infection Guidelines include a more complete discussion of the diagnosis and treatment of TB disease in people with HIV.

The TB Trials Consortium Study 31/ AIDS Clinical Trials Group (ACTG) A5349 demonstrated success with a shorter, 4-month regimen.[21] This randomized, open-label, controlled Phase 3 trial compared two 4-month rifapentine-containing regimens to the standard 6-month control regimen of isoniazid plus rifampin. In 2,516 participants, including 193 (8%) with HIV, the rifapentine-moxifloxacin regimen was non-inferior to the control regimen, with 11.6% versus 9.6% unfavorable outcomes, respectively (difference 2.0%; 95% confidence interval, −1.1% to +5.1%), and it was safe and well tolerated. Participants with HIV were either already on an EFV-based ART or initiating an EFV-based ART.[22] In both groups, EFV concentrations were decreased slightly, but most maintained EFV concentrations of >1 mg/L and undetectable viremia.[23] This 4-month TB regimen with DTG-based ART is currently under investigation in the ACTG A5406 trial (NCT05630872).

Tuberculosis Diagnosed While a Person Is Receiving Antiretroviral Therapy

ART should be continued when TB is diagnosed in a person receiving ART, but the ARV regimen should be assessed with particular attention to potential drug interactions between ARVs and TB drugs (discussed below). The person's ARV regimen may need to be modified to permit use of the optimal TB treatment regimen **(AII)** (see Tables 24a through 24g for dosing recommendations).

Tuberculosis Diagnosed in a Person With HIV Not Yet Receiving Antiretroviral Therapy

ART should not be delayed until TB treatment is completed, because this strategy was associated with higher mortality rates in the SAPiT-1 study.[24] The timing of ART in specific populations is discussed below.

People with HIV and CD4 counts <50 cells/mm^3: Three large randomized clinical trials in people with HIV/TB disease, conducted in Africa and Asia, all convincingly showed that early ART in those with CD4 counts <50 cell/mm^3 significantly reduced AIDS events or deaths.[25-27] In these studies, early ART was defined as either ≤2 weeks[26] or ≤4 weeks[25] after initiation of TB therapy.

Collectively these three trials support the initiation of ART within the first 2 weeks of TB treatment in people with CD4 counts <50 cells/mm^3 **(AI).**

People with HIV and CD4 counts ≥50 cells/mm^3: In two of the three studies mentioned above,[26,27] no survival benefit was seen for people with CD4 counts ≥50 cells/mm^3 who initiated ART at <2 weeks versus later (8–12 weeks), after beginning TB treatment. Importantly, none of the studies demonstrated harm from earlier ART initiation, and many benefits of ART in people with HIV are well documented, regardless of TB coinfection. It is unlikely that more trials will be conducted to specifically inform the decision on when to start ART in people with TB and CD4 counts ≥50 cells/mm^3.

However, given the growing body of evidence supporting early ART in general and the lack of data showing any harm in people with TB coinfection, the Panel recommends ART initiation within 2 to 8 weeks after starting TB treatment for people with CD4 counts ≥50 cells/mm^3 **(AI).**

People with HIV and drug-resistant TB: People may have single-drug-resistant TB, multidrug-resistant TB (MDR-TB) (defined as strains with resistance to both isoniazid and rifampin); pre-extensively drug-resistant (pre-XDR) TB (defined as MDR-TB plus resistance to any fluoroquinolone), or extensively drug-resistant TB (XDR-TB) (defined as MDR-TB plus resistance to any fluoroquinolone and at least one additional Group A drug listed in the WHO guidelines).[28] Historically, mortality rates in people with MDR-TB or XDR-TB and HIV have been high,[29] but more recent data suggest that treatment outcomes are similar for people with MDR-TB with and without HIV infection. In the Nix-TB study of an all-oral, 6-month regimen of bedaquiline, pretomanid, and linezolid for MDR-TB and XDR-TB, 51% of the 109 participants also had HIV. Rates of cure, serious adverse events, and mortality were similar among those with and without HIV.[30]

Although randomized clinical trial data to guide the optimal timing for ART initiation are lacking, the WHO guidelines recommend ART for all people with HIV and drug-resistant TB, irrespective of CD4 count, as early as possible (within the first 8 weeks), following the initiation of TB treatment.

Management of people with HIV and drug-resistant TB is complex, and expert consultation is advised **(AIII).**

People with TB meningitis: TB meningitis is often associated with severe complications and a high mortality rate. In a study conducted in Vietnam, people with HIV-associated TB meningitis were randomized to immediate ART or to ART deferred until 2 months after initiation of TB treatment. A significantly higher rate of severe (Grade 4) adverse events was seen in people who received immediate ART than in those who received deferred ART (80.3% vs. 69.1% for immediate and deferred ART, respectively; $P = 0.04$).[31]

Despite these study results, in the setting of TB meningitis, many experts would recommend initiating ART early in settings where close monitoring of drug-related toxicities and central nervous system adverse events is feasible (see Adult and Adolescent Opportunistic Infection Guidelines) **(BIII).** ART should be started after TB meningitis is under control and after at least 2 weeks of anti-TB treatment to reduce the risk of life-threatening inflammation in a closed space as a result of immune reconstitution **(AIII).**

Managing people with HIV and TB meningitis is complex, and expert consultation is advised **(AIII).**

Pregnant people: All people with HIV and active TB who are pregnant should be started on ART as early as feasible, both for the treatment of the person with HIV and prevention of HIV transmission to the infant **(AIII).** The choice of ART should be based on efficacy and safety in pregnancy and should take into account potential drug–drug interactions between ARVs and rifamycins (see Perinatal Guidelines for more detailed discussions).

Drug Interaction Considerations

Rifamycin antibiotics (rifabutin, rifampin, and rifapentine) are an important component of TB treatment regimens because of their sterilizing ability. However, they are associated with a considerable potential for drug interactions due to their ability to affect various drug-metabolizing enzymes and transporters. Rifampin is a potent inducer of the CYP (mostly 3A and 2C subfamilies) enzyme system, P-glycoprotein (P-gp), and uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1). Rifabutin and rifapentine are both substrates and inducers of CYP3A4. As potent inducers of metabolic enzymes and drug transporters, rifamycin-related drug interactions may result in significant reduction in ARV drug exposure. The ARV drugs most affected include all protease inhibitors (PIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), INSTIs, the CCR5 antagonist maraviroc (MVC), the gp120 attachment inhibitor fostemsavir, and the capsid inhibitor lenacapavir. Coadministration of rifamycins with long-acting injectable cabotegravir with rilpivirine or lenacapavir is contraindicated.[32] Most NRTIs, the fusion inhibitor enfuvirtide, and the CD4 post-attachment inhibitor ibalizumab are not expected to have significant drug interactions with the rifamycins. Tables 24a through 24g outline the magnitude of these interactions and provide dosing recommendations when rifamycin antibiotics and selected ARV drugs are used concomitantly.

Because TAF is a P-gp substrate, its plasma concentrations may be reduced by rifamycin antibiotics. Current labeling does not recommend concomitant administration of TAF and any rifamycin antibiotic.[33] However, in a healthy volunteer study, following administration of TAF/FTC with rifampin, intracellular tenofovir-diphosphate concentrations were still 4.2-fold higher than those achieved by TDF.[34] TAF can be used with rifampin with caution and close monitoring of virologic response.

Several ARV drugs are not recommended for use with rifampin; clinicians should refer to Tables 24a through 24g before prescribing these drugs in combination. When DTG, RAL, or MVC are used with rifampin for TB treatment, the ARV doses must be increased. In contrast to its effect on other ARV drugs, rifampin leads to only a modest reduction in EFV concentrations.[35,36] Even though the current EFV label recommends increasing the EFV dose from 600 mg once daily to 800 mg once daily in people weighing >50 kg,[37] this dosage increase is generally not necessary. The Panel recommends EFV 600 mg for individuals receiving rifampin therapy. High-dose (up to 35 mg/kg/day) rifampin is currently being evaluated for treatment of TB meningitis. The data on the magnitude and extent of interactions between high-dose rifampin and ARV drugs are limited.[38-40]

Rifabutin, a weaker CYP3A4 enzyme inducer, is an alternative to rifampin for TB treatment, especially in people taking PI- or INSTI-based ARV regimens. Because rifabutin is a substrate of the CYP450 enzyme system, its metabolism may be affected by NNRTIs or PIs. Therefore, rifabutin dosage adjustment is generally recommended (see Tables 24a through 24g for dosing recommendations).

Rifapentine is a long-acting rifamycin that may be given once weekly or once daily. When given daily, it is a more potent inducer than rifampin.[41] Once-daily rifapentine did not affect the oral clearance of EFV 600 mg in individuals with HIV in the BRIEF TB study,[42] and once-weekly rifapentine has demonstrated minimal impact on EFV 600 mg exposure.[9] Once-weekly rifapentine led to an increase, rather than a decrease, in RAL drug exposure in healthy volunteers.[11] A PK study conducted in South Africa found that once-weekly isoniazid-rifapentine plus once-daily DTG was well tolerated in participants with HIV, with only 3 of 60 participants experiencing a Grade 3 adverse effect (two with elevated creatinine and one with hypertension). The extent of the interaction varied by day, with a 23% reduction on Day 1, 64% reduction on Day 2, and 56% reduction on Days 5 and 6 after isoniazid-rifapentine dose.[12] In a multicenter PK study (A5372), 32 adults with HIV and virologic suppression on DTG-containing ART received DTG 50 mg twice daily during 1HP and for 14 days after.[13] DTG trough concentrations were comparable with standard-dose DTG once daily without 1HP.

Tuberculosis-Associated Immune Reconstitution Inflammatory Syndrome

Immune reconstitution inflammatory syndrome (IRIS) is a clinical condition caused by ART-induced restoration of pathogen-specific immune responses to opportunistic infections, such as TB, resulting in either the deterioration of a treated infection (paradoxical IRIS) or a new presentation of a previously subclinical infection (unmasking IRIS). Manifestations of unmasking TB-associated IRIS (TB-IRIS) are characterized by their marked inflammatory nature, such as high fever, respiratory distress, lymphadenitis, abscesses, and sepsis syndrome. Manifestations of paradoxical TB-IRIS include fevers, new or worsening lymphadenopathy, new or worsening pulmonary infiltrates, enlarging pleural effusions, and new or enlarging tuberculomas.

TB-IRIS has been reported in 8% to more than 40% of people who start ART after being diagnosed with TB, although the incidence depends on the definition of IRIS and the intensity of monitoring.[43,44] IRIS is infrequently associated with mortality.

Predictors of IRIS include a baseline CD4 count <50 cells/mm^3; higher on-ART CD4 counts; high pre-ART and lower on-ART HIV viral loads; severity of TB disease, especially high pathogen burden; and <30-day interval between initiation of TB and HIV treatments.[45] Most IRIS in HIV/TB disease occurs ≤3 months from the start of ART.

In general, the Panel recommends continuing ART without interruption during IRIS **(AIII).**

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Limitations to Treatment Safety and Efficacy

Adherence to the Continuum of Care

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Key Considerations and Recommendations

• Linkage to HIV care and adherence to both antiretroviral therapy (ART) and clinic appointments should be regularly assessed.
• An individual's barriers to ART and clinic appointment adherence should be assessed before or shortly after the initiation of ART and regularly thereafter.
• Rapid access to ART is one of the pillars of the United States' plan to end the HIV epidemic; therefore, delays in access to ART should be addressed and treatment initiated as soon as possible.
• People with HIV having ART adherence problems should be placed on regimens with high genetic barriers to resistance, such as dolutegravir, bictegravir, or boosted darunavir. Side effects, out-of-pocket costs, convenience, and individual preferences should also be considered.
• People with HIV having difficulties with adherence to appointments or ART should be provided additional adherence support using a constructive, collaborative, nonjudgmental, and problem-solving approach.
• The approach taken to improve adherence should be tailored to each person's needs and barriers to care. Approaches could include, but are not limited to—
  ○ Changing ART to simplify dosing or to reduce side effects
  ○ Allowing flexible appointment scheduling
  ○ Finding resources to assist with treatment costs to maintain uninterrupted access to both ART and appointments
  ○ Linkage to resources to assist with unmet social and economic needs, such as transportation, food, housing, and other support services
  ○ Linkage to services to overcome stigma, substance use, or mental illness
• A multidisciplinary approach—including collaborations with nursing, pharmacy, social work, and case management (to the extent available—is often necessary to identify solutions to ART and appointment adherence. The clinician's role is to help people with HIV understand the importance of adherence to the continuum of care, identify the barriers to adherence and address those that are within their purview, and link them to resources to overcome other barriers.
• Single-tablet ART regimens are generally recommended when clinically appropriate, but high-quality evidence to definitively recommend them is lacking and shared decision-making between clinicians and people with HIV is essential **(BIII).**
• At this time, evidence does not support the use of financial incentives to engage people with HIV in ongoing routine care.
• Methods to estimate adherence based on drug levels measured in plasma, dried blood spots, urine, and hair samples are available. Measuring adherence with these methods has not been shown in randomized studies to improve outcomes. However, these methods should be used in a collaborative manner to avoid an adversarial relationship between the provider and people with HIV.
• Because delayed administration of long-acting cabotegravir plus rilpivirine (LA CAB/RPV) may lead to the emergence of drug resistance, LA CAB/RPV is not generally recommended as a complete regimen in people with viremia due to suboptimal adherence to ART, or in people who have ongoing challenges with retention in HIV care. However, based on very limited data, the Panel for the Use of Antiretroviral Agents in Adults and Adolescents With HIV recommends the use of LA CAB/RPV on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral ART, and who have no evidence of resistance to rilpivirine RPV or CAB and, with shared decision-making between providers and people with HIV **(CIII).** See Virologic Failure for a more detailed discussion.

- A summary of best practice interventions to improve linkage, retention, and adherence can be found in the Centers for Disease Control and Prevention's Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention.

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

HIV treatment adherence includes initiating care with an HIV provider (linkage to care), regularly engaging in appointments (retention in care), and adhering to antiretroviral therapy (ART). The concept of a "continuum of care" has been used to describe the process of HIV testing, linkage to HIV care, initiation of ART, adherence to ART, retention in care, and virologic suppression.[1-3] The Centers for Disease Control and Prevention (CDC) estimates that about 13% of people with HIV are undiagnosed in the United States.[4] Based on 2022 data, about 82% of individuals were linked to care within 30 days of receiving an HIV diagnosis.[5,6] However, only 54% of people with diagnosed HIV were retained in HIV care. It is estimated that only approximately 69% of people with complete data were virologically suppressed within 6 months of diagnosis. This low rate of viral suppression is primarily due to poor adherence to clinic appointments and ART.[5,7] Outcomes along the continuum of care also vary by geographic region and other population characteristics, such as sex, race and ethnicity, and HIV risk factors.[7] To achieve optimal clinical outcomes and to realize the potential public health benefit of treatment as prevention, adherence to each step in the continuum of care is critical.[8] It is important to note that retention and adherence may fluctuate as a result of life events, changes in insurance status, comorbid conditions, and health system changes, causing people with HIV to shift back and forth on the continuum. Knowledgeable providers and high-quality system processes are vital in promoting rapid linkage and sustained retention in care and adherence to ART. Finally, clinicians should recognize that adherence is a complex behavior requiring knowledge, motivation, memory, behavior change, external resources, and successful and persistent interaction with complex and, sometimes, challenging health care systems.[9-11] The patient–provider relationship is central to improving HIV care engagement and adherence to treatment. Providers must recognize that adherence is a collaborative effort between clinicians and people with HIV.

Addressing social determinants of health (SDOH) is critical to adherence along the HIV continuum of care. The CDC defines SDOH as "the conditions in which people are born, grow, work, live, and age" and "that influence health outcomes."[12] SDOH include access to education, income, nutritious food, transportation, stable housing, and health insurance coverage, as well as policies that may lead to structural racism, HIV criminalization, and stigma related to sexual and gender minority identification or immigration status. There are several commonly used screening tools for health-related social needs, including the Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences (PRAPARE),[13] the American Academy of Family Physicians Social Needs Screening Tool (long and short forms),[14,15] and the Centers for Medicare & Medicaid Services (CMS) Accountable Health Communities Health-Related Social Needs (AHC-HRSN) Screening Tool.[16] The CMS Accountable Health Communities Model conducted a randomized trial connecting beneficiaries to community resources for five core health-related social needs compared with a referral-only group. Individuals in the community resources group received an in-depth assessment of social needs, planning, referral to community services, and follow-up until the needs were resolved or determined unresolvable. The beneficiaries who received community service navigation experienced reduced emergency department visits and a trend toward lower expenditures and improved hospital-based utilization outcomes compared with the referral-only group.[17] Any unmet

social and economic needs identified via screening should be addressed, either through direct service provision or by community referrals.

This section provides guidance on linking people with HIV to care, assessing and improving retention in care, and assessing and improving adherence to ART. The CDC maintains a Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention to improve linkage, retention, and adherence, and the Health Resources and Services Administration (HRSA) has multiple tools to assist clinics housed in the Ryan White HIV/AIDS Program (RWHAP) Best Practices Compilation. In addition, a number of other groups and organizations have provided guidance for improving adherence to the steps in the care continuum.[8,18]

Linkage to Care

Receiving an HIV diagnosis can be traumatic, and linkage to care efforts must be delivered with compassion and persistence. The time from diagnosis to linkage to care can be affected by many factors, including insufficient socioeconomic resources, active substance use, mental health problems, stigma, and disease severity (symptomatic HIV is associated with more successful linkage).[19-23] In the United States, youth, people who use injection drugs, and Black/African American people have lower rates of linkage to care.[7] Some health system factors have also been associated with linkage success or failure. Co-location of testing and treatment services[22] and active linkage services (e.g., assistance in setting up HIV care appointments, maintaining an active relationship with individuals until linkage is completed, providing linkage case management services)[24-26] bolster linkage to care. Conversely, passive linkage (e.g., only providing names and contact information for treatment centers) is associated with lower linkage to care.

Monitoring Linkage to Care

Linking to HIV care after a new HIV diagnosis is defined as completing an outpatient appointment with a clinical provider who has the skills and ability to treat HIV, including prescribing ART. People with HIV should be linked to care as soon as possible after HIV diagnosis, preferably within 30 days. Monitoring linkage is critical to ensure that interventions can effectively reach people who are not linked to care. If the facilities that diagnose and treat an individual are the same or share the same electronic medical record system, it is relatively straightforward to monitor linkage to care. Monitoring linkage for people whose HIV is diagnosed outside the treatment provider's health care system is difficult and generally is the responsibility of the diagnosing provider or entity and the public health authority. However, once people with HIV make contact with the treating clinical system, they should be engaged in linkage efforts. The referring entity should monitor for successful linkage to and retention in HIV care.

Improving Linkage to Care

Strategies to improve linkage to care are summarized in Table 19 below. Linkage efforts should include immediate referral to care at diagnosis, appointment reminders, and outreach efforts if needed.[24] The only intervention shown to increase linkage to care in a randomized trial conducted in the United States is the Anti-Retroviral Treatment and Access to Services (ARTAS) intervention.[25] In this study, participants randomized to the control arm received information about HIV and care resources and a referral to a local HIV medical provider, whereas participants in the intervention arm worked with an ARTAS interventionist for five sessions, 90 days, or until linkage—whichever came first. The interventionist helped participants to identify and use their strengths, abilities, and skills to

link to HIV care; participants were also linked to community resources. Linkage to care, defined in this study as completing at least one visit with an HIV clinician within the first 6 months, was greater among the ARTAS participants than the control participants (78% vs. 60%, adjusted risk ratio = 1.36, $P < 0.001$). Furthermore, a greater percentage of ARTAS participants were retained in care, defined as visiting an HIV clinician at least once in each of the first two 6-month blocks after enrollment (64% vs. 49% for ARTAS and control participants, respectively; adjusted risk ratio = 1.41, $P = 0.006$). The results from the ARTAS intervention have been replicated in a community-based study.[26] The CDC supports free training in the ARTAS intervention. Other studies support the importance of post-test counseling to educate, motivate, and present positive messages about HIV,[27] peer support,[28] and engaging people with HIV at the clinic in advance of the visit with the provider.[29] Financial incentives did not increase linkage to care within 90 days in a large randomized trial.[30]

Retention in Care

Poor retention in HIV care is associated with a greater risk of death.[31,32] Poor retention is more common in people who use substances, have serious mental health problems, have unmet socioeconomic needs (e.g., housing, food, transportation), lack financial resources or health insurance, have schedules that complicate adherence, have been recently incarcerated, or face stigma.[33-36] At the provider and health system level, low trust in providers and a poor relationship between providers and people with HIV have been associated with lower retention, as has lower satisfaction with the clinic experience.[37-39] Availability of appointments and timeliness of appointments (i.e., long delay between the appointment request and the appointment date) and scheduling convenience are also factors.

Monitoring Retention in Care

Retention in care should be routinely monitored.[8] There are various ways to measure retention, including measures based on attended visits over a defined period of time (constancy measures) and measures based on missed visits.[40] Both approaches are valid and independently predict survival.[41] Missed visits and a prolonged time since the last visit are relatively easy to measure and should trigger efforts to retain or reengage a person in care. Constancy measures (e.g., at least two visits that are at least 90 days apart over 1 year, or at least one visit every 6 months over the last 2 years) can be used as clinic quality assurance measures.

Improving Retention in Care

Strategies to improve retention in care are summarized in Table 19 below. The Retention through Enhanced Personal Contact (REPC) intervention was tested in a randomized trial in six clinics in the United States. The study enrolled people with HIV who had a history of inconsistent clinic attendance. The intervention relied on personal contact and included a brief face-to-face meeting upon returning to care and at each subsequent clinic visit, plus three types of phone calls (check-ins between visits, to provide appointment reminders just before visits, and to attempt to reschedule missed visits). REPC resulted in small but significant improvements in retention in care, including in racial/ethnic minority populations and people with detectable plasma HIV RNA.[42] When necessary, in-clinic opioid replacement therapy helps opioid users remain in care.[43] An intervention using the electronic medical record to alert providers when people had suboptimal follow-up or high viral loads also improved retention in care.[44]

Telehealth has emerged as an important modality for retention in HIV care during the COVID-19 pandemic. A cluster-randomized study conducted in the U.S. Department of Veterans Affairs health facilities before the pandemic showed that the availability of telehealth resulted in improvements in viral suppression and the number of completed visits.[45] Reengaging and retaining people who are out of care remains particularly challenging.

Navigation services for out-of-care individuals with HIV in a New York City Medicaid health plan resulted in faster re-linkage to care but did not improve retention in care.[46] In two randomized trials involving out-of-care, hospitalized people with HIV, peer counselors and patient navigators did not improve re-linkage to care after hospital discharge.[47,48] Two randomized studies tested a Data to Care intervention, which uses clinic and public health data to reach and reengage out-of-care people with HIV.[49] One trial conducted in Seattle found that the intervention did not result in significantly faster time to re-linkage or viral suppression.[50] However, only people with unsuppressed viremia and CD4 T lymphocyte (CD4) cell counts <350 cells/mm^3 or people with no laboratory values in the preceding 12 months were included, reflecting the HIV treatment guidelines at the time. The Cooperative Re-Engagement Controlled Trial (CoRECT) was more recently conducted in the Northeast United States (Connecticut, Massachusetts, Philadelphia) and included people with HIV with no evidence of a clinic visit or laboratory measurement in the preceding 6 months, regardless of their most recent laboratory results. The proportion of people re-linked to care within 90 days and retained in care at 12 months was significantly higher in the intervention group, but no differences were observed in the proportion who achieved viral suppression in 12 months. Time to viral suppression among those who achieved viral suppression in 12 months was shorter for participants who were randomized to the Data to Care arm compared with the standard of care. Using the Data to Care approach requires substantial resources and notable privacy concerns; although short-term re-linkage may be improved, there is no evidence of an impact on long-term re-linkage or time to viral suppression.

Data from nonrandomized studies are less conclusive, but many interventions bear mentioning. Clinic-wide marketing (e.g., posters, brochures) and customer service training of staff to promote attending scheduled visits and provide people with a welcoming and courteous experience have improved retention.[51] People with HIV who rated their experience with their doctor more highly were more likely to stay in care.[52] Stepped-case management and social and outreach services,[53] including mobile health applications that enhance communication and provide support, are beneficial, although the applications that have been developed and studied are not available for widespread public use. Differentiated care approaches reduce the need for appointments and other expectations for people doing well and allow extra resources to be devoted to people not achieving optimal health outcomes. The evidence to support the use of differentiated care is strongest in low-resource settings, whereas in the United States, the evidence is limited to observational data, which suggests the approach has a beneficial impact.[54]

Overall, these data support the concept that all clinic personnel, from the facilities' staff to nurses to providers, play important roles in supporting retention in care by providing the optimal care experiences, constructively affirming attendance rather than criticizing non-attendance, and collaboratively solving problems with people to overcome barriers to care.[38,42,51] Flexible appointment schedules, expanded clinic hours, and copay or other financial or insurance assistance—such as that provided by the RWHAP—also facilitate uninterrupted access to clinical care. Navigation services, telehealth, and engaging with people through mobile health applications are likely to improve outcomes, although the evidence is not sufficient to support their use unequivocally.

The use of financial incentives or rewards to promote retention in care has been studied. A large study randomized clinic sites to financial incentives or standard of care. At baseline, 45% of the participants were retained in care in these clinics. The relative increase in the proportion of participants retained in care was 9% higher in clinics offering incentives than in standard-of-care clinics. Viral suppression also improved by 4% at financial incentive clinics, from a baseline of 62%.[30] Evidence from a *post hoc* analysis of a subset of the sites involved in that trial shows a reduced but persistent improvement in retention in care after the withdrawal of the incentives without a persistent effect on viral suppression.[55] In another large, randomized study of people who were out of care and hospitalized, financial incentives plus patient navigation did not lead to sustained improvement in retention or viral load suppression compared to standard care.[47] At this time, financial incentives remain experimental in the context of improved retention due to a lack of data supporting their use in routine care.

Adherence to Antiretroviral Therapy

Adherence to ART can be influenced by several factors, including a person's social situation, clinical condition, the prescribed regimen, and the patient–provider relationship.[56] Poor adherence is often a consequence of one or more behavioral, structural, and psychosocial barriers (e.g., depression and other mental illnesses, neurocognitive impairment, low health literacy, low levels of social support, stressful life events, busy or unstructured daily routines, active substance use, homelessness, poverty, nondisclosure of HIV serostatus, denial, stigma, inconsistent access to medications due to financial and insurance status).[57-60]

Characteristics of one or more components of the prescribed regimen can affect adherence. Once-daily regimens,[61] including those with low pill burden (even if not one pill once daily), no food requirement, and few side effects or toxicities, are associated with higher levels of adherence.[62,63] Single-tablet regimens (STRs) that include all antiretroviral (ARV) drugs in one pill taken once daily are easier for people to use. However, data to support or refute the superiority of an STR versus a once-daily multi-tablet regimen (MTR), as might be required for the use of some generic-based ARV regimens, are limited. Comparisons of these regimens are hampered because not all drugs and classes are available as STRs. There are demonstrated beneficial effects on virologic suppression in a meta-analysis of MTRs versus STRs.[64,65] Whether an STR is beneficial in people with HIV who are ART-naive is not known, with observational cohort studies showing the benefit of a once-daily STR versus a once-daily MTR.[63,66-69] On the other hand, observational data from Spain showed that co-formulated dolutegravir (DTG)/abacavir (ABC)/lamivudine (3TC) resulted in similar viral suppression compared to DTG plus ABC/3TC when used both at treatment initiation and when people with viral suppression on STR were switched to the two-pill formulation as a cost-saving strategy.[70] Given these findings and their wide availability, STRs are generally recommended when clinically appropriate, but high-quality evidence to definitively recommend them is lacking, and shared decision-making is essential **(BIII).**

Characteristics of the clinical setting can also have important structural influences on the success or failure of medication adherence. Settings that provide comprehensive multidisciplinary care (e.g., by case managers, pharmacists, social workers, mental health and substance use providers) support the complex needs of individuals, including those related to medication adherence. Treatment programs for substance use may offer services that promote adherence, such as directly observed therapy (DOT) (see Substance Use Disorders and HIV).

Monitoring Adherence to Antiretroviral Therapy

Adherence to ART should be assessed and addressed in a constructive and nonjudgmental manner at every clinic visit. Given the potency of contemporary ART, a detectable viral load identified during chronic care for a person with stable access to ART is most likely the result of poor adherence. Self-report, the most frequently used method for evaluating medication adherence, remains a useful tool. Carefully assessed self-report of high-level adherence to ART has been associated with favorable viral load responses,[71-73] whereas admission of suboptimal adherence is highly correlated with poor therapeutic response. The reliability of self-reporting often depends on how the clinician elicits the information. It is most reliable when ascertained in a simple, nonjudgmental, routine, and structured format that normalizes less-than-perfect adherence and minimizes socially desirable responses. To allow people to disclose lapses in adherence, some experts suggest inquiring about the number of missed doses during a defined period. For example, for a person with a detectable viral load, a provider might state, "I know it is difficult to take medicine every day. Most people miss doses at least sometimes. Thinking about the last 2 weeks, how many times have you missed doses? Please give me a rough estimate so I can help you take the best care of yourself." Other research supports simply asking people to rate their adherence during the last 4 weeks on a 5- or 6-point Likert scale[74,75] or using qualitative response categories.[73]

Other measures of adherence include pharmacy records and pill counts. Pharmacy records can be valuable when medications are obtained exclusively from a single source. Because pill counts can be altered, are labor intensive, and can be perceived as confrontational, they are generally not used in routine care. Electronic measurement devices are costly and are generally reserved for research settings. Finally, methods to estimate adherence based on drug levels measured in plasma, dried blood spots, urine, and hair samples are available.[76] Some of these are commercially available, but none have been shown in randomized studies to improve outcomes. However, if these methods are used, they should be implemented collaboratively between the provider and the person with HIV to avoid an adversarial relationship.

Improving Adherence to Antiretroviral Therapy

Strategies to improve adherence to ART are summarized in Table 19 below. Just as they support retention in care, all health care team members play integral roles in successful ART adherence programs.[72,77-79] An increasing number of interventions have proven effective in improving adherence to ART (for descriptions of the interventions, see the CDC's Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention). These interventions can be customized to suit a range of needs and settings. Many interventions that are efficacious in randomized trials require specialized training and resources before they can be implemented in routine care, and this has limited their impact. Nonetheless, these interventions have contributed to our knowledge in developing general principles of improving and maintaining adherence.

Every person with HIV must receive and understand basic information about HIV infection, including the goals of therapy (achieving and maintaining viral suppression, which will decrease HIV-associated complications and prevent transmission), the prescribed regimen (including dosing schedule and potential side effects), the importance of adherence to ART, and the potential for the development of drug resistance as a consequence of suboptimal adherence. People with HIV must also be positively motivated to initiate therapy, which can be assessed by simply asking people if they want to start treatment for HIV. Clinicians should assist people with HIV in identifying facilitating factors and potential barriers to adherence and develop multidisciplinary plans to attempt

to overcome those barriers. Processes for obtaining medications and refills should be clearly described. Transportation to pharmacy and clinic visits should be assessed with linkage to appropriate services as needed. Plans to ensure uninterrupted access to ART via insurance, copay assistance, pharmaceutical company assistance programs, or AIDS Drug Assistance Programs (ADAP), for example, should be made and reviewed with each person with HIV. Much of this effort to inform, motivate, and reduce barriers can be achieved by nonphysician members of the multidisciplinary team and can be accomplished concomitantly with, or even after, starting therapy.[80-83]

While delaying the initiation of ART is rarely indicated, some people may not be comfortable starting treatment right away. People expressing reluctance to initiate ART should be engaged to understand and overcome barriers to ART initiation. Although homelessness, substance use, and mental health problems are associated with poorer adherence, they are not predictive enough at the individual level to warrant withholding or delaying therapy given the simplicity, potency, and tolerability of contemporary ART. Rapid ART initiation at the time of HIV diagnosis has been pursued as a strategy to increase viral load suppression and retention in care, but safety data, data on intermediate or long-term outcomes, and data from randomized controlled trials conducted in high-resource settings are currently lacking.[80-86] In low-resource settings, data from randomized trials suggest that rapid ART probably increases ART use and viral suppression at 12 months, but data on other important outcomes—such as retention in care, regimen switching, and mortality—are not sufficient to draw conclusions.[87,88] Rapid access to ART has become a pillar of the United States' plan to end the HIV epidemic, and delays in access to ART should be addressed.[89] For more details, see Initiation of Antiretroviral Therapy.

Successful treatment requires a regimen that the individual can adhere to,[90,91] considering their daily schedule, tolerance of pills (number, size, and frequency), and any issues affecting absorption (e.g., use of acid-suppressing therapy, food requirements). As reviewed above, STRs have been associated with high rates of adherence. People with risk factors for poor adherence or a history of poor adherence should be offered regimens with high genetic barriers to resistance (e.g., a second-generation integrase strand transfer inhibitor [INSTI] or a boosted protease inhibitor), if clinically appropriate. Using shared decision-making, a medication choice and administration schedule should be tailored to each person's daily activities. Clinicians should explain to people that their first regimen is usually the best option for a simple regimen, which affords long-term treatment success. Establishing a trusting patient–provider relationship and maintaining good communication will help to improve adherence and long-term outcomes. Medication adherence can also be enhanced using medication reminder aids. The evidence is strongest for text messaging, although pillbox monitors, pill boxes, and alarms may also improve adherence.[92-96]

Positive reinforcement, such as informing people of their low or suppressed viral load and increased CD4 counts, can greatly help maintain high levels of adherence. Motivational interviewing has also been used with some success.[97-99] Other effective interventions include nurse home visits, a five-session group intervention, and couples- or family-based interventions. Interventions involving several approaches are generally more successful than single-strategy interventions, and interventions based on cognitive behavioral therapy and supporter interventions have been shown to improve viral suppression.[100] Problem-solving approaches that vary in intensity and culturally tailored approaches are also promising.[99,101,102] Providing additional therapy (e.g., for substance use or mental health) and social support may be important to maintain high levels of adherence. DOT has been effective in providing ART to people actively using drugs[103] but not to people in a general clinic population[104] or in home-based settings with partners responsible for DOT.[105,106] The use of incentives or rewards to

promote adherence has been studied, demonstrating improved adherence in one study conducted by the HIV Prevention Trials Network (HPTN)[30] and reduce viral load in another study that required very frequent viral load measurement and incentives.[107] Although the durability and feasibility of financial incentives are limited, and behavior change is generally not sustained after the incentives are withdrawn, the HPTN study did find some evidence of sustained adherence after 9 months.[55] Data are too limited to support the use of financial rewards for adherence to routine care.[47,108,109]

Transitions of Care

Transitions of HIV care are critical periods during which people may be more likely to fall out of care. Some important examples of transitions of care are discussed in further detail below.

Transition From Pediatric to Adult HIV Care

The transition from pediatric to adult HIV care requires proactive attention to the medical and psychosocial needs of adolescents as they move from a child-focused to an adult-focused health care system, with the goal of preventing disruption in care and ensuring ART adherence.[110] Recommendations for transition planning from pediatric to adult HIV care can be found in the Adolescents and Young Adults With HIV section of these guidelines and the Pediatric Antiretroviral Guidelines.

Transition From Obstetric to Primary HIV Care Postpartum

Pregnancy and the postpartum period offer a unique opportunity to engage in HIV care, both for people newly diagnosed with HIV during pregnancy and for people with HIV prior to pregnancy. Childcare responsibilities and postpartum depression can contribute to decreased adherence to HIV care in the postpartum period, thus requiring additional support services. Guidance on postpartum follow-up for people with HIV can be found in the Perinatal Guidelines.

Transitions Between Health Care Providers or Settings

Transitions in health care providers or settings can occur between hospitals, primary HIV care practices, ambulatory specialty care practices, long-term care facilities, home health, and rehabilitation facilities.[111] Safe transitions in HIV care can be supported by coordinating with HIV care providers and educating people with HIV and their support systems. In the setting of a health care facility discharge, bedside medication delivery or "Meds to Beds" programs may enhance post-discharge medication adherence by eliminating the need to visit a pharmacy to fill post-discharge medications.[112,113] In the setting of a residential move from one geographic area to another, a new HIV care provider would ideally be identified ahead of the move so that communication and transfer of medical records occur in a timely manner. This is particularly important for people with HIV who are receiving RWHAP services because not all HIV care providers receive RWHAP funding. HRSA provides an online resource for identifying RWHAP providers nationally. Provision of at least a 30-day ART supply at the time of a residential move may mitigate gaps in adherence due to delays in health care access in a new geographic area.

Reengagement in HIV Care After Loss to Follow-up

Adherence along the HIV care continuum is fluid and can change depending on an individual's life circumstances. In general, guidance around reengagement in care is similar to the guidance for

individuals who are newly diagnosed with HIV. However, specific attention should be paid to understanding the reasons for previous disengagement from care, and shared decision-making should be used to identify strategies to address these barriers using a multidisciplinary approach. Hospitalization can provide an important opportunity for reengagement when an acute illness may increase an individual's motivation for behavior change. As noted above, bedside medication delivery or "Meds to Beds" programs have the potential to enhance post-discharge medication adherence.[112,113]

Individuals in Custody Released From Jails and Prisons

HIV continues to disproportionately affect individuals who are incarcerated at a rate three times that of the general population. Approximately 1.1% of individuals in custody have HIV, compared with 0.4% of the general population.[114,115] Incarceration presents an opportunity to identify and treat previously undiagnosed people with HIV, reengage those who had fallen out of HIV care in the community before incarceration, and stabilize HIV treatment among those who struggled with adherence and retention in care in the community. HIV treatment inside carceral facilities should mirror treatment in the community with respect to ART selection. Treatment interruptions should be avoided when people enter and leave such facilities. HIV treatment outcomes can be improved by having HIV specialty care teams within carceral facilities to communicate and coordinate care with community-based providers. There are unique considerations when treating HIV inside prisons and jails, given a lack of individual privacy, restricted movement to the health care unit, HIV stigma, and solitary confinement—all of which can negatively impact ART adherence while in custody. Conversely, this setting can allow the individual in custody to focus on adherence and allow the health care team to assess the safety, tolerability, and effectiveness of an ART regimen.

Adherence challenges can increase exponentially upon release from custody and include lapses in medical and prescription benefits (including for mental health and substance use disorders), housing instability, lack of transportation, lack of identification and other important documents (e.g., birth certificate, social security card) needed to secure medical benefits, relapse to substance use, and risk of overdose. Interventions to reduce barriers to HIV treatment should be assessed during the prerelease discharge planning process when feasible and can be enhanced by accessing assistance through community-based organizations that provide post-release services.[116] Factors that promote treatment adherence post-release include registering for health insurance and completing an ADAP application prior to release,[117] coordinating follow-up HIV care with community providers, and providing a 30-day supply of ART at the time of release.[118] Various interventions to improve post-release treatment adherence have demonstrated the efficacy of an interdisciplinary medical team, including case management and patient navigation resources.[119-124]

Long-Acting Antiretroviral Therapy

An ART regimen of long-acting intramuscular cabotegravir and rilpivirine (LA CAB/RPV) given monthly or every 2 months has been studied and approved for use in populations with viral suppression. In addition, preliminary data from a randomized clinical trial suggest that LA CAB/RPV may be safe and effective among people without viral suppression despite intensive adherence support on oral ART; however, final data and long-term outcomes are not yet available.[125] The long pharmacologic tail of LA CAB/RPV after the last dose raises concerns about the emergence of drug-resistance mutations in people who discontinue therapy without rapidly transitioning to oral therapy. Further, efficacy data from randomized clinical trials do not always translate to effectiveness in real-world settings.

The use of the LA CAB/RPV as a complete regimen is generally not recommended in people with viremia due to suboptimal adherence to ART, or in people who have ongoing challenges with retention in HIV care. However, limited data from small observational studies found that LA CAB/RPV can lead to high levels of viral suppression in people who have struggled with adherence to oral ART and who are viremic at treatment initiation.[126-128] It should be noted that these studies were conducted in settings where LA CAB/RPV was available on Medicaid and ADAP formularies. Further, significant social and case management support, including full-time dedicated staff, was provided to ensure adherence to the regimen. This support was provided by multidisciplinary teams involving clinicians, pharmacists, and case managers and included appointment reminders, assistance with transportation, financial incentives, and assistance with rescheduling missed injection appointments. Additionally, injections were offered in people's homes, at harm-reduction sites, and via street medicine. It is unknown whether similar responses can be achieved in clinics without the resources to provide the level of adherence support seen in previous studies.

Based on these limited data, the Panel recommends the use of LA CAB/RPV on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral ART, who have no evidence of resistance to RPV or CAB, and with shared decision-making between providers and people with HIV **(CIII)**.

This approach may provide alternatives for individuals with viremia and difficulties with adherence to oral ART, especially for those at the highest risk for disease progression or death. If LA CAB/RPV is used, close monitoring is recommended, with drug-resistance testing performed if virologic response is inadequate. Importantly, conventional adherence support is likely inadequate, and expanded, intensive, multidisciplinary case management and outreach support are needed when using this strategy to assure adherence and adequate monitoring for people while on LA CAB/RPV. People with HIV and providers need to be aware of the significant risk of developing resistance to non-nucleoside reverse transcriptase inhibitors and particularly INSTIs if virologic failure occurs on LA CAB/RPV, which may limit future treatment options and may also lead to transmission of HIV; these concerns should be balanced with the given individual's HIV-related risk for disease progression and death. See Virologic Failure for a more detailed discussion.

Conclusion

Clinicians should obtain accurate information about a person's adherence and barriers to ART and appointment adherence, followed by meaningful discussions on solutions, rather than simply instructing adherence and warning about potential consequences of poor adherence. The latter approach fails to acknowledge a person's barriers to adherence, fails to provide actionable information, erodes rather than builds the patient–provider relationship, and has been demonstrated to not improve adherence.[129,130] At the same time, however, many of the interventions shown to improve adherence are difficult to implement in routine care. Nonetheless, effective lessons from this body of research can be applied to routine care to improve linkage to care, adherence to ART, and adherence to appointments. These lessons include the following:

- Regularly assess adherence to ART and appointments.
- Engage people struggling with adherence at any step on the care continuum with a constructive, collaborative, nonjudgmental, and problem-solving approach rather than reprimanding them or lecturing them on the importance of adherence.

- Elicit an individual's barriers to adherence, which may include personal, behavioral, medical, or structural barriers (e.g., substance use, housing instability, stigma, lack of transportation), clinic barriers (e.g., limited clinic hours, processes that make it more difficult to obtain prescriptions or schedule appointments), and system barriers (e.g., copays, prior approvals, processes that complicate maintaining pharmacy benefits or obtaining refills).
- Tailor approaches to improve adherence to an individual's specific needs and barriers, for example, by changing ART to simplify dosing or reduce side effects, finding resources to assist with copays or other out-of-pocket costs (see Table 19 below), to maintain an uninterrupted supply of ART, and to assure access to clinicians, or linking people to counseling to overcome stigma, substance use, or mental illness.
- Utilize ART regimens with high genetic barriers to resistance—such as DTG, bictegravir, or boosted darunavir regimens—for people with adherence problems. When selecting the regimen, consider possible side effects, out-of-pocket costs, convenience, and individual preferences, because the only regimen that will work is the one that people can obtain and are willing and able to take.
- Recognize the need for multidisciplinary approaches to identify and address barriers. Clinicians should help people with HIV understand the importance of adherence to the continuum of care, identify and address immediate barriers, and link them to resources for overcoming other obstacles.

Table 19. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy

Strategies	Examples
Provide an accessible, trustworthy, nonjudgmental multidisciplinary health care team.	• Include care providers, nurses, social workers, case managers, pharmacists, medication managers, and administrative staff on the care team; train all members on providing compassionate and person-centered care.
Strengthen early linkage to care and retention in care.	• Encourage health care team participation in linkage to and retention in care. • Use ARTAS training (if available). • Actively support linkage to care with assistance in making appointments and linkage to services to overcome barriers to care. • Streamline Ryan White HIV/AIDS Program eligibility verification processes for uninsured and underinsured clients.
Evaluate an individual's knowledge about HIV, HIV prevention, and HIV treatment and provide information based on this assessment.	• Keeping the current knowledge base in mind, provide information about HIV, including the natural history of the disease, HIV viral load and CD4 count and expected clinical outcomes according to these parameters, therapeutic and prevention consequences of poor adherence, and the importance of staying in HIV care.
Identify facilitators, potential barriers to adherence, and necessary medication management skills both when starting ART and thereafter.	• Assess each individual's cognitive competence and impairment. • Assess behavioral and psychosocial challenges, including mental illnesses, trauma, social support levels, alcohol consumption, substance use, nondisclosure of HIV serostatus, and stigma. • Identify and address language and literacy barriers. • Assess beliefs, perceptions, and expectations about taking ART (e.g., impact on health, side effects, disclosure issues, consequences of poor adherence). • Ask about medication-taking skills and foreseeable challenges with adherence (e.g., past difficulty keeping appointments, adverse effects from previous medications, issues managing other chronic medications, need for medication reminders and organizers). • Assess structural issues, including unstable housing, lack of income, unpredictable daily schedule, lack of prescription drug coverage, lack of continuous access to medications, and transportation problems.
Provide needed resources.	• Provide or refer for mental health and/or substance use treatment. • Provide resources to obtain prescription drug coverage (e.g., AIDS Drug Assistance Programs, Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs). • Assist people during insurance enrollment periods to facilitate enrollment in plans that cover antiretrovirals. • Provide resources about stable housing, social support, transportation assistance, income, and food security.

Table 19. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy

Strategies	Examples
Involve people with HIV in ARV regimen selection.	• Review potential side effects, dosing frequency, pill burden, storage requirements, food requirements, and consequences of poor adherence. • Assess daily activities and tailor a regimen to predictable and routine daily events. • Consider preferential use of ART regimen with a high barrier to resistance, such as BIC-, DTG-, or boosted DRV-based ART if poor adherence is anticipated. • Consider the use of STR or fixed-dose-combination formulations to reduce pill burden and/or dosing frequency. • Consider the use of LA CAB/RPV if clinically appropriate (see the Long-Acting Antiretroviral Therapy section above for further discussion). • Assess if the cost or copayment for drugs will affect adherence and access to medications.
Assess adherence at every clinic visit.	• Monitor viral load as a strong biological measure of adherence. • Use a simple behavioral rating scale or self-reported assessment. • Employ a structured format that normalizes or assumes less-than-perfect adherence and minimizes socially desirable or "white-coat adherence" responses. • Ensure that other members of the health care team also assess and support adherence.
Use positive reinforcement to foster adherence success.	• Inform people of the benefits of low or nondetectable levels of HIV viral load (e.g., "Undetectable = Untransmittable") and increases in CD4 counts. • Thank people for attending their appointments.
Identify the type of and reasons for poor adherence and target ways to improve adherence.	Identify if any of the following have contributed to poor adherence: • Failure to understand dosing instructions. • Complexity of regimen (e.g., pill burden, size, dosing schedule, food requirements, polypharmacy). • Pill aversion or pill fatigue. • Adverse effects. • Inadequate understanding of drug resistance and its relationship to adherence. • Appointment reminders and incorporation of input from people with HIV in appointment scheduling. • Cost-related issues (e.g., copays for medications or visits, missed work time). • Mental illness, drug and alcohol use, homelessness, or poverty. • Stigma of taking pills or attending HIV-related appointments. • Nondisclosure of status or privacy concerns leading to missed doses, refills, or appointments.

Table 19. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy

Strategies	Examples
Select from among available effective adherence and retention interventions.	• See the CDC's Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention for a summary of best practice interventions to improve linkage, retention, and adherence. • Use adherence-related tools to complement education and counseling interventions (e.g., text messaging, pill box monitors, pill boxes, alarms). • Use community resources to support adherence (e.g., visiting nurses, community workers, family, peer advocates, transportation assistance, pharmacy delivery). • Use prescription assistance programs (see "Provide needed resources" above in this table). • Use motivational interviews. • Provide outreach for people who drop out of care. • Use peer or paraprofessional treatment navigators. • Recognize positive clinical outcomes resulting from better adherence. • Arrange for DOT for people in substance use treatment (if feasible). • Enhance clinic support and structures to promote linkage and retention (e.g., reminder calls, flexible scheduling, assessment of clinic service satisfaction). • Offer telehealth services for primary care, as well as supportive services when appropriate.
Systematically monitor retention in care.	• Record and follow up on missed visits.

Key: ART = antiretroviral therapy; ARTAS = Anti-Retroviral Treatment and Access to Services; ARV = antiretroviral; BIC = bictegravir; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; DOT = directly observed therapy; DRV = darunavir; DTG = dolutegravir; LA CAB/RPV = long-acting cabotegravir/rilpivirine; STR = single-tablet regimen

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Adverse Effects of Antiretroviral Agents

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Adverse effects have been reported with all antiretroviral (ARV) drugs and were among the most common reasons for switching or discontinuing therapy, and for medication nonadherence in the earlier era of combination antiretroviral therapy (ART).[1] Fortunately, newer ARV regimens are associated with fewer serious and intolerable adverse effects than regimens used in the past. Generally, <10% of ART-naive patients enrolled in randomized trials experience treatment-limiting adverse events. However, the long-term complications of ART can be underestimated because most clinical trials use highly specific inclusion criteria which exclude individuals with certain underlying medical conditions, and the duration of participant follow-up is relatively short. As ART is recommended for all patients regardless of CD4 T lymphocyte (CD4) cell count, and because therapy must be continued indefinitely, the focus of patient management has evolved from identifying and managing early ARV-related toxicities to individualizing therapy to avoid long-term adverse effects, including diabetes and other metabolic complications, atherosclerotic cardiovascular disease, kidney dysfunction, bone loss, and weight gain. To achieve and sustain viral suppression over a lifetime, both long-term and short-term ART toxicities must be anticipated and managed. When selecting an ARV regimen, clinicians must consider potential adverse effects, as well as the individual's comorbidities, concomitant medications, and prior history of drug intolerances.

Several factors may predispose individuals to adverse effects of ARV medications and include the following:

- Concomitant use of medications with overlapping and additive toxicities.
- Comorbid conditions that increase the risk of adverse effects. For example, underlying liver disease from alcohol use, coinfection with viral hepatitis, and/or liver steatosis[2,3] may increase the risk of hepatotoxicity when efavirenz (EFV) or protease inhibitors are used; and borderline or mild renal dysfunction increases the risk of nephrotoxicity from tenofovir disoproxil fumarate (TDF).
- Certain ARVs that may exacerbate pre-existing conditions. For example, psychiatric disorders may be exacerbated by EFV, rilpivirine, and, infrequently, by integrase strand transfer inhibitors.[4,5]
- Drug-drug interactions that may increase toxicities of ARV drugs or concomitant medications. For example, when pharmacokinetic boosters such as ritonavir or cobicistat are used, or when isoniazid is used with EFV.[6]
- Genetic factors that predispose patients to abacavir (ABC) hypersensitivity reaction,[7,8] EFV neuropsychiatric toxicity,[6,9] QTc prolongation,[10,11] and atazanavir (ATV)-associated hyperbilirubinemia.[12]

Information on the adverse effects of ARVs is outlined in several tables in these Guidelines. Table 20 provides clinicians with a list of the most common and/or severe ARV-associated adverse events for each drug class. The most common adverse effects of individual ARV agents are summarized in Appendix B, Tables 3, 4, 5, 6, 7, 8, 9, and 10.

Table 20. Common and/or Severe Adverse Effects Associated With Antiretroviral Therapy

Adverse effects for ARV drugs that are no longer commonly used in clinical practice (ddI, d4T, FPV/r, IDV, NFV, SQV/r, and TPV/r) have been removed from this table, with the exception of lipodystrophy and peripheral neuropathy associated with ddI and d4T. Because these effects may persist long after discontinuation of ddI or d4T, and patients may still present with these long-lasting toxicities, the drugs remain listed among the ARVs associated with these two effects. Refer to the product labels or to the archived July 10, 2019, version of the Guidelines for information regarding the adverse effects associated with these older ARVs.

This table focuses on ARV-associated adverse effects that a patient may experience as a result of taking an ARV regimen. For information regarding potential adverse effects of ARVs on fetuses and newborns when certain ARVs are taken around the time of conception or during pregnancy, refer to the Perinatal Guidelines.

In this table, N/A indicates either that there are no reported cases for that particular side effect or that data for that specific ARV drug class are not available. See Appendix B, Tables 3, 4, 5, 6, 7, 8, 9, and 10 for additional information listed by drug.

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Bone Density Effects	**TDF:** Associated with greater loss of BMD than other NRTIs, especially when given with a PK booster. Osteomalacia may be associated with renal tubulopathy and urine phosphate wasting. **TAF:** Associated with smaller declines in BMD than those seen with TDF.	Decreases in BMD observed after the initiation of any ART regimen			N/A	Not evaluated
Bone Marrow Suppression	**ZDV:** Anemia, neutropenia.	N/A	N/A	N/A	N/A	N/A
Cardiac Conduction Effects	N/A	**RPV and EFV:** QTc prolongation	**ATV/r and LPV/r:** PR prolongation. Risk factors include pre-existing heart disease and concomitant use of medications that may cause PR prolongation.	N/A	**FTR:** QTc prolongation was seen at four times the recommended dose. Use with caution in patients with pre-existing heart disease or QTc prolongation, or concomitant	N/A

Table 20. Common and/or Severe Adverse Effects Associated With Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
					use of medications that may prolong QTc interval.	
Cardiovascular Disease	**ABC:** Associated with an increased risk of MI in some cohort studies. Absolute risk greatest in patients with traditional CVD risk factors.	N/A	**Boosted DRV and LPV/r:** Associated with cardiovascular events in some cohorts	N/A	N/A	N/A
Cholelithiasis	N/A	N/A	**ATV:** Cholelithiasis and kidney stones may present concurrently. Median onset is 42 months after ARV initiation.	N/A	N/A	N/A
Diabetes Mellitus and Insulin Resistance	ZDV	N/A	LPV/r, but not with boosted ATV or DRV	N/A	N/A	N/A
Dyslipidemia	**ZDV > ABC:** ↑ TG and ↑ LDL **TAF:** ↑ TG, ↑ LDL, and ↑ HDL (no change in TC:HDL ratio) TDF has been associated with lower lipid levels than ABC or TAF.	**EFV**: ↑ TG, ↑ LDL, ↑ HDL	**All RTV- or COBI-boosted PIs:** ↑ TG, ↑ LDL, ↑ HDL **LPV/r > DRV/r and ATV/r:** ↑ TG	**EVG/c:** ↑ TG, ↑ LDL, ↑ HDL	N/A	N/A
Gastrointestinal Effects	**ZDV > other NRTIs:** Nausea and vomiting	N/A	GI intolerance (e.g., diarrhea, nausea, vomiting) **LPV/r > DRV/r and ATV/r:** Diarrhea	**EVG/c:** Nausea and diarrhea	N/A	**LEN:** Nausea and diarrhea

Table 20. Common and/or Severe Adverse Effects Associated With Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Hepatic Effects	**When TAF, TDF, 3TC, and FTC are withdrawn in patients with HBV/HIV coinfection or when HBV resistance develops:** Patients with HBV/HIV coinfection may develop severe hepatic flares. **ZDV:** Steatosis	**EFV:** Most cases relate to an increase in transaminases. Fulminant hepatitis leading to death or hepatic failure requiring transplantation have been reported. **NVP:** Severe hepatotoxicity associated with skin rash or hypersensitivity. A 2-week NVP dose escalation may reduce risk. Risk is greater for women with pre-NVP CD4 counts >250 cells/mm^3 and men with pre-NVP CD4 counts >400 cells/mm^3. NVP should **never** be used for post-exposure prophylaxis. EFV and NVP **are not recommended** in patients with hepatic insufficiency (Child-Pugh class B or C).	**All PIs:** Drug-induced hepatitis and hepatic decompensation have been reported. **ATV:** Jaundice due to indirect hyperbilirubinemia	**DTG:** Persons with HBV or HCV coinfection may be at higher risk of DTG-associated hepatotoxicity.	**MVC:** Hepatotoxicity with or without rash or HSRs has been reported. **FTR:** Transaminase elevation was seen more commonly in patients with HBV/HCV. Transient elevation of bilirubin observed in clinical trials.	N/A

Table 20. Common and/or Severe Adverse Effects Associated With Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Hypersensitivity Reaction Excluding rash alone or Stevens-Johnson syndrome	**ABC: Contraindicated** if patient is HLA-B*5701 positive. Median onset for HSR is 9 days after treatment initiation; 90% of reactions occur within 6 weeks. **HSR symptoms (in order of descending frequency):** Fever, rash, malaise, nausea, headache, myalgia, chills, diarrhea, vomiting, abdominal pain, dyspnea, arthralgia, and respiratory symptoms Symptoms worsen with continuation of ABC. Patients should not be rechallenged with ABC if HSR is suspected, regardless of their HLA-B*5701 status.	**NVP:** Hypersensitivity syndrome of hepatotoxicity and rash that may be accompanied by fever, general malaise, fatigue, myalgias, arthralgias, blisters, oral lesions, conjunctivitis, facial edema, eosinophilia, renal dysfunction, granulocytopenia, or lymphadenopathy Risk is greater for ARV-naive women with pre-NVP CD4 counts >250 cells/mm^3 and men with pre-NVP CD4 counts >400 cells/mm^3. Overall, risk is higher for women than men. A 2-week dose escalation of NVP reduces risk.	N/A	**RAL:** HSR reported when RAL is given with other drugs also known to cause HSRs. All ARVs should be stopped if HSR occurs. **DTG:** Reported in <1% of patients in clinical development program	**MVC:** HSR reported as part of a syndrome related to hepatotoxicity.	N/A

Table 20. Common and/or Severe Adverse Effects Associated With Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Injection Site Reaction		**RPV IM injection:** Reported in >80% of patients; reactions may include localized pain/discomfort (most common), nodules, induration, swelling, erythema, hematoma.		**CAB IM injection:** Reported in >80% of patients; reactions may include localized pain/discomfort (most common), nodules, induration, swelling, erythema, hematoma.	**T-20 SQ injection:** Reported in almost all patients; reactions may include pain, tenderness, nodules, induration, ecchymosis, erythema.	**LEN SQ injection:** Reported in 47–62% of patients; reactions may include swelling, erythema, pain, nodules, inflammation, induration. Nodules and induration may persist for months in some patients.
Lactic Acidosis	**Reported with older NRTIs, d4T, ZDV, and ddI,** but not with ABC, 3TC, FTC, TAF, or TDF.	N/A	N/A	N/A	N/A	N/A
Lipodystrophy	**Lipoatrophy:** Associated with history of exposure to d4T or ZDV (d4T > ZDV). Not reported with ABC, 3TC or FTC, or TAF or TDF.	**Lipohypertrophy:** Trunk fat increase is observed with EFV-, PI-, and RAL-containing regimens; however, a causal relationship has not been established.			N/A	N/A
Myopathy/Elevated Creatine Phosphokinase	**ZDV:** Myopathy	N/A	N/A	**RAL and DTG:** ↑ CPK, rhabdomyolysis, and myopathy or myositis have been reported.	N/A	N/A

Table 20. Common and/or Severe Adverse Effects Associated With Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Nervous System/Psychiatric Effects	**History of exposure to ddI, ddC, or d4T:** Peripheral neuropathy (can be irreversible)	**Neuropsychiatric events:** EFV > RPV, DOR, ETR **EFV:** Somnolence, insomnia, abnormal dreams, dizziness, impaired concentration, depression, psychosis, suicidal ideation, ataxia, encephalopathy. Some symptoms may subside or diminish after 2–4 weeks. Bedtime dosing and taking without food may reduce symptoms. Risk factors include psychiatric illness, concomitant use of agents with neuropsychiatric effects, and genetic factors. **RPV:** Depression, suicidality, sleep disturbances **DOR:** Sleep disorders and disturbances, dizziness, altered sensorium; depression and suicidality and self-harm	N/A	**All INSTIs:** Insomnia, depression, and suicidality have been reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.	N/A	**LEN:** Headache
Rash	**FTC:** Hyperpigmentation	All NNRTIs	ATV, DRV, and LPV/r	All INSTIs	MVC, IBA, FTR	N/A

Table 20. Common and/or Severe Adverse Effects Associated With Antiretroviral Therapy

Adverse Effect	Drug Class					
	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Renal Effects/ Urolithiasis	**TDF:** ↑ SCr, proteinuria, hypophosphatemia, urinary phosphate wasting, glycosuria, hypokalemia, and non-anion gap metabolic acidosis. Concurrent use of TDF with COBI- or RTV-containing regimens appears to increase risk. **TAF:** Less impact on renal biomarkers and lower rates of proteinuria than TDF	**RPV:** Inhibits Cr secretion without reducing renal glomerular function	**ATV and LPV/r:** Associated with increased risk of chronic kidney disease in a large cohort study. **ATV:** Stone or crystal formation; adequate hydration may reduce risk **COBI (as a boosting agent for DRV or ATV):** Inhibits Cr secretion without reducing renal glomerular function	**DTG, COBI (as a boosting agent for EVG), and BIC:** Inhibits Cr secretion without reducing renal glomerular function	**IBA:** SCr abnormalities ≥Grade 3 reported in 10% of trial participants **FTR:** SCr >1.8 x ULN seen in 19% in a clinical trial, but primarily with underlying renal disease or other drugs known to affect creatinine	N/A
Stevens-Johnson Syndrome/Toxic Epidermal Necrosis	N/A	NVP > EFV, ETR, RPV	Some reported cases for DRV, LPV/r, and ATV	RAL	N/A	N/A
Weight Gain	Weight gain has been associated with initiation of ART and subsequent viral suppression. The increase appears to be greater with INSTIs than with other drug classes. Greater weight increase has also been reported with TAF than with TDF and with DOR than with EFV.			INSTI > other ARV drug classes	N/A	N/A

Key: 3TC = lamivudine; ABC = abacavir; ART= antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; CAB = cabotegravir; CD4 = CD4 T lymphocyte; CI = capsid inhibitor; CNS = central nervous system; COBI = cobicistat; CPK = creatine phosphokinase; Cr = creatinine; CVD = cardiovascular disease; d4T = stavudine; ddC = zalcitabine; ddI = didanosine; DLV = delavirdine; DOR = doravirine; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; EI = entry inhibitor; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; FTR = fostemsavir; GI = gastrointestinal; HBV = hepatitis B virus; HCV = hepatitis C virus; HDL = high-density lipoprotein; HSR = hypersensitivity reaction; IBA = ibalizumab; IDV = indinavir; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; MI = myocardial infarction; MVC = maraviroc; NFV = nelfinavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; SQ = subcutaneous; SQV = saquinavir; SQV/r = saquinavir/ritonavir; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; TPV = tipranavir; TPV/r = tipranavir/ritonavir; ULN = upper limit of normal; ZDV = zidovudine

Switching Antiretroviral Drugs Due to Adverse Effects

Some patients experience treatment-limiting toxicities associated with ART. In these cases, ART must be modified. ART-associated adverse events can range from acute and potentially life-threatening to chronic and insidious. Serious life-threatening events (e.g., hypersensitivity reaction due to ABC, symptomatic hepatotoxicity, severe cutaneous reactions) require the immediate discontinuation of all ARV drugs and re-initiation of an alternative regimen without overlapping toxicity. Toxicities that are not life threatening (e.g., urolithiasis with ATV, renal tubulopathy with TDF) can usually be managed by substituting another ARV agent for the presumed causative agent without interrupting ART. Other chronic, non–life-threatening adverse events (e.g., dyslipidemia) can be addressed either by switching the potentially causative agent for another agent or by managing the adverse event with pharmacological or nonpharmacological interventions. Management strategies must be individualized for each patient. When adverse effects occur during the use of a long-acting ARV, management might be challenging due to the persistence of drug in the body over the course of many months. Oral lead-in regimens for cabotegravir plus rilpivirine are available to assess short-term tolerability.

Switching a patient from an effective ARV agent or regimen to a new agent or regimen must be done carefully, and only when the potential benefits of the change outweigh the potential risks of altering treatment. The fundamental principle of regimen switching is to maintain viral suppression. When selecting a new agent or regimen, providers should be aware that drug-resistant viruses previously acquired or selected, even those not detected by past genotypic resistance testing, are archived in HIV reservoirs. The resistant virus, even if absent from subsequent resistance test results, may reappear under selective drug pressure. See Optimizing Antiretroviral Therapy in the Setting of Viral Suppression for further discussion. It is critical that providers review the following information before implementing any treatment switch:

- The patient's medical and complete ARV history, including prior virologic responses to ART;
- All previous drug resistance test results;
- Viral tropism (if maraviroc [MVC] is being considered);
- HLA-B*5701 status (if ABC is being considered);
- Comorbidities;
- The patient's pregnancy status, ability to use effective contraceptives, and desire for pregnancy;
- Hepatitis B virus (HBV) status. Patients with evidence of chronic HBV infection should not discontinue ARVs active against HBV (e.g., TDF, tenofovir alafenamide, lamivudine, emtricitabine). If discontinuation is necessary due to adverse effects, consult the HBV/HIV Coinfection section for guidance;
- Adherence history;
- Prior intolerances to any ARVs; and
- Concomitant medications and supplements, considering any potential drug interactions with ARVs.

A patient's willingness to accept new food requirements or dosing schedule must also be assessed. In some cases, medication costs may also be a factor to consider before switching treatment. Signs and

symptoms of comorbidities, adverse effects of concomitant medications, or HIV itself may mimic adverse effects caused by ART. Therefore, clinicians should investigate all potential causes for an adverse event. In the case of a severe adverse event, it may be necessary to discontinue or switch ARVs pending the outcome of such an investigation. For the first few months after an ART switch, the patient should be closely monitored for any new adverse events. The patient's HIV viral load should also be monitored to assure continued viral suppression.

Table 21 lists several major ART-associated adverse events and the options for appropriate switches between agents in an ARV regimen. The table focuses on the ARVs most commonly used in the United States and lists substitutions that are supported by ARV switch studies, the findings of comparative ARV trials and observational cohort studies, or expert opinion. Switching agents in an effective ARV regimen should be done carefully and only when the potential benefits of the change outweigh the potential risks of altering treatment.

Table 21. Antiretroviral Therapy–Associated Adverse Effects That Can Be Managed With Substitution of Alternative Antiretroviral Agents

This table focuses on ARV-associated adverse effects that patients may experience as a result of a current ARV regimen. For information regarding ARV choices to use in individuals of childbearing potential and during pregnancy to avoid potential ARV adverse effects on fetuses and newborns refer to the Perinatal Guidelines.

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Bone Density Effects	TDF[a]	TAF or ABC[b] NRTI-sparing regimens or regimens using only 3TC or FTC as the NRTI may be considered, if appropriate.	Declines in BMD have been observed upon initiation of most ART regimens. Switching from TDF to alternative ARV agents has been shown to increase bone density, but the clinical significance of this increase remains uncertain. TAF is associated with smaller declines in BMD than TDF, and patients show improvement in BMD upon switching to TAF. The long-term impact of TAF on patients with osteopenia or osteoporosis is unknown; close clinical monitoring is recommended in this setting.
Bone Marrow Suppression	ZDV	Regimen not including ZDV	ZDV has been associated with neutropenia and macrocytic anemia.
Calculi Nephrolithiasis and cholelithiasis	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	This switch should be made if ATV is the presumed cause of the calculi.
Cardiac QTc Interval Prolongation	EFV, RPV, FTR	Boosted ATV or DRV, DOR, or INSTI-based regimen (that does not combine with RPV)	High EFV, RPV, and FTR exposures may cause QT prolongation. Consider switching from EFV- or RPV- based regimens if patient is taking other medications with known risk of Torsades de Pointes, or in patients at higher risk of Torsades de Pointes. For FTR, if there is no alternative ARV drug option, consider switching the concomitant medication.
Cardiovascular Events Myocardial infarction, ischemic stroke	ABC	TDF or TAF	ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies. TDF has been associated with lower lipid levels than TAF.
	RTV- or COBI-boosted PI regimens, EFV	INSTI, RPV, or DOR	If lipids are a concern, see Dyslipidemia below. Large observation cohorts have found an association between some PIs (DRV, FPV, IDV, LPV/r) and an increased risk of CV events. However, this association has not been seen with ATV. Further study is needed.

Table 21. Antiretroviral Therapy–Associated Adverse Effects That Can Be Managed With Substitution of Alternative Antiretroviral Agents

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Dyslipidemia Hypertriglyceridemia (with or without elevated LDL level)	RTV- or COBI-boosted PI, EFV-based regimens	INSTI, DOR, or RPV	Elevated TG and LDL levels are more common with LPV/r and FPV/r than with other RTV-boosted PIs. Improvements in TG and LDL levels have been observed with switch from LPV/r to ATV or ATV/r.[c]
Gastrointestinal Effects Nausea, diarrhea	LPV/r	Boosted ATV or DRV, INSTI, NNRTI	GI intolerance is common with boosted PIs and is linked to the total dose of RTV. More GI toxicity is seen with LPV/r than with ATV/r or DRV/r. GI effects are often transient and do not warrant ARV substitution unless they are persistent and intolerable.
	Other RTV- or COBI-boosted regimens	BIC, DTG, RAL, or NNRTI	In a trial of treatment-naive patients, rates of diarrhea and nausea were similar for EVG/c/TDF/FTC and ATV/r plus TDF/FTC.
Hypersensitivity Reaction	ABC	Any appropriate ABC-sparing regimen	Never rechallenge with ABC following a suspected HSR, regardless of the patient's HLA-B*5701 status.
	EFV, ETR, NVP, RPV	Non-NNRTI ART	Risk of HSR with NVP is higher for women and those with high CD4 counts.
	DTG, RAL	Non-INSTI ART	Reactions to NVP, ETR, RAL, DTG, and MVC may be accompanied by elevated liver transaminases.
	MVC	Suitable alternative ART	
Insulin Resistance	LPV/r	INSTI, NNRTI	Results of switch studies have been inconsistent. Studies in HIV-negative patients suggest a direct causal effect of LPV/r on insulin resistance. However, traditional risk factors for insulin resistance may be stronger risk factors than the use of any PI.
Jaundice and Icterus	ATV, ATV/c, ATV/r	DRV/c, DRV/r, INSTI, or NNRTI	Increases in unconjugated bilirubin are common with ATV and generally do not require modification of therapy unless resultant symptoms are distressing to the patient.
Lipoatrophy	Peripheral lipoatrophy (loss of subcutaneous fat of the limbs, face, and buttocks) is associated with prior thymidine analog (d4T and ZDV) use. Despite switching from these ARVs, fat recovery remains slow (may take years) and incomplete.		
Lipohypertrophy	Accumulation of visceral, truncal, dorsocervical, and breast fat has been observed during ART, particularly during use of older PI-based regimens (e.g., IDV), but whether ART directly causes fat accumulation remains unclear. There is no clinical evidence that switching to another first line regimen will reverse lipohypertrophy.		
Neuropsychiatric Side Effects Dizziness, suicidal ideation, abnormal dreams, depression, ataxia, encephalopathy	EFV, RPV	DOR, ETR, PI/c, or PI/r INSTIs may be used, but monitoring is recommended (see Comments column).	In most patients, EFV-related CNS effects subside within 4 weeks after initiation of the drug, but in some patients, ataxia or encephalopathy may appear months to years after EFV-initiation. Persistent or intolerable effects should prompt substitution of EFV. INSTIs are associated with insomnia. Depression and suicidality have been infrequently reported with INSTI use, primarily in patients with pre-existing psychiatric conditions.

Table 21. Antiretroviral Therapy–Associated Adverse Effects That Can Be Managed With Substitution of Alternative Antiretroviral Agents

Adverse Event	ARV Agent(s) or Drug Class		Comments
	Switch from	Switch to	
Rash	NNRTIs (especially NVP and EFV)	PI- or INSTI-based regimen	Mild rashes that develop after initiation of NNRTIs other than NVP rarely require treatment switch. When serious rash develops due to any NNRTI, switch to another drug class.
	DRV/c, DRV/r	ATV/c, ATV/r, or another drug class (e.g., INSTI)	Mild rashes following DRV/r use may resolve without modification of therapy. For more severe reactions, change to an alternative boosted PI or an agent from another drug class.
Renal Effects Including proximal renal tubulopathy and elevated creatinine	TDF[a]	ABC,[b] TAF (for patients with CrCl >30 mL/min, unless on chronic hemodialysis), NRTI-sparing regimens, or regimens using only 3TC or FTC as the NRTI may be considered if appropriate.	TDF may cause tubulopathy. Switching from TDF to TAF is associated with improvement in proteinuria and renal biomarkers. The long-term impact of TAF on patients with pre-existing renal disease, including overt proximal tubulopathy, is unknown, and close clinical monitoring is recommended in this setting.
	ATV/c, ATV/r, LPV/r	BIC, DTG, EVG/c/TAF/FTC, RAL, boosted DRV, or NNRTI	COBI, DTG, BIC, and, to a lesser extent, RPV, can increase SCr through inhibition of creatinine secretion. This effect does not affect glomerular filtration. However, assess patient for renal dysfunction if SCr increases by >0.4 mg/dL.

[a] In patients with chronic active HBV infection, another agent that is active against HBV should be substituted for TDF.

[b] ABC should be used only in patients known to be HLA-B*5701 negative.

[c] TDF reduces ATV levels; therefore, unboosted ATV should not be coadministered with TDF.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; BMD = bone mineral density; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; CrCl = creatine clearance; CV = cardiovascular; d4T = stavudine; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FPV = fosamprenavir; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; FTR = fostemsavir; GI = gastrointestinal; HBV = hepatitis B virus; HSR = hypersensitivity reaction; IDV = indinavir; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; ZDV = zidovudine

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Cost Considerations and Antiretroviral Therapy

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The clinical benefits, public health impact, and cost-effectiveness of HIV treatment have been well-established since the advent of combination antiretroviral therapy (ART),[1-6] and the expanded use of ART is one of the four pillars of the *Ending the HIV Epidemic in the U.S.* initiative.[7,8] However, HIV treatment with ART is costly. A 2015 study using 2012 health care expenditure data estimated that the discounted lifetime medical costs for an individual who acquires HIV at 35 years of age are $326,500 ($597,300 undiscounted), with 60% of the costs attributable to ART.[9] The estimated total direct expenditure for HIV care and treatment between 2002 and 2011 was $10.7 billion annually, which is 800% to 900% higher than similar expenditures for other chronic conditions.[10] Since the addition of the cost table in these guidelines in 2012,[11] the overall cost of brand-name, first-line antiretroviral (ARV) regimens increased by over 30% from 2012 to 2018,[12] which is 3.5 times higher than the rate of inflation for the same period. Total annual undiscounted spending on ARV drugs has more than doubled since 2010, reaching $22.5 billion in 2018.[13,14]

This section provides guidance on cost considerations related to HIV clinical care. The cost of ART, especially out-of-pocket costs to the person with HIV, should be one of the many considerations in regimen selection, because such expenditures may directly affect adherence. Overall costs to the health care system, to insurers, and to society are also important, especially given the increasing number of people with HIV, rising drug costs, and increasing multimorbidity among people aging with HIV. Providers should make every effort to prevent costs from limiting HIV care.

Cost Sharing in the United States

Prescription drug pricing in the United States involves complex systems with varying requirements for mandatory and voluntary discounts, rebates, and reimbursement rates, and much of the pricing information is confidential. Prices can vary depending on the state, purchaser, type of public or private insurance coverage in use, and number of generic competitors to branded drugs (see Table 22b below). Additionally, provider-administered drugs and biologics, including those used in the management of HIV (e.g., intramuscular injections of long-acting cabotegravir plus rilpivirine [LA CAB/RPV]), are typically associated with product, administration, and/or office visit costs. Therefore, providers may find it difficult to navigate payer cost-containment practices, including formulary restrictions; prior authorization requirements; and cost-sharing arrangements, such as copayments (a fixed dollar amount per prescription), coinsurance (a fixed percentage of the prescription cost), and insurance deductible payments.

Out-of-pocket costs for people with HIV can be prohibitive, creating a barrier to the initiation and continuation of ART. Cost sharing results in higher rates of people not initiating ART, prescription abandonment at the pharmacy, decreased adherence, and more frequent drug discontinuation. In turn, these may lead to worse health outcomes and an increased use of the medical system, especially among people with chronic diseases.[15-20] Conversely, reducing out-of-pocket costs (e.g., through manufacturer copayment-assistance programs or by prescribing generic drugs instead of more costly brand-name products) has been associated with improved adherence.[21] Given the clear association between out-of-pocket costs and the ability to pay for and adhere to medications, clinicians should minimize out-of-pocket drug-related expenses for people with HIV whenever possible. However,

many of the cost-sharing arrangements that determine out-of-pocket costs are not transparent to clinicians or people with HIV at the time decisions on ART are made.

Maximum allowable copayments on prescription drugs covered by Medicaid can vary by family income, but they are usually nominal. For commercial insurers, cost sharing is generally subject to maximum payment rules under the Affordable Care Act (ACA). Manufacturer cost-sharing assistance programs are available for most brand-name ARV products but may be restricted by pharmacy and by state. Manufacturer copay assistance may also be subject to copay accumulator programs implemented by insurers' pharmacy benefit managers, whereby manufacturer payments do not count toward a person's deductible or out-of-pocket maximum.

Medicare Part D plan cost sharing can include deductibles and copayments or coinsurance, including out-of-pocket payments of up to 25% on prescription drugs, until total out-of-pocket spending reaches approximately $3,300 in 2024 and $2,000 in 2025.[22-25] Medicare Part B cost sharing on provider-administered drugs, such as LA CAB/RPV or ibalizumab-uiyk (IBA) infusions, can be up to 20% of all medication costs.[26] Low-income beneficiaries may qualify for subsidies to defray Part D cost-sharing payments or for the Qualified Medicare Beneficiary program to defray Part B cost-sharing payments. Beginning in 2025, Medicare Advantage and Part D plans will be required to offer beneficiaries an option to enroll in a Medicare Prescription Payment Plan authorized under the Inflation Reduction Act of 2022, allowing beneficiaries to pay out-of-pocket prescription drug costs in the form of capped monthly payments instead of a single payment in full at the pharmacy.[27] Manufacturer copay assistance programs may not be applied toward Medicare plan cost sharing, but assistance from independent foundations (e.g., Patient Access Network Foundation, Patient Advocate Foundation) may provide cost-sharing support if financial eligibility criteria are met.

AIDS Drug Assistance Programs (ADAPs), through the Ryan White HIV/AIDS Program (RWHAP), make ARVs and other prescription drugs accessible to people with HIV who are underinsured and have limited financial resources. Furthermore, many ADAPs provide premium and cost-sharing assistance to eligible clients covered by Medicaid, commercial insurance plans, or Medicare.[28]

Generic Antiretrovirals and Multi-Tablet Regimens

The U.S. health care system saved $408 billion in 2022 from using generic drugs and biosimilar products, including $130 billion in Medicare savings and $194 billion in savings for commercial insurers.[29]

With substantial improvements in the long-term safety and effectiveness of contemporary ART, a number of regimens and regimen components in Tables 6a and 6b remain listed beyond their patent protection date and are or will be available as lower-cost generic options. In one study, the savings associated with a transition to a hypothetical lower-cost generic ART could potentially help cover the 20-year, $480 billion projected costs to reach national treatment targets.[5]

Some research informs the cost impact of using specific generic ARV regimens or regimen components. In a cost-effectiveness analysis conducted before the availability of integrase strand transfer inhibitors (INSTIs), the use of generic efavirenz (EFV) had an estimated savings of nearly $1 billion, and a regimen with generic EFV was very cost-effective.[2] Another study described a 25% reduction in both the wholesale acquisition cost (WAC)and federal supply schedule cost associated with switching from branded coformulated dolutegravir (DTG)/abacavir (ABC)/lamivudine (3TC) to branded DTG plus generic ABC and generic 3TC.[2,30]

A number of generic options for ARV regimen components included in Tables 6a and 6b are commercially available. See Table 22b below for a summary of the costs associated with commonly used generic and proprietary ARV regimen components and coformulations.

There is keen interest in assessing the economic value of using newer, more expensive drugs compared with older, less expensive drugs that have established clinical safety and efficacy. One study investigated the cost-effectiveness of TDF-based versus tenofovir alafenamide (TAF)–based regimens.[22] The study demonstrated that the similar efficacy—but slightly improved toxicity profile—of the TAF-based regimens would justify a $1,000 higher annual premium for the TAF-based regimens. The study further highlighted that once generic TDF becomes available at much lower costs, TAF-based regimens will remain cost-effective only if their annual cost is no more than $1,000 above that of generically available TDF-based regimens. Of note, generic TDF was approved in 2018.

The use of DTG plus generic 3TC for initial therapy has been evaluated in a cost-containment analysis. One study projected that if just 50% of people with newly diagnosed HIV initiated a two-pill regimen consisting of branded DTG plus generic 3TC, the cost savings would reach $550 million to $800 million over 5 years.[31] If 25% of people with sustained viral suppression switched to branded DTG plus generic 3TC maintenance therapy, cost savings were projected to exceed $3 billion in just 5 years.[31]

Because all commercially available STRs are branded products, including those containing ARV components that are no longer patent protected, use of generics in the United States may necessitate modest increases in pill burden, but without changes in drug frequency. One study of Medicare Part D spending, which included expenditures for one ARV fixed-dose combination tablet (ABC/3TC), demonstrated that separating brand-name coformulated products into their generic components could have saved Medicare an estimated $2.7 billion from 2011 through 2016, and it highlighted this approach as a critical cost-containment measure.[32] A benefit of STRs is that they eliminate the risk that one drug in the regimen will be temporarily or permanently discontinued because of prescribing error, unsynchronized refill schedules, or prohibitive out-of-pocket costs. Data to support or refute the superiority of once-daily STRs versus once-daily multi-tablet regimens, particularly based on virologic outcomes and especially following viral suppression, remain limited. One large observational cohort study demonstrated a small but statistically significant virologic efficacy benefit associated with STRs.[33] In this study, the time to treatment discontinuation was shorter for non-STRs than for STR once-daily regimens; however, this difference disappeared when modifications for regimen simplification were included in the analysis. On the other hand, observational data from Spain showed that coformulated DTG/ABC/3TC resulted in similar viral suppression compared to DTG plus ABC/3TC, both when used as an initial ARV regimen and when persons with viral suppression on STR were switched to the two-pill formulation as a cost-saving strategy.[34]

Importantly, when the costs of brand-name drug products and generic ARV drugs are compared, savings associated with generic ARV drugs may vary when branded drugs are subject to discounts or rebates across public and private payer systems. Although generic drug products may be associated with societal cost savings and, specifically, savings for public payers, commercial insurers, and people with HIV with significant out-of-pocket pharmacy expenses, manufacturer copay assistance is not generally available to commercially insured individuals. In cases where manufacturer copay assistance may be available for a brand-name ARV product but not for the equivalent generic product, the generic drug prescription may paradoxically result in higher out-of-pocket costs.

Costs and Cost-Effectiveness of ARV Regimens for Highly Treatment-Experienced People With Multidrug-Resistant HIV

For people with multidrug-resistant (MDR) HIV, an ARV regimen that includes intravenous IBA, subcutaneous lenacapavir, or oral fostemsavir can be effective in achieving viral suppression, but with high associated costs. Two cost-effectiveness analyses using independent simulation models have demonstrated that IBA-containing ARV regimens would substantially improve survival for people with MDR HIV but at a high cost per quality-adjusted life-year, given the high cost of IBA. However, the overall budget impact of such regimens would be relatively small, given the limited number of people for whom IBA would be necessary.[35,36]

Laboratory Services

In the context of lifelong ART, the amount of money saved by performing infrequent or one-time tests (e.g., genotypes, serologies) is modest, even for expensive tests. Even so, judicious use of laboratory testing, without compromising individual care, can still be an important way to reduce costs. For people with deductibles for laboratory tests, decreasing the use of tests with limited clinical value could reduce costs and improve adherence to a care plan. Several studies have examined the value of laboratory services in HIV care. One cost analysis study suggested that there may be no clinical benefit to continuing CD4 T lymphocyte (CD4) cell monitoring in people with suppressed viral loads and CD4 counts >200 cells/mm^3 after 48 weeks of therapy.[19] In the United States, reducing biannual CD4 monitoring to annual monitoring could save approximately $10 million per year.[37] Another study reviewed the records of 429 hospitalizations for 274 people with HIV at a single site during a 6-month period. The inpatient chart review demonstrated that 45% of ordered laboratory tests were not indicated, including hepatitis serologies, other serologies, and cytomegalovirus polymerase chain reaction tests. During this 6-month period, the estimated cost of excess and inappropriate laboratory testing totaled between $14,000 and $92,000.[38]

Cost-effectiveness analyses from 2001 and 2005 demonstrated the value of genotypic resistance testing in people who are ART-experienced and ART-naive and supported the recommendation by the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) to perform resistance testing before ART initiation and at time of virologic failure.[39,40] More recent cost-effectiveness analyses have revisited the value of baseline, pre-treatment genotype testing in the setting of INSTI plus two-nucleoside reverse transcriptase inhibitor (NRTI) regimens. One modeling study suggested that INSTI-specific genotype testing before initiation of a regimen including DTG plus two NRTIs was not cost-effective and may lead to underutilization of INSTIs; the results highlighted that some people with minor INSTI resistance mutations would still become virologically suppressed on a DTG-based regimen.[41] A second modeling study found that standard (NRTI, non-nucleoside reverse transcriptase inhibitor, protease inhibitor) genotype testing before ART initiation was also not cost-effective, because it may have little impact on outcomes given the use of regimens including an INSTI plus two NRTIs in first-line treatment.[42] Both of these modeling studies assessed the use of genotype testing only for decision-making for initial ART and presumed that such testing would be available for use at the time of first-line failure. The results of these modeling studies suggest that additional clinical research is needed to define the role of genotypic resistance testing before initiation of a regimen including an INSTI plus two NRTIs. Importantly, these modeling data do not apply to the initiation of two-drug ARV regimens (e.g., DTG plus 3TC) or to people who have received cabotegravir (CAB) as pre-exposure prophylaxis (PrEP), which are both being prescribed increasingly in clinical practice. It should be noted that the Panel continues to recommend baseline

testing for clinically relevant protease and reverse transcriptase mutations for most people, with additional genotypic resistance testing for integrase mutations for individuals with a history of CAB use for PrEP (see Drug-Resistance Testing).

Costs and Cost-Effectiveness of Comprehensive HIV Care

Comprehensive person-centered HIV care offers substantial clinical benefits.[43] Such programs include integration of social service needs and services for mental health, substance use disorders, sexual health, and age-associated multimorbidity (see Substance Use Disorders and HIV, Transgender People With HIV, Adherence to the Continuum of Care, and HIV and the Older Person). Integrated services can improve engagement in care and virologic suppression among people with HIV, but they require investment and resources. Several cost-effectiveness analyses have demonstrated that integrated care programs can offer excellent value, especially if delivered to people at increased risk of disengagement in care.[44-46]

Health care access in the United States can be inequitable and limited, depending on location and income. Although the ACA has substantially improved access to HIV clinical services in many regions of the United States since 2010, an estimated 36% of people with HIV in the United States live in the 11 states that had not expanded Medicaid in accordance with the ACA as of August 2020.[28]

The RWHAP provides a critical source of outpatient HIV clinical care for people with HIV who have low income and remain uninsured or underinsured under the ACA, or who require wraparound support.[28] A recent cost-effectiveness analysis underscored the value of this safety net program and projected its clinical and cost impact over 50 years. Given higher rates of virologic suppression among people with HIV attending RWHAP clinics (compared with estimated virologic suppression in the absence of such supports), the analysis projects fewer HIV incident infections and longer life expectancy and demonstrates the cost-effectiveness of RWHAP.[47] However, because RWHAP is focused on HIV care and support services, people with HIV who have other important outpatient and inpatient health needs may experience underdiagnosis and undertreatment if they cannot pay the out-of-pocket costs of clinical care.

Comprehensive HIV care and treatment often require navigating a complex, dynamic patchwork of service delivery, and both payer and financing mechanisms. Provider awareness of this patchwork, including the array of services available to people with HIV eligible for RWHAP, is therefore essential to maximizing clinical outcomes.

Conclusion

Ideally, costs should not drive clinical care, yet they are a factor in contemporary health care. Because regimen costs may affect the ability of people with HIV to afford and adhere to therapy, understanding ART-related costs in the United States is increasingly important. Providers play a key role in ensuring optimal care while working to both (1) minimize costs for ARV drugs and avoid or minimize unnecessary laboratory monitoring and (2) retain excellent clinical outcomes in an environment of cost-containment strategies, including formulary restrictions, utilization management (e.g., prior authorization), and cost-sharing. Therefore, providers should remain informed of current insurance and payment structures, ART costs (see Table 22b below for estimates of average drug prices), out-of-pocket expenditure requirements, and available generic ARV options. Providers should work with people with HIV and their pharmacists, social workers, case managers, and peer

navigators to understand the medication benefits and any potential financial barriers to prescription fulfillment and full adherence for each person with HIV. This information will help providers identify treatment options that are safe, effective, and affordable. Engaging people with HIV in discussion about cost constraints during regimen selection will likely facilitate adherence. Additionally, providers should familiarize themselves with ARV affordability resources (such as ADAP and pharmaceutical company assistance programs for people who qualify) and refer them to such assistance if needed. Similarly, providers should help people with HIV to find comprehensive clinical care coverage when available and consider opportunities to integrate care when feasible.

Table 22a. Insurance and Health Program Prescription Drug Pricing and Access

Insurance/Health Program	Prescription Drug Pricing and Access
Medicaid	Drug manufacturers must participate in the MDRP for their drugs to be covered by Medicaid and under Medicare Part B. Manufacturers are required to pay Medicaid programs a rebate of at least 23.1% of the AMP for most brand-name drugs (13% for generics) sold to retail pharmacies or outpatient care providers (notably infused, injected, implanted, inhaled, or instilled drugs). Manufacturers pay additional rebates if this confidential AMP increases faster than the CPI-U rate of inflation. Additionally, many states negotiate with manufacturers for supplemental rebates. States are permitted to require "nominal" cost sharing for medical and pharmacy benefits for some beneficiaries, although many elect not to do so. States can obtain a waiver to allow them to apply higher cost sharing.
Medicare	ARVs are one of six "protected drug classes" under Medicare Part D. Part D plans must provide access to all, or substantially all, FDA-approved ARVs. Part D plan sponsors, or PBMs on their behalf, negotiate rebates on outpatient drugs with manufacturers; the extent of rebating is unclear. Most physician-administered drugs and biologics are covered under Medicare Part B at a set cost: ASP plus 6%. This pricing mechanism controls spending by narrowing the spread between what is actually paid for the drug and what is actually billed to Medicare. Premiums and cost-sharing payments may be significant for both services and prescription drugs, although caps on out-of-pocket spending for drugs covered under Medicare Part D went into effect in 2024; Part A (hospital care) and Part B place no cap on out-of-pocket spending. Some subsidies and supplemental coverage are offered for low-income beneficiaries. Manufacturer copay assistance programs cannot be applied to Part B or Part D cost sharing; cost-sharing support is available from ADAPs, foundations, and other sources and is based on financial eligibility criteria.
Commercial Insurance	Private insurance plans, or PBMs on their behalf, negotiate rebates on inpatient and outpatient drugs with manufacturers; the extent of rebating is unclear. Formulary restrictions and utilization management (prior authorization, step therapy, higher cost sharing) involving drugs and biologics covered under plans' pharmacy benefit or medical benefit (e.g., infused or injected ARVs) are possible cost-containment measures. Cost sharing can be highly variable. Manufacturer copay assistance programs can be applied in most cases but may not count toward annual ACA cost-sharing limits; cost-sharing support is also available from ADAPs, foundations, and other sources and is based on financial eligibility criteria.

Table 22a. Insurance and Health Program Prescription Drug Pricing and Access

Insurance/Health Program	Prescription Drug Pricing and Access
ADAPs	Significant discounting on most ARVs negotiated by the ADAP Crisis Task Force is allowed under the 340B Drug Pricing Program. There is usually no cost sharing for ADAP clients who are uninsured. ADAP can assist with commercial or public insurance out-of-pocket costs.
Veterans Affairs	The FCP is the maximum price manufacturers may charge the four largest federal purchasers of pharmaceuticals (the "Big Four"): the U.S. Department of Veterans Affairs (VA), Department of Defense, Public Health Service (including the Indian Health Service), and the Coast Guard. The FCP of a drug includes a 24% discount on a drug's average price paid by non-federal purchasers. Additional discounts may be applied if non-federal purchase prices increase faster than the CPI-U inflation rate. Big Four prices may be 40% to 50% below list prices. The VA may negotiate further price reductions. Prescription drug cost sharing is generally nominal; medications are not withheld from those who cannot afford cost-sharing expenses.
Community Health Centers	Many community health centers are enrolled in the 340B Drug Pricing Program, which allows discounted drug purchasing using the MDRP formula. Discounts start at 23.1% off AMP, with additional discounts if the AMP increases faster than the CPI-U rate of inflation. Cost sharing in community health centers is first driven by payer source. For clients who are uninsured, cost sharing, if required, is typically based on a sliding fee scale.

Key: ACA = Affordable Care Act; ADAP = AIDS Drug Assistance Program; AMP = average manufacturer price; ARV = antiretroviral; ASP = average sales price; CPI-U = consumer price index-urban; FCP = federal ceiling price; FDA = U.S. Food and Drug Administration; MDRP = Medicaid Drug Rebate Program; PBM = pharmacy benefits manager

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

Table 22b includes three benchmark prices, rounded to the nearest dollar, for commonly used antiretroviral (ARV) drugs[a] as a general reference for health care providers when considering the cost of HIV treatment. Health care providers should contact pharmacies or payers regarding actual prices, comparative cost savings, formulary restrictions, and cost-sharing requirements. The wholesale acquisition cost (WAC) is the list price published by manufacturers for prescription drugs or biologics sold to wholesalers. The WAC price approximates what retail pharmacies pay wholesalers for single-source (e.g., brand-name) drugs. There is a range of WAC prices for generic ARV drugs because these are multiple-source products with variable list prices. With increasing competition, actual transactional prices of generic drugs decrease substantially among wholesalers and pharmacies. Average wholesale price (AWP) has historically been used as the basis for setting public (e.g., Medicaid) and private (e.g., commercial insurer) reimbursement rates for pharmacies. Neither WAC nor AWP includes variable price concessions along supply and payment chains, including discounts and rebates to wholesalers, pharmacies, federal purchasers (e.g., the Department of Veterans Affairs), pharmacy benefit managers, commercial insurers, Medicaid, 340B pharmacies, and AIDS Drug Assistance Programs. The availability of these discounts and rebates depends on product demand, market competition, and WAC price increases set by manufacturers. Maximum Medicaid payment rates are assigned to generic products with three or more therapeutically and pharmaceutically equivalent products, as determined by the U.S. Food and Drug Administration. This federally established pharmacy reimbursement limit is the federal upper limit (FUL). Federal Medicaid will reimburse state Medicaid programs up to this limit for multiple-source drugs (plus the dispensing fee); states may set their own state maximum allowable costs and commercial insurers set their own reimbursement upper limits with pharmacies. While WACs and AWPs are generally set annually, FULs are adjusted on a monthly basis, particularly for multiple-source drugs with fluctuating pharmacy acquisition costs. In this table, the FUL for a drug is described as "pending" if a generic drug currently lacks the required competition.

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
NRTIs					
Abacavir					
Generic	300-mg tablet	60 tablets	$100 to $150	$578 to $603	$48
Ziagen	300-mg tablet	60 tablets	$559	$670	N/A
Emtricitabine					
Generic	200-mg capsule	30 capsules	$390 to $464	$482 to $579	Pending

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Emtriva	200-mg capsule	30 capsules	$537	$644	N/A
Lamivudine					
Generic	300-mg tablet	30 tablets	$40 to $415	$429	$39
Epivir	300-mg tablet	30 tablets	$416	$499	N/A
Tenofovir Disoproxil Fumarate					
Generic	300-mg tablet	30 tablets	$27 to $300	$167 to $1,216	$42
Viread	300-mg tablet	30 tablets	$1,254	$1,504	N/A
Zidovudine					
Generic	300-mg tablet	60 tablets	$36 to $54	$54 to $365	$13
NRTI Combination Products					
Abacavir/Lamivudine					
Generic	600-mg/300-mg tablet	30 tablets	$100 to $302	$1,393 to $1,395	$40
Tenofovir Alafenamide/Emtricitabine					
Descovy	25-mg/200-mg tablet	30 tablets	$2,202	$2,643	N/A
Tenofovir Disoproxil Fumarate/Emtricitabine					
Generic	300-mg/200-mg tablet	30 tablets	$25 to $420	$70 to $2,100	$15
Truvada	300-mg/200-mg tablet	30 tablets	$1,842	$2,211	N/A
Tenofovir Disoproxil Fumarate/Lamivudine					
Cimduo	300-mg/300-mg tablet	30 tablets	$1,185	$1,422	N/A
Zidovudine/Lamivudine					
Generic	300-mg/150-mg tablet	60 tablets	$125 to $578	$265 to $932	$44

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
NNRTIs					
Efavirenz					
Generic	600-mg tablet	30 tablets	$80 to $894	$1,043 to $1,118	$55
Doravirine					
Pifeltro	100-mg tablet	30 tablets	$1,760	$2,112	N/A
Etravirine					
Generic	200-mg tablet	60 tablets	$1,287	$1,609	$878
Intelence	200-mg tablet	60 tablets	$1,469	$1,762	N/A
Nevirapine					
Generic	200-mg tablet	60 tablets	$10 to $45	$648 to $651	$47
Generic XR	400-mg tablet	30 tablets	$135 to $565	$595 to $706	$149
Viramune XR	400-mg tablet	30 tablets	$840	$1,008	N/A
Rilpivirine					
Edurant	25-mg tablet	30 tablets	$1,483	$1,780	N/A
PIs					
Atazanavir					
Generic	200-mg capsule	60 capsules	$178 to $316	$1,502 to $1,668	$711
Reyataz	200-mg capsule	60 capsules	$1,463	$1,756	N/A
Generic	300-mg capsule	30 capsules	$178 to $316	$1,502 to $1,652	$187
Reyataz	300-mg capsule	30 capsules	$1,449	$1,739	N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Atazanavir/Cobicistat					
Evotaz	300-mg/150-mg tablet	30 tablets	$1,605	$1,927	N/A
Darunavir					
Generic	600-mg tablet	60 tablets	$60 to $1,145	$1,373 to $2,388	Pending
Prezista	600-mg tablet	60 tablets	$2,158	$2,590	N/A
Generic	800-mg tablet	30 tablets	$60 to $1,153	$1,384 to $2,388	Pending
Prezista	800-mg tablet	30 tablets	$2,158	$2,590	N/A
Prezista	100-mg/mL suspension	200 mL	$1,199	$1,439	N/A
Darunavir/Cobicistat					
Prezcobix	800-mg/150-mg tablet	30 tablets	$2,467	$2,960	N/A
Lopinavir/Ritonavir					
Generic	200-mg/50-mg tablet	120 tablets	$885	$1,106	Pending
Kaletra	200-mg/50-mg tablet	120 tablets	$1,024	$1,229	N/A
Tipranavir					
Aptivus	250-mg capsule	120 capsules	$2,054	$2,466	N/A
INSTIs					
Dolutegravir					
Tivicay	50-mg tablet	30 tablets	$2,257	$2,709	N/A
Tivicay	50-mg tablet	60 tablets	$4,514	$5,418	N/A
Raltegravir					
Isentress	400-mg tablet	60 tablets	$1,997	$2,396	N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Isentress HD	600-mg tablet	60 tablets	$1,997	$2,396	N/A
Fusion Inhibitor					
Enfuvirtide					
Fuzeon	90-mg injection kit	60 doses (1 kit)	$3,586	$4,303	N/A
CCR5 Antagonist					
Maraviroc					
Generic	150-mg tablet	60 tablets	$1,141	$1,764	$1,659
Selzentry	150-mg tablet	60 tablets	$1,730	$2,076	N/A
Generic	300-mg tablet	60 tablets	$1,141	$1,764	$1,518
Selzentry	300-mg tablet	60 tablets	$1,730	$2,076	N/A
Selzentry	300-mg tablet	120 tablets	$3,460	$4,152	N/A
CD4-Directed Post-Attachment Inhibitor					
Ibalizumab-uiyk					
Trogarzo	200-mg vial	8 vials	$11,840	$14,208	N/A
gp120-Directed Attachment Inhibitor					
Fostemsavir					
Rukobia	600-mg tablet	60 tablets	$9,010	$10,812	N/A
Capsid Inhibitor					
Lenacapavir					
Sunlenca	300-mg tablet	4 tablets	$3,250	$3,900	N/A
Sunlenca	300-mg tablet	5 tablets	$4,063	$4,875	N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Sunlenca	927-mg injection kit	2 vials (1 kit every 6 months)	$19,500 (every 6 months)	$23,400 (every 6 months)	N/A
Coformulated Combination Products as Single-Tablet Regimens					
Bictegravir/Tenofovir Alafenamide/Emtricitabine					
Biktarvy	50-mg/25-mg/200-mg tablet	30 tablets	$3,981	$4,777	N/A
Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine					
Symtuza	800-mg/150-mg/10-mg/ 200-mg tablet	30 tablets	$4,717	$5,660	N/A
Dolutegravir/Abacavir/Lamivudine					
Triumeq	50-mg/600-mg/300-mg tablet	30 tablets	$3,748	$4,497	N/A
Dolutegravir/Lamivudine					
Dovato	50-mg/300-mg tablet	30 tablets	$2,977	$3,572	N/A
Dolutegravir/Rilpivirine					
Juluca	50-mg/25-mg tablet	30 tablets	$3,512	$4,215	N/A
Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine					
Delstrigo	100-mg/300-mg/300-mg tablet	30 tablets	$2,680	$3,216	N/A
Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine					
Generic	600-mg/300-mg/200-mg tablet	30 tablets	$82 to $252	$302 to $3,414	$54
Atripla	600-mg/300-mg/200-mg tablet	30 tablets	$2,995	$3,594	N/A
Efavirenz/Tenofovir Disoproxil Fumarate/Lamivudine					
Symfi	600-mg/300-mg/150-mg tablet	30 tablets	$1,926	$2,312	N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Symfi Lo	400-mg/300-mg/150-mg tablet	30 tablets	$1,926	$2,312	N/A
Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine					
Genvoya	150-mg/150-mg/10-mg/ 200-mg tablet	30 tablets	$33,981	$4,777	N/A
Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine					
Stribild	150-mg/150-mg/300-mg/ 200-mg tablet	30 tablets	$4,176	$5,012	N/A
Rilpivirine/Tenofovir Alafenamide/Emtricitabine					
Odefsey	25-mg/25-mg/200-mg tablet	30 tablets	$3,623	$4,348	N/A
Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine					
Complera	25-mg/300-mg/200-mg tablet	30 tablets	$3,454	$4,145	N/A
Copackaged Combination Products as Injectable Regimens					
Cabotegravir + Rilpivirine					
Cabenuva	600 mg (3 mL) 900 mg (3 mL)	2 vials (every other month)	$6,624 (every other month)	$7,948 (every other month)	N/A
Cabenuva	400 mg (2 mL) 600 mg (2 mL)	2 vials	$4,416	$5,299	N/A
PK Enhancers (Boosters)					
Cobicistat					
Tybost	150-mg tablet	30 tablets	$297	$357	N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	Strength, Formulation	Capsules, mLs, Tablets, or Vials	Wholesale Acquisition Cost[b]	Average Wholesale Price[b]	Federal Upper Limit (As of July 31, 2024)[c]
		(Monthly Values, Unless Otherwise Noted)			
Ritonavir					
Generic	100-mg tablet	30 tablets	$80 to $160	$278	$74
Norvir	100-mg tablet	30 tablets	$257	$309	N/A

[a] The following less commonly used ARV drugs are not included in this table: fosamprenavir and nelfinavir.

[b] **Source:** Micromedex Red Book [database]. Merative. 2024. Available at: https://www.micromedexsolutions.com.

[c] **Source:** Federal Upper Limits–March 2024 [database]. Medicare & Medicaid Services. 2024. Available at: https://www.medicaid.gov/medicaid/prescription-drugs/pharmacy-pricing/index.html.

Key: ARV = antiretroviral; CD4 = CD4 T lymphocyte; HD = high dose; INSTI = integrase strand transfer inhibitor; N/A = not applicable; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; XR = extended release

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Drug–Drug Interactions

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Overview

Pharmacokinetic (PK) drug–drug interactions between antiretroviral (ARV) drugs and concomitant medications are common and may lead to increased or decreased drug exposure. In some instances, changes in drug exposure may increase the frequency and/or severity of toxicities or affect therapeutic responses. When prescribing or switching one or more drugs in an ARV regimen, clinicians must consider the potential for drug–drug interactions—both those affecting ARVs and those affecting concomitant drugs. A thorough review of concomitant medications in consultation with an expert in ARV pharmacology can help in designing a regimen that minimizes undesirable interactions. Recommendations for managing a specific drug interaction may differ depending on whether a new ARV is being initiated in a patient on a stable concomitant medication or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of interactions are difficult to predict when several drugs with competing metabolic pathways and drug transporter systems are prescribed concomitantly. When it is necessary to prescribe interacting drugs, clinicians should be vigilant in monitoring for therapeutic efficacy and/or concentration-related toxicities. Tables 24a through 25b provide information on known or suspected drug interactions between ARV agents and commonly prescribed medications based on published PK data or information from product labels. The tables provide general guidance on drugs that should not be coadministered and recommendations for dose modification of ARVs or concomitant medicines or for alternative therapy.

Mechanisms of Pharmacokinetic Interactions

PK interactions may occur during absorption, metabolism, or elimination of the ARV and/or the interacting drugs. The most common drug interaction mechanisms are described and listed for individual ARV drugs in Table 23 below.

Pharmacokinetic Interactions Affecting Drug Absorption

The extent of oral absorption of drugs can be affected by the following mechanisms:

- Acid-reducing agents—such as proton pump inhibitors, H2 antagonists, or antacids—can reduce the absorption of ARV drugs that require gastric acidity for optimal absorption (i.e., atazanavir and rilpivirine).
- Products that contain polyvalent cations—such as supplements, iron products, or antacids that contain aluminum, calcium, or magnesium—can bind to integrase strand transfer inhibitors (INSTIs) and reduce absorption of these ARV agents.
- Drugs that induce or inhibit the enzyme cytochrome P450 (CYP) 3A4 or efflux transporter P-glycoprotein in the intestines may reduce or promote the absorption of other drugs.

Pharmacokinetic Interactions Affecting Hepatic Metabolism

Two major enzyme systems are most frequently responsible for clinically significant drug interactions:

- The CYP enzyme system is responsible for the metabolism of many drugs, including non-nucleoside reverse transcriptase inhibitors, protease inhibitors, the CCR5 antagonist maraviroc, and the INSTI elvitegravir. CYP3A4 is the most common enzyme responsible for drug metabolism, though multiple enzymes may be involved in the metabolism of a drug. ARV drugs and concomitant medications may be inducers, inhibitors, and/or substrates of these enzymes.
- The uridine diphosphate glucuronosyltransferase (UGT) 1A1 enzyme is the primary enzyme responsible for the metabolism of the INSTIs cabotegravir and raltegravir. Drugs that induce or inhibit the UGT enzyme can affect the PK of these INSTIs.
- The INSTIs bictegravir and dolutegravir (DTG) and the capsid inhibitor lenacapavir have mixed metabolic pathways, including both CYP3A4 and UGT1A1. Drugs that induce or inhibit these enzymes may have variable impact on the PK of these ARVs.

Pharmacokinetic Enhancers (Boosters)

PK enhancing is a strategy used to increase exposure of an ARV by concomitantly administering a drug that inhibits the enzymes that metabolize the ARV. Currently, two agents are used as PK enhancers: ritonavir (RTV) and cobicistat (COBI). Both drugs are potent inhibitors of the CYP3A4 enzyme and, thus, when coadministered with ARVs metabolized by the CYP3A4 pathway, the resultant systemic exposure of the ARVs is higher. Importantly, RTV and COBI have different effects on other CYP- or UGT-metabolizing enzymes and drug transporters. Complex or unknown mechanisms of PK-based interactions preclude extrapolation of RTV drug interactions to certain COBI interactions, such as interactions with warfarin, direct oral anticoagulants, phenytoin, voriconazole, oral contraceptives, and certain hydroxy-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (or statins).

Other Mechanisms of Pharmacokinetic Interactions

Drug transporters are expressed in various tissues, and they play an important role in drug disposition. Knowledge of drug transporters is evolving, elucidating additional drug interaction mechanisms. For example, DTG decreases the renal clearance of metformin by inhibiting organic cation transporters in renal tubular cells. Similar transporters aid hepatic, renal, and biliary clearance of drugs and may be susceptible to drug interactions. ARVs and concomitant medications may be inducers, inhibitors, and/or substrates of these drug transporters. The influence of drug transporters on drug–drug interactions is complex, and the clinical significance of these interactions is unclear but is under investigation. Further research is needed to better understand these pathways and the clinical significance of this drug interaction mechanism.

Role of Therapeutic Drug Monitoring in Managing Drug–Drug Interactions

Therapeutic drug monitoring (TDM) can guide the dosing of certain medications by using measured drug concentrations to improve the likelihood of desired therapeutic and safety outcomes. Drugs suitable for TDM are characterized by a known exposure-response relationship and a therapeutic range of concentrations. The “therapeutic range” is a range of concentrations established through clinical investigations that are associated with a greater likelihood of achieving the desired therapeutic response and/or reducing the frequency of drug-associated adverse reactions.

When concomitant use of an ARV drug and another medication is likely to result in a clinically important drug–drug interaction, the first step is to assess whether other, equally effective treatment options can be

used to avoid the interaction. If that is not possible, TDM may be useful in assessing whether a dose adjustment is needed.

Drug concentration assays for some ARV drugs are commercially available; however, result reporting may take 1 week or longer. When interpreting assay results, clinicians should consider the patient's medication adherence, the timing of the patient's last ARV dose and blood draw, and the time elapsed since coadministration of the interacting drug combination. If needed, a specialist in ARV clinical pharmacology should be consulted when interpreting the results and deciding what actions to take. If a dose adjustment is needed, TDM must be repeated after the dose-adjusted drug reaches steady state to ensure appropriate dosing.

TDM information should not be used alone; it must be considered in conjunction with other clinical information—including virologic response, medication adherence, and signs and symptoms of drug toxicities—to assure safe and effective therapy.

Table 23. Mechanisms of Antiretroviral-Associated Drug Interactions

Pharmacokinetic interactions may occur during absorption, metabolism, or elimination of the antiretroviral (ARV) drug and/or the interacting drug. This table does not include a comprehensive list of all possible mechanisms of interactions for individual ARV drugs (e.g., transporters); however, the table lists the most common mechanisms of known interactions and focuses on absorption and cytochrome P450 (CYP)– and uridine diphosphate glucuronosyltransferase (UGT) 1A1–mediated interactions.

Note: N/A indicates that there are no clinically relevant interactions by the mechanism. Identified mechanisms are specific to the ARV drugs described in the row and may not be reflective of complete ARV regimens. Some older ARVs—unboosted atazanavir, fosamprenavir, nelfinavir, nevirapine, tipranavir, and zidovudine—are not commonly used in clinical practice and are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions for these ARVs.

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or Are Induced or Inhibited by ARV Drugs			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
INSTIs							
BIC	N/A	Concentrations of PO INSTIs are decreased by-products that contain polyvalent cations (e.g., Ca, Mg, Al, Fe, Zn).	Substrate	3A4	N/A	N/A	Substrate
CAB	N/A		Substrate	N/A	N/A	N/A	Substrate
DTG	N/A		Substrate	3A4 (minor)	N/A	N/A	Substrate
EVG/c	N/A		Inhibitor	3A4	3A4, 2D6	2C9	Substrate
RAL	N/A		N/A	N/A	N/A	N/A	Substrate
PIs							
ATV/c	Concentration decreased	N/A	Substrate, inhibitor	3A4	3A4, 2D6, 2C8	N/A	Inhibitor
ATV/r	Concentration decreased	N/A	Substrate, inhibitor	3A4, 2D6	3A4, 2D6, 2C8	1A2, 2B6, 2C8, 2C9, 2C19	**ATV:** Inhibitor **RTV:** Inducer
DRV/c	N/A	N/A	Substrate, inhibitor	3A4	3A4, 2D6	N/A	No data
DRV/r	N/A	N/A	Substrate, inhibitor	3A4, 2D6	3A4, 2D6	1A2, 2B6, 2C8, 2C9, 2C19	Inducer
LPV/r	N/A	N/A	Substrate	3A4, 2D6	3A4	1A2, 2B6, 2C8, 2C9, 2C19	Inducer

Table 23. Mechanisms of Antiretroviral-Associated Drug Interactions

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or Are Induced or Inhibited by ARV Drugs			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
NNRTIs							
DOR	N/A	N/A	N/A	3A4, 3A5	N/A	N/A	N/A
EFV	N/A	N/A	N/A	2B6 (primary), 2A6, 3A4	3A4	3A4, 2B6, 2C19	N/A
ETR	N/A	N/A	N/A	3A4, 2C9, 2C19	2C9, 2C19	3A4	N/A
RPV	**Only RPV PO:** Concentration decreased	N/A	N/A	3A4	N/A	N/A	N/A
NRTIs							
ABC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
FTC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
3TC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
TAF	N/A	N/A	Substrate	N/A	N/A	N/A	N/A
TDF	N/A	N/A	Substrate	N/A	N/A	N/A	N/A
Capsid Inhibitor							
LEN (SQ and PO)	N/A	N/A	Substrate	3A4	3A4	N/A	Substrate
CCR5 Antagonist							
MVC	N/A	N/A	Substrate	3A4	N/A	N/A	N/A
gp120-Directed Attachment Inhibitor							
FTR	N/A	N/A	Substrate	3A4	N/A	N/A	N/A
Fusion Inhibitor							
T-20	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Table 23. Mechanisms of Antiretroviral-Associated Drug Interactions

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or Are Induced or Inhibited by ARV Drugs			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
Post-Attachment Inhibitor							
IBA	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; Ca = calcium; CAB = cabotegravir; CCR5 = C-C chemokine receptor type 5; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; FTR = fostemsavir; gp120 = glycoprotein 120; IBA = ibalizumab; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; Mg = magnesium; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitors; NRTI = nucleoside reverse transcriptase inhibitors; P-gp = P-glycoprotein; PI = protease inhibitor; PO = oral; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT = uridine diphosphate glucuronosyltransferase; Zn = zinc

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

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This table provides information on the known or predicted interactions between protease inhibitors (PIs) and non-antiretroviral (ARV) drugs. The term "PI" refers to atazanavir (ATV) or darunavir (DRV) boosted with either ritonavir (RTV or r) or cobicistat (COBI or c). This table does not include interactions for unboosted ATV, fosamprenavir (FPV), lopinavir (LPV), nelfinavir (NFV), or tipranavir (TPV). For information regarding interactions between PIs and other ARV drugs, including dosing recommendations, refer to Tables 24c, 25a, and 25b.

Recommendations for managing a particular drug interactions may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Note: Unboosted ATV, FPV, LPV/r, NFV, and TPV are no longer commonly used in clinical practice in the United States and are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between these PIs and concomitant medications. Information regarding these agents may also be found in archived versions of this guideline.

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	ATV/c, ATV/r	**When Given Simultaneously** • ↓ ATV expected	Administer ATV at least 2 hours before or 2 hours after antacids or buffered medications.
H2 Receptor Antagonists	ATV/c, ATV/r	↓ ATV expected	H2RA dose should not exceed a dose equivalent to famotidine 40 mg twice daily in ART-naive patients or famotidine 20 mg twice daily in ART-experienced patients. Give ATV 300 mg (plus COBI 150 mg **or** RTV 100 mg) with food simultaneously with and/or ≥10 hours after the dose of H2RA.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			If using TDF and H2RA in ART-experienced patients, administer ATV 400 mg plus RTV 100 mg with food simultaneously with and/or ≥10 hours after the dose of H2RA. **Do not coadminister** ATV/c with TDF and H2RA in ART-experienced patients.
	DRV/c, DRV/r	**With Ranitidine** • ↔ DRV/r	No dose adjustment needed
Proton Pump Inhibitors	ATV/c, ATV/r	**With Omeprazole 40 mg** • ATV AUC ↓ 76% **When Omeprazole 20 mg Is Given 12 Hours Before ATV/c or ATV/r** • ATV AUC ↓ 42%	PPI dose should not exceed a dose equivalent to omeprazole 20 mg daily in PI-naive patients. PPIs should be administered at least 12 hours before ATV/c or ATV/r. **Do not coadminister** in PI-experienced patients.
	DRV/c	↔ PI expected	No dose adjustment needed
	DRV/r	↔ DRV/r Omeprazole AUC ↓ 42%	Consider alternative ARV or acid reducer. If coadministered, monitor for omeprazole effectiveness. If the patient does not experience symptomatic relief, increase the dose to no more than omeprazole 40 mg daily.
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ alfuzosin expected	**Contraindicated**
Doxazosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ doxazosin possible	Initiate doxazosin at lowest dose and titrate. Monitor blood pressure. Dose reduction may be necessary.
Tamsulosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ tamsulosin expected	**Do not coadminister** unless benefits outweigh risks. If coadministered, monitor blood pressure.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Terazosin	ATV/c, ATV/r, DRV/c, DRV/r	↔ or ↑ terazosin possible	Initiate terazosin at lowest dose and titrate. Monitor blood pressure. Dose reduction may be necessary.
Silodosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ silodosin expected	**Contraindicated**
Antibacterials—Antimycobacterials			
Bedaquiline	ATV/c, ATV/r, DRV/c, DRV/r	• ↑ bedaquiline possible	**Do not coadminister** unless benefits outweigh risks. If coadministered, consider therapeutic drug monitoring and monitor for bedaquiline-related adverse effects, including hepatotoxicity and QTc prolongation.
Rifabutin	ATV/r	**Compared With Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Once Daily) Plus ATV/r** • Rifabutin AUC ↑ 110% and metabolite AUC ↑ 2,101%	Recommended dose is rifabutin 150 mg once daily. Monitor for antimycobacterial activity and consider therapeutic drug monitoring. Monitor for rifabutin-related adverse events, including neutropenia and uveitis. PK data in this table are results from healthy volunteer studies. Lower rifabutin exposure has been reported in patients with HIV than in healthy study participants.
	DRV/r	**Compared With Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Every Other Day) Plus DRV/r** • ↔ rifabutin AUC and metabolite AUC ↑ 881%	
	ATV/c, DRV/c	↑ rifabutin expected ↓ COBI expected	**Do not coadminister.**
Rifampin	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI concentration by >75%	**Contraindicated.** Increasing the dose of RTV does not overcome this interaction and may increase hepatotoxicity. Increasing the COBI dose **is not recommended.** Consider rifabutin if a rifamycin is indicated.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rifapentine	ATV/c, ATV/r, DRV/c, DRV/r	**Daily and Weekly Dosing** • ↓ PI expected	**Do not coadminister.**
Antibacterials—Macrolides			
Azithromycin	ATV/c, ATV/r	↑ azithromycin possible	No dose adjustment needed
	DRV/c, DRV/r	↔ azithromycin expected	No dose adjustment needed
Clarithromycin	ATV/c, ATV/r, DRV/c	↑ clarithromycin expected ↑ ATV/r and PI/c expected	Consider alternative ARV or azithromycin.
	DRV/r	DRV/r ↑ clarithromycin AUC 57% RTV 500 mg twice daily ↑ clarithromycin 77%	Consider alternative ARV or azithromycin. If use of clarithromycin is necessary in a patient with impaired renal function, reduce clarithromycin dose by 50% in patients with CrCl 30 to 60 mL/min. In patients with CrCl <30 mL/min, reduce clarithromycin dose by 75%. Monitor for clarithromycin-related adverse events, including QTc prolongation.
Erythromycin	ATV/c, ATV/r, DRV/c, DRV/r	↑ erythromycin expected ↑ PI expected	Consider alternative ARV or use azithromycin.
Anticoagulants			
Apixaban	ATV/c, ATV/r, DRV/c, DRV/r	↑ apixaban expected	**Do not coadminister** in patients who require apixaban 2.5 mg twice daily. **In Patients Requiring Apixaban 5 mg or 10 mg Twice Daily** • Reduce apixaban dose by 50%.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Dabigatran	ATV/c, ATV/r	**With COBI 150 mg Alone** • Dabigatran AUC ↑ 110% to 127% **With ATV/r** • ↑ dabigatran expected	**Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation in Adult Patients** • CrCl >30 mL/min: no dose adjustment needed • CrCl ≤30 mL/min: do not coadminister. **Treatment and Reduction in the Risk of Recurrence of DVT and PE or Prophylaxis of DVT and PE Following Hip Replacement Surgery in Adult Patients** • CrCl ≥50 mL/min: no dose adjustment needed • CrCl <50 mL/min: do not coadminister.
	DRV/c, DRV/r	**With DRV/c** • Single dose DRV/c: dabigatran AUC ↑ 164% • After 14 days of DRV/c: dabigatran AUC ↑ 88% **With DRV/r** • Single dose DRV/r: dabigatran AUC ↑ 72% • After 14 days of daily DRV/r: dabigatran AUC ↑ 18%	
Edoxaban	ATV/c, ATV/r, DRV/c	↑ edoxaban expected	**Treatment of Nonvalvular Atrial Fibrillation** • No dose adjustment needed **Treatment of DVT and PE** • Reduce edoxaban dose to 30 mg once daily.
	DRV/r	↑ edoxaban expected	**Treatment of Nonvalvular Atrial Fibrillation** • No dose adjustment needed **Treatment of DVT and PE** • No dose adjustment needed
Rivaroxaban	ATV/c, ATV/r, DRV/c, DRV/r	↑ rivaroxaban expected	**Do not coadminister.**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Warfarin	ATV/c, DRV/c	↑ warfarin possible	Monitor INR closely when stopping or starting PI/c or PI/r and adjust warfarin dose accordingly. If switching between RTV and COBI, the effect of COBI on warfarin is not expected to be equivalent to RTV's effect on warfarin.
	ATV/r, DRV/r	↓ warfarin possible	
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
Antidepressants, Anxiolytics			
Bupropion	ATV/r, DRV/r	↓ bupropion possible	Titrate bupropion dose based on clinical response.
	ATV/c, DRV/c	↔ bupropion expected	No dose adjustment needed
Buspirone	ATV/c, ATV/r, DRV/c, DRV/r	↑ buspirone expected	Administer lowest dose of buspirone with caution and titrate buspirone dose based on clinical response. Dose reduction may be necessary. Monitor for buspirone-related adverse events.
Desvenlafaxine	ATV/c, ATV/r, DRV/c, DRV/r	↑ desvenlafaxine possible	No dose adjustment needed
Duloxetine	ATV/c, DRV/c	↑ duloxetine possible	No dose adjustment needed
	ATV/r, DRV/r	↑ or ↓ duloxetine possible	
Mirtazapine	ATV/c, ATV/r, DRV/c, DRV/r	↑ mirtazapine possible	Monitor for mirtazapine-related adverse events. Mirtazapine dose reduction may be necessary.
Nefazodone	ATV/c, ATV/r, DRV/c, DRV/r	↑ nefazodone expected ↑ PI possible	Monitor for nefazodone-related adverse events and PI tolerability.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	DRV/r	Paroxetine AUC ↓ 39% Sertraline AUC ↓ 49%	Titrate SSRI dose based on clinical response.
	ATV/c, ATV/r, DRV/c	↑ or ↓ SSRI possible	Titrate SSRI dose using the lowest available initial or maintenance dose.
Trazodone	ATV/c, ATV/r, DRV/c, DRV/r	**RTV 200 mg Twice Daily (For 2 Days)** • Trazodone ↑ AUC 240%	Administer lowest dose of trazodone and titrate dose based on clinical response. Monitor for trazodone-related adverse events, including CNS and CV adverse events.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	ATV/c, ATV/r, DRV/c, DRV/r	↑ TCA expected	Administer lowest possible TCA dose and titrate based on clinical assessment and/or drug concentrations. Monitor for TCA-related adverse events.
Venlafaxine	ATV/c, ATV/r, DRV/c, DRV/r	↑ venlafaxine and O-desmethylvenlafaxine expected	Monitor for venlafaxine-related adverse events. Consider venlafaxine dose reduction.
Antipsychotics			
Aripiprazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for effectiveness/adverse events. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6-poor metabolizers.
Brexpiprazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate the dose based on clinical monitoring for effectiveness/adverse events. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6-poor metabolizers.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cariprazine	ATV/c, ATV/r, DRV/c, DRV/r	↑ cariprazine expected	**Starting Cariprazine in a Patient Who Is Already Receiving a PI** • Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum of cariprazine 3 mg daily. If the PI is withdrawn, cariprazine dose may need to be increased. **Starting a PI in a Patient Who Is Already Receiving Cariprazine** • For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce the dose by half. For patients taking cariprazine 4.5 mg daily, the dose should be reduced to cariprazine 1.5 mg or cariprazine 3 mg daily. For patients taking cariprazine 1.5 mg daily, change to cariprazine 1.5 mg every other day. If PI is withdrawn, the cariprazine dose may need to be increased.
Iloperidone	ATV/c, ATV/r, DRV/c, DRV/r	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lumateperone	ATV/c, ATV/r, DRV/c, DRV/r	↑ lumateperone expected	**Do not coadminister.**
Lurasidone	ATV/c, ATV/r, DRV/c, DRV/r	↑ lurasidone expected	**Contraindicated**
Olanzapine, Olanzapine/Samidorphan	ATV/c, DRV/c	↔ olanzapine expected ↑ samidorphan possible	No dose adjustment needed
	ATV/r, DRV/r	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Other Antipsychotics CYP3A4 and/or CYP2D6 substrates (e.g., clozapine, perphenazine, risperidone, thioridazine)	ATV/c, ATV/r, DRV/c, DRV/r	↑ antipsychotic possible	Titrate the antipsychotic dose using the lowest initial dose or adjust the maintenance dose accordingly. Monitor for adverse events, including QTc prolongation.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Pimavanserin	ATV/c, ATV/r, DRV/c, DRV/r	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg once daily.
Pimozide	ATV/c, ATV/r, DRV/c, DRV/r	↑ pimozide expected	**Contraindicated**
Quetiapine	ATV/c, ATV/r, DRV/c, DRV/r	↑ quetiapine expected	**Starting Quetiapine in a Patient Receiving a PI** • Initiate quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine effectiveness and adverse events, including QTc prolongation. **Starting a PI in a Patient Receiving a Stable Dose of Quetiapine** • Consider alternative ARV. If coadministered, reduce quetiapine dose to 1/6 of the current dose. Closely monitor for quetiapine effectiveness and adverse events, including QTc prolongation.
Ziprasidone	ATV/c, ATV/r, DRV/c, DRV/r	↑ ziprasidone expected	Monitor for ziprasidone-related adverse events, including QTc prolongation.
Antimigraine			
Ergot Derivatives	ATV/c, ATV/r, DRV/c, DRV/r	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Contraindicated**
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ atogepant expected	Chronic migraine: **Do not coadminister.** Episodic migraine: Administer atogepant at a dose of 10 mg once daily.
Rimegepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ rimegepant expected	**Do not coadminister.**
Ubrogepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ ubrogepant expected	**Contraindicated**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Zavegepant	ATV/r, ATV/c, DRV/c	↑ zavegepant expected	**Do not coadminister.**
	DRV/r	↔ zavegepant expected	No dose adjustment needed
Serotonin 5-HT1B, 1D Receptor Agonists			
Almotriptan	ATV/c, ATV/r, DRV/c, DRV/r	↑ almotriptan expected	Administer single dose of almotriptan 6.25 mg. Maximum dose should not exceed 12.5 mg in a 24-hour period.
Eletriptan	ATV/c, ATV/r, DRV/c, DRV/r	↑ eletriptan expected	**Contraindicated**
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan Zolmitriptan	ATV/c, ATV/r, DRV/c, DRV/r	↔ triptan expected	No dose adjustment needed
Antifungals			
Fluconazole	ATV/c, ATV/r, DRV/c, DRV/r	↔ PI expected ↔ fluconazole expected	No dose adjustment needed
Isavuconazole	ATV/c, DRV/c	↑ isavuconazole expected ↓ PI possible	**Contraindicated**
	ATV/r, DRV/r	↑ isavuconazole expected ↓ PI possible	If coadministered, monitor isavuconazole concentrations and monitor for isavuconazole-related adverse events. Monitor for PI tolerability.
Ibrexafungerp	ATV/c, ATV/r, DRV/c, DRV/r	↑ ibrexafungerp expected	Reduce ibrexafungerp dose to 150 mg twice daily.
Itraconazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ itraconazole expected ↑ PI expected	Itraconazole doses >200 mg/day **are not recommended** unless dosing is guided by itraconazole concentrations.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Posaconazole	ATV/r	ATV AUC ↑ 146% ↔ posaconazole possible	If coadministered, monitor for PI-related adverse events.
	ATV/c, DRV/c, DRV/r	↑ PI expected ↔ posaconazole possible	
Voriconazole	ATV/c, DRV/c	No data	**Do not coadminister** voriconazole and RTV or COBI unless benefits outweigh risks. If coadministered, monitor voriconazole concentration and adjust dose accordingly.
	ATV/r, DRV/r	RTV 100 mg twice daily ↓ voriconazole AUC 39%	
Antimalarials			
Artemether/Lumefantrine	ATV/c, DRV/c	↑ lumefantrine expected ↑ artemether possible	Clinical significance is unknown. If coadministered, monitor closely for antimalarial effectiveness and lumefantrine-related adverse events, including QTc prolongation.
	DRV/r	↔ artemether expected ↔ DHA[a] expected Lumefantrine AUC ↑ 175% ↔ DRV	
Artesunate	ATV/c	↑ DHA[a] possible	Monitor for artesunate-related adverse effects.
	DRV/c	↔ DHA[a] expected	No dose adjustment needed
	ATV/r, DRV/r	↓ DHA[a] possible	Monitor for clinical response to artesunate.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Atovaquone/Proguanil	ATV/r, DRV/r	**With ATV/r** • Atovaquone AUC ↓ 46% • Proguanil AUC ↓ 41% **With DRV/r** • ↓ atovaquone/proguanil possible	Clinical significance is unknown. Consider alternative ARV or malaria prophylaxis.
	ATV/c, DRV/c	↔ atovaquone/proguanil expected	No dose adjustment needed
Mefloquine	ATV/c, ATV/r, DRV/c, DRV/r	**With RTV 200 mg Twice Daily** • RTV AUC ↓ 31% and C_{min} ↓ 43% • ↔ mefloquine **With ATV (Unboosted), PI/c, or PI/r** • ↑ mefloquine possible	Clinical significance is unknown. Consider alternative ARV or antimalarial drug. If coadministered, monitor for mefloquine-related adverse events, including psychiatric symptoms and QTc prolongation. Monitor virologic response.
Antiplatelets			
Clopidogrel	ATV/c, ATV/r, DRV/c, DRV/r	Clopidogrel active metabolite AUC ↓ 69% in people with HIV on RTV or COBI-boosted regimens compared with healthy volunteers without HIV. Impaired platelet inhibition observed in people with HIV.	**Do not coadminister.**
Prasugrel	ATV/c, ATV/r, DRV/c, DRV/r	Prasugrel active metabolite AUC ↓ 52% in people with HIV on RTV or COBI-boosted regimens compared to healthy volunteers without HIV. Adequate platelet inhibition observed in people with HIV.	No dose adjustment needed
Ticagrelor	ATV/c, ATV/r, DRV/c, DRV/r	↑ ticagrelor expected	**Do not coadminister.**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Vorapaxar	ATV/c, ATV/r, DRV/c, DRV/r	↑ vorapaxar expected	**Do not coadminister.**
Antipneumocystis and Antitoxoplasmosis			
Atovaquone Oral suspension	ATV/r	↔ atovaquone	No dose adjustment needed
	ATV/c, DRV/c, DRV/r	↔ atovaquone expected	No dose adjustment needed
Antiseizure			
Carbamazepine	ATV/r	↑ carbamazepine possible May ↓ PI concentrations substantially	Consider alternative ARV or anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assess virologic response. Carbamazepine dose reduction may be necessary.
	DRV/r	Carbamazepine AUC ↑ 45% ↔ DRV	Monitor anticonvulsant concentration and adjust dose accordingly.
	ATV/c, DRV/c	↑ carbamazepine possible ↓ COBI expected ↓ PI expected	**Contraindicated**
Eslicarbazepine	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Ethosuximide	ATV/c, ATV/r, DRV/c, DRV/r	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.
Lamotrigine	ATV/r	Lamotrigine AUC ↓ 32%	A dose increase of lamotrigine may be needed; monitor lamotrigine concentration or consider alternative ARV or anticonvulsant.
	DRV/r	↓ lamotrigine possible	

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	ATV/c	No data	Monitor anticonvulsant concentration and adjust dose accordingly.
	DRV/c	↔ lamotrigine expected	No dose adjustment needed.
Oxcarbazepine	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Phenobarbital	ATV/r, DRV/r	↓ phenobarbital possible ↓ PI possible	Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	ATV/c, DRV/c	↓ COBI expected ↓ PI expected	**Contraindicated**
Phenytoin	ATV/r, DRV/r	↓ phenytoin possible ↓ PI possible	Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	ATV/c, DRV/c	↓ COBI expected ↓ PI expected	**Contraindicated**
Primidone	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI expected	**Do not coadminister.**
Valproic Acid	ATV/c, ATV/r, DRV/c, DRV/r	↓ or ↔ VPA possible	Monitor VPA concentrations and monitor for PI tolerability.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antivirals—Hepatitis C			
Elbasvir/Grazoprevir	ATV/r	Elbasvir AUC ↑ 4.8-fold Grazoprevir AUC ↑ 10.6-fold Elbasvir ↔ ATV Grazoprevir ↑ ATV AUC 43%	**Contraindicated** May increase the risk of ALT elevations due to a significant increase in grazoprevir plasma concentrations caused by OATP1B1/3 inhibition.
	DRV/r	Elbasvir AUC ↑ 66% Grazoprevir AUC ↑ 7.5-fold ↔ DRV	
	ATV/c, DRV/c	↑ grazoprevir expected	
Glecaprevir/Pibrentasvir	ATV/c, ATV/r	**With (ATV 300 mg Plus RTV 100 mg) Once Daily** • Glecaprevir AUC ↑ 6.5-fold • Pibrentasvir AUC ↑ 64%	**Contraindicated**
	DRV/c, DRV/r	**With (DRV 800 mg Plus RTV 100 mg) Once Daily** • Glecaprevir AUC ↑ fivefold • ↔ pibrentasvir	**Do not coadminister.**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ledipasvir/Sofosbuvir	ATV/r	ATV AUC ↑ 33% Ledipasvir AUC ↑ 113% ↔ sofosbuvir	No dose adjustment needed Coadministration of ledipasvir/sofosbuvir with TDF and a PI/r results in increased exposure to TDF. The safety of the increased TDF exposure has not been established. Consider alternative HCV or ARV drugs to avoid increased risk of TDF toxicities. If coadministration is necessary, monitor for TDF-related adverse events.
	ATV/c, DRV/c, DRV/r	↔ PI expected ↔ ledipasvir and sofosbuvir	
Sofosbuvir/Velpatasvir	ATV/r	↔ ATV/r ↔ sofosbuvir Velpatasvir AUC ↑ 2.4-fold	No dose adjustment needed
	DRV/r	↔ DRV/r Sofosbuvir AUC ↓ 28% ↔ velpatasvir	No dose adjustment needed
	ATV/c, DRV/c	↔ sofosbuvir and velpatasvir expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/ Voxilaprevir	ATV/c, ATV/r	**With ATV/r** • Voxilaprevir AUC ↑ 4.3-fold • Velpatasvir AUC ↑ 93% • Sofosbuvir AUC ↑ 40%	**Do not coadminister.**
	DRV/c, DRV/r	**With DRV/r** • Voxilaprevir AUC ↑ 2.4-fold • ↔ DRV/r, velpatasvir, and sofosbuvir	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	ATV/c, ATV/r, DRV/c, DRV/r	↑ brincidofovir possible	Give PI dose at least 3 hours after administering brincidofovir and monitor for brincidofovir-related adverse events (i.e., elevations in ALT/AST and bilirubin and GI adverse events).
Cidofovir	ATV/c, ATV/r, DRV/c, DRV/r	↔ cidofovir	No dose adjustment needed
Tecovirimat	ATV/c, ATV/r, DRV/c, DRV/r	↔ tecovirimat	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	ATV/c, ATV/r, DRV/c, DRV/r	↔ molnupiravir	No dose adjustment needed
Remdesivir	ATV/c, ATV/r, DRV/c, DRV/r	↔ remdesivir	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	ATV/r, ATV/c, DRV/c, DRV/r	↑ PI expected ↑ ritonavir-boosted nirmatrelvir expected	No dose adjustment needed. Monitor for increased ritonavir-boosted nirmatrelvir and PI-related adverse events.
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	ATV/c, ATV/r	↑ arformoterol possible	No dose adjustment needed
	DRV/c, DRV/r	↔ arformoterol expected	No dose adjustment needed
Indacaterol	ATV/c, ATV/r, DRV/c, DRV/r	**With RTV 300 mg Twice Daily** • Indacaterol AUC ↑ 1.7-fold	No dose adjustment needed in patients receiving indacaterol 75 mcg daily.
Olodaterol	ATV/c, ATV/r, DRV/c, DRV/r	↑ olodaterol expected	No dose adjustment needed
Salmeterol	ATV/c, ATV/r, DRV/c, DRV/r	↑ salmeterol possible	**Do not coadminister,** due to potential increased risk of salmeterol-related CV events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications			
Antiarrhythmics			
Amiodarone	ATV/r	↑ amiodarone possible ↑ PI possible	**Contraindicated**
	ATV/c, DRV/c, DRV/r	↑ amiodarone possible ↑ PI possible	**Do not coadminister** unless the benefits outweigh the risks. If coadministered, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone drug concentration.
Digoxin	ATV/c, ATV/r, DRV/c, DRV/r	RTV 200 mg twice daily ↑ digoxin AUC 29% and ↑ half-life 43% DRV/r ↑ digoxin AUC 36% COBI ↑ digoxin C_{max} 41% and ↔ AUC	Monitor digoxin concentrations. Digoxin dose may need to be decreased. Titrate initial digoxin dose.
Disopyramide	ATV/c, ATV/r, DRV/c, DRV/r	↑ disopyramide possible	**Do not coadminister.**
Dofetilide	ATV/c, ATV/r, DRV/c, DRV/r	↑ dofetilide possible	**Do not coadminister.**
Dronedarone	ATV/c, ATV/r, DRV/c, DRV/r	↑ dronedarone expected	**Contraindicated**
Flecainide	ATV/c, ATV/r, DRV/c, DRV/r	↑ flecainide possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor flecainide concentrations and for antiarrhythmic-related adverse events.
Lidocaine	ATV/c, ATV/r, DRV/c, DRV/r	↑ lidocaine possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor lidocaine concentrations and for antiarrhythmic-related adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Mexiletine	ATV/c, ATV/r, DRV/c, DRV/r	↑ mexiletine possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor mexiletine concentrations and for antiarrhythmic-related adverse events.
Propafenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ propafenone possible	**Do not coadminister.**
Quinidine	ATV/r	↑ quinidine expected	**Contraindicated**
	ATV/c, DRV/c, DRV/r	↑ quinidine possible	**Do not coadminister.**
Sotalol	ATV/c, ATV/r, DRV/c, DRV/r	↔ sotalol expected	No dose adjustment needed
Beta-Blockers			
Atenolol, Labetalol	ATV/c, ATV/r, DRV/c, DRV/r	↑ beta-blockers possible	No dose adjustment needed
Bisoprolol, Carvedilol, Metoprolol, Nebivolol	ATV/c, ATV/r, DRV/c, DRV/r	↑ beta-blockers possible	May need to decrease beta-blocker dose; adjust dose based on clinical response. Consider using beta-blockers that are not metabolized by CYP2D6 enzymes (e.g., atenolol, labetalol, nadolol).
Calcium Channel Blockers			
Amlodipine, Diltiazem, Felodipine, Nifedipine, Verapamil	ATV/c, ATV/r, DRV/c, DRV/r	↑ dihydropyridine possible ↑ verapamil possible	Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB is used with ATV.
Diltiazem	ATV/c, ATV/r	Unboosted ATV ↑ diltiazem AUC 125% Greater ↑ of diltiazem AUC is likely with ATV/c or ATV/r	Decrease diltiazem dose by at least 50%. If starting diltiazem, start with the lowest dose and titrate according to clinical response and adverse events. ECG monitoring is recommended.
	DRV/c, DRV/r	↑ diltiazem possible	Titrate diltiazem dose according to clinical response and adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac—Other			
Bosentan	ATV/c, ATV/r, DRV/c, DRV/r	**With ATV (Unboosted)** • ↓ ATV expected **With PI/r or PI/c** • ↑ bosentan expected	**Do not coadminister** bosentan and unboosted ATV. **In Patients on a PI (Other Than Unboosted ATV) >10 Days** • Start bosentan at 62.5 mg once daily or every other day. **In Patients on Bosentan Who Require a PI (Other Than Unboosted ATV)** • Stop bosentan ≥36 hours before PI initiation and restart bosentan 10 days after PI initiation at 62.5 mg once daily or every other day. **When Switching Between COBI and RTV** • Maintain same bosentan dose.
Eplerenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ eplerenone expected	**Contraindicated**
Ivabradine	ATV/c, ATV/r, DRV/c, DRV/r	↑ ivabradine expected	**Contraindicated**
Mavacamten	ATV/c, ATV/r, DRV/c, DRV/r	↑ mavacamten expected	**Contraindicated**
Ranolazine	ATV/c, ATV/r, DRV/c, DRV/r	↑ ranolazine expected	**Contraindicated**
Corticosteroids			
Beclomethasone Inhaled or intranasal	DRV/r	↔ 17-BMP (active metabolite) AUC RTV 100 mg twice daily ↑ 17-BMP AUC 2-fold	No dose adjustment needed
	ATV/c, ATV/r, DRV/c	↔ 17-BMP expected	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids possible RTV 100 mg twice daily ↑ fluticasone AUC 350-fold	**Do not coadminister** unless the potential benefits of inhaled or intranasal corticosteroid outweigh the risks of adverse events associated with corticosteroids. Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider alternative inhaled/intranasal corticosteroid (e.g., beclomethasone).
Betamethasone, Budesonide Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids possible ↓ PI possible	**Do not coadminister** unless the potential benefits of systemic corticosteroid outweigh the risks of adverse events associated with systemic corticosteroids. Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Dexamethasone Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids possible ↓ PI possible	Consider alternative corticosteroid for long-term use. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ prednisolone possible	Coadministration may be considered if the potential benefits outweigh the risks of adverse events associated with systemic corticosteroids. If coadministered, monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Betamethasone, Methylprednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids expected	**Do not coadminister.** Coadministration can result in adrenal insufficiency and Cushing's syndrome.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Glucose-Lowering			
Canagliflozin	ATV/c, DRV/c	↔ canagliflozin	No dose adjustment needed
	ATV/r, DRV/r	↓ canagliflozin expected	If a patient is already tolerating canagliflozin 100 mg daily, increase canagliflozin dose to 200 mg daily. If a patient is already tolerating canagliflozin 200 mg daily and requires additional glycemic control, management strategy is based on renal function. **In Patients With eGFR ≥60 mL/min/1.73 m²** • Canagliflozin dose may be increased to 300 mg daily. **In Patients With eGFR <60 mL/min/1.73 m²** • Consider adding another antihyperglycemic agent.
Saxagliptin	ATV/c, ATV/r, DRV/c, DRV/r	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/Saxagliptin	ATV/c, ATV/r, DRV/c, DRV/r	↑ saxagliptin expected	**Do not coadminister.** Dapagliflozin is only available as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination **is not recommended.**
Herbal Products			
St. John's Wort	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI expected	**Contraindicated**
Hormonal Therapies—Contraceptives			
Injectable Contraceptives Depot MPA	ATV/c, ATV/r, DRV/c, DRV/r	↔ expected	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate, norethindrone)	ATV/c	Drospirenone AUC ↑ 130% Ethinyl estradiol AUC ↓ 22%	**Contraindicated** with drospirenone-containing hormonal contraceptive due to potential for hyperkalemia**.** Use alternative ARV or alternative contraceptive methods.
		↔ ethinyl estradiol AUC and C_{min} ↓ 25% ↔ levonorgestrel	No dose adjustment needed
	ATV/r	Ethinyl estradiol AUC ↓ 19% and C_{min} ↓ 37% Norgestimate AUC ↑ 85% Norethindrone AUC ↑ 51% and C_{min} ↑ 67%	Oral contraceptive should contain at least 35 mcg of ethinyl estradiol.[c]
		↑ drospirenone expected ↔ estetrol	Clinical monitoring is recommended due to the potential for hyperkalemia. Use alternative ARV or contraceptive methods.
	DRV/c	Drospirenone AUC ↑ 58% Ethinyl estradiol AUC ↓ 30%	Clinical monitoring is recommended due to the potential for hyperkalemia. Use alternative ARV or contraceptive methods.
	DRV/r	Ethinyl estradiol AUC ↓ 44% and C_{min} ↓ 62% Norethindrone AUC ↓ 14% and C_{min} ↓ 30%	**When Used for Contraception** • Consider alternative ARV or contraceptive methods. If combined, consider using an oral contraceptive with at least 35 mcg of ethinyl estradiol. **When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation)** • Monitor for clinical effectiveness of hormonal therapy.
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	ATV/c, ATV/r, DRV/c, DRV/r	↑ etonogestrel, levonorgestrel expected	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Transdermal Contraceptives (e.g., ethinyl estradiol/norelgestromin, ethinyl estradiol/levonorgestrel)	ATV/c, ATV/r, DRV/c, DRV/r	↓ ethinyl estradiol possible with ritonavir ↑ ethinyl estradiol possible with cobicistat ↑ norelgestromin, levonorgestrel possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	ATV/r	Ethinyl estradiol AUC ↓ 26% Etonogestrel AUC ↑ 79%	No dose adjustment needed with etonogestrel/ethinyl estradiol vaginal rings. Use alternative ARV or contraceptive methods with segesterone/ethinyl estradiol vaginal rings.
	ATV/c, DRV/c, DRV/r	↓ ethinyl estradiol possible with ritonavir ↑ ethinyl estradiol possible with cobicistat	
Emergency Contraceptives Levonorgestrel (oral)	ATV/c, ATV/r, DRV/c, DRV/r	↑ levonorgestrel expected	No dose adjustment needed
Hormonal Therapies—Gender Affirming and Menopause			
Estradiol	ATV/c, DRV/c	↓ or ↑ estradiol possible	Adjust estradiol dose as needed based on clinical effects and endogenous hormone concentrations.
	ATV/r, DRV/r	↓ estradiol possible	
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	ATV/c, ATV/r, DRV/c, DRV/r	↑ dutasteride possible ↑ finasteride possible	Adjust dutasteride dose as needed based on clinical effects and endogenous hormone concentrations. No dose adjustment needed for finasteride.
Testosterone	ATV/c, ATV/r, DRV/c, DRV/r	↑ testosterone possible	Adjust testosterone dose as needed based on clinical effects and endogenous hormone concentrations.
Other Gender-Affirming Medications	ATV/c, ATV/r, DRV/c, DRV/r	↔ goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, MPA, progesterone)	ATV/c, ATV/r, DRV/c, DRV/r	↓ or ↑ estrogen possible with estradiol or conjugated estrogen (equine and synthetic)	Adjust estrogen dose as needed based on clinical effects.
	ATV/c, ATV/r, DRV/c, DRV/r	↑ drospirenone possible ↑ MPA ↑ micronized progesterone See the Hormonal Therapies—Contraceptives section for other progestin-PI interactions.	Adjust progestin/progesterone dose as needed based on clinical effects. Drospirenone is not contraindicated with ATV/c products because it is prescribed at a lower dose for menopausal HRT than products used for hormonal contraceptives.
Immunosuppressants			
Cyclosporine, Sirolimus, Tacrolimus	ATV/c, ATV/r, DRV/c, DRV/r	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
Everolimus	DRV/c, DRV/r	↑ immunosuppressant expected	**Do not coadminister.**
	ATV/c, ATV/r	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lipid-Modifying			
Atorvastatin	ATV/r	↑ atorvastatin possible	Administer the lowest effective atorvastatin dose while monitoring for adverse events.
	ATV/c	Atorvastatin AUC ↑ 9.2-fold and C_{max} ↑ 18.9-fold	**Do not coadminister.**
	DRV/c	Atorvastatin AUC ↑ 3.9-fold and C_{max} ↑ 4.2-fold	Administer the lowest effective atorvastatin dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
	DRV/r	DRV/r plus atorvastatin 10 mg similar to atorvastatin 40 mg administered alone	Administer the lowest effective atorvastatin dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
Fluvastatin	ATV/c, DRV/c	↑ fluvastatin expected	Administer the lowest effective fluvastatin dose while monitoring for adverse events.
	ATV/r, DRV/r	↑ or ↓ fluvastatin possible	
Lomitapide	ATV/c, ATV/r, DRV/c, DRV/r	↑ lomitapide expected	**Contraindicated**
Lovastatin	ATV/c, ATV/r, DRV/c, DRV/r	Significant ↑ lovastatin expected	**Contraindicated**
Pitavastatin	ATV/c, DRV/c	No data	No dose adjustment needed. Monitor for pitavastatin-related adverse events.
	ATV/r, DRV/r	**With ATV/r** • ↔ pitavastatin expected • ↔ ATV/r expected **With DRV/r** • ↓ pitavastatin AUC 26% • ↔ DRV/r	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Pravastatin	ATV/c, ATV/r	No data	Administer the lowest effective pravastatin dose while monitoring for adverse events.
	DRV/c, DRV/r	**With DRV/r** • Pravastatin AUC ↑ 81% following single dose of pravastatin • Pravastatin AUC ↑ 23% at steady state	Administer the lowest effective pravastatin dose while monitoring for adverse events.
Rosuvastatin	ATV/r	Rosuvastatin AUC ↑ 3-fold and C_{max} ↑ 7-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events. Do not exceed rosuvastatin 10 mg daily.
	ATV/c	Rosuvastatin AUC ↑ 3.4-fold and C_{max} ↑ 10.6-fold	
	DRV/c	Rosuvastatin AUC ↑ 1.9-fold and C_{max} ↑ 3.8-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events. Do not exceed rosuvastatin 20 mg daily.
	DRV/r	Rosuvastatin AUC ↑ 48% and C_{max} ↑ 2.4-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events.
Simvastatin	ATV/c, ATV/r, DRV/c, DRV/r	Significant ↑ simvastatin expected	**Contraindicated**
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	ATV/r	Buprenorphine AUC ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 105%	Monitor for sedation and other signs or symptoms of overmedication. Buprenorphine dose reduction may be necessary. It may be necessary to remove implant and treat with a formulation that permits dose adjustments.
	DRV/r	↔ buprenorphine Norbuprenorphine (active metabolite) AUC ↑ 46% and C_{min} ↑ 71%	No dose adjustment needed. Monitor for buprenorphine-related adverse events. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	ATV/c, DRV/c	↑ buprenorphine possible	Titrate buprenorphine dose using the lowest initial dose. Dose adjustment of buprenorphine may be needed. It may be necessary to remove implant and treat with a formulation that permits dose adjustments. Monitor for buprenorphine-related adverse events.
Fentanyl	ATV/c, ATV/r, DRV/c, DRV/r	↑ fentanyl possible	Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression.
Lofexidine	ATV/c, ATV/r, DRV/c, DRV/r	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	ATV/c, DRV/c	No data	Titrate methadone dose using the lowest feasible initial dose. Dose adjustment of methadone may be needed. Monitor for methadone-related adverse events.
	ATV/r, DRV/r	ATV/r and DRV/r ↓ R-methadone[d] AUC 16% to 18%	Opioid withdrawal is unlikely but may occur. Monitor for opioid withdrawal and increase methadone dose as clinically indicated.
Oxycodone	ATV/c, ATV/r, DRV/c, DRV/r	↑ oxycodone expected	Monitor for opioid-related adverse events, including potentially fatal respiratory depression. Oxycodone dose reduction may be necessary.
Tramadol	ATV/c, ATV/r, DRV/c, DRV/r	↑ tramadol expected ↓ M1 (active metabolite) possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors			
Avanafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 600 mg twice daily (for 5 days) ↑ avanafil AUC 13-fold and ↑ C_{max} 2.4-fold	**Do not coadminister.**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sildenafil	ATV/c, ATV/r, DRV/c, DRV/r	DRV/r plus sildenafil 25 mg similar to sildenafil 100 mg alone RTV 500 mg twice daily ↑ sildenafil AUC 1,000%	**For Treatment of Erectile Dysfunction** • Start with sildenafil 25 mg every 48 hours and monitor for sildenafil-related adverse events. **Contraindicated** for treatment of PAH.
Tadalafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 200 mg twice daily ↑ tadalafil AUC 124%	**For Treatment of Erectile Dysfunction** *As-Needed Use* • Start with tadalafil 5 mg and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for tadalafil-related adverse events. *Once-Daily Use* • Do not exceed tadalafil 2.5 mg once daily. Monitor for tadalafil-related adverse events. **For Treatment of PAH** *In Patients on a PI >7 Days* • Start with tadalafil 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. *In Patients on Tadalafil Who Require a PI* • Stop tadalafil ≥24 hours before PI initiation. Seven days after PI initiation, restart tadalafil at 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. *In Patients Switching Between COBI and RTV* • Maintain tadalafil dose. **For Treatment of Benign Prostatic Hyperplasia** • Maximum recommended daily dose is tadalafil 2.5 mg per day. Monitor for tadalafil-related adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Vardenafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 600 mg twice daily ↑ vardenafil AUC 49-fold	Start with vardenafil 2.5 mg every 72 hours and monitor for vardenafil-related adverse events.
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Clonazepam, Diazepam	ATV/c, ATV/r, DRV/c, DRV/r	↑ benzodiazepine possible RTV 200 mg twice daily (for 2 days) ↑ alprazolam half-life 222% and ↑ AUC 248%	Consider alternative benzodiazepines, such as lorazepam, oxazepam, or temazepam.
Lorazepam, Oxazepam, Temazepam	ATV/c, ATV/r, DRV/c, DRV/r	No data	These benzodiazepines are metabolized via non-CYP450 pathways and, therefore, have less interaction potential than other benzodiazepines.
Midazolam	ATV/c, ATV/r, DRV/c, DRV/r	↑ midazolam expected	Oral midazolam is **contraindicated** with PIs. Parenteral midazolam can be used with caution when given in a monitored situation with appropriate medical management available in case of respiratory sedation and/or prolonged sedation. Consider dose reduction, especially if more than a single dose of midazolam is administered.
Triazolam	ATV/c, ATV/r, DRV/c, DRV/r	↑ triazolam expected RTV 200 mg twice daily ↑ triazolam half-life 1,200% and ↑ AUC 2,000%	**Contraindicated**
Orexin Receptor Antagonist			
Daridorexant, Lemborexant, Suvorexant	ATV/c, ATV/r, DRV/c, DRV/r	↑ daridorexant, lemborexant, suvorexant expected	**Do not coadminister.**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Other Sedatives			
Eszopiclone	ATV/c, ATV/r, DRV/c, DRV/r	↑ eszopiclone expected	Start with lowest dose and increase to a maximum of 2 mg daily; monitor for eszopiclone-related adverse events.
Zolpidem	ATV/c, ATV/r, DRV/c, DRV/r	↑ zolpidem possible	Initiate zolpidem at a low dose and monitor for zolpidem-related adverse events. Dose reduction may be necessary.
Miscellaneous			
Calcifediol	ATV/c, ATV/r, DRV/c, DRV/r	↑ calcifediol possible	Dose adjustment of calcifediol may be required, and serum 25-hydroxyvitamin D, intact PTH, and serum calcium concentrations should be closely monitored.
Cisapride	ATV/c, ATV/r, DRV/c, DRV/r	↑ cisapride expected	**Contraindicated**
Colchicine	ATV/c, ATV/r, DRV/c, DRV/r	RTV 100 mg twice daily ↑ colchicine AUC 296% and C_{max} ↑ 184% Significant ↑ colchicine expected with all PIs, with or without COBI or RTV	**For Treatment of Gout Flares** • Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. **For Prophylaxis of Gout Flares** • If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day. **For Treatment of Familial Mediterranean Fever** • Do not exceed colchicine 0.6 mg once daily or colchicine 0.3 mg twice daily. **Contraindicated** in patients with hepatic (Child-Pugh Score A, B, or C) or renal impairment (CrCl <60 mL/min)
Dronabinol	ATV/c, ATV/r, DRV/c, DRV/r	↑ dronabinol possible	Monitor for dronabinol-related adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Eluxadoline	ATV/c, ATV/r, DRV/c, DRV/r	↑ eluxadoline expected	Administer eluxadoline at a dose of 75 mg twice daily and monitor for eluxadoline-related adverse events.
Finerenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ finerenone expected	**Contraindicated**
Flibanserin	ATV/c, ATV/r, DRV/c, DRV/r	↑ flibanserin expected	**Contraindicated**
Naloxegol	ATV/c, ATV/r, DRV/c, DRV/r	↑ naloxegol expected	**Contraindicated**
Praziquantel	ATV/c, ATV/r, DRV/c, DRV/r	↑ praziquantel possible	Consider alternative ARV. If coadministration is necessary, monitor for praziquantel-related adverse events.

[a] DHA is an active metabolite of artemether and artesunate.

[b] The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Lo Minastrin Fe; Lo Loestrin Fe; Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Minastrin 24 Fe; Ortho Tri-Cyclen Lo. Generic formulations also may be available.

[c] The following products contain at least 35 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Brevicon; Femcon Fe; Modicon; Norinyl 1/35; Ortho-Cyclen; Ortho-Novum 1/35, 7/7/7; Ortho Tri-Cyclen; Ovcon 35; Tri-Norinyl. Generic formulations also may be available.

[d] R-methadone is the active form of methadone.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 17-BMP = beclomethasone 17-monopropionate; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CCB = calcium channel blocker; CNS = central nervous system; COBI = cobicistat; CrCl = creatinine clearance; CMV = cytomegalovirus; CV = cardiovascular; CYP = cytochrome P; DHA = dihydroartemisinin; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DVT = deep vein thrombosis; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; EVG/c = elvitegravir/cobicistat; GI = gastrointestinal; H2RA = H2 receptor antagonist; HCV = hepatitis C virus; HRT = hormone replacement therapy; INR = international normalized ratio; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MPA = medroxyprogesterone acetate; OATP = organic anion-transporting polypeptide; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PE = pulmonary embolism; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RTV = ritonavir; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; TDF = tenofovir disoproxil fumarate; VPA = valproic acid

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between non-nucleoside reverse transcriptase inhibitors (NNRTIs) and non-antiretroviral drugs. Cabotegravir (CAB) intramuscular (IM) plus rilpivirine (RPV) IM are co-packaged into a single product and are coadministered as a complete regimen; therefore, the dosing recommendations and clinical comments reflect the combination of CAB IM and RPV IM treatments. Drug interaction studies were not conducted with either CAB IM or RPV IM. Drug interaction studies with oral CAB and RPV were leveraged to make the dosing recommendations for CAB IM and RPV IM. For information regarding interactions between NNRTIs and other antiretroviral (ARV) drugs, including dosing recommendations, refer to Tables 24c, 24e, 24f, 25a, and 25b.

Recommendations for managing a particular drug interaction may differ, depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. When an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Oral doses of RPV at 75 mg and 300 mg once daily (equivalent to 3 and 12 times the recommended dose) were associated with prolonged QTc (or QT corrected for heart rate) interval. Known and expected/theoretical pharmacokinetic interactions, resulting in increased RPV exposures, are included in this table due to the safety concern of QTc prolongation. There is limited information about the potential for pharmacodynamic interactions between RPV (in the absence of increased RPV exposures) and drugs that prolong the QTc interval; therefore, these are not included in this table.

Nevirapine (NVP) is no longer commonly used in clinical practice in the United States and is not included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between NVP and concomitant medications. Information may also be found in archived versions of this guideline.

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	DOR, EFV	↔ NNRTI AUC	No dose adjustment needed
	ETR	↔ ETR expected	No dose adjustment needed
	RPV IM	↔ RPV expected	No dose adjustment needed
	RPV PO	↓ RPV expected when given simultaneously	Give antacids at least 2 hours before or at least 4 hours after RPV.
H2 Receptor Antagonists	DOR	↔ DOR expected	No dose adjustment needed
	EFV	↔ EFV AUC	No dose adjustment needed
	ETR	↔ ETR AUC	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV IM	↔ RPV expected	No dose adjustment needed
	RPV PO	RPV AUC ↓ 76% when famotidine 40 mg is taken 2 hours prior	Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.
Proton Pump Inhibitors	DOR	↔ DOR AUC and C_{min}	No dose adjustment needed
	EFV	↔ EFV expected	
	ETR	**With Omeprazole 40 mg Daily** • ETR AUC ↑ 41%	
	RPV IM	↔ RPV expected	No dose adjustment needed
	RPV PO	**With Omeprazole 20 mg Daily** • RPV AUC ↓ 40% to 65% and C_{min} ↓ 33%	**Contraindicated**
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin, Doxazosin, Silodosin, Terazosin	DOR, RPV IM, RPV PO	↔ alpha-adrenergic antagonists expected	No dose adjustment needed
	EFV, ETR	↓ alpha-adrenergic antagonists expected	Consider alternative ARV or alpha-antagonist therapy. If coadministration is necessary, monitor for therapeutic effectiveness of alpha antagonist.
Tamsulosin	DOR, RPV IM, RPV PO	↔ tamsulosin expected	No dose adjustment needed
	EFV, ETR	↓ tamsulosin expected	Monitor for therapeutic effectiveness of tamsulosin after 2–4 weeks. May need to increase dose to tamsulosin 0.8 mg once daily for patients who fail to respond to the 0.4-mg dose.
Antibacterials—Antimycobacterials			
Bedaquiline	DOR, RPV IM, RPV PO	↔ bedaquiline expected	No dose adjustment needed
	EFV, ETR	↓ bedaquiline possible	**Do not coadminister.**
Rifabutin	DOR	DOR AUC ↓ 50%	Increase DOR dose to 100 mg twice daily. No dose adjustment is needed for rifabutin.
	EFV	Rifabutin ↓ 38%	Increase rifabutin dose to 450–600 mg per day.
	ETR	↔ rifabutin and metabolite AUC ETR AUC ↓ 37%	**Do not coadminister** ETR plus PI/r with rifabutin. Use rifabutin 300 mg once daily if ETR is administered without PI/r.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV IM	↓ RPV expected	**Contraindicated**
	RPV PO	**Rifabutin Plus RPV 50 mg PO Once Daily Compared to RPV 25 mg Once Daily Alone** • ↔ RPV AUC and C_{min}	Increase RPV dose to 50 mg PO once daily during coadministration. No dose adjustment for rifabutin is needed.
Rifampin	DOR	DOR AUC ↓ 88%	**Contraindicated.** After stopping rifampin, wait 4 weeks before initiating DOR**.**
	EFV	EFV AUC ↓ 26%	**Do not use** EFV 400 mg with rifampin. Maintain EFV dose at 600 mg once daily and monitor for virologic response.
	ETR	Significant ↓ ETR possible	**Do not coadminister.**
	RPV IM	↓ RPV possible	**Contraindicated**
	RPV PO	RPV AUC ↓ 80%	**Contraindicated**
Rifapentine	DOR	**Once-Weekly Rifapentine Plus Isoniazid and DOR 100 mg Twice Daily Compared to DOR 100 mg Twice Daily Alone** • DOR AUC ↓ 29%, C_{min} ↓ 31%	**Contraindicated.** After stopping rifapentine, wait 4 weeks before initiating DOR**.**
	EFV	**Daily Rifapentine (Max 600 mg) With EFV** • ↔ EFV **Weekly Rifapentine (Max 900 mg) With EFV** • ↔ EFV	No dose adjustment needed
	ETR	↓ ETR possible	**Do not coadminister.**
	RPV IM, RPV PO	↓ RPV possible	**Contraindicated**
Antibacterials—Macrolides			
Azithromycin	DOR, EFV, ETR, RPV IM, RPV PO	↔ azithromycin expected	No dose adjustment needed
Clarithromycin	DOR	↔ clarithromycin expected ↑ DOR possible	Monitor for ARV tolerability if used in combination.
	EFV	Clarithromycin AUC ↓ 39%	Monitor for effectiveness, or consider alternative agent (e.g., azithromycin) for MAC prophylaxis and treatment.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	ETR	Clarithromycin AUC ↓ 39% ETR AUC ↑ 42%	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.
	RPV IM, RPV PO	↔ clarithromycin expected ↑ RPV possible	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment. If coadministered, monitor for QTc prolongation.
Erythromycin	DOR	↑ DOR possible	Monitor for ARV tolerability if used in combination.
	EFV, ETR	↑ EFV and ETR possible ↓ erythromycin possible	Monitor for ARV tolerability and antibiotic efficacy if used in combination.
	RPV IM, RPV PO	↑ RPV possible	Consider alternative macrolide (e.g., azithromycin). If coadministered, monitor for QTc prolongation.
Anticoagulants			
Apixaban	DOR, RPV IM, RPV PO	↔ apixaban expected	No dose adjustment needed
	EFV, ETR	↓ apixaban possible	Consider alternative ARV or anticoagulant therapy.
Dabigatran, Edoxaban	DOR, EFV, ETR, RPV IM, RPV PO	↔ DOAC expected	No dose adjustment needed
Rivaroxaban	DOR, RPV IM, RPV PO	↔ rivaroxaban expected	No dose adjustment needed
	EFV, ETR	↓ rivaroxaban possible	Consider alternative ARV or anticoagulant therapy.
Warfarin	DOR, RPV IM, RPV PO	↔ warfarin expected	No dose adjustment needed
	EFV, ETR	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Antiseizure			
Carbamazepine, Phenobarbital, Phenytoin, Primidone	DOR	↓ DOR possible	**Contraindicated.** After stopping antiseizure medication, wait 4 weeks before initiating DOR.
	EFV	**Carbamazepine Plus EFV** • Carbamazepine AUC ↓ 27%	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor antiseizure drug and EFV concentrations.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		• EFV AUC ↓ 36% **Phenytoin Plus EFV** • ↓ EFV • ↑ or ↓ phenytoin possible **Phenobarbital or Primidone Plus EFV** • ↓ EFV and antiseizure agent possible	
	ETR	↓ antiseizure agent and ETR possible	**Do not coadminister.**
	RPV IM, RPV PO	↓ RPV possible	**Contraindicated**
Eslicarbazepine	DOR, EFV, ETR, RPV IM, RPV PO	↓ NNRTI possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Oxcarbazepine	DOR, RPV IM, RPV PO	↓ NNRTI possible	**Contraindicated**
	EFV, ETR	↓ NNRTI possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Ethosuximide, Lacosamide, Tiagabine, Zonisamide	DOR, RPV IM, RPV PO	↔ antiseizure agent expected	No dose adjustment needed
	EFV, ETR	↓ antiseizure agent possible	Monitor seizure control. Consider anticonvulsant therapeutic drug monitoring.
Lamotrigine	DOR, ETR, RPV IM, RPV PO	↔ lamotrigine expected	No dose adjustment needed
	EFV	↓ lamotrigine possible	Monitor seizure control and plasma concentrations of lamotrigine.
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below.			
Antidepressants and Anxiolytics			
Bupropion	DOR, ETR, RPV IM, RPV PO	↔ bupropion expected	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EFV	Bupropion AUC ↓ 55%	Titrate bupropion dose based on clinical response.
Citalopram, Escitalopram	DOR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
	EFV, ETR	↓ antidepressant possible	Titrate antidepressant dose based on clinical response.
Desvenlafaxine, Venlafaxine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Duloxetine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Fluoxetine, Fluvoxamine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Mirtazapine	DOR, RPV IM, RPV PO	↔ mirtazapine expected	No dose adjustment needed
	EFV, ETR	↓ mirtazapine possible	Monitor antidepressant effect. Titrate dose as necessary based on clinical response.
Nefazodone	DOR, RPV IM, RPV PO	↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ nefazodone expected ↑ NNRTI possible	Monitor antidepressant effect. Titrate dose as necessary based on clinical response.
Paroxetine	DOR, ETR, RPV IM, RPV PO	↔ paroxetine expected	No dose adjustment needed
	EFV	↔ EFV and paroxetine	No dose adjustment needed
Sertraline	DOR, RPV IM, RPV PO	↔ sertraline expected	No dose adjustment needed
	EFV	Sertraline AUC ↓ 39%	Monitor the antidepressant effect. Titrate dose as necessary based on clinical response.
	ETR	↓ sertraline possible	

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Trazodone	DOR, RPV IM, RPV PO	↔ trazodone expected	No dose adjustment needed
	EFV, ETR	↓ trazodone possible	Monitor for therapeutic effectiveness of trazodone and titrate dose as necessary.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Antipsychotics			
Aripiprazole	DOR, RPV IM, RPV PO	↔ aripiprazole expected	No dose adjustment needed
	EFV, ETR	↓ aripiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling usual dose of aripiprazole over 1–2 weeks. Refer to aripiprazole prescribing information for dose recommendations.
Brexpiprazole	DOR, RPV IM, RPV PO	↔ brexpiprazole expected	No dose adjustment needed
	EFV, ETR	↓ brexpiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling the usual dose of brexpiprazole and making further adjustments based on clinical response. Refer to brexpiprazole prescribing information.
Cariprazine	DOR, RPV IM, RPV PO	↔ cariprazine expected	No dose adjustment needed
	EFV, ETR	↓ cariprazine and ↑ or ↓ active metabolite possible	**Do not coadminister.**
Iloperidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Lumateperone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	**Do not coadminister.**

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lurasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Olanzapine, Olanzapine/Samidorphan	DOR, ETR, RPV IM, RPV PO	↔ olanzapine expected	No dose adjustment needed
	EFV	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Other Antipsychotics **CYP3A4 Substrates** (e.g., clozapine, haloperidol, perphenazine, risperidone, thioridazine)	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Pimavanserin	DOR, RPV IM, RPV PO	↔ pimavanserin expected	No dose adjustment needed
	EFV, ETR	↓ pimavanserin expected	**Do not coadminister.**
Pimozide	DOR, RPV IM, RPV PO	↔ pimozide expected	No dose adjustment needed
	EFV, ETR	↓ pimozide possible	Monitor for therapeutic effectiveness of pimozide.
Quetiapine	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Ziprasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Antifungals			
Fluconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV	↔ fluconazole expected ↔ EFV AUC	No dose adjustment needed
	ETR	ETR AUC ↑ 86%	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Ibrexafungerp	DOR, RPV PO	↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ ibrexafungerp expected ↑ NNRTI possible	**Do not coadminister.**
	RPV IM	↔ ibrexafungerp expected ↔ RPV IM expected	No dose adjustment needed
Isavuconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV, ETR	↓ isavuconazole possible	Monitor isavuconazole concentration and antifungal response. Dose adjustments for isavuconazole may be necessary.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Itraconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV	**EFV With Itraconazole Solution** • Itraconazole and OH-itraconazole AUC, C_{max}, and C_{min} ↓ 37% to 44% **EFV With Itraconazole Capsules** • Itraconazole AUC ↓ 86% and OH-itraconazole AUC 84%	**Do not coadminister** unless potential benefits outweigh the risks. Failure to achieve therapeutic itraconazole concentrations has been reported. If coadministration is necessary, closely monitor itraconazole concentration and adjust dose accordingly.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole concentration and antifungal response.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Posaconazole	DOR, ETR	↑ NNRTI possible	No dose adjustment needed
	EFV	Posaconazole AUC ↓ 50% ↔ EFV AUC	**Do not coadminister** unless potential benefits outweigh the risks. If coadministration is necessary, monitor posaconazole concentration and adjust dose accordingly.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Voriconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV	Voriconazole AUC ↓ 77% EFV AUC ↑ 44%	**Contraindicated at standard doses** Adjust dose to voriconazole 400 mg twice daily plus EFV 300 mg daily.
	ETR	↔ voriconazole AUC ETR AUC ↑ 36%	No dose adjustment needed
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Antimalarials			
Artemether/Lumefantrine	DOR, RPV IM, RPV PO	↔ antimalarial expected	No dose adjustment needed
	EFV	Artemether AUC ↓ 79% DHA AUC ↓ 75% Lumefantrine AUC ↓ 30% to 56%	Consider alternative ARV or antimalarial drug. If used in combination, monitor closely for antimalarial efficacy.
	ETR	Artemether AUC ↓ 38% ↔ DHA AUC ↔ lumefantrine AUC ↔ ETR AUC	Clinical significance of the reduced antimalarial drug concentrations is unknown. If used in combination with ETR, monitor for antimalarial efficacy.
Atovaquone/Proguanil	DOR, ETR, RPV IM, RPV PO	No data	Monitor for antimalarial efficacy.
	EFV	Atovaquone AUC ↓ 75% Proguanil AUC ↓ 43%	No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.
Antimigraine			
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	DOR RPV IM, RPV PO	↔ atogepant expected	No dose adjustment needed
	EFV, ETR,	↓ atogepant possible	Episodic migraine: Increase atogepant dose to 30–60 mg once daily. Chronic migraine: **Do not coadminister.**

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rimegepant	DOR, RPV IM, RPV PO	↔ rimegepant expected	No dose adjustment needed
	EFV, ETR,	↓ rimegepant possible	Consider alternative ARV or migraine medication.
Ubrogepant	DOR, RPV IM, RPV PO	↔ ubrogepant expected	No dose adjustment needed
	EFV, ETR	↓ ubrogepant expected	Use initial dose of 100 mg, followed by second dose of 100 mg if needed.
Zavegepant	DOR, RPV IM, RPV PO	↔ zavegepant expected	No dose adjustment needed
	EFV, ETR,	↓ zavegepant possible	
Serotonin 5-HT1B, 1D Receptor Agonists			
Almotriptan, Eletriptan	DOR RPV IM, RPV PO	↔ almotriptan expected	No dose adjustment needed
	EFV, ETR,	↓ almotriptan possible	
Frovatriptan, Naratripan, Rizatriptan, Sumatriptan, Zolmitriptan	DOR, EFV, ETR, RPV IM, RPV PO	↔ migraine medication expected	No dose adjustment needed
Antiplatelets			
Clopidogrel	DOR, RPV IM, RPV PO	↔ clopidogrel expected	No dose adjustment needed
	EFV, ETR	↓ activation of clopidogrel possible	Consider alternative ARV or antiplatelet. ETR may prevent metabolism of clopidogrel to its active metabolite.
Prasugrel	All NNRTIs	↔ prasugrel expected	No dose adjustment needed
Ticagrelor	DOR, RPV IM, RPV PO	↔ ticagrelor expected	No dose adjustment needed
	EFV, ETR	↓ ticagrelor expected	Consider alternative ARV or anticoagulant therapy.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Vorapaxar	DOR, RPV IM, RPV PO	↔ vorapaxar expected	No dose adjustment needed
	EFV, ETR	↓ vorapaxar expected	Insufficient data to make a dose recommendation.
Antipneumocystis and Antitoxoplasmosis			
Atovaquone (oral solution)	DOR, ETR, RPV IM, RPV PO	No data	Monitor for therapeutic effectiveness of atovaquone.
	EFV	Atovaquone AUC ↓ 44% to 47%	Consider alternative ARV or agent for PCP or toxoplasmosis treatment or prophylaxis. If coadministration is necessary, monitor for therapeutic effectiveness of atovaquone.
Antivirals—Hepatitis C			
Elbasvir/Grazoprevir	DOR	↔ elbasvir and grazoprevir DOR AUC ↑ 56% and C_{min} ↑ 41%	No dose adjustment needed
	EFV	Elbasvir AUC ↓ 54% Grazoprevir AUC ↓ 83% ↔ EFV	**Contraindicated**
	ETR	↓ elbasvir and grazoprevir expected	**Do not coadminister.**
	RPV IM	↔ elbasvir and grazoprevir expected ↔ RPV expected	No dose adjustment needed
	RPV PO	↔ elbasvir and grazoprevir ↔ RPV AUC and C_{min}	No dose adjustment needed
Glecaprevir/Pibrentasvir	DOR	↑ DOR expected	No dose adjustment needed
	EFV	↓ glecaprevir and pibrentasvir expected	**Do not coadminister.**
	ETR	↓ glecaprevir and pibrentasvir possible	**Do not coadminister.**
	RPV IM	↔ glecaprevir and pibrentasvir expected ↑ RPV expected	No dose adjustment needed
	RPV PO	↔ glecaprevir and pibrentasvir RPV AUC ↑ 84%	No dose adjustment needed
Ledipasvir/Sofosbuvir	DOR	↔ ledipasvir and sofosbuvir ↔ DOR	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EFV	Ledipasvir AUC, C_{min}, and C_{max} ↓ 34% ↔ sofosbuvir	
	ETR	No significant effect expected	
	RPV IM	↔ ledipasvir, sofosbuvir, and RPV expected	
	RPV PO	↔ ledipasvir and sofosbuvir ↔ RPV	
Sofosbuvir/Velpatasvir	DOR, RPV IM, RPV PO	No significant effect expected	No dose adjustment needed
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47%	**Do not coadminister.**
	ETR	↓ velpatasvir expected	**Do not coadminister.**
Sofosbuvir/Velpatasvir/ Voxilaprevir	DOR, RPV IM, RPV PO	No significant effect expected	No dose adjustment needed.
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47% ↓ voxilaprevir expected	**Do not coadminister.**
	ETR	↓ voxilaprevir expected ↓ velpatasvir expected	**Do not coadminister.**
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	All NNRTIs	↔ brincidofovir expected	No dose adjustment needed
Cidofovir	All NNRTIs	↔ cidofovir expected	No dose adjustment needed
Maribavir	DOR, RPV IM, RPV PO	↔ maribavir expected	No dose adjustment needed
	EFV, ETR	↓ maribavir possible	
Tecovirimat	DOR, RPV PO	↓ DOR or RPV expected but not likely to be clinically relevant	No dose adjustment needed
	EFV, ETR	↔ EFV or ETR expected	No dose adjustment needed
	RPV IM	↓ RPV expected but not likely to be clinically relevant	No dose adjustment needed. If there is a concern for suboptimal RPV exposure, seek expert consultation. Do not initiate CAB/RPV IM during or within 2 weeks after tecovirimat treatment. (Refer to Table 24d for interaction with CAB.)

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antivirals—SARS-CoV-2			
Molnupiravir	All NNRTIs	↔ expected	No dose adjustment needed
Remdesivir	All NNRTIs	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	DOR	**With Ritonavir 100 mg Twice Daily** • DOR AUC ↑ 254%	No dose adjustment needed
	EFV, ETR, RPV PO, RPV IM	↔ expected	No dose adjustment needed
Cardiac Medications			
Beta-Blockers			
Atenolol, Metoprolol, Nebivolol	DOR, EFV, ETR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed
Bisoprolol, Carvedilol	DOR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed
	EFV, ETR	↓ beta-blocker possible	No dose adjustment needed. Monitor blood pressure and heart rate and titrate to clinical effect.
Labetalol	DOR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed
	EFV, ETR	↑ beta-blocker possible	No dose adjustment needed. Monitor blood pressure and heart rate and adjust dose to achieve desired clinical effect.
Calcium Channel Blockers			
Dihydropyridine Calcium Channel Blockers (e.g., amlodipine, nifedipine)	DOR, RPV IM, RPV PO	↔ CCBs expected	No dose adjustment needed
	EFV, ETR	↓ CCBs possible	Titrate CCB dose based on clinical response.
Non-Dihydropyridine Calcium Channel Blockers (e.g., diltiazem, verapamil)	DOR, RPV IM, RPV PO	↔ CCBs expected ↑ NNRTI possible	No dose adjustment needed
	EFV	Diltiazem AUC ↓ 69% ↓ verapamil possible	Titrate diltiazem or verapamil dose based on clinical response.
	ETR	↓ diltiazem or verapamil possible	

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac—Other			
Bosentan	DOR	↓ DOR possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
	EFV, ETR	↓ NNRTI possible ↓ bosentan possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor bosentan efficacy and virologic response.
	RPV IM, RPV PO	↓ RPV possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
Eplerenone	DOR, RPV IM, RPV PO	↔ eplerenone expected	No dose adjustment needed
	EFV, ETR	↓ eplerenone possible	Titrate eplerenone dose based on clinical response.
Ivabradine	DOR, RPV IM, RPV PO	↔ ivabradine expected	No dose adjustment needed
	EFV, ETR	↓ ivabradine expected	**Contraindicated**
Mavacamten	DOR, RPV IM, RPV PO	↔ mavacamten expected ↓ NNRTI possible	Consider alternative ARV or alternative to mavacamten. If coadministration is necessary, monitor virologic response.
	EFV, ETR	↓ mavacamten expected ↓ NNRTI possible	**Contraindicated**
Ranolazine	DOR, RPV IM, RPV PO	↔ ranolazine expected	No dose adjustment needed
	EFV, ETR	↓ ranolazine expected	**Contraindicated**
Corticosteroids			
Beclomethasone, Ciclesonide	DOR, EFV, ETR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
Budesonide, Fluticasone, Mometasone	DOR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
	EFV, ETR,	↓ corticosteroid possible	Monitor corticosteroid efficacy and titrate as needed. May consider alternative corticosteroid for long-term use.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Dexamethasone	DOR, EFV, ETR	↓ NNRTI possible	Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.
	RPV IM, RPV PO	Significant ↓ RPV possible	**Contraindicated** with more than a single dose of dexamethasone.
Prednisone, Prednisolone	DOR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
	EFV, ETR,	↓ corticosteroid possible	Monitor corticosteroid efficacy and titrate as needed. May consider alternative corticosteroid for long-term use.
Glucose-Lowering			
Linagliptin, Sitagliptin	DOR, RPV IM, RPV PO	↔ antihyperglycemic expected	No dose adjustment needed
	EFV, ETR	↓ antihyperglycemic possible	Monitor glycemic control.
Metformin	DOR	↔ metformin AUC DOR AUC ↓ 26% and C_{max} ↓ 24%	No dose adjustment needed
	EFV, ETR, RPV IM	↔ metformin expected	No dose adjustment needed
	RPV PO	↔ metformin AUC	No dose adjustment needed
Sodium-Glucose Cotransporter-2 Inhibitors (e.g., canagliflozin, dapagliflozin, empagliflozin)	DOR, EFV, ETR, RPV IM, RPV PO	↔ antihyperglycemic expected	No dose adjustment needed
Herbal Products			
St. John's Wort	DOR	↓ DOR expected	**Contraindicated.** After stopping St. John's Wort, wait 4 weeks before initiating DOR.
	EFV, ETR	↓ EFV or ETR expected	**Do not coadminister.**
	RPV IM, RPV PO	↓ RPV expected	**Contraindicated**
Hormonal Therapies—Contraceptives			
Injectable Contraceptives Depot MPA	DOR, ETR, RPV IM, RPV PO	↔ MPA expected	No dose adjustment needed
	EFV	↔ MPA	No dose adjustment needed. Refer to Women With HIV section for people on EFV and RIF.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate)	DOR	↔ ethinyl estradiol ↔ levonorgestrel ↔ drospirenone expected	No dose adjustment needed
	EFV	↔ ethinyl estradiol Etonogestrel (metabolite of oral desogestrel) C_{min} ↓ 61% Levonorgestrel (metabolite of oral norgestimate) AUC ↓ 83% Norelgestromin (metabolite of oral norgestimate) AUC ↓ 64% ↓ drospirenone possible	**When Used for Contraception** Use alternative ARV or contraceptive methods. **When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation)** Monitor for clinical effectiveness of hormonal therapy.
	ETR	Ethinyl estradiol AUC ↑ 22% ↔ norethindrone ↓ drospirenone possible	No dose adjustment needed for regimens that do not contain drospirenone For drospirenone-containing regimens used for contraception, use alternative ARV or alternative contraceptive method. If using drospirenone for other clinical indications, monitor for clinical effectiveness of hormonal therapy.
	RPV IM	↔ ethinyl estradiol expected ↔ norethindrone expected ↔ drospirenone expected	No dose adjustment needed
	RPV PO	↔ ethinyl estradiol ↔ norethindrone ↔ drospirenone expected	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	DOR, RPV IM, RPV PO	↔ etonogestrel expected ↔ levonorgestrel expected	No dose adjustment needed
	EFV	Etonogestrel AUC ↓ 63% to 82% Levonorgestrel AUC ↓ 42% to 47% **Levonorgestrel 300 mg Implant With 600 mg EFV Compared to Levonorgestrel 150 mg Implant** • Levonorgestrel AUC ↓ 34%	Use alternative ARV or contraceptive methods. Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	ETR	↓ etonogestrel possible ↓ levonorgestrel possible	Consider using alternative ARV or contraceptive methods.
Transdermal Contraceptives (e.g., ethinyl estradiol/norelgestromin, ethinyl estradiol/levonorgestrel)	DOR, RPV IM, RPV PO	↔ ethinyl estradiol or norelgestromin expected	No dose adjustment needed
	EFV	↓ ethinyl estradiol or norelgestromin possible	Consider alternative ARV or contraceptive method.
	ETR	↓ ethinyl estradiol or norelgestromin possible	Consider alternative ARV or contraceptive method.
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	DOR, RPV IM, RPV PO	↔ etonogestrel and ethinyl estradiol expected ↔ segesterone and ethinyl estradiol expected	No dose adjustment needed
	EFV	Ethinyl estradiol (intravaginal ring) AUC ↓ 56% Etonogestrel (intravaginal ring) AUC ↓ 81%	Use alternative ARV or contraceptive method.
		↓ segesterone and ethinyl estradiol possible	Consider alternative ARV or contraceptive method.
	ETR	↓ etonogestrel and ethinyl estradiol possible ↓ segesterone and ethinyl estradiol possible	Consider alternative ARV or contraceptive method.
Emergency Contraceptives Levonorgestrel (oral)	DOR, RPV IM, RPV PO	↔ levonorgestrel expected	No dose adjustment needed.
	EFV	**Levonorgestrel 1.5 mg Plus 600 mg EFV** • Levonorgestrel AUC ↓ 58% **Levonorgestrel 3 mg Plus 600 mg EFV Compared to Levonorgestrel 1.5 mg Alone** • ↔ levonorgestrel AUC	Increase dose of levonorgestrel to 3mg when used for emergency postcoital contraception.
	ETR	↓ levonorgestrel possible	Consider alternative ARV or contraceptive method.
Hormonal Therapies—Gender Affirming and Menopause			
Estradiol	DOR, RPV IM, RPV PO	↔ estradiol expected	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EFV	Estradiol AUC ↓ 28% ↔ EFV AUC	Monitor feminizing effects of estrogen and therapy. Titrate dose as necessary to achieve therapeutic goals
	ETR	↓ estradiol possible	
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	DOR, RPV IM, RPV PO	↔ dutasteride and finasteride expected	No dose adjustment needed
	EFV, ETR	↓ dutasteride and finasteride possible	Monitor masculinizing effects of testosterone. Titrate testosterone dose as necessary to achieve therapeutic goals.
Testosterone	DOR, RPV IM, RPV PO	↔ testosterone expected	No dose adjustment needed
	EFV, ETR	↓ testosterone possible	Monitor masculinizing effects of testosterone. Titrate testosterone dose as necessary to achieve therapeutic goals.
Other Gender-Affirming Medications	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed
	EFV, ETR	↓ cyproterone and progestogens possible ↔ goserelin, leuprolide acetate, and spironolactone expected	Monitor feminizing effects of estrogen and antiandrogen therapy. Titrate dose as necessary to achieve therapeutic goals.
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed
	EFV, ETR	↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic) ↓ medroxyprogesterone possible ↓ micronized progesterone possible ↓ drospirenone possible See Contraceptives—Oral above for other progestin-NNRTI interactions	Monitor menopausal symptoms. Titrate to the dose of hormonal therapy that achieves menopausal symptom relief.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Immunosuppressants			
Cyclosporine	DOR, RPV IM, RPV PO	↔ cyclosporine expected ↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ cyclosporine possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Everolimus, Sirolimus, Tacrolimus	DOR, RPV IM, RPV PO	↔ immunosuppressant expected	No dose adjustment needed
	EFV, ETR	↓ immunosuppressant possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Lipid-Modifying			
Atorvastatin	DOR	↔ atorvastatin AUC	No dose adjustment needed
	EFV, ETR	Atorvastatin AUC ↓ 32% to 43%	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	RPV IM	↔ atorvastatin expected	No dose adjustment needed
	RPV PO	↔ atorvastatin AUC	No dose adjustment needed
Fluvastatin	DOR, RPV IM, RPV PO	↔ fluvastatin expected	No dose adjustment needed
	EFV, ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary. Monitor for fluvastatin toxicity.
Lovastatin, Simvastatin	DOR, RPV IM, RPV PO	↔ lovastatin and simvastatin expected	No dose adjustment needed
	EFV	Simvastatin AUC ↓ 60% to 68% Simvastatin active metabolite AUC ↓ 60%	Adjust simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	ETR	↓ lovastatin possible ↓ simvastatin possible	Adjust lovastatin or simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
Pitavastatin	DOR, ETR, RPV IM, RPV PO	↔ pitavastatin expected	No dose adjustment needed
	EFV	↔ pitavastatin AUC	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Pravastatin	DOR, RPV IM, RPV PO	↔ pravastatin expected	No dose adjustment needed
	EFV	Pravastatin AUC ↓ 44%	Adjust statin dose according to lipid responses, but do not exceed the maximum recommended dose.
	ETR	↓ pravastatin possible	
Rosuvastatin	DOR, EFV, ETR, RPV IM, RPV PO	↔ rosuvastatin expected	No dose adjustment needed
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual or buccal	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed
	EFV	Buprenorphine AUC ↓ 50% Norbuprenorphine (active metabolite) AUC ↓ 71%	No dose adjustment needed, monitor for withdrawal symptoms.
	ETR	Buprenorphine AUC ↓ 25%	No dose adjustment needed
Buprenorphine Implant	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed
	EFV, ETR	No data	Clinical monitoring is recommended when NNRTI is initiated after insertion of buprenorphine implant.
Lofexidine	DOR, EFV, ETR, RPV IM, RPV PO	↔ lofexidine expected	No dose adjustment needed
Methadone	DOR	↔ methadone AUC DOR AUC ↓ 26%	No dose adjustment needed
	EFV	Methadone AUC ↓ 52%	Opioid withdrawal common; monitor and increase methadone dose as necessary.
	ETR	↔ methadone AUC	No dose adjustment needed
	RPV IM	↓ methadone AUC expected	No dose adjustment needed; monitor for withdrawal symptoms.
	RPV PO	↔ R-methadone[a] AUC	No dose adjustment needed; monitor for withdrawal symptoms.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PDE5 Inhibitors			
Avanafil, Tadalafil, Vardenafil	DOR, RPV IM, RPV PO	↔ PDE5 inhibitor expected	No dose adjustment needed
	EFV, ETR	↓ PDE5 inhibitor possible	May need to titrate dose based on clinical effect.
Sildenafil	DOR	↔ sildenafil expected	No dose adjustment needed
	EFV	↓ sildenafil possible	May need to titrate sildenafil dose based on clinical effect.
	ETR	Sildenafil AUC ↓ 57%	May need to titrate sildenafil dose based on clinical effect.
	RPV IM	↔ sildenafil expected	No dose adjustment needed
	RPV PO	↔ sildenafil AUC and C_{max}	No dose adjustment needed
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Triazolam	DOR, RPV IM, RPV PO	↔ alprazolam or triazolam expected	No dose adjustment needed
	EFV, ETR	↓ alprazolam or triazolam possible	Monitor for therapeutic effectiveness of benzodiazepine.
Diazepam	DOR, RPV IM, RPV PO	↔ diazepam expected	No dose adjustment needed
	EFV	↓ diazepam possible	Monitor for therapeutic effectiveness of diazepam.
	ETR	↑ diazepam possible	Decreased dose of diazepam may be necessary. Monitor for diazepam toxicity.
Lorazepam	DOR, ETR, RPV IM, RPV PO	↔ lorazepam expected	No dose adjustment needed
	EFV	↔ lorazepam AUC	No dose adjustment needed
Midazolam	DOR	↔ midazolam AUC	No dose adjustment needed
	EFV	↑ or ↓ midazolam possible	Monitor for therapeutic effectiveness and toxicity of midazolam.
	ETR	Midazolam AUC ↓ 31% Midazolam active metabolite C_{max} ↑ 57%	Monitor for therapeutic effectiveness of midazolam.
	RPV IM, RPV PO	↔ midazolam expected	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Orexin Receptor Antagonists			
Daridorexant	DOR, RPV IM, RPV PO	↔ daridorexant expected	No dose adjustment needed
	EFV	Daridorexant AUC ↓ 61%	**Do not coadminister.**
	ETR	↓ daridorexant possible	
Lemborexant, Suvorexant	DOR, RPV IM, RPV PO	↔ lemborexant expected	No dose adjustment needed
	EFV, ETR	↓ lemborexant possible	**Do not coadminister.**
Other Sedatives			
Eszopiclone, Zolpidem	DOR, RPV IM, RPV PO	↔ eszopiclone or zolpidem expected	No dose adjustment needed
	EFV, ETR	↓ eszopiclone or zolpidem possible	Monitor for therapeutic effectiveness of sedative and titrate to clinical effect.
Miscellaneous			
Finerenone	DOR, RPV IM, RPV PO	↔ finerenone expected	No dose adjustment needed
	EFV, ETR	↓ finerenone expected	Consider alternative ARV or alternative to finerenone. If coadministration is necessary, monitor finerenone efficacy.
Praziquantel	DOR, RPV IM, RPV PO	↔ praziquantel expected	No dose adjustment needed
	EFV	R-praziquantel and S-praziquantel AUC ↓ 74% to 75%	**Do not coadminister**. If coadministration is necessary, consider alternative ARVs.
	ETR	↓ praziquantel possible	**Do not coadminister.** If coadministration is necessary, consider alternative ARVs.

[a] R-methadone is the active form of methadone.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ARV = antiretroviral; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CAB = cabotegravir; CCB = calcium channel blocker; DAA = direct-acting antiviral; DHA = dihydroartemisinin; DOAC = direct oral anticoagulants; DOR = doravirine; EFV = efavirenz; ETR = etravirine; IM = intramuscular; INR = international normalized ratio; isoniazid = isonicotinic acid hydrazide; MAC = *Mycobacterium avium* complex; MPA = medroxyprogesterone acetate; CMV = cytomegalovirus; NNRTI = non-nucleoside reverse transcriptase inhibitor; OH-itraconazole = active metabolite of itraconazole; PCP = *Pneumocystis jirovecii* pneumonia; PDE5 = phosphodiesterase type 5; PI/r = protease inhibitor/ritonavir; PO = orally; QTc = QT corrected for heart rate; RPV = rilpivirine

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between nucleoside reverse transcriptase inhibitors (NRTIs) and non-antiretroviral drugs.

Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

This table focuses on interactions with pharmacokinetic study data and interactions without study data but where there is a clinical recommendation. Interactions associated with zidovudine (ZDV) are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between ZDV and other drugs.

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Antimycobacterials			
Rifabutin	3TC, ABC, FTC,	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	**Use with caution.** If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed
Rifampin	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF With Rifampin Compared With TDF Alone** • TFV-DP AUC ↑ 4.2-fold **TAF With Rifampin Compared With TAF Alone** • TAF AUC ↓ 55% • TFV-DP AUC ↓ 36% **TAF 25 mg Twice Daily With Rifampin Compared With TAF Once Daily Alone** • TAF AUC ↓ 14% • TFV-DP AUC ↓ 24%	**Use with caution.** If coadministered, monitor virologic response. Intracellular TFV-DP levels are higher when TAF is coadministered with rifampin than when TDF is administered alone, but clinical outcomes have not been studied.
	TDF	↔ AUC TFV	No dose adjustment needed

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rifapentine	3TC, ABC, FTC,	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	**Use with caution.** If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed
Antiseizure			
Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin	ABC	↑ carbamazepine possible ↓ ABC possible with oxcarbazepine, phenobarbital, phenytoin	No dose adjustment needed
	3TC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	**With Carbamazepine** • TAF AUC ↓ 55% • ↓ TAF possible with other anticonvulsants	**Do not coadminister.**
Antivirals—Hepatitis C			
Glecaprevir/Pibrentasvir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↔ TFV AUC	No dose adjustment needed
	TDF	TFV AUC ↑ 29%	No dose adjustment needed
Ledipasvir/Sofosbuvir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	TFV AUC ↑ 27%	No dose adjustment needed
	TDF	Ledipasvir ↑ TFV AUC 35% to 98% when TDF is given with various PIs and NNRTIs. Ledipasvir ↑ TFV C_{min} 55% to 80% when TDF is given with various PIs, NNRTIs, or INSTIs. Further ↑ TFV AUC and C_{max} possible when TDF, ledipasvir/sofosbuvir, and PIs are coadministered.	**Do not coadminister** with EVG/c, TDF, or FTC. If TDF is used, monitor for TDF toxicities. Consider using TAF in patients at risk of TDF-associated adverse events. Consider using TAF or alternative HCV therapy in patients on TDF plus a PI/r or PI/c. The safety of increased TFV exposure with this combination has not been established.
Ribavirin	3TC	↔ 3TC AUC	No dose adjustment needed
	ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	**Ribavirin With Sofosbuvir 400 mg** • ↔ TFV AUC	No dose adjustment needed

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sofosbuvir/Velpatasvir	3TC, ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	TFV C_{max} ↑ 44% to 46% and AUC ↑ 40% when coadministered with various ARV combinations.	If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Sofosbuvir/Velpatasvir/ Voxilaprevir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	TAF AUC ↑ 52% to 57%	No dose adjustment needed
	TDF	TFV C_{max} ↑ 48% and AUC ↑ 39% when coadministered with various ARV combinations.	Monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Antivirals—Miscellaneous (e.g., for Herpesvirus, CMV, HBV, Mpox)			
Adefovir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↑ TFV possible	**Do not coadminister.** Serum concentrations of TDF and/or other renally eliminated drugs may increase.
	TDF	↔ TFV	**Do not coadminister.**
Brincidofovir	3TC, ABC, FTC, TAF, TDF	↔ brincidofovir expected	No dose adjustment needed
Cidofovir	3TC, ABC, FTC, TAF	↔ cidofovir expected	No dose adjustment needed
	TDF	↑ TDF and cidofovir possible	Potential for renal toxicity when TDF is given with a nephrotoxic agent, such as cidofovir. If concomitant use is necessary, closely monitor renal function.
Famciclovir	3TC, ABC, TAF, TDF	↔ expected	No dose adjustment needed
	FTC	↔ AUC FTC, famciclovir	No dose adjustment needed
Ganciclovir, Valganciclovir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF, TDF	↑ ganciclovir or TFV possible	Monitor for dose-related toxicities.
Tecovirimat	3TC, ABC, FTC, TAF, TDF	↔ tecovirimat expected	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
Remdesivir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies—Contraceptives			
Injectable Contraceptives Depot MPA	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC, TDF	↔ FTC AUC ↔ TFV AUC	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norelgestromin, norgestimate, norgestrel)	3TC, ABC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	↔ ethinyl estradiol AUC ↔ norelgestromin AUC ↔ norgestrel AUC	No dose adjustment needed
Hormonal Therapies—Gender Affirming and Menopause			
Estradiol Valerate	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC	↔ FTC AUC ↔ estradiol AUC	
	TDF	↔ TFV AUC ↔ estradiol	
17-β-estradiol	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC	FTC AUC ↓ 14% to 24%	
	TDF	TFV AUC ↓ 12% to 27%	
Other Medications Used for Gender-Affirming Therapy or Menopausal Replacement Therapy	ABC, 3TC, FTC, TAF, TDF	↔ NRTI expected	No dose adjustment needed
Narcotics and Treatment for Opioid Dependence			
Buprenorphine	ABC, FTC	↔ expected	No dose adjustment needed
	3TC, TDF	↔ 3TC, TDF, and buprenorphine	No dose adjustment needed
	TAF	↔ TAF expected	No dose adjustment needed
Methadone	3TC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
	ABC	Methadone clearance ↑ 22%	No dose adjustment needed

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Miscellaneous			
Ethanol	ABC	ABC AUC ↑ 41%	No dose adjustment needed
Riociguat	3TC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
	ABC	Riociguat AUC ↑ 200%	If coadministered, initiate riociguat at 0.5 mg three times daily and monitor for riociguat-related adverse effects (e.g., hypotension).
St. John's Wort	3TC, ABC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	**Do not coadminister.**
Antiretrovirals			
Capsid Inhibitor			
LEN (SQ and PO)	3TC, ABC, FTC	↔ 3TC, ABC, FTC, LEN expected	No dose adjustment needed
	TAF	TAF AUC ↑ 32% ↔ LEN	No dose adjustment needed
	TDF	TDF AUC ↑ 47% ↔ LEN	No dose adjustment needed
INSTIs			
DTG	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↔ TAF AUC	No dose adjustment needed
	TDF	↔ TDF AUC ↔ DTG AUC	No dose adjustment needed
RAL	3TC, ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	RAL AUC ↑ 49%	No dose adjustment needed
PIs			
ATV/c, ATV/r	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF 10 mg With ATV/r** • TAF AUC ↑ 91% **TAF 10 mg With ATV/c** • TAF AUC ↑ 75%	No dose adjustment needed (use TAF 25 mg)

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	TDF	**With ATV (Unboosted)** • ATV AUC ↓ 25% and C_{min} ↓ 23% to 40% (higher C_{min} with RTV than without RTV) • TFV AUC ↑ 24% to 37%	Use ATV 300 mg plus (RTV 100 mg or COBI 150 mg) daily when coadministering TDF 300 mg daily. If using TDF and an H2 receptor antagonist in an ART-experienced patient, use ATV 400 mg plus (RTV 100 mg or COBI 150 mg) daily. Monitor for TDF-associated toxicities.
DRV/c	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF 25 mg With DRV/c** • ↔ TAF	No dose adjustment needed
	TDF	TFV ↑ possible	Monitor for TDF-associated toxicities.
DRV/r	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF 10 mg With DRV/r** • ↔ TAF AUC	No dose adjustment needed
	TDF	TFV AUC ↑ 22% and C_{min} ↑ 37%	Clinical significance is unknown. If coadministered, monitor for TDF-associated toxicities.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; COBI = cobicistat; CMV = cytomegalovirus; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HBV = hepatitis B virus; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MPA = medroxyprogesterone acetate; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PO: oral; RAL = raltegravir; RTV = ritonavir; SQ = subcutaneous; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; TFV-DP = tenofovir diphosphate

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between integrase strand transfer inhibitors (INSTIs) (bictegravir [BIC], dolutegravir [DTG], elvitegravir [EVG], or raltegravir [RAL]) and non-antiretroviral drugs. EVG is always coadministered with cobicistat (COBI or c). Cabotegravir (CAB) intramuscular (IM) plus rilpivirine (RPV) IM are co-packaged into a single product and are coadministered as a complete regimen; therefore, the dosing recommendations and clinical comments reflect the combination of CAB IM and RPV IM treatments. Because drug interaction studies were not conducted with either IM CAB or RPV, dosing recommendations for the IM formulations are based on drug interaction studies using oral CAB and RPV. For information regarding interactions between INSTIs and other antiretroviral (ARV) drugs, including dosing recommendations, refer to Tables 24c, 24e, 24f, and 25b.

Recommendations for managing a particular drug interaction may differ, depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Al, Mg **+/–** **Ca-Containing Antacids** Please refer to the Miscellaneous Drugs section of this table for recommendations on use with other polyvalent cation products (e.g., Fe and Ca supplements, multivitamins).	BIC	**Al/Mg Hydroxide Antacid** • ↔ BIC AUC if antacid is administered 2 hours after BIC and under fasting conditions • BIC AUC ↓ 52% if antacid is administered 2 hours before BIC • BIC AUC ↓ 47% to 79% if administered simultaneously with antacid **$CaCO_3$ Antacid** • ↔ BIC AUC if administered with food • BIC AUC ↓ 33% if administered under fasting conditions	**With Antacids That Contain Al/Mg** • Administer antacids that contain Al/Mg at least 2 hours after or 6 hours before BIC. **With Antacids That Contain Ca** • Administer BIC and antacids that contain Ca together with food. • **Do not coadminister** BIC simultaneously with antacids that contain Ca on an empty stomach.
	CAB PO	CAB PO ↓ expected	**With Antacids That Contain Polyvalent Cations (Al, Mg, or Ca)** • Administer antacid products at least 2 hours before or 4 hours after taking CAB PO.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	CAB IM	↔ CAB IM expected	No dose adjustment needed
	DTG	DTG AUC ↓ 74% if administered simultaneously with antacid DTG AUC ↓ 26% if administered 2 hours before antacid	Administer DTG at least 2 hours before or at least 6 hours after antacids that contain polyvalent cations.
	EVG/c	EVG AUC ↓ 40% to 50% if administered simultaneously with antacid EVG AUC ↓ 15% to 20% if administered 2 hours before or after antacid; ↔ with a 4-hour interval	Separate EVG/c and antacid administration by more than 2 hours.
	RAL	**Al/Mg Hydroxide Antacid** • RAL C_{min} ↓ 49% to 63% **$CaCO_3$ Antacid** • RAL 400 mg twice daily: C_{min} ↓ 32% • RAL 1,200 mg once daily: C_{min} ↓ 48% to 57%	**Do not coadminister** RAL and Al/Mg hydroxide antacids. Use alternative acid-reducing agent. **With $CaCO_3$ Antacids** • RAL 1,200 mg once daily: **Do not coadminister.** • RAL 400 mg twice daily: No dose adjustment or separation needed
H2-Receptor Antagonists	BIC, CAB (PO and IM), DTG, EVG/c	↔ INSTI	No dose adjustment needed
	RAL	RAL AUC ↑ 44% and C_{max} ↑ 60%	No dose adjustment needed
Proton Pump Inhibitors	BIC, CAB (PO and IM), DTG, EVG/c	↔ INSTI	No dose adjustment needed
	RAL	RAL AUC ↑ 37% and C_{min} ↑ 24%	No dose adjustment needed
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin	BIC, CAB (PO and IM), DTG, RAL	↔ alfuzosin expected	No dose adjustment needed
	EVG/c	↑ alfuzosin expected	**Contraindicated**
Doxazosin	BIC, CAB (PO and IM), DTG, RAL	↔ doxazosin expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ doxazosin possible	Initiate doxazosin at lowest dose. Titrate based on doxazosin efficacy. Monitor blood pressure. Doxazosin dose reduction may be needed.
Tamsulosin	BIC, CAB (PO and IM), DTG, RAL	↔ tamsulosin expected	No dose adjustment needed
	EVG/c	↑ tamsulosin expected	**Do not coadminister** unless the benefits outweigh the risks. If coadministered, monitor blood pressure.
Terazosin	BIC, CAB (PO and IM), DTG, RAL	↔ terazosin expected	No dose adjustment needed
	EVG/c	↑ terazosin possible	Initiate terazosin at lowest dose. Titrate based on terazosin efficacy. Monitor blood pressure. Terazosin dose reduction may be necessary.
Silodosin	BIC, CAB (PO and IM), DTG, RAL	↔ silodosin expected	No dose adjustment needed
	EVG/c	↑ silodosin expected	**Contraindicated**
Antibacterials—Antimycobacterials			
Bedaquiline	BIC, CAB (PO and IM), DTG, RAL	↔ bedaquiline	No dosage adjustment needed
	EVG/c	↑ bedaquiline possible	**Do not coadminister** unless benefits outweigh risks. If coadministered, consider therapeutic drug monitoring and monitor for bedaquiline-related adverse effects, including hepatotoxicity and QTc prolongation.
Rifabutin	BIC	**Rifabutin 300 mg Once Daily** • BIC AUC ↓ 38% and C_{min} ↓ 56%	**Do not coadminister.**
	CAB PO	CAB PO AUC ↓ 23% and C_{min} ↓ 26% ↔ rifabutin	No dose adjustment needed
	CAB IM	↓ CAB IM and RPV expected ↔ rifabutin expected	**Contraindicated** due to ↓ RPV, which is co-packaged and coadministered with CAB IM.
	DTG	**Rifabutin 300 mg Once Daily** • ↔ DTG AUC and C_{min} ↓ 30%	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	**Rifabutin 150 mg Every Other Day With EVG/c Once Daily Compared to Rifabutin 300 mg Once Daily Alone** • ↔ rifabutin AUC • 25-O-desacetyl-rifabutin AUC ↑ 625% • EVG AUC ↓ 21% and C_{min} ↓ 67%	**Do not coadminister.**
	RAL	↔ RAL AUC and C_{min} ↓ 20%	No dose adjustment needed
Rifampin	BIC	BIC AUC ↓ 75%	**Contraindicated**
	CAB PO	CAB PO AUC ↓ 59% and C_{min} ↓ 50%	**Contraindicated**
	CAB IM	CAB IM ↓ expected	**Contraindicated**
	DTG	**Rifampin With DTG 50 mg Twice Daily Compared to DTG 50 mg Twice Daily Alone** • DTG AUC ↓ 54% and C_{min} ↓ 72% **Rifampin With DTG 50 mg Twice Daily Compared to DTG 50 mg Once Daily Alone** • DTG AUC ↑ 33% and C_{min} ↑ 22%	Use DTG 50 mg twice daily (instead of DTG 50 mg once daily) in patients without suspected or documented INSTI-associated resistance mutations. Consider an alternative to rifampin, such as rifabutin, in patients with certain suspected or documented INSTI-associated resistance mutations.
	EVG/c	Significant ↓ EVG and COBI expected	**Contraindicated**
	RAL	**RAL 400 mg** • RAL AUC ↓ 40% and C_{min} ↓ 61% **Rifampin With RAL 800 mg Twice Daily Compared to RAL 400 mg Twice Daily Alone** • RAL AUC ↑ 27% and C_{min} ↓ 53%	Use RAL 800 mg twice daily instead of 400 mg twice daily. **Do not coadminister** RAL 1,200 mg once daily with rifampin. Monitor closely for virologic response or consider using rifabutin as an alternative rifamycin.
Rifapentine	BIC, EVG/c	Significant ↓ BIC, EVG, and COBI expected	**Do not coadminister.**
	CAB (PO and IM)	Significant ↓ CAB (PO and IM) expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DTG	**Rifapentine 900 mg Once Weekly** • DTG AUC ↓ 26% and C_{min} ↓ 47% **Rifapentine 600 mg Once Daily With DTG 50 mg Twice Daily vs DTG 50 mg Once Daily Alone** • ↔ DTG AUC and C_{min}	With **once-weekly** rifapentine, DTG 50 mg daily may be used in patients with viral suppression on daily DTG. Monitor for virologic efficacy. **Do not coadminister** in patients who require twice-daily DTG. With **once-daily** rifapentine for 4 weeks (1HP), use DTG 50 mg twice daily. See Tuberculosis/HIV Coinfection for more on rifapentine and DTG use.
	RAL	**Rifapentine 900 mg Once Weekly** • RAL AUC ↑ 71% and C_{min} ↓ 12% **Rifapentine 600 mg Once Daily** • RAL C_{min} ↓ 41%	For once-weekly rifapentine and RAL 400 mg twice daily, no dose adjustment is needed. **Do not coadminister** with once-daily rifapentine.
Antibacterials—Macrolides			
Azithromycin	All INSTIs	↔ azithromycin expected	No dose adjustment needed
Clarithromycin	BIC	↑ BIC possible	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ clarithromycin expected	No dose adjustment needed
	EVG/c	↑ clarithromycin expected ↑ COBI possible	Reduce clarithromycin dose by 50% in patients with CrCl 50 to 60 mL/min. **Do not coadminister** in patients with CrCl <50 mL/min. Consider alternative ARV or use azithromycin.
Erythromycin	BIC	↑ BIC possible	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ erythromycin expected	No dose adjustment needed
	EVG/c	↑ erythromycin expected ↑ COBI possible	No data available for dose recommendation. Consider alternative ARV or use azithromycin.
Anticoagulants			
Apixaban	BIC, CAB (PO and IM), DTG, RAL	↔ apixaban expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ apixaban expected	**Do not coadminister** in patients who require apixaban 2.5 mg twice daily. Reduce apixaban dose by 50% in patients who require apixaban 5 mg or 10 mg twice daily.
Dabigatran	BIC, CAB (PO and IM), DTG, RAL	↔ dabigatran expected	No dose adjustment needed
	EVG/c	↑ dabigatran expected **With COBI 150 mg Alone** • Dabigatran AUC ↑ 110% to 127%	**Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation in Adult Patients** • CrCl >30 mL/min: no dose adjustment needed • CrCl ≤30 mL/min: **do not coadminister.** **Treatment and Reduction in the Risk of Recurrence of DVT and PE or Prophylaxis of DVT and PE Following Hip Replacement Surgery in Adult Patients** • CrCl ≥50 mL/min: no dose adjustment needed • CrCl <50 mL/min: **do not coadminister.**
Edoxaban	BIC, CAB (PO and IM), DTG, RAL	↔ edoxaban expected	No dose adjustment needed
	EVG/c	↑ edoxaban expected	**Stroke Prevention in Nonvalvular Atrial Fibrillation** • No dose adjustment needed **DVT and PE** • Administer edoxaban 30 mg once daily.
Rivaroxaban	BIC, CAB (PO and IM), DTG, RAL	↔ rivaroxaban expected	No dose adjustment needed
	EVG/c	↑ rivaroxaban expected	**Do not coadminister.**
Warfarin	BIC, CAB (PO and IM), DTG, RAL	↔ warfarin expected	No dose adjustment needed
	EVG/c	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Antiseizure			
Carbamazepine	BIC	↓ BIC possible	**Do not coadminister.**
	CAB (PO and IM)	↓ CAB expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DTG	DTG AUC ↓ 49%	Increase DTG dose to 50 mg twice daily in ART-naive or ART-experienced (but INSTI-naive) patients. **Do not coadminister** in INSTI-experienced patients with known or suspected INSTI resistance.
	EVG/c	Carbamazepine AUC ↑ 43% EVG AUC ↓ 69% and C_{min} ↓ >99% ↓ COBI expected	**Contraindicated**
	RAL	↓ or ↔ RAL possible	**Do not coadminister.**
Eslicarbazepine	All INSTIs	↓ INSTI possible ↓ COBI possible	Consider alternative ARV or anticonvulsant.
Ethosuximide	BIC, CAB (PO and IM), DTG, RAL	↔ ethosuximide expected	No dose adjustment needed
	EVG/c	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.
Lamotrigine	BIC, CAB (PO and IM), DTG, RAL	↔ lamotrigine expected	No dose adjustment needed
	EVG/c	No data	Monitor anticonvulsant concentrations and adjust dose accordingly.
Oxcarbazepine	BIC, DTG	↓ BIC and DTG possible	**Do not coadminister.**
	CAB (PO and IM)	↓ CAB expected	**Contraindicated**
	EVG/c, RAL	↓ EVG/c and RAL possible	Consider alternative ARV or anticonvulsant.
Phenobarbital, Phenytoin, Primidone	BIC, DTG, RAL	↓ BIC and DTG possible ↓ or ↔ RAL possible	**Do not coadminister.**
	CAB (PO and IM), EVG/c	↓ CAB and EVG/c expected	**Contraindicated**
Valproic Acid	DTG	DTG ↓ possible	No dose adjustment needed. Take with food and monitor virologic response.
	BIC, CAB (PO and IM), RAL	No data	No dose adjustment needed. Monitor virologic response.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
Antidepressants, Anxiolytics			
Bupropion	BIC, CAB (PO and IM), DTG, RAL	↔ bupropion expected	No dose adjustment needed
	EVG/c	↑ bupropion possible	Titrate bupropion dose based on clinical response.
Buspirone	BIC, CAB (PO and IM), DTG, RAL	↔ buspirone expected	No dose adjustment needed
	EVG/c	↑ buspirone possible	Initiate buspirone at a low dose. Buspirone dose reduction may be needed.
Desvenlafaxine	All INSTIs	↔ desvenlafaxine expected	No dose adjustment needed
Duloxetine	BIC, CAB (PO and IM), DTG, RAL	↔ duloxetine expected	No dose adjustment needed
	EVG/c	↑ duloxetine possible	No dose adjustment needed
Mirtazapine	BIC, CAB (PO and IM), DTG, RAL	↔ mirtazapine expected	No dose adjustment needed
	EVG/c	↑ mirtazapine possible	Monitor for mirtazapine-related adverse events. Mirtazapine dose reduction may be necessary.
Nefazodone	BIC, CAB (PO and IM), DTG, RAL	↔ nefazodone expected	No dose adjustment needed
	EVG/c	↑ nefazodone expected	Consider alternative ARV or antidepressant.
Trazodone	BIC, CAB (PO and IM), DTG, RAL	↔ trazodone expected	No dose adjustment needed
	EVG/c	↑ trazodone possible	Titrate dose based on antidepressant response and monitor for trazodone-related adverse events.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Tricyclic Antidepressants (e.g., amitriptyline, desipramine, doxepin, imipramine, nortriptyline)	BIC, CAB (PO and IM), DTG, RAL	↔ TCA expected	No dose adjustment needed
	EVG/c	Desipramine AUC ↑ 65%	Initiate with lowest dose of TCA and titrate dose carefully.
		↑ TCA expected	Initiate with lowest dose of TCA. Titrate dose carefully based on antidepressant response and/or drug concentrations.
Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	EVG/c	↔ sertraline	No dose adjustment needed
	EVG/c	↑ other SSRIs possible	Initiate with lowest dose of SSRI. Titrate dose carefully based on antidepressant response.
	BIC, CAB (PO and IM), DTG, RAL	↔ SSRI expected	No dose adjustment needed
Venlafaxine	BIC, CAB (PO and IM), DTG, RAL	↔ venlafaxine expected	No dose adjustment needed
	EVG/c	↑ venlafaxine possible	Monitor for venlafaxine-related adverse events.
Antipsychotics			
Aripiprazole	BIC, CAB (PO and IM), DTG, RAL	↔ aripiprazole expected	No dose adjustment needed
	EVG/c	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate based on aripiprazole effectiveness and adverse events. Refer to aripiprazole label for dosing recommendations in patients who are known to be CYP2D6-poor metabolizers or who have major depressive disorder.
Brexpiprazole	BIC, CAB (PO and IM), DTG, RAL	↔ brexpiprazole expected	No dose adjustment needed
	EVG/c	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate based on brexpiprazole effectiveness and adverse events. Refer to brexpiprazole label for dosing recommendations in patients who are known to be CYP2D6-poor metabolizers or who have major depressive disorder.
Cariprazine	BIC, CAB (PO and IM), DTG, RAL	↔ cariprazine expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ cariprazine expected	**Starting Cariprazine in a Patient Who Is Already Receiving EVG/c** • Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum of cariprazine 3 mg daily. If EVG/c is withdrawn, cariprazine dose may need to be increased. **Starting EVG/c in a Patient Who Is Already Receiving Cariprazine** • For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce the dose by half. For patients receiving cariprazine 4.5 mg daily, reduce dose to cariprazine 1.5 mg or cariprazine 3 mg daily. For patients receiving cariprazine 1.5 mg daily, change to cariprazine 1.5 mg every other day. If EVG/c is withdrawn, cariprazine dose may need to be increased.
Iloperidone	BIC, CAB (PO and IM), DTG, RAL	↔ iloperidone expected	No dose adjustment needed
	EVG/c	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lumateperone	BIC, CAB (PO and IM), DTG, RAL	↔ lumateperone expected	No dose adjustment needed
	EVG/c	↑ lumateperone expected	**Do not coadminister.**
Lurasidone	BIC, CAB (PO and IM), DTG, RAL	↔ lurasidone expected	No dose adjustment needed
	EVG/c	↑ lurasidone expected	**Contraindicated**
Olanzapine, Olanzapine/ Samidorphan	All INSTIs	↔ olanzapine expected	No dose adjustment needed
	EVG/c	↔ olanzapine expected ↑ samidorphan possible	No dose adjustment needed
Other Antipsychotics CYP3A4 and/or CYP2D6 substrates (e.g., perphenazine, risperidone, thioridazine)	EVG/c	↑ antipsychotic possible	Initiate antipsychotic at a low dose. Antipsychotic dose reduction may be needed.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Pimavanserin	BIC, CAB (PO and IM), DTG, RAL	↔ pimavanserin expected	No dose adjustment needed
	EVG/c	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg.
Pimozide	BIC, CAB (PO and IM), DTG, RAL	↔ pimozide expected	No dose adjustment needed
	EVG/c	↑ pimozide expected	**Contraindicated**
Quetiapine	BIC, CAB (PO and IM), DTG, RAL	↔ quetiapine expected	No dose adjustment needed
	EVG/c	↑ quetiapine AUC expected	**Starting Quetiapine in a Patient Receiving EVG/c** • Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse events. **Starting EVG/c in a Patient Receiving a Stable Dose of Quetiapine** • Reduce quetiapine dose to 1/6 of the current dose. Closely monitor for quetiapine efficacy and adverse events.
Ziprasidone	BIC, CAB (PO and IM), DTG, RAL	↔ ziprasidone expected	No dose adjustment needed
	EVG/c	↑ ziprasidone possible	Monitor for ziprasidone-related adverse events.
Antimigraine			
Ergot Derivatives	BIC, CAB (PO and IM), DTG, RAL	↔ dihydroergotamine, ergotamine, and methylergonovine expected	No dose adjustment needed
	EVG/c	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Contraindicated**
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	BIC, CAB (PO and IM), DTG, RAL	↔ atogepant expected ↑ atogepant expected	No dose adjustment needed
	EVG/c	↑ atogepant expected	Chronic migraine: **Do not coadminister.** Episodic migraine: Administer atogepant at a dose of 10 mg once daily.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rimegepant	BIC, CAB (PO and IM), DTG, RAL	↔ rimegepant expected	No dose adjustment needed
	EVG/c	↑ rimegepant expected	**Do not coadminister.**
Ubrogepant	BIC, CAB (PO and IM), DTG, RAL	↔ ubrogepant expected	No dose adjustment needed
	EVG/c	↑ ubrogepant expected	**Contraindicated**
Zavegepant	BIC, CAB (PO and IM), DTG, RAL	↔ zavegepant expected	No dose adjustment needed
	EVG/c	↑ zavegepant expected	**Do not coadminister.**
Serotonin 5-HT1B, 1D Receptor Agonist			
Almotriptan	BIC, CAB (PO and IM), DTG, RAL	↔ almotriptan expected	No dose adjustment needed
	EVG/c	↑ almotriptan expected	Administer single dose of almotriptan 6.25 mg. Maximum dose should not exceed 12.5 mg in a 24-hour period.
Eletriptan	BIC, CAB (PO and IM), DTG, RAL	↔ eletriptan expected	No dose adjustment needed
	EVG/c	↑ eletriptan expected	**Contraindicated**
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan Zolmitriptan	All INSTIs	↔ triptan expected	No dose adjustment needed
Antifungals			
Ibrexafungerp	BIC, CAB (PO and IM), DTG, RAL	↔ ibrexafungerp expected	No dose adjustment needed
	EVG/c	↑ ibrexafungerp expected	Reduce ibrexafungerp dose to 150 mg twice daily.
Isavuconazole	BIC, CAB (PO and IM), DTG, RAL	↑ INSTI possible	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ isavuconazole expected ↑ or ↓ EVG and COBI possible	**Contraindicated**
Itraconazole	BIC	↑ BIC expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ itraconazole expected	No dose adjustment needed
	EVG/c	↑ itraconazole expected ↑ EVG and COBI possible	Consider monitoring itraconazole concentrations to guide dose adjustments. **Do not coadminister** with high itraconazole doses (>200 mg/day) unless guided by itraconazole concentrations.
Posaconazole	BIC	↑ BIC expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ posaconazole expected	No dose adjustment needed
	EVG/c	↑ EVG and COBI possible ↑ posaconazole possible	If coadministered, monitor posaconazole concentrations.
Voriconazole	BIC	↑ BIC possible	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ voriconazole expected	No dose adjustment needed
	EVG/c	↑ voriconazole expected ↑ EVG and COBI possible	**Do not coadminister** voriconazole and COBI, unless the benefit outweighs the risk. If coadministered, consider monitoring voriconazole concentrations and adjust dose accordingly.
Antimalarials			
Artemether/ Lumefantrine	BIC	↔ antimalarial expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ antimalarial expected	No dose adjustment needed
	EVG/c	↑ artemether and lumefantrine possible	Monitor for artemether and lumefantrine-related adverse events, including QTc prolongation.
Artesunate	All INSTIs	↔ dihydroartemisinin expected	No dose adjustment needed
Atovaquone/ Proguanil	All INSTIs	↔ atovaquone/proguanil expected	No dose adjustment needed
Mefloquine	CAB (PO and IM), DTG, RAL	↔ mefloquine expected	No dose adjustment needed
	EVG/c	↑ mefloquine possible	Monitor for mefloquine-related adverse events, including psychiatric symptoms and QTc prolongation.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Glucose-Lowering			
Metformin	BIC	Metformin AUC ↑ 39%	Monitor for adverse events of metformin.
	CAB (PO and IM), RAL	↔ metformin expected	No dose adjustment needed
	DTG	**DTG 50 mg Once Daily Plus Metformin 500 mg Twice Daily** • Metformin AUC ↑ 79% and C_{max} ↑ 66% **DTG 50 mg Twice Daily Plus Metformin 500 mg Twice Daily** • Metformin AUC ↑ 2.4-fold and C_{max} ↑ 2-fold	Start metformin at the lowest dose and titrate based on glycemic control. Monitor for adverse events of metformin. When starting/stopping DTG in patients on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize adverse events of metformin.
	EVG/c	↑ metformin possible	No dose adjustment needed
Saxagliptin	BIC, CAB (PO and IM), DTG, RAL	↔ saxagliptin expected	No dose adjustment needed
	EVG/c	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/ Saxagliptin	BIC, CAB (PO and IM), DTG, RAL	↔ dapagliflozin or saxagliptin expected	No dose adjustment needed
	EVG/c	↑ saxagliptin expected	**Do not coadminister.** Dapagliflozin is available only as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination **is not recommended.**
Antiplatelets			
Clopidogrel	BIC, CAB (PO and IM), DTG, RAL	↔ clopidogrel expected	No dose adjustment needed
	EVG/c	↓ clopidogrel active metabolite, with impaired platelet inhibition expected	**Do not coadminister.**
Prasugrel	BIC, CAB (PO and IM), DTG, RAL	↔ prasugrel expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↓ prasugrel active metabolite, with no impairment of platelet inhibition expected	No dose adjustment needed
Ticagrelor	BIC, CAB (PO and IM), DTG, RAL	↔ ticagrelor expected	No dose adjustment needed
	EVG/c	↑ ticagrelor expected	**Do not coadminister.**
Vorapaxar	BIC, CAB (PO and IM) DTG, RAL	↔ vorapaxar expected	No dose adjustment needed
	EVG/c	↑ vorapaxar expected	**Do not coadminister.**
Antipneumocystis and Antitoxoplasmosis			
Atovaquone	All INSTIs	↔ atovaquone expected	No dose adjustment needed
Antivirals—Hepatitis C			
Elbasvir/Grazoprevir	BIC	↔ BIC expected	No dose adjustment needed
	CAB (PO and IM)	↔ CAB, elbasvir, and grazoprevir expected	No dose adjustment needed
	DTG	↔ DTG ↔ elbasvir ↔ grazoprevir	No dose adjustment needed
	EVG/c	↑ elbasvir expected ↑ grazoprevir expected	**Do not coadminister.**
	RAL	↔ RAL with elbasvir RAL AUC ↑ 43% with grazoprevir ↔ elbasvir ↔ grazoprevir	No dose adjustment needed
Glecaprevir/ Pibrentasvir	BIC, CAB (PO and IM)	↔ BIC or CAB expected	No dose adjustment needed
	DTG	↔ DTG and glecaprevir/ pibrentasvir	No dose adjustment needed
	RAL	No significant effect RAL AUC ↑ 47%	
	EVG/c	Glecaprevir AUC ↑ 3-fold Pibrentasvir AUC ↑ 57%	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		EVG AUC ↑ 47%	If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.
Ledipasvir/ Sofosbuvir	BIC, DTG, RAL	↔ BIC, DTG, and RAL	No dose adjustment needed
	CAB (PO and IM)	↔ CAB expected	No dose adjustment needed
	EVG/c/TDF/ FTC	↑ TDF expected ↑ ledipasvir expected	**Do not coadminister.**
	EVG/c/TAF/ FTC	↔ EVG/c/TAF/FTC expected	No dose adjustment needed
Sofosbuvir	BIC, CAB (PO and IM), DTG, EVG/C	↔ INSTI expected ↔ sofosbuvir expected	No dose adjustment needed
	RAL	↔ RAL and sofosbuvir	No dose adjustment needed
Sofosbuvir/ Velpatasvir	BIC, DTG, RAL	↔ sofosbuvir and velpatasvir	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events.
	CAB (PO and IM)	↔ CAB expected ↔ sofosbuvir and velpatasvir expected	
	EVG/c	↔ EVG/c/TAF/FTC Velpatasvir AUC ↑ 50%	
Sofosbuvir/ Velpatasvir/ Voxilaprevir	BIC	**When Administered With Sofosbuvir/Velpatasvir/ Voxilaprevir (400 mg/ 100 mg/100 mg) Plus Voxilaprevir 100 mg** • ↔ BIC, sofosbuvir, velpatasvir, voxilaprevir	No dose adjustment needed
	EVG/c	**When Administered With Sofosbuvir/Velpatasvir/ Voxilaprevir (400 mg/ 100 mg/100 mg) Plus Voxilaprevir 100 mg** • Sofosbuvir AUC ↑ 22% • ↔ velpatasvir • Voxilaprevir AUC ↑ 2-fold	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.
	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ sofosbuvir, velpatasvir, and voxilaprevir expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected	No dose adjustment needed
	EVG/c	↑ brincidofovir possible ↑ EVG possible	Administer EVG/c dose at least 3 hours after administering brincidofovir and monitor for brincidofovir-related adverse events, including elevations in ALT/AST and bilirubin and GI adverse events.
Cidofovir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI expected ↔ cidofovir expected	No dose adjustment needed
Tecovirimat	CAB (IM)	↔ CAB expected	No dose adjustment needed Do not initiate CAB/RPV IM during or within 2 weeks after tecovirimat treatment. (Refer to Table 24b for interaction with RPV.)
	BIC, CAB (PO), DTG, EVG/c, RAL	↔ INSTI expected	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI and molnupiravir expected	No dose adjustment needed
Ritonavir-boosted Nirmatrelvir	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI and ritonavir-boosted nirmatrelvir expected	No dose adjustment needed.
	EVG/c/FTC/TAF	↑ TAF possible ↔ ritonavir-boosted nirmatrelvir expected	No dose adjustment needed
Remdesivir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI and remdesivir expected	No dose adjustment needed
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	All INSTIs	↔ arformoterol or formoterol expected	No dose adjustment needed
Indacaterol	BIC, CAB (PO and IM), DTG, RAL	↔ indacaterol expected	No dose adjustment needed
	EVG/c	↑ indacaterol expected	

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Olodaterol	BIC, CAB (PO and IM), DTG, RAL	↔ olodaterol expected	No dose adjustment needed
	EVG/c	↑ olodaterol expected	
Salmeterol	BIC, CAB (PO and IM), DTG, RAL	↔ salmeterol expected	No dose adjustment needed
	EVG/c	↑ salmeterol possible	**Do not coadminister** due to the potential for increased risk of salmeterol-associated cardiovascular events.
Cardiac Medications			
Antiarrhythmics			
Amiodarone	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ amiodarone expected	No dose adjustment needed
	EVG/c	↑ amiodarone expected	**Do not coadminister** unless the benefits outweigh the risks. If coadministration is necessary, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone concentrations.
Digoxin	BIC, CAB (PO and IM), RAL	↔ digoxin expected	No dose adjustment needed
	EVG/c	Digoxin C_{max} ↑ 41% and ↔ AUC	Therapeutic drug monitoring for digoxin is recommended if available.
Dofetilide	CAB (PO and IM)	↔ dofetilide expected	No dose adjustment needed
	BIC, DTG	↑ dofetilide expected	**Contraindicated**
	EVG/c	↑ dofetilide possible	**Do not coadminister.**
Disopyramide	BIC, CAB (PO and IM), RAL	↔ disopyramide expected	No dose adjustment needed
	DTG	↑ disopyramide possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor disopyramide concentrations and for antiarrhythmic-related adverse events.
	EVG/c	↑ disopyramide expected	**Do not coadminister.**
Dronedarone	BIC, CAB (PO and IM), DTG, RAL	↔ dronedarone expected	No dose adjustment needed
	EVG/c	↑ dronedarone expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Flecainide	BIC, CAB (PO and IM), DTG, RAL	↔ flecainide expected	No dose adjustment needed
	EVG/c	↑ flecainide possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor flecainide concentrations and for antiarrhythmic-related adverse events.
Propafenone	BIC, CAB (PO and IM), DTG, RAL	↔ propafenone expected	No dose adjustment needed
	EVG/c	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor propafenone concentrations and for antiarrhythmic-related adverse events.
Mexiletine	BIC, CAB (PO and IM), DTG, RAL	↔ mexiletine expected	No dose adjustment needed
	EVG/c	↑ mexiletine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor mexiletine concentrations and for antiarrhythmic-related adverse events.
Systemic Lidocaine	BIC, CAB (PO and IM), DTG, RAL	↔ lidocaine expected	No dose adjustment needed
	EVG/c	↑ lidocaine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor lidocaine concentrations and for antiarrhythmic-related adverse events.
Quinidine	BIC, CAB (PO and IM), DTG, RAL	↔ quinidine expected	No dose adjustment needed
	EVG/c	↑ quinidine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor quinidine concentrations and for antiarrhythmic-related adverse events.
Beta-Blockers			
Atenolol, Bisoprolol, Carvedilol, Metoprolol, Nadolol, Nebivolol, Sotalol	CAB (PO and IM), RAL	↔ beta-blocker expected	No dose adjustment needed
	BIC, DTG, EVG/c	↑ beta-blocker possible	Beta-blocker dose may need to be decreased; adjust dose based on clinical response.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Calcium Channel Blockers			
Calcium Channel Blockers	BIC	↑ BIC possible with diltiazem ↔ expected for all other CCBs	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ CCB expected	No dose adjustment needed
	EVG/c	↑ CCB possible	Titrate CCB dose and monitor for CCB efficacy and adverse events.
Cardiac—Other			
Bosentan	BIC, DTG	↓ BIC and DTG possible	No dose adjustment needed
	CAB (PO and IM)	↔ bosentan expected	Consider using alternative ARV or an alternative to bosentan because bosentan may ↓ RPV, which is co-packaged and coadministered with CAB IM. If bosentan is used with RPV, monitor virologic response to ART.
	RAL	↔ bosentan expected	No dose adjustment needed
	EVG/c	↑ bosentan possible	**In Patients on EVG/c ≥10 Days** • Start bosentan at 62.5 mg once daily or every other day based on individual tolerability. **In Patients on Bosentan Who Require EVG/c** • Stop bosentan ≥36 hours before EVG/c initiation. At least 10 days after initiation of EVG/c, resume bosentan at 62.5 mg once daily or every other day based on individual tolerability.
Dofetilide	BIC, DTG	↑ dofetilide expected	**Contraindicated**
	CAB (PO and IM), RAL	↔ dofetilide expected	No dose adjustment needed
	EVG/c	↑ dofetilide possible	**Do not coadminister.**
Eplerenone	BIC, CAB (PO and IM), DTG, RAL	↔ eplerenone expected	No dose adjustment needed
	EVG/c	↑ eplerenone expected	**Contraindicated**
Ivabradine	BIC, CAB (PO and IM), DTG, RAL	↔ ivabradine expected	No dose adjustment needed
	EVG/c	↑ ivabradine expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Mavacamten	BIC, CAB (PO and IM), DTG, RAL	↔ mavacamten expected	No dose adjustment needed
	EVG/c	↑ mavacamten expected	**Contraindicated**
Ranolazine	BIC, CAB (PO and IM), DTG, RAL	↔ ranolazine expected	No dose adjustment needed
	EVG/c	↑ ranolazine expected	**Contraindicated**
Corticosteroids			
Beclomethasone Inhaled or intranasal	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ glucocorticoid expected	No dose adjustment needed
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	BIC, CAB (PO and IM), DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed
	EVG/c	↑ glucocorticoid possible	**Do not coadminister** unless the potential benefits of inhaled or intranasal corticosteroid outweigh the risks of systemic corticosteroid adverse effects. Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider using an alternative corticosteroid (e.g., beclomethasone).
Betamethasone, Budesonide Systemic	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ glucocorticoid expected	No dose adjustment needed
	EVG/c	↑ glucocorticoid possible ↓ EVG possible	**Do not coadminister** unless the potential benefits of systemic budesonide outweigh the risks of systemic corticosteroid adverse effects. Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Dexamethasone Systemic	BIC	↓ BIC possible	Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART.
	CAB (PO and IM), DTG, RAL	↔ INSTI expected	No dose adjustment needed
	EVG/c	↓ EVG and COBI possible	Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	BIC, CAB (PO and IM), DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ prednisolone possible	Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministration is necessary, monitor for adrenal insufficiency and Cushing's syndrome.
Betamethasone, Methylprednisolone, Prednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	BIC, CAB (PO and IM), DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed
	EVG/c	↑ glucocorticoid expected	**Do not coadminister.** Coadministration may result in adrenal insufficiency and Cushing's syndrome.
Herbal Products			
St. John's Wort	BIC, CAB (PO and IM), DTG	↓ BIC and DTG possible	**Do not coadminister.**
	EVG/c	↓ EVG and COBI expected	**Contraindicated**
Hormonal Therapies			
Injectable Contraceptives Depot MPA	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI and injectable contraceptive expected	No dose adjustment needed
	EVG/c	↑ MPA possible	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norethindrone, norgestimate)	BIC, CAB (PO, IM), DTG, RAL	↔ ethinyl estradiol and norgestimate with DTG ↔ ethinyl estradiol and levonorgestrel with CAB PO ↔ ethinyl estradiol and norgestimate expected with BIC, RAL ↔ norgestimate expected with CAB PO and IM ↔ levonorgestrel expected ↔ drospirenone expected ↔ norethindrone expected	No dose adjustment needed
	EVG/c	Norgestimate AUC, C_{max}, and C_{min} ↑ > 2-fold Ethinyl estradiol AUC ↓ 25% and C_{min} ↓ 44%	The effects of increases in progestin (norgestimate) are not fully known and may include insulin resistance, dyslipidemia, acne, and venous thrombosis. Decreased ethinyl estradiol may lead to more intermenstrual bleeding. Weigh the risks and benefits of using the drug and consider using an alternative ARV or contraceptive method.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		↑ drospirenone possible	Clinical monitoring is recommended due to the potential for hyperkalemia. Consider using alternative ARV or contraceptive method.
		↑ levonorgestrel possible ↑ norethindrone expected	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	BIC, CAB (PO and IM), DTG, RAL	Etonogestrel ↑ 27% with DTG ↔ etonogestrel or levonorgestrel expected with BIC, CAB, RAL	No dose adjustment needed
	EVG/c	↑ etonogestrel expected ↑ levonorgestrel expected	No dose adjustment needed
Transdermal Contraceptives (e.g., ethinyl estradiol/ norelgestromin, ethinyl estradiol/ levonorgestrel)	BIC, CAB (PO, IM), DTG, RAL	↔ contraceptive expected	No dose adjustment needed
	EVG/c	↑ progestin possible ↓ ethinyl estradiol possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ ethinyl estradiol, segesterone/ethinyl estradiol)	BIC, CAB (PO, IM), DTG, RAL	↔ contraceptive expected	No dose adjustment needed
	EVG/c	↑ progestin possible ↓ ethinyl estradiol possible	For segesterone/ethinyl estradiol vaginal rings, use alternative ARV or contraceptive methods.
Emergency Contraceptives Levonorgestrel (PO)	BIC, CAB (PO, IM), DTG, RAL	↔ levonorgestrel expected	No dose adjustment needed
	EVG/c	↑ levonorgestrel possible	No dose adjustment needed
Hormonal Therapies—Gender-Affirming and Menopause			
Gender-Affirming Therapy	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment needed
	BIC, CAB (PO and IM), DTG, RAL	↔ estrogen expected	No dose adjustment needed
		↔ testosterone expected	No dose adjustment needed
	EVG/c	↑ or ↓ estradiol possible ↑ cyproterone, dutasteride, and finasteride possible	Adjust dutasteride dose as needed based on clinical effects and endogenous hormone concentrations.
		↑ testosterone possible	Monitor masculinizing effects of testosterone and monitor for adverse effects. Adjust testosterone dose as necessary.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Menopausal Replacement Therapy	BIC, CAB (PO and IM), DTG, RAL	↔ estrogen expected with estradiol or conjugated estrogen (equine and synthetic) ↔ drospirenone, MPA, and micronized progesterone expected	No dose adjustment needed
	EVG/c	↓ or ↑ estrogen possible ↑ drospirenone possible ↑ oral MPA possible ↑ oral micronized progesterone possible	Adjust estrogen and progestin dose as needed based on clinical effects.
Immunosuppressants			
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	BIC, CAB (PO and IM), DTG, RAL	↔ immunosuppressant expected	No dose adjustment needed
	EVG/c	↑ immunosuppressant possible	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant. Monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
Lipid-Modifying			
Atorvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ atorvastatin expected	No dose adjustment needed
	EVG/c	Atorvastatin AUC ↑ 2.6-fold and C_{max} ↑ 2.3-fold	Administer the lowest effective dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
Fluvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ fluvastatin expected	No dose adjustment needed
	EVG/c	↑ fluvastatin possible	Administer the lowest effective fluvastatin dose while monitoring for adverse events.
Lomitapide	BIC, CAB (PO and IM), DTG, RAL	↔ lomitapide expected	No dose adjustment needed
	EVG/c	↑ lomitapide expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lovastatin	BIC, CAB (PO and IM), DTG, RAL	↔ lovastatin expected	No dose adjustment needed
	EVG/c	Significant ↑ lovastatin expected	**Contraindicated**
Pitavastatin, Pravastatin	BIC, CAB (PO and IM), DTG, RAL	↔ statin expected	No dose adjustment needed
	EVG/c	No data	No dose adjustment needed. Monitor for adverse events.
Rosuvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ rosuvastatin expected	No dose adjustment needed
	EVG/c	Rosuvastatin AUC ↑ 38% and C_{max} ↑ 89%	Administer the lowest effective dose while monitoring for adverse events.
Simvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ simvastatin expected	No dose adjustment needed
	EVG/c	Significant ↑ simvastatin expected	**Contraindicated**
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	BIC, CAB (PO and IM), DTG	↔ buprenorphine and norbuprenorphine (active metabolite) expected	No dose adjustment needed
	EVG/c	Buprenorphine AUC ↑ 35% and C_{min} ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 42% and C_{min} ↑ 57%	No dose adjustment needed. Monitor for adverse events of buprenorphine. When transferring buprenorphine from transmucosal administration to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	RAL	↔ buprenorphine and norbuprenorphine (active metabolite) (sublingual) ↔ buprenorphine or norbuprenorphine (active metabolite) expected (implant)	No dose adjustment needed
Fentanyl	BIC, CAB (PO and IM), DTG, RAL	↔ fentanyl expected	No dose adjustment needed
	EVG/c	↑ fentanyl	Monitor for fentanyl efficacy and adverse events, including potentially fatal respiratory depression.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lofexidine	BIC, CAB (PO and IM), DTG, RAL	↔ lofexidine expected	No dose adjustment needed
	EVG/c	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	All INSTIs	↔ methadone	No dose adjustment needed
Tramadol	BIC, CAB (PO and IM), DTG, RAL	↔ tramadol and M1 (active metabolite) expected	No dose adjustment needed
	EVG/c	↑ tramadol expected ↓ M1 (active metabolite) possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors			
Avanafil	BIC, CAB (PO and IM), DTG, RAL	↔ avanafil expected	No dose adjustment needed
	EVG/c	No data	**Do not coadminister.**
Sildenafil	BIC, CAB (PO and IM), DTG, RAL	↔ sildenafil expected	No dose adjustment needed
	EVG/c	↑ sildenafil expected	**For Treatment of Erectile Dysfunction** • Start with sildenafil 25 mg every 48 hours and monitor for sildenafil-related adverse events. **Contraindicated** for treatment of PAH.
Tadalafil	BIC, CAB (PO and IM), DTG, RAL	↔ tadalafil expected	No dose adjustment needed
	EVG/c	↑ tadalafil expected	**For Treatment of Erectile Dysfunction** • Start with tadalafil 5 mg. Do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for tadalafil-related adverse events. **For Treatment of PAH** *In Patients on EVG/c >7 Days* • Start with tadalafil 20 mg once daily. Increase to tadalafil 40 mg once daily based on tolerability.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			In Patients on Tadalafil who Require EVG/c • Stop tadalafil ≥24 hours before EVG/c initiation. Seven days after EVG/c initiation, restart tadalafil at 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability.
Vardenafil	BIC, CAB (PO and IM), DTG, RAL	↔ vardenafil expected	No dose adjustment needed
	EVG/c	↑ vardenafil expected	Start with vardenafil 2.5 mg every 72 hours and monitor for vardenafil-related adverse events.
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Clonazepam, Clorazepate, Diazepam, Estazolam, Flurazepam	BIC, CAB (PO and IM), DTG, RAL	↔ benzodiazepine expected	No dose adjustment needed
	EVG/c	↑ benzodiazepine possible	Dose reduction of benzodiazepine may be necessary. Initiate with a low dose and monitor for benzodiazepine-related adverse events. Consider using an alternative benzodiazepine, such as lorazepam, oxazepam, or temazepam.
Midazolam, Triazolam	BIC, CAB (PO and IM), RAL	↔ benzodiazepine expected	No dose adjustment needed
	DTG	**With DTG 25 mg** • ↔ midazolam AUC	No dose adjustment needed
	EVG/c	↑ midazolam expected ↑ triazolam expected	**Contraindicated** **Do not coadminister** triazolam or oral midazolam and EVG/c. Parenteral midazolam can be administered in a closely monitored setting. Consider dose reduction, especially if >1 dose is administered.
Orexin Receptor Antagonists			
Daridorexant, Lemborexant, Suvorexant	BIC, CAB (PO and IM), DTG, RAL	↔ daridorexant, lemborexant, suvorexant expected	No dose adjustment needed
	EVG/c	↑ daridorexant, lemborexant, suvorexant expected	**Do not coadminister.**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Other Sedatives			
Eszopiclone	BIC, CAB (PO and IM), DTG, RAL	↔ eszopiclone expected	No dose adjustment needed
	EVG/c	↑ eszopiclone expected	Start with lowest dose and increase to a max of 2 mg daily. Monitor for eszopiclone-related adverse events.
Zolpidem	BIC, CAB (PO and IM), DTG, RAL	↔ zolpidem expected	No dose adjustment needed
	EVG/c	↑ zolpidem expected	Initiate zolpidem at a low dose. Dose reduction of zolpidem may be necessary.
Miscellaneous Drugs			
Calcifediol	BIC, CAB (PO and IM), DTG, RAL	↔ calcifediol expected	No dose adjustment needed
	EVG/c	↑ calcifediol possible	Dose adjustment of calcifediol may be required. Monitor serum 25-hydroxyvitamin D, intact PTH, and serum Ca concentrations.
Cisapride	BIC, CAB (PO and IM), DTG, RAL	↔ cisapride expected	No dose adjustment needed
	EVG/c	↑ cisapride expected	**Contraindicated**
Colchicine	BIC, CAB (PO and IM), DTG, RAL	↔ colchicine expected	No dose adjustment needed
	EVG/c	↑ colchicine expected	**Do not coadminister** in patients with hepatic or renal impairment. **For Treatment of Gout Flares** • Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. **For Prophylaxis of Gout Flares** • If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			For Treatment of Familial Mediterranean Fever • Do not exceed colchicine 0.6 mg once daily or 0.3 mg twice daily.
Dronabinol	BIC, CAB (PO and IM), DTG, RAL	↔ dronabinol expected	No dose adjustment needed
	EVG/c	↑ dronabinol possible	Monitor for dronabinol-related adverse events.
Eluxadoline	BIC, CAB (PO and IM), DTG, RAL	↔ eluxadoline expected	No dose adjustment needed
	EVG/c	↑ eluxadoline possible	Monitor for eluxadoline-related adverse events.
Ergot Derivatives	BIC, CAB (PO and IM), DTG, RAL	↔ dihydroergotamine, ergotamine, and methylergonovine expected	No dose adjustment needed
	EVG/c	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Contraindicated**
Finerenone	BIC, CAB (PO and IM), DTG, RAL	↔ finerenone expected	No dose adjustment needed
	EVG/c	↑ finerenone expected	**Contraindicated**
Flibanserin	BIC, CAB (PO and IM), DTG, RAL	↔ flibanserin expected	No dose adjustment needed
	EVG/c	↑ flibanserin expected	**Contraindicated**
Naloxegol	BIC, CAB (PO and IM), DTG, RAL	↔ naloxegol expected	No dosage adjustment needed
	EVG/c	↑ naloxegol expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Polyvalent Cation Supplements Mg, Al, Fe, Ca, Zn, including multivitamins with minerals. **Note:** Please refer to the Acid Reducers section in this table for recommendations on use with Al-, Mg-, and Ca-containing antacids.	BIC	↔ BIC AUC if administered simultaneously with Fe or Ca and food BIC AUC ↓ 33% if administered simultaneously with $CaCO_3$ under fasting conditions BIC AUC ↓ 63% if administered simultaneously with Fe under fasting conditions	**With Supplements That Contain Ca or Fe** • Administer BIC and supplements that contain Ca or Fe together with food. **Do not coadminister** BIC under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.
	CAB	↓ INSTI possible	If coadministration is necessary, administer INSTI at least 2 hours before or at least 4 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.
	DTG	DTG AUC ↓ 39% if administered simultaneously with $CaCO_3$ under fasting conditions DTG AUC ↓ 54% if administered simultaneously with Fe under fasting conditions ↔ DTG when administered with Ca or Fe supplement simultaneously with food	**With Supplements That Contain Ca or Fe** • Administer DTG and supplements that contain Ca or Fe together with food, or administer DTG at least 2 hours before or at least 6 hours after supplement. **Do not coadminister** DTG under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.
	EVG/c, RAL	↓ INSTI possible	If coadministration is necessary, administer INSTI at least 2 hours before or at least 6 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Praziquantel	BIC, CAB (PO and IM), DTG, RAL	↔ praziquantel and INSTI expected	No dose adjustment needed
	EVG/c	↑ praziquantel possible	Consider alternative ARV. If coadministration is necessary, monitor for praziquantel-related adverse events.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: Al = aluminum; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; AUC = area under the curve; BIC = bictegravir; Ca = calcium; CAB = cabotegravir; $CaCO_3$ = calcium carbonate; CCB = calcium channel blocker; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CMV = cytomegalovirus; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P450; DTG = dolutegravir; DVT = deep vein thrombosis; ECG = electrocardiogram; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; GI = gastrointestinal; IM = intramuscular; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; MPA = medroxyprogesterone acetate; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PE = pulmonary embolism; PO = orally; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; SSRI = selective serotonin reuptake inhibitors; TAF = tenofovir alafenamide; TCA = tricyclic antidepressants; TDF = tenofovir disoproxil fumarate; Zn = zinc

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Updated: September 12, 2024
Reviewed: September 12, 2024

In the table below, "no dose adjustment needed" indicates that the U.S. Food and Drug Administration–approved dose of maraviroc (MVC) 300 mg twice daily should be used. Recommendations for managing a particular drug interaction may differ, depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Macrolides		
Azithromycin	↔ MVC expected	No dose adjustment needed
Clarithromycin	↑ MVC possible	MVC 150 mg twice daily
Erythromycin	↑ MVC possible	No dose adjustment needed
Antifungals		
Fluconazole	↑ MVC possible	No dose adjustment needed
Isavuconazole	↑ MVC possible	No dose adjustment needed
Itraconazole	↑ MVC possible	MVC 150 mg twice daily
Posaconazole	↑ MVC possible	MVC 150 mg twice daily
Voriconazole	↑ MVC possible	MVC 150 mg twice daily
Antimycobacterials		
Rifabutin	MVC AUC ↔ and C_{min} ↓ 30%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 300 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
Rifampin	MVC AUC ↓ 63%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • Consider alternative ARV or antimycobacterial
Rifapentine	**Rifapentine Weekly and Daily** ↓ MVC expected	Do not coadminister.

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiseizure		
Carbamazepine, Phenobarbital, Phenytoin	↓ MVC possible	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
Eslicarbazepine	↓ MVC possible	Consider alternative ARV or anticonvulsant.
Oxcarbazepine	↓ MVC possible	Consider alternative ARV or anticonvulsant.
Antivirals—Hepatitis C Direct-Acting Antivirals		
Elbasvir/Grazoprevir	↔ MVC expected	No dose adjustment needed
Ledipasvir/Sofosbuvir	↔ MVC expected	No dose adjustment needed
Glecaprevir/Pibrentasvir	↔ MVC expected	No dose adjustment needed
Simeprevir	↔ MVC expected	No dose adjustment needed
Sofosbuvir	↔ MVC expected	No dose adjustment needed
Sofosbuvir/Velpatasvir	↔ MVC expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/Voxilaprevir	↔ MVC expected	No dose adjustment needed
Antivirals—Miscellaneous (e.g., for CMV, Mpox)		
Brincidofovir	↔ MVC expected	No dose adjustment needed
Cidofovir	↔ MVC expected	No dose adjustment needed
Tecovirimat	**When Given With MVC Without a Boosted PI or Other Potent CYP3A4 Inhibitors** • ↓ MVC possible but not expected to be clinically relevant **When Given With MVC Plus a Boosted PI or Other Potent CYP3A4 Inhibitors** • ↑ MVC expected	**If Used *Without* a Strong CYP3A Inhibitor** • No dose adjustment needed **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
Antivirals—SARS-CoV-2		
Molnupiravir	↔ MVC expected	No dose adjustment needed
Remdesivir	↔ MVC expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	**MVC With Ritonavir 100 mg Twice Daily** • MVC AUC ↑ 161%	MVC 150 mg twice daily
Herbal Products		
St. John's Wort	↓ MVC expected	Do not coadminister.

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies		
Hormonal Contraceptives	↔ ethinyl estradiol or levonorgestrel	No dose adjustment needed
Gender-Affirming Hormone Therapies	↔ MVC or gender-affirming hormones expected	No dose adjustment needed
Menopausal Hormone Replacement Therapy	↔ MVC or hormone replacement therapies expected	No dose adjustment needed
Antiretroviral Drugs		
Attachment Inhibitor		
FTR[a]	MVC AUC ↑ 25% ↔ TMR[a]	No dose adjustment needed
Capsid Inhibitor		
LEN (SQ and PO)	↑ MVC possible	No dose adjustment needed
INSTIs		
BIC, CAB (IM and PO), DTG	↔ MVC expected	No dose adjustment needed
EVG/c	↑ MVC possible	MVC 150 mg twice daily.
RAL	MVC AUC ↓ 21% RAL AUC ↓ 37%	No dose adjustment needed
NNRTIs		
DOR, RPV (IM and PO)	↔ MVC expected	No dose adjustment needed
EFV	MVC AUC ↓ 45%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
ETR	MVC AUC ↓ 53%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
PIs		
ATV/c, ATV/r	**With (ATV/r 300 mg/100 mg) Once Daily** • MVC AUC ↑ 388%	MVC 150 mg twice daily.

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
DRV/c, DRV/r	**With (DRV/r 600 mg/100 mg) Twice Daily** • MVC AUC ↑ 305% **With (DRV/r 600 mg/100 mg) Twice Daily and ETR** • MVC AUC ↑ 210%	MVC 150 mg twice daily

[a] FTR is a prodrug metabolized to its active moiety, TMR. Therefore, the effect on gp120-directed attachment inhibitor in the table refers to TMR concentrations.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; CAB = cabotegravir; C_{min} = minimum plasma concentration; CMV = cytomegalovirus; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTR = fostemsavir; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; ; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; TMR = temsavir

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Updated: September 12, 2024
Reviewed: September 12, 2024

Fostemsavir (FTR), an HIV-1 gp120-directed attachment inhibitor, is a prodrug of temsavir (TMR). In this table, the effect on gp120-directed attachment inhibitor refers to TMR concentrations. Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. Providers should exercise their clinical judgment to select the most appropriate alternative medication to use in cases where an interacting drug needs to be replaced with an alternative.

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers		
H2 Receptor Antagonists	↔ TMR	No dose adjustment needed
Anticonvulsants		
Carbamazepine, Phenobarbital, Phenytoin	↓ TMR expected	**Contraindicated**
Antibacterials—Antimycobacterials		
Rifabutin	**With Rifabutin 300 mg Once Daily and Without RTV** • TMR AUC ↓ 30% **With Rifabutin 150 mg Once Daily and With RTV 100 mg Once Daily** • TMR AUC ↑ 66%	**If Used *Without* PI/r** • No dose adjustment needed **If Used *With* PI/r** • Recommended dose is rifabutin 150 mg once daily. • No dose adjustment of FTR
Rifampin	TMR AUC ↓ 82%	**Contraindicated**
Rifapentine	**Daily and Weekly Dosing** ↓ TMR expected	**Do not coadminister.**

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antivirals—Hepatitis C Direct-Acting Antivirals		
Elbasvir/Grazoprevir	↑ grazoprevir expected	Increased grazoprevir exposures may increase the risk of ALT elevations. **Use an alternative** HCV regimen.
Ledipasvir/Sofosbuvir	↔ expected	No dose adjustment needed
Glecaprevir/Pibrentasvir	↔ expected	No dose adjustment needed
Sofosbuvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/Voxilaprevir	↑ voxilaprevir expected	**Use an alternative** HCV regimen if possible.
Antivirals—Miscellaneous (e.g., for CMV, Mpox)		
Brincidofovir	↑ brincidofovir possible	Give FTR dose at least 3 hours after administering brincidofovir, and monitor for brincidofovir-related adverse events (i.e., elevations in ALT/AST and bilirubin and GI adverse events).
Cidofovir	↔ TMR expected	No dose adjustment needed
Tecovirimat	↔ TMR expected	No dose adjustment needed
Antivirals—SARS-CoV-2		
Molnupiravir	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	TMR AUC ↑ 45%	No dose adjustment needed
Remdesivir	↔ expected	No dose adjustment needed
Herbal Products		
St. John's Wort	↓ TMR expected	**Contraindicated**
Hormonal Therapies		
Hormonal Contraceptives	Ethinyl estradiol AUC ↑ 40% ↔ norethindrone	Prescribe oral contraceptive that contains no more than 30 mcg of ethinyl estradiol[a] or use alternative ARV or contraceptive methods.

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Gender-Affirming Hormone Therapies (e.g., estradiol, 5-alpha reductase inhibitors, testosterone)	↑ estradiol possible	Use lowest effective dose for estrogen-containing regimens.
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	↑ estrogens, estradiol possible	Use lowest effective dose for estrogen-containing regimens.
Lipid-Modifying Agents		
Atorvastatin, Fluvastatin, Pitavastatin, Simvastatin	↑ statin possible ↔ expected	Increased statin concentration may not be clinically relevant. Follow clinical guidelines. Administer the lowest effective statin dose while monitoring for adverse events.
Rosuvastatin	Rosuvastatin AUC ↑ 69%	Increased rosuvastatin concentration may not be clinically relevant. Follow clinical guidelines. Administer the lowest effective dose while monitoring for adverse events.
Narcotics and Treatment for Opioid Dependence		
Buprenorphine/Naloxone	Buprenorphine AUC ↑ 30% Norbuprenorphine (active metabolite) AUC ↑ 39%	No dose adjustment needed
Methadone	↔ Total methadone ↔ R(−) methadone (active metabolite) ↔ S(+) methadone	No dose adjustment needed
Antiretroviral Drugs		
Capsid Inhibitor		
LEN (SQ and PO)	↔ TMR expected ↔ LEN expected	No dose adjustment needed

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
CCR5 Antagonist		
MVC	↔ TMR MVC AUC ↑ 25%	No dose adjustment needed
CD4 Post-Attachment Inhibitor		
IBA	↔ expected	No dose adjustment needed
INSTIs		
BIC, CAB (IM and PO), DTG, EVG/c	↔ TMR expected	No dose adjustment needed
RAL plus TDF	↔ TMR	No dose adjustment needed
NRTIs		
TDF	↔ TMR ↔ TDF	No dose adjustment needed
NNRTIs		
DOR, RPV (IM and PO)	↔ TMR expected	No dose adjustment needed
EFV	↓ TMR possible ↔ EFV expected	No dose adjustment needed
ETR	TMR AUC ↓ 50% ↔ ETR	No dose adjustment needed
ETR plus DRV/r	TMR C_{max} and AUC ↑ 34% to 53% ↔ DRV, RTV ETR AUC ↑ 28%	No dose adjustment needed
PIs		
ATV/c	↑ TMR expected ↔ ATV expected	No dose adjustment needed

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
ATV/r	TMR C_{max} and AUC ↑ 54% to 58% ↔ ATV, RTV	No dose adjustment needed
DRV/c	TMR C_{max} and AUC ↑ 79% to 97% ↔ DRV, RTV expected	No dose adjustment needed
DRV/r	TMR C_{max} and AUC ↑ 52% to 63% ↔ DRV, RTV	No dose adjustment needed

[a] The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Lo Minastrin Fe; Lo Loestrin Fe; Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Minastrin 24 Fe; Ortho Tri-Cyclen Lo. Generic formulations also may be available.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ALT = alanine aminotransferase; ARV = antiretroviral; AST = aspartate aminotransferase; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{max} = maximum plasma concentration; CAB = cabotegravir; CCR5 = C-C chemokine receptor type 5; CMV = cytomegalovirus; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTR = fostemsavir; GI = gastrointestinal; gp120 = glycoprotein 120; HCV = hepatitis C virus; IBA = ibalizumab; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/r = ritonavir-boosted PI; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; TDF = tenofovir disoproxil fumarate; TMR = temsavir

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between lenacapavir (LEN), an HIV capsid inhibitor, and other drugs, including antiretroviral (ARV) drugs.

LEN is available as an oral tablet (to be used only as initial therapy) and a long-acting injectable formulation that is administered every 6 months. LEN is a moderate cytochrome P450 (CYP) 3A4 inhibitor and may increase the concentration of drugs metabolized by CYP3A4. Due to the long half-life of the injectable formulation, this inhibitory effect may persist, and clinicians should continue to assess for drug interactions for up to 9 months after the last LEN injection. Recommendations for managing a particular drug interaction may differ depending on whether LEN is being initiated in a patient on a stable concomitant medication or whether a new medication is being initiated in a patient on a stable LEN-containing ARV regimen.

The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. Providers should exercise their clinical judgment to select the most appropriate alternative medication to use in cases where an interacting drug needs to be replaced with an alternative. People with HIV should be counseled about the importance of informing all their health care providers about their HIV regimen prior to starting any new concomitant medications (e.g., prescription, over-the-counter, and herbal or dietary supplements) to minimize the risk of drug–drug interactions.

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers		
Antacids, H2 Receptor Antagonists, Proton Pump Inhibitors	↔ expected	No dose adjustment needed
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia		
Alfuzosin	↑ alfuzosin expected	Consider an alternative to alfuzosin or an alternative ARV. If coadministered, monitor blood pressure.
Doxazosin	↑ doxazosin possible	No dose adjustment needed. Monitor blood pressure.
Tamsulosin	↑ tamsulosin possible	Initiate tamsulosin at 0.4 mg/day. Monitor blood pressure.
Terazosin	↔ expected	No dose adjustment needed
Silodosin	↑ silodosin possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Antimycobacterials		
Bedaquiline	↑ bedaquiline expected	Consider alternatives unless benefits outweigh risks. Monitor liver function and ECG for QTc prolongation.
Rifabutin	↓ LEN expected	**Do not coadminister.**
Rifampin	LEN AUC ↓ 84%	**Contraindicated**
Rifapentine	**Daily and Weekly Dosing** • ↓ LEN expected	**Do not coadminister.**
Antibacterials—Macrolides		
Azithromycin	↔ expected	No dose adjustment needed
Clarithromycin	↑ LEN possible	No dose adjustment needed
Erythromycin	↑ LEN possible	No dose adjustment needed
Anticoagulants		
Apixaban	↑ apixaban possible	No dose adjustment needed Monitor for apixaban-related adverse events, such as increased bleeding.
Dabigatran	↑ dabigatran possible	No dose adjustment needed Monitor for dabigatran-related adverse events, such as increased bleeding.
Edoxaban	↑ edoxaban possible	No dose adjustment needed Monitor for edoxaban-related adverse events, such as increased bleeding.
Rivaroxaban	↑ rivaroxaban possible	Monitor for rivaroxaban-related adverse events, such as increased bleeding, and adjust rivaroxaban dose accordingly.
Warfarin	↑ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below.		
Bupropion	↔ expected	No dose adjustment needed
Buspirone	↑ buspirone expected	Administer lowest dose of buspirone with caution and titrate buspirone dose based on clinical response. Dose reduction may be necessary. Monitor for buspirone-related adverse events.
Desvenlafaxine	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Duloxetine	↔ expected	No dose adjustment needed
Mirtazapine	↑ mirtazapine possible	No dose adjustment needed. Monitor for mirtazapine-related adverse events.
Nefazodone	↑ LEN possible	No dose adjustment needed
Selective Serotonin Reuptake Inhibitor (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	↑ paroxetine possible ↔ citalopram, escitalopram, fluoxetine, fluvoxamine, sertraline, vortioxetine expected	Dose reduction may be necessary with paroxetine. No dose adjustment needed
Trazodone	↑ trazodone expected	Administer lowest dose of trazodone and monitor for CNS and CV adverse events.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	↔ expected	No dose adjustment needed
Venlafaxine	↔ expected	No dose adjustment needed
Antipsychotics		
Aripiprazole	↑ aripiprazole possible	No dose adjustment needed
Brexpiprazole	↑ brexpiprazole expected	If patient is a known CYP2D6 poor metabolizer, then administer one-quarter of usual brexpiprazole dose.
Cariprazine	↑ cariprazine possible	No dose adjustment needed
Iloperidone	↑ iloperidone possible	No dose adjustment needed or consider dose reduction. Monitor for iloperidone-related adverse events.
Lumateperone	↑ lumateperone expected	Reduce dose of lumateperone to 21 mg once daily.
Lurasidone	↑ lurasidone expected	If LEN is added to lurasidone therapy, administer half of lurasidone dose. If lurasidone is added to LEN therapy, the recommended starting dose of lurasidone is 20 mg daily, and the maximum recommended dose is 80 mg daily.
Olanzapine **Olanzapine/Samidorphan**	↔ LEN olanzapine expected ↑ samidorphan possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Other Antipsychotics (e.g., clozapine, risperidone, thioridazine)	↑ clozapine possible	No dose adjustment needed. Monitor for clozapine-related adverse events.
	↑ risperidone possible	No dose adjustment needed
	↑ thioridazine possible ↓ LEN possible	**Do not coadminister.**
Pimavanserin	↑ pimavanserin possible	No dose adjustment needed. Monitor ECG for QTc prolongation.
Pimozide	↑ pimozide expected	**Contraindicated**
Quetiapine	↑ quetiapine expected	Consider alternatives unless benefits outweigh risks. Monitor ECG for QTc prolongation and consider dose reduction accordingly.
Ziprasidone	↔ expected	No dose adjustment needed
Antimigraine		
Ergot Derivatives	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Do not coadminister.**
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists		
Atogepant	↑ atogepant expected	No dose adjustment needed
Rimegepant	↑ rimegepant expected	Avoid a second dose of rimegepant within 48 hours.
Ubrogepant	↑ ubrogepant expected	Avoid a second dose of ubrogepant within 24 hours.
Zavegepant	↔ expected	No dose adjustment needed
Serotonin 5-HT1B, 1D Receptor Agonist		
Almotriptan	↔ expected	No dose adjustment needed
Eletriptan	↑ eletriptan expected	No dose adjustment needed. Monitor for eletriptan-related adverse events.
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan Zolmitriptan	↔ expected	No dose adjustment needed
Antifungals		
Fluconazole	↑ LEN possible	No dose adjustment needed
Ibrexafungerp	↑ ibrexafungerp possible	No dose adjustment needed
Isavuconazole	↔ expected	No dose adjustment needed
Itraconazole	↑ LEN possible	No dose adjustment needed
Posaconazole	↑ LEN possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Voriconazole	↑ LEN AUC 41%	No dose adjustment needed
Antimalarials		
Artemether/Lumefantrine	↑ artemether and lumefantrine possible	Monitor for lumefantrine-related adverse events, including QTc prolongation.
Artesunate	↔ expected	No dose adjustment needed
Atovaquone/Proguanil	↔ expected	No dose adjustment needed
Mefloquine	↑ mefloquine possible	Monitor for mefloquine-related adverse events, including QTc prolongation.
Antiplatelets		
Clopidogrel	↓ clopidogrel active metabolite possible	Consider alternative ARV or antiplatelet drug. If coadministered, monitor for clopidogrel-related adverse events.
Prasugrel	↔ expected	No dose adjustment needed
Ticagrelor	↑ ticagrelor possible	No dose adjustment needed. Monitor for ticagrelor-related adverse events.
Vorapaxar	↑ vorapaxar possible	No dose adjustment needed
Antipneumocystis and Antitoxoplasmosis		
Atovaquone Oral suspension	↔ expected	No dose adjustment needed
Antiseizure		
Carbamazepine	↓ LEN expected	**Contraindicated**
Eslicarbazepine	↓ LEN expected	**Do not coadminister.**
Ethosuximide	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events and adjust ethosuximide dose accordingly.
Lamotrigine	↔ expected	No dose adjustment needed
Oxcarbazepine	↓ LEN expected	**Do not coadminister.**
Phenobarbital	↓ LEN expected	**Do not coadminister.**
Phenytoin	↓ LEN expected	**Contraindicated**
Primidone	↓ LEN expected	**Do not coadminister.**
Valproic Acid	↔ expected	No dose adjustment needed
Antivirals—Hepatitis C		
Elbasvir/Grazoprevir	↔ expected	No dose adjustment needed
Glecaprevir/Pibrentasvir	↔ expected	No dose adjustment needed
Ledipasvir/Sofosbuvir	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sofosbuvir/Velpatasvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/Voxilaprevir	↔ expected	No dose adjustment needed
Antivirals—Miscellaneous (e.g., for CMV, Mpox)		
Brincidofovir	↔ expected	No dose adjustment needed
Cidofovir	↔ expected	No dose adjustment needed
Maribavir	↔ expected	No dose adjustment needed
Tecovirimat	↓ LEN possible	No dose adjustment needed
Valganciclovir	↔ expected	No dose adjustment needed
Antivirals—SARS-CoV-2		
Molnupiravir	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	↑ LEN possible	No dose adjustment needed
Remdesivir	↔ expected	No dose adjustment needed
Antiretroviral Drugs		
CCR5 Antagonist		
MVC	↔ expected	No dose adjustment needed
CD4 Post-attachment Inhibitor		
IBA	↔ expected	No dose adjustment needed
gp120 Attachment Inhibitor		
FTR	↔ expected	No dose adjustment needed
INSTIs		
BIC, CAB (IM or PO), DTG, EVG/c, RAL	↔ expected	No dose adjustment needed
NRTIs		
ABC, 3TC, FTC	↔ expected	No dose adjustment needed
TAF	TAF AUC ↑ 32%	No dose adjustment needed
TDF	TDF AUC ↑ 47%	No dose adjustment needed
NNRTIs		
EFV	LEN AUC↓ 56%	**Do not coadminister.**
ETR	↓ LEN expected	**Do not coadminister.**
DOR	↑ DOR possible	No dose adjustment needed
RPV (IM or PO)	↑ RPV possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PIs		
ATV/r	↑ LEN expected	**Do not coadminister.**
ATV/c	LEN AUC ↑ 4-fold	**Do not coadminister.**
DRV/c	DRV/c AUC ↑ 94%	No dose adjustment needed
DRV/r	↑ LEN expected	No dose adjustment needed
Beta-Agonists, Long-Acting Inhaled		
Arformoterol, Formoterol, Indacaterol, Olodaterol, Salmeterol	↔ expected	No dose adjustment needed
Cardiac Medications		
Antiarrhythmics		
Amiodarone	↑ amiodarone expected ↑ LEN possible	**Do not coadminister.**
Digoxin	↑ digoxin expected	Consider alternative ARV or antiarrhythmic. If coadministered, monitor digoxin therapeutic concentration.
Disopyramide	↑ disopyramide expected	**Do not coadminister.**
Dofetilide	↔ expected	No dose adjustment needed
Dronedarone	↑ dronedarone possible ↑ LEN possible	Consider alternative ARV or cardiac medication. If coadministered, monitor for dronedarone-related adverse events.
Flecainide	↔ expected	No dose adjustment needed
Lidocaine	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events and monitor concentrations, if available.
Mexiletine	↔ expected	No dose adjustment needed
Propafenone	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events and monitor concentrations, if available.
Quinidine	↑ quinidine expected	**Do not coadminister.**
Sotalol	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Beta-Blockers		
Atenolol, Bisoprolol, Carvedilol, Labetalol, Metoprolol, Nebivolol, Timolol	↔ expected	No dose adjustment needed
Calcium Channel Blockers		
Amlodipine, Felodipine, Nifedipine	↑ amlodipine, felodipine expected ↑ nifedipine possible	Monitor and dose adjust according to clinical response and adverse events.
Diltiazem, Verapamil	↑ diltiazem possible ↔ verapamil expected	No dose adjustment needed
Cardiac – Other		
Bosentan	↓ LEN expected	**Do not coadminister.**
Eplerenone	↑ eplerenone expected	**For Post-MI CHF** • Dosing of eplerenone should not exceed 25 mg daily. **For Hypertension** • Initiate at 25 mg once daily. Dosing may be increased to a maximum of 25 mg twice daily.
Ivabradine	↑ ivabradine expected	**Do not coadminister.**
Mavacamten	↓ LEN possible ↑ mavacamten expected	Initiate mavacamten at the recommended starting dose of 5 mg daily in patients who are on stable therapy with LEN. Reduce dose of mavacamten by one level (i.e., 15 to 10 mg, 10 to 5 mg, or 5 to 2.5 mg) in patients who are on mavacamten treatment and intend to initiate LEN.
Ranolazine	↑ ranolazine expected	Limit ranolazine to 500 mg twice daily.
Corticosteroids		
Beclomethasone Inhaled or intranasal **Ciclesonide** Inhaled	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Budesonide, Fluticasone, Mometasone Inhaled or intranasal	↑ glucocorticoids possible	Initiate with the lowest starting dose and titrate carefully and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Betamethasone Systemic	↑ betamethasone possible ↓ LEN possible	**Do not coadminister.**
Budesonide, Prednisone, Prednisolone Systemic	↑ glucocorticoids expected	Initiate with the lowest starting dose, titrate carefully, and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Dexamethasone Systemic	↑ dexamethasone expected ↓ LEN expected if used with dexamethasone >16 mg/day	Initiate with the lowest starting dose, titrate carefully, and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events. **Do not coadminister** with dexamethasone >16 mg/day**.**
Betamethasone, Methylprednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	↑ glucocorticoids possible	Monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Glucose-Lowering		
Canagliflozin	↔ expected	No dose adjustment needed
Saxagliptin	↑ saxagliptin possible	No dose adjustment needed
Dapagliflozin/Saxagliptin	↑ saxagliptin possible	No dose adjustment needed
Herbal Products		
St. John's Wort	↓ LEN expected	**Contraindicated**
Hormonal Therapies—Contraceptives		
Injectable Contraceptives Depot MPA	↑ MPA possible	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate)	↑ contraceptive exposures possible	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	↑ contraceptive exposures possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Transdermal Contraceptives (e.g., ethinyl estradiol/norelgestromin, ethinyl estradiol/levonorgestrel)	↑ contraceptive exposures possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	↑ contraceptive exposures possible	No dose adjustment needed
Emergency Contraceptives Levonorgestrel (oral)	↑ levonorgestrel possible	No dose adjustment needed
Hormonal Therapies—Gender Affirming and Menopause		
Estradiol	↔ expected	No dose adjustment needed
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	↑ dutasteride and finasteride possible	No dose adjustment needed
Testosterone	↑ testosterone possible	No dose adjustment needed
Other Gender-Affirming Medications	↔ goserelin, leuprolide acetate expected	No dose adjustment needed
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	↑ estrogen and progesterone possible ↑ drospirenone possible	No dose adjustment needed
Immunosuppressants		
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
Lipid-Modifying		
Atorvastatin	↑ atorvastatin possible	No dose adjustment needed
Fluvastatin	↔ expected	No dose adjustment needed
Lomitapide	↑ lomitapide expected	**Contraindicated**
Lovastatin	↑ lovastatin expected	Administer the lowest effective lovastatin dose while monitoring for adverse events.
Pitavastatin	↔ expected	No dose adjustment needed
Pravastatin	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rosuvastatin	↑ rosuvastatin possible	No dose adjustment needed
Simvastatin	↑ simvastatin expected	Administer the lowest effective simvastatin dose while monitoring for adverse events.
Narcotics and Treatment for Opioid Dependence		
Buprenorphine Sublingual, buccal, or implant	↑ buprenorphine possible	**Initiation of Buprenorphine in Patients Taking LEN** • Titrate buprenorphine dose to desired effect and use the lowest feasible initial dose. **Initiation of LEN in Patients Taking Buprenorphine** • Dose adjustment for buprenorphine may be needed. Monitor for buprenorphine-related adverse events.
Fentanyl	↑ fentanyl possible	Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression. Fentanyl dose reduction may be necessary.
Lofexidine	↔ expected	No dose adjustment needed
Methadone	↑ methadone possible	**Initiation of Methadone in Patients Taking LEN** • Titrate methadone dose to desired effect and use the lowest feasible initial dose. **Initiation of LEN in Patients Taking Methadone** • Dose adjustment for methadone may be needed. Monitor for buprenorphine-related adverse events.
Oxycodone	↑ oxycodone possible	Monitor for opioid-related adverse events, including potentially fatal respiratory depression. Oxycodone dose reduction may be necessary.
Tramadol	↑ tramadol possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PDE5 Inhibitors		
Avanafil	↑ avanafil expected	Avanafil dose should not exceed 50 mg once every 24 hours.
Sildenafil	↑ sildenafil expected	**For Treatment of Erectile Dysfunction** • Start with sildenafil 25 mg and monitor for sildenafil-related adverse events. **For Treatment of PAH** • Reduce the dose of sildenafil to 20 mg three times a day when discontinuing treatment with LEN.
Tadalafil	↑ tadalafil expected	**For Treatment of Erectile Dysfunction** • For once-daily use: Consider maximum dose of 2.5 mg daily. If higher dose is needed, consider alternative PDE5 inhibitor. • For use as needed: Consider maximum dose of 10 mg every 72 hours. If higher dosing is needed, consider alternative PDE5 inhibitor. **For Treatment of PAH** • **Do not coadminister.** **For Treatment of Benign Prostatic Hyperplasia** • Consider maximum dose of 2.5 mg daily. Use caution and monitor for AEs if dose increases to 5 mg.
Vardenafil	↑ vardenafil expected	Vardenafil dose should not exceed 5 mg once every 24 hours.
Sedative/Hypnotics		
Benzodiazepines		
Alprazolam, Diazepam, Triazolam	↑ alprazolam expected	Consider lowest dose and monitor for benzodiazepine-related adverse events.
Clonazepam	↑ clonazepam possible	Use with caution and consider alternative benzodiazepines.
Lorazepam, Oxazepam, Temazepam	↔ expected	No dose adjustment needed
Midazolam (Oral), Triazolam	↑ midazolam AUC 259-308%	Use with caution and consider alternative benzodiazepine.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Orexin Receptor Antagonist		
Daridorexant, Lemborexant, Suvorexant	↑ daridorexant expected ↑ lemborexant expected ↑ suvorexant expected	Maximum recommended daridorexant dose is 25 mg. **Do not coadminister** with lemborexant. Initiate suvorexant dose at 5 mg daily. Suvorexant dose can be increased to 10 mg once per night if the 5 mg dose is not effective. **Do not exceed** 10 mg per night.
Other Sedatives		
Eszopiclone	↑ eszopiclone expected	Consider lowest dose and monitor for eszopiclone-related adverse events.
Zolpidem	↑ zolpidem possible	Consider initiating zolpidem at a low dose.
Miscellaneous Drugs		
Calcifediol	↑ calcifediol possible	No dose adjustment needed
Cisapride	↑ cisapride expected	**Do not coadminister.**
Colchicine	↑ colchicine expected	**For Treatment of Gout Flares** • Administer single colchicine dose of 1.2 mg. Do not repeat dose for at least 3 days. **For Treatment of Familial Mediterranean Fever** • Colchicine dose should not exceed 1.2 mg daily (may be given as 0.6 mg twice a day).
Dronabinol	↔ expected	No dose adjustment needed
Eluxadoline	↔ expected	No dose adjustment needed
Finerenone	↑ finerenone expected	Monitor serum potassium at initiation and during therapy according to finerenone product labeling.
Flibanserin	↑ flibanserin expected	**Contraindicated**
Naloxegol	↑ naloxegol expected	Avoid use; if coadministration is necessary, decrease dosage of naloxegol and monitor for naloxegol-related adverse events.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Praziquantel	↑ praziquantel possible	Consider alternative antiretroviral. If coadministration is necessary, monitor for praziquantel-related adverse events.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse event; AUC = area under the curve; ARV = antiretroviral; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; CD4 = CD4 T lymphocyte; CHF = congestive heart failure; CMV = cytomegalovirus; CNS = central nervous system; CV = cardiovascular; CYP = cytochrome P450; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; FTR = fostemsavir; IBA = ibalizumab; IM = intramuscular; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; QTc = QT corrected for heart rate; LEN = lenacapavir; MI = myocardial infarction; MPA = medroxyprogesterone acetate; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

Updated: September 12, 2024
Reviewed: September 12, 2024

Note: Interactions associated with unboosted atazanavir (ATV), delavirdine (DLV), fosamprenavir (FPV), indinavir (IDV), lopinavir (LPV), nelfinavir (NFV), nevirapine (NVP), saquinavir (SQV), and tipranavir (TPV) are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding interactions between these drugs and other concomitant drugs.

Rilpivirine (RPV) intramuscular (IM) is not included in this table, because the combination of cabotegravir (CAB) IM plus RPV IM is a two-drug co-packaged product. Therefore, RPV IM is not expected to be used with a protease inhibitor.

PIs		NNRTIs			
		DOR	**EFV**	**ETR**	**RPV**
ATV/c	**PK Data**	↑ DOR expected ↔ ATV expected	↔ EFV expected ↓ ATV possible ↓ COBI possible	↑ ETR possible ↓ ATV possible ↓ COBI possible	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed	**ATV/c in ART-Naive Patients** • ATV 400 mg plus COBI 150 mg once daily • **Do not use** coformulated ATV 300 mg/COBI 150 mg. **ATV/c in ART-Experienced Patients** • **Do not coadminister.** No dose adjustment needed for EFV.	**Do not coadminister.**	No dose adjustment needed

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

PIs		NNRTIs			
		DOR	**EFV**	**ETR**	**RPV**
ATV/r	**PK Data**	↑ DOR expected ↔ ATV expected	↔ EFV expected **(ATV 400 mg Plus RTV 100 mg) Once Daily** • ATV concentrations similar to (ATV 300 mg plus RTV 100 mg) without EFV	**(ATV 300 mg Plus RTV 100 mg) Once Daily** • ETR AUC and C_{min} both ↑ ~30% • ↔ ATV AUC and C_{min}	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed	**ATV/r in ART-Naive Patients** • (ATV 400 mg plus RTV 100 mg) once daily **ATV/r in ART-Experienced Patients** • **Do not coadminister.** No dose adjustment needed for EFV	No dose adjustment needed	No dose adjustment needed
DRV/c	**PK Data**	↑ DOR expected ↔ DRV expected	↔ EFV expected ↓ DRV possible ↓ COBI possible	**ETR 400 mg Once Daily With (DRV 800 mg Plus COBI 150 mg) Once Daily** • ↔ ETR AUC and C_{min} • ↔ DRV AUC and C_{min} ↓ 56% • COBI AUC ↓ 30% and C_{min} ↓ 66%	↔ DRV expected ↑ RPV PO possible
	Dose	No dose adjustment needed	**Do not coadminister.**	**Do not coadminister.**	No dose adjustment needed

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

PIs		NNRTIs			
		DOR	**EFV**	**ETR**	**RPV**
DRV/r	**PK Data**	↑ DOR expected ↔ DRV expected	**With (DRV 300 mg Plus RTV 100 mg) Twice Daily** • EFV AUC ↑ 21% • ↔ DRV AUC and C_{min} ↓ 31%	**ETR 100 mg Twice Daily With (DRV 600 mg Plus RTV 100 mg) Twice Daily** • ETR AUC ↓ 37% and C_{min} ↓ 49% • ↔ DRV	**RPV 150 mg PO Once Daily With (DRV 800 mg Plus RTV 100 mg) Once Daily** • RPV PO AUC ↑ 130% and C_{min} ↑ 178% • ↔ DRV
	Dose	No dose adjustment needed	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	No dose adjustment needed Despite reduced ETR concentration, safety and efficacy of this combination have been established in a clinical trial.	No dose adjustment needed

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ART = antiretroviral therapy; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PO = oral; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

Updated: September 12, 2024
Reviewed: September 12, 2024

Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication, or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

Information on drug interactions with oral (PO) cabotegravir (CAB) is not included in this table. The CAB PO tablet is not available in retail pharmacies and will be provided directly to people with HIV for short-term use only (PO lead-in and to bridge if intramuscular [IM] administration is delayed).

CAB IM and rilpivirine (RPV) IM are not included in this table because the combination is a two-drug, co-packaged product. Therefore, it is not anticipated that they will be used with PO non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (PIs).

ARV Drugs by Drug Class		INSTIs			
		BIC	**DTG**	**EVG/c**	**RAL**
NNRTIs					
DOR	**PK Data**	↔ DOR and BIC expected	↔ DOR DTG AUC ↑ 36% and C_{min} ↑ 27%	↑ DOR expected ↔ EVG	↔ DOR and RAL expected
	Dose	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.
EFV	**PK Data**	↓ BIC expected	**With DTG 50 mg Once Daily** • DTG AUC ↓ 57% and C_{min} ↓ 75%	↑ or ↓ EVG, COBI, and EFV possible	**With RAL 400 mg Twice Daily** • RAL AUC ↓ 36% and C_{min} ↓ 21% **With RAL 1,200 mg Once Daily** • ↔ RAL AUC and C_{min}

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
	Dose	**Do not coadminister.**	**In Patients Without INSTI Resistance** • DTG 50 mg twice daily **In Patients With Certain INSTI-Associated Resistance[a] or Clinically Suspected INSTI Resistance** • Consider alternative combination	**Do not coadminister.**	No dose adjustment needed.
ETR	**PK Data**	↓ BIC expected	**ETR 200 mg Twice Daily Plus DTG 50 mg Once Daily** • DTG AUC ↓ 71% and C_{min} ↓ 88% **ETR 200 mg Twice Daily With (DRV 600 mg Plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily** • DTG AUC ↓ 25% and C_{min} ↓ 37%	↑ or ↓ EVG, COBI, and ETR possible	**ETR 200 mg Twice Daily Plus RAL 400 mg Twice Daily** • ETR C_{min} ↑ 17% • RAL C_{min} ↓ 34%
	Dose	**Do not coadminister.**	**Do not coadminister** ETR and DTG without concurrently administering ATV/r or DRV/r. **In Patients Without INSTI Resistance** • DTG 50 mg once daily with ETR (concurrently with ATV/r or DRV/r)	**Do not coadminister.**	RAL 400 mg twice daily Coadministration with RAL 1,200 mg once daily **is not recommended.**

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
			In Patients With Certain INSTI-Associated Resistance[a] or Clinically Suspected INSTI Resistance • DTG 50 mg twice daily with ETR (concurrently with ATV/r or DRV/r)		
RPV	**PK Data**	No data	**With DTG 50 mg Once Daily** • ↔ DTG AUC and C_{min} ↑ 22% • ↔ RPV PO AUC and C_{min} ↑ 21%	↑ RPV PO possible	↔ RPV PO RAL C_{min} ↑ 27%
	Dose	No dose adjustment needed.	No dose adjustment needed.	**Do not coadminister.**	No dose adjustment needed.
PIs					
ATV/c	**PK Data**	BIC AUC ↑ 306%	No data	Not applicable	No data
	Dose	**Do not coadminister.**	No dose adjustment needed.	**Do not coadminister** two COBI-containing products.	No dose adjustment needed.
ATV/r	**PK Data**	↑ BIC expected	**(ATV 300 mg Plus RTV 100 mg) Once Daily Plus DTG 30 mg Once Daily** • DTG AUC ↑ 62% and C_{min} ↑ 121%	Not applicable	**With (ATV 300 mg Plus RTV 100 mg) Once Daily** • RAL AUC ↑ 41%
	Dose	**Do not coadminister.**	No dose adjustment needed.	**Do not coadminister** RTV and COBI.	No dose adjustment needed.
DRV	**PK Data**	Not applicable	Not applicable	↔ DRV or EVG expected	Not applicable
	Dose	**Do not administer** DRV without RTV or COBI.	**Do not administer** DRV without RTV or COBI.	No dose adjustment needed.	**Do not administer** DRV without RTV or COBI.

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
DRV/c	**PK Data**	BIC AUC ↑ 74%	**DRV/c Plus DTG Once Daily** • ↔ DTG, DRV, and COBI **DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c** • DTG C_{min} ↑ 100%	Not applicable	No data
	Dose	No dose adjustment needed.	No dose adjustment needed.	**Do not coadminister** two COBI-containing products.	No dose adjustment needed.
DRV/r	**PK Data**	No data	**(DRV 600 mg Plus RTV 100 mg) Twice Daily With DTG 30 mg Once Daily** • DTG AUC ↓ 22% and C_{min} ↓ 38%	Not applicable	**With (DRV 600 mg Plus RTV 100 mg) Twice Daily** • RAL AUC ↓ 29% and Cmin ↑ 38%
	Dose	No dose adjustment needed.	No dose adjustment needed.	**Do not coadminister** RTV and COBI.	No dose adjustment needed.

[a] Refer to DTG product label for details.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ARV = antiretroviral; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{min} = minimum plasma concentration; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; PO = oral; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir

Appendix A: Key to Acronyms

Updated: September 12, 2024
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Drug Name Abbreviations

Abbreviation	Definition
3TC	lamivudine
ABC	abacavir
ATV	atazanavir
ATV/c	atazanavir/cobicistat
ATV/r	atazanavir/ritonavir
BIC	bictegravir
CAB	cabotegravir
CAB-LA	long-acting cabotegravir
COBI or c	cobicistat
d4T	stavudine
ddI	didanosine
DLV	delavirdine
DOR	doravirine
DRV	darunavir
DRV/c	darunavir/cobicistat
DRV/r	darunavir/ritonavir
DTG	dolutegravir
EFV	efavirenz
ETR	etravirine
EVG	elvitegravir
EVG/c	elvitegravir/cobicistat
FPV	fosamprenavir
FPV/r	fosamprenavir/ritonavir
FTC	emtricitabine
FTR	fostemsavir
IBA	ibalizumab
IDV	indinavir
LA CAB/RPV	long-acting cabotegravir plus rilpivirine

Abbreviation	Definition
LEN	lenacapavir
LPV	lopinavir
LPV/r	lopinavir/ritonavir
MVC	maraviroc
NFV	nelfinavir
NVP	nevirapine
RAL	raltegravir
RPV	rilpivirine
RTV or r	ritonavir
SQV	saquinavir
T-20	enfuvirtide
TAF	tenofovir alafenamide
TDF	tenofovir disoproxil fumarate
TFV	tenofovir
TFV-DP	tenofovir-diphosphate
TMP-SMX	trimethoprim-sulfamethoxazole
TMR	temsavir
TPV	tipranavir
TPV/r	tipranavir/ritonavir
ZDV	zidovudine

General Terms

Abbreviation	Definition
17-BMP	beclomethasone 17-monopropionate
ACA	Affordable Care Act
ADAP	AIDS Drug Assistance Program
AE	adverse event
Ag/Ab	antigen/antibody
AHA	American Heart Association
AHC-HRSN	Accountable Health Communities Health-Related Social Needs
Al	aluminum
ALT	alanine aminotransferase
AMP	average manufacturer price
aPR	adjusted prevalence ratio
ART	antiretroviral therapy
ARTAS	Anti-Retroviral Treatment and Access to Services
ARV	antiretroviral
ASP	average sales price
ASCVD	atherosclerotic cardiovascular disease
AST	aspartate aminotransferase
AUC	area under the curve
AUD	alcohol use disorder
AUDIT-C	Alcohol Use Disorders Identification Test-Consumption
AV	atrioventricular
AWP	average wholesale price
AYA	adolescents and young adults
BMD	bone mineral density
BMI	body mass index
BMT	bone marrow transplant
BUN	blood urea nitrogen
Ca	calcium
$CaCO_3$	calcium carbonate
CBC	complete blood count
CCB	calcium channel blocker
CD4	CD4 T lymphocyte
CDC	Centers for Disease Control and Prevention

Abbreviation	Definition
CGRP	calcitonin gene-related peptide
CHF	congestive heart failure
CI	confidence interval capsid inhibitor
CKD	chronic kidney disease
Cl	chloride
C_{max}	maximum plasma concentration
C_{min}	minimum plasma concentration
CMS	Centers for Medicare & Medicaid Services
CMV	cytomegalovirus
CNS	central nervous system
COC	combined oral contraceptive
CPI-U	consumer price index-urban
CPK	creatine phosphokinase
Cr	creatinine
CrCl	creatinine clearance
CsA	cyclosporine
CSF	cerebrospinal fluid
CV	cardiovascular
CVD	cardiovascular disease
CYP	cytochrome P450
D/M	dual/mixed
DAA	direct-acting antiviral
DDI	drug–drug interaction
DHA	dihydroartemisinin
DILI	drug-induced liver injury
DM	diabetes mellitus
DMPA	depo-medroxyprogesterone acetate
DOAC	direct oral anticoagulant
DOT	directly observed therapy
DSMB	Data Safety Monitoring Board
DVT	deep vein thrombosis
EBV	Epstein-Barr virus
ECG	electrocardiogram

Abbreviation	Definition
eGFR	estimated glomerular filtration rate
ESRD	end-stage renal disease
FCP	federal price ceiling
FDA	U.S. Food and Drug Administration
FDC	fixed-dose combination
Fe	iron
FUL	federal upper limit
GAHT	gender-affirming hormone therapy
GFR	glomerular filtration rate
GHB	gamma-hydroxybutyrate
GI	gastrointestinal
GnRH	gonadotropin-releasing hormone
GVHD	graft versus host disease
H2	histamine type 2
H2RA	H2 receptor antagonist
HAND	HIV-associated neurocognitive disorder
HAV	hepatitis A virus
HbA1C	hemoglobin A1c
HBcAb	hepatitis B core antibody
HBeAg	hepatitis B e antigen
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCO_3	bicarbonate
HCT	hematopoietic cell transplant
HCV	hepatitis C virus
HD	hemodialysis high-dose
HDL	high-density lipoprotein
HDV	hepatitis D virus
HHS	U.S. Department of Health and Human Services
HIV	human immunodeficiency virus
HIV RNA	HIV viral load

Abbreviation	Definition
HIV-1	human immunodeficiency virus type 1
HIV-2	human immunodeficiency virus type 2
HIVMA/IDSA	HIV Medicine Association of the Infectious Diseases Society of America
HLA	human leukocyte antigen
HMG-CoA	hydroxy-methylglutaryl-coenzyme A
HR	hazard ratio
HRSA	Health Resources and Services Administration
HRT	hormone replacement therapy
hs-CRP	high-sensitivity C-reactive protein
HSR	hypersensitivity reaction
HTLV-1	human T-lymphotropic virus-1 type I
IC_{50}	median inhibitory concentration
IL	interleukin
IM	intramuscular
IMF	illicitly manufactured fentanyl
IN	integrase
INR	international normalized ratio
INSTI	integrase strand transfer inhibitor
IPT	isoniazid preventive therapy
IRIS	immune reconstitution inflammatory syndrome
ISR	injection site reactions
IUD	intrauterine device
IV	intravenous
K	potassium
LA	long-acting
LDL	low-density lipoprotein
LGBTQ	lesbian, gay, bisexual, transgender, or queer
LLOD	lower limits of detection
LTBI	latent tuberculosis infection
MAC	*Mycobacterium avium* complex
MATE	multidrug and toxin extrusion transporter
MDMA	methylenedioxymethamphetamine
MDR	multidrug resistant
MDR-TB	multidrug-resistant tuberculosis

Abbreviation	Definition
MDRP	Medicaid Drug Rebate Program
MET	motivational enhancement therapy
Mg	magnesium
MHC	major histocompatibility complex
MI	motivational interviewing myocardial infarction
MPA	medroxyprogesterone acetate
MRI	magnetic resonance imaging
MSM	men who have sex with men
MTR	multi-tablet regimen
N/A	not applicable
Na	sodium
NIH	National Institutes of Health
NNRTI	non-nucleoside reverse transcriptase inhibitor
NRTI	nucleoside/nucleotide reverse transcriptase inhibitor
NTD	neural tube defect
OARAC	Office of AIDS Research Advisory Council
OATP	organic anion-transporting polypeptide
OBR	optimized background regimen
OCT2	organic cation transporter 2
OH-itraconazole	active metabolite of itraconazole
OI	opportunistic infection
ONDCP	Office of National Drug Control Policy
OR	odds ratio
OTP	opioid treatment program
OUD	opioid use disorder
P	phosphorus
P-gp	p-glycoprotein
PAH	pulmonary arterial hypertension
PBM	pharmacy benefit manager
PCP	*Pneumocystis jirovecii* pneumonia
PCR	polymerase chain reaction
PDE5	phosphodiesterase type 5
PEP	post-exposure prophylaxis

Abbreviation	Definition
PI	protease inhibitor
PI/c	cobicistat-boosted protease inhibitor
PI/r	ritonavir-boosted protease inhibitor
PK	pharmacokinetic
PO	orally
PPI	proton pump inhibitor
PR	protease
PRAPARE	Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences
PrEP	pre-exposure prophylaxis
PTH	parathyroid hormone
QTc	QT corrected for heart rate
REPC	Retention through Enhanced Personal Contact
RNA	ribonucleic acid
RT	reverse transcriptase
RWHAP	Ryan White HIV/AIDS Program
SAMHSA	Substance Abuse and Mental Health ServicesAdministration
SCr	serum creatinine
SDOH	social determinants of health
SMR	sexual maturity rating
SOT	solid organ transplantation
SPT	skin patch test
SQ	subcutaneous
SSP	syringe service program
SSRI	selective serotonin reuptake inhibitor
STI	sexually transmitted infection
STR	single-tablet regimen
SUD	substance use disorder
TasP	treatment as prevention
TB	tuberculosis
TC	total cholesterol
TCA	tricyclic antidepressant
TDM	therapeutic drug monitoring
TDR	transmitted drug resistance
TG	triglyceride

Abbreviation	Definition
The Panel	The Panel on Antiretroviral Guidelines for Adults and Adolescents
U=U	Undetectable = Untransmittable
UGT	uridine diphosphate glucuronosyltransferase
UGT1	uridine diphosphate glucuronosyltransferase 1 family
UGT1A1	uridine diphosphate glucuronosyltransferase 1A1
ULN	upper limit of normal
UW	University of Washington
VL	viral load
VPA	valproic acid
WAC	wholesale acquisition cost
WBC	white blood cell
WHO	World Health Organization
WPATH	World Professional Association for Transgender Health
XDR	extensively drug-resistant
XR	extended release
Zn	zinc

Study and Trial Names

Acronym/Abbreviation	Name
ACTG	AIDS Clinical Trials Group
ADVANCE	Assessing Donor Variability And New Concepts in Eligibility
ARDENT	ACTG A5257 trial
ARTEMIS	Affordability and Real-World Antiplatelet Treatment Effectiveness After Myocardial Infarction Study
ATLAS	Antiretroviral Therapy as Long-Acting Suppression
CARES	Cabotegravir and Rilpivirine Efficacy and Safety
CoRECT	Cooperative Re-Engagement Controlled Trial
D:A:D	Data Collection on Adverse Events of Anti-HIV Drugs
D^2EFT	Dolutegravir and Darunavir Evaluation in Adults Failing Therapy
ECHO	Evidence for Contraceptive Options in HIV
ENCORE	Evaluation of Novel Concepts in Optimization of antiRetroviral Efficacy
FLAIR	First Long-Acting Injectable Regimen
HPTN	HIV Prevention Trials Network
LATITUDE	Long-Acting Therapy to Improve Treatment Success in Daily LifE
NADIA	Nucleosides And Darunavir/Dolutegravir In Africa
REPRIEVE	Randomized Trial to Prevent Vascular Events in HIV
STaR	Single-Tablet Regimen
START	Strategic Timing of AntiRetroviral Treatment
THRIVE	Targeting HIV Retention and Improved Viral Load Through Engagement
VACS	Veterans Aging Cohort Study
WIHS	Women's Interagency HIV Study

Appendix B. Drug Characteristics Tables

Appendix B, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Updated: September 12, 2024
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The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved coformulated and copackaged antiretroviral regimens for adults with HIV. Not all products are FDA approved for adolescents with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines. Please see the class-specific drug characteristics tables (Appendix B, Tables 3, 4, 5, and 6) for details about the individual drugs included in these products, including information on elimination and metabolic pathways, serum and intracellular half-lives, and adverse effects. The products in this table are listed by drug class and arranged **in alphabetical order** by trade name within each class.

Trade Name (Abbreviation)	**ARV Drugs Included in the Regimen**	**Dosing Recommendation**[a]
INSTI Plus Two NRTIs		
Biktarvy (BIC/TAF/FTC)	Bictegravir 50 mg/tenofovir alafenamide 25 mg/emtricitabine 200 mg	One tablet PO once daily
Genvoya (EVG/c/TAF/FTC)	Elvitegravir 150 mg/cobicistat 150 mg/tenofovir alafenamide 10 mg/ emtricitabine 200 mg	One tablet PO once daily with food
Stribild (EVG/c/TDF/FTC)	Elvitegravir 150 mg/cobicistat 150 mg/tenofovir disoproxil fumarate 300 mg/ emtricitabine 200 mg	One tablet PO once daily with food
Triumeq (DTG/ABC/3TC)	Dolutegravir 50 mg/abacavir 600 mg/lamivudine 300 mg	One tablet PO once daily
INSTI Plus One NRTI		
Dovato (DTG/3TC)	Dolutegravir 50 mg/lamivudine 300 mg	One tablet PO once daily

Appendix B, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Trade Name (Abbreviation)	ARV Drugs Included in the Regimen	Dosing Recommendation[a]
INSTI Plus One NNRTI		
Cabenuva (CAB IM and RPV IM)	**Cabenuva 600-mg/900-mg Kit:** • CAB 600-mg/3-mL vial and RPV 900-mg/3-mL vial **Cabenuva 400-mg/600-mg Kit:** • CAB 400-mg/2-mL vial and RPV 600-mg/2-mL vial	**Optional Lead-In With Oral CAB and RPV** • CAB 30 mg PO and RPV 25 mg PO once daily with food for 4 weeks **Monthly IM CAB and RPV** • Loading dose: CAB 600 mg/3 mL IM for 1 dose and RPV 900 mg/3 mL IM for 1 dose • Continuation phase: CAB 400 mg/2 mL IM every 4 weeks and RPV 600 mg/2 mL IM every 4 weeks **Every-2-Month IM CAB and RPV** • Loading dose: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM **once monthly** for 2 doses • Continuation phase: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM every 2 months
Juluca (DTG/RPV)	Dolutegravir 50 mg/rilpivirine 25 mg	One tablet PO once daily with food
NNRTI Plus Two NRTIs		
Atripla (EFV/TDF/FTC)	Efavirenz 600 mg/tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg	One tablet PO once daily on an empty stomach, preferably at bedtime
Complera (RPV/TDF/FTC)	Rilpivirine 25 mg/tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg	One tablet PO once daily with food
Delstrigo (DOR/TDF/3TC)	Doravirine 100 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet PO once daily
Odefsey (RPV/TAF/FTC)	Rilpivirine 25 mg/tenofovir alafenamide 25 mg/emtricitabine 200 mg	One tablet PO once daily with food
Symfi (EFV/TDF/3TC)	Efavirenz 600 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet PO once daily on an empty stomach, preferably at bedtime
Symfi Lo (EFV/TDF/3TC)	Efavirenz 400 mg/tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet PO once daily on an empty stomach, preferably at bedtime

Appendix B, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Trade Name (Abbreviation)	ARV Drugs Included in the Regimen	Dosing Recommendation[a]
PI Plus Two NRTIs		
Symtuza (DRV/c/TAF/FTC)	Darunavir 800 mg/cobicistat 150 mg/tenofovir alafenamide 10 mg/emtricitabine 200 mg	One tablet PO once daily with food

[a] For dose adjustments in people with renal or hepatic insufficiency, see Appendix B, Table 12. When no food restriction is listed, the product can be taken with or without food.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; IM = intramuscularly; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PO = orally; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix B, Table 2. Nucleoside Reverse Transcriptase Inhibitor-Based, Fixed-Dose Combination Tablets for Use as Part of an Antiretroviral Regimen

Updated: May 26, 2023
Reviewed: September 12, 2024

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved dual nucleoside reverse transcriptase inhibitor fixed-dose combination (FDC) products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines. These FDC tablets are not complete regimens and must be administered in combination with other antiretroviral drugs. FDC products that contain zidovudine (ZDV) have been removed from this table. Please refer to the FDA product labels for information regarding ZDV-containing FDCs. Please see the class-specific drug characteristics tables (Appendix B, Tables 3, 4, 5, and 6) for details about the individual drugs contained in these FDC products, including information on elimination and metabolic pathways, serum and intracellular half-lives, and adverse effects. The FDC tablets in this table are listed by trade name.

Trade Name (Abbreviation)	**ARV Drugs Included in the FDC Tablet**	**Dosing Recommendation**[a]
TAF or TDF Plus an NRTI		
Descovy (TAF/FTC)	Tenofovir alafenamide 25 mg/emtricitabine 200 mg	One tablet PO once daily
Cimduo (TDF/3TC)	Tenofovir disoproxil fumarate 300 mg/lamivudine 300 mg	One tablet PO once daily
Truvada (TDF/FTC)	Tenofovir disoproxil fumarate 300 mg/emtricitabine 200 mg	One tablet PO once daily
Other NRTI-Based, FDC Tablets		
Epzicom (ABC/3TC) **Note:** Generic product is available.	Abacavir 600 mg/lamivudine 300 mg	One tablet PO once daily

[a] For dose adjustments in people with renal or hepatic insufficiency, see Appendix B, Table 12. All FDC tablets listed in this table can be taken without regard to food.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; FDC = fixed-dose combination; FTC = emtricitabine; NRTI = nucleoside reverse transcriptase inhibitor; PO = orally; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

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The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved nucleoside reverse transcriptase inhibitor products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines. The older nucleoside reverse transcriptase inhibitors didanosine (ddI) and stavudine (d4T) have been discontinued in the United States. Zidovudine (ZDV) is no longer used commonly in clinical practice. Therefore, these antiretrovirals have been removed from this table. Please refer to the FDA product label for ZDV for information regarding this drug.

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum/ Intracellular Half-Lives**	**Adverse Events**[b]
Abacavir (ABC) *Ziagen* **Note:** Generic tablet formulation is available.	**Ziagen** • 300-mg tablet • 20-mg/mL oral solution **Generic** • 300-mg tablet • Also available as FDC with 3TC **FDC Tablets That Contain ABC**[c] • Epzicom (ABC/3TC) **STRs That Contain ABC**[d] • Triumeq (DTG/ABC/3TC)	**Ziagen** • ABC 600 mg PO once daily, *or* • ABC 300 mg PO twice daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain ABC.	Metabolized by alcohol dehydrogenase and glucuronyl transferase 82% of ABC dose is excreted in the urine as metabolites of ABC. Dose adjustment is recommended in people with hepatic insufficiency (see Appendix B, Table 12).	1.5 hours/12–26 hours	People who test positive for HLA-B*5701 are at the highest risk of experiencing HSRs. HLA screening should be done before initiating ABC. For people with a history of HSRs, rechallenge **is not recommended.** Symptoms of HSRs may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, fatigue, or respiratory symptoms (e.g., sore throat, cough, or shortness of breath). Some cohort studies suggest an increased risk of MI with recent or current use of ABC, but this risk is not substantiated in other studies.

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events[b]
Emtricitabine (FTC) *Emtriva*	**Emtriva** • 200-mg hard gelatin capsule • 10-mg/mL oral solution **FDC Tablets That Contain FTC[c]** • Descovy (TAF/FTC) • Truvada (TDF/FTC) **STRs That Contain FTC[d]** • Atripla (EFV/TDF/FTC) • Biktarvy (BIC/TAF/FTC) • Complera (RPV/TDF/FTC) • Genvoya (EVG/c/TAF/FTC) • Odefsey (RPV/TAF/FTC) • Stribild (EVG/c/TDF/FTC) • Symtuza (DRV/c/TAF/FTC)	**Emtriva** *Capsule* • FTC 200 mg PO once daily *Oral Solution* • FTC 240 mg (24 mL) PO once daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain FTC.	86% of FTC dose is excreted renally. See Appendix B, Table 12 for dosing recommendations in people with renal insufficiency.	10 hours/ >20 hours	Minimal toxicity Hyperpigmentation/skin discoloration Severe acute exacerbation of hepatitis may occur in people with HBV/HIV coinfection who discontinue FTC.
Lamivudine (3TC) *Epivir* **Note:** Generic products are available.	**Epivir** • 150-mg and 300-mg tablets • 10-mg/mL oral solution **Generic** • 150-mg and 300-mg tablets • Also available as FDC with ABC **FDC Tablets That Contain 3TC[c]** • Cimduo (TDF/3TC) • Epzicom (ABC/3TC)	**Epivir** • 3TC 300 mg PO once daily, *or* • 3TC 150 mg PO twice daily See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain 3TC.	70% of 3TC dose is excreted renally. See Appendix B, Table 12 for dose recommendations in people with renal insufficiency.	5–7 hours/ 18–22 hours	Minimal toxicity Severe acute exacerbation of hepatitis may occur in people with HBV/HIV coinfection who discontinue 3TC.

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum/ Intracellular Half-Lives**	**Adverse Events**[b]
	STRs That Contain 3TC[d] • Delstrigo (DOR/TDF/3TC) • Dovato (DTG/3TC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/TDF/3TC) • Triumeq (DTG/ABC/3TC)				
Tenofovir Alafenamide (TAF) *Vemlidy* **Note:** Vemlidy is available as a 25-mg tablet for the treatment of HBV.	**FDC Tablets That Contain TAF**[c] • Descovy (TAF/FTC) **STRs That Contain TAF**[d] • Biktarvy (BIC/TAF/FTC) • Genvoya (EVG/c/TAF/FTC) • Odefsey (RPV/TAF/FTC) • Symtuza (DRV/c/TAF/FTC)	See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain TAF.	Metabolized by cathepsin A See Appendix B, Table 12 for dosing recommendations in people with renal insufficiency.	0.5 hour/ 150–180 hours	Renal insufficiency, Fanconi syndrome, and proximal renal tubulopathy are less likely to occur with TAF than with TDF. Osteomalacia and decreases in BMD are less likely to occur with TAF than with TDF. Severe acute exacerbation of hepatitis may occur in people with HBV/HIV coinfection who discontinue TAF. Diarrhea, nausea, headache Greater weight increase has been reported with TAF than with TDF.

Appendix B, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum/ Intracellular Half-Lives	Adverse Events[b]
Tenofovir Disoproxil Fumarate (TDF) *Viread* **Note:** Generic product is available.	**Viread** • 300-mg tablet • 40-mg/g oral powder **Generic** • 300-mg tablet **FDC Tablets That Contain TDF[c]** • Cimduo (TDF/3TC) • Truvada (TDF/FTC) **STRs That Contain TDF[d]** • Atripla (EFV/TDF/FTC) • Complera (RPV/TDF/FTC) • Delstrigo (DOR/TDF/3TC) • Stribild (EVG/c/TDF/FTC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/TDF/3TC)	**Viread** • TDF 300 mg PO once daily, *or* • 7.5 level scoops of oral powder PO once daily (dosing scoop dispensed with each bottle; one level scoop contains 1 g of oral powder). Mix oral powder with 2–4 ounces of a soft food that does not require chewing (e.g., applesauce, yogurt). **Do not mix oral powder with liquid.** See Appendix B, Tables 1 and 2 for dosing information for FDC tablets that contain TDF.	Renal excretion is the primary route of elimination. See Appendix B, Table 12 for dose recommendations in people with renal insufficiency.	17 hours/ >60 hours	Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy Osteomalacia, decrease in BMD Asthenia, headache, diarrhea, nausea, vomiting, flatulence Severe acute exacerbation of hepatitis may occur in people with HBV/HIV coinfection who discontinue TDF.

[a] For dose adjustments in people with renal or hepatic insufficiency, see Appendix B, Table 12. When no food restriction is listed, the antiretroviral drug can be taken with or without food.

[b] Also see Table 20.

[c] See Appendix B, Table 2 for information about these formulations.

[d] See Appendix B, Table 1 for information about these formulations.

Key: 3TC = lamivudine; ABC = abacavir; BIC = bictegravir; BMD = bone mineral density; DOR = doravirine; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; MI = myocardial infarction; PO = orally; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors

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The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved non-nucleoside reverse transcriptase inhibitor (NNRTI) products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines. The older NNRTIs delavirdine (DLV) and nevirapine (NVP) are **not** listed in this table; DLV has been discontinued and NVP is no longer commonly used in clinical practice in the United States.

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum Half-Life**	**Adverse Events**[b]
Doravirine (DOR) *Pifeltro*	**Pifeltro** • 100-mg tablet **STRs That Contain DOR**[c] • Delstrigo (DOR/TDF/3TC)	**Pifeltro** • DOR 100 mg PO once daily See Appendix B, Table 1 for dosing information for Delstrigo.	CYP3A4/5 substrate	15 hours	Nausea Dizziness Abnormal dreams
Efavirenz (EFV) **Note:** The branded product Sustiva has been discontinued.	**Efavirenz** (generic) • 600-mg tablet **STRs That Contain EFV**[c] • Atripla (EFV/TDF/FTC) • Symfi (EFV 600 mg/TDF/3TC) • Symfi Lo (EFV 400 mg/TDF/3TC)	**Efavirenz** (generic) • EFV 600 mg PO once daily on an empty stomach, preferably at or before bedtime See Appendix B, Table 1 for dosing information for STRs that contain EFV.	Metabolized by CYP2B6 (primary), 3A4, and 2A6 CYP3A4 mixed inducer/inhibitor (more an inducer than an inhibitor) CYP2B6 and 2C19 inducer	40–55 hours	Rash[d] Neuropsychiatric symptoms[e] Serum transaminase elevations Hyperlipidemia QT interval prolongation Use of EFV may lead to false-positive results with some cannabinoid and benzodiazepine screening assays.
Etravirine (ETR) *Intelence*	**Intelence** • 100-mg and 200-mg tablets	**Intelence** • ETR 200 mg PO twice daily following a meal.	CYP3A4, 2C9, and 2C19 substrate CYP3A4 inducer CYP2C9 and 2C19 inhibitor	41 hours	Rash, including Stevens-Johnson syndrome[d] HSRs, characterized by rash, constitutional findings, and sometimes organ dysfunction (including hepatic failure), have been reported. Nausea

Appendix B, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum Half-Life**	**Adverse Events**[b]
Rilpivirine (RPV) *Edurant*	**Edurant** • 25-mg tablet **STRs That Contain RPV**[c] • Complera (RPV/TDF/FTC) • Juluca (DTG/RPV) • Odefsey (RPV/TAF/FTC) **Copackaged Intramuscular Regimen** • Cabenuva (CAB plus RPV)	**Edurant** • RPV 25 mg PO once daily with food. See Appendix B, Table 1 for dosing information for coformulated and copackaged regimens that contain RPV.	CYP3A4 substrate	PO: 50 hours IM: 13–28 weeks	Rash[d] Depressive disorders, insomnia, headache Hepatotoxicity QT interval prolongation **IM Formulation Only** • Injection site reactions (pain, induration, swelling, nodules) • Rare postinjection reaction (dyspnea, agitation, abdominal cramps, flushing) occurring within a few minutes after RPV IM injection; possibly associated with inadvertent IV administration.

[a] For dose adjustments in people with renal or hepatic insufficiency, see Appendix B, Table 12. When no food restriction is listed, the antiretroviral drug can be taken with or without food.

[b] Also see Table 20.

[c] See Appendix B, Table 1 for information about these formulations.

[d] Rare cases of Stevens-Johnson syndrome have been reported with the use of most NNRTIs.

[e] Adverse events can include dizziness, somnolence, insomnia, abnormal dreams, depression, suicidality (e.g., suicide, suicide attempt or ideation), confusion, abnormal thinking, impaired concentration, amnesia, agitation, depersonalization, hallucinations, and euphoria. Approximately 50% of people who are receiving EFV may experience any of these symptoms. Symptoms usually subside spontaneously after 2–4 weeks, but discontinuation of EFV may be necessary in a small percentage of people. Late-onset neurotoxicities, including ataxia and encephalopathy, have been reported.

Key: 3TC = lamivudine; ARV = antiretroviral; CAB = cabotegravir; CD4 = CD4 T lymphocyte; CYP = cytochrome P; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; FTC = emtricitabine; HSR = hypersensitivity reaction; IM = intramuscular; IV = intravenous; NNRTI = non-nucleoside reverse transcriptase inhibitor; PO = orally; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix B, Table 5. Characteristics of Protease Inhibitors

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The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved protease inhibitor products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines. The older protease inhibitors indinavir (IDV) and saquinavir (SQV) have been discontinued in the United States; fosamprenavir (FPV), lopinavir/ritonavir (LPV/r), nelfinavir (NFV), and tipranavir (TPV) are no longer used commonly in clinical practice. These agents have been removed from this table. Please refer to the July 10, 2019, version of the guidelines (found in the Adult and Adolescent Antiretroviral Archived Guidelines section of the Archived Guidelines webpage on the Clinicalinfo website) or to the FDA product labels for information regarding these drugs.

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum Half-Life**	**Adverse Events**[b]
Atazanavir (ATV) *Reyataz* (ATV/c) *Evotaz* **Note:** Generic products of ATV are available.	**Reyataz** • 200-mg and 300-mg capsules • 50-mg oral powder/packet **Generic** • 200-mg and 300-mg capsules **Evotaz** • ATV 300-mg/COBI 150-mg tablet	**Reyataz** *In People Without Prior ARV Treatment* • (ATV 300 mg plus RTV 100 mg) PO once daily with food; *or* • ATV 400 mg PO once daily with food. *With TDF or in ARV-Experienced People* • (ATV 300 mg plus RTV 100 mg) PO once daily with food. • Unboosted ATV **is not recommended**. *With EFV in People Without Prior ARV Treatment* • (ATV 400 mg plus RTV 100 mg) PO once daily with food. **Evotaz** • One tablet PO once daily with food.	**ATV** • CYP3A4 inhibitor and substrate • Weak CYP2C8 inhibitor • UGT1A1 inhibitor **COBI** • CYP3A inhibitor and substrate • CYP2D6 inhibitor Dose adjustment is recommended in people with hepatic insufficiency (see Appendix B, Table 12).	7 hours	Indirect hyperbilirubinemia Cholelithiasis Nephrolithiasis Renal insufficiency Serum transaminase elevations Hyperlipidemia (especially with RTV boosting) Skin rash Hyperglycemia Lipodystrophy An increase in serum creatinine may occur when ATV is administered with COBI.

Appendix B, Table 5. Characteristics of Protease Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
		• The use of ATV/c **is not recommended** for people who are taking TDF and who have baseline CrCl <70 mL/min (see Appendix B, Table 12 for the equation for calculating CrCl). For dosing recommendations for people who also are receiving H2 antagonists and PPIs, refer to Table 24a.			PR interval prolongation: First-degree symptomatic AV block has been reported. Use with caution in people who have underlying conduction defects or who are on concomitant medications that can cause PR prolongation.
Darunavir (DRV) *Prezista* (DRV/c) *Prezcobix*	**Prezista** • 600-mg and 800-mg tablets • 100-mg/mL oral suspension **Prezcobix** • DRV 800-mg/COBI 150-mg tablet Also available as part of the STR Symtuza (DRV/c/TAF/FTC)	**Prezista** *In People Without Prior ARV Treatment or ARV-Experienced Treatment With No DRV Mutations* • (DRV 800 mg plus RTV 100 mg) PO once daily with food. *In ARV-Experienced People With One or More DRV Resistance Mutations* • (DRV 600 mg plus RTV 100 mg) PO twice daily with food. Unboosted DRV **is not recommended.** **Prezcobix** • One tablet PO once daily with food. • **Not recommended** for people with one or more DRV resistance-associated mutations. • Coadministering Prezcobix and TDF **is not recommended** for people with baseline CrCl <70 mL/min (see Appendix B, Table 12 for the equation for calculating CrCl). See Appendix B, Table 1 for dosing information for Symtuza.	**DRV** • CYP3A4 inhibitor and substrate • CYP2C9 inducer **COBI** • CYP3A inhibitor and substrate • CYP2D6 inhibitor	15 hours when combined with RTV 7 hours when combined with COBI	Hepatotoxicity Diarrhea, nausea Headache Hyperlipidemia Serum transaminase elevation Hyperglycemia Lipodystrophy An increase in serum creatinine may occur when DRV is administered with COBI. Skin rash: DRV has a sulfonamide moiety; however, incidence and severity of rash are similar in those with or without a sulfonamide allergy—Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme have been reported.

Appendix B, Table 5. Characteristics of Protease Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
Ritonavir (RTV) *Norvir* **Note:** Generic is available. RTV was initially developed as a PI for HIV treatment but is now primarily used at a lower dose of 100 mg once or twice daily as a PK enhancer to increase the concentrations of other PIs.	**Norvir** • 100-mg tablet • 100-mg single packet oral powder Also available as part of the FDC tablet Kaletra (LPV/r)	**As a PK Booster (or Enhancer) for Other PIs** • RTV 100–200 mg PO per day in one or two divided doses (refer to other PIs for specific dosing recommendations) with food.	CYP3A4 > 2D6 substrate Potent CYP3A4 and 2D6 inhibitor Inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19	3–5 hours	GI intolerance, nausea, vomiting, diarrhea Paresthesia (circumoral and extremities) Hyperlipidemia (especially hypertriglyceridemia) Hepatitis Asthenia Dysgeusia Hyperglycemia Fat maldistribution

[a] For dose adjustments in people with hepatic insufficiency, see Appendix B, Table 12.

[b] Also see Table 20.

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; AV = atrioventricular; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; EFV = efavirenz; FDC = fixed-dose combination; FTC = emtricitabine; GI = gastrointestinal; H2 = histamine H2 receptor; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; PK = pharmacokinetic; PO = orally; PPI = proton pump inhibitor; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT1 = uridine diphosphate glucuronyl transferase 1 family

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors

Updated: September 12, 2024
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The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved integrase strand transfer inhibitor products for adults with HIV. Not all products are FDA-approved for adolescents with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines.

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathways**	**Serum Half-Life**	**Adverse Events**[b]
Bictegravir (BIC)	BIC is available only as a component of the STR Biktarvy (BIC/TAF/FTC).[c]	**Biktarvy** • One tablet PO once daily	CYP3A4 substrate UGT1A1-mediated glucuronidation	~17 hours	Diarrhea Nausea Headache Weight gain
Cabotegravir (CAB)	Available as part of the copackaged IM long-acting regimen Cabenuva (CAB IM and RPV IM) • 400-mg/2-mL vial • 600-mg/3-mL vial Also available as an individual product for IM long-acting pre-exposure prophylaxis Apretude (CAB IM) • 600-mg/3-mL vial Also available in oral tablet formulation Vocabria (CAB PO) • 30-mg tablet • Must be obtained from manufacturer for oral lead-in and oral bridging during administration of Cabenuva (CAB IM/RPV IM)	See Appendix B, Table 1 for dosing information for coformulated and copackaged regimens that contain CAB.	UGT1A1 and UGT1A9-mediated glucuronidation	Oral: 41 hours IM: 6–12 weeks	IM formulation only: Injection site reactions (e.g., pain, induration, swelling, nodules) The following AEs were reported when CAB was administered in combination with RPV: Headache Nausea Abnormal dreams Anxiety Insomnia Depressive disorders Hepatotoxicity

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathways**	**Serum Half-Life**	**Adverse Events**[b]
Dolutegravir (DTG) *Tivicay*	**Tivicay** • 50-mg tablet **STRs That Contain DTG**[c] • Dovato (DTG/3TC) • Juluca (DTG/RPV) • Triumeq (DTG/ABC/3TC)	**In People Without Prior ARV Treatment or ARV-Experienced People Who Had Never Received INSTIs** • DTG 50 mg PO once daily **In People Without Prior ARV Treatment or ARV-Experienced People Who Had Never Received INSTIs When Coadministered With EFV, FPV/r, TPV/r, or Rifampin** • DTG 50 PO mg twice daily **In INSTI-Experienced People With Certain INSTI Mutations (See Product Label) or With Clinically Suspected INSTI Resistance** • DTG 50 mg PO twice daily See Appendix B, Table 1 for dosing information for STRs that contain DTG.	UGT1A1-mediated glucuronidation Minor substrate of CYP3A4	~14 hours	Insomnia Headache Depressive disorders and suicidal ideation (rare; usually occurs in people with preexisting psychiatric conditions) Weight gain Hepatotoxicity HSRs, including rash, constitutional symptoms, and organ dysfunction (including liver injury), have been reported.

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathways	Serum Half-Life	Adverse Events[b]
Elvitegravir (EVG)	EVG is only available as a component of an STR tablet that also contains COBI, FTC, and either TDF or TAF. **STRs That Contain EVG[c]** • Genvoya (EVG/c/TAF/FTC) • Stribild (EVG/c/TDF/FTC)	**Genvoya** • One tablet PO once daily with food. • See Appendix B, Table 12 for recommendations on dosing in persons with renal insufficiency. **Stribild** • One tablet PO once daily with food. • **Not recommended** for people with baseline CrCl <70 mL/min (see Appendix B, Table 12 for the CrCl calculation equation).	**EVG** • CYP3A and UGT1A1/3 substrate **COBI** • CYP3A inhibitor and substrate • CYP2D6 inhibitor	EVG/c: ~13 hours	Nausea Diarrhea Depression and suicidal ideation (rare; usually occurs in people with preexisting psychiatric conditions)
Raltegravir (RAL) *Isentress* *Isentress HD*	**Isentress** • 400-mg tablet • 100-mg single-use packet for oral suspension **Isentress HD** • 600-mg tablet	**Isentress** • 400 mg PO twice daily *With Rifampin* • 800 mg PO twice daily **Isentress HD** *In People Without Prior ARV Treatment or ARV-Experienced People With Virologic Suppression on a Regimen Containing RAL 400 mg Twice Daily* • 1,200 mg (two 600-mg tablets) PO once daily *With Rifampin* • **Not recommended**	UGT1A1-mediated glucuronidation	~9 hours	Rash, including Stevens-Johnson syndrome, HSR, and toxic epidermal necrolysis Nausea Headache Diarrhea Pyrexia CPK elevation, muscle weakness, and rhabdomyolysis Weight gain Insomnia

Appendix B, Table 6. Characteristics of Integrase Strand Transfer Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathways**	**Serum Half-Life**	**Adverse Events**[b]
					Depression and suicidal ideation (rare; usually occurs in people with preexisting psychiatric conditions)

[a] For dose adjustments in people with hepatic insufficiency, see Appendix B, Table 12. When no food restriction is listed, the antiretroviral drug can be taken with or without food.

[b] Also see Table 20.

[c] See Appendix B, Table 1 for information about these formulations.

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse event; ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; COBI = cobicistat; CPK = creatine phosphokinase; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; HSR = hypersensitivity reaction; IM = intramuscular; INSTI = integrase strand transfer inhibitor; NTD = neural tube defect; PO = orally; RAL = raltegravir; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir; UGT1 = uridine diphosphate glucuronyl transferase 1 family

Appendix B, Table 7. Characteristics of the Fusion Inhibitor

Updated: May 26, 2023
Reviewed: September 12, 2024

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved fusion inhibitor. For additional information regarding the use of this medication in adolescents with HIV, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines.

Generic Name (Abbreviation) *Trade Name*	**Formulation**	**Dosing Recommendation**	**Serum Half-Life**	**Elimination**	**Adverse Events**[a]
Enfuvirtide (T-20) *Fuzeon*	**Fuzeon** • Injectable; supplied as lyophilized powder. • Each vial contains 108 mg of T-20; reconstitute with 1.1 mL of sterile water for injection for delivery of approximately 90 mg/1 mL. • Refer to prescribing information for storage instruction.	**Fuzeon** • T-20 90 mg/1 mL SQ twice daily	3.8 hours	Expected to undergo catabolism to its constituent amino acids, with subsequent recycling of the amino acids in the body pool.	Local injection site reactions (e.g., pain, erythema, induration, nodules and cysts, pruritus, ecchymosis) in almost all people Increased incidence of bacterial pneumonia HSR occurs in <1% of people. Symptoms may include rash, fever, nausea, vomiting, chills, rigors, hypotension, or elevated serum transaminases. **Rechallenge is not recommended.**

[a] Also see Table 20.

Key: HSR = hypersensitivity reaction; SQ = subcutaneous; T-20 = enfuvirtide

Appendix B, Table 8. Characteristics of the CCR5 Antagonist

Updated: May 26, 2023
Reviewed: September 12, 2024

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved CCR5 antagonist. For additional information regarding the use of this medication in adolescents with HIV, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines.

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations[a]	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events[b]
Maraviroc (MVC) *Selzentry*	**Selzentry** • 150-mg and 300-mg tablets • 20-mg/1-mL oral solution	**Selzentry** • MVC 150 mg PO twice daily when given with drugs that are strong CYP3A inhibitors (with or without CYP3A inducers), including PIs (except TPV/r) • MVC 300 mg PO twice daily when given with NRTIs, T-20, TPV/r, NVP, RAL, and other drugs that are not strong CYP3A inhibitors or inducers • MVC 600 mg PO twice daily when given with drugs that are CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor) Take MVC without regard to food.	14–18 hours	CYP3A4 substrate	Abdominal pain Cough Dizziness Musculoskeletal symptoms Pyrexia Rash Upper respiratory tract infections Hepatotoxicity, which may be preceded by severe rash or other signs of systemic allergic reactions Orthostatic hypotension, especially in people with severe renal insufficiency

[a] For dose adjustments in people with hepatic insufficiency, see Appendix B, Table 12.

[b] Also see Table 20.

Key: CYP = cytochrome P; EFV = efavirenz; ETR = etravirine; MVC = maraviroc; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = orally; RAL = raltegravir; T-20 = enfuvirtide; TPV/r = tipranavir/ritonavir

Appendix B, Table 9. Characteristics of the CD4 Post-Attachment Inhibitor

Updated: May 26, 2023
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The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved CD4 post-attachment inhibitor. Ibalizumab is not FDA approved for use in adolescents with HIV.

Generic Name (Abbreviation) *Trade Name*	**Formulation**	**Dosing Recommendations**	**Serum Half-Life**	**Elimination/ Metabolic Pathway**	**Adverse Events**[a]
Ibalizumab (IBA) *Trogarzo*	**Trogarzo** • Single-dose 2-mL vial containing 200 mg/1.33 mL (150 mg/mL) of ibalizumab	**Trogarzo** • Administer a single loading dose of IBA 2,000-mg IV infusion over 30 minutes, followed by a maintenance dose of IBA 800-mg IV infusion over 15 minutes or IV push over 30 seconds every 2 weeks. • See prescribing information for additional instructions for preparing, storing, and administering IBA, and for monitoring people who are receiving IBA.	~64 hours	Not well defined	Diarrhea Dizziness Nausea Rash HSRs, including anaphylaxis and infusion-related reactions, have been reported.

[a] Also see Table 20.

Key: HSR = hypersensitivity reaction; IBA = ibalizumab; IV = intravenous

Appendix B, Table 10. Characteristics of the gp120 Attachment Inhibitor

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The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved gp120 attachment inhibitor. Fostemsavir is not FDA approved for use in adolescents with HIV.

Generic Name (Abbreviation) *Trade Name*	**Formulation**	**Dosing Recommendations**	**Serum Half-Life**	**Elimination/ Metabolic Pathway**	**Adverse Events**[a]
Fostemsavir (FTR) *Rukobia*	• 600-mg extended-release tablets	• FTR 600 mg PO twice daily	11 hours	Hydrolysis (esterases), CYP3A4	Nausea Transaminase elevation; transient bilirubin elevation Sleep disturbance, dizziness QTc prolongation was seen at four times the recommended dose. Use with caution in people with preexisting heart disease, QTc prolongation, or concomitant use of medications that may prolong QTc interval.

[a] also see Table 20.

Key: CYP = cytochrome P; FTR = fostemsavir; PO = orally; QTc = corrected QT interval

Appendix B, Table 11. Characteristics of the Capsid Inhibitor

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The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved capsid inhibitor. Lenacapavir is not FDA approved for use in adolescents with HIV.

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations	Serum Half-Life	Elimination/ Metabolic Pathway	Adverse Events[a]
Lenacapavir (LEN) *Sunlenca*	• 300-mg tablet • Single-dose 463.5-mg/1.5-mL vial for injection	**Initiation Option 1** • Day 1: 927 mg SQ x 1 dose + 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose **Initiation Option 2** • Day 1: 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose • Day 8: 300 mg PO x 1 dose • Day 15: 927 mg SQ x 1 dose **Maintenance Dosing** • 927 mg by SQ injection every 6 months from the date of the last injection (+/-2 weeks) **Note:** Each SQ dose requires two injections.	PO: 10–12 days SQ: 8–12 weeks	Substrate of P-glycoprotein, CYP3A (minor), UGT1A1 (minor) CYP3A4 inhibitor (moderate)	Injection site reactions, including nodules and induration Nausea, diarrhea, headache

[a] Also see Table 20.

Key: CYP = cytochrome P; LEN = lenacapavir; PO = orally; SQ = subcutaneous

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Updated: September 12, 2024
Reviewed: September 12, 2024

Not all products are Food and Drug Administration (FDA)–approved for adolescents with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines.

The older antiretroviral drugs fosamprenavir (FPV), lopinavir/ritonavir (LPV/r) , nelfinavir (NFV), nevirapine (NVP), tipranavir (TPV), and zidovudine (ZDV) have been removed from this table. Please refer to the FDA product labels for these drugs for recommendations on dosing in adults and adolescents with renal or hepatic insufficiency.

See the reference section at the end of this table for creatinine clearance calculation formulas and criteria for Child-Pugh classification.

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Recommendations for FDCs based on CrCl level are outlined in the table below.			
NRTIs			
Abacavir (ABC) *Ziagen*	ABC 300 mg PO twice daily *or* ABC 600 mg PO once daily	No dose adjustment necessary.	*Child-Pugh Class A:* ABC 200 mg PO twice daily (use oral solution) *Child-Pugh Class B or C:* **Contraindicated**
Abacavir/Lamivudine (ABC/3TC) *Epzicom*	One tablet PO once daily	Not FDA recommended if CrCl <30 mL/min due to the 3TC component. **Note:** There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. Some Panel members use full-dose 3TC to allow people to remain on the FDC product. See the 3TC entry for more information.	*Child-Pugh Class A:* People with mild hepatic impairment require a dose reduction of ABC. Use the individual drugs instead of the FDC tablet in these people. *Child-Pugh Class B or C:* **Contraindicated** due to the ABC component
Emtricitabine (FTC) *Emtriva*		**Dose by Formulation** **CrCl (mL/min)** / **Capsule** / **Solution** 30–49[b] / No dose adjustment necessary.	No dose recommendation.

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**			**Dosing in Adults With Hepatic Impairment**
	FTC 200-mg oral capsule once daily *or* FTC 240-mg (24-mL) oral solution once daily **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min who are not on HD. To allow people to remain on certain TAF-containing FDC products, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min who are not on HD.	15–29 (see **Note**)	200 mg every 72 hours	80 mg every 24 hours	
		<15 (not on HD) (see **Note**)	200 mg every 96 hours	60 mg every 24 hours	
		On HD[b]	No dose adjustment necessary. On HD days, administer after dialysis.		
Lamivudine[c] (3TC) *Epivir*	3TC 300 mg PO once daily *or* 3TC 150 mg PO twice daily **Note:** PK and safety data are limited on the use of 3TC doses higher than those recommended by the FDA in people with CrCl <30 mL/min. Clinicians may consider using the nearest available tablet strength (100 mg or 150 mg), as outlined in the "Alternative Dose" column **(BIII)** (see rationale[d]). There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. Some Panel members use full-dose 3TC to allow people to remain on certain ABC and/or DTG-containing FDC products.	**CrCl (mL/min)**	**Epivir Label Dose**	**Alternative Dose**[d]	No dose adjustment necessary
		15–29 (see **Note**)	1 × 150 mg, then 100 mg every 24 hours	100–150 mg every 24 hours	
		5–14 (see **Note**)	1 × 150 mg, then 50 mg every 24 hours	100–150 mg every 24 hours	
		<5 or on HD (see **Note**)	1 × 50 mg, then 25 mg every 24 hours	100–150 mg every 24 hours	

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults With Renal Insufficiency		Dosing in Adults With Hepatic Impairment
Tenofovir Alafenamide (TAF) *Vemlidy*	Vemlidy is available as a 25-mg tablet for the treatment of HBV.	**CrCl (mL/min)**	**Dose**	*Child-Pugh Class A:* No dose adjustment *Child-Pugh Class B or C:* **Not recommended**
		<15 (not on HD)	**Not recommended**	
		On HD	No dose adjustment necessary. On HD days, administer after dialysis.	
Tenofovir Alafenamide/ Emtricitabine (TAF/FTC) *Descovy*	TAF for HIV treatment is only available as a component of FDC tablets (i.e., in Descovy, Genvoya, Odefsey, Biktarvy, and Symtuza). • TAF 10 mg PO daily with EVG/c (Genvoya) or DRV/c (Symtuza) • TAF 25 mg PO daily in other FDC tablets	**CrCl (mL/min)**	**Dose**	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C*: No dose recommendation
		15–29	**Not recommended** **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose FTC in people with CrCl 15–29 mL/min.	
		<15 (not on HD)	**Not recommended**	
		On HD	No dose adjustment necessary. On HD days, administer after dialysis.	
Tenofovir Disoproxil Fumarate (TDF) *Viread*	TDF 300 mg PO once daily	**CrCl (mL/min)**	**Dose**	No dose adjustment necessary
		30–49	300 mg every 48 hours	
		10–29	300 mg twice weekly (every 72–96 hours)	
		<10 (not on HD)	No recommendation	
		On HD	300 mg every 7 days (administer after completion of HD)	
Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC) *Truvada*	One tablet PO once daily	**CrCl (mL/min)**	**Dose**	No dose recommendation
		30–49	One tablet every 48 hours	
		<30 or on HD	FDC of TDF/FTC **not recommended**	

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults With Renal Insufficiency		Dosing in Adults With Hepatic Impairment
Tenofovir Disoproxil Fumarate/Lamivudine (TDF/3TC) *Cimduo*	One tablet PO once daily	**CrCl (mL/min)**	**Dose**	No dose recommendation
		<50 or on HD	FDC of TDF/3TC **not recommended**	
NNRTIs				
Doravirine (DOR) *Pifeltro*	DOR 100 mg PO once daily	No dose adjustment required in mild, moderate, or severe renal impairment. Has not been studied in individuals with ESRD or on HD.		*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* Not studied
Doravirine/Tenofovir Disoproxil Fumarate/ Lamivudine (DOR/TDF/3TC) *Delstrigo*	One tablet PO once daily	FDC of DOR/TDF/3TC **not recommended** if CrCl <50 mL/min or on HD		*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* Not studied
Efavirenz (EFV) *Sustiva*	EFV 600 mg PO once daily on an empty stomach, preferably at bedtime	No dose adjustment necessary		No dose recommendation; use with caution in people with hepatic impairment.
Efavirenz/Tenofovir Disoproxil Fumarate/ Emtricitabine (EFV/TDF/FTC) *Atripla*	One tablet PO once daily on an empty stomach, preferably at bedtime	FDC of EFV/TDF/FTC **not recommended** if CrCl <50 mL/min or if on HD		No dose recommendation; use with caution in people with hepatic impairment.
Efavirenz 600 mg/ Tenofovir Disoproxil Fumarate/ Lamivudine (EFV/TDF/3TC) *Symfi*	One tablet PO once daily on an empty stomach, preferably at bedtime	FDC of EFV/TDF/3TC **not recommended** if CrCl <50 mL/min or if on HD		**Not recommended** for people with moderate or severe hepatic impairment. Use with caution in people with mild hepatic impairment.
Efavirenz 400 mg/ Tenofovir Disoproxil Fumarate/Lamivudine (EFV/TDF/3TC) *Symfi Lo*	One tablet PO once daily on an empty stomach, preferably at bedtime	FDC of EFV/TDF/3TC **not recommended** if CrCl <50 mL/min or if on HD		**Not recommended** for people with moderate or severe hepatic impairment. Use with caution in people with mild hepatic impairment.

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Etravirine (ETR) *Intelence*	ETR 200 mg PO twice daily	No dose adjustment necessary	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Rilpivirine (RPV PO) *Edurant*	RPV 25 mg PO once daily with food	No dose adjustment necessary	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Rilpivirine IM Plus Cabotegravir IM (RPV IM and CAB IM) *Cabenuva*	**Monthly Dosing** • Loading dose: RPV 900 mg/3 mL IM × 1 dose and CAB 600 mg/3 mL IM × 1 dose • Continuation phase: RPV 600 mg/2 mL IM every 4 weeks and CAB 400 mg/2 mL IM every 4 weeks **Every-2-Months Dosing** • Loading dose: RPV 900 mg/3 mL IM and CAB 600 mg/3 mL IM monthly for 2 doses • Continuation phase: RPV 900 mg/3 mL IM and CAB 600 mg/3 mL IM every 2 months	No dose adjustment necessary for mild or moderate renal impairment For people with severe renal impairment or on HD, increase monitoring for adverse events.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No recommendation

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults With Renal Insufficiency	Dosing in Adults With Hepatic Impairment
Rilpivirine/Tenofovir Alafenamide/Emtricitabine (RPV/TAF/FTC) *Odefsey*	One tablet PO once daily with food	**In People With CrCl 15–29 mL/min** • **Not recommended** • **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. **In People With CrCl <15 mL/min (not on HD)** • **Not recommended** **In People on Chronic HD** • No dose adjustment necessary. On HD days, administer after dialysis.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine (RPV/TDF/FTC) *Complera*	One tablet PO once daily with food	FDC of RPV/TDF/FTC **not recommended** if CrCl <50 mL/min or on HD	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Rilpivirine/Dolutegravir (RPV/DTG) *Juluca*	One tablet PO once daily with food	No dose adjustment necessary In people with CrCl <30 mL/min, monitor closely for adverse effects.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
PIs			
Atazanavir (ATV) *Reyataz*	ATV 400 mg PO once daily with food *or* (ATV 300 mg plus RTV 100 mg) PO once daily with food	**In People Without Prior ARV Treatment on HD** • (ATV 300 mg plus RTV 100 mg) once daily with food. **In ARV-Experienced People on HD** • ATV and ATV/r **are not recommended.**	*Child-Pugh Class A:* No dose adjustment *Child-Pugh Class B:* ATV 300 mg once daily (unboosted) for people without prior ARV treatent *Child-Pugh Class C:* **Not recommended** RTV boosting **is not recommended** in people with hepatic impairment.

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Atazanavir/Cobicistat (ATV/c) *Evotaz*	One tablet PO once daily with food	**If Used With TDF** • **Not recommended** if CrCl <70 mL/min	**Not recommended** in people with hepatic impairmen.
Darunavir (DRV) *Prezista*	**In People Without Prior ARV Treatment or ARV-Experienced Treatment With No DRV Mutations** • (DRV 800 mg plus RTV 100 mg) PO once daily with food. **In ARV-Experienced People With at Least One DRV Resistance Mutation** • (DRV 600 mg plus RTV 100 mg) PO twice daily with food.	No dose adjustment necessary	*In People With Mild-to-Moderate Hepatic Impairment:* No dose adjustment *In People With Severe Hepatic Impairment:* **Not recommended**
Darunavir/Cobicistat (DRV/c) *Prezcobix*	One tablet PO once daily with food	**If Used With TDF** • **Not recommended** if CrCl <70 mL/min	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Darunavir/Cobicistat/ Tenofovir Alafenamide/ Emtricitabine (DRV/c/TAF/FTC) *Symtuza*	One tablet PO once daily with food	**In People With CrCl 15–29 mL/min** • **Not recommended** • **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. **In People With CrCl <15 mL/min (not on HD)** • **Not recommended** **In People on Chronic HD** • No dose adjustment necessary. On HD days, administer after dialysis.	**Not recommended** for people with severe hepatic impairment

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Ritonavir (RTV) *Norvir*	**As a PI-Boosting Agent** • RTV 100–400 mg PO per day with food.	No dose adjustment necessary	Refer to recommendations for the primary (i.e., boosted) PI.
INSTIs			
Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/TAF/FTC) *Biktarvy*	One tablet PO once daily	**In People With CrCl 15–29 mL/min** • **Not recommended** • **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. **In People With CrCl <15 mL/min (not on HD)** • **Not recommended** **In People on Chronic HD** • No dose adjustment necessary. On HD days, administer after dialysis.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Cabotegravir (CAB PO) *Vocabria*	**Treatment (As Optional Oral Lead-In or As Oral Bridging)** • CAB 30 mg PO once daily, given with RPV 25 mg PO, with food before switching to CAB IM and RPV IM **Pre-exposure Prophylaxis (Optional Oral Lead-In)** • CAB 30 mg PO once daily before switching to CAB IM	No dose adjustment necessary	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No recommendation

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults With Renal Insufficiency	Dosing in Adults With Hepatic Impairment
Cabotegravir (CAB IM) *Apretude*	**Pre-exposure Prophylaxis** • Loading dose: CAB 600 mg/3 mL IM monthly for 2 doses • Continuation phase: CAB 600 mg/3 mL IM every 2 months	No dose adjustment necessary	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No recommendation
Cabotegravir IM plus Rilpivirine IM (CAB IM plus RPV IM) *Cabenuva*	**Monthly Dosing** • Loading dose: CAB 600 mg/3 mL IM × 1 dose and RPV 900 mg/3 mL IM × 1 dose • Continuation phase: CAB 400 mg/2 mL IM every 4 weeks and RPV 600 mg/2 mL IM every 4 weeks **Every 2-Month Dosing** • Loading dose: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM monthly for 2 doses • Continuation phase: CAB 600 mg/3 mL IM and RPV 900 mg/ 3 mL IM every 2 months	No dose adjustment necessary for mild or moderate renal impairment For people with severe renal impairment or on HD, increase monitoring for adverse events.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No recommendation
Dolutegravir (DTG) *Tivicay*	DTG 50 mg PO once daily *or* DTG 50 mg PO twice daily	No dose adjustment necessary	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Dolutegravir/Abacavir/ Lamivudine (DTG/ABC/3TC) *Triumeq*	One tablet PO once daily	Not FDA recommended if CrCl <30 mL/min due to the 3TC component **Note:** There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. Some Panel members use full-dose 3TC to allow people to remain on the FDC product.[d]	*Child-Pugh Class A:* People with mild hepatic impairment require a dose reduction of ABC. Use the individual drugs instead of the FDC tablet in these people. *Child-Pugh Class B or C:* **Contraindicated** due to the ABC component

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Dolutegravir/Lamivudine (DTG/3TC) *Dovato*	One tablet PO once daily	Not FDA recommended if CrCl <30 mL/min due to 3TC component **Note:** There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. Some Panel members use full-dose 3TC to allow people to remain on the FDC product.[d]	*Child-Pugh Class C:* **Not recommended**
Dolutegravir/Rilpivirine (DTG/RPV) *Juluca*	One tablet PO once daily with food	No dose adjustment necessary In people with CrCl <30 mL/min, monitor closely for adverse effects.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Elvitegravir/Cobicistat/ Tenofovir Alafenamide/ Emtricitabine (EVG/c/TAF/FTC) *Genvoya*	One tablet PO once daily with food	**In People With CrCl 15–29 mL/min** • **Not recommended** • **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. **In People With CrCl <15 mL/min (not on HD)** • **Not recommended** **In People on Chronic HD** • No dose adjustment necessary. On HD days, administer after dialysis.	*In People With Mild-to-Moderate Hepatic Insufficiency:* No dose adjustment necessary *In People With Severe Hepatic Insufficiency:* **Not recommended**
Elvitegravir/Cobicistat/ Tenofovir Disoproxil Fumarate/Emtricitabine (EVG/c/TDF/FTC) *Stribild*	One tablet PO once daily with food	EVG/c/TDF/FTC **should not be initiated** in people with CrCl <70 mL/min. Discontinue EVG/c/TDF/FTC if CrCl declines to <50 mL/min while on therapy.	*In People With Mild-to-Moderate Hepatic Insufficiency:* No dose adjustment necessary *In People With Severe Hepatic Insufficiency:* **Not recommended**

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults With Renal Insufficiency	Dosing in Adults With Hepatic Impairment
Raltegravir (RAL) *Isentress* *Isentress HD*	RAL 400 mg PO twice daily (using Isentress formulation) *or* RAL 1,200 mg PO once daily (using Isentress HD formulation only)	No dose adjustment necessary	*In People With Mild-to-Moderate Hepatic Insufficiency:* No dose adjustment necessary *In People With Severe Hepatic Insufficiency:* No recommendation
Fusion Inhibitor			
Enfuvirtide (T-20) *Fuzeon*	T-20 90 mg SQ twice daily	No dose adjustment necessary	No dose adjustment necessary
CCR5 Antagonist			
Maraviroc (MVC) *Selzentry*	The recommended dose differs based on concomitant medications and potential for drug–drug interactions. See Appendix B, Table 8 for detailed dosing information.	**In People With CrCl <30 mL/min or People Who Are on HD** *Without Potent CYP3A Inhibitors or Inducers* • MVC 300 mg twice daily; if postural hypotension occurs, reduce to MVC 150 mg twice daily *With Potent CYP3A Inducers or Inhibitors* • **Not recommended**	No dose recommendations. MVC concentrations will likely be increased in people with hepatic impairment.
CD4 Post-Attachment Inhibitor			
Ibalizumab (IBA) *Trogarzo*	Loading dose: IBA 2,000 mg IV Maintenance dose: IBA 800 mg IV every 2 weeks	No dose adjustment recommended	No recommendation
gp-120 Attachment Inhibitor			
Fostemsavir (FTR) *Rukobia*	FTR 600 mg PO twice daily	No dose adjustment recommended	No dose adjustment recommended

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	Usual Dose[a]	Dosing in Adults With Renal Insufficiency	Dosing in Adults With Hepatic Impairment
Capsid Inhibitor			
Lenacapavir (LEN) *Sunlenca*	**Initiation Option 1** • Day 1: 927 mg SQ x 1 dose plus 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose **Initiation Option 2** • Day 1: 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose • Day 8: 300 mg PO x 1 dose • Day 15: 927 mg SQ x 1 dose **Maintenance Dosing** • 927 mg by SQ injection every 6 months from the date of the last injection (+/-2 weeks)	No dose adjustment recommended	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No recommendation

[a] Refer to Appendix B, Tables 1–10 for additional dosing information.

[b] The prescribing information for FTC (Emtriva) recommends adjusted doses for people with CrCl 30–49 mL/min and people on hemodialysis. However, the prescribing information for several FDC products that contain FTC (including Descovy, Biktarvy, Genvoya, and Odefsey) recommends that the standard dose (FTC 200 mg) can be given once daily in these people. The recommendations in this table incorporates the dosing guidance from the FDC products.

[c] The prescribing information for 3TC (Epivir) recommends dosage adjustment from 300 mg once daily to 150 mg once daily for people with CrCl 30–49 mL/min. However, the prescribing information for several FDC products that contain 3TC (including Epzicom, Dovato, and Triumeq) recommends no dose adjustment for CrCl 30–49 mL/min. The recommendation in this table incorporates the dosing guidance from the FDC products.

[d] Use of 3TC doses higher than those recommended by the FDA for people with CrCl <30 mL/min has been reported in clinical practice [1-4] and endorsed in the Guidelines for Chronic Kidney Disease in People With HIV for many years [5]; limited published literature has supported the safety of this practice [2,3]. 3TC has a wide therapeutic index with no established correlation between elevated concentrations and AEs. Serious AEs, such as lactic acidosis and severe hematologic toxicities, have been reported in rare cases; however, these effects typically occurred when 3TC was used in combination with older NRTIs (such as didanosine, stavudine, zidovudine). Clinicians may consider using the nearest available tablet strength (100 mg or 150 mg) to avoid the need for 3TC oral solution, thereby simplifying ARV regimens and facilitating adherence **(BIII).** See the Alternative Dose column in 3TC table entry. There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. Some Panel members use full-dose 3TC to allow people to remain on certain FDC products.

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse effect; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; ESRD = end stage renal disease; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; FTR = fostemsavir; HBV = hepatitis B virus;

Appendix B, Table 12. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

HD = hemodialysis; IBA = ibalizumab; IM = intramuscular; INSTI = integrase strand transfer inhibitor; IV = intravenous; LEN = lenacapavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PK: pharmacokinetic; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Creatinine Clearance Calculation	
Male: $\frac{(140 - age\ in\ years) \times weight\ in\ kg}{72 \times serum\ creatinine}$	**Female:** $\frac{(140 - age\ in\ years) \times weight\ in\ kg \times 0.85}{72 \times serum\ creatinine}$

Child-Pugh Score			
Component	**Points Scored**		
	1	**2**	**3**
Encephalopathy[a]	None	Grade 1–2	Grade 3–4
Ascites	None	Mild or controlled by diuretics	Moderate or refractory despite diuretics
Albumin	>3.5 g/dL	2.8–3.5 g/dL	<2.8 g/dL
Total Bilirubin, *or*	<2 mg/dL (<34 μmol/L)	2–3 mg/dL (34–50 μmol/L)	>3 mg/dL (>50 μmol/L)
Modified Total Bilirubin[b]	<4 mg/dL	4–7 mg/dL	>7 mg/dL
Prothrombin Time (Seconds Prolonged), *or*	<4	4–6	>6
International Normalized Ratio (INR)	<1.7	1.7–2.3	>2.3

[a] **Encephalopathy Grades**

Grade 1: Mild confusion, anxiety, restlessness, fine tremor, slowed coordination

Grade 2: Drowsiness, disorientation, asterixis

Grade 3: Somnolent but rousable, marked confusion, incomprehensible speech, incontinence, hyperventilation

Grade 4: Coma, decerebrate posturing, flaccidity

[b] Modified total bilirubin is used for people who have Gilbert's syndrome or who are taking atazanavir.

Child-Pugh Classification	Total Child-Pugh Score[a]
Class A	5–6 points
Class B	7–9 points
Class C	>9 points

[a] Sum of points for each component of the Child-Pugh Score.

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Weddle Declaration
Exhibit G

GUIDELINES FOR THE USE OF ANTIRETROVIRAL AGENTS IN ADULTS AND ADOLESCENTS WITH HIV



Developed by the HHS Panel on Antiretroviral Guidelines for Adults and Adolescents—A Working Group of the NIH Office of AIDS Research Advisory Council (OARAC)

How to Cite the Adult and Adolescent Antiretroviral Guidelines:

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It is emphasized that concepts relevant to HIV management evolve rapidly. The Panels have a mechanism to update recommendations on a regular basis, and the most recent information is available on the Clinicalinfo website (https://clinicalinfo.hiv.gov/).

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Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs) *M-112*

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors *M-127*

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors *M-130*

WHAT'S NEW IN THE GUIDELINES

Updated: September 25, 2025
Reviewed: September 25, 2025

These guidelines were updated by the U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) based on key new clinical evidence on the use of antiretroviral therapy (ART) for the treatment of people with HIV.

New Chapter Added to the Guidelines

Cardiovascular and Metabolic Complications in People With HIV

With the success of ART, the life expectancy of people with HIV is approaching that of people without HIV. As a result, many people with HIV are experiencing age-related comorbidities. This new chapter aims to provide guidance on the prevention and management of cardiovascular disease and metabolic complications in people with HIV and includes the following sections:

- Introduction
- Immune Activation and Inflammation Among People With HIV Receiving Antiretroviral Therapy
- Cardiovascular Complications in People With HIV
- Statin Therapy as Primary Prevention of Atherosclerotic Disease in People With HIV
- Weight Gain in People With Treated HIV

Key Revisions to the Guidelines

Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy

Updates made to the Laboratory Testing section include the following:

- Updated recommended monitoring frequencies for CD4 T lymphocyte (CD4) cell count, basic metabolic panel, liver enzymes, and lipid profile (see Table 3).
- A new table (Table 4. Laboratory Monitoring If ART Is Deferred) provides guidance on initial laboratory assessments and recommended follow-up frequency if ART is deferred.

Plasma HIV-1 RNA (Viral Load) and CD4 Count Monitoring

Updates made to the Plasma HIV-1 RNA (Viral Load) and CD4 Count Monitoring section include the following:

- The Panel previously considered repeat HIV-1 RNA monitoring optional when ART was deferred. To support ongoing discussions about the benefits of ART, for both HIV treatment and the prevention of transmission to others, the Panel now recommends testing every 3 to 6 months when ART is deferred.
- Updated the rationale for the changes in recommended CD4 count monitoring frequency, as noted in Table 3

Initiation of Antiretroviral Therapy

Two new subsections have been added to the Initiation of Antiretroviral Therapy section:

- **Early (Acute/Recent) HIV Infection:** This subsection focuses on the importance of initiating ART as soon as possible, as ART can provide immunologic benefits for people with early HIV infection. Additionally, early HIV is a period of high infectivity, and ART substantially reduces the risk of transmission.
- **Antiretroviral Therapy Initiation in Hospitalized People With HIV:** This subsection discusses the benefits of initiating ART in people who receive an HIV diagnosis during hospitalization, while acknowledging that this may not be possible in all settings. Based on the discussion, the Panel recommends initiating ART during hospitalization whenever possible **(BIII).** The Panel notes that if ART is initiated before hospital discharge, clinicians should ensure sufficient ART supply is available until the outpatient clinic appointment.

The Elite HIV Controllers subsection was updated with two recommendations based on discussion of new observational studies regarding clinical outcomes of this population:

- The Panel strongly recommends ART for elite controllers with evidence of HIV-related complications, declining CD4 counts, intermittent detectable viral loads, or comorbidities (e.g., cardiovascular disease, cancer, hepatitis B virus/hepatitis C virus coinfection) or for those who are pregnant **(AIII).**
- The Panel also recommends initiation of ART for all other HIV elite controllers **(BII).**

Suboptimal CD4 Cell Recovery Despite Viral Suppression

This section—previously titled “Poor CD4 Cell Recovery and Persistent Inflammation Despite Viral Suppression”—has been renamed following the relocation of content on persistent inflammation to the new Immune Activation and Inflammation section. Additional updates to the Suboptimal CD4 Cell Recovery section include the following:

- Updated evidence on the clinical consequences of suboptimal CD4 recovery, including the increased risk of AIDS and non-AIDS events.
- The Panel notes that promptly initiating ART in people diagnosed early with HIV provides the best opportunity for maximal CD4 recovery.
- The Panel emphasizes that to date, there is no effective therapeutic intervention to improve CD4 count in people with suboptimal CD4 recovery.
- The Panel notes that efforts to decrease morbidity and mortality should focus on preventive care, addressing modifiable risk factors for chronic disease, and optimizing management of comorbidities.

Cost Considerations and Antiretroviral Therapy

Several new subsections have been added to the Cost Considerations and Antiretroviral Therapy section:

- Health Care Coverage to Maximize Access to Antiretroviral Therapy
- Medicare Beneficiaries With HIV
- Long-Acting Injectables

- 340B Drug Pricing Program, Prescription Drug Affordability, and Program Savings for People With HIV

Table 22a (Insurance and Health Program Prescription Drug Pricing and Access) and Table 22b (Monthly Average Prices of Commonly Used Antiretroviral Drugs) have been updated with the most recent information.

Other Updates

Minor updates have been made to the following sections of the guidelines:

- Antiretroviral Therapy to Prevent Sexual Transmission of HIV (Treatment as Prevention)
- Adverse Effects of Antiretroviral Medications
- Appendix A: Drug Characteristics Tables
- Appendix B: Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

PANEL ROSTER

Updated: September 25, 2025
Reviewed: September 25, 2025

Members and Consultants of the U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents

These guidelines were developed by the U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents (a working group of the National Institutes of Health Office of AIDS Research Advisory Council).

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FINANCIAL DISCLOSURE

Updated: September 25, 2025
Reviewed: September 25, 2025

U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents: Financial Disclosure for Companies Related to HIV Treatment or Diagnostics for the Period of April 1, 2024, to March 31, 2025

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Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents: Financial Disclosure for Companies Related to HIV Treatment or Diagnostics for the Period of April 1, 2024, to March 31, 2025

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Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents: Financial Disclosure for Companies Related to HIV Treatment or Diagnostics for the Period of April 1, 2024, to March 31, 2025

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Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents: Financial Disclosure for Companies Related to HIV Treatment or Diagnostics for the Period of April 1, 2024, to March 31, 2025

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Key: AC = Acting Co-chair; C = Co-chair; CC = Community Consultant; ES = Executive Secretary; M = Member; N/A = not applicable; PC = Pharmacology Consultant

INTRODUCTION

Updated: September 21, 2022
Reviewed: September 21, 2022

Antiretroviral therapy (ART) for the treatment of HIV infection has improved steadily since the advent of potent combination therapy in 1996. ART has dramatically reduced HIV-associated morbidity and mortality and has transformed HIV infection into a manageable chronic condition, with life expectancy approaching that for people without HIV.[1,2] ART is also highly effective at preventing sexual transmission of HIV in patients who have adequately suppressed viral loads.[3-5] Lack of viral load suppression is mostly due to undiagnosed HIV infection and failure to link or retain patients with HIV in care.

The U.S. Department of Health and Human Services (HHS) Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) is a working group of the Office of AIDS Research Advisory Council (OARAC). The Panel's primary goal is to provide HIV care practitioners with recommendations that are based on current knowledge of the antiretroviral (ARV) drugs that are used to treat adults and adolescents with HIV in the United States. The Panel reviews new evidence and updates recommendations when needed. These guidelines include recommendations on baseline laboratory evaluations, treatment goals, benefits of ART and considerations when initiating therapy, choice of the initial regimen for ART-naive people with HIV, ARV drugs or combinations to avoid, management of treatment failure, optimizing ARV regimens, management of adverse effects and drug interactions, and special ART-related considerations in specific populations. This Panel works closely with the HHS Panel on Antiretroviral Therapy and Medical Management of Children Living with HIV to provide recommendations for adolescents at different stages of growth and development. Recommendations for ARV regimens in these guidelines are most appropriate for postpubertal adolescents (i.e., those with sexual maturity ratings [SMR] of 4 and 5). Clinicians should follow recommendations in the Pediatric Antiretroviral Guidelines when initiating ART in adolescents with an SMR of 3 or lower. For recommendations related to pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) for people who do not have HIV, clinicians should consult recommendations from the Centers for Disease Control and Prevention.[6]

These guidelines represent current knowledge regarding the use of ARV drugs. Because the science of HIV evolves rapidly, the availability of new agents and new clinical data may change therapeutic options and preferences. Information included in these guidelines may not always be consistent with approved labeling for the specific drugs or indications, and the use of the terms "safe" and "effective" may not be synonymous with the U.S. Food and Drug Administration–defined legal standards for drug approval. The Panel frequently updates the guidelines (current and archived versions of the guidelines are available on the Clinical Info website). However, updates to the guidelines may not keep pace with the release of new data, and the guidelines cannot offer guidance on care for all patients. Patient management decisions should be based on clinical judgement and attention to unique patient circumstances.

The Panel recognizes the importance of clinical research in generating evidence to address unanswered questions related to the optimal safety and efficacy of ART and encourages both the development of protocols and patient participation in well-designed Institutional Review Board–approved clinical trials.

HIV Expertise in Clinical Care

Several studies have demonstrated that overall outcomes in patients with HIV are better when care is delivered by clinicians with HIV expertise (e.g., those who have cared for a large group of patients

with HIV),[7-11] reflecting the complexity of HIV transmission and its treatment. Appropriate training, continuing education, and clinical experience are all components of optimal care. Providers who do not have this requisite training and experience should consult HIV experts when needed.

Guidelines Development Process

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Goal of the guidelines	Provide guidance to HIV care practitioners on the optimal use of antiretroviral (ARV) agents for the treatment of HIV in adults and adolescents in the United States.
Panel members	The Panel is composed of approximately 50 voting members who have expertise in HIV care and research and includes at least one representative from each of the following U.S. Department of Health and Human Services (HHS) agencies: Centers for Disease Control and Prevention (CDC), U.S. Food and Drug Administration (FDA), Health Resource and Services Administration (HRSA), and National Institutes of Health (NIH). Approximately two-thirds of the Panel members are nongovernmental scientific members. The Panel also includes four to five community members with knowledge of HIV treatment and care. The U.S. government representatives are appointed by their respective agencies; other Panel members are selected after an open call for nominations. Each member serves on the Panel for a 4-year term, with an option for reappointment for an additional term. See the Panel Roster for a list of current Panel members.
Financial disclosure	All members of the Panel submit a written financial disclosure annually, reporting any association with manufacturers of ARV drugs or diagnostics used to manage HIV infection. The latest version of the Financial Disclosure list is available on the Clinical Info website.
Users of the guidelines	HIV treatment providers
Developer	Panel on Antiretroviral Guidelines for Adults and Adolescents—a working group of the Office of AIDS Research Advisory Council (OARAC)
Funding source	Office of AIDS Research, NIH
Evidence collection	The recommendations in the guidelines are based on studies published in peer-reviewed journals or data available in FDA drug labels. On some occasions, particularly when new information may affect patient safety, unpublished data presented at major conferences or prepared by the FDA and/or manufacturers as warnings to the public may be used as evidence to revise the guidelines.
Recommendation grading	As described in Table 2 below
Method of synthesizing data	Each section of the guidelines is assigned to a working group of Panel members with expertise in the section's area of interest. The working groups synthesize available data and propose recommendations to the Panel. The Panel discusses all proposals during monthly teleconferences. Recommendations endorsed by the Panel are included in the guidelines.

Table 1. Outline of the Guidelines Development Process

Topic	Comment
Other guidelines	These guidelines focus on antiretroviral therapy (ART) for adults and adolescents with HIV. For a more detailed discussion on the use of ART in children and prepubertal adolescents (those with sexual maturity ratings of 1 to 3), clinicians should refer to the Pediatric Antiretroviral Guidelines. These guidelines also include a brief discussion on the management of women of childbearing potential and pregnant women. For more details on the use of ARV drugs during pregnancy, see the Perinatal Guidelines.
Update plan	The Panel meets monthly by teleconference to review data that may warrant modification of the guidelines. Updates may be prompted by new drug approvals (or new indications, dosing formulations, or frequency of dosing), new safety or efficacy data, or other information relating to ARV drugs that may have an impact on the clinical care of people with HIV. In the event of new data of clinical importance, the Panel may post an interim announcement with recommendations on the Clinical Info website until the guidelines can be updated with the appropriate changes. Updated guidelines are available on the Clinical Info website.
Public comments	A 2-week public comment period follows the release of the updated guidelines on the Clinical Info website. The Panel reviews comments to determine whether additional revisions to the guidelines are indicated. The public also may submit comments to the Panel at any time at HIVinfo@NIH.gov.

Basis for Recommendations

Recommendations in these guidelines are based on scientific evidence and expert opinion. Each recommendation statement includes a letter **(A, B,** or **C)** that represents the strength of the recommendation and a Roman numeral **(I, II,** or **III)** that represents the quality of the evidence that supports the recommendation (see Table 2 below).

Table 2. Rating Scheme for Recommendations

Strength of Recommendation	Quality of Evidence for Recommendation
A: Strong recommendation for the statement **B:** Moderate recommendation for the statement **C:** Weak recommendation for the statement	**I:** One or more randomized trials with clinical outcomes and/or validated laboratory endpoints **II:** One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes **III:** Expert opinion

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BASELINE EVALUATION

Updated: September 21, 2022
Reviewed: September 21, 2022

Every patient with HIV entering into care should have a complete medical history, physical examination, and laboratory evaluation and should be counseled regarding the implications of HIV infection. The goals of this initial evaluation are to confirm the diagnosis of HIV infection, obtain appropriate baseline historical and laboratory data, ensure patient understanding about HIV infection and its transmission, and initiate care as recommended in the HIV Medicine Association of the Infectious Diseases Society of America's (HIVMA/IDSA) Primary Care Guidance for Persons with HIV[1] and the Adult and Adolescent Opportunistic Infections Guidelines.[2] The initial evaluation also should include discussion of the benefits of antiretroviral therapy (ART) for the patient's health and to prevent HIV transmission, as well as strategies to optimize care engagement and treatment adherence **(AIII).** Information obtained in this baseline evaluation then can be used to define treatment management goals and plans. The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating ART at the time of diagnosis (when possible) or as soon as possible afterward to increase the uptake of ART, decrease the time required to achieve linkage to care and virologic suppression, improve the rate of virologic suppression, and reduce HIV transmission **(AII).**

The following laboratory tests performed during initial patient visits can be used to stage HIV progression and to assist in the selection of antiretroviral (ARV) drug regimens:

- HIV antigen/antibody testing (if prior documentation is not available or if HIV RNA is below the assay's limit of detection) **(AI)**
- CD4 T lymphocyte (CD4) cell count **(AI)**
- Plasma HIV RNA (viral load) **(AI)**
- Complete blood count; chemistry profile, including glucose, blood urea nitrogen and creatinine, liver enzymes and bilirubin, urinalysis, and serologies for hepatitis A, B, and C viruses **(AIII)**
    - If random blood glucose level is abnormal, repeat fasting
- Serum lipids (if random levels are abnormal, fasting lipids should be obtained)
- HLA-B*5701 test (if abacavir is being considered) **(AI)**
- Genotypic drug-resistance testing **(AII).** Based on current rates of transmitted drug resistance to different ARV medications, standard genotypic drug-resistance testing in ARV-naive people should focus on testing for mutations in the reverse transcriptase (RT) and protease (PR) genes. If transmitted integrase strand transfer inhibitor (INSTI) resistance is a concern in people with newly diagnosed HIV or in people who acquired HIV after receipt of long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP), testing for mutations in the integrase gene also should be performed.
- For patients who have HIV RNA levels <1,000 copies/mL, viral amplification for drug-resistance testing should still be performed; however, it may not always be successful **(BII)** (see Drug-Resistance Testing).

In addition, other tests (including screening tests for sexually transmitted infections, opportunistic infections, and cancer) should be performed as recommended in the HIVMA/IDSA's Primary Care Guidance for Persons with HIV[1] and the Adult and Adolescent Opportunistic Infections Guidelines.[2]

Many clinics have adopted a rapid start policy to initiate ART on the day of HIV diagnosis in order to increase ART uptake and engagement in care and to accelerate the time to viral suppression. Rapid ART initiation also reduces the time during which people with newly diagnosed HIV can transmit HIV. Prior to ART initiation, HIV infection should be confirmed. HIV RNA and CD4 count also should be obtained, but results need not be available before starting ART. CD4 count will determine the need for prophylaxis for certain opportunistic infections.

- If available, results of safety testing—such as complete blood count, renal function tests, and liver enzymes—should be reviewed. If safety test results are not available, ART can still be started, but a clinician should review the results as soon as possible.
- Genotypic resistance testing for RT and PR (and INSTI resistance testing if patient has a history of CAB PrEP use or if INSTI transmission is suspected) should be obtained before ART initiation. It is not necessary to delay ART until results are available, but results should be reviewed as soon as possible in order to make adjustments to the regimen, if needed.
- Screening for viral hepatitis should be done before starting ART, and if ART initiation occurs before results are available, a regimen that has activity against hepatitis B virus should be selected.
- In patients who do not have reliable methods of contact, rapid ART may be initiated, with a plan for a return clinic visit soon after ART initiation to review test results.
- Screening for sexually transmitted infections should, ideally, occur at the initial visit, but results do not need to be available before starting ART.

For previously treated patients who present for an initial evaluation with a new health care provider, it is critical to obtain a complete ARV history (including drug-resistance testing results, if available), preferably through the review of past medical records. A complete immunization history (including for SARS-CoV-2) also should be obtained. Newly diagnosed patients also should be asked about any prior use of ARV agents for prevention of HIV infection.

People with HIV often must cope with many social, psychiatric, and medical issues that are best addressed through a patient-centered, multidisciplinary approach. The baseline evaluation should include consideration of the patient's readiness for ART, including an assessment of substance use (including tobacco use), social support, mental health, medical comorbidities, economic factors (e.g., unstable housing, food instability), medical insurance status and adequacy of coverage, and other factors that are known to impair adherence to ART and increase the risk of HIV transmission. Once evaluated, these factors should be managed accordingly. The baseline evaluation also should include a discussion of risk reduction and disclosure to sexual and/or needle-sharing partners, especially with untreated patients who are still at high risk of HIV transmission. People with HIV should be informed that maintaining a plasma HIV RNA of <200 copies/mL, including any measurable value below this threshold, with ART prevents sexual transmission of HIV to their partners **(AII).** Patients may recognize this concept as Undetectable = Untransmittable or U=U.

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LABORATORY TESTING

Laboratory Testing for Initial Assessment and Monitoring of People With HIV

Updated: September 25, 2025
Reviewed: September 25, 2025

Several laboratory tests are important for initial evaluation of people with HIV upon entry into care. Some tests should be performed before and after initiation or modification of antiretroviral therapy (ART) to assess the virologic and immunologic efficacy of ART and to monitor for laboratory abnormalities that may be associated with antiretroviral (ARV) drugs.

Two surrogate markers have been used to monitor people with HIV: (1) plasma HIV RNA (viral load) to assess the level of HIV viremia and (2) CD4 T lymphocyte (CD4) cell count to assess immune function. Standard (reverse transcriptase and protease) genotypic drug-resistance testing should be used to guide selection of an ARV regimen; if integrase strand transfer inhibitor (INSTI) resistance is a concern due to potential transmitted resistance or previous use of an INSTI for pre-exposure prophylaxis (e.g., long-acting cabotegravir), post-exposure prophylaxis, or treatment, providers should ensure that genotypic resistance testing also includes the integrase gene (see Drug-Resistance Testing). For guidance on the choice of ARV regimens before drug-resistance testing results become available, clinicians should consult the What to Start and Early (Acute or Recent) HIV Infection sections. A viral tropism assay should be performed before initiation of a CCR5 antagonist or at the time of virologic failure if a person is receiving a CCR5 antagonist. HLA-B*5701 testing should be performed before initiation of abacavir (ABC) to reduce the risk of hypersensitivity reaction, and HLA-B*5701-positive people should not be prescribed ABC. People should be screened for hepatitis B virus (HBV) and hepatitis C virus infections before initiating ART and, if indicated, periodically after ART initiation, because treatment of these coinfections may affect the choice of ART and likelihood of drug-induced hepatotoxicity. Before initiating nucleoside reverse transcriptase inhibitor (NRTI)–sparing or NRTI-limited ARV regimens, HBV serology testing should be performed in people who are not known to have chronic HBV (see Hepatitis B Virus/HIV Coinfection). The rationale for and utility of some of these laboratory tests are discussed in the corresponding sections of the guidelines.

Currently available newer ARVs are generally easy to take and typically do not cause significant laboratory abnormalities. Most people with HIV achieve and maintain viral suppression and have improvement in CD4 count within 1 year after starting ART. Table 3 provides general guidance on the frequency of laboratory monitoring before initiation of and throughout treatment with ART. However, more frequent monitoring of selected tests may be needed as clinically indicated, based on issues such as responses to therapy, underlying medical conditions, drug-related adverse effects, engagement in care, and adherence to therapy. ART is recommended for all people with HIV **(AI);** Table 4 provides guidance for laboratory monitoring in the rare occasions when ART initiation is deferred.

Table 3. Laboratory Testing Schedule Before and After Antiretroviral Therapy Initiation[a]

This table provides general guidance for laboratory monitoring for people with HIV before and after antiretroviral therapy (ART) initiation. Clinicians should use their clinical judgment to determine the monitoring frequency for an individual person based on clinical needs. This schedule is not intended to be a guide on how often people with HIV should undergo clinical evaluation, as some individuals may need to be seen more frequently to accomplish other aspects of clinical care. Please refer to Table 4 for laboratory monitoring guidance if ART initiation is deferred.

Laboratory Test	Timepoint or Frequency of Testing							
	Entry Into Care	ART Initiation[b] or Modification	After ART Initiation or Modification	Every 3–4 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated
HIV Antigen/ Antibody Test	✓ If HIV diagnosis not confirmed							
HIV Viral Load	✓	✓	✓[c] At 4–8 weeks	✓[d]	✓[d]		✓	✓
CD4 Count	✓	✓	✓ 3 months (after ART initiation only)	✓[e] If CD4 count is <300 cells/mm^3	✓ During the First 1–2 Years on ART and With Viral Suppression, if CD4 Count Is ≥300 Cells/mm^3: • Every 6 months After 1–2 Years on ART With Consistently Suppressed Viral Load and CD4 Count ≥300 Cells/mm^3: • Optional unless clinically indicated		✓ Monitor CD4 count every 3–6 months.	✓

Table 3. Laboratory Testing Schedule Before and After Antiretroviral Therapy Initiation

Laboratory Test	Timepoint or Frequency of Testing							
	Entry Into Care	ART Initiation[b] or Modification	After ART Initiation or Modification	Every 3–4 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated
Genotypic Resistance Testing (PR/RT Genes)[f]	✓	✓					✓	✓
Genotypic Resistance Testing (Integrase Genes)[f]	✓ If transmitted INSTI resistance is suspected or if there is a history of CAB-LA use for PrEP or INSTI use for PEP	✓ If transmitted INSTI resistance is suspected or if there is a history of INSTI use					✓ If there is a history of INSTI use for treatment or prevention	✓
Tropism Testing		✓ If considering a CCR5 antagonist					✓ If considering a CCR5 antagonist, or upon virologic failure on a CCR5 antagonist	✓

Table 3. Laboratory Testing Schedule Before and After Antiretroviral Therapy Initiation

Laboratory Test	Timepoint or Frequency of Testing							
	Entry Into Care	ART Initiation[b] or Modification	After ART Initiation or Modification	Every 3–4 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated
HLA-B*5701 Testing		✓ If considering ABC (perform once; keep result in health record)						
Hepatitis B Serology (HBsAb, HBsAg, HBcAb total)[g,h,i] Also see Hepatitis B Virus/HIV Coinfection	✓	✓ In people not immune to HBV, repeat testing if switching to a regimen that does not contain TAF or TDF.						✓ Before starting HCV DAA In people not immune to HBV and at high risk for HBV,[j] periodic testing may be considered.
Hepatitis C Screening (HCV antibody or, if indicated, HCV RNA)[k]	✓					✓ Repeat HCV screening for at-risk people.[j]		✓

Table 3. Laboratory Testing Schedule Before and After Antiretroviral Therapy Initiation

Laboratory Test	Timepoint or Frequency of Testing							
	Entry Into Care	ART Initiation[b] or Modification	After ART Initiation or Modification	Every 3–4 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated
Basic Metabolic Panel[l,m]	✓	✓	✓ At 4–8 weeks For people with preexisting conditions or at risk of laboratory changes after ART initiation		✓ Every 6–12 months			✓
ALT, AST, Total Bilirubin	✓	✓	✓ At 4–8 weeks For people with preexisting conditions, at risk for laboratory changes after ART initiation, or with HBV coinfection		✓ Every 6–12 months			✓
CBC With Differential[n]	✓	✓		✓ When monitoring CD4 count (if required by lab)	✓ When monitoring CD4 count (if required by lab)	✓ When no longer monitoring CD4 count		✓

Table 3. Laboratory Testing Schedule Before and After Antiretroviral Therapy Initiation

Laboratory Test	Timepoint or Frequency of Testing							
	Entry Into Care	ART Initiation[b] or Modification	After ART Initiation or Modification	Every 3–4 Months	Every 6 Months	Every 12 Months	Treatment Failure	Clinically Indicated
Lipid Profile[o]	✓	✓	At 3–6 months once viral suppression is reached			✓ If aged ≥40 years or on a statin (Every 1–3 years if aged <40 years **and** not on a statin)		✓ If there are changes in CV risk factors[p]
Random or Fasting Glucose[q]	✓	✓						✓
Urinalysis[m,r]	✓							✓ e.g., in people with CKD or DM
Pregnancy Test[s]	✓	✓						✓

[a] This table pertains to laboratory tests done to select an ARV regimen and monitor for treatment responses or ART toxicities. Please refer to the HIV Medicine Association of the Infectious Diseases Society of America's (HIVMA/IDSA) Primary Care Guidance for Providers Who Care for Persons With HIV for other laboratory tests generally recommended for primary health care maintenance of HIV people.[1]

[b] If ART is initiated soon after HIV diagnosis and entry into care, repeat baseline laboratory testing is not necessary.

[c] If HIV RNA is detectable at 4–8 weeks, repeat testing every 4–8 weeks until viral load is suppressed to <50 copies/mL. Thereafter, repeat testing every 3–6 months.

[d] For people on ART, viral load is typically measured every 3–6 months. More frequent monitoring may be considered in individuals having difficulties with ART adherence or at risk for nonadherence. However, for adherent people with consistently suppressed viral load and stable immunologic status for more than 1 year, monitoring can be extended to 6-month intervals.

[e] After 1–2 years of consistently suppressed HIV RNA, less frequent monitoring (e.g., every 6 months) may be considered.

[f] Standard genotypic drug-resistance testing in ARV-naive persons should focus on testing for mutations in the PR and RT genes. If transmitted INSTI resistance is a concern, or if a person may have a history of INSTI use as PrEP, PEP, or treatment, or a person presents with viremia while on an INSTI, providers also should

Table 3. Laboratory Testing Schedule Before and After Antiretroviral Therapy Initiation

test for resistance mutations in the integrase gene. In people who are ARV-naive and who do not immediately begin ART, repeat testing before initiation of ART is optional if drug-resistance testing was performed at entry into care. In people with virologic suppression who are switching therapy because of toxicity or for convenience, viral amplification will not be possible; see the Drug-Resistance Testing section for a discussion of the potential limitations and benefits of proviral DNA assays in this situation. Results from prior drug-resistance testing should be used in constructing a new regimen.

[g] If a person has HBV infection (as determined by a positive HBsAg or HBV DNA test result), TDF or TAF plus either FTC or 3TC should be used as part of the ARV regimen to treat both HBV and HIV infections (see the Hepatitis B Virus/HIV Coinfection section).

[h] If HBsAg, HBsAb, and HBcAb test results are negative, HBV vaccine series should be administered. Refer to the HIVMA/IDSA's Primary Care Guidance for Persons With HIV and the Adult and Adolescent Opportunistic Infection Guidelines for detailed recommendations.[1,2]

[i] Most people with isolated HBcAb have resolved HBV infection with loss of HBsAb. Consider performing an HBV viral load test for confirmation. If the HBV viral load test is positive, the person may be acutely infected (and will usually display other signs of acute hepatitis) or chronically infected. If the test is negative, the person should be vaccinated. Refer to the HIVMA/IDSA's Primary Care Guidance for Persons With HIV and the Adult and Adolescent Opportunistic Infection Guidelines for more detailed recommendations.[2]

[j] Injection drug users, people with a history of incarceration, men with HIV who have unprotected sex with men, and people with percutaneous/parenteral exposure to blood in unregulated settings are at risk of HBV or HCV infection.

[k] The HCV antibody test may not be adequate for screening in the setting of recent HCV infection (acquisition within the past 6 months) or advanced immunodeficiency (CD4 count <100 cells/mm^3). HCV RNA screening is indicated in persons who have been successfully treated for HCV or who spontaneously cleared prior infection. HCV antibody-negative people with elevated ALT may need HCV RNA testing.

[l] Serum Na, K, HCO_3, Cl, BUN, creatinine, glucose, and Cr-based eGFR. Serum P should be monitored in people with CKD who are on TDF-containing regimens.[3]

[m] Consult the HIVMA/IDSA's Clinical Practice Guideline for the Management of Chronic Kidney Disease in People Infected With HIV for recommendations on managing people with renal disease.[3] More frequent monitoring may be indicated for people with evidence of kidney disease (e.g., proteinuria, decreased glomerular dysfunction) or increased risk of renal insufficiency (e.g., people with diabetes, hypertension).

[n] CBC with differential should be done when a CD4 count is performed. When CD4 count is no longer being monitored, the recommended frequency of CBC with differential is once a year. More frequent monitoring may be indicated for people receiving medications that potentially cause cytopenia (e.g., TMP-SMX).

[o] If random lipids are abnormal, fasting lipids should be obtained. Consult the American College of Cardiology/American Heart Association's 2018 Guideline on the Management of Blood Cholesterol for diagnosis and management of people with dyslipidemia.[4]

[p] Changes in CV risk factors such as new diagnosis of hypertension, weight gain, or new medications (including ART) that may raise lipid levels or overall CV risk.

[q] If random glucose is abnormal, fasting glucose should be obtained. HbA1C is no longer recommended for diagnosis of diabetes in people with HIV on ART (see the American Diabetes Association Guidelines).[5]

[r] Urine glucose and protein should be assessed before initiating TAF- or TDF-containing regimens and monitored during treatment with these regimens.

[s] For women of childbearing potential.

Key: 3TC = lamivudine; ABC = abacavir; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; BUN = blood urea nitrogen; CAB-LA = cabotegravir long-acting; CBC = complete blood count; CD4 = CD4 T lymphocyte; CKD = chronic kidney disease; Cl = chloride; Cr = creatinine; CV = cardiovascular; DAA = direct-acting antiviral; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; FTC = emtricitabine; HbA1C = hemoglobin A1c; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCO_3 = bicarbonate; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; K = potassium; Na = sodium; P = phosphorus; PEP = post-exposure prophylaxis; PR = protease; PrEP = pre-exposure prophylaxis; RT = reverse transcriptase; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TMP-SMX = trimethoprim-sulfamethoxazole

Table 4. Laboratory Monitoring If ART Is Deferred

Antiretroviral therapy (ART) is recommended for all people with HIV **(AI).** People with HIV should be advised to begin ART as soon as feasible to reduce morbidity and mortality and to prevent transmission of HIV to others. This table provides guidance for laboratory monitoring in the rare occasions when ART initiation is deferred.

Laboratory Test	Initial Assessment	Monitoring Frequency If ART Is Deferred	Comments
CD4 Count	✓	Every 3–6 months	To assess for urgency of ART initiation and the need for OI prophylaxis
HIV Viral Load	✓	Every 3–6 months	
Genotypic Resistance Testing (PR/RT +/- integrase gene) See Drug Resistance Testing for more information.	✓		Repeat genotypic resistance testing at the time of ART initiation is optional.
Hepatitis B Serology (HBsAb, HBsAg, HBcAb) See Hepatitis B in the Adult OI Guidelines for more detailed guidance.	✓	Clinically indicated	Before starting HCV DAA If HBsAg Positive: • ART with HBV-active drugs that include TAF or TDF should be initiated. If Not Immune at Baseline: • Repeat after vaccination or before starting an NRTI-sparing (or limited) ART regimen.
Hepatitis C Screening (HCV antibody, or, if indicated, HCV RNA)	✓	Every 12 months for at-risk people, or if clinically indicated	
Basic Metabolic Panel	✓	Every 6–12 months or if clinically indicated	
ALT, AST, Total Bilirubin	✓	Every 6–12 months or if clinically indicated	
CBC With Differential	✓	When monitoring CD4 count or if clinically indicated	
Pregnancy Test (when pregnancy is possible)	✓	If clinically indicated	ART should be initiated as soon as possible after confirming pregnancy to prevent perinatal HIV transmission.

Key: ALT = alanine aminotransferase; ART = antiretroviral therapy; AST = aspartate aminotransferase; CBC = complete blood count; CD4 = CD4 T lymphocyte; DAA = direct-acting antiviral; HBcAb = hepatitis B core antibody; HBsAb = hepatitis B surface antibody; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HCV = hepatitis C virus; NRTI = nucleoside reverse transcriptase inhibitor; OI = opportunistic infection; PR = protease; RT = reverse transcriptase; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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Plasma HIV-1 RNA (Viral Load) and CD4 Count Monitoring

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HIV RNA (viral load) and CD4 T lymphocyte (CD4) cell count are the two surrogate markers of antiretroviral therapy (ART) responses and HIV disease progression that have been used for decades to manage and monitor HIV infection.

Viral load is a marker of response to ART. A person's pre-ART viral load level and the magnitude of viral load decline after initiation of ART provide prognostic information about the probability of disease progression.[1-4] The key goal of ART is to achieve and maintain durable viral suppression. Thus, an important use of the viral load is to monitor the effectiveness of therapy after initiation of ART. The use of viral load testing to confirm the attainment and maintenance of viral suppression is instrumental in the operationalization of Undetectable = Untransmittable (or U=U)/Treatment as Prevention (see the Antiretroviral Therapy to Prevent Sexual Transmission of HIV [Treatment as Prevention] section).

It should be noted that commercially available HIV-1 RNA assays do not detect HIV-2 viral load. For further discussion on HIV-2 RNA monitoring in people with HIV-1/HIV-2 coinfection or HIV-2 mono-infection, see the HIV-2 Infection section.

CD4 count provides information on the overall immune function of a person with HIV. Measurement of CD4 count at entry into care and **before** initiation of ART is particularly useful in establishing the need to initiate opportunistic infection (OI) prophylaxis. Monitoring **after** initiation of ART is important for assessing immunologic response and establishing the need to discontinue OI prophylaxis.

The management of people with HIV has changed substantially with the availability of newer, more potent, easier-to-use, and less toxic antiretroviral (ARV) drugs. ART is recommended for all people with HIV regardless of their viral load or CD4 count **(AI)** (see the Initiation of Antiretroviral Therapy section). Because almost all people with HIV in care now receive ART and achieve good immunologic responses, the rationale for frequent CD4 count monitoring is weaker. The roles and usefulness of these two tests in clinical practice are discussed below.

Plasma HIV-1 RNA (Viral Load) Monitoring

Viral load is the most important indicator of initial and sustained response to ART and should be measured in all people with HIV at entry into care **(AI),** at initiation of therapy (if treatment is delayed) **(AI),** and on a regular basis thereafter. For those people in whom therapy is delayed, repeat viral load testing is recommended approximately every 3 to 6 months **(BIII),** aligning with CD4 count testing. Repeating viral load testing at these intervals provides an opportunity for discussions about the benefits of ART, both for the treatment of HIV and prevention of HIV transmission. Pre-treatment viral load level is also an important factor in the selection of an initial ARV regimen because some ARV drugs or regimens have been associated with poorer responses in people with high baseline viral load (see the What to Start section).

Several systematic reviews of data from clinical trials involving thousands of participants in the early era of potent ART have established that decreases in viral load following initiation of ART are associated with reduced risk of progression to AIDS or death.[1-4] Thus, viral load testing is an established surrogate marker for treatment response. The minimal change in viral load considered to be statistically significant (2 standard deviations) is a threefold change (equivalent to a 0.5 $\log_{10}$ copies/mL change). Optimal viral suppression is defined as a confirmed HIV RNA level below the lower limit of detection of available assays (generally <20 copies/mL, depending on the assay used). After virologic suppression, an isolated detectable HIV RNA level that is followed by a return to virologic suppression, known as a "blip," may occur in successfully treated people and is not usually predictive of virologic failure.[5] Furthermore, the data on

the association between persistently low-level but quantifiable viremia (HIV RNA <200 copies/mL) and virologic failure is conflicting. Several studies showed an increased risk of subsequent failure, drug resistance, morbidity, and mortality at this level of viremia[6-12]; however, the association was not observed in other studies.[10,11,13-17] These guidelines now define virologic failure as the inability to achieve or maintain suppression of viral replication to HIV RNA levels of <200 copies/mL—a threshold that eliminates most cases of apparent viremia caused by viral load blips or assay variability[18] (see the Virologic Failure section).

Individuals who are adherent to their ARV regimens and do not harbor resistance mutations to the component drugs can generally achieve viral suppression 8 to 12 weeks after ART initiation or after modification due to virologic failure; rarely, it may take longer in some people. Recommendations on the frequency of viral load monitoring are summarized below:

- **After initiation of ART:** Plasma viral load should be measured when ART is initiated **(AI)** and within 4 to 8 weeks after treatment initiation **(AIII).** The purpose of these measurements is to confirm an adequate virologic response to ART, indicating appropriate regimen selection and individual adherence to therapy. Repeat viral load measurement should be performed every 4 to 8 weeks until the level falls below the assay's limit of detection **(BIII).**
- **In people with viral suppression, with ART modification because of regimen simplification or drug toxicity:** Viral load measurement should be performed within 4 to 8 weeks after changing therapy **(AIII).** The purpose of viral load monitoring at this point is to confirm the effectiveness of the new regimen.
- **In people on a stable, suppressive ARV regimen:** Viral load measurement should be repeated every 3 to 4 months **(AIII)** or as clinically indicated to confirm continuous viral suppression. Clinicians may extend the interval to 6 months for adherent people whose viral load has been suppressed for more than a year, whose clinical and immunologic status is stable, and who are not at risk for inadequate adherence **(AIII).**
- **In people with virologic failure who require a change in ARV regimen:** Plasma viral load should be measured before ART change and within 4 to 8 weeks after treatment modification **(AIII).** The purpose of the measurements is to confirm an adequate virologic response to the new regimen. Repeat viral load measurement should be performed every 4 to 8 weeks until the level falls below the assay's limit of detection **(BIII).** If viral suppression is not possible, repeat viral load measurement every 3 months or more frequently if indicated **(AIII).**
- **In people with suboptimal response:** The frequency of viral load monitoring will depend on clinical circumstances, such as adherence and availability of further treatment options. In addition to viral load monitoring, several other factors—such as individual adherence to prescribed medications, suboptimal drug exposure, or drug interactions—should be assessed. People who fail to achieve viral suppression should undergo drug-resistance testing to aid in the selection of an alternative ARV regimen (see the Drug-Resistance Testing and Virologic Failure sections).

CD4 Count Monitoring

The CD4 count is the most important laboratory indicator of immune function in people with HIV. Low pre-treatment CD4 count is the strongest predictor of disease progression and mortality according to findings from clinical trials and cohort studies.[4,19] CD4 counts are highly variable; a significant change (2 standard deviations) between two tests is approximately a 30% change in the absolute count, or an increase or decrease in CD4 percentage by three percentage points. Monitoring of lymphocyte subsets other than CD4 (e.g., CD8, CD19) **is not recommended (BIII)** because it has not been proven to be clinically useful and is more expensive than monitoring CD4 count alone.

Use of CD4 Count for Initial Assessment

CD4 count should be measured in all people with HIV at entry into care **(AI).** It is the key factor in determining the need to initiate OI prophylaxis (see the Adult and Adolescent Opportunistic Infections Guidelines)[20] and the urgency to initiate ART **(AI),** even though ART is recommended for all people with HIV, regardless of CD4 count **(AI)** (see the Initiation of Antiretroviral Therapy section). Although most OIs occur in people with CD4 counts <200 cells/mm^3, some OIs can occur in people with higher CD4 counts.[21]

Use of CD4 Count for Monitoring Response to ART

The CD4 count is used to assess a person's immunologic response to ART. It is also used to determine whether prophylaxis for OIs can be discontinued (see the Adult and Adolescent Opportunistic Infections Guidelines).[20] For most people, an adequate response is defined as an increase in CD4 count in the range of 50 cells/mm^3 to 150 cells/mm^3 in the first year of ART, generally with an accelerated response in the first 3 months of treatment. Subsequent increases average approximately 50 cells/mm^3 to 100 cells/mm^3 per year until a steady state level is reached.[22] People who initiate therapy with a low CD4 count[23,24] or at an older age[25] may have a blunted increase in their counts despite virologic suppression.

Frequency of CD4 Count Monitoring

ART is recommended for all people with HIV. For people with HIV and pre-treatment CD4 count <300 cells/mm^3, repeating CD4 count 3 months after ART initiation will provide information regarding the magnitude of immune reconstitution **(AIII).** This repeat measurement is most important in people who initiate ART with more advanced disease and require OI prophylaxis or treatment. In these individuals, the magnitude and duration of CD4 count increase can be used to determine whether to discontinue OI prophylaxis and/or treatment as recommended in the Adult and Adolescent Opportunistic Infections Guidelines. After ART initiation, CD4 count should be repeated every 3 to 4 months for the first 1 to 2 years of suppressive ART for those with CD4 counts <300 cells/mm^3 **(BII)** and every 6 months if CD4 count is ≥300 cells/mm^3 with viral suppression **(BIII).** After 1 to 2 years of suppressive ART, reducing CD4 count monitoring to every 6 months may be considered for some people whose CD4 counts remain at <300 cells/mm^3 **(BIII);** for those with CD4 counts ≥300 cells/mm^3, CD4 count monitoring is optional unless clinically indicated **(BIII).**

The CD4 count response to ART varies widely, but a poor CD4 response in a person with viral suppression is rarely an indication for modifying an ARV regimen (see the Suboptimal CD4 Recovery section). In people with consistently suppressed viral loads who have already experienced ART-related immune reconstitution (i.e., CD4 count ≥300 cells/mm^3), the CD4 count provides limited information. Frequent testing is unnecessary because the results rarely lead to a change in clinical management. One retrospective study found that declines in CD4 count to <200 cells/mm^3 are rare in people with viral suppression and CD4 counts >300 cells/mm^3.[26] Similarly, the ARTEMIS trial found that CD4 count monitoring had no clinical benefit in people who had suppressed viral loads and CD4 counts >200 cells/mm^3 after 48 weeks of therapy.[27] Furthermore, the risk of *Pneumocystis jirovecii* pneumonia is extremely low in people on suppressive ART who have CD4 counts between 100 cells/mm^3 and 200 cells/mm^3.[28] Although uncommon, CD4 count declines can occur in a small percentage of virologically suppressed people and may be associated with adverse clinical outcomes, such as cardiovascular disease, malignancy, and death.[29,30]

An analysis of costs associated with CD4 count monitoring in the United States estimated that reducing CD4 count monitoring in treated people from every 6 months to every 12 months could result in annual savings of approximately $10 million.[31]

CD4 count should be monitored more frequently, as clinically indicated, when there are changes in a person's clinical status that may decrease CD4 count and thus prompt OI prophylaxis. Examples of such changes include the appearance of new HIV-associated clinical symptoms or initiation of treatment known

to reduce CD4 count (e.g., chronic corticosteroids, antineoplastic agents) **(AIII).** In people who do not maintain viral suppression while on ART, CD4 count monitoring should be done every 3 to 6 months **(AIII).**

In people who remain untreated for whatever reason, CD4 count should be monitored every 3 to 6 months to monitor for disease progression and assess the urgency of ART initiation and the need for OI prophylaxis **(AIII).**

Factors That Affect Absolute CD4 Count

The absolute CD4 count is a calculated value based on the total white blood cell (WBC) count and the percentages of total and CD4 T lymphocytes. This absolute number may fluctuate in individuals or may be influenced by factors that may affect the total WBC count and lymphocyte percentages, such as use of bone marrow–suppressive medications, chronic corticosteroids, or the presence of acute infections. Splenectomy[32,33] or coinfection with human T-lymphotropic virus type I[34] may cause misleadingly elevated CD4 counts. In all these settings, CD4 percentage remains stable and may be a more appropriate parameter to assess a person's immune function.[35]

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Drug-Resistance Testing

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Panel's Recommendations

For Initial Treatment of HIV

- HIV drug-resistance testing is recommended at entry into care for people with HIV to guide the selection of the initial antiretroviral (ARV) regimen **(AII).** If antiretroviral therapy (ART) is deferred, repeat testing may be considered at the time of ART initiation **(CIII).**
- The Panel on Antiretroviral Guidelines for Adults and Adolescents recommends genotypic, rather than phenotypic, testing as the preferred resistance testing to guide therapy in ARV-naive people **(AIII).**
- In people with early (acute and recent) HIV infection, in pregnant women with HIV, or in people who will initiate ART on the day of or soon after HIV diagnosis, ART initiation should not be delayed while awaiting resistance testing results; the regimen can be modified once results are reported **(AIII).**
- Standard genotypic drug-resistance testing in ARV-naive people involves testing for mutations in the reverse transcriptase and protease genes. If transmitted integrase strand transfer inhibitor (INSTI) resistance is suspected, if the person has ever used long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis, or if the person has ever received an INSTI-based regimen for post-exposure prophylaxis, providers should ensure that genotypic resistance testing also includes the integrase gene **(AIII).**

For Antiretroviral Therapy–Experienced People

- HIV drug-resistance testing should be performed to assist the selection of active drugs when changing ARV regimens in—
  - People with virologic failure and HIV RNA levels >200 copies/mL (**AI** for >1,000 copies/mL**, AIII** for 501–1,000 copies/mL**, CIII** for confirmed HIV RNA 201–500 copies/mL). For people with confirmed HIV RNA levels >200 copies/mL but <500 copies/mL, drug-resistance testing may be unsuccessful but should still be considered.
  - People with suboptimal viral load reduction **(AII).**
- Reverse transcriptase and protease genotypic resistance testing should be performed on people with virologic failure. Integrase resistance testing should be performed on individuals who have virologic failure and have a history of prior use of an INSTI (for prevention or treatment) or are currently receiving an INSTI-based regimen **(AII).**
- For people taking a non–long-acting ARV regimen, drug-resistance testing in the setting of virologic failure should be performed while the person is still taking their ARV regimen or, if that is not possible, within 4 weeks after discontinuing their ARV regimen **(AII).** If more than 4 weeks have elapsed since the non–long-acting agents have been discontinued, resistance testing may still provide useful information to guide therapy; however, it is important to recognize that previously selected resistance mutations can be missed due to lack of drug-selective pressure **(CIII).**
- For people who previously received long-acting cabotegravir and rilpivirine (LA CAB/RPV) and present with virologic failure, resistance testing (including INSTI genotypic testing) should be performed regardless of the time since the last dose of LA CAB/RPV **(AIII).**
- Genotypic testing is preferred over phenotypic-resistance testing to guide therapy in people with suboptimal virologic response or virologic failure while on first- or second-line regimens and in people in whom resistance mutation patterns are known or not expected to be complex **(AII).**
- The addition of phenotypic to genotypic resistance testing is recommended for people with known or suspected complex drug-resistance mutation patterns **(BIII).**

- All prior and current drug-resistance test results, when available, should be reviewed and considered when constructing a new regimen **(AIII).**
- When the use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed **(AI).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Genotypic and Phenotypic-Resistance Assays

Genotypic and phenotypic-resistance assays are used to assess viral strains and select treatment strategies. These assays provide information on resistance to nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), and integrase strand transfer inhibitors (INSTIs). In some circumstances, INSTI-resistance tests may need to be ordered separately, and clinicians should check this with the testing laboratory. INSTI-resistance testing is particularly important in people who experience virologic failure while taking an INSTI-containing regimen or in those with prior use of injectable long-acting cabotegravir (CAB-LA) (either for treatment of HIV or as pre-exposure prophylaxis [PrEP]). Testing for fusion inhibitor resistance can be ordered separately when needed. There is currently no commercially available resistance test for the CD4 T lymphocyte post-attachment inhibitor ibalizumab, the gp120 attachment inhibitor fostemsavir, or the capsid inhibitor lenacapavir. For a description of co-receptor tropism testing, see Co-Receptor Tropism Assays.

Genotypic Assays

Genotypic assays detect drug-resistance mutations in relevant viral genes; in general, these assays require a plasma viral load of at least 500 to 1,000 copies/mL. Most genotypic assays involve conventional Sanger sequencing of the reverse transcriptase (RT), protease (PR), and integrase (IN) genes of circulating RNA in plasma to detect mutations that are known to confer drug resistance. A genotypic assay that assesses mutations in the gp41 (envelope) gene associated with resistance to the fusion inhibitor enfuvirtide is also commercially available. Genotypic assays can be performed rapidly, and results are available within 1 to 2 weeks of sample collection. Interpreting these test results requires knowledge of the mutations selected by different antiretroviral (ARV) drugs and of the potential for cross-resistance to other drugs conferred by certain mutations. The International AIDS Society–USA maintains an updated list of significant resistance-associated mutations in the RT, PR, IN, and envelope genes. The Stanford University HIV Drug Resistance Database also provides helpful guidance for interpreting genotypic resistance test results.[1] Various additional tools are available to assist providers in interpreting genotypic test results.[2-5] Clinical trials have demonstrated that consulting with specialists in HIV drug resistance improves virologic outcomes.[6] Clinicians are thus encouraged to consult a specialist to interpret genotypic test results and design new, optimal ARV regimens.

A next-generation sequencing genotypic resistance assay that analyzes HIV-1 proviral DNA in host cells is now commercially available. This test aims to detect archived resistance mutations in people with HIV RNA below the limit of detection or with low-level viremia.

Phenotypic Assays

Phenotypic assays measure the ability of a virus to grow in different concentrations of ARV drugs. RT, PR, and, more recently, IN and envelope gene sequences derived from a person's plasma HIV RNA are inserted into the backbone of a laboratory clone of HIV or used to generate pseudotyped

viruses that express that person's HIV genes of interest. Replication of these viruses at different drug concentrations is monitored by expression of a reporter gene and is compared with the replication of a reference HIV strain. The drug concentration that inhibits viral replication by 50% (i.e., the median inhibitory concentration [IC_{50}]) is calculated, and the ratio of the IC_{50} of test and reference viruses is reported as the fold increase in IC_{50} (i.e., fold resistance).

Automated phenotypic assays that can produce results in 2 to 3 weeks are commercially available, but they cost more to perform than genotypic assays. In addition, interpreting phenotypic assay results can be complicated by incomplete information regarding the specific resistance level (i.e., fold increase in IC_{50}) associated with drug failure, although clinically significant fold increase cutoffs have been described for some drugs.[7-11] Again, consulting with a specialist to interpret test results can be helpful.

Limitations of Genotypic and Phenotypic Assays

Limitations of both genotypic and phenotypic assays include lack of uniform quality assurance testing for all available assays, relatively high cost, and insensitivity to minor viral species. Drug-resistant viruses that constitute <10% to 20% of the circulating virus population will probably not be detected by commercially available assays. This limitation is important to note because a wild-type virus often re-emerges as the predominant population in the plasma after discontinuation of drugs that exert selective pressure on drug-resistant populations. As a consequence, the proportion of virus with resistance mutations can decrease to below the 10% to 20% threshold.[12-14] In the case of some oral ARV drugs, this reversion to predominantly wild-type virus can occur in the first 4 to 6 weeks after the drugs are discontinued. However, with injectable agents that have prolonged half-lives (e.g., long-acting cabotegravir and rilpivirine [LA CAB/RPV]), drug pressure may persist for prolonged periods. Prospective studies have demonstrated that despite plasma reversion, reinitiating the same ARV agents (or those with similar resistance pathways) often leads to early treatment failure; the virus responsible for this failure is derived from a previously archived resistant virus.[15] Therefore, for people taking a non–long-acting ARV regimen, drug-resistance testing in the setting of virologic failure should be performed while the person is still taking their ARV regimen or, if that is not possible, within 4 weeks after discontinuing their ARV regimen **(AII).** If more than 4 weeks have elapsed since the non–long-acting agents were discontinued, resistance testing may still provide useful information to guide therapy; however, it is important to recognize that previously selected resistance mutations can be missed due to lack of drug-selective pressure **(CIII).** Given the long half-lives of the long-acting injectable ARV drugs, resistance testing (including testing for resistance to INSTIs) should be performed in all people who have experienced virologic failure on a regimen of LA CAB/RPV or acquired HIV after receiving CAB-LA as PrEP, regardless of the amount of time since drug discontinuation **(AIII).** However, the absence of detectable resistance in people not currently on antiretroviral therapy (ART) must be interpreted with caution when designing subsequent ARV regimens. Importantly, in addition to considering prior ART history, prior genotypic- or phenotypic-resistance test results should be obtained from old records when possible. Because the most current drug-resistance test may not be able to detect resistance mutations that were previously detected, these prior test results are clinically important and should be reviewed and considered when designing a new ARV regimen **(AIII).**

A next-generation sequencing genotypic assay that analyzes HIV-1 proviral DNA may provide additional information on drug resistance in people with low levels of plasma HIV RNA or in people whose levels are below the limit of detection **(CIII).** However, these assays might miss some or all previous drug-resistance mutations, and they should be interpreted with caution. The usefulness of these assays in the clinic is still under investigation and has yet to be fully determined.

Use of Resistance Assays in Clinical Practice

Note: See Table 5 below for recommendations for the use of drug resistance assays.

Use of Resistance Assays in Determining Initial Treatment

Transmission of drug-resistant HIV strains is well documented and associated with suboptimal virologic response to initial ART.[16-19] The risk of acquiring drug-resistant virus is related to the prevalence of drug resistance in people with HIV who engage in activities that may result in HIV transmission within a given community. The prevalence of resistance and mutations by ARV drug class depends upon the population being studied (e.g., people with previous ARV exposure versus ARV-naive people), geography, and ARV class available in the region.[20] Pre-existing HIV drug resistance before initiation of ART is recognized as an issue for both high- and low-income countries. The prevalence of transmitted drug resistance (TDR) in high-income countries ranges from 9% to 14% and varies by country.[21-23] Pre-treatment drug resistance—which includes people exposed to ARVs prior to initiating first-line therapy (e.g., for PrEP or for the prevention of perinatal transmission), as defined by the World Health Organization—exceeds 10% in many countries.[20] In most TDR surveys, NNRTI resistance and NRTI resistance are the most common mutation class types detected, followed by PI- and INSTI-resistance mutations, respectively.[21-23]

Resistance testing is recommended to guide therapy selection to optimize virologic response in all people starting ART **(AII).** A genotypic assay is preferred for this purpose **(AIII).** In early (acute and recent) HIV infection, in pregnant women with HIV, or in people willing and able to initiate ART on the day or soon after HIV diagnosis, treatment initiation should not be delayed pending resistance testing results. Once results are reported, the regimen can be modified if warranted (see Early [Acute and Recent] HIV Infection) **(AIII).** In the absence of ART, resistant viruses may decline over time to less than the detection limit of standard resistance tests. However, when ART is eventually initiated, even low levels of resistant viruses may still increase the risk of treatment failure.[24-26] Therefore, if ART is deferred, resistance testing should still be performed at the time of entry into care to optimize the chance of capturing transmitted resistance **(AIII).** In this situation, the genotypic resistance test result should be used for regimen selection in the future when the person begins ART. If a person received CAB-LA as part of ART or PrEP, genotypic resistance testing should include the IN gene.

The rate at which transmitted resistance-associated mutations revert to wild-type virus has not been completely delineated, but mutations present at the time of HIV transmission are more stable than those selected under drug pressure. It is often possible to detect resistance-associated mutations in viruses that were transmitted several years earlier.[27-29] Though no prospective trial has directly addressed whether drug-resistance testing before initiation of therapy confers benefit in this population, data from several studies, including one prospective clinical trial, suggest that virologic responses in people with baseline resistance mutations are suboptimal.[16-19,30-34] In addition, an analysis of early RT and PR genotypic resistance testing in ARV-naive people suggests that baseline testing in this population is cost-effective and should be performed.[35] Therefore, resistance testing in people with chronic HIV is recommended at the time of entry into HIV care **(AII).**

Although no definitive prospective data exist to support the choice of one type of resistance testing over another, genotypic testing is generally preferred over phenotypic testing because of lower cost, faster turnaround time, greater sensitivity for detecting mixtures of wild-type and resistant virus, and easier interpretation of test results **(AIII).** If therapy is deferred, repeat testing shortly before initiating ART may be considered, because the person may have acquired drug-resistant virus (i.e., superinfection) **(CIII).**[36] Standard genotypic drug-resistance testing in ARV-naive people involves testing for mutations in the RT and PR genes. Although reports of transmission of INSTI-resistant virus are rare, as use of INSTIs increases, the potential for transmission of INSTI-

resistant virus also may increase. The prior use of CAB-LA for PrEP also may increase the risk of INSTI resistance at the time of HIV diagnosis. When INSTI resistance is possible, providers should supplement standard, baseline, genotypic resistance testing with genotypic testing of the IN gene, which may need to be ordered separately **(AIII).**

The next-generation sequencing genotypic resistance assay that analyzes proviral DNA in host cells can be considered in people with baseline HIV RNA <1,000 copies/mL or when conventional HIV RNA drug-resistance testing is unsuccessful **(CIII).** As outlined above, the results should be interpreted with caution, as this assay might miss some or all previously existing drug-resistance mutations.

Use of Resistance Assays in the Event of Virologic Failure

Resistance assays are important tools to inform treatment decisions for people who experience virologic failure while on ART. Several prospective studies have assessed the utility of resistance testing to guide ARV drug selection in people who experience virologic failure. These studies have involved genotypic assays, phenotypic assays, or both.[6,37-43] In general, these studies have found that changes in therapy based on resistance test results produce better early virologic response to salvage regimens than regimen changes guided only by clinical judgment.

In addition, one observational cohort study found that the use of genotypic drug-resistance testing in ART-experienced people with detectable plasma HIV RNA was independently associated with improved survival.[44] Thus, resistance testing is recommended as a tool for selecting active drugs when changing ARV regimens because of virologic failure in people with HIV RNA >200 copies/mL (**AI** for >1,000 copies/mL, **AIII** for 501 to 1,000 copies/mL, **CIII** for confirmed HIV RNA 201 to 500 copies/mL) (see Virologic Failure). In people with HIV RNA >200 copies/mL but <500 copies/mL, testing may be difficult to obtain outside of a research setting but still should be considered. Conventional drug-resistance testing in people with plasma viral loads ≤200 copies/mL **is not recommended** because there are unclear benefits and drug-resistance assays cannot be consistently performed at very low HIV RNA levels **(AIII).**

Resistance testing can also help to guide treatment decisions for people with HIV who have suboptimal viral load reduction **(AII).** Virologic failure in the setting of ART is, for certain people with HIV, associated with resistance to only one component of the regimen.[45-47] In this situation, substituting individual drugs in a failing regimen may be an option, but this concept will require clinical validation (see Virologic Failure).

Genotyping is preferred for resistance testing in people with HIV who experience virologic failure or suboptimal viral load reduction while on a first or second ARV drug regimen and in people for whom resistance mutation patterns are known or not expected to be complex (i.e., mutations that are straightforward, usually limited in number, or those that have clear significance) **(AII).** Often in these situations, the mutation patterns detected can be interpreted by algorithms used to predict the impact of subsequent regimens on virologic response. For people with HIV who have extensive treatment history, complex mutational patterns may occur. In such situations, the interpretation of complex genotypes and the impact of the mutation pattern on subsequent treatment regimens can be challenging. For these individuals, phenotypic-resistance testing may provide additional helpful information **(BIII).** Rather than only predicting the impact of the detected mutations, these assays can measure *in vitro* the actual fold change in drug susceptibility, as well as the actual impact of mutation combinations and interactions on each drug under consideration.

When compared with phenotypic testing, genotypic testing costs less to perform and has a faster turnaround time and greater sensitivity for detecting mixtures of wild-type and resistant virus. In addition, observations show that genotypic and phenotypic assays are comparable predictors of

virologic response to subsequent ARV regimens.[48] In people with HIV who experience virologic failure while on INSTI-based regimens or in those with prior INSTI exposure, including to CAB-LA for HIV treatment or prevention, testing for INSTI resistance should be performed to determine whether to include drugs from this class in subsequent regimens **(AII).** In this circumstance, clinicians should confirm that, when they order a resistance test, their laboratory is testing for INSTI resistance in addition to NNRTI, NRTI, and PI resistance. If INSTI-resistance testing needs to be ordered separately (as is the case in some laboratories), clinicians should request this assay in addition to standard drug-resistance testing. The addition of phenotypic to genotypic testing is generally indicated for people with known or suspected complex drug-resistance mutation patterns **(BIII).**

The next-generation sequencing genotypic resistance assay that analyzes proviral DNA can be considered for people with HIV who are experiencing treatment failure and for whom conventional HIV RNA genotypic drug-resistance testing is unsuccessful or unavailable due to low HIV RNA levels **(CIII).** As outlined above, results should be interpreted with caution, as these assays might miss some or all previously existing drug-resistance mutations.

When the use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed **(AI)** (see Co-Receptor Tropism Assays).

Use of HIV Proviral DNA Resistance Assays for Optimizing Antiretroviral Regimen in People With Viral Suppression

In the past decade, simpler, more potent, and better-tolerated ARV drugs have become available, and new ARV drugs will likely continue to emerge. Switching individual or multiple ARV drugs in a regimen is sometimes considered for people with HIV with suppressed viral load to simplify a regimen, avoid drug interactions or toxicity, or for other reasons. If a person's viral load is suppressed, standard drug-resistance testing will not be successful.

The next-generation sequencing genotypic resistance assay that analyzes proviral DNA can be considered for people with viral suppression, particularly if complex or semi-complex pre-existing resistance is suspected. In individuals who have experienced no prior virologic failures and who are on their first or second regimen, or who have genotypic testing results from when they had prior virologic failures, the use of the proviral DNA genotypic test is unlikely to provide additional useful information. However, in individuals who have experienced multiple prior failures, have a prolonged history of prior ARV regimens, or for whom prior genotypic resistance test results are not available, it may be appropriate to utilize proviral DNA genotypic testing **(CIII).** When such testing is obtained, results should be combined with all prior genotypic and phenotypic test results to construct a cumulative genotype, which incorporates all current and previously detected drug-resistance mutations. Results from proviral DNA genotypes should be interpreted with caution, as these assays might miss some or all previously existing drug-resistance mutations.[49,50] The usefulness of these assays in the clinic is still under investigation and has yet to be fully determined.

Use of Resistance Assays in Pregnancy

In pregnancy, the goal of ART is to rapidly and maximally reduce plasma HIV RNA in order to provide optimal therapy for the pregnant woman and to prevent perinatal transmission of HIV. Genotypic resistance testing is recommended for all pregnant women with HIV before initiation of therapy **(AIII)** and for those entering pregnancy with detectable HIV RNA levels while on therapy **(AI).** Phenotypic testing in those found to have complex drug-resistance mutation patterns may provide additional information **(BIII).** Optimal prevention of perinatal transmission requires prompt initiation of ART pending resistance testing results. Once the results are available, the ARV regimen can be changed as needed.

Table 5. Recommendations for the Use of Drug-Resistance Assays

Clinical Setting and Recommendation	Rationale
In Early (Acute and Recent) HIV Drug-resistance testing is recommended **(AII).** A genotypic assay is generally preferred **(AIII).** Treatment should not be delayed while awaiting resistance testing results **(AIII).** See Early (Acute and Recent) HIV Infection for discussion on ART selection.	Drug-resistance testing can determine whether drug-resistant virus was transmitted or acquired while using PrEP. The initial ARV regimen can be modified, if necessary, once resistance test results are available. Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.
If ART is deferred, repeat genotypic resistance testing may be considered when therapy is initiated **(CIII).** A genotypic assay is preferred **(AIII).**	Repeat testing when ART is initiated may be considered because the person may have acquired a drug-resistant virus (i.e., superinfection).
Before ART Initiation in People With Chronic HIV Drug-resistance testing is recommended at entry into HIV care to guide the selection of initial ART **(AII).** A genotypic assay is generally preferred **(AIII).** Treatment should not be delayed while awaiting resistance testing results **(AIII).**	Transmitted HIV with baseline resistance to at least one drug has been reported, and suboptimal virologic responses may be seen in people with baseline resistance mutations to ARVs in the prescribed regimen. Some drug-resistance mutations can remain detectable for years in untreated people with chronic HIV.
If transmitted or acquired INSTI resistance (including among people who had received INSTI for post-exposure prophylaxis) is a concern, providers should supplement standard resistance testing with a specific INSTI genotypic resistance assay, which may need to be ordered separately **(AIII).** Given the prolonged half-life of CAB-LA, INSTI-resistance testing should be considered in all people with HIV who previously received CAB-LA for PrEP, regardless of the time since drug discontinuation **(AIII).** See What to Start for discussion on ART selection.	Genotypic assays provide information on resistance to NRTIs, NNRTIs, PIs, and INSTIs. In some circumstances, INSTI-resistance tests need to be ordered separately (clinicians should check with the testing laboratory). Currently, transmitted INSTI resistance is infrequent, but the risk of people acquiring INSTI-resistant strains may be greater in certain known exposure settings. INSTI-resistance testing should be ordered for all people with prior exposure to CAB-LA for PrEP or an INSTI-based regimen for post-exposure prophylaxis.
For pregnant women or people who will initiate ART on the day of or soon after HIV diagnosis, treatment can be initiated prior to receiving resistance testing results.	If necessary, the ARV regimen can be modified once resistance test results are available.
If therapy is deferred, repeat genotypic resistance testing may be considered before initiation of ART **(CIII).** A genotypic assay is generally preferred **(AIII).**	Repeat testing before initiation of ART may be considered, because the person may have acquired a drug-resistant virus (i.e., a superinfection). Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant virus.

Table 5. Recommendations for the Use of Drug-Resistance Assays

Clinical Setting and Recommendation	Rationale
In People With Virologic Failure Drug-resistance testing is recommended in people on ART with HIV RNA >200 copies/mL (**AI** for >1,000 copies/mL**, AIII** for 501–1,000 copies/mL) and a confirmed HIV RNA 201–500 copies/mL **(CIII).** In people with confirmed HIV RNA levels between 201–500 copies/mL, testing may not be successful but should still be considered.	Drug-resistance testing can help determine the role of resistance in virologic failure and maximize the ability to select active drugs for the new regimen. Resistance testing for HIV RNA levels 201–500 copies/mL may need to be conducted within a research setting.
Resistance testing should be done while the person is taking ART or, if that is not possible, within 4 weeks after discontinuation of non–long-acting ARV drugs **(AII).** If >4 weeks have elapsed, resistance testing may still be useful to guide therapy; however, previously selected mutations can be missed due to lack of drug-selective pressure **(CIII).**	The absence of detectable resistance in such people with HIV must be interpreted with caution when designing subsequent ARV regimens, as mutations may decay with time.
For people who previously received LA CAB/RPV and present with virologic failure, resistance testing (including INSTI genotypic testing) should be performed regardless of the time since the last dose of LA CAB/RPV **(AIII).**	Because of the long half-lives of LA CAB and RPV, resistance mutations to INSTI and NNRTI may emerge even months after the last doses of these drugs.
Reverse transcriptase and protease genotypic resistance testing should be performed on people with virologic failure. Integrase resistance testing should be performed on individuals who have virologic failure and have a history of prior use of an INSTI (for prevention or treatment) or are currently receiving an INSTI-based regimen **(AII).**	Genotypic testing is preferred to phenotypic testing because of lower cost, faster turnaround time, and greater sensitivity for detecting mixtures of wild-type and resistant HIV. INSTI-resistance tests may need to be ordered separately. (Clinicians should check with the testing laboratory.)
All prior and current drug-resistance testing results should be reviewed and considered when designing a new ARV regimen for a person experiencing virologic failure **(AIII).**	Drug-resistance mutations may decay with time, and mutations detected in prior resistance tests may not be detected in current tests, though they remain clinically relevant.
Adding phenotypic testing to genotypic testing is generally preferred in people with known or suspected complex drug-resistance patterns **(BIII).**	Phenotypic testing can provide additional useful information in people with complex drug-resistance mutation patterns.
If use of a CCR5 antagonist is being considered, a co-receptor tropism assay should be performed **(AI).**	See Co-Receptor Tropism Assays section.
In People With Suboptimal Suppression of Viral Load Drug-resistance testing is recommended in people with suboptimal viral load suppression after initiation of ART **(AII).**	Testing can determine the role of resistance in suboptimal viral suppression, and it can help the clinician identify the number of active drugs available in the current ARV regimen and assess the need for a new regimen.

Table 5. Recommendations for the Use of Drug-Resistance Assays

Clinical Setting and Recommendation	Rationale
In Pregnant Women With HIV Genotypic resistance testing is recommended for all pregnant women before initial ART **(AIII)** and for those entering pregnancy with detectable HIV RNA levels while on therapy **(AI).**	The goals of ART in pregnant women with HIV are to achieve maximal viral suppression for treatment of HIV in the pregnant woman and to prevent perinatal transmission of HIV. Genotypic resistance testing will assist the clinician in selecting the optimal ARV regimen. However, treatment should not be delayed while awaiting resistance testing results. The initial regimen can be modified once resistance test results are available, if needed.
In People With Undetectable Viral Load or Low-Level Viremia Who Are Planning to Change Their ARV Regimen HIV-1 proviral DNA resistance assays may be useful if HIV RNA is below the limit of detection or with low-level viremia, where an HIV RNA genotypic assay is unlikely to be successful **(CIII).**	HIV-1 proviral DNA resistance assays may provide information about previously circulating resistant viral variants that are archived within proviral DNA. These assays may miss some or all prior resistance mutations that have occurred within the viral quasi-species and, therefore, they should be interpreted with caution. The clinical utility of HIV-1 proviral DNA assays has not been fully determined.

Key: ART = antiretroviral therapy; ARV = antiretroviral; CAB-LA = long-acting cabotegravir; CCR5 = cysteine-cysteine chemokine receptor 5; INSTI = integrase strand transfer inhibitor; LA = long-acting; LA CAB/RPV = long-acting cabotegravir/rilpivirine; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PrEP = pre-exposure prophylaxis; RPV = rilpivirine

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Co-Receptor Tropism Assays

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Reviewed: October 25, 2018

Panel's Recommendations
• A co-receptor tropism assay should be performed whenever the use of a CCR5 co-receptor antagonist is being considered **(AI).** • Co-receptor tropism testing is recommended for patients who exhibit virologic failure on a CCR5 antagonist **(BIII).** • A phenotypic tropism assay is preferred to determine HIV-1 co-receptor usage **(AI).** • A genotypic tropism assay should be considered as an alternative test to predict HIV-1 co-receptor usage **(BII).** • A proviral DNA tropism assay can be utilized for patients with undetectable HIV-1 RNA when a CCR5 antagonist is considered for use in a new regimen (e.g., as part of a regimen switch or simplification) **(BII).**
***Rating of Recommendations**: A = Strong; B = Moderate; C = Weak* ***Rating of Evidence**: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

HIV enters cells by a complex process that involves sequential attachment to the CD4 T lymphocyte (CD4) receptor followed by binding to either the CCR5 or CXCR4 molecules and fusion of the viral and cellular membranes.[1] CCR5 co-receptor antagonists prevent HIV entry into target cells by binding to the CCR5 receptors.[2] Phenotypic and genotypic assays have been developed that can determine or predict the co-receptor tropism (i.e., use of CCR5, CXCR4, or both as either dual-tropic virus or a mixed population of viruses referred to for purposes of assay results as dual/mixed [D/M]) of the patient's dominant virus population. An older generation assay (Trofile,® Monogram Biosciences, Inc., South San Francisco, CA) was used to screen patients who were participating in clinical trials that led to the approval of maraviroc (MVC), the only CCR5 antagonist currently available. The assay has been improved and is now available with enhanced sensitivity. In addition, genotypic assays to predict co-receptor usage are commercially available.

During acute/recent infection, the vast majority of patients harbor a CCR5-utilizing virus (R5 virus), which suggests that the R5 variant is preferentially transmitted; however, up to 19% of individuals with acute/recent infection can harbor CXCR4-tropic virus.[3-5] Viruses in many untreated patients eventually exhibit a shift in co-receptor tropism from CCR5 usage to either CXCR4 usage or D/M tropism. This shift is temporally associated with a more rapid decline in CD4 counts,[6,7] but whether this tropism shift is a cause or a consequence of progressive immunodeficiency remains undetermined.[1] Antiretroviral-treated patients with extensive drug resistance or persistently high-level viremia are more likely to harbor CXCR4- or D/M-tropic variants than untreated patients with comparable CD4 counts.[8,9] The prevalence of CXCR4- or D/M-tropic variants increases to more than 50% in treated patients who have CD4 counts <100 cells/mm^3.[8,10] Since CXCR4-tropic viruses may be present at initial presentation or a patient may shift to CXCR4-tropism over the course of infection, co-receptor tropism should always be assessed prior to the use of CCR5 antagonists for treatment. Once a patient has ever been documented with detectable CXCR4- or D/M-tropic virus, it is assumed that such viruses will always be present. CCR5 co-receptor antagonists will no longer be active for that patient and should not be used.

Phenotypic Assays

Phenotypic assays characterize the co-receptor usage of plasma-derived virus. These assays involve the generation of laboratory viruses that express patient-derived envelope proteins (i.e., gp120 and gp41). These pseudoviruses, which are replication-defective, are used to infect target cell lines that express either CCR5 or CXCR4.[11,12] Using the Trofile® assay, the co-receptor tropism of the patient-derived virus is confirmed by testing the susceptibility of the virus to specific CCR5 or CXCR4 inhibitors *in vitro*. This assay takes about 2 weeks to perform and requires a plasma HIV RNA level ≥1,000 copies/mL.

The performance characteristics of these assays have evolved. Most, if not all, patients enrolled in premarketing clinical trials of MVC and other CCR5 antagonists were screened with an earlier, less sensitive version of the Trofile® assay.[12] This earlier assay failed to routinely detect low levels of CXCR4-utilizing variants. As a consequence, some patients enrolled in these clinical trials harbored low levels of such variants at baseline, which were below the assay limit of detection, and these patients exhibited rapid virologic failure after initiation of a CCR5 antagonist.[13] The assay has been improved and is now able to detect lower levels of CXCR4-utlizing viruses. *In vitro*, the assay can detect CXCR4-utilizing clones with 100% sensitivity when those clones represent 0.3% or more of the virus population.[14] Although this more sensitive assay has had limited use in prospective clinical trials, it is now the only assay that is commercially available. For unclear reasons, a minority of samples cannot be successfully phenotyped with either generation of the Trofile® assay.

In patients with an undetectable viral load or detectable plasma HIV RNA <1,000 copies/mL, phenotypic co-receptor usage can be determined using proviral DNA obtained from peripheral blood mononuclear cells (e.g., Trofile® DNA, Monogram Sciences); however, the clinical utility of this assay remains to be determined.[15]

Genotypic Assays

Genotypic determination of HIV-1 co-receptor usage is based on sequencing of the V3-coding region of HIV-1 *env*, the principal determinant of co-receptor usage. A variety of algorithms and bioinformatics programs can be used to predict co-receptor usage from the V3 sequence.[16] When compared to the phenotypic assay, genotypic methods show high specificity (~90%) but only modest sensitivity (~50% to 75%) for the presence of a CXCR4-utilizing virus. Studies in which V3 genotyping was performed on samples from patients screened for clinical trials of MVC suggest that genotyping performed as well as phenotyping in predicting the response to MVC.[17-19] An important caveat is that the majority of patients who received MVC were first shown to have R5 virus by a phenotypic assay (Trofile®). Consequently, the opportunity to assess treatment response to MVC in patients whose virus was considered R5 by genotype but D/M or X4 by phenotype was limited to a relatively small number of patients. Other studies have also demonstrated relatively high concordance between genotypic- and phenotypic-assessed tropism;[20,21] however, there is variability between different genotypic platforms.[22]

Given these performance characteristics, genotypic tropism assays may not be sufficiently robust to completely rule out the presence of an X4 or D/M variant;[23] therefore, the Panel preferentially recommends phenotypic testing. Based on accessibility, capacity, logistics, and cost, European guidelines currently include genotypic testing as an equivalent option to phenotypic testing when determining co-receptor usage among patients with HIV RNA >1,000 copies/mL and preferentially for those with HIV RNA ≤1,000 copies/mL.[24]

HIV-1 proviral DNA genotypic tropism testing is available for patients with HIV RNA <1,000 copies/mL. These assays evaluate the HIV-1 proviral DNA integrated within infected cells for CXCR4-utilizing viral strains.[25] As discussed above, caution is advised when using such assays, as

their detection limit, concordance with plasma HIV RNA tropism, and clinical utility are not yet fully determined.

Use of Assays to Determine Co-receptor Usage in Clinical Practice

An assay for HIV-1 co-receptor usage should be performed whenever the use of a CCR5 antagonist is being considered **(AI).** This is true even in the setting of prior tropism testing showing CCR5 usage, as viral evolution may occur over the course of infection. In addition, because virologic failure may occur due to a shift from CCR5-using to CXCR4-using virus, testing for co-receptor usage is recommended in patients who exhibit virologic failure on a CCR5 antagonist **(BIII).** Virologic failure may also be caused by resistance of a CCR5-using virus to a CCR5 antagonist, but such resistance is uncommon. Compared to genotypic testing, phenotypic testing has more evidence supporting its utility. Therefore, a phenotypic test for co-receptor usage is generally preferred **(AI).** However, because phenotypic testing is more expensive, requires more time to perform, and may have logistic challenges, a genotypic test to predict HIV-1 co-receptor usage should be considered as an alternative test **(BII).**

As with HIV resistance testing, the results of all prior tropism tests should be obtained. If CXCR4-utlizing or D/M-tropic viruses have ever been detected previously, then repeat testing is not necessary and a CCR5 co-receptor antagonist **should not be used.**

If a CCR5 co-receptor antagonist is being considered in a patient with an undetectable HIV RNA (e.g., in cases of regimen simplification or a toxicity-related switch), a proviral DNA tropism assay can be utilized **(BII).**[26-28] If CXCR4-utlizing or D/M-tropic viruses are detected, then the CCR5 co-receptor antagonist **should not be used.**

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HLA-B*5701 Screening

Updated: December 1, 2007
Reviewed: January 10, 2011

Panel's Recommendations
• The Panel recommends screening for HLA-B*5701 before starting patients on an abacavir (ABC)-containing regimen to reduce the risk of hypersensitivity reaction (HSR) **(AI).** • HLA-B*5701-positive patients should not be prescribed ABC **(AI).** • The positive status should be recorded as an ABC allergy in the patient's medical record **(AII).** • When HLA-B*5701 screening is not readily available, it remains reasonable to initiate ABC with appropriate clinical counseling and monitoring for any signs of HSR **(CIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = data from randomized controlled trials; II = data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = expert opinion*

The abacavir (ABC) hypersensitivity reaction (HSR) is a multiorgan clinical syndrome typically seen within the initial 6 weeks of ABC treatment. This reaction has been reported in 5% to 8% of patients participating in clinical trials when using clinical criteria for the diagnosis, and it is the major reason for early discontinuation of ABC. Discontinuing ABC usually promptly reverses HSR, whereas subsequent rechallenge can cause a rapid, severe, and even life-threatening recurrence.[1]

Studies that evaluated demographic risk factors for ABC HSR have shown racial background as a risk factor, with white patients generally having a higher risk (5%–8%) than black patients (2%–3%). Several groups reported a highly significant association between ABC HSR and the presence of the major histocompatibility complex (MHC) class I allele HLA-B*5701.[2, 3] Because the clinical criteria used for ABC HSR are overly sensitive and may lead to false-positive ABC HSR diagnoses, an ABC skin patch test (SPT) was developed as a research tool to immunologically confirm ABC HSR.[4] A positive ABC SPT is an ABC-specific delayed HSR that results in redness and swelling at the skin site of application. All ABC SPT–positive patients studied were also positive for the HLA-B*5701 allele.[5] The ABC SPT could be falsely negative for some patients with ABC HSR and, at this point, is not recommended for use as a clinical tool. The PREDICT-1 study randomized participants with HIV before starting ABC either to be prospectively screened for HLA-B*5701 (with HLA-B*5701–positive patients not offered ABC) or to standard of care at the time of the study (i.e., no HLA screening, with all patients receiving ABC).[6] The overall HLA-B*5701 prevalence in this predominately white population was 5.6%. In this cohort, screening for HLA-B*5701 eliminated immunologic ABC HSR (defined as ABC SPT positive) compared with standard of care (0% vs. 2.7%), yielding a 100% negative predictive value with respect to SPT and significantly decreasing the rate of clinically suspected ABC HSR (3.4% vs. 7.8%). The SHAPE study corroborated the low rate of immunologically validated ABC HSR in black patients and confirmed the utility of HLA-B*5701 screening for the risk of ABC HSR (100% sensitivity in black and white populations).[7]

On the basis of the results of these studies, the Panel recommends screening for HLA-B*5701 before starting an ABC-containing regimen in a person with HIV **(AI).** HLA-B*5701–positive patients should not be prescribed ABC **(AI),** and the positive status should be recorded as an ABC allergy in the patient's medical record **(AII).** HLA-B*5701 testing is needed only once in a patient's lifetime; thus, efforts to carefully record and maintain the test result and to educate the patient about its implications are important. The specificity of the HLA-B*5701 test in predicting ABC HSR is lower than the sensitivity (i.e., 33%–50% of HLA-B*5701–positive patients would likely not develop

confirmed ABC HSR if exposed to ABC). HLA-B*5701 should not be used as a substitute for clinical judgment or pharmacovigilance, because a negative HLA-B*5701 result does not absolutely rule out the possibility of some form of ABC HSR. When HLA-B*5701 screening is not readily available, it remains reasonable to initiate ABC with appropriate clinical counseling and monitoring for any signs of ABC HSR **(CIII).**

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TREATMENT GOALS

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Antiretroviral therapy (ART) has reduced HIV-related morbidity and mortality at all stages of HIV infection[1-4] and has reduced HIV transmission.[5-8] Maximal and durable suppression of plasma viremia delays or prevents the selection of drug-resistance mutations, preserves or improves CD4 T lymphocyte (CD4) cell numbers, and confers substantial clinical benefits, all of which are important treatment goals.[9,10] HIV suppression with ART may also decrease inflammation and immune activation thought to contribute to higher rates of cardiovascular and other end-organ damage reported in cohorts with HIV (see Initiating Antiretroviral Therapy). Despite these benefits, eradication of HIV infection cannot be achieved with available antiretrovirals (ARVs). Treatment interruption has been associated with rebound viremia, worsening of immune function, and increased morbidity and mortality.[11] Thus, once initiated, ART should be continued, with the following key treatment goals:

- Maximally and durably suppress plasma HIV RNA;
- Restore and preserve immunologic function;
- Reduce HIV-associated morbidity and prolong the duration and quality of survival; and
- Prevent HIV transmission.

Achieving viral suppression currently requires the use of combination ARV regimens that generally include three active drugs from two or more drug classes. Baseline patient characteristics and results from drug resistance testing should guide design of the specific regimen (see What to Start: Initial Combination Regimens for People With HIV). When initial HIV suppression is not achieved or not maintained, changing to a new regimen with at least two active drugs is often required (see Virologic Failure). The increasing number of ARV drugs and drug classes makes viral suppression below detection limits an achievable goal in most patients.

After initiation of effective ART, viral load reduction to below limits of assay detection usually occurs within the first 12 to 24 weeks of therapy. Predictors of virologic success include the following:

- Low baseline viremia;
- High potency of the ARV regimen;
- Tolerability of the regimen;
- Convenience of the regimen; and
- Excellent adherence to the regimen.

Strategies to Achieve Treatment Goals

Selection of Initial Combination Regimen

Several ARV regimens are recommended for use in ART-naive patients (see What to Start). Most of the recommended regimens have comparable efficacy but vary in pill burden, potential for drug interactions and/or side effects, and propensity to select for resistance mutations if ART adherence is suboptimal. Regimens should be tailored for the individual patient to enhance adherence and support long-term treatment success. Considerations when selecting an ARV regimen for an

individual patient include potential side effects, patient comorbidities, possible interactions with concomitant medications, results of pretreatment genotypic drug-resistance testing, and regimen convenience (see Table 7).

Improving Adherence

Suboptimal adherence may result in reduced treatment response. Incomplete adherence can result from complex medication regimens; patient-related factors, such as active substance abuse, depression, or the experience of adverse effects; and health system issues, including interruptions in patient access to medication and inadequate treatment education and support. Conditions that promote adherence should be maximized before and after initiation of ART (see Adherence to Antiretroviral Therapy).

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INITIATION OF ANTIRETROVIRAL THERAPY

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Panel's Recommendations
• The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends antiretroviral therapy (ART) for all people with HIV to reduce morbidity and mortality **(AI)** and to prevent transmission of HIV to others **(AI).** • The Panel recommends initiating ART immediately (or as soon as possible) after HIV diagnosis in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients, and improve the rate of virologic suppression among people with HIV **(AII).** • When initiating ART, people with HIV should be counseled on the benefits, lifelong need, and importance of adherence to ART; clinicians should also identify and address barriers to care engagement and ART adherence **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

The primary goals of antiretroviral therapy (ART) are to prevent HIV-associated morbidity and mortality and to prevent transmission of HIV to others. These goals are accomplished by using effective ART to achieve and maintain plasma HIV-1 RNA levels (viral load) below the quantification limits of commercially available assays. Durable viral suppression lowers the risk of both AIDS-defining and other HIV-related complications, improves immune function and overall health, and allows people with HIV to live a lifespan approaching that of people without HIV.[1,2] High plasma viral load is a major risk factor for HIV transmission; effective ART suppresses viremia and, consequently, substantially reduces the risk of sexual[3-7] and perinatal HIV transmission.[8,9] Modeling studies and ecological studies of populations with high ART uptake and high viral suppression rates suggest that expanded use of ART lowers the incidence of HIV and, eventually, the prevalence of HIV on a community or population level.[10-12]

Early clinical trials of combination ART focused on people with advanced HIV and low CD4 T lymphocyte (CD4) cell counts.[13-15] Consequently, treatment guidelines at that time recommended the initiation of ART based on CD4 count thresholds or the development of AIDS-defining conditions. The benefits of ART for people with high CD4 counts were unclear, along with concerns about the toxicities of some antiretroviral (ARV) drugs. However, two large randomized controlled trials, START[16] and TEMPRANO[17], both published in 2015, addressed the optimal time to initiate ART. Both studies demonstrated reductions in morbidity and mortality among people with HIV who had CD4 counts >500 cells/mm^3 and who initiated ART immediately when compared with people who delayed initiation of ART.

Deferring ART until CD4 counts decline puts people with HIV at risk of both AIDS-defining conditions and certain serious non-AIDS–defining conditions. Furthermore, the magnitude of CD4 recovery is directly correlated with CD4 count at ART initiation. Consequently, some individuals who start treatment with CD4 counts <350 cells/mm^3 do not achieve CD4 counts >500 cells/mm^3 after up to

10 years on ART,[18,19] and they have a shorter life expectancy than those who initiated therapy at higher CD4 count thresholds.[18-20]

Fundamental to the recommendation for earlier initiation of ART is the assumption that HIV will be diagnosed early in the course of the disease. The Centers for Disease Control and Prevention (CDC) recommends HIV screening to be performed for all people aged 13 to 64 years, including during pregnancy, using an opt-out screening approach.[21] More frequent HIV screening is recommended for certain populations with higher HIV prevalence.[22] The U.S. Preventive Services Task Force (USPSTF) also recommends HIV testing for people aged 15 to 65 years and for all pregnant women. This recommendation has been designated a Grade A recommendation by the USPSTF, meaning that third-party payers should cover this service without cost to patients.[23] HIV testing should also be performed for people younger than 15 and older than 65 years of age when indicated or requested.

Unfortunately, in some individuals, the diagnosis of HIV is not made until the later stages of the disease. In a survey conducted between 2016 and 2017, it was noted that fewer than 40% of American adults had ever had an HIV test.[24] Delayed diagnosis of HIV has been reported more often in people who inject drugs, people who live in rural communities, older adults, and among Black and Hispanic persons.[25-27] Many people with HIV access health care years before their HIV diagnosis but are not offered HIV testing.[28]

To ensure that the current treatment guidelines have maximum impact, routine HIV screening per current CDC or USPSTF recommendations is essential.[23,29] Early diagnosis also has clinical and economic benefits, including prolonging life, improving the quality of life, and decreasing the costs related to the management of AIDS and its comorbidities.[30,31] Additionally, HIV screening is a key step in the Ending the HIV Epidemic initiative to prevent the transmission of HIV to others.[32] It is critical that everyone who receives an HIV diagnosis be educated about HIV disease; initiated on ART; and linked to care for full evaluation, follow-up, and management as soon as possible. In order for people with HIV and their sexual partners to fully benefit from early diagnosis, clinicians should initiate ART as soon as possible and provide support to enhance engagement in care and full ART adherence (see Adherence to the Continuum of Care and Treatment as Prevention).

Initiating Antiretroviral Therapy

The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends ART for all people with HIV to reduce the morbidity and mortality associated with HIV infection **(AI)** and to prevent HIV transmission to sexual partners and infants **(AI).** ART should be initiated as soon as possible after HIV diagnosis **(AII).** Clinicians should refer to What to Start for guidance on ART regimen selection for all adults and adolescents with HIV, including those who received pre-exposure prophylaxis (PrEP) before HIV diagnosis; the Perinatal Guidelines provide guidance on ART regimen selection during pregnancy. When initiating ART, people with HIV should be counseled on the benefits, lifelong need, and importance of adherence to ART; clinicians should also identify and address barriers to care engagement and ART adherence **(AIII).** People with HIV should also understand that the currently available ART does not cure HIV. To improve and maintain immunologic function and maintain viral suppression, ART should be continued indefinitely without interruption. Initiating ART as soon as possible is particularly important for people with AIDS-defining conditions, those with acute or recent HIV infection, and during pregnancy. Delaying therapy in these subpopulations may increase risks for morbidity, mortality, and HIV transmission. Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy provides recommendations for baseline and follow-up laboratory monitoring for people starting ART.

Early (Acute/Recent) HIV Infection

The term "early HIV" refers to both acute and recent infection. "Acute HIV" occurs soon after transmission (onset of symptoms typically within 2–4 weeks after infection) and is characterized by the presence of HIV RNA alone or with positive p24 antigen and nonreactive or indeterminate HIV antibody results on the confirmatory immunoassay. "Recent HIV" refers to the first 6 months after infection, during which anti-HIV antibodies and HIV RNA become detectable.[33,34] Detailed discussion on the diagnosis of acute HIV can be found in Early (Acute and Recent) HIV Infection.

Early HIV is considered a period of high infectivity,[35] and early ART substantially reduces the risk of HIV transmission.[4-7] Additionally, clinical trial data indicate that individuals who are treated during early HIV may experience immunologic and virologic benefits.[36-41] Therefore, ART should be initiated as soon as possible after a positive qualitative test result or a quantitative HIV RNA test result **(AII).** Before starting ART, and without delaying its initiation, a blood sample should be sent for genotypic resistance testing (see Drug Resistance Testing and What to Start). Same-day or rapid ART initiation in people with acute HIV has been shown to be safe, acceptable, and effective.[42] When initiating ART, clinicians should identify and address barriers to ART adherence and engagement in care for each person with HIV (see Adherence to the Continuum of Care).

To verify the diagnosis of acute HIV, a new blood specimen should be collected for a confirmatory HIV antibody test and a quantitative plasma HIV RNA test. Given the sensitivity of current HIV RNA assays,[43] a positive result by quantitative or qualitative plasma HIV RNA testing in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. If acute HIV is highly suspected, ART should be initiated without delay while awaiting confirmation of diagnosis[44]; if the pending test results later rule out HIV infection, then ART for the treatment of HIV should be discontinued. People who tested negative but remain at risk of sexual HIV transmission should be offered ARV PrEP per recommendations from the CDC.

Some individuals with early HIV may decline ART initially. Individuals who do not begin ART immediately should be maintained in care, and every effort should be made to initiate therapy as soon as they are ready.

Immediate Antiretroviral Therapy Initiation on the Day of HIV Diagnosis

ART initiation on the same day of HIV diagnosis in the outpatient setting may be used as a strategy to increase ART uptake and engagement in care, to accelerate the time to ART-mediated viral suppression, and, consequently, to reduce the potential for HIV transmission. Benefits of rapid ART initiation are supported by randomized controlled trials that were performed in resource-limited settings outside of the United States[45-47] and observational trials in the United States that included both immediate initiation of ART (on the day of diagnosis)[48-50] and rapid ART initiation (within days or weeks of diagnosis).[50,51] Two randomized trials were performed in South Africa (n = 377)[45] and Haiti (n = 703).[46] In these trials, same-day ART initiation increased the proportion of participants who had suppressed viral loads about a year after HIV diagnosis compared with those who initiated ART between 3 weeks and 3 months after diagnosis. In addition, these studies demonstrated that rapid ART initiation can be feasible and beneficial in resource-limited settings. While no randomized controlled trials have been conducted in the United States, several prospective observational studies have demonstrated the feasibility of same-day ART initiation. City-wide implementation of the San Francisco RAPID program among 225 patients who were newly diagnosed with HIV resulted in ART initiation on the day of diagnosis for more than half of the patients and a median time from ART initiation to viral suppression (defined as <200 copies/mL) of 41 days. Over a median follow-up of 1.1 years (range 0–3.9 years), 92.1% of patients achieved virologic suppression. In the RAPID

study, a substantial proportion of participants had a major substance use disorder (51.4%), a major mental health disorder (48.1%), or unstable housing (30.6%).[49]

It should be emphasized that ART initiation on the same day of HIV diagnosis can be resource intensive. This strategy may require additional staff, multidisciplinary coordination, provision of ART starter packs, and consolidation of "usual care" patient services (e.g., clinical evaluation, education, counseling, initiation or optimization of insurance coverage, intake laboratory testing) into a 2- or 3-hour visit.[49] While the infrastructure and resources necessary to implement an immediate ART program may not be available in all health care settings, facilitating rapid ART initiation may improve treatment outcomes. The Panel recommends initiating ART at the time of diagnosis (when possible) or soon afterwards to increase the uptake of ART, decrease the time required to achieve linkage to care and virologic suppression, and improve the rate of virologic suppression **(AII).** The rating for this recommendation reflects the fact that randomized trials have only been conducted in low-resource countries, while evidence for benefit in the United States is based on observational studies.

Antiretroviral Therapy for Persons With Acute Opportunistic Infections and Malignancies

Initiation of ART in the setting of an acute, AIDS-associated opportunistic infection (OI) or malignancy can improve immune function and potentially enhance treatment success for the OI. Clinicians should refer to the Adult and Adolescent Opportunistic Infection Guidelines for a more in-depth discussion on specific OIs. Below are some important factors to consider when initiating ART in these situations.

- **When no effective therapy exists for the treatment of the OI (e.g., cryptosporidiosis, microsporidiosis, progressive multifocal leukoencephalopathy):** In these situations, ART is the only treatment that can improve immune function and clinical outcomes. ART should be initiated without delay.
- **Concerns about immune reconstitution inflammatory syndrome (IRIS):** For some OIs, such as cryptococcal and tuberculosis (TB) meningitis, immediate ART initiation may increase the risk of serious IRIS. A short delay before initiating ART may be warranted.[52-55] After ART initiation, the patient should be closely monitored for signs and symptoms associated with IRIS.
- **Nonmeningeal TB:** In these patients, initiating ART during treatment for TB confers a significant survival advantage[56-60]; therefore, ART should be initiated as recommended in Tuberculosis/HIV Coinfection.
- **For people with mild to moderate cutaneous Kaposi sarcoma:** Prompt initiation of ART alone without chemotherapy has been associated with improvement of cutaneous Kaposi sarcoma lesions, even though initial transient progression of Kaposi sarcoma lesions as a manifestation of IRIS can also occur.[61]
- **For people with other OIs:** After starting treatment for the OI, ART should be initiated as soon as feasible to improve immune function.
- **For patients with malignancies that require chemotherapy:**
  - A diagnosis of malignancy should not delay initiation of ART, nor should initiation of ART delay treatment for the malignancy.
  - Although an IRIS-like presentation of non-Hodgkin's lymphoma after initiation of ART has been described,[62] ART-mediated viral suppression is associated with longer survival among individuals undergoing treatment for AIDS-related lymphoma.[63]

Importantly, drug interactions should be considered when selecting ART, as there is the potential for significant interactions between some ARV drugs (particularly ritonavir- or cobicistat-boosted regimens) and drugs for treatment of OIs (particularly with rifamycins and azole antifungal drugs) and chemotherapy drugs.

Antiretroviral Therapy Initiation in Hospitalized People With HIV

Some people receive their first HIV diagnosis while hospitalized for HIV-related or unrelated conditions.[64] The test-and-treat concept of initiating ART has been successful in the outpatient setting as described above; however, newly diagnosed people with HIV who are hospitalized seldom start ART before hospital discharge.[65] Some concerns about initiating ART during hospitalization include the potential for drug–drug interactions or ART-related adverse effects that may complicate management of the acute condition that prompted hospitalization, the risk of paradoxical or unmasking IRIS in the context of OIs, and limited HIV care experience among hospital staff. Additionally, securing ART prescription coverage for a person with newly diagnosed HIV requires a multidisciplinary approach, including coordination with social workers/case managers to navigate through some complex insurance/patient assistance programs. As a result, some clinicians prefer to leave this task to the primary HIV clinic.

Although receiving an HIV diagnosis during an acute illness can be overwhelming, several reasons make this an opportune time to initiate ART. For example, being hospitalized allows more time for the person with HIV to receive education and ask questions about HIV and treatment goals and to receive ART-related counseling. Upon patient approval, having family or caregivers participate in these discussions will allow them to assist with adherence to ART (and concomitant medications) and clinic follow-up after discharge. Administering the first doses of ART during hospitalization allows clinicians to assess ART tolerance while under observation. Using a multidisciplinary team approach (e.g., HIV specialists, pharmacists, social workers) during the hospital stay to assist with ART initiation can facilitate transition to outpatient care. Clinical pharmacists can assess for potential drug–drug and drug–nutrient interactions and provide counseling on ART and adherence. Social workers/patient navigators can assist with exploring options for outpatient ARV coverage and facilitate linkage to HIV primary care. A multicenter study that enrolled hospitalized people with HIV from 2012 to 2014 demonstrated that starting ART in hospitalized patients who had a recent history of substance use was associated with shorter time to linkage to their first HIV clinical appointment after discharge and more clinic visits in the first 12 months after ART initiation than those who were not started on ART before discharge; however, no difference was observed in the rate of viral suppression and retention in care over 12 months.[66]

Certain situations, such as in the setting of TB meningitis or cryptococcal meningitis, may warrant a short delay in ART initiation due to concerns of severe consequences related to paradoxical IRIS; however, in most other situations, the benefits of starting ART during hospitalization outweigh the concerns listed above. Therefore, the Panel recommends initiating ART during hospitalization whenever possible **(BIII).**

Before starting ART, and without delaying its initiation, a blood sample should be sent for genotypic resistance testing (see Drug Resistance Testing and What to Start). If the resistance testing results are not available before hospital discharge, they should be forwarded to the outpatient HIV provider as soon as they become available. If ART is initiated before hospital discharge, clinicians should coordinate with their multidisciplinary team to ensure sufficient ART supply (e.g., at least 2–4 weeks'

supply) is available until the outpatient clinic appointment. See Adherence to the Continuum of Care for more discussions on the transition of care between different health care settings.

Evidence Supporting the Benefits of Antiretroviral Therapy in Preventing Morbidity and Mortality

Randomized Controlled Trials of Early Versus Deferred Antiretroviral Therapy

Two large randomized controlled trials, START and TEMPRANO, published in 2015, provided the evidence for the Panel's recommendation to initiate ART in all patients regardless of CD4 count **(AI).** The results of these two studies are summarized below.

START was a large, multinational, randomized controlled clinical trial designed to evaluate the role of early ART initiation in asymptomatic adults with high CD4 counts in reducing AIDS-defining illnesses, serious non-AIDS events, or death. In this study, ART-naive adults (aged >18 years) with CD4 counts >500 cells/mm^3 were randomized to initiate ART at randomization (immediate arm) or to wait to initiate ART until their CD4 counts declined to <350 cells/mm^3 or until they developed a clinical indication for therapy (deferred arm).

The study enrolled 4,685 participants. Initial results were unblinded early (after a mean follow-up of 3 years) because of the superiority of the immediate ART strategy. The primary endpoint of serious AIDS or non-AIDS events was reported in 42 participants (1.8%, or 0.60 events per 100 person-years) in the immediate ART arm and 96 participants (4.1%, or 1.38 events per 100 person-years) in the deferred ART arm (hazard ratio [HR] 0.43, favoring early ART; 95% confidence interval [CI], 0.30–0.62, $P < 0.001$). The majority of clinical events (59%) in the deferred ART arm occurred in participants whose CD4 counts were still above 500 cells/mm^3, evidence for a benefit of initiating ART even before CD4 count declines below this threshold. Furthermore, the benefit of immediate ART was consistent across all participant subgroups, including sex, age, plasma HIV RNA levels, and country income level. The benefit appeared to be particularly strong for AIDS events (HR 0.28), TB (HR 0.29), malignancies (HR 0.36), and severe bacterial infections (HR 0.39). The benefit at lower CD4 counts was primarily a reduction in the number of AIDS events, while the benefit at higher CD4 counts was primarily a reduction in the number of serious non-AIDS events. In addition to AIDS-related events, early ART initiation also significantly reduced the rate of pooled serious non-AIDS events (HR 0.61).[16,67]

The TEMPRANO ANRS 12136 study was a randomized controlled trial conducted in Cote d'Ivoire. Using a two-by-two factorial design, participants with HIV who had CD4 counts <800 cells/mm^3 and who did not meet the criteria for starting ART according to World Health Organization guidelines at that time were randomized to start ART early (upon enrollment) or defer ART based on the national guidelines criteria for starting treatment. Half of the participants in each group received isoniazid for prevention of TB for 6 months and half did not. The primary study endpoint was a combination of all-cause deaths, AIDS diseases, non-AIDS malignancies, and non-AIDS invasive bacterial diseases. More than 2,000 participants enrolled in the trial, with a median follow-up of 30 months. Among the 849 participants who had baseline CD4 counts >500 cells/mm^3, early ART reduced the rate of primary events compared with deferred ART, with an HR of 0.56 (95% CI, 0.33–0.94).[17]

The TEMPRANO and START trials had very similar estimates for the protective effect of ART among individuals with HIV who had CD4 counts >500 cells/mm^3. Guidelines around the world now recommend starting ART irrespective of CD4 count at the time or soon after HIV diagnosis.

Use of Antiretroviral Therapy to Prevent HIV Transmission

Prevention of Sexual Transmission

A randomized clinical trial[4] and several large observational cohort studies[5-7] have provided strong evidence that achieving sustained viral suppression prevents sexual transmission of HIV. Thus, a key goal of ART is to prevent transmission of HIV to seronegative sexual partners **(AI).** All people with HIV should be informed that maintaining a plasma HIV RNA (viral load) of <200 copies/mL (including any measurable value below this threshold value) with ART prevents sexual transmission of HIV to partners **(AII).** People with HIV may recognize this concept as Undetectable = Untransmittable, or U=U. The results of these studies are summarized in Antiretroviral Therapy to Prevent Sexual Transmission of HIV. Clinicians should also discuss with these individuals the potential harm of non-adherence to ART, including that it can lead to viremia, which may affect their own health, lead to drug resistance, and potentially transmission to sexual partners.

Prevention of Perinatal Transmission

The first well-established example of ART reducing the risk of HIV transmission is the use of ART during pregnancy to prevent perinatal transmission of HIV. Effective suppression of HIV replication is a key determinant in reducing the risk of perinatal transmission. In the setting of maternal viral load suppressed to <50 copies/mL near delivery, the use of combination ART during pregnancy has reduced the rate of perinatal HIV transmission from approximately 20%–30% to 0.1%–0.5%.[8,9] ART is thus recommended during all pregnancies in the context of HIV, for both maternal health and for the prevention of HIV transmission to the newborn. In ART-naive pregnant women, ART should be initiated as soon as possible, with the goal of suppressing plasma viremia throughout pregnancy. HIV testing should be performed upon confirmation of pregnancy, with testing repeated throughout pregnancy as needed for those at risk of HIV acquisition (see Pregnancy and Postpartum HIV Testing and Identification of Perinatal and Postnatal HIV Exposure in the Perinatal Guidelines).

Considerations When Initiating Antiretroviral Therapy

The ART regimens that are currently recommended as initial therapy in these guidelines (see What to Start) can suppress and maintain viral loads below the level of quantification in most people who fully adhere to their regimens. Most of the recommended regimens have a low pill burden (one or two pills once daily) and are well tolerated. People with HIV should be assessed for coexisting medical conditions and medications that may influence the selection of ART regimens or require dose adjustments or additional monitoring (see What to Start). Once started on treatment, patients must continue ART indefinitely, although future switches to alternative ART regimens may occur due to adverse events, drug–drug or drug–food interactions, cost, regimen simplification, or other reasons.

Optimizing Adherence, Antiretroviral Therapy Access, and Care Engagement

The key to successfully maintaining viral suppression is continuous access to ART and full adherence to the prescribed regimen. Lack of adherence or intermittent access to ART can result in treatment failure and the emergence of drug resistance mutations that may compromise future treatment options. While optimizing adherence and linkage to care and ensuring continuous access

are critical regardless of the timing of ART initiation, the evidence thus far indicates that drug resistance occurs more frequently in individuals who initiate therapy later in the course of infection than in those who initiate ART earlier.[68-70] It is important to discuss strategies to optimize adherence, care engagement, and ART access with all patients.

Several clinical, behavioral, and social factors have been associated with poor adherence. These factors include untreated psychiatric disorders, neurocognitive impairment, substance use disorder, unstable housing, patient concerns about side effects, difficulty remembering, demanding or irregular daily routines, experiences of HIV-related stigma, and ongoing adjustment to HIV diagnosis. Clinicians should identify areas in which additional intervention is needed to improve adherence both before and after initiation of therapy. Some strategies to improve adherence are discussed in Adherence to the Continuum of Care. However, mental illness, substance use disorder, and psychosocial challenges are not reasons to withhold ART from a patient. Rather, these issues indicate the need for additional interventions to support adherence, and they may influence the ART regimen that is recommended (see What to Start).

Considerations for Special Populations

Elite HIV Controllers

A small subset of people with HIV maintains plasma viral load below the level of quantification for years without ART. These individuals are often referred to as elite HIV controllers.[71,72] Data on the role of ART and the optimal management of elite controllers are sparse, and clinicians should engage in shared decision-making with the elite controller.

Despite the absence of detectable viremia, ongoing HIV replication occurs even in HIV elite controllers. In addition, even with normal CD4 counts, elite controllers show evidence of abnormally high immune activation, chronic inflammation, immune aging, and surrogate markers of atherosclerosis, which may contribute to an increased risk of non-AIDS–related diseases.[71,73-77] One observational multisite study in the United States suggested that elite controllers not receiving ART are hospitalized more often for cardiovascular and psychiatric disease than well-controlled patients on ART.[78] A subsequent observational study did not show an increase in the incidence of hospitalization, but the study population was younger and had a lower incidence of hepatitis C virus (HCV) coinfection than that of the previous study.[79] In additional cohort studies of HIV elite controllers, loss of viral control, older age, and HCV coinfection were independently associated with a higher incidence of non-AIDS–defining events.[79-82]

Elite controllers with preserved CD4 counts appear to experience a decline in immune activation and the size of the HIV reservoir after ART initiation, suggesting that treatment may be beneficial.[77,83] Whether this potential immunologic benefit of ART in elite controllers outweighs the potential risks of ART-associated adverse effects is unclear.[77] Unfortunately, given the very low prevalence of elite controllers, it is unlikely that randomized controlled trials will be able to address this question.[84] Nevertheless, there is a clear rationale for prescribing ART to some elite controllers even in the absence of detectable plasma viral load.

Based on discussions above, the Panel strongly recommends ART for elite controllers with evidence of HIV-related complications, declining CD4 counts, intermittent detectable viral load, or comorbidities (e.g., cardiovascular disease, cancer, hepatitis B virus/HCV coinfection), or for those who are pregnant **(AIII).** The Panel also recommends initiation of ART for all other HIV elite controllers **(BII).** If

ART is deferred, elite controllers should be followed closely, as some may experience CD4 count decline, loss of viral control, or complications related to HIV infection.

Adolescents and Young Adults With HIV

Neither the START trial nor the TEMPRANO trial included adolescents aged <18 years. The Panel's recommendation to initiate ART in all people with HIV is extrapolated to adolescents based on the expectation that they will derive benefits from early ART initiation similar to those observed in adults. However, adolescence is marked by socioemotional, cognitive, and developmental changes that can increase the risk of treatment nonengagement. Compared with adults, adolescents have demonstrated significantly lower levels of ART adherence and viral suppression, as well as higher rates of viral rebound following initial viral suppression.[85] In recent years, more adolescents have been prescribed once-daily regimens, which has increased the rate of viral suppression in this population.[86] Because youth often face psychosocial and other barriers to adherence, their ability to adhere to therapy should be carefully considered when making decisions about ART initiation. Although some adolescents and young adults may not be immediately ready to initiate therapy, clinicians should offer ART, preferably fixed-dose, once-daily regimens with a high barrier to drug resistance, alongside effective interventions to assess and address existing and potential barriers to care and adherence. To optimize the benefits of ART for youths, multidisciplinary care teams should individualize psychosocial and adherence support to adolescents and young adults (see Adolescents and Young Adults With HIV).[87]

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ANTIRETROVIRAL THERAPY TO PREVENT SEXUAL TRANSMISSION OF HIV (TREATMENT AS PREVENTION)

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Reviewed: September 25, 2025

Panel's Recommendations
• All people with HIV should be informed that maintaining a plasma HIV RNA (viral load) of <200 copies/mL, including any measurable value below this threshold value, with antiretroviral therapy (ART) prevents sexual transmission of HIV. This concept may be recognized as Undetectable = Untransmittable or U=U **(AII).** • People with HIV who are starting ART should use another form of prevention with sexual partners (e.g., condoms, sexual abstinence, pre-exposure prophylaxis [PrEP] for the sexual partner who is HIV-negative) for at least the first 6 months of ART and until a viral load of <200 copies/mL has been documented **(AII).** Many experts would recommend confirming sustained suppression before assuming that there is no further risk of sexual transmission of HIV **(AIII).** • When the viral load is ≥200 copies/mL, at least one additional HIV prevention method (e.g., condoms, sexual abstinence, or PrEP for the HIV-negative partner) is recommended to prevent sexual HIV transmission until resuppression to <200 copies/mL is confirmed **(AIII).** • People with HIV who intend to rely on ART as prevention need to maintain high levels of ART adherence **(AIII).** They should be informed that transmission is possible during periods of poor adherence or treatment interruption **(AIII).** • At each visit for HIV care, clinicians should assess adherence to ART and counsel people with HIV on the importance of ART for their own health as well as its role in preventing sexual HIV transmission **(AIII).** • Providers should inform people with HIV that maintaining a viral load of <200 copies/mL does not prevent acquisition or transmission of other sexually transmitted infections (STIs) **(AII).** • Providers should also routinely screen all people with HIV who are sexually active for STIs, both for their own health and to prevent transmission of STIs to others **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Antiretroviral therapy (ART) not only reduces morbidity and mortality for people with HIV but has been definitively shown to prevent sexual transmission of the virus when the plasma HIV RNA (viral load) is consistently suppressed to <200 copies/mL, which includes any measurable viral load that is lower than this threshold value. Providers who manage people with HIV need to be aware of the data supporting treatment as prevention (TasP, which may be recognized as Undetectable = Untransmittable or U=U), its implications, and how to operationalize this prevention strategy in clinical practice. For people with HIV who intend to rely on TasP to prevent sexual transmission, providers should make an individualized assessment that considers the person's risk tolerance, personal health, history of maintaining viral suppression on treatment, and access to health care services and ART, as well as other factors that may affect their ability to maintain a high level of adherence to ART.

Evidence That Viral Load Suppression Prevents Sexual HIV Transmission

Suppressing the HIV viral load to <200 copies/mL with ART prevents sexual transmission of HIV. Observational data collected in the early 1990s from heterosexual couples demonstrated that sexual transmission from untreated people with HIV was rare at viral loads of <1,000 copies/mL to 1,500 copies/mL and that the risk of transmission increased in a dose–response fashion with increasing viral load.[1,2] Additional reports[3-7] and a meta-analysis[8] supported the observation that sexual HIV transmission risk in heterosexual persons was correlated with plasma viral load, and transmission was infrequent below the lowest limits of quantification for the viral load assays used at the time (range <50 to <500 copies/mL).

The first prospective clinical trial designed specifically to address this question was HPTN 052, which randomized people with HIV with CD4 T lymphocyte cell (CD4) count between 350 cells/mm^3 and 550 cells/mm^3 who were in mixed–HIV status relationships (previously referred to as serodiscordant couples) to initiate ART early or to delay initiation. Initial results from this study were reported in 2011,[9] with final results reported in 2016.[10] The 2016 analysis reported that no phylogenetically linked sexual transmissions of HIV occurred among 1,763 couples who were followed a median of 5.5 years, in which the partners with HIV were on ART and had a viral load <400 copies/mL for at least 6 months. Notably, four phylogenetically linked infections occurred within the 90 days after the partner with HIV had started ART and had presumably not yet achieved viral suppression. Four other transmissions occurred after the partner with HIV experienced virologic failure. A number of transmission events occurred that were not phylogenetically linked, indicating acquisition from someone other than the partner enrolled in the study.[11] HPTN 052 was conducted almost exclusively among heterosexual couples who lived in Africa and Asia and did not track the number or type of sexual exposures. In addition, ART was used as an adjunct to a comprehensive prevention package that provided condoms and encouraged condom use, as well as frequent testing for HIV and other sexually transmitted infections (STIs).

Three prospective observational studies—PARTNER 1,[12] PARTNER 2,[13] and Opposites Attract[14]—provided data from more diverse populations of mixed–HIV status couples in which condomless sex was common. Clinical follow-up in these studies closely mimicked that of routine clinical care. Conducted in 14 European countries (PARTNER 1 and PARTNER 2) as well as Australia, Thailand, and Brazil (Opposites Attract), the investigators followed 548 heterosexual and 1,481 male–male mixed–HIV status couples that engaged in 144,631 episodes of condomless vaginal or anal sex while the partner with HIV had a suppressed viral load on ART, defined as <200 copies/mL. In these studies, no phylogenetically linked transmissions were observed; however, as in HPTN 052, there were numerous non-phylogenetically linked transmissions attributed to partners outside the enrolled study couple relationship.

Integrating the Principles of Treatment as Prevention Into Clinical Care

The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends that providers inform all persons with HIV that maintaining an HIV viral load <200 copies/mL with ART prevents sexual transmission of HIV **(AII).** This information may help reduce stigma and provide additional motivation for individuals to get tested, enter into and engage in care, initiate and adhere to ART, and ultimately achieve and maintain viral suppression.[15] Although the PARTNER 1, PARTNER 2, and Opposites Attract trials were designed to follow participants in the study as they would typically be followed in clinical care for HIV, the participants reported high levels of ART adherence at study entry and many reported at least 1 year of condomless sex with an established

sexual partner without transmission. As the principles of TasP are integrated into the clinical management of people with HIV who are on ART, implementation research will be critical to maximize the effectiveness of TasP in practice.

Frequency of Viral Load Assessment

The Panel has issued recommendations for viral load monitoring to manage the health of persons with HIV (see Plasma HIV-1 RNA [Viral Load] and CD4 Count Monitoring). However, current data are insufficient to determine whether these recommendations represent the optimal monitoring schedule for the purpose of preventing sexual transmission of HIV. In the PARTNER and Opposites Attract studies, viral loads were generally assessed every 3 to 6 months during study follow-up, usually during the course of regular HIV care. The Panel recommends a similar frequency for monitoring viral load (every 3–6 months) as in the section of the guidelines **(BII).**

Time to Adequate Suppression After Starting Antiretroviral Therapy

A subgroup analysis from the Partners PrEP Study provided data regarding the risk of HIV transmission during and after the first 6 months on ART for the partner with HIV.[16] This analysis only included the 1,573 heterosexual East African couples in which the partners without HIV were randomized to the placebo arm of the study and were tested monthly for HIV, while the viral load of the partner with HIV was assessed every 6 months. Three phylogenetically linked infections were diagnosed in the 6 months prior to the first follow-up visit for the partners with HIV. The observed incidence rate of 1.79 per 100 person-years during this initial 6-month period after the partner with HIV started ART was slightly less than the 2.08 per person-years incidence rate observed in couples in which the person with HIV was not receiving ART. Viral suppression in this study was defined as <40 copies/mL, and the three infections were diagnosed at 0 days, 56 days, and 149 days after the partner with HIV started ART and before documented viral suppression. After the partners with HIV had been taking ART for ≥6 months, no further transmissions were observed.

At this time, the Panel recommends that people with HIV who are starting ART should use another form of prevention with sexual partners (e.g., consistent condom use, sexual abstinence, pre-exposure prophylaxis [PrEP] for sexual partners without HIV) for at least the first 6 months of treatment and until a viral load of <200 copies/mL has been documented **(AII).** Confirming sustained viral suppression is recommended before assuming that sexual transmission of HIV is no longer a risk **(AIII).**

Adherence to Antiretroviral Therapy

Adherence to ART is paramount for persons who intend to prevent HIV transmission by achieving and maintaining a suppressed viral load. Viral rebound typically occurs within days to weeks after ART cessation and has been observed as early as 3 to 6 days after stopping oral ARV medications.[17-31] The minimum level of adherence that is required to prevent sexual transmission has not been determined and may vary depending on the ART regimen and the route of administration (orally vs. parenterally). In the key studies that defined the efficacy of TasP, adherence levels prior to study entry and during follow-up were very high. In clinical practice, most people who start ART will achieve a viral load <200 copies/mL within 6 months, but maintaining viral suppression can be a challenge for some people, especially for those who have difficulty accessing ART and other HIV care. The Centers for Disease Control and Prevention (CDC) estimates that during 2023, 76.3% of persons aged 13 years or older with HIV were engaged in clinical care, and only 67.2% had viral loads <200 copies/mL at their most recent assessment.[32] Observational cohort data have demonstrated that within the first year of starting ART, up to 10% of persons with HIV can

experience loss of viral suppression; however, the likelihood of maintaining a suppressed viral load generally improves over time. After a few years, typically no more than 5% to 10% of people on ART experience loss of viral suppression.[33-35]

Adherence can be especially challenging for certain groups, such as adolescents and young adults, people with unstable housing, people with active substance use disorder(s), and people who are justice-involved. Recommendations to help manage and maximize ART adherence can be found in Adolescents and Young Adults With HIV. Persons for whom there is concern about adherence also merit counseling on how to properly use other prevention methods, especially barrier methods that prevent STIs.

The Panel recommends that persons with HIV who intend to rely upon TasP be made aware of the need for high levels of ART adherence **(AIII).** The Panel further recommends that adherence be assessed and counseling be provided at each visit for HIV care to reinforce the importance of adherence for the individual's health as well as its role in preventing HIV transmission **(AIII).** People with HIV should be informed that transmission is possible during periods of poor adherence or treatment interruption **(AIII).**

Managing Transient Viremia, or "Blips"

Occasionally, some people who are highly adherent may experience intermittent or transient viremia, commonly termed "viral blips." Blips are defined in the context of effective treatment as a single, measurable HIV RNA level, typically <200 copies/mL, that is followed by a return to a viral load below the limit of detection or quantification. With some earlier ART regimens, up to 16% of persons per year who are adherent to ART may experience a blip.[36-39] Most blips likely represent normal biological fluctuation (i.e., variation around a mean undetectable viral load) or laboratory artifact and not inadequate adherence.[40-42] Persistent viremia ≥200 copies/mL has been associated with increasing risk of virologic failure[36,39,43-46] that, in the context of TasP, can lead to increased risk of sexual transmission of HIV.[10] The PARTNER and Opposites Attract studies excluded observation time when the viral load of the participant with HIV was ≥200 copies/mL. The frequency of blips <200 copies/mL was not reported in Opposites Attract; however, in PARTNER 1 and PARTNER 2, transient elevations in viral loads >50 copies/mL but <200 copies/mL were observed for 6% and 4% of the total follow-up time, respectively, during which time no phylogenetically linked infections were observed.

One of the clinical challenges with blips is that they can only be defined retrospectively once the viral load has returned to a suppressed value. The Panel recommends that any time the viral load is ≥200 copies/mL, people with HIV and their sexual partners should be counseled to use another form of prevention (e.g., condoms, pre-exposure prophylaxis for sexual partners without HIV, sexual abstinence) to protect against HIV transmission until a viral load <200 copies/mL is achieved and sustained **(AII).** This recommendation applies both to persons who are starting ART (as noted earlier) and to those who have been taking ART and have achieved viral suppression but develop viral loads ≥200 copies/mL.

In cases where a person achieves resuppression to <200 copies/mL after a detectable viral load ≥200 copies/mL (e.g., blips, viremia), or when a person with a viral load <200 copies/mL switches regimens (e.g., for regimen simplification or to avoid certain side effects), providers should follow situation-specific viral load monitoring recommendations **(AIII)** (see Plasma HIV-1 RNA [Viral Load] and CD4 Count Monitoring). There are presently no data to guide how long, if at all, a person might need to continue to use another form of prevention in these two circumstances. Individualized assessment is recommended based on the length and quality of adherence and time with viral load <200 copies/mL preceding the viral load ≥200 copies/mL.

Effect of Sexually Transmitted Infections on Treatment as Prevention

The presence of STIs in a person with HIV does not appear to meaningfully alter the risk of sexual transmission when the person's viral load is <200 copies/mL. The PARTNER studies and the Opposites Attract study regularly assessed participants for STIs, which were diagnosed in 6% of heterosexual participants and 13% to 27% of men who have sex with men. Although the authors of the studies noted that their findings could not rule out the possibility that STIs in participants with viral loads <200 copies/mL might affect the risk of HIV transmission, when viewed collectively, these data suggest that any effect is very small, since STIs were common and no linked HIV transmissions were observed. The Panel recommends that patients using TasP be informed that maintaining a viral load of <200 copies/mL does not prevent acquisition or transmission of other STIs, and that it is not a substitute for condoms or behavioral modifications **(AII).** Providers should also routinely screen all sexually active persons with HIV for STIs, both for their own health and to prevent transmission of STIs to others **(AIII).** Refer to the CDC's Sexually Transmitted Infections Treatment Guidelines for details.

Treatment as Prevention Applies Only to Sexual Transmission of HIV

Available clinical data only support the use of TasP to prevent sexual HIV transmission in patients with viral loads <200 copies/mL. The effectiveness of this strategy in preventing transmission from blood exposure has not been determined. In addition, while suppression of maternal viral load substantially reduces the risk of perinatal transmission and transmission through breastfeeding, it does not eliminate these risks, and transmission has occurred via breastfeeding despite continuous viral suppression (refer to the Perinatal Guidelines for details).

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WHAT TO START: INITIAL COMBINATION ANTIRETROVIRAL REGIMENS FOR PEOPLE WITH HIV

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Introduction

More than 30 antiretroviral (ARV) drugs in nine mechanistic classes are U.S. Food and Drug Administration (FDA)–approved for treatment of HIV infection. These nine classes include nucleos(t)ide reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase strand transfer inhibitors (INSTIs), a fusion inhibitor, a CCR5 antagonist, a CD4 T lymphocyte (CD4) cell post-attachment inhibitor, a gp120 attachment inhibitor, and a capsid inhibitor. In addition, two drugs—ritonavir (RTV) and cobicistat (COBI)—are used as pharmacokinetic (PK) enhancers (or boosters) to improve the PK profiles of PIs and the INSTI elvitegravir (EVG).

Over time, incremental improvements in potency, tolerability, safety, convenience, drug interactions and genetic barriers to the emergence of drug resistance have led to streamlined recommendations for initial ARV regimens for most people with HIV. The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) now recommends initial ARV regimens based on an oral second-generation INSTI plus two NRTIs—bictegravir (BIC)/tenofovir alafenamide (TAF)/emtricitabine (FTC) **(AI)** or dolutegravir (DTG) plus TAF/FTC or tenofovir disoproxil fumarate (TDF)/ FTC or TDF/lamivudine (3TC) **(AI)**—for most people with HIV. In some people with HIV, the two-drug regimen DTG/3TC can be used **(AI).** When INSTI resistance is possible, such as after exposure to long-acting injectable cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP) and/or if INSTI genotype results are not yet available, a boosted PI (boosted darunavir [DRV]) in combination with two NRTIs (TAF or TDF with FTC or 3TC) is recommended **(AIII).** The Panel's recommendations are summarized in Tables 6a and 6b.

Table 6a. Recommended Initial Regimens for Most People With HIV

Selection of antiretroviral therapy (ART) should be based on the regimen's virologic efficacy, potential adverse effects, pill burden, dosing frequency, drug–drug interaction potential, cost, access, resistance test results, and the comorbid condition of the person with HIV. A pregnancy test should be performed in women of childbearing potential, and choice of ART for pregnant women should be guided by recommendations from the Perinatal Guidelines. Drug classes and regimens within each class are arranged first by evidence rating and, when ratings are equal, in alphabetical order. Additional initial ARV regimen options for certain clinical scenarios are listed in Table 6b below.

Table 6a. Recommended Initial Regimens for Most People With HIV

Table 6a. Recommended Initial Regimens for Most People With HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. Choice of ART during pregnancy should be guided by recommendations from the Perinatal Guidelines.

For people who do not have a history of using CAB-LA as PrEP, one of the following regimens is recommended[a]:

- BIC/TAF/FTC **(AI)**
- DTG plus (TAF or TDF)[b] plus (FTC or 3TC) **(AI)**
- DTG/3TC **(AI),** except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.

For people who have a history of CAB-LA use as PrEP, INSTI genotype resistance testing should be performed before starting ART. If ART is to be started before results of genotypic testing results, the following regimen is recommended:

- DRV/c[c] or DRV/r with (TAF or TDF)[b] plus (FTC or 3TC)—pending the results of the genotype test **(AIII)**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion*

[a] Because of the current low rates of transmitted INSTI resistance in the United States, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started pending the results of the INSTI genotype.

[b] TAF and TDF are two forms of TFV approved by the U.S. Food and Drug Administration. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

[c] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters. For further information, refer to the Perinatal Guidelines.

Note: The following are available as coformulated drugs: BIC/TAF/FTC, DRV/c/TAF/FTC, DTG/3TC, TAF/FTC, TDF/3TC, and TDF/FTC.

Key: 3TC = lamivudine; ART = antiretroviral therapy; BIC = bictegravir; CAB-LA = long-acting cabotegravir; COBI = cobicistat; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; HBV = hepatitis B virus; INSTI = integrase strand transfer inhibitor; PrEP = pre-exposure prophylaxis; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Table 6b. Other Initial Antiretroviral Regimens for Certain Clinical Scenarios

Several antiretroviral regimens are found to be effective and tolerable as initial regimens but have some disadvantages or have fewer supporting data from randomized clinical trials compared with the recommended regimens listed in Table 6a. However, one of these regimens may be preferred for an individual with HIV in certain clinical situations (also see Table 7). These regimens are listed below.

Type of Regimen	ARV Regimen	For Certain Clinical Scenarios	Other Considerations
INSTI Plus Two NRTIs	DTG/ABC/3TC **(BI)** (if HLA-B*5701-negative)	When concern about renal- or bone-associated AEs precludes the use of TDF or TAF	Test for HLA-B*5701 before prescribing ABC; do not prescribe if HLA-B*5701-positive. Consider avoiding ABC for people with multiple CV risk factors or known CV disease. Do not use in people with HBV coinfection unless an HBV-active drug, such as entecavir, TAF, or TDF is also used. Do not use following exposure to CAB-LA unless INSTI genotype shows sensitivity.
Boosted PI Plus Two NRTIs	(DRV/c[a] or DRV/r) plus (TAFor TDF[b]) plus (FTC or 3TC) **(BI)**	To avoid an INSTI-based regimen (e.g., documented INSTI resistance).	Assess for potential RTV- or COBI-related DDIs.
	(DRV/c[a] or DRV/r) plus ABC/3TC **(BII)** (if HLA-B*5701-negative)	To avoid an INSTI-based regimen (e.g., with suspected or documented INSTI resistance), *and* When concern about renal or bone-associated AEs precludes the use of TDF or TAF	Test for HLA-B*5701 before prescribing ABC; do not prescribe if HLA-B*5701-positive. Consider avoiding ABC for people with multiple CV risk factors or known CV disease. Do not use in people with HBV coinfection unless used with an HBV-active drug other than 3TC. Assess for potential RTV- or COBI-related DDIs.

Table 6b. Other Initial Antiretroviral Regimens for Certain Clinical Scenarios

Type of Regimen	ARV Regimen	For Certain Clinical Scenarios	Other Considerations
NNRTI Plus Two NRTIs	DOR/TDF/3TC[b] **(BI)** or DOR plus TAF/FTC[b] **(BIII)**	To avoid an INSTI-based regimen (e.g., with suspected or documented INSTI resistance), *and* To avoid a PI-based regimen (e.g., with significant DDIs with concomitant medications)	
	RPV/TAF/FTC **(BII)** Only if HIV RNA <100,000 copies/mL **and** CD4 count >200 cells/mm^3	To avoid an INSTI-based regimen (e.g., with suspected or documented INSTI resistance), *and* To avoid a PI-based regimen (e.g., with significant DDIs with concomitant medications), *and* When a single-tablet regimen containing an NNRTI and TAF is desired	Cannot take with PPI; space apart from H2 antagonist. Needs to be taken with a meal.
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion*			

[a] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been observed during the second and third trimesters. For further information, refer to the Perinatal Guidelines.

[b] TAF and TDF are two forms of TFV approved by the U.S. Food and Drug Administration. TAF has fewer bone and kidney toxicities than TDF, while TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

Note: The following are available as coformulated drugs: ABC/3TC, DOR/TDF/3TC, DRV/c, DRV/c/TAF/FTC, DTG/ABC/3TC, RPV/TAF/FTC, TAF/FTC, TDF/3TC, and TDF/FTC.

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse event; ARV = antiretroviral; CD4 = CD4 T lymphocyte; COBI = cobicistat; CV = cardiovascular; DDI = drug–drug interaction; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; H2 = histamine type 2; HBV = hepatitis B virus; HLA = human leukocyte antigen; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Supporting Evidence and Rationale Used for the Panel's Recommendations

The Panel's recommendations are primarily based on clinical trial data published in peer-reviewed journals and on data prepared by drug manufacturers for FDA review. In select cases, the Panel considers data from abstracts presented at major scientific meetings. The Panel considers published

information from randomized prospective clinical trials with adequate sample size that demonstrate that an ARV regimen produces high rates of viral suppression, increases CD4 count, and has a favorable safety profile to be the strongest evidence on which to base recommendations. Comparative clinical trials of initial treatments generally are not designed to show significant differences in HIV-related clinical endpoints (such as progression to AIDS-defining conditions) or survival. Thus, the assessment of regimen efficacy and safety is primarily based on surrogate marker endpoints (i.e., rates of HIV RNA suppression) and the incidence and severity of adverse events.

In some instances, the Panel recommends regimens that include ARV drugs approved by the FDA based on bioequivalence or relative bioavailability studies that demonstrate that the exposure of the drug(s) in the new formulation or combination is comparable to the exposure of a reference drug(s) that has demonstrated safety and efficacy in randomized clinical trials. When developing recommendations, the Panel may also consider data from randomized switch studies in which a drug in an ARV initial regimen that suppressed patients' viral loads is replaced by a new drug from the same class. Switch trials do not evaluate the ability of a drug or regimen to induce viral suppression; they only examine the drug or regimen's ability to maintain suppression. Therefore, results from switch trials may not be directly applicable to the selection of an initial regimen and should be considered in conjunction with other data, including data from bioavailability/bioequivalence studies and from trials conducted in people taking their first ARV treatment regimen. In this section of the guidelines, the definition of an evidence rating of **II** is expanded to include supporting data from bioavailability/bioequivalence studies or randomized switch studies.

When developing recommendations, the Panel also considers tolerability and toxicity profiles, pill burden and dosing frequency, drug interaction potential, cost and access, postmarketing safety data, observational cohort data published in peer-reviewed publications, the experience of clinicians who are actively engaged in patient care, and the views of community members.

The Panel reviewed the available data to arrive at two classifications for initial ARV treatment regimens: (1) *Recommended Initial Regimens for Most People With HIV* (Table 6a) and (2) *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b). *Recommended Initial Regimens for Most People With HIV* are those regimens with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use. The Panel also recognizes that in certain clinical situations, other regimens may be preferred; these options are included in Table 6b. See Table 7 for examples of clinical scenarios in which certain drugs in these regimens may be particularly advantageous.

Many other ARV regimens are effective for initial therapy but have disadvantages when compared with the regimens listed in Tables 6a and 6b. These disadvantages include greater toxicity, higher pill burden, less supporting data from large comparative clinical trials, and limitations for use in certain populations. These regimens are no longer included in Tables 6a and 6b. For people with HIV who have a suppressed viral load and are not experiencing any adverse effects while on a regimen that is not listed, changing to a regimen listed in Table 6a or 6b is not necessary. Clinicians should refer to Optimizing Antiretroviral Therapy in the Setting of Viral Suppression for further guidance if switching to a new regimen is desired.

Several tables in these guidelines provide clinicians with guidance on selecting and prescribing an optimal regimen for a person with HIV. Table 7 provides information on considerations based on specific clinical scenarios and ARV drug characteristics. Table 9 lists the potential advantages and disadvantages of the different ARV drug components. Appendix A, Tables 3–10, lists characteristics of individual ARV agents for initial therapy (e.g., formulations, dosing recommendations, PK, common adverse effects). Appendix B provides ARV dosing recommendations for people who have renal or hepatic insufficiency.

Changes Since the Last Revision of the Guidelines

Since the last revision of these guidelines, the Panel has made several important changes to the recommendations for initial therapy in people with HIV. Among these changes, the following deserve emphasis:

Changes in the Panel's Recommendations for Initial Regimens in Most People With HIV:

- The single-tablet regimen (STR) DTG/abacavir (ABC)/3TC has moved from *Recommended Initial Regimens for Most People With HIV* (Table 6a) to *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b) due to the necessity of obtaining an HLA-B*5701 assay to avoid ABC-associated hypersensitivity, data suggesting increased risk for cardiovascular events associated with ABC, and the availability of several other options for initial therapy (see the Nucleoside Reverse Transcriptase Inhibitor Options as Part of Initial Therapy section for more information).
- Because of the current low rates of transmitted INSTI resistance in the United States, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started pending the results of the INSTI genotype test.

No Longer Recommended as Initial Antiretroviral Regimens:

- Raltegravir (RAL)-, elvitegravir/cobicistat (EVG/c)-, boosted atazanavir (ATV)-, and efavirenz (EFV)-based regimens and rilpivirine (RPV)/TDF/FTC are no longer recommended as initial therapy due to the following disadvantages compared with other regimens:
  - RAL: Low genetic barrier to resistance and higher pill burden
  - EVG/c: Drug–drug interactions with COBI and low genetic barrier to resistance of EVG
  - Boosted ATV: Toxicities, including hyperbilirubinemia, and drug–drug interactions
  - EFV: Toxicities, including neuropsychiatric effects and suicidality; low barrier to resistance; and drug–drug interactions
  - RPV/TDF/FTC: Availability of doravirine (DOR)/TDF/3TC as an STR, more drug–drug interactions than DOR, food restrictions, and HIV RNA and CD4 restrictions. RPV/TAF/3TC remains an option for those who wish to use an STR containing RPV and TAF
- The two-drug regimens darunavir/ritonavir (DRV/r) plus RAL and DRV/r plus 3TC are no longer recommended for initial therapy.
  - DRV/r plus RAL is not recommended due to the higher rate of virologic failure in people with HIV RNA >100,000 copies/mL, the low genetic barrier to resistance, and the high pill burden of RAL.[1-3]
  - DRV/r plus 3TC is not recommended because it requires a PK booster with accompanying drug interactions, and published clinical trial data are lacking.[4] For further information, see Other Antiretroviral Regimens for Initial Therapy.

Selecting an Initial Antiretroviral Regimen

The goal of ART is to improve health and prolong life for people with HIV and to prevent the transmission of HIV to others by maximizing virologic suppression. This is achieved by initiating therapy with a potent, safe, tolerable, and easy-to-adhere-to ARV regimen as soon as possible after diagnosis. Table 6a provides a list of Panel-recommended ARV regimens for most people with HIV. Some factors listed below may influence the selection of a regimen. See Table 6b and Table 7 for additional regimen recommendations to use in specific clinical scenarios.

Initial Characteristics to Consider in All People With HIV

- Pre-treatment HIV RNA level (viral load)
- Pre-treatment CD4 count
- History of prior exposure to CAB-LA or oral TDF/FTC or TAF/FTC as PrEP, or use of INSTI-based post-exposure prophylaxis (PEP)
- Suspected drug resistance (prior to availability of genotypic testing results)
- HIV genotypic drug resistance test results
  - Genotypic drug resistance testing in people without prior ARV exposure should focus on testing for mutations in the reverse transcriptase and protease genes.
  - If transmitted INSTI resistance is a concern, providers should also test for resistance mutations to this class of drugs.
- Individual preferences
- Anticipated adherence to the regimen

Presence of Specific Conditions

- Comorbid conditions: Cardiovascular disease; hyperlipidemia; renal disease; liver disease; osteopenia, osteoporosis, or other conditions associated with bone mineral density loss; psychiatric illness; neurologic disease; substance use disorder requiring narcotic replacement therapy
- Coinfections: Hepatitis B virus (HBV), hepatitis C virus, tuberculosis
- Pregnancy and potential for pregnancy: See below in General Considerations for Women of Childbearing Potential Initiating Antiretroviral Therapy

Regimen-Specific Considerations

- Regimen's barrier to resistance
- HLA-B*5701 status (only for those considering initiation of ABC). Those who are HLA-B*5701 positive should not receive ABC. See Table 7 for regimens to initiate.
- Potential adverse effects and drug toxicities, including risk for the development of comorbid diseases
- Known or potential drug interactions with other medications (see Drug–Drug Interactions)
- Convenience (e.g., pill burden, dosing frequency, availability of a fixed-dose combination or of STR formulations, food requirements)
- Cost and access (see Cost Considerations and Antiretroviral Therapy)

Considerations for People With Prior Use of Pre- or Post-Exposure Prophylaxis

- For people who acquired HIV after taking oral PrEP with TAF/FTC or TDF/FTC, there is concern for transmitted resistance, especially related to FTC or 3TC with the M184V/I mutation. In a cohort of people in New York City with newly diagnosed HIV, 2% had the M184V/I mutation. People who had used prior oral PrEP were four to seven times more likely to harbor resistance

than people who had never used oral PrEP.[5] This reinforces the Panel's recommendation not to initiate DTG/3TC without the results of genotypic resistance testing.

- For people who acquired HIV after exposure to CAB-LA as PrEP, there is concern for INSTI resistance. CAB-LA may remain detectable after treatment discontinuation for up to 3 years in men and 4 years in women.[6] This long PK tail may contribute to the selection of drug-resistant variants in the setting of incident infection. In the HPTN 083 trial of CAB-LA as PrEP in cisgender men and transgender women, 10 of 32 people who acquired HIV after exposure to CAB-LA were found to harbor major INSTI resistance mutations.[7] This is the basis for the Panel's recommendation to obtain INSTI genotypic drug resistance testing in people with prior CAB-LA exposure and not to initiate INSTIs before these results are available and show INSTI sensitivity. If therapy is initiated before INSTI sensitivity is confirmed, the Panel recommends initiating a boosted DRV regimen with TAF/FTC or TDF/FTC while awaiting INSTI genotype results; once INSTI sensitivity is confirmed by genotypic resistance testing, a switch to an INSTI-based regimen can occur **(AIII).**
- For people with no history of using CAB-LA for PrEP and who acquire HIV despite INSTI-based PEP use, an INSTI genotype should be obtained prior to beginning an INSTI-based regimen. However, because selection of INSTI-resistant virus is likely to be uncommon in this setting, an INSTI-based regimen could be started prior to the return of genotype results **(CIII).** This recommendation is based largely on theoretical concerns that INSTI resistance could occur in the setting of INSTI-based PEP failure, but it is likely to be uncommon. In addition, transmitted INSTI resistance remains low in the United States. For these reasons, the Panel supports using INSTI-based regimens in this setting.

General Considerations for Women of Childbearing Potential Initiating Antiretroviral Therapy

- A pregnancy test should be performed before initiating ART.
- Clinicians should discuss intentions regarding pregnancy with all women of childbearing potential.
- People with HIV should attain maximum viral suppression before attempting conception in order to protect their own health, prevent sexual HIV transmission to partners without HIV, and minimize the risk of perinatal HIV transmission to the infant.
- For individuals who are trying to conceive, the Panel recommends initiating a regimen designated as a *Preferred* regimen during pregnancy, as detailed in the Perinatal Guidelines.

General Considerations for INSTI-, PI-, or NNRTI-Based Regimens

Except when HIV is acquired after exposure to CAB-LA as PrEP and results from INSTI genotypic resistance testing are not available, INSTIs (specifically BIC and DTG) are recommended for initial therapy in most people because of their demonstrated efficacy, high barrier to resistance, tolerability, low potential for drug–drug interactions, convenience, and better adverse effects profile compared with NNRTIs and boosted PIs (see Tables 7 and 9).

INSTI-Based Regimens

The Panel's *Recommended Initial Regimens for Most People With HIV*, as listed in Table 6a, include one of two INSTIs: BIC coformulated with TAF/FTC **(AI);** or DTG plus TAF or TDF plus FTC or 3TC **(AI);** or coformulated DTG/3TC **(AI)** for people who have not had exposure to CAB-LA as PrEP. In those with prior exposure to CAB-LA as PrEP, these regimens should not be initiated unless a

recent genotype test result showing no INSTI resistance mutations is available. If an INSTI-based regimen is initiated and viral suppression is not achieved in 8 to 12 weeks, genotypic resistance testing should be repeated, including for INSTIs.

For most people, these INSTI-containing regimens will be highly effective and have relatively infrequent treatment-limiting adverse effects and few drug interactions. In several head-to-head comparisons between boosted PI- and INSTI-containing regimens, the INSTI-based regimens were better tolerated and caused fewer treatment discontinuations.[8-10]

The Panel recommends a two-drug regimen of DTG/3TC for initial therapy if certain criteria are met. Data from two randomized trials showed that, in terms of virologic efficacy, DTG plus 3TC was non-inferior to a three-drug regimen of DTG plus TDF/FTC. No treatment-emergent resistance was seen in either the two-drug or the three-drug group.[11] Based on these data, DTG/3TC is not currently recommended for rapid ARV initiation as initial therapy before the availability of HBV serology, HIV RNA level, and an HIV genotypic test demonstrating sensitivity to 3TC.

Among the INSTI-based regimens, BIC- and DTG-containing regimens have a higher barrier to resistance than the first-generation INSTI-based regimens containing EVG or RAL and do not require a PK booster. Transmitted resistance to BIC or DTG is rare. Treatment-emergent resistance has been reported in individuals who failed three-drug DTG-based therapy[12-15] and BIC-based regimens.[16-19] Because of this high barrier to resistance and tolerability, BIC- and DTG-containing regimens may be used in people who have not previously used CAB-LA for PrEP and plan to start ART before resistance testing results are available (e.g., with rapid initiation of ART after diagnosis). BIC-based regimens have been shown to be non-inferior to DTG-based regimens in clinical trials.[20-22]

There are data suggesting greater weight gain after initiating therapy with certain INSTI-based regimens and TAF than with other ARV drugs. The reasons for differences in weight gain are unclear and should not be a reason to withhold an INSTI- or TAF-based regimen.[23-30]

EVG- and RAL-based regimens have the disadvantage of having lower barriers to resistance than DTG- or BIC-containing regimens and therefore are no longer recommended as initial therapy. Additionally, the pill burden with RAL is higher than for other INSTI-based regimens whereas EVG-based regimens have a greater potential for drug interactions because EVG is combined with COBI, a strong cytochrome P3A4 inhibitor (see Table 7).

PI-Based Regimens

In the setting of HIV acquisition following CAB-LA exposure, an RTV- or COBI-boosted DRV regimen containing TAF or TDF plus FTC or 3TC is recommended as initial therapy if a genotypic drug resistance test indicating INSTI sensitivity is not available at the time of ART initiation **(AIII),** if resistance to INSTI is confirmed **(BI),** or in certain clinical situations, such as when INSTIs must be avoided **(BI).** DRV/c/TAF/FTC is available as an STR. Large observational cohorts found an association between some PIs, including DRV/r, and an increased risk of cardiovascular events; however, further study is needed.[31-36] COBI-boosted regimens should not be initiated during pregnancy because of inadequate drug levels. Boosted ATV is no longer recommended as initial therapy due to frequent adverse events (e.g., hyperbilirubinemia) and high rates of drug–drug interactions, including with tenofovir and acid-suppressive therapy.

Boosted ATV is no longer recommended as initial therapy due to frequent adverse events, such as hyperbilirubinemia and higher rates of drug–drug interactions (including with tenofovir and acid-suppressive therapy) compared to boosted DRV.

NNRTI-Based Regimens

NNRTI-based regimens are not recommended for initial therapy in most people with HIV, but selected regimens may be useful in some circumstances. The NNRTI-based regimens that are currently recommended by the Panel to be used in certain clinical scenarios include DOR/TDF/3TC **(BI),** DOR plus TAF/FTC **(BIII),** and RPV/TAF/FTC **(BII).** The emergence of drug resistance at the time of virologic failure has been reported with all NNRTIs, which generally have a lower barrier to resistance than INSTIs or boosted PIs.

DOR is available both as a single-drug tablet to be used with two NRTIs and as part of an STR with TDF/3TC. In randomized trials, DOR was non-inferior to both EFV and DRV/r when either of these drugs was taken in combination with two NRTIs,[37,38] but DOR has not yet been compared against INSTIs. DOR has fewer central nervous system (CNS) side effects than EFV and more favorable lipid effects than both DRV/r and EFV. DOR also has fewer potential drug interactions than EFV or RPV, and unlike RPV, the virologic efficacy of DOR is not compromised in people with high HIV RNA levels and low CD4 counts.

RPV has fewer adverse effects than EFV, and RPV/TAF/FTC is available as one of the smallest tablet sizes among STRs. However, RPV has lower virologic efficacy in people with baseline HIV RNA levels >100,000 copies/mL and CD4 counts <200 cells/mm^3 and is subject to numerous drug–drug interactions.[39] EFV is no longer recommended for initial therapy due to a relatively high rate of CNS-related side effects, reported suicidality, high rates of drug discontinuation, and numerous drug–drug interactions.

Regimens When Abacavir, Tenofovir Alafenamide, and Tenofovir Disoproxil Fumarate Cannot Be Used or Are Not Optimal

In people in whom ABC, TDF, or TAF cannot be used or are not optimal, only DTG/3TC is recommended by the Panel **(AI).** Several other NRTI-sparing/limiting two-drug regimens have been evaluated in clinical trials but are not currently recommended for initial therapy due to insufficient data. For more information on these regimens, see Other Antiretroviral Regimens for Initial Therapy. Two-drug ARV options **should not be used** in pregnancy due to insufficient data, or in those with known pre-existing resistance to any of the ARVs in the combination. Tenofovir-sparing regimens **should not be used** in individuals with HBV coinfection unless a drug with HBV activity (i.e., entecavir) is also used.

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Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

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This table guides clinicians in choosing an initial antiretroviral (ARV) regimen according to various patient and regimen characteristics and specific clinical scenarios. ARV drugs/regimens that are listed in Table 6a as *Recommended Initial Regimens for Most People With HIV* and in Table 6b as *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* are included in this table (see Initial Combination Antiretroviral Regimens for People With HIV). When more than one scenario applies to a person with HIV, clinicians should review considerations for each relevant scenario and use their clinical judgment to select the most appropriate regimen. Please see Table 9 for additional information regarding the advantages and disadvantages of particular ARV medications recommended to be used as initiation therapy.

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
Pre-ART Characteristics	CD4 count <200 cells/mm^3	**Do not use** RPV-based regimens.	Higher rates of virologic failure have been observed in those with low pre-treatment CD4 counts.
	HIV RNA >100,000 copies/mL (also see next row if HIV RNA >500,000 copies/mL)	**Do not use** RPV-based regimens.	Higher rates of virologic failure have been observed in those with high pre-treatment HIV RNA levels.
	HIV RNA >500,000 copies/mL	**Do Not Use** the Following Regimens: • RPV/TAF/FTC • DTG/3TC	For DTG/3TC, limited data are available in patients with viral loads above this threshold.
	HLA-B*5701 positive or result unknown	**Do not use** ABC-containing regimens.	ABC hypersensitivity is a potentially fatal reaction that is highly associated with the HLA-B*5701 allele.
	Prior exposure to oral TDF/(3TC or FTC) or TAF/3TC PrEP	Use DTG or BIC plus two NRTIs. DTG/3TC could be considered if testing confirms no 3TC resistance mutations.	DTG/3TC should be avoided if resistance testing results are not available, as presence of 3TC resistance mutations may lead to use of DTG monotherapy.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	Prior exposure to CAB-LA for PrEP	INSTI genotype resistance testing should be performed. **If INSTI Resistance Is Present or If ART Needs to Be Started Before Genotype Test Results** • (DRV/r or DRV/c) plus (TAF or TDF)[a] plus (3TC or FTC) **If No INSTI Resistance Is Identified** • BIC/TAF/FTC, *or* • DTG plus (TAF or TDF)[a] plus (3TC or FTC)	Mutations conferring resistance to INSTIs have been seen in association with CAB-LA PrEP. CAB-LA has a very long half-life, and drug exposure may persist at levels suboptimal to prevent infection and may select for INSTI-resistant virus.
	People with **no prior exposure** to CAB-LA for PrEP and ARV regimen should be started rapidly and before HIV drug resistance results are available.	**Avoid** ABC, DTG/3TC, and NNRTI-based regimens. **Use** • BIC/TAF/FTC, *or* • DTG plus (TAF or TDF)[a] plus (3TC or FTC) **In People Who Used INSTI-Based ART for PEP or Who Are Suspected to Have Acquired HIV From Someone Failing an INSTI-Based Regimen** • Obtain INSTI genotypic resistance test and start one of the following regimens: ○ BIC/TAF/FTC, *or* ○ DTG plus (TAF or TDF)[a] plus (3TC or FTC)	Transmitted mutations conferring NNRTI and NRTI resistance are more likely than mutations associated with PI or INSTI resistance. HLA-B*5701 results may not be available rapidly; thus, ABC is not recommended. Because of the current low rates of transmitted INSTI resistance in the United States, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started, pending the results of the INSTI genotype.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
ART-Specific Characteristics	A one-pill, once-daily regimen is desired.	**STR Options as Initial ART Include the Following:** • BIC/TAF/FTC • DOR/TDF/3TC • DRV/c/TAF/FTC • DTG/ABC/3TC • DTG/3TC • RPV/TAF/FTC	**Do not use** DTG/ABC/3TC if the patient is HLA-B*5701 positive. DTG/3TC **is not recommended** if HIV RNA is >500,000 copies/mL. **Do not use** DTG/ABC/3TC or DTG/3TC in the setting of HBV coinfection without another HBV agent. **Do not use** RPV/TAF/FTC if HIV RNA is >100,000 copies/mL and CD4 count is <200 cells/mm^3.
	Food effects	**Regimens That Can Be Taken Without Regard to Food** • BIC-, DOR-, or DTG-based regimens	Oral bioavailability of these regimens is not significantly affected by food.
		Regimens That Should Be Taken With Food • DRV/r- or DRV/c-based regimens • RPV/TAF/FTC	Food improves absorption of these regimens. RPV-containing regimens should be taken with ≥390 calories of food.
Presence of Other Conditions	Chronic kidney disease (defined as CrCl <60 mL/min)	In general, **avoid TDF.** For patients with progressively declining renal function, consider avoiding all TFV-containing (TAF or TDF) regimens. Refer to Appendix B for specific ARV drug dosing recommendations in patients with renal impairment.	TDF has been associated with proximal renal tubulopathy. Higher rates of renal dysfunction have been reported in patients using TDF in conjunction with RTV-containing regimens. TAF has less impact on renal dysfunction than TDF. Avoid the use of TDF- or TAF-sparing regimens in the setting of HBV coinfection or unknown HBV status unless also receiving a fully active HBV regimen (see Hepatitis B Virus/HIV Coinfection).

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	Liver disease with cirrhosis	Some ARVs are contraindicated or may require dosage modification in patients with Child-Pugh class B or C disease.	Refer to Appendix B for specific dosing recommendations. Patients with cirrhosis should be carefully evaluated by an expert in advanced liver disease.
	Concern for weight gain	For many people with HIV, gaining weight after starting ART is part of a "return to health." However, some ARV regimens are associated with greater weight increase than others.	Reasons for differences in weight gain among ART regimens are unknown. **Note:** Weight gain should not be a reason to avoid taking an INSTI-based regimen.
	Osteoporosis	**Avoid TDF.**[a]	TDF is associated with decreases in BMD, along with renal tubulopathy, urine phosphate wasting, and resultant osteomalacia. TAF[a] and ABC are associated with smaller declines in BMD than TDF.
	Psychiatric illnesses	**Consider avoiding** RPV-based regimens. Patients on INSTI-based regimens who have preexisting psychiatric conditions should be closely monitored. Some ARVs are contraindicated, and some psychiatric medications need dose adjustments when coadministered with certain ARVs.	RPV can exacerbate psychiatric symptoms and may be associated with suicidality. Some INSTIs have been associated with adverse neuropsychiatric effects in some retrospective cohort studies and case series. See the drug–drug interaction tables (Tables 24a, 24b, 24d, and 24g) for dosing recommendations when drugs used for psychiatric illnesses are used with certain ARVs.
	Cardiac QTc interval prolongation	Consider avoiding RPV-based regimens if the patient is taking other medications with known risk of Torsades de Pointes or in patients at higher risk of Torsades de Pointes.	High RPV concentrations may cause QTc prolongation.

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	High risk for CV events	Consider avoiding ABC-based regimens. Refer to Hyperlipidemia, below, for regimens associated with more favorable lipid profiles.	An increased risk of CV events with ABC has been observed in some, but not all, studies. Certain ARV regimens are associated with more favorable lipid profiles than other regimens.
	Hyperlipidemia	PI/c and PI/r have been associated with hyperlipidemia. BIC, DOR, DTG, and RPV have fewer lipid effects.	TDF has been associated with lower lipid levels than ABC or TAF.
	Patients with history of poor adherence to non-ARV medications or inconsistent engagement in care	Consider using regimens with a boosted PI or BIC or DTG.	These regimens have a high genetic barrier to resistance.
	Pregnancy	Refer to the Perinatal Guidelines for further guidance on ARV use during pregnancy.	
Presence of Coinfections	HBV infection	**Avoid regimens** that do not contain NRTIs. Use (TDF or TAF) with (FTC or 3TC) as part of the ARV regimen. **If TDF and TAF Are Contraindicated** • For treatment of HBV, use FTC or 3TC with entecavir and a suppressive ARV regimen (see Hepatitis B Virus/HIV Coinfection).	TDF, TAF, FTC, and 3TC are active against both HIV and HBV. 3TC- or FTC-associated HBV resistance mutations can emerge when these drugs are used without another drug that is active against HBV.
	HCV treatment required	Refer to recommendations in Hepatitis C Virus/HIV Coinfection, with special attention to potential interactions between ARV drugs and HCV drugs.	

Table 7. Antiretroviral Regimen Considerations for Initial Therapy Based on Specific Clinical Scenarios

Patient or Regimen Characteristics	Clinical Scenario	Consideration(s)	Rationale/Comments
	Concomitant use with rifamycin antibiotics (e.g., rifabutin, rifampin, and rifapentine)	Recommended regimens may require dose adjustment. See the drug–drug interaction tables (Tables 24a, 24b, 24c, 24d, 24e, 24f, 24g, 25a, and 25b) and Tuberculosis/HIV Coinfection for information on ARV use with rifamycin antibiotics.	Rifamycin antibiotics are inducers of CYP3A4 and UGT1A1 enzymes, causing significant decreases in concentrations of PIs, INSTIs, and RPV.

[a] TAF and TDF are two U.S. Food and Drug Administration–approved forms of TFV. TAF has fewer bone and kidney toxicities than TDF, whereas TDF is associated with lower lipid levels. Safety, cost, and access are among the factors to consider when choosing between these drugs.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BMD = bone mineral density; CAB-LA = long-acting cabotegravir; CD4 = CD4 T lymphocyte; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; FTC = emtricitabine; HBV = hepatitis B virus; HCV = hepatitis C virus; HLA = human leukocyte antigen; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PEP = post-exposure prophylaxis; PrEP = pre-exposure prophylaxis; QTc = QT corrected for heart rate; RPV = rilpivirine; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; UGT = uridine diphosphate glucuronosyltransferase

Nucleoside Reverse Transcriptase Inhibitor Options as Part of Initial Therapy

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The following sections provide detailed information on antiretroviral (ARV) drugs that the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends for initial therapy for most people with HIV and for initial therapy in certain clinical scenarios (see Tables 6a and 6b in the Initial Combination Antiretroviral Regimens for People With HIV section), including ARV drug characteristics, adverse effects, clinical trial results, and Panel recommendations on their use.

Table 8a. Characteristics of Nucleoside Reverse Transcriptase Inhibitor Options for People Without Prior Antiretroviral Treatment

Note: Listed in order of the Panel's recommendations in Tables 6a and 6b.

Characteristics	TAF/FTC	TDF/FTC	TDF/3TC	3TC	ABC/3TC
Dosing Frequency	Once daily	Once daily	Once daily	Once daily	Once daily
Available Coformulations for People Without Prior ARV Treatment	• TAF 25 mg/FTC • BIC/TAF 25 mg/FTC • DRV/c/TAF 10 mg/FTC • RPV/TAF 25 mg/FTC	• TDF/FTC	• TDF/3TC • DOR/TDF/3TC	• DTG/3TC	• ABC/3TC • DTG/ABC/3TC
Adverse Effects	**TAF** • Renal insufficiency, proximal renal tubulopathy (less frequent than with TDF) • Decrease in BMD (less than with TDF)	**TDF** • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters.	**TDF** • Renal insufficiency, proximal renal tubulopathy • Decrease in BMD • Renal and bone toxicity are exacerbated by pharmacologic boosters.	**3TC** • No notable adverse effects	**ABC** • HSR to ABC is associated with the presence of HLA-B*5701 allele.[b] • Increase in CV events is associated with ABC use in some but not all cohort studies.

Table 8a. Characteristics of Nucleoside Reverse Transcriptase Inhibitor Options for People Without Prior Antiretroviral Treatment

Characteristics	TAF/FTC	TDF/FTC	TDF/3TC	3TC	ABC/3TC
Other Considerations	• Also used for HBV treatment. Discontinuation may precipitate HBV flare. • See Appendix B for dosing recommendations in people with renal insufficiency. • Some studies reported less weight gain and lower LDL, HDL, TC, and triglycerides with TDF than with TAF.			• 3TC or ABC/3TC **should not be used** as treatment for HBV without adding another HBV-active drug.	

[a] 3TC is recommended for use with DTG in some people as initial ART. See Table 6a and the discussion below for more information. Otherwise, dual-NRTI backbones are recommended.

[b] Perform HLA-B*5701 testing before initiating ABC; if result is positive, do not start ABC and add ABC to patient's allergy list. See the HLA-B*5701 Screening section for more information.

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BMD = bone mineral density; CV = cardiovascular; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; FTC = emtricitabine; HBV = hepatitis B virus; HDL = high-density lipoprotein; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; LDL = low-density lipoprotein; NRTI = nucleoside reverse transcriptase inhibitor; RPV = rilpivirine; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate

Summary

The U.S. Food and Drug Administration (FDA)–approved nucleos(t)ide reverse transcriptase inhibitors (NRTIs) include zidovudine (ZDV), stavudine (d4T), didanosine (ddI), abacavir (ABC), tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF), lamivudine (3TC), and emtricitabine (FTC). Older NRTIs (ZDV, d4T, ddI) are no longer recommended for use in clinical practice in the United States because of high rates of serious toxicities. All of these drugs can cause mitochondrial toxicity that may lead to myopathy, hepatic steatosis, lactic acidosis, or lipoatrophy; ZDV may cause bone marrow suppression, whereas peripheral neuropathy is commonly seen with ddI or d4T use. The incidence of these complications is substantially lower with 3TC, FTC, ABC, TDF, and TAF than with older NRTIs.[1,2]

TAF/FTC, TDF/3TC, and TDF/FTC are NRTI combinations that are part of *Recommended Initial Regimens for Most People With HIV* (see Table 6a). In addition, 3TC may be used as a single NRTI with dolutegravir (DTG), except in individuals with HIV RNA >500,000 copies/mL or in whom antiretroviral therapy (ART) is to be started before the results of HIV RNA and HIV genotypic resistance tests are available. If used in those with hepatitis B virus (HBV) coinfection, another HBV-active drug should be added. Tables 6a and 6b provide recommendations and ratings for the individual regimens. These recommendations are based on the virologic potency and durability, short- and long-term toxicity, and dosing convenience of these drugs. TDF has been associated with bone and kidney toxicities, especially when used with a pharmacologic booster.[3] TAF is less likely to cause kidney and bone toxicities than TDF, whereas TDF is associated with lower lipid levels than TAF. Like TDF, TAF is a recommended option in pregnancy because of reassuring data from a multinational trial in pregnant women with HIV[4] and data from the Antiretroviral Pregnancy Registry that show no evidence of teratogenicity. Please refer to the Perinatal Guidelines for more information on the use of ARVs during pregnancy.

ABC/3TC, including DTG/ABC/3TC, is no longer recommended for initial therapy in most people with HIV but may be considered in circumstances in which tenofovir (TFV)-containing regimens or DTG/3TC cannot be used. Before starting any regimen with ABC, screening for the HLA-B*5701 allele is necessary because there is a strong link with a potentially life-threatening hypersensitivity

reaction in people who test positive for this allele. In addition, some data continue to support an association between ABC and an increased risk for serious cardiovascular events.[5,6]

Along with safety and efficacy, cost and access are among the factors to consider when choosing among available options. ABC/3TC, TDF/3TC, TDF/FTC, and 3TC are available as generic formulations.

Clinical Trials Comparing Nucleoside Reverse Transcriptase Inhibitors

Tenofovir Alafenamide Compared to Tenofovir Disoproxil Fumarate

Safety and HIV Efficacy

Two randomized double-blind Phase 3 clinical trials compared the safety and efficacy of elvitegravir/cobicistat (EVG/c)/TDF/FTC and EVG/c/TAF/FTC in 1,733 ART-naive adults with estimated glomerular filtration rate (eGFR) ≥50 mL/min.

- TAF/FTC was virologically non-inferior to TDF/FTC at Week 48 (92% vs. 90% of participants had plasma HIV RNA <50 copies/mL, respectively),[7] but TAF/FTC was superior to TDF/FTC at Week 144 (84.2% vs. 80% of participants with plasma HIV RNA <50 copies/mL), largely driven by a higher rate of treatment discontinuation in the TDF arm.[8]
- Participants in the TAF arm had significantly smaller reductions in bone mineral density (BMD) at the spine and hip than those in the TDF arm through 144 weeks.[8] Those receiving TAF also had less pronounced changes in eGFR and renal biomarkers and fewer clinically significant renal events through Week 96.[9] Conversely, levels of fasting low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides increased more in the TAF group than in the TDF group at Week 96, with no change in total cholesterol to HDL ratio.[10]

Two randomized studies have compared the safety and efficacy of TAF/FTC to TDF/FTC, with each combination administered with boosted darunavir (DRV) in ART-naive participants:

- A Phase 2 study of coformulated darunavir/cobicistat (DRV/c) plus TAF/FTC versus DRV/c plus TDF/FTC in treatment-naive participants demonstrated similar virologic suppression rates in both arms (75% vs. 74%).[11] In the TAF arm, fewer participants developed proteinuria. Changes in BMD were also less pronounced among participants in the TAF group.
- The AMBER study randomized ART-naive participants to receive either coformulated DRV/c/TAF/FTC or DRV/c plus TDF/FTC. At Week 48, HIV RNA <50 copies/mL was achieved in 91% of the DRV/c/TAF/FTC participants versus 88% of the DRV/c plus TDF/FTC participants. Participants in the TAF/FTC arm showed less decline in hip and spine BMD and eGFR than participants in the TDF/FTC arm.[12]

One analysis evaluated data from 14 randomized trials that compared the virologic efficacy, frequency of renal events, and bone density changes associated with the use of TDF and TAF when either drug was taken with or without pharmacokinetic (PK) boosters (ritonavir [RTV] or cobicistat [COBI]). No significant differences appeared between unboosted regimens with TDF and TAF in terms of virologic efficacy. When used with PK boosters, TAF resulted in a clinically small but statistically significant greater virologic efficacy than TDF (94% vs. 92%; $P = 0.0004$). No difference was seen in bone-related toxicities and clinical or laboratory adverse events between TAF and TDF, regardless of whether used with a boosting agent. The rate of discontinuation due to renal adverse

events was higher for those on boosted regimens containing TDF compared with those containing TAF, with a small but statistically significant difference (P = 0.03).[13]

Although conducted in people without HIV for pre-exposure prophylaxis (PrEP), the DISCOVER trial, with 5,387 treated participants, was the largest trial to directly compare the adverse effects of TAF/FTC with those of TDF/FTC.[14] The following findings were observed after 48 weeks of follow-up:

- Adverse events did not significantly vary between the two groups, including Grade 3 and 4 events, serious adverse events, discontinuations due to adverse events, and overall.
- Changes in renal biomarkers and bone density significantly favored the TAF arm over TDF. One case of proximal tubular disease occurred in the TDF arm.
- LDL, HDL, and total cholesterol were significantly lower in the TDF arm than in the TAF arm, with no significant difference in the total cholesterol to HDL ratio.
- Participants in the TAF arm gained an average of 1.1 kg whereas those in the TDF arm had a mean loss of 0.1 kg.

Efficacy in People With HIV and HBV

To assess the ability of TAF to maintain HIV and HBV suppression, 72 people with HIV/HBV coinfection who had HIV RNA <50 copies/mL and HBV DNA <9 $\log_{10}$ IU/mL on a stable regimen were switched to EVG/c/TAF/FTC.[15] In this study, 96% of participants were on a TDF/FTC-containing regimen before the switch. Key results of the study showed the following:

- Among those who switched to EVG/c/TAF/FTC, HIV suppression was maintained in 91.7% of participants at Week 48, and 91.7% of participants had HBV DNA <29 IU/mL.
- Markers of proximal tubular proteinuria and biomarkers of bone turnover decreased in those who switched to EVG/c/TAF/FTC.[15]

Lamivudine Compared to Tenofovir Disoproxil Fumarate/Emtricitabine

A single-tablet regimen (STR) of DTG/3TC has now been approved as an initial ARV regimen. Please refer to the Integrase Strand Transfer Inhibitor-Based Regimens section for a full discussion.

GEMINI 1 and GEMINI 2 were identically designed randomized, double-blind clinical trials that found DTG plus 3TC non-inferior to DTG plus TDF/FTC in ART-naive adults with HIV RNA <500,000 copies/mL and eGFR ≥50 mL/min.[16,17]

Abacavir/Lamivudine Compared to Tenofovir Disoproxil Fumarate/Emtricitabine

Several randomized controlled trials in ART-naive participants compared ABC/3TC to TDF/FTC, each administered in combination with a third ARV drug[18-20] (see the Integrase Strand Transfer Inhibitor-Based Regimen section).[21]

- The ACTG 5202 study, a randomized controlled trial in >1,800 participants, evaluated the efficacy and safety of ABC/3TC and TDF/FTC when each combination was used with either efavirenz (EFV) or atazanavir/ritonavir (ATV/r). In people with baseline HIV RNA ≥100,000 copies/mL, the time to virologic failure was significantly shorter with ABC/3TC than

with TDF/FTC, regardless of whether the third active drug was EFV or ATV/r. In addition, time to first adverse event was also shorter in the ABC/3TC groups.[18]

- In the HEAT study, 688 participants received ABC/3TC or TDF/FTC with once-daily lopinavir/ritonavir. Virologic efficacy was similar in the two study arms, including in a subgroup of participants with HIV RNA ≥100,000 copies/mL.[20]
- The ASSERT study compared open-label ABC/3TC with TDF/FTC in 385 HLA-B*5701-negative people with HIV who were ART-naive; all participants also received EFV. The primary study endpoint was renal safety of the regimens. Although eGFR did not differ significantly between the regimens, biomarkers associated with tubular dysfunction (retinol-binding protein and beta-2 microglobulin) increased significantly, to a greater extent in the TDF/FTC arm than the ABC/3TC arm (+50% vs. +24% and no change vs. −47%, respectively). At Week 48, the proportion of participants with HIV RNA <50 copies/mL was lower among ABC/3TC-treated participants (59%) than among TDF/FTC-treated participants (71%).[19]

Nucleoside Reverse Transcriptase Inhibitor Options for Initial Therapy

Tenofovir Alafenamide/Emtricitabine

TAF, an oral prodrug of TFV, is hydrolyzed to TFV in plasma and then converted to TFV-diphosphate (TFV-DP) intracellularly, where it exerts its activity as an NRTI. Unlike TDF, which readily converts to TFV in plasma after oral absorption, TAF remains relatively stable in plasma, resulting in lower plasma and higher intracellular TFV concentrations. After oral administration, TAF 25 mg resulted in plasma TFV concentrations that were 90% lower than those seen with TDF 300 mg. Intracellular TFV-DP concentrations, however, were substantially higher with TAF.

Adverse Effects

Renal and Bone Effects

- In randomized controlled trials that compared TAF and TDF in people without prior ARV treatment experience or those with virologic suppression, TAF had more favorable effects on renal biomarkers and bone density than TDF.

Lipid Effects

- In randomized controlled trials in ART-naive participants, in switch studies, and in a large study of PrEP, levels of LDL and HDL cholesterol and triglycerides were lower in participants who received TDF than those who received TAF. However, total cholesterol to HDL ratios did not differ between participants receiving TAF and those receiving TDF. The clinical significance of this finding is not clear.[7,22,23]

Weight Gain

- Initiation of TAF in previously untreated individuals and in people without HIV has been associated with greater weight gain than initiation of TDF[24-26] and ABC.[25] In ADVANCE, an open-label trial conducted in South Africa that compared EFV/TDF/FTC versus DTG plus TDF/FTC versus DTG plus TAF/FTC in ART-naive participants, a greater increase in body weight was reported with initiation of TAF than with TDF.[24] This area is under intense investigation, and the reason for the difference in weight gain between regimens is still uncertain. It is also unclear whether change of ART results in reversal of weight gain.

Other Factors and Considerations

- TAF/FTC is available in fixed-dose combinations (FDCs) with bictegravir (BIC), DRV/c, EVG/c, and rilpivirine (RPV), allowing the regimens to be administered as a single pill taken once daily.
- TAF-containing regimens are approved for people with eGFR ≥30 mL/min. Renal function, urine glucose, and urine protein should be assessed before initiating treatment with TAF, and these assessments should be repeated periodically during treatment. EVG/c/FTC/TAF was safe and effective in a single-arm switch study that was conducted in people on hemodialysis.[27] Based on the results from this study, TAF/FTC can be used without dosage adjustment in people with HIV who require hemodialysis.
- Both TAF and FTC are active against HBV. In people with HIV/HBV coinfection, TAF/FTC may be used as the NRTI pair in an ARV regimen because these drugs have activity against both viruses (see Hepatitis B Virus/HIV Coinfection).[15]
- TAF is recommended as a preferred drug in pregnancy because of reassuring data from a multinational trial of pregnant women and data from the Antiretroviral Pregnancy Registry that show no evidence of teratogenicity.[4]

The Panel's Recommendation

- On the basis of clinical trial safety and efficacy data, and its availability as a component of various FDCs, the Panel considers TAF/FTC a recommended NRTI combination for initial ART in most people with HIV when prescribed with BIC or DTG **(AI),** and as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (see Table 6b) when given with RPV, DOR, RTV-boosted DRV (DRV/r), or DRV/c.

Tenofovir Disoproxil Fumarate/Emtricitabine and Tenofovir Disoproxil Fumarate/Lamivudine

TDF, with either 3TC or FTC, has been studied in combination with DOR, EFV, RPV, several boosted protease inhibitors (PIs), EVG/c, RAL, and DTG in randomized clinical trials.[28-37]

Adverse Effects

Renal Effects

- New onset or worsening renal impairment has been associated with TDF use.[38,39] Risk factors may include advanced HIV disease, longer treatment history, low body weight (especially in women),[40] and preexisting renal impairment.[41] Adverse effects on renal biomarkers, such as proteinuria, especially tubular proteinuria, were more frequent with TDF than with TAF.[42]
- Adverse renal outcomes are more likely when TDF/FTC is coadministered with PK boosters (RTV or COBI). A meta-analysis of randomized trials found that discontinuation due to renal adverse events is more frequent in people who take TDF/FTC than TAF/FTC with PK boosters.[13]

Bone Effects

- Although initiation of all NRTI-containing regimens has been associated with a decrease in BMD, the loss of BMD is greater with TDF-containing regimens. For example, in two randomized studies that compared TDF/FTC with ABC/3TC, participants who received TDF/FTC experienced a significantly greater decline in BMD than ABC/3TC-treated participants.[43,44] BMD generally

stabilizes following an early decline after ART initiation. Loss of BMD is also greater with TDF than with TAF.

- Cases of osteomalacia associated with proximal renal tubulopathy have been reported with the use of TDF.[45] Adverse bone outcomes have been found to be more likely when TDF/FTC is coadministered with PK boosters. However, a meta-analysis found no difference in bone-related toxicities between TAF and TDF, regardless of boosting.[13]

Other Factors and Considerations

- TDF/3TC is available as a coformulated generic drug.
- TDF/3TC is available in an FDC with DOR 100 mg.
- Renal function, urine glucose, and urine protein should be assessed before initiating treatment with TDF and periodically during treatment (see Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy). In people who have preexisting renal insufficiency (CrCl <60 mL/min),[46] use of TDF generally should be avoided. If TDF is used, a dose adjustment is required if the person's CrCl falls below 50 mL/min (see Appendix B for dose recommendations).
- TDF, FTC, and 3TC are active against HBV. In people with HBV/HIV coinfection, TDF/FTC or TDF/3TC may be used as the NRTI pair of the ARV regimen because these drugs have activity against both viruses (see Hepatitis B Virus/HIV Coinfection).

The Panel's Recommendations

- On the basis of clinical trial safety and efficacy data, long-term experience in clinical practice, and the combination's availability as a component of FDC drugs, the Panel considers TDF/FTC and TDF/3TC as recommended NRTI combinations for initial ART in most people with HIV when combined with DTG, and as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b).
- TDF should be used with caution or avoided in people with renal disease and/or osteopenia/osteoporosis.
- When TDF is used, especially in conjunction with a PK booster, clinicians should monitor for renal and bone safety during therapy. Boosters should be avoided when possible in people taking TDF.

Emtricitabine Versus Lamivudine

FTC and 3TC generally are used interchangeably in combination with other ARVs, based on the results of randomized clinical trials and a meta-analysis of 12 trials that compared virologic efficacy and safety.[47,48] In the ATHENA cohort, virologic efficacy of TDF/FTC was compared to TDF/3TC when either was combined with a non-nucleoside reverse transcriptase inhibitor (NNRTI)—EFV or nevirapine[49]—or with a boosted PI.[50] No difference was reported in the rates of virologic failure in people who were taking TDF/FTC and people who were taking TDF/3TC when these drug combinations were used with a boosted PI. TDF/3TC was associated with higher rates of virologic failure than TDF/FTC in the NNRTI analysis; however, participants in the NNRTI cohort who were taking 3TC generally had higher viral loads and lower CD4 T lymphocyte cell counts and were more likely to be using injection drugs at the start of the study than those taking FTC.

Adverse Effects

- Both FTC and 3TC have been well tolerated with no significant treatment-limiting adverse effects.
- In early clinical trials, FTC was infrequently associated with mild hyperpigmentation of palms and soles.

Other Factors and Considerations

- 3TC is now generic in the United States and is coformulated with other drugs, such as DOR/TDF/3TC and DTG/ABC/3TC.
- Both 3TC and FTC have activity against hepatitis B but are insufficient for HBV treatment when used alone due to the emergence of resistance. Discontinuation of FTC or 3TC can precipitate a flare in HBV if no other HBV-active drugs are in the regimen.
- See Appendix B for dosing recommendations in people with renal impairment.
- No significant drug interactions have been identified with FTC. Sorbitol-containing drugs can decrease 3TC concentration, and coadministration should be avoided.
- Both FTC and 3TC select for the M184V mutation when viral suppression is suboptimal.

The Panel's Recommendation

- FTC and 3TC are considered interchangeable in combination with other ARV drugs.

Lamivudine as a Single Nucleoside Reverse Transcriptase Inhibitor

Based on the GEMINI-1 and GEMINI-2 studies[17] that found DTG plus 3TC non-inferior to DTG plus TDF/FTC in ART-naive people with HIV RNA <500,000 copies/mL, 3TC may be used as a single NRTI with DTG (see Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs for more information).

Other Factors and Considerations

- 3TC with DTG is available as a STR.
- 3TC is active against HBV but is insufficient for HBV treatment when used alone due to the emergence of resistance. Discontinuation of 3TC can precipitate a flare in HBV if no other HBV-active drugs are in the regimen.
- 3TC is available in two brand-name formulations (one for HIV and the other for HBV), but the doses are different. The dose for HIV treatment is 3TC 300 mg daily.
- See Appendix B for dosing recommendations in people with renal impairment.
- Sorbitol-containing drugs can decrease 3TC concentration, and coadministration should be avoided.

The Panel's Recommendations

The Panel recommends the use of DTG/3TC **(AI)** as a *Recommended Initial Regimen for Most People With HIV,* with four exceptions. DTG/3TC **is not recommended** for:

- Individuals with HIV RNA >500,000 copies/mL.
- Individuals with HBV coinfection unless receiving another HBV-active drug.
- Individuals who have received long-acting injectable cabotegravir as PrEP and do not have integrase strand transfer inhibitor (INSTI) genotype resistance testing results available demonstrating INSTI sensitivity.
- Individuals starting ART before the results of genotypic resistance testing for reverse transcriptase are available.

Abacavir/Lamivudine

ABC plus 3TC has been studied in combination with EFV, several PIs, and DTG in people who are ART-naive.[21,51-53]

Adverse Effects

Hypersensitivity Reactions

- Clinically suspected hypersensitivity reactions (HSRs) were observed in 5% to 8% of individuals who started ABC in clinical trials conducted before the use of HLA-B*5701 testing. The risk of HSRs is highly associated with the presence of the HLA-B*5701 allele; approximately 50% of people who are HLA-B*5701-positive and are given ABC will have a related HSR.[54,55] HLA-B*5701 testing should be done if the use of ABC is being considered. A person who tests positive for HLA-B*5701 should not be given ABC, and ABC hypersensitivity should be noted on the person's allergy list. People who are HLA-B*5701 negative are far less likely to experience an HSR, but they should be counseled about the symptoms of the reaction. People who discontinue ABC because of a suspected HSR **should never be rechallenged,** regardless of their HLA-B*5701 status.

Cardiovascular Risk

- An association between ABC use and myocardial infarction (MI) was first reported in the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study. This large, multinational, observational study group found that recent (i.e., within 6 months) or current use of ABC was associated with an increased risk of an MI, particularly in participants with preexisting cardiac risk factors.[5,6]
- Since the D:A:D report, several studies have evaluated the relationship between ABC therapy and cardiovascular events. Some studies have found an association.[56-63] Others, including an FDA meta-analysis of 26 randomized clinical trials that evaluated ABC, have not.[64-68]
- No consensus has been reached on the association between ABC use and MI risk or the mechanism for such an association.

Other Factors and Considerations

- ABC/3TC is available as a coformulated tablet and as a coformulated STR with DTG.
- ABC and 3TC are available separately and as a coformulated tablet in generic tablet formulations.
- ABC does not cause renal dysfunction and can be used instead of TDF in people with underlying renal dysfunction or in those who are at high risk for renal effects. No dose adjustment is required in people with renal dysfunction.

The Panel's Recommendations

- ABC should be prescribed only for people who are HLA-B*5701 negative.
- Due to the need for HLA-B*5701 testing before use, ongoing concerns about increased risk of cardiovascular events seen in association with ABC (observed in some but not all studies), and the availability of other effective and well-tolerated options, the Panel no longer recommends DTG/ABC/3TC for most individuals initiating ART and now classifies DTG/ABC/3TC as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (see Table 6b) **(BI)** (see Characteristics of Integrase Strand Transfer Inhibitors for discussion regarding the clinical efficacy data for ABC/3TC plus DTG).
- ABC/3TC use with DRV/r or DRV/c is also recommended as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b) **(BII).**
- ABC should be used with caution or avoided in people with cardiovascular disease or known high cardiovascular risk.

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Integrase Strand Transfer Inhibitor–Based Regimens as Initial Antiretroviral Therapy

Updated: September 12, 2024
Reviewed: September 12, 2024

Table 8b. Characteristics of Integrase Strand Transfer Inhibitors That Are Recommended as Part of Initial Antiretroviral Therapy

	BIC	DTG
Dosing Frequency	Once daily	**Once Daily** • As initial ART or in people with no INSTI-resistance mutations **Twice Daily** • If used with certain CYP3A4 and UGT1A1 inducers; *or* • In people with certain INSTI drug resistance mutations
STR Available as Initial ART	BIC/TAF/FTC	• DTG/ABC/3TC • DTG/3TC
Available as a Single Drug Tablet	No	Yes
Virologic Efficacy Against EVG- or RAL-Resistant HIV	*In vitro* data indicate activity, but clinical trial data are not available.	Yes, for some isolates; effective with DTG 50 mg twice-daily dose
Adverse Reactions	• ↑ CPK 4% • CNS side effects were rarely reported in clinical trials. • Diarrhea, nausea, and headache may occur in some cases.	• ↑ CPK, myositis • CNS side effects such as insomnia and headache have been reported; depression and suicidality are rare, occurring primarily in people with preexisting conditions. • Hypersensitivity, hepatotoxicity
CYP3A4 Drug–Drug Interactions	CYP3A4 substrate	CYP3A4 substrate (minor)
Chelation With Polyvalent Cation Supplements and Antacids	Oral absorption may be reduced by polyvalent cations. See Table 24d for recommendations regarding dosing separations and these drugs.	

Table 8b. Characteristics of Integrase Strand Transfer Inhibitors That Are Recommended for Antiretroviral Therapy–Naive Patients

	BIC	DTG
Other Key Potential Drug Interaction Mechanisms	P-gp substrate, UGT1A1 substrate, OCT2 and MATE1 inhibitor	P-gp substrate, UGT1A1 substrate
Other Factors	Both BIC and DTG decrease tubular secretion of creatinine without affecting glomerular function. This may result in an increase in serum creatinine of approximately 0.1–0.2 mg/dL.	

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; BIC = bictegravir; CNS = central nervous system; CPK = creatine phosphokinase; CYP = cytochrome P450; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; MATE1 = multidrug and toxic compound extrusion 1; OCT2 = organic cation transporter 2; P-gp = p-glycoprotein; RAL = raltegravir; STR = single-tablet regimen; TAF = tenofovir alafenamide; UGT = uridine diphosphate glucuronosyltransferase

Four oral integrase strand transfer inhibitors (INSTIs)—bictegravir (BIC), dolutegravir (DTG), elvitegravir (EVG), and raltegravir (RAL)—are approved for use in people with HIV as their initial ARV treatment. Intramuscular cabotegravir (CAB) is approved for use with rilpivirine (RPV) (with or without an oral CAB + RPV lead-in) as part of a long-acting injectable complete antiretroviral (ARV) regimen to replace a stable oral regimen in people with HIV and viral suppression. The role of this combination is discussed in the Optimizing Antiretroviral Therapy in the Setting of Viral Suppression section. Long-acting injectable cabotegravir (CAB-LA) is also approved for pre-exposure prophylaxis (PrEP). The first-generation INSTIs EVG and RAL have some disadvantages, which include a low barrier to resistance. In addition, because EVG has to be given with cobicistat (COBI), a pharmacokinetic (PK) booster, it has a high potential for drug–drug interactions, whereas RAL-based regimens have a higher pill burden than other INSTI regimens. Because of these disadvantages, elvitegravir/cobicistat (EVG/c) and RAL are no longer recommended by the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) as initial ART. Because the second-generation INSTIs BIC and DTG have high barriers to resistance, BIC/tenofovir alafenamide (TAF)/emtricitabine (FTC) and DTG plus TAF/FTC or tenofovir disoproxil fumarate (TDF)/FTC are recommended for most people with HIV (see Appendix A, Table 6 for more information on the INSTIs BIC and DTG).

This section of the guidelines will focus on BIC and DTG, the two INSTIs recommended by the Panel as part of the *Recommended Initial Regimens for Most People With HIV* (Table 6a) and *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b) (also see Table 7).

Panel's Recommendations for Integrase Strand Transfer Inhibitor–Based Regimens as Initial Therapy

The Panel recommends one of the following INSTI-based regimens as initial ART for people with HIV who do not have a history of using CAB-LA as PrEP (see Table 6a):

- BIC/TAF/FTC **(AI)**
- DTG plus (TAF or TDF) with (FTC or lamivudine [3TC]) **(AI)**
- DTG/3TC **(AI),** except for those with HIV RNA >500,000 copies/mL, with hepatitis B virus (HBV) coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.

INSTI resistance has been reported in people who acquired HIV following exposure to CAB-LA as PrEP.[1] For a person who has had exposure to CAB-LA as PrEP, an INSTI-containing regimen

should not be initiated unless an INSTI genotypic resistance test result is available and shows no INSTI-resistance mutations **(AIII).** If treatment is initiated before genotypic test results are available, boosted darunavir (DRV) plus (TAF or TDF) plus (FTC or 3TC) should be used, pending INSTI resistance results **(AIII).** See Table 6a for more details.

Because of the low rates of transmitted INSTI resistance in the United States at present, when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started pending the results of the INSTI genotype test.

For people who have never used CAB-LA for PrEP and who acquired HIV despite using INSTI-based post-exposure prophylaxis, an INSTI genotype should be obtained prior to beginning an INSTI-based regimen. However, because selection of INSTI-resistant virus is likely to be uncommon in this setting, an INSTI-based regimen could be started prior to the return of genotype results **(CIII).**

The Panel also recommends using DTG/abacavir (ABC)/3TC **(BI)** when concerns about renal or bone-associated adverse events preclude the use of TAF or TDF. However, ABC should only be given to people who are documented to be HLA-B*5701-negative.

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Adverse Effects

BIC and DTG are generally well tolerated, although there are reports of insomnia in some people. Depression and suicidal ideation, primarily in people with a history of psychiatric illnesses, have been reported rarely in those receiving INSTI-based regimens.[2-5]

Among people with HIV who have not yet received ART, initiation of INSTI-containing regimens has been associated with greater weight increases compared to non-nucleoside reverse transcriptase inhibitor (NNRTI) or boosted protease inhibitor (PI) regimens.[6-11] In randomized trials of ARV-naive individuals, the mean increase in weight from baseline associated with BIC and DTG was similar and greater than with EVG/c or with efavirenz (EFV).[8,12-14] Weight gain was also greater in those initiating TAF than other nucleoside reverse transcriptase inhibitors (NRTIs).[7,8,15] These weight increases appear to disproportionately affect women and Black and Hispanic people,[6-8,16] yet predictors and mechanisms for the weight gain are still unclear. In general, concerns for weight gain should not be a reason to avoid an INSTI- or TAF-based regimen.

Integrase Strand Transfer Inhibitor Use in Women of Childbearing Potential

Clinicians should refer to the Perinatal Guidelines for detailed recommendations on ARV regimens in treatment-naive people, including recommendations on the use of INSTI-based regimens during conception and throughout pregnancy.

- Earlier data from a birth outcomes surveillance study in Botswana raised concern about an increased risk of neural tube defects (NTDs) (0.9%) in infants born to women who were receiving DTG at the time of conception.[17,18] Updated data from the same study showed that the prevalence of NTDs in infants born to women on DTG at the time of conception is not significantly different from those on non-DTG regimens at the time of conception.[19] Based on

these data, DTG is now one of the *Preferred* INSTIs during pregnancy. See the Perinatal Guidelines for further discussion.

- BIC is also recommended as a *Preferred* INSTI during pregnancy based on safety and PK data in pregnancy. See the Perinatal Guidelines for more details.

Bictegravir

BIC is approved by the U.S. Food and Drug Administration for initial therapy in adults with HIV as a component of a once-daily single-tablet regimen with TAF and FTC.

Efficacy in Clinical Trials

- The efficacy of BIC in ART-naive adults has been evaluated in two large Phase 3 randomized double-blind clinical trials that compared BIC to DTG administered in combination with two NRTIs. The primary efficacy endpoint was the proportion of participants with plasma HIV RNA <50 copies/mL at Week 48.
  - The GS-US-380-1490 trial randomized participants 1:1 to receive either BIC/TAF/FTC or DTG with coformulated TAF/FTC. Both regimens were given once daily. At Week 96, 84% of participants in the BIC arm and 86% of those in the DTG arm achieved HIV RNA <50 copies/mL.[15]
  - The GS-US-380-1489 trial randomized participants 1:1 to receive BIC/TAF/FTC or coformulated DTG/ABC/3TC once daily. At Week 96, 88% of participants in the BIC/TAF/FTC arm and 90% of those in the DTG/ABC/3TC arm achieved HIV RNA <50 copies/mL.[20]
  - Week 144 follow-up from both trials demonstrated noninferiority of the BIC/TAF/FTC regimen to both DTG-containing regimens, with high levels of virologic suppression and no treatment-emergent resistance.

Adverse Effects

- BIC is generally well tolerated.
- Neuropsychiatric adverse events have been reported with INSTIs. BIC-associated serious neuropsychiatric effects were uncommon (<1%) in clinical trials and mainly occurred in the setting of preexisting depression, other psychiatric illness, or prior suicide attempt.[21]

Drug–Drug Interactions

Note: See Table 24d for a comprehensive list of potential INSTI-related drug–drug interactions.

- BIC is a cytochrome P450 (CYP) 3A4 substrate and a uridine diphosphate glucuronosyltransferase (UGT) 1A1 substrate; therefore, its metabolism may be affected by concomitant use of CYP3A4 and UGT1A1 inducers or inhibitors. Rifampin or other rifamycins may decrease BIC or TAF concentrations, which may result in loss of therapeutic effect of the ART. For people who require rifamycins, BIC/FTC/TAF should not be used. Use of certain anti-seizure medications and St. John's wort should also be avoided.[21]
- BIC is an inhibitor of the drug transporters OCT2 (organic cation transporter 2) and MATE1 (multidrug and toxic compound extrusion 1); therefore, BIC may increase concentrations of drugs that are substrates of these transporters. For this reason, dofetilide is **contraindicated** with BIC/TAF/FTC.

- Like other INSTIs, oral absorption of BIC may be reduced when BIC is coadministered with polyvalent cations (e.g., aluminum-, magnesium-, or calcium-containing antacids; calcium or iron supplements).

Other Factors and Considerations

- BIC decreases tubular secretion of creatinine without affecting glomerular function. Increases in serum creatinine are observed typically within the first 4 weeks of BIC therapy (with a median increase of 0.10 mg/dL after 48 weeks). This increase is comparable to that seen with other ARV drugs that have a similar effect on creatinine secretion, including DTG, RPV, and COBI.
- Treatment-emergent mutations that confer BIC resistance have rarely been reported in people receiving BIC for initial therapy.[22] BIC has not been studied in prospective trials for people with prior INSTI failure or INSTI-related resistance mutations. One analysis of 20 individuals with preexisting INSTI-related resistance mutations showed maintenance of virologic suppression in 19 people after switch to BIC, and viral suppression after beginning BIC in one person without prior ARV treatment. There are, however, insufficient data at present to recommend BIC use in such cases.

The Panel's Recommendation

The Panel recommends the use of BIC/TAF/FTC as a *Recommended Initial Regimen for Most People With HIV* **(AI)** (see Table 6a and Table 7 for more detailed recommendations).

Dolutegravir

As initial ARV regimens, both DTG plus two NRTIs and DTG/3TC demonstrated high efficacy in achieving HIV suppression in clinical trials. DTG is given once daily, with or without food.

Efficacy in Clinical Trials

The efficacy of DTG in ART-naive individuals has been evaluated in several fully powered randomized controlled clinical trials. In these trials, DTG-based regimens were noninferior or superior to a comparator INSTI-, NNRTI-, or PI-based regimen. The primary efficacy endpoint in these clinical trials was the proportion of participants with plasma HIV RNA <50 copies/mL.[13,23,24]

DTG Plus Two NRTIs Versus Other INSTIs Plus Two NRTIs

- DTG-based regimens (with TAF/FTC or ABC/3TC) have been compared to BIC/TAF/FTC in two randomized controlled trials. These regimens have virologic efficacy that is similar to BIC/TAF/FTC (see discussion in the BIC section above).[15,20,23,25]

DTG Plus Two NRTIs Versus EFV Plus Two NRTIs

- The SINGLE trial compared DTG 50 mg once daily plus ABC/3TC to EFV/TDF/FTC in 833 participants. At Week 48, DTG plus ABC/3TC was superior to EFV/TDF/FTC, primarily because the study treatment discontinuation rate was higher in the EFV arm than in the DTG arm.[26] At Week 144, DTG plus ABC/3TC remained superior to EFV/TDF/FTC.[27]
- The ADVANCE trial, an open-label, noninferiority trial conducted in South Africa, compared DTG with either TDF/FTC or TAF/FTC to EFV/TDF/FTC. At Week 96, the DTG-based regimens were noninferior to the EFV regimen based on the proportion of participants with HIV RNA levels <50 copies/mL (79% in DTG/TAF/FTC vs. 78% in DTG/TDF/FTC vs. 74% in EFV/TDF/FTC

arms). More participants discontinued the trial regimen in the EFV group than in the DTG group. Mean weight gain was 7.1 kg in the DTG/TAF/FTC group, 4.3 kg in the DTG/TDF/FTC group, and 2.3 kg in the EFV/TDF/FTC group and was greater among women than men.[14]

DTG Plus Two NRTIs Versus Ritonavir-Boosted Darunavir Plus Two NRTIs

- The FLAMINGO study, a randomized open-label clinical trial, compared DTG 50 mg once daily to the boosted PI—darunavir/ritonavir (DRV/r) 800 mg/100 mg once daily—each administered in combination with investigator-selected ABC/3TC or TDF/FTC. At Week 48, DTG was superior to DRV/r, with 90% and 83% of participants achieving HIV RNA <50 copies/mL, respectively. More participants discontinued their assigned regimen in the DRV/r arm.[28] The difference in efficacy between the DTG and DRV/r regimens was more pronounced in people with pre-treatment HIV RNA levels >100,000 copies/mL. At Week 96, DTG remained superior to DRV/r.[29]

DTG/3TC

- In the GEMINI-1 and GEMINI-2 trials, 1,433 ART-naive participants with baseline HIV RNA <500,000 copies/mL and no evidence of HBV infection were randomized to receive DTG plus 3TC or DTG plus TDF/FTC. At Week 96, DTG plus 3TC was noninferior to DTG plus TDF/FTC with 86% of participants in the DTG plus 3TC group and 89.5% in the DTG plus TDF/FTC group with viral load <50 copies/mL.[30] Virologic nonresponse was uncommon, occurring in 3.1% of participants who received DTG plus 3TC and 2% of participants who received DTG plus TDF/FTC. No treatment-emergent NRTI or INSTI resistance occurred in either treatment group. Among participants who started the study with CD4 counts <200 cells/mm^3, the rate of HIV RNA <50 copies/mL at Week 96 was lower in the DTG plus 3TC group than in the DTG plus TDF/FTC group; however, the difference was not related to a higher rate of virologic failure in the two-drug group. Overall mean change in weight from baseline was 3.1 kg in the DTG plus 3TC group and 2.1 kg in the DTG plus TDF/FTC group. At Week 144, DTG plus 3TC maintained noninferiority to DTG plus TDF/FTC with 82% versus 84% of participants maintaining viral load <50 copies/mL, respectively. The proportion of participants with viral load ≥50 copies/mL was 3% in both treatment groups. A lower risk of drug-related adverse events was found with DTG plus 3TC versus DTG plus TDF/FTC (20% vs. 27%; relative risk, 0.76 [95% confidence interval, 0.63–0.92]).[30]
- Two other small, nonrandomized single-arm studies showed similar rates of viral suppression with DTG plus 3TC.[31,32]

Adverse Effects

- DTG is generally well tolerated. The most reported adverse reactions of moderate-to-severe intensity were insomnia and headache.
- Some studies have shown greater weight increase among people initiating INSTI-based regimens, including regimens with DTG.[7,8,33,34] In a pooled analysis of eight randomized controlled trials in ART-naive individuals, the weight gain at 96 weeks with BIC- and DTG-based regimens was similar (approximately 3.5 kg). The clinical significance of weight gain in this setting is unclear.[8]
- Neuropsychiatric adverse events (e.g., sleep disturbances, depression, anxiety, suicidal ideation) associated with the initiation of DTG and other INSTIs have been reported.[2,3,35,36] However, analyses of data from large randomized controlled trials and a health care database demonstrated similar rates of neuropsychiatric adverse events between DTG-based regimens

and regimens that included RAL, EFV, DRV, and ATV.[37] Neuropsychiatric events rarely led to DTG discontinuation.

Drug–Drug Interactions

Note: See Table 24d for a comprehensive list of potential INSTI-related drug–drug interactions.

- DTG has fewer drug interactions than BIC.
- DTG oral absorption may be reduced when the ARV is coadministered with polyvalent cations. DTG should be taken at least 2 hours before or 6 hours after cation-containing antacids or laxatives are taken. Alternatively, DTG and supplements containing calcium or iron can be taken simultaneously with food.

Other Factors and Considerations

- DTG decreases tubular secretion of creatinine without affecting glomerular function, with increases in serum creatinine observed within the first 4 weeks of treatment.
- Treatment-emergent mutations that confer DTG resistance have been rarely reported in people receiving DTG as part of a three-drug regimen for initial therapy.[38-40] The incidence of resistance with DTG is much lower than with EVG or RAL, which suggests that DTG, like BIC, has a higher barrier to resistance than EVG or RAL.

The Panel's Recommendations

- The Panel classifies the following as *Recommended Initial Regimens for Most People With HIV* (see Table 6a and Table 7 for more detailed recommendations):
  - DTG plus (TAF or TDF) plus (FTC or 3TC) **(AI)**
  - DTG/3TC **(AI)—not recommended** for those with HIV RNA >500,000 copies/mL, with HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.
- The Panel recommends DTG/ABC/3TC **(BI)** in certain clinical scenarios for people with HIV who are documented to be HLA-B*5701-negative and who have concerns about renal or bone toxicities associated with TAF or TDF. This regimen should not be used in people with HBV coinfection unless an HBV-active drug (i.e., entecavir) other than 3TC is used.

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Non-Nucleoside Reverse Transcriptase Inhibitor–Based Regimens as Initial Antiretroviral Therapy

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Table 8c. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors That Are Recommended as Initial Antiretroviral Therapy in Certain Clinical Scenarios

Characteristics	DOR	RPV[a]
Dosing Frequency	Once daily	Once daily
Food Requirement	With or without food	With a meal
STR Available as Initial ART Recommended in Table 6b	DOR/TDF/3TC	RPV/TAF/FTC
Available as a Single-Drug Tablet	Yes	Yes
Adverse Effects	Generally well tolerated	• Depression • Headache • Skin rash • QTc prolongation
CYP3A4 Drug–Drug Interactions	CYP3A4 substrate	CYP3A4 substrate
Other Significant Drug Interactions	None	RPV oral absorption is reduced with increased gastric pH. Use of RPV with PPIs is not recommended; see Drug–Drug Interactions for dosing recommendations when RPV is coadministered with an H2 blocker or antacids.

[a] See Optimizing Antiretroviral Therapy section and Appendix A, Table 4 for information regarding injectable RPV.

Key: 3TC = lamivudine; ART = antiretroviral therapy; CYP = cytochrome P; DOR = doravirine; FTC = emtricitabine; H2 = histamine 2; PPI = proton pump inhibitor; QTc = QT corrected for heart rate; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Summary

Four non-nucleoside reverse transcriptase inhibitors (NNRTIs)—doravirine (DOR), efavirenz (EFV), nevirapine (NVP), and rilpivirine (RPV)—are currently approved by the U.S. Food and Drug Administration (FDA) for the initial treatment of HIV when used in combination with other antiretroviral (ARV) drugs. A fifth NNRTI, etravirine (ETR), is approved only for people who are ART-experienced.

NNRTI-based regimens have demonstrated virologic potency and durability. The major disadvantages of currently available NNRTIs (especially EFV and RPV) include the prevalence of NNRTI-resistant viral strains in people without prior antiretroviral therapy (ART),[1] a low barrier for the development of resistance, and potential for drug–drug interactions, although drug–drug interactions are less common with DOR. Resistance testing should be performed before initiation of an NNRTI-based regimen in people without prior ART. High-level resistance to all NNRTIs (except ETR or DOR) may occur with a single mutation. In people treated with RPV, the presence of RPV resistance mutations at virologic failure may confer cross-resistance to other NNRTIs, including ETR.[2,3] DOR-based regimens and one of the RPV-based regimens are now categorized as recommended *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios*. More details about these NNRTIs are provided below.

This section of the guidelines focuses on DOR and RPV, the two NNRTIs recommended by the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) as part of an initial ART regimen for people with HIV in certain clinical scenarios (see Table 6b in the Initial Combination Antiretroviral Regimens for People With HIV section and Table 7). There is no clinical trial comparing the efficacy of these two NNRTIs as initial ARV regimens. The Panel no longer recommends EFV as initial therapy because of the high incidence of serious toxicities, including neuropsychiatric effects and suicidality. NVP is no longer commonly used in clinical practice in the United States due to a relatively high potential for adverse effects compared to other NNRTIs.

Doravirine

Efficacy in Clinical Trials

The efficacy of DOR-based therapy as initial ART was demonstrated in two randomized, double-blind, placebo-controlled trials.

Doravirine-Based Regimen Versus Efavirenz-Based Regimen

- In the DRIVE-AHEAD trial, 734 participants received either DOR/tenofovir disoproxil fumarate (TDF)/lamivudine (3TC) or EFV/TDF/emtricitabine (FTC), both as a daily fixed-dose combination (FDC) tablet.[4]
    - At 96 weeks, DOR/TDF/3TC was noninferior to EFV/TDF/FTC, with 77.5% of participants who received DOR/TDF/3TC and 73.6% of those who received EFV/TDF/FTC achieving HIV RNA <50 copies/mL. Although virologic responses to ART overall were lower in participants with pre-treatment HIV RNA >100,000 copies/mL or pre-treatment CD4 T lymphocyte (CD4) cell counts of ≤200 cells/mm^3, there was no difference between the DOR-treated and EFV-treated participants.
    - Virologic rebound and virologic nonresponse were similar in the DOR/TDF/3TC (9.3%) and EFV/TDF/FTC (7.7%) treatment groups. At 96 weeks, genotype resistance results were reported for 21 participants with protocol-defined virologic failure in the DOR arm and 15 participants in the EFV arm. For the DOR arm, 7 of 21 (33.3%) participants had NNRTI resistance and 6 of 21 (28.6%) had NRTI resistance. For EFV, 10 of 15 (66.7%) participants had NNRTI resistance and 5 of 15 (33.3%) had NRTI resistance.
    - More participants in the EFV arm discontinued their assigned ART due to adverse events than in the DOR arm (6.6% vs. 3.0%). Neuropsychiatric side effects and rash were more common in the EFV arm.

Doravirine-Based Regimen Versus Darunavir/Ritonavir-Based Regimen

- In the DRIVE-FORWARD trial, 769 participants received DOR or darunavir/ritonavir (DRV/r) once daily along with two investigator-selected nucleoside reverse transcriptase inhibitors (NRTIs), either abacavir (ABC)/3TC or TDF/FTC.[5]
  - At 48 weeks, DOR was noninferior to DRV/r with 84% of study participants who received DOR versus 80% of those who received DRV/r achieving HIV RNA <50 copies/mL. Participants who received DOR plus ABC/3TC (n = 48) and those who received DOR plus TDF/FTC (n = 316) had similar virologic responses.
  - At 96 weeks, DOR was superior to DRV/r in terms of virologic suppression (73% vs. 66%).[5]
  - Protocol-defined virologic failure was similar in the DOR and DRV/r groups (9% vs. 11%) by Week 96. Genotype resistance results were reported for 11 and 14 participants with virologic failure in the DOR and DRV/r arms, respectively. Treatment-emergent resistance to any study drug occurred in 2 of 11 participants in the DOR group and 1 of 14 participants in the DRV/r group.
  - Treatment-related diarrhea was more frequently reported in the DRV/r arm. Greater increases in fasting low-density lipoprotein cholesterol, triglycerides, non–high-density lipoprotein cholesterol, and total cholesterol were seen in the participants who received DRV/r than in those who received DOR.
- In a pooled analysis of DRIVE-AHEAD and DRIVE-FORWARD participants who entered an open-label extension phase following the initial 96 weeks of randomized treatment, 550 participants continued their DOR-based regimen and 502 participants switched to a DOR-based regimen from the control arms. At 192 weeks, 83% percent of participants who continued on DOR and 81% of participants in the switch arm maintained viral suppression. Discontinuation due to drug-related adverse events was <1% overall and similar between the two arms, with no discontinuations due to renal adverse events.[6]

Other Factors and Considerations

- DOR is available as a single-drug 100-mg tablet[7] and as part of a single-tablet regimen (STR) that contains DOR/TDF/3TC 100 mg/300 mg/300 mg[8] and is dosed once daily, with or without food.
- DOR-based regimens have not been directly compared to integrase strand transfer inhibitor (INSTI)–based regimens in clinical trials and have not been studied with tenofovir alafenamide (TAF) in clinical trials.
- A post hoc analysis of three randomized controlled trials examined weight gain among ART-naive participants receiving DOR versus DRV/r or EFV. At week 96, mean weight gain was similar in the DOR group (2.4 kg), DRV/r group (1.8 kg), and EFV group (1.6 kg). No significant differences between treatment groups were found in the proportion of participants whose body mass index classification increased to overweight or obese at Week 48 or Week 96.[9]
- DOR is primarily metabolized by the CYP3A4 enzyme and should not be coadministered with strong CYP3A4 inducers. DOR concentration may increase in the presence of a CYP3A4 inhibitor (see Table 24b). DOR is not a CYP3A4 inducer or inhibitor; thus, it is not expected to affect the concentrations of concomitant CYP3A4 substrates.
- Treatment-emergent resistance mutations to DOR may confer cross-resistance to certain other NNRTIs. Most isolates with DOR mutations remain susceptible to ETR.[10]
- There are currently no data on the safety of DOR use during pregnancy.

- There are limited clinical trial data with the combination of DOR + ABC/3TC, so the Panel is less certain about the efficacy of this regimen.

The Panel's Recommendations

- Based on the clinical trial data discussed above, the Panel classifies DOR/TDF/3TC **(BI)** and DOR plus two NRTIs (**BI** for TDF/FTC and **BIII** for TAF/FTC) as *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios*.

Rilpivirine

Oral RPV is approved for use in combination with two NRTIs as initial ART for people with HIV who have pre-treatment viral loads <100,000 copies/mL. RPV is also approved as an extended-release injectable suspension as part of a long-acting (LA) injectable complete ARV regimen when used with cabotegravir (CAB), an INSTI. This regimen is approved to replace oral ART in people with virologic suppression and no history of resistance to RPV or INSTIs (see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression for discussion of LA CAB/RPV).

Efficacy in Clinical Trials

- Two Phase 3 randomized, double-blind clinical trials—ECHO and THRIVE—compared RPV and EFV, each combined with two NRTIs.[11] At 96 weeks, the following findings were reported:
  - RPV was noninferior to EFV overall.
  - Among participants with pre-ART viral loads >100,000 copies/mL, more RPV-treated participants experienced virologic failure than EFV-treated participants. NNRTI and NRTI resistance were more frequently found in RPV-treated participants with virologic failure.
  - Among the RPV-treated participants, the rate of virologic failure was greater in those with pre-treatment CD4 counts <200 cells/mm^3 than in those with CD4 counts ≥200 cells/mm^3.
- STaR, a Phase 3b, open-label study, compared two STRs—RPV/TDF/FTC and EFV/TDF/FTC—as initial ART in 786 people with HIV. The results at 96 weeks[12] were similar to those reported at 48 weeks.[13]
  - RPV was noninferior to EFV overall.
  - RPV was superior to EFV in participants with pre-ART viral loads ≤100,000 copies/mL and noninferior in those with pre-ART viral loads >100,000 copies/mL. Among participants with pre-ART viral loads >500,000 copies/mL, virologic failure was more common in RPV-treated than in EFV-treated participants.
  - At Week 96, there were more participants with emergent resistance in the RPV/FTC/TDF arm than in the EFV/FTC/TDF arm (5.3% vs. 1.0%, respectively).
- The STR of RPV/TAF/FTC was approved by the FDA based on results from a bioequivalence study. In this study, plasma concentrations of RPV, FTC, and TAF 25 mg in participants taking the coformulated drug were similar to those seen in participants who received RPV as the single-drug tablet and TAF/FTC as part of the STR of EVG/c/TAF 10 mg/FTC.[14]

Adverse Effects

- RPV is generally well tolerated. In the ECHO, THRIVE, and STaR trials, fewer instances of CNS adverse events (e.g., abnormal dreams, dizziness, psychiatric side effects), skin rash, and dyslipidemia were reported in the RPV arms than in the EFV arms, and fewer people in the RPV

arms discontinued therapy due to adverse events. However, up to 9% of clinical trial participants experienced depressive disorders, including approximately 1% of participants who had suicidal thoughts or who attempted suicide. People receiving RPV who have severe depressive symptoms should be evaluated to assess whether the symptoms may be due to RPV and if the risks of continuing the same regimen outweigh the benefits.

Other Factors and Considerations

- Oral RPV is formulated both as a single-drug tablet and in STRs with TAF/FTC, with TDF/FTC, and with DTG. Among available STRs, RPV/TDF/FTC is no longer recommended by the Panel for initial therapy.
- RPV is also available as part of an LA injectable ARV regimen for use in combination with LA CAB in people with HIV who are virologically suppressed and do not have resistance to these drugs (see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression).
- The STR of RPV/TAF/FTC is given once daily and must be administered with a meal (containing at least 390 kcal).
- RPV is also coformulated as a once-daily FDC tablet with DTG that is used as continuation therapy for people with HIV who have achieved viral suppression.[15] However, this combination has not been studied in people with HIV and no prior ART, and it **is not recommended** for initial therapy (see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression).
- The oral drug absorption of RPV can be significantly reduced in the presence of acid-reducing agents. RPV is **contraindicated** in people who are receiving proton pump inhibitors and should be used with caution in those receiving H2 antagonists or antacids (see Drug–Drug Interactions for dosing recommendations).
- RPV is primarily metabolized in the liver by the CYP3A enzyme; its plasma concentration may be affected in the presence of CYP3A inhibitors or inducers (see Drug–Drug Interactions).
- At doses above the approved dose of 25 mg, RPV may cause QTc interval prolongation. RPV should be used with caution when coadministered with a drug known to increase the risk of Torsades de Pointes.

The Panel's Recommendations

- Given the availability of other effective regimens that do not have virologic and immunologic prerequisites to initiate treatment, substantial drug–drug interactions, and a low genetic barrier to resistance, RPV is **not recommended** for initial therapy in most persons with HIV. RPV/TDF/FTC is no longer recommended as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios*, largely due to the limitations of RPV and the availability of DOR/TDF/3TC, which has fewer drug–drug interactions and no virologic and immunologic prerequisites. The Panel continues to recommend RPV/TAF/FTC as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (see Table 6b), largely to retain an STR option containing an NNRTI and TAF.
- Use of RPV with TAF/FTC **(BII)** should be limited to persons with pre-treatment viral loads <100,000 copies/mL and CD4 counts >200 cells/mm^3.
- Data on RPV plus ABC/3TC are insufficient to consider recommending this regimen.

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Protease Inhibitor–Based Regimens

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Table 8d. Characteristics of Protease Inhibitor Options as Initial Antiretroviral Therapy in Certain Clinical Scenarios

Characteristic	DRV
Dosing Frequency	Once daily for persons with no prior PI experience.
PK Boosting	DRV should only be used with a PK booster (i.e., RTV or COBI).
Fixed-Dose Formulation	• DRV/c • DRV/c/TAF/FTC
Available as a Single-Drug Tablet	Yes
Adverse Effects	• Skin rash • Increase in serum transaminase • Hyperlipidemia • Diarrhea, nausea
CYP3A4 Drug–Drug Interactions	CYP34A substrate, inhibitor
Other Significant Drug Interactions	N/A

Key: COBI = cobicistat; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; FTC = emtricitabine; N/A = not applicable; PI = protease inhibitor; PK = pharmacokinetic; RTV = ritonavir; TAF = tenofovir alafenamide

Summary

The U.S. Food and Drug Administration (FDA)–approved protease inhibitors (PIs) include atazanavir (ATV), atazanavir/cobicistat (ATV/c), darunavir (DRV), darunavir/cobicistat (DRV/c), fosamprenavir (FPV), indinavir (IDV), lopinavir/ritonavir (LPV/r), nelfinavir (NFV), ritonavir (RTV), saquinavir (SQV), and tipranavir (TPV). PI-based regimens using pharmacokinetic (PK) enhancement with either cobicistat (COBI) or RTV (also called PK boosting) increase concentration and prolong the half-lives of the PI. These regimens have demonstrated virologic potency, durability in people who are ART-naive, and a high barrier to resistance. Because LPV/r, fosamprenavir/ritonavir (FPV/r), ATV (with or without a PK enhancer), and saquinavir/ritonavir (SQV/r) have disadvantages—such as greater pill burden, lower efficacy, or increased toxicity—only boosted DRV in combination with two nucleoside reverse transcriptase inhibitors (NRTIs) is recommended as initial therapy in certain clinical situations (see Table 6b in Initial Combination Antiretroviral Regimens for People With HIV).

Because transmitted PI resistance is uncommon, boosted DRV-based regimens are preferred over a non-nucleoside reverse transcriptase inhibitor (NNRTI)-based regimen as an option for treatment initiation before resistance test results are available. In addition, a boosted DRV-based regimen can be used for rapid antiretroviral therapy (ART) initiation, in the setting of acute HIV infection, and as the preferred option while awaiting resistance test results for people with a history of long-acting

cabotegravir (CAB-LA) use as pre-exposure prophylaxis (PrEP). Few or no PI mutations are detected when a patient's first PI-based regimen fails, which is not the case with non-nucleoside reverse transcriptase inhibitor (NNRTI)–based regimens and regimens with a first-generation integrase strand transfer inhibitor (INSTI) (e.g., raltegravir or elvitegravir).[1] Because of their high barrier to resistance, PI-based regimens may be useful for people at risk for intermittent therapy because of poor adherence.

DRV requires PK boosting with either RTV or COBI to inhibit the cytochrome P3A4 (CYP3A4) isoenzyme, which may lead to significant drug–drug interactions (see Drug–Drug Interactions). The specific characteristics of DRV are listed in Appendix A, Table 5.

Darunavir/Ritonavir

Efficacy in Clinical Trials

Darunavir/ritonavir (DRV/r) has been studied in several large, randomized controlled trials in people with HIV without prior antiretroviral (ARV) experience. These trials compared DRV/r-based regimens to PI-, INSTI-, or NNRTI-based regimens. Summaries of the results from some key trials are listed below.

- The FLAMINGO study compared DRV/r with dolutegravir (DTG), each administered in combination with two NRTIs—either tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) or abacavir (ABC)/lamivudine (3TC)—in 488 participants who were ART-naive. The rate of virologic suppression at Week 96 was significantly higher among those who received DTG than in those who received DRV/r. The higher rate of virologic failure observed in the DRV/r group was related primarily to the number of failures among those with a viral load >100,000 copies/mL and secondarily to more drug discontinuations in the DRV/r group.[2]
- The AIDS Clinical Trial Group (ACTG) study A5257 (ARDENT), a large, randomized, open-label trial, compared atazanavir/ritonavir (ATV/r) to DRV/r or raltegravir (RAL) over 96 weeks, each given with TDF/FTC. The trial showed similar virologic efficacy for DRV/r, ATV/r, and RAL, but more participants in the ATV/r group discontinued randomized treatment because of adverse events.[3]
- The DRIVE-FORWARD study compared DRV/r to doravirine (DOR), both administered with two investigator-selected NRTIs, in 769 ART-naive participants. At 48 weeks, DOR was found to be non-inferior to DRV/r, with 80% and 84% of participants achieving HIV RNA levels <50 copies/mL, respectively.[4] At Week 96, DOR was superior to DRV/r in terms of virologic suppression (73% vs. 66%).[4] Rates of virologic failure were low and similar in the DOR and DRV/r groups (9% vs. 11%). Treatment-emergent resistance to any study drug was infrequent, occurring in <1% of participants in both the DOR group (2 of 383) and the DRV/r group (1 of 383).

Adverse Effects

- People with HIV who take DRV/r may develop a skin rash, which is usually mild-to-moderate in severity and self-limited. Treatment discontinuation is necessary on rare occasions when severe rash occurs with fever or elevated transaminases.
- ACTG A5257 showed similar lipid changes in participants in the ATV/r and DRV/r arms. Bone mineral density decreased to a greater extent in participants in the ATV/r and DRV/r arms compared to participants in the RAL arm.[3] The likelihood of developing metabolic syndrome was equivalent among the three arms, although a larger increase in waist circumference was

observed at 96 weeks in participants assigned to the RAL arm than in those assigned to the DRV/r arm (P = 0.023).[5]

- In the DRIVE-FORWARD study, treatment-related diarrhea was more frequently reported in the DRV/r arm, and greater increases were observed in fasting low-density lipoprotein cholesterol, triglycerides, non–high-density lipoprotein cholesterol, and total cholesterol compared to the DOR arm.[4]

Other Factors and Considerations

- DRV/r is administered once daily with food in people who are ART-naive.
- DRV has a sulfonamide moiety and should be used with caution in people with severe sulfonamide allergies. In clinical trials, the incidence and severity of rash were similar in participants with and without a history of sulfonamide allergy. Most people with sulfonamide allergy can tolerate DRV.
- DRV/r is a potent CYP3A4 inhibitor, which may lead to significant interactions with other medications metabolized through this same pathway (see Drug–Drug Interactions).
- Unlike DRV/c, DRV/r may be used in pregnancy.

The Panel's Recommendations

- Based on efficacy and safety data from clinical trials and clinical experience, the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) classifies DRV/r with (tenofovir alafenamide [TAF] or TDF) plus (FTC or 3TC) as a *Recommended Initial Regimen for Most People With HIV* who have a history of CAB-LA use as PrEP, pending the results of INSTI genotype testing **(AIII)** (see Table 6a). DRV/r plus (TAF or TDF) plus (FTC or 3TC) **(BI)** and DRV/r plus ABC/3TC **(BII)** are also part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (see Table 6b and Table 7).

Darunavir/Cobicistat

Efficacy in Clinical Trials

- The AMBER trial enrolled 725 ART-naive participants in a Phase 3 randomized controlled trial that compared the single-tablet regimen (STR) DRV/c/TAF/FTC with DRV/c plus TDF/FTC. At 48 weeks, similar virologic suppression rates among participants were achieved in both arms of the study (91% and 88% had HIV RNA <50 copies/mL, respectively). No treatment-emergent mutations associated with DRV or TAF/TDF resistance were observed in either group.[6] At 96 weeks, 85% of participants on the STR maintained HIV RNA levels <50 copies/mL compared to 84% in the DRV/c plus TDF/FTC arm.[7]
- The DIAMOND study evaluated DRV/c/TAF/FTC as an STR in 109 participants in a rapid-initiation model of care. At Week 48, 97 (89%) participants completed the study and 92 (84%) achieved HIV-1 RNA <50 copies/mL by the FDA snapshot analysis. No protocol-defined virologic failures occurred, and incidences of adverse events at least possibly related to study drugs (33%) were low. No study drug-related serious adverse events occurred, and only one (<1%) participant discontinued because of a study drug-related adverse event.[8]

Adverse Effects

- The most common drug-related adverse events were diarrhea, nausea, fatigue, flatulence, rash, and headache.

Other Factors and Considerations

- DRV/c 800 mg/150 mg is available as a coformulated boosted PI or as an STR with TAF/FTC 10 mg/200 mg.
- Both DRV and COBI exposures are reduced markedly during the second and third trimesters of pregnancy, and should be avoided if possible.[9] However, if pregnant women with viral suppression while on DRV/c elect to continue on the drug, frequent viral load monitoring is recommended. For further information, please refer to the Perinatal Guidelines.

The Panel's Recommendations

- The Panel recommends DRV/c plus (TAF or TDF) plus (FTC or 3TC) **(BI)** and DRV/c plus ABC/3TC **(BII)** as part of *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios*.
- Per product label recommendation, DRV/c plus TDF/FTC **is not recommended** for people with creatinine clearance (CrCl) <70 mL/min, whereas DRV/c plus TAF/FTC **is not recommended** for people with CrCl <30 mL/min.
- For people who have a history of CAB-LA use as PrEP, INSTI genotype resistance testing should be performed before starting ART. If ART is to be started before genotypic testing results are available, DRV/c with (TAF or TDF) plus (FTC or 3TC) can be started **(AIII).**

Rating of Recommendations: A = Strong; B = Moderate; C = Weak

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

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Antiretroviral Regimens for Initial Therapy When Abacavir, Tenofovir Alafenamide, and Tenofovir Disoproxil Fumarate Cannot Be Used or Are Not Optimal

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Most of the currently recommended antiretroviral (ARV) regimens for initial therapy consist of two nucleoside reverse transcriptase inhibitors (NRTIs) plus a third active drug. In addition, dolutegravir (DTG)/lamivudine (3TC) is a two-drug, NRTI-limiting regimen that is a recommended option for people with HIV (see Table 6a in Initial Combination Antiretroviral Regimens for People With HIV) and would be preferred over others in situations where it is desirable to avoid abacavir (ABC), tenofovir alafenamide (TAF), and tenofovir disoproxil fumarate (TDF). Several other NRTI-limiting/sparing two-drug regimens have been evaluated in clinical studies, but are not yet recommended by the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) due to insufficient evidence. Note that two-drug regimens **are not currently recommended** during pregnancy and tenofovir-sparing regimens **are not recommended** in people with hepatitis B virus (HBV)/HIV coinfection unless another HBV-active drug (i.e., entecavir) is added. Clinicians should refer to HBV/HIV Coinfection for guidance on treatment of people with HBV infection when TAF or TDF cannot be used as part of the ARV regimen.

Strategies Supported by Evidence From Clinical Trials

Dolutegravir/Lamivudine

- In the GEMINI-1 and GEMINI-2 trials, 1,433 antiretroviral therapy (ART)–naive participants with baseline HIV RNA <500,000 copies/mL and no evidence of HBV infection were randomized to receive a two-drug regimen of DTG plus 3TC or a three-drug regimen of DTG plus TDF/emtricitabine (FTC). At Week 96, DTG plus 3TC was non-inferior to DTG plus TDF/FTC based on the proportion of participants with viral loads <50 copies/mL (86% in DTG plus 3TC group and 89.5% in DTG plus TDF/FTC group).[1] Virologic nonresponse was uncommon, occurring in 3.1% of participants who received DTG plus 3TC and 2% of participants who received DTG plus TDF/FTC. No instances of treatment-emergent NRTI or integrase strand transfer inhibitor (INSTI) resistance occurred in either treatment group. Among participants who started the study with CD4 counts <200 cells/mm^3, the proportion of participants with HIV RNA <50 copies/mL at Week 96 was lower in the DTG plus 3TC group than in the DTG plus TDF/FTC group; however, the difference was not related to a higher rate of virologic failures in the two-drug group. At Week 144, DTG plus 3TC maintained noninferiority to DTG plus TDF/FTC with 82% versus 84% of participants maintaining viral load <50 copies/mL, respectively. The proportion of participants with viral load ≥50 copies/mL was similar between both treatment groups at 3%. There was a lower risk of drug-related adverse events with DTG plus 3TC versus DTG plus TDF/FTC (19.6% vs. 25.0%; relative risk ratio, 0.78; 95% confidence interval, 0.64–0.95).[1]

The Panel's Recommendation

When ABC, TAF, or TDF cannot be used or are not optimal, the Panel recommends DTG/3TC as an initial regimen for people with HIV **(AI)** who—

- Have a viral load ≤500,000 copies/mL,
- Have a genotype available that demonstrates sensitivity to 3TC,
- Do not have a history of long-acting cabotegravir (CAB-LA) use as pre-exposure prophylaxis, *or*
- Have CAB-LA exposure but with documented INSTI sensitivity on genotypic resistance testing.

HBV status must be determined, and if HBV/HIV coinfection is present, another HBV-active drug should be added (see HBV/HIV Coinfection).

Nucleoside-Limiting Regimens With Some Supporting Data but Not Recommended as Initial Therapy

The Panel **does not recommend** the following nucleoside-limiting or nucleoside-sparing regimens for initial therapy due to insufficient clinical trial data.

Darunavir/Ritonavir Plus Lamivudine

- In the ANDES trial, 336 participants were randomized 1:1 to receive open-label, once-daily dual therapy with darunavir/ritonavir (DRV/r) plus 3TC or triple therapy with DRV/r plus TDF/3TC. This study was conducted in Argentina, and the researchers used an FDC of DRV/r 800 mg/100 mg that is available in that country. The median baseline HIV RNA was 4.5 $\log_{10}$ copies, and 23% of participants had HIV RNA >100,000 copies/mL. At Week 48, 91% of the participants in the dual-therapy group and 93% of the participants in the triple-therapy group achieved an HIV RNA <50 copies/mL, demonstrating that dual therapy was non-inferior to triple therapy.[2] The rates of virologic suppression among study participants who had pre-therapy HIV RNA levels >100,000 copies/mL were similar in the dual- and triple-therapy groups (87% and 90%, respectively). The Panel **does not recommend** this regimen as initial therapy as the results from this study have not yet been published.

Darunavir/Ritonavir Plus Raltegravir

- In the NEAT/ANRS 143 study, 805 treatment-naive participants were randomized to receive twice-daily raltegravir (RAL) or once-daily TDF/FTC, each with DRV/r (800 mg/100 mg once daily). At Week 96, DRV/r plus RAL was non-inferior to DRV/r plus TDF/FTC based on the primary endpoint, the proportion of people with virologic or clinical failure. Among those with baseline CD4 counts <200 cells/mm^3; however, there were more virologic failures in the RAL plus DRV/r arm. A trend towards more failure was also observed among those with pre-treatment HIV RNA ≥100,000 copies/mL.[3] High rates of virologic failure in participants with HIV RNA >100,000 copies/mL were also seen in two smaller studies of DRV/r plus RAL.[4,5] The Panel **does not recommend** DRV/r plus RAL as initial ART because of the higher rate of virologic failure in participants with HIV RNA ≥100,000 copies/mL and the higher pill burden of this regimen compared to other Panel-recommended initial ARV regimens.

Darunavir/Ritonavir Plus Rilpivirine

- In a single-arm, open-label pilot study, 36 ART-naive participants without genotypic evidence of resistance to DRV or rilpivirine (RPV) received DRV/r plus RPV for 48 weeks. Half of the participants (18 of 36) had baseline HIV viral loads >100,000 copies/mL. By Week 36, 97% of participants (35 of 36) achieved HIV RNA <50 copies/mL, and by Week 48, all achieved viral suppression (HIV RNA < 50 copies/mL).[6] The Panel **does not recommend** this regimen as initial ART given the small sample size of the study described above and the lack of comparative data evaluating DRV/r plus RPV as initial therapy for people with HIV.

Long-Acting Injectable Cabotegravir With Rilpivirine

- The long-acting injectable combination of CAB plus RPV (LA CAB/RPV) has not been studied in ART-naive participants. In the Phase 3 trial FLAIR and Phase IIb trial LATTE-2,[7,8] ART-naive participants were first treated with 20 weeks of DTG/ABC/3TC or oral CAB+ABC/3TC, respectively. Study participants who achieved virologic suppression were eligible for randomization to receive LA CAB/RPV every month or to continue oral daily ART. The Panel **does not recommend** the LA CAB/RPV as initial therapy for people with HIV because of the lack of data supporting the efficacy of this combination in people who are ART-naive **(AIII).** People desiring to use LA CAB/RPV early in their treatment history should first attain viral suppression on a recommended regimen before transitioning to LA CAB/RPV. See Optimizing Antiretroviral Therapy in the Setting of Viral Suppression for more discussion.

Rating of Recommendations: A = Strong; B = Moderate; C = Weak

Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

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Table 9. Advantages and Disadvantages of Antiretroviral Components of Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

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Note: All drugs within an ARV class are listed in alphabetical order. Information based on Table 6a and Table 6b in the Initial Combination Antiretroviral Regimens for People With HIV section.

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
Dual-NRTI	**ABC/3TC**	• Coformulated with DTG • Generic formulations are available for ABC/3TC, ABC, and 3TC.	• May cause life-threatening HSRs in people who test positive for the HLA-B*5701 allele. As a result, HLA-B*5701 testing is required before use. • ABC use has been associated with CV disease and cardiac events in some, but not all, observational studies.
	TAF/FTC	• Coformulated with BIC, DRV/c, or RPV • Active against HBV; a recommended dual-NRTI option for people with HBV/HIV coinfection • Smaller decline in renal function, less proteinuria, and smaller reductions in BMD than TDF/FTC • Approved for people with eGFR ≥30 mL/min • Can be used in people on chronic hemodialysis	• See text in the NRTI section regarding weight gain with TAF.
	TDF/3TC	• Coformulated with DOR • Generic formulations are available for TDF, 3TC, or TDF/3TC. • Long-term clinical experience • Active against HBV	• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters • Osteomalacia has been reported as a consequence of proximal tubulopathy. • Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.
	TDF/FTC	• Active against HBV; a recommended dual-NRTI option for people with HIV/HBV coinfection • TDF is associated with lower lipid levels than TAF.	• Renal toxicity, including proximal tubulopathy and acute or chronic renal insufficiency, especially when combined with pharmacologic boosters • Osteomalacia has been reported as a consequence of proximal tubulopathy.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
			• Decreased BMD has been associated with use of TDF, especially when combined with pharmacologic boosters.
Single NRTI	**3TC**	• Coformulated with DTG as STR • Avoids potential toxicities associated with TDF, TAF, ABC	• DTG/3TC **is not recommended** for individuals with HIV RNA >500,000 copies/mL, HBV coinfection unless on another HBV active drug, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.
INSTI	**BIC**	• Coformulated with TAF/FTC • Higher barrier to resistance than EVG and RAL • No food requirement	• Oral absorption of BIC can be reduced by simultaneous administration with drugs or supplements containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements or multivitamin tablets with minerals). See dosing recommendations in Table 24d. • CYP3A4 and UGT1A1 substrate (but not a CYP3A4 inducer or inhibitor); potential for drug–drug interactions. • See text in the INSTI section regarding weight gain and INSTI use.
	DTG	• Higher barrier to resistance than EVG or RAL • Coformulated with ABC/3TC and 3TC as STR • No food requirement • Minimal CYP3A4 interactions • Favorable lipid profile	• Oral absorption of DTG can be reduced by simultaneous administration with drugs containing polyvalent cations (e.g., Al-, Ca-, or Mg-containing antacids or supplements or multivitamin tablets with minerals). See dosing recommendations in Table 24d. • UGT1A1 substrate; potential for drug interactions (see Table 24d) • Depression and suicidal ideation (rare; usually in people with preexisting psychiatric conditions) • See text in the INSTI section regarding weight gain and INSTI use.
NNRTI	**DOR**	• Coformulated with TDF/3TC • Fewer CNS side effects compared to EFV and RPV • No food requirement	• Shorter-term clinical experience than with RPV • Potential for CYP450 drug interactions (see Tables 24b, 25a, and 25b) • Treatment-emergent DOR resistance mutations may confer resistance to certain NNRTIs.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)

	RPV	• Coformulated with TAF/FTC	• **Not recommended** in people with pre-ART HIV RNA >100,000 copies/mL or CD4 counts <200 cells/mm^3 because of higher rate of virologic failure in these people.
			• Depression and suicidality
			• QTc interval prolongation; consider using an alternative to RPV in people taking medications with known risk of causing Torsades de Pointes or in those at higher risk of Torsades de Pointes.
			• Rash
			• Transmitted resistance is more common than with PIs and INSTIs.
			• More NNRTI-, TDF-, and 3TC-associated mutations at virologic failure than with regimens that contain EFV and two NRTIs
			• Potential for CYP450 drug interactions (see Tables 24b and 25a)
			• Meal requirement (>390 kcal)
			• Requires acid for adequate absorption
			  ○ Contraindicated with PPIs.
			  ○ Use with H2 antagonists or antacids with caution (see Table 24a for detailed dosing information).

PI	**DRV/c** or **DRV/r**	• Higher barrier to resistance than NNRTIs • PI resistance at the time of treatment failure is uncommon with PK-enhanced PIs.	• Skin rash • Food requirement • GI adverse effects • CYP3A4 inhibitors and substrates: potential for drug interactions (see Table 24a) • Increased CV risk reported in one observational cohort study[a] • Hepatotoxicity has been reported, especially in those with preexisting liver disease.

Table 9. Advantages and Disadvantages of Antiretroviral Components Recommended as Initial Antiretroviral Therapy Listed in Table 6a and Table 6b

ARV Class	ARV Agent(s)	Advantage(s)	Disadvantage(s)
	DRV/c Specific considerations	• Coformulated as DRV/c and DRV/c/TAF/FTC	• COBI inhibits active tubular secretion of Cr and can increase serum Cr without affecting renal glomerular function. • Coadministration with TDF **is not recommended** in people with CrCl <70 mL/min. • COBI (like RTV) is a potent CYP3A4 inhibitor, which can result in significant interactions with CYP3A substrates. • COBI should be avoided in pregnancy because levels of COBI and its boosted drugs are lower in the second and third trimesters. If women who are pregnant with suppressed virus on DRV/c elect to continue on the drug, frequent viral load monitoring is recommended.

[a] D:A:D international prospective multicohort study[1]

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; BMD = bone mineral density; Ca = calcium; CD4 = CD4 T lymphocyte; CNS = central nervous system; COBI = cobicistat; Cr = creatinine; CrCl = creatinine clearance; CV = cardiovascular; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; eGFR = estimated glomerular filtration rate; FTC = emtricitabine; GI = gastrointestinal; H2 = histamine 2; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; INSTI = integrase strand transfer inhibitor; Mg = magnesium; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; PPI = proton pump inhibitor; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT = uridine diphosphate glucuronosyltransferase

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MANAGEMENT OF PEOPLE WITH HIV AND ANTIRETROVIRAL THERAPY EXPERIENCE

Virologic Failure

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Key Considerations and Recommendations
• Assessing and managing a person with HIV who is experiencing antiretroviral therapy (ART) failure can be complex. Expert advice can be critical and should be sought in many instances. • Evaluation of virologic failure should include an assessment of ART adherence, drug–drug and drug–food interactions, drug tolerability, HIV RNA level and CD4 T lymphocyte (CD4) cell count trends over time, ART history, and prior and current drug-resistance test results. • Drug-resistance testing should be performed while the person is taking the failing antiretroviral (ARV) regimen **(AI)** or within 4 weeks of discontinuing a non–long-acting ARV regimen **(AII).** If more than 4 weeks have elapsed since non–long-acting ARV regimens were discontinued, resistance testing still can provide useful information to guide therapy, although it may not detect previously selected resistance mutations **(CIII).** • For people who previously received long-acting (LA) cabotegravir (CAB) plus rilpivirine (RPV), or LA CAB/RPV, and present with virologic failure, resistance testing (including integrase strand transfer inhibitor [INSTI] genotypic testing) should be performed regardless of the time since the last dose of LA CAB/RPV **(AIII).** • The goal of treatment for people with HIV with drug resistance who are experiencing virologic failure is to establish virologic suppression (i.e., HIV RNA levels below the lower limits of detection of currently used assays) **(AI).** • A new ARV regimen should preferably include two fully active drugs if at least one has a high resistance barrier, such as a second-generation INSTI or a boosted protease inhibitor (PI) **(AI).** • A new ARV regimen can also include a second-generation INSTI (i.e., dolutegravir [DTG]) plus a boosted PI (preferably boosted darunavir) without nucleoside reverse transcriptase inhibitors (NRTIs) if both are fully active **(AI)**. • If the above two options are not feasible, a new ARV regimen that includes at least one drug with a high resistance barrier plus two partially active NRTIs—particularly tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF) with lamivudine (3TC) or emtricitabine (FTC)—can also be considered, although this is a less well-defined strategy and is based on an extrapolation of existing data. Caution with close monitoring of virologic response is advised **(BII),** as discussed below. • If no fully active drug with a high resistance barrier is available, every effort should be made to include three fully active drugs in the new ARV regimen **(AI).** • In general, adding a single ARV drug to a virologically failing regimen **is not recommended,** because this would rarely result in full virologic suppression and may risk the development of resistance to all drugs in the regimen **(BII).** • In some rare instances, it might not be possible to achieve maximal virologic suppression in people with HIV who are highly ART-experienced and have extensive drug resistance. In this case, ART should be continued **(AI)** with regimens that are designed to maintain CD4 counts, preserve treatment options, delay clinical progression, and minimize toxicity.

- When it is not possible to construct a viable suppressive regimen for a person with multidrug-resistant HIV, the clinician should consider enrolling the person in a clinical trial of investigational agents or contacting pharmaceutical companies that may have investigational agents available.
- In people with HIV and virologic failure, it is crucial to provide continuous adherence support before and after ARV regimen changes.
- When switching an ARV regimen in a person with hepatitis B virus (HBV)/HIV coinfection, the person should remain on an ARV agent that is active against HBV and has a high resistance barrier to HBV (i.e., TAF, TDF, or entecavir) to avoid HBV rebound and hepatocellular damage **(AII)** (see Hepatitis B Virus/HIV Coinfection for more information).
- Discontinuing or briefly interrupting therapy may lead to a rapid increase in HIV RNA, a decrease in CD4 count, and an increase in the risk of clinical progression. Therefore, discontinuing or interrupting ART **is not recommended** in the setting of virologic failure **(AI).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Antiretroviral (ARV) regimens that are currently recommended for initial therapy in people with HIV have a high likelihood of achieving and maintaining plasma HIV RNA levels that are below the lower limits of detection (LLOD) of currently used assays (see Initial Combination Antiretroviral Regimens for People With HIV). People on antiretroviral therapy (ART) who do not achieve this treatment goal or who experience virologic rebound can develop resistance mutations to one or more components of their ARV regimen with possible cross-resistance to other ARVs. Adherence to ARV regimens can be challenging for some people with HIV, and poor adherence can result in detectable HIV RNA levels. The extent of drug resistance varies based on ARV treatment history, with some people having minimal or no resistance and others with extensive resistance. Managing people with extensive resistance is complex and usually requires consultation with an HIV expert. This section of the guidelines defines virologic failure in people on ART and discusses strategies to manage ART in these individuals.

Virologic Response Definitions

The following definitions are used in this section to describe the different levels of virologic response to ART.

- **Virologic suppression:** A confirmed HIV RNA level below the LLOD of available assays.
- **Virologic failure:** The inability to achieve or maintain suppression of viral replication to HIV RNA level <200 copies/mL.
- **Incomplete virologic response:** Two consecutive plasma HIV RNA levels ≥200 copies/mL after 24 weeks on an ARV regimen in a person who has not yet had documented virologic suppression on that regimen. A person's baseline HIV RNA level may affect the time course of response, and some regimens may take longer than others to suppress HIV RNA levels.
- **Virologic rebound:** After virologic suppression, confirmed HIV RNA level ≥200 copies/mL.
- **Virologic blip:** After virologic suppression, an isolated detectable HIV RNA level that is followed by a return to virologic suppression.
- **Low-level viremia:** Confirmed HIV RNA level above the LLOD but <200 copies/mL.

Antiretroviral Therapy Goals and Presence of Viremia While on Antiretroviral Therapy

The goal of ART is to suppress HIV replication to a level below which drug-resistance mutations cannot emerge. Although not conclusive, the evidence suggests that selection of drug-resistance mutations does not occur in people with HIV RNA levels that are persistently suppressed below the LLOD of current assays.[1]

Virologic blips are not usually associated with subsequent virologic failure.[2] In contrast, there is controversy regarding the clinical implications of low-level viremia, i.e., persistent HIV RNA levels between the LLOD and <200 copies/mL in people on ART. Viremia at this threshold is detected with some frequency by commonly used real-time polymerase chain reaction (PCR) assays, which are more sensitive than the PCR-based HIV RNA platforms used in the past.[3-5] Several retrospective studies support the supposition that virologic failure is more likely to occur in people with HIV RNA levels ≥200 copies/mL than in those with low-level viremia between 50 copies/mL and 199 copies/mL.[6-8] However, other studies have suggested that detectable viremia at <200 copies/mL can be predictive of virologic failure[9] and can be associated with the evolution of drug resistance[10] and non-AIDS morbidities.[11]

Persistent HIV RNA levels ≥200 copies/mL are often associated with evidence of viral evolution and accumulation of drug-resistance mutations.[12] This association is particularly common with HIV RNA levels >500 copies/mL.[13] Therefore, people who have persistent HIV RNA levels ≥200 copies/mL are considered to be experiencing virologic failure.

Causes of Virologic Failure

Virologic failure can occur for many reasons. Data from cohorts in the earlier era of combination ART suggested that suboptimal adherence and drug intolerance/toxicity are key contributors to virologic failure and regimen discontinuations.[14,15] Current ARVs are easier to tolerate and have less pill burden, which may improve adherence.[16-18] Virologic failure may be associated with a variety of factors, including the following:

HIV-Related Factors

- Presence of transmitted or acquired drug-resistant virus that may or may not be documented by current or past drug-resistance test results
- Prior ARV treatment failure
- Innate drug resistance to prescribed ARV drugs
- Higher pre-treatment HIV RNA levels (e.g., HIV RNA >100,000 copies/mL; some regimens may be less effective at higher levels)

Antiretroviral Regimen–Related Factors

- Suboptimal pharmacokinetics (PK) (e.g., variable absorption, metabolism, penetration into reservoirs)
- Suboptimal virologic potency
- Low barrier to resistance
- Reduced efficacy due to prior exposure to suboptimal regimens (e.g., monotherapy, dual–nucleoside reverse transcriptase inhibitor [NRTI] therapy, or the sequential introduction of drugs)

- Food requirements
- Drug–drug interactions with concomitant medications, which may reduce concentrations of the ARV drugs
- Adverse drug effects
- High pill burden and/or dosing frequency
- Prescription (prescribing or dispensing) errors

Social and Adherence-Related Factors

Note: Each of the social and adherence-related factors listed below are discussed in the Adherence to the Continuum of Care section.

- Active substance use, mental health disorders, or neurocognitive impairment
- Unstable housing and other psychosocial factors
- Missed clinic appointments
- Interruption of or intermittent access to ART
- Cost and affordability of ARV drugs, which may affect the ability to access or continue therapy (see the Cost Considerations and Antiretroviral Therapy section)

Managing People With HIV and Virologic Failure

If virologic failure is suspected or confirmed, a thorough assessment of whether one or more of the above factors could have been the cause(s) of failure is indicated. The causes of virologic failure can usually be identified but may not be obvious in some cases. Distinguishing among the causes of virologic failure is important, because the approaches to subsequent therapy may differ, depending on the cause. Potential causes of virologic failure should be explored in depth. Once virologic failure is confirmed, steps should be taken to improve virologic outcomes. If a new ARV regimen is needed, approaches to designing a new regimen are discussed below.

Key Factors to Consider When Designing a New Antiretroviral Regimen After Virologic Failure

General Principles on Antiretroviral Use in Virologic Failure

- When designing a new ARV regimen for a person with virologic failure, it is important to consider the factors outlined above on causes of virologic failure and, if possible, consider better tolerated and adherence-friendly regimens.
- A new ARV regimen should be selected based on ART history, current and previous drug-resistance test results, and whether a fully susceptible ARV drug with a high barrier to resistance and other fully active drugs are available.[9,19-31]
- ARV drugs with a high barrier to resistance are those in which emergent resistance is uncommon in people experiencing virologic failure. These include boosted darunavir (DRV), dolutegravir (DTG), and bictegravir (BIC).
- Fully active drugs may include—
    - Drugs in classes for which the person has not previously selected for drug-resistant virus.

  - Newer drugs in existing drug classes that are predicted to be fully active against HIV isolates despite the presence of resistance mutations for some drugs in the same drug class. For example, the non-nucleoside reverse transcriptase inhibitors (NNRTIs) etravirine and possibly doravirine (DOR), the protease inhibitor DRV, and the integrase strand transfer inhibitors (INSTIs) DTG and BIC. However, clinical data supporting the use of DOR or BIC in the setting of virologic failure are limited.
  - Drugs with novel mechanisms of action that the person with HIV has not received before, such as the post-attachment inhibitor ibalizumab (IBA), the gp120 attachment inhibitor fostemsavir (FTR), the capsid inhibitor lenacapavir (LEN), the fusion inhibitor enfuvirtide (T-20), or the CCR5 antagonist maraviroc (MVC) in people with no detectable CXCR4-using virus.

- ARV drugs with partial activity are those predicted to have antiviral activity but to a lesser extent than when there is no underlying drug resistance.
- Administering a drug that a person has never used does not ensure that the drug will be fully or partially active; the potential exists for cross-resistance among drugs from the same class.
- Discontinuing or briefly interrupting therapy in a person with viremia **is not recommended** because it may increase HIV RNA levels, decrease CD4 T lymphocyte (CD4) cell count, and increase the risk of clinical progression **(AI)**[32,33] (see Discontinuation or Interruption of Antiretroviral Therapy).
- The presence of preexisting (transmitted) drug resistance also may lead to virologic failure.[34,35]

Drug-Resistance Testing to Guide New Antiretroviral Regimens

- The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends that drug-resistance testing should be used to guide ARV regimen design and should be performed while the person with HIV is still taking the failing regimen **(AI)** or within 4 weeks of discontinuation of a non–long-acting regimen **(AII).** If more than 4 weeks have elapsed since discontinuation of a non–long-acting regimen, drug-resistance testing still may provide useful information to guide therapy, although it may not detect previously selected resistance mutations **(CIII).**
- Drug-resistance testing is recommended in persons with confirmed virologic failure, i.e., HIV RNA repeatedly >200 copies/mL (**AI** for >1,000 copies/mL, **AIII** for 501–1,000 copies/mL, **CIII** for confirmed 201–500 copies/mL), although at low HIV RNA levels, testing may be difficult to obtain outside of a research setting. In persons with HIV RNA >200 copies/mL but <500 copies/mL, testing may be unsuccessful, but it still should be considered.
- Drug resistance is cumulative, meaning that once a mutation is detected in a resistance assay, it should be considered present in that person's HIV thereafter (this is sometimes referred to as "archived" resistance), regardless of whether it appears on subsequent drug-resistance assays. Thus, clinicians should evaluate the extent of drug resistance, taking into account all of the person's ART history and, importantly, prior genotypic- or phenotypic-resistance test results.
- Activity of ART based on current and cumulative genotypic mutations can be estimated by tools and interpretation algorithms, such as the Stanford University HIV Drug-Resistance Database. Also see Drug-Resistance Testing.
- Some drug-resistance assays only detect resistance to NRTIs, NNRTIs, or protease inhibitors (PIs); INSTI-resistance testing may need to be ordered separately. INSTI-resistance testing should be ordered in people who experience virologic failure on an INSTI-based regimen. Additional drug-resistance tests for people who experience failure on a fusion inhibitor **(AII),** and viral tropism tests for people who experience failure on a CCR5 antagonist **(BIII)** are also

available. There is currently no commercially available resistance test for IBA, FTR, or LEN (see Drug-Resistance Testing).

Strategies for New Antiretroviral Regimen Design

- A new ARV regimen should preferably include two fully active drugs if at least one has a high resistance barrier, such as a second-generation INSTI or a boosted PI **(AI).**[36]
- A new ARV regimen can also include a second-generation INSTI (e.g., DTG) plus a boosted PI (preferably boosted DRV) without NRTIs if both are fully active **(AI);**[37-41] see more detailed discussion in *Managing Virologic Failure in Different Clinical Scenarios* below. If this regimen is used in people with hepatitis B virus (HBV)/HIV coinfection, an HBV-active drug with a high barrier to resistance (e.g., tenofovir alafenamide [TAF], tenofovir disoproxil fumarate [TDF], or entecavir) should be continued or started to avoid HBV rebound and hepatocellular damage.
- If the above two options are not feasible, a new ARV regimen can also include a fully active drug with a high resistance barrier plus two partially active NRTIs—particularly TAF or TDF with lamivudine (3TC) or emtricitabine (FTC)—though this is less well-defined and close monitoring is advised **(BII);** this is discussed in more detail in *Managing Virologic Failure in Different Clinical Scenarios* below.[36,37,42,43]
- If no fully active drug with a high resistance barrier is available, every effort should be made to include three fully active drugs in the regimen **(AI).** See the clinical scenarios below for further guidance on the number of fully active drugs a regimen should contain.
- Despite the presence of drug-resistance mutations, some ARV drugs in the regimen may still have partial activity against the person's HIV and may be retained as part of a salvage regimen. These drugs may include NRTIs, PIs, and second-generation INSTIs, although dosing of some drugs (e.g., DRV and DTG) may need to be increased when treating people with relevant resistance mutations to achieve drug concentrations necessary to be at least partially active against a less sensitive virus.[44-46]
- In contrast, other agents in which resistance may be expected should be discontinued, because their continued use is unlikely to contribute to virologic suppression. These drugs include NNRTIs (especially efavirenz, nevirapine, and rilpivirine [RPV]), the first-generation INSTIs raltegravir (RAL) and elvitegravir (EVG), and T-20.[47-49]
- Long-acting (LA) cabotegravir (CAB)/rilpivirine (RPV) is currently approved as a complete ART regimen for individuals engaged in care who have good adherence to an oral regimen, sustained undetectable HIV RNA levels for >3 months, no known or suspected resistance to either drug, and no active HBV infection. To date, no large or randomized clinical trials have been published using any INSTI plus NNRTI, including LA CAB/RPV, as a complete regimen for people without viral suppression. However, a few small observational studies have shown that people with viremia despite intensive efforts on oral ART, without resistance to CAB or RPV, can achieve viral suppression with LA CAB/RPV when intensive supportive services are available.[50-53] If considering LA CAB/RPV in this population, it is important to note that data are limited, and this is not an approved indication of the regimen. If the regimen is used in people with inconsistent adherence and virologic failure, there is a high likelihood of developing acquired resistance to CAB and/or RPV, which might limit future treatment options. The approaches and considerations for the use of LA CAB/RPV in people with viremia is further outlined below.
- When changing an ARV regimen in a person with HBV/HIV coinfection, ARV drugs that are active against HBV (especially TAF or TDF) should be continued as part of the new regimen or, if not possible, entecavir should be initiated **(AII).** Using 3TC or FTC as the only drug with HBV activity in a regimen **is not recommended (AII)** because HBV resistance to these drugs can

emerge. Discontinuation of these drugs may lead to the reactivation of HBV, which may result in serious hepatocellular damage (see Hepatitis B Virus/HIV Coinfection).

- Virologic responses should be closely monitored after regimen switch (e.g., HIV RNA level testing performed within 4 to 8 weeks), with prompt drug-resistance testing if virologic response is inadequate.

Managing Virologic Failure in Individuals With Different Levels of Viremia

People with HIV and detectable HIV RNA levels while on ART comprise a heterogeneous group of individuals with different ART exposure histories, degrees of drug resistance, durations of virologic failure, and levels of plasma viremia. Management strategies should be individualized. The first steps are to confirm the level of HIV viremia and to assess and address adherence and potential drug–drug interactions (including interactions with over-the-counter products and supplements) and drug–food interactions. Some general approaches based on the level of viremia are addressed below.

- **Low-level viremia (HIV RNA above the LLOD and <200 copies/mL):** People who have these HIV RNA levels do not typically require a change in treatment **(AII).**[4] Although there is no consensus on how to manage these individuals, the risk that drug resistance will emerge is believed to be relatively low. Therefore, these individuals should continue their current regimens and have their HIV RNA levels monitored at least every 3 months to assess the need for changes to ART in the future **(AIII).**
- **HIV RNA ≥200 copies/mL and <1,000 copies/mL:** In contrast to people with detectable HIV RNA levels that are persistently <200 copies/mL, people with levels that are persistently ≥200 copies/mL often develop drug resistance, particularly when HIV RNA levels are >500 copies/mL.[6,7] People who have persistent plasma HIV RNA levels in the range of 200 copies/mL to 1,000 copies/mL are considered to be experiencing virologic failure, and drug-resistance testing should be attempted, particularly in people with HIV RNA levels >500 copies/mL (at <500 copies/mL, testing may not be possible for technical reasons). Management approaches should be the same as for people with HIV RNA >1,000 copies/mL (as outlined below). When drug-resistance testing cannot be performed because of low HIV RNA levels, the decision of whether to empirically change ARV drugs should be made on a case-by-case basis, taking into account whether a new regimen that is expected to fully suppress viremia can be constructed. If genotypic-resistance test results cannot be obtained because of low HIV RNA levels, proviral DNA genotypic testing may be considered. Results from this test should be interpreted with caution because these assays might miss some or all previously existing drug-resistance mutations. However, mutations that are detected using proviral DNA genotypic testing may be significant and can affect the effectiveness of future regimens (see Drug-Resistance Testing).
- **HIV RNA ≥1,000 copies/mL and no drug-resistance mutations identified using current or previous genotypic-resistance test results:** This scenario is almost always associated with suboptimal adherence. A thorough assessment should be conducted to evaluate the level of adherence, identify and address the underlying cause(s) for incomplete adherence and, if possible, simplify the regimen (e.g., decrease pill count, simplify food requirement or dosing frequency; see Adherence to the Continuum of Care). Assessment includes the following:
    - Assessing the person's access to ART, including access to pharmacy, refills, and copays or patient assistance programs, and seeking assistance to overcome any barriers to consistent access to ART.

- Assessing social determinants that may impact adherence (e.g., substance use, unstable housing, mental health challenges, etc.).
- Assessing the person's tolerance of the current ARV regimen and the severity and duration of side effects if intolerance is a concern, while considering that even minor side effects can affect adherence.
- Addressing intolerance by treating symptoms (e.g., with antiemetics or antidiarrheals), switching one ARV agent in a regimen to another agent in the same drug class, or switching from one drug class to another class (e.g., from an NNRTI to a PI or an INSTI; see Adverse Effects of Antiretroviral Agents).
- Reviewing food requirements for each medication and assessing whether the person adheres to the requirements.
- Assessing whether a recent history of gastrointestinal symptoms (e.g., vomiting, diarrhea) may result in short-term malabsorption.
- Reviewing concomitant medications (including over-the-counter medications and dietary supplements) for possible adverse drug–drug interactions (consult Drug–Drug Interactions and Tables 24a through 25b for common interactions) and, if possible, making appropriate substitutions for ARV agents and/or concomitant medications.
- Considering therapeutic drug monitoring if PK drug–drug interactions (e.g., when used with rifamycin) or impaired drug absorption (e.g., using polyvalent cations with an INSTI) leading to decreased ARV drug exposure is suspected.
- Considering the timing of the drug-resistance test (e.g., was the person mostly or completely nonadherent to oral ART for >4 weeks before testing?) (see Drug-Resistance Testing).
- After a thorough assessment, the following approaches may be considered:
  - If the current regimen is well tolerated, with no significant drug–drug or drug–food interactions, it is reasonable to continue the same regimen while focusing on improving adherence.
  - If the agents are poorly tolerated or have important drug–drug or drug–food interactions, changing the regimen to an equally effective but more tolerable regimen should be considered.
  - HIV RNA level testing should be repeated 4 to 8 weeks after treatment adherence is encouraged or treatment is modified **(AII);** if RNA levels remain >200 copies/mL, genotypic drug-resistance testing should be performed to determine whether a resistant viral strain has emerged (**AI** for >1,000 copies/mL, **AIII** for 501–1,000 copies/mL, **CIII** for 201–500 copies/mL), though at low RNA levels, testing may be difficult to obtain outside of a research setting.

- **HIV RNA >1,000 copies/mL and drug resistance identified:** If new or previously detected resistance mutations compromise the regimen, the regimen should be modified as soon as possible to avoid progressive accumulation of resistance mutations.[54] In addition, several studies have shown that virologic responses to new and fully active regimens are greater in individuals with lower HIV RNA levels and/or higher CD4 counts at the time of regimen changes; thus, the change is best done before viremia worsens or before CD4 count declines.[9,55] The availability of newer ARV drugs, including some with new mechanisms of action, makes it possible to suppress HIV RNA levels to below the LLOD in most people with HIV. The options in this setting depend on the extent of drug resistance and are addressed in the clinical scenarios outlined below.

Managing Virologic Failure in Different Clinical Scenarios

Note: See Table 10 below for a summary of these recommendations.

Virologic Failure on the First Antiretroviral Regimen

The Panel recommends that drug-resistance testing should be performed upon treatment failure to inform regimen design **(AI).**

NNRTI plus NRTI regimen failure: Although an NNRTI plus NRTI regimen is no longer considered a preferred first-line ART option in treatment guidelines, data from clinical trials comparing different ARV regimens after NNRTI plus NRTI failure provide the most robust evidence to inform second-line treatment strategies and, therefore, are included here.

In this setting, people with HIV often have viral resistance to the NNRTI, with or without the M184V/I mutation, which confers high-level resistance to 3TC and FTC. Additional NRTI mutations also may be present. Below are some treatment options.

- **Second-generation INSTI (BIC or DTG) plus NRTIs:** The Panel recommends that fully active DTG plus two NRTIs, at least one of which is fully active, can be a treatment option after failure of a first-line NNRTI-based therapy **(AI).** BIC, which is available only in a combination pill with FTC/TAF, also has a high resistance barrier and may have similar activity to that of DTG in this setting, and is also an option **(AIII);** however, no clinical trial data for this strategy with BIC is available. If at least one fully active NRTI cannot be assured and a clinician wants to avoid using a boosted PI or a drug from other classes, a regimen that includes fully active DTG plus two NRTIs that are estimated to be only partially active (particularly TAF or TDF with 3TC or FTC) can be considered, with caution and close monitoring of viral response, as further discussed below **(BII).**

  In the DAWNING trial, participants from 13 countries who experienced virologic failure while on a first-line NNRTI-based regimen were randomized to receive either lopinavir/ritonavir(LPV/r) or DTG, each with two NRTIs, one of which had to be fully active based on real-time drug-resistance testing. The study was stopped early after an interim analysis showed that the DTG arm was superior to the LPV/r arm. The superiority of DTG was somewhat counterbalanced by the finding that 2 of 11 participants in the DTG arm who met virologic withdrawal criteria selected for INSTI resistance, with no PI resistance selected for in the LPV/r arm.[36]

  In the NADIA trial, participants in Uganda, Kenya, and Zimbabwe who experienced virologic failure while on a first-line NNRTI plus TDF and 3TC or FTC were randomized to receive either darunavir/ritonavir (DRV/r) or DTG, each with 3TC; participants were assigned by a second randomization to receive a third ARV, either TDF or zidovudine (ZDV). Unlike the DAWNING study, full activity of the NRTIs based on genotype testing at the time of switch was not required.[42,43] The primary study outcome was virologic suppression <400 copies/mL; at 48 and 96 weeks, >85% of participants had HIV RNA levels <400 copies/mL in all arms, and the DTG-based regimens were non-inferior to the DRV/r-based regimens. However, at 96 weeks, 9 of 235 (4%) participants in the DTG group developed DTG resistance. This represented 45% of participants in the DTG group with HIV RNA levels >400 copies/mL, six of whom were assigned to ZDV. In contrast, no PI resistance was selected for in the DRV/r group. When comparing TDF with ZDV, the two NRTIs demonstrated virologic suppression noninferiority at 48 weeks, but TDF was superior to ZDV at 96 weeks. These results included 84 of 92 (91%) participants in the DTG group who had virologic suppression <400 copies/mL despite no predicted active NRTIs at the time of failure of first-line NNRTI-based regimens, and a large proportion of this group had the K65R and M184V/I mutations. Individual-level drug-resistance data would have enabled further examination of specific mutation patterns and their association with patient characteristics and

treatment outcomes. Although such data are not available, these results suggest that ZDV should not be used over TDF in a public health approach. The decision to use DTG or DRV/r without another fully active drug should balance the overall efficacy data of these regimens, with considerations for potential emergent drug resistance, drug–drug interactions, convenience, and tolerability. The results from these studies should be interpreted with caution, as individual-level drug-resistance data and their linkage to patient characteristics and outcomes were not available, thus preventing full interpretation of these results. Additionally, these results may not be generalizable to settings and populations outside of the trials due to differences in geography, HIV-1 subtype, study population, ART availability, and treatment monitoring practice.

- **Boosted PI plus NRTIs:** The Panel recommends that a boosted PI (preferably boosted DRV) plus two NRTIs, at least one of which is fully active, can be an option after failure of a first-line NNRTI-based therapy **(AI).** However, if full activity of at least one NRTI in the regimen cannot be assured, fully active boosted DRV plus two NRTIs estimated to be only partially active (particularly TAF or TDF with 3TC or FTC) can be considered, with close monitoring **(BII).** Notably, boosted PIs as monotherapy **are not recommended (AI).**[37,39,40,42,43,56]

  Several large, randomized controlled trials (primarily conducted in resource-limited settings where NNRTI-based regimens have been used as first-line therapy) have explored different second-line regimen options. The studies found that regimens that contained LPV/r or DRV/r plus at least two NRTIs were as effective as regimens that contained LPV/r plus RAL or DTG plus two NRTIs. Participants in some of these studies did not undergo drug-resistance testing before randomization. In the NADIA trial (summarized above), virologic efficacy of DTG and DRV/r-based regimens were non-inferior at 48 and 96 weeks, with TDF being non-inferior at 48 weeks and superior at 96 weeks compared with ZDV. Although there were nine participants in the DTG group who developed DTG resistance (six on ZDV and three on TDF), no participant in the DRV/r group developed PI resistance. Additionally, 74 of 80 (93%) participants in the DRV/r group had virologic suppression <400 copies/mL at 96 weeks despite no predicted active NRTIs at the time of failure of first-line NNRTI-based regimens. As outlined above in the discussion about second-generation INSTI plus no estimated fully active NRTIs based on current drug-resistance algorithms, these results should be interpreted with caution within, and particularly beyond, the study populations and settings.

- **Boosted PI plus an INSTI:** The Panel recommends that boosted DRV plus DTG, both with high barriers to resistance, should be the preferred boosted PI plus INSTI option **(AI).** In a setting where a two-drug boosted PI and INSTI combination are being considered and both boosted DRV and DTG cannot be used, LPV/r plus RAL can be a treatment option for those who experienced virologic failure on an NNRTI-based regimen **(CI).**

  D^{2}EFT is an open-label multinational randomized controlled trial that assessed the efficacies of DRV/r plus DTG versus DTG plus two NRTIs versus standard of care (DRV/r plus two NRTIs) for participants with first-line failure of an NNRTI-based regimen.[41] In D^{2}EFT, TDF plus 3TC or FTC were the NRTIs used. At 48 weeks, the proportion of participants who achieved HIV RNA <50 copies/mL was 84% for the DRV/r + DTG arm, 75% for the DRV/r plus two NRTI arm, and 78% for the DTG plus two NRTI arm, showing that the DRV/r + DTG arm was non-inferior to the other two regimens, with more participants achieving viral suppression. Several other small retrospective studies have found that a regimen of boosted DRV plus DTG is effective in achieving viral suppression in people with documented resistance to multiple drug classes.[57-59] Three randomized controlled trials have found that a regimen that consisted of LPV/r plus RAL can be as effective as LPV/r plus at least two NRTIs as second-line therapy for people who failed first-line ART (mostly with an NNRTI-based regimen).[37,39,40]

  If this regimen is used in people with HBV coinfection, an HBV-active drug with a high barrier to resistance (i.e., TAF, TDF, or entecavir) should be continued or started to avoid HBV rebound and hepatocellular damage.

Boosted PI plus NRTI regimen failure: In this scenario, because boosted PI has a high barrier to resistance, most people will have either no resistance or resistance that is limited to 3TC and FTC, though additional NRTI mutations also may be present.[60,61] Failure in this setting is often attributed to poor adherence, drug–drug interactions, or drug–food interactions. Below are some management options.

- **Switch to a second-generation INSTI plus NRTIs regimen:** Second-generation INSTIs have increasingly become preferred options over boosted PIs due to lower drug–drug interaction potential, improved tolerability, comparable efficacy, and a high barrier to resistance. Therefore, consideration should be given to switching to DTG or possibly BIC plus two NRTIs (if at least one of them is fully active) **(AIII).** If only one of the NRTIs is fully active or if adherence is a concern, DTG is currently preferred over BIC **(AIII).** If full activity of at least one NRTI in the regimen cannot be assured, DTG plus two NRTIs estimated to be only partially active based on current drug-resistance algorithms (particularly TAF or TDF with 3TC or FTC) can be considered **(CIII).** As outlined above, results from studies that may suggest such extrapolations should be interpreted with caution, as they did not involve failure of first-line boosted PI plus NRTIs regimens and as individual-level drug-resistance data and their linkage to patient characteristics and outcomes were not available, thus preventing full interpretation of these results. Additionally, these results may not be generalizable to settings and populations outside of the trials due to differences in geography, HIV-1 subtype, patient population, ART availability, and treatment monitoring practice.
- **Maintain the same regimen:** A systematic review of multiple randomized trials that investigated the failures of first-line ritonavir-boosted PI-based regimens showed that taking actions to improve adherence to the original regimen is as effective as changing to new regimens with or without drugs from new classes **(AII).**[62] If the regimen is well tolerated with no concerns about drug–drug or drug–food interactions or drug resistance, then the regimen can be continued with adherence support and viral monitoring.
- **Switch to another PI-based regimen:** If a regimen with an INSTI plus two NRTIs is not an option and poor tolerability is contributing to virologic failure, the regimen can be modified with a different boosted PI that has no evidence for cross-resistance, plus a second-generation INSTI **(AIII),** or plus two NRTIs (at least one of which is fully active) **(AIII).** If full activity of at least one NRTI in the regimen cannot be assured, another fully active boosted PI plus two NRTIs estimated to be only partially active (particularly TAF or TDF with 3TC or FTC) can be considered, with close monitoring of viral response **(BIII).**

INSTI plus NRTI regimen failure: Virologic failure in people on a regimen that consists of RAL or EVG plus two NRTIs may be associated with emergent resistance to 3TC or FTC (with/without additional NRTI mutations) and, possibly, the INSTI.[63] Viruses with EVG or RAL resistance often remain susceptible to DTG and BIC.[55] However, in the presence of certain INSTI mutations, DTG dose should be increased from once daily to twice daily.[44] The effective dose of BIC in these situations is unknown. In contrast, in clinical trials, people who experienced virologic failure while receiving DTG or BIC plus two NRTIs as first-line therapy were unlikely to develop resistance to DTG or BIC.[63-65] No existing clinical trial data guide therapy for first-line INSTI failures; therefore, treatment strategy should be based on drug-resistance test results and the potential potency of the next regimen. Below are some treatment options, based on drug-resistance pattern considerations.

- **Virologic failure without any resistance mutations:** The person with HIV should be managed as outlined above in the section on virologic failure without drug resistance.
- **Virologic failure without INSTI resistance:** The regimen can be modified to one of the following:
    - A boosted PI plus two NRTIs (preferably at least one of which is fully active) **(AIII);** *or*

- DTG, or likely BIC, plus two NRTIs (preferably at least one of which is fully active) **(AIII);** *or*
- A boosted PI plus DTG **(AIII).**

- **Virologic failure with resistance to RAL and/or EVG but susceptibility to DTG:** The regimen can be modified to one of the following:
  - A boosted PI plus two NRTIs (preferably at least one of which is fully active) **(AIII);** *or*
  - DTG (twice daily) plus two NRTIs (at least one of which is fully active) **(BIII);** *or*
  - DTG (twice daily) plus a boosted PI **(AIII).**

Although BIC has a high resistance barrier, there are no data on whether the current BIC dose is efficacious in settings with RAL or EVG resistance and, therefore, it **is not currently recommended (BIII).**

INSTI plus NNRTI regimen failure: Virologic failure in people on a regimen that consists of an INSTI (e.g., DTG or CAB) plus an NNRTI (e.g., RPV) may be associated with resistance to one or both of the medications in the regimen.[66,67] Experience to guide therapy upon failure of these regimens is limited. Therefore, treatment strategies should be based on past treatment history, drug-resistance test results, and the potential potency of the next regimen, based on the guidance provided above.

Second-Line Regimen Failure and Beyond

Drug resistance with fully active commonly used ARV drug options: Using a person's complete ARV treatment history and drug-resistance data, a clinician can decide whether to include a fully active boosted PI or INSTI in future regimens. For example, those who have no documented PI resistance and who have never been treated with an unboosted PI likely harbor virus that is fully susceptible to PIs. Similarly, people who have no documented INSTI resistance and who have never been treated with an INSTI are likely to have virus susceptible to DTG or BIC. In this setting, virologic suppression should be achievable using a boosted PI plus either two NRTIs (preferably at least one of which is fully active), a boosted PI plus an active INSTI, or DTG or BIC plus two NRTIs (preferably at least one of which is fully active). Drugs should be selected based on the likelihood that they will be fully active, as determined by the person's treatment history, past and present drug-resistance testing, and tropism testing if a CCR5 antagonist is being considered.

Multidrug resistance without fully active commonly used ARV drug options: Use of currently available ARV drugs has resulted in a dramatic decline in the number of people with HIV who have few treatment options because of multiclass drug resistance.[68,69] Despite this progress, some people have experienced toxicities with and/or developed resistance to most currently available commonly used ARV drugs. Maximal virologic suppression should remain the goal; however, if it cannot be achieved, the goals of ART will be to preserve immunologic function, prevent clinical progression, and minimize the development of further resistance that may compromise future regimens.

Consensus on the optimal management of people with multidrug-resistant HIV is lacking. If neither a fully active boosted PI nor a second-generation INSTI (e.g., DTG or BIC) is available, the new regimen should include at least two, and preferably three, fully active agents. If less than three fully active drugs are available, the regimen should include as many fully active drugs as possible, along with potentially partially active agents **(BII).** If resistance to NNRTIs, T-20, MVC, BIC, DTG, CAB, EVG, or RAL are identified, there is rarely a reason to continue using these drugs, because there is little evidence that keeping them in the regimen helps delay disease progression **(BII).** Moreover, continuing these drugs (in particular, early-generation INSTIs) may allow selection of additional resistance mutations and development of within-class cross-resistance that may limit

future treatment options. It should be noted that even partial virologic suppression of HIV RNA to >0.5 $\log_{10}$ copies/mL from baseline correlates with clinical benefit.[68,70] Cohort studies provide evidence that even in the presence of viremia and no improvement in CD4 count, continuing ART reduces the risk of disease progression.[71] Other cohort studies suggest that even modest reductions in HIV RNA levels continue to confer immunologic and clinical benefits.[72,73] However, these potential benefits must be balanced with the ongoing risk of accumulating additional resistance mutations. In general, adding a single, fully active ARV drug to the regimen **is not recommended** because of the risk of rapid development of resistance **(BII).**

People with HIV and ongoing detectable viremia who lack sufficient treatment options due to an inability to construct a fully suppressive regimen with common ARVs may be candidates for the first-in-class CD4 post-attachment inhibitor IBA,[74] the gp120-directed attachment inhibitor FTR,[75] and/or the capsid inhibitor LEN.[76]

- **Ibalizumab (IBA)** is a long-acting CD4 post-attachment inhibitor that is given intravenously every 2 weeks. A single-arm, multicenter clinical trial enrolled 40 heavily ART-experienced participants who had multidrug-resistant HIV-1 and who were experiencing virologic failure on an ARV regimen. Subjects received intravenous IBA infusions every 2 weeks, in addition to an optimized background regimen (OBR) that included at least one additional agent to which the subject's virus was susceptible. At Week 24, 43% of participants achieved HIV RNA <50 copies/mL, and 50% achieved HIV RNA <200 copies/mL.[77] Of the 27 participants who continued to the 48-week follow-up study, 59% and 63% had HIV RNA <50 copies/mL and <200 copies/mL, respectively. All 15 participants who had HIV RNA <50 copies/mL at Week 24 maintained virologic suppression up to Week 48.[78]
- **Fostemsavir (FTR)** is a gp120 attachment inhibitor that is given orally twice daily. A Phase 3 multicenter trial enrolled 371 heavily ART-experienced participants who had multidrug-resistant HIV-1 and who were experiencing virologic failure. Participants were enrolled into two cohorts, according to their remaining treatment options. The randomized cohort (n = 272) included those with at least one fully active approved ARV drug in at least one but no more than two classes. These individuals were randomized to FTR (oral 600 mg twice daily) or placebo for 8 days, followed by open-label FTR plus OBR. In the nonrandomized cohort (n = 99), participants with no remaining ARV options were started on open-label FTR (oral 600 mg twice daily) plus OBR on Day 1. The primary endpoint for the randomized cohort was a change in HIV RNA level from baseline at Day 8. In the FTR group, the mean RNA level decrease was 0.79 $\log_{10}$ copies/mL compared to 0.17 $\log_{10}$ copies/mL in the placebo group ($P < 0.001$). At Week 96, 60% of participants in the randomized cohort and 37% of those in the nonrandomized cohort had HIV RNA levels <40 copies/mL, with mean CD4 increases of 205 cells/mm^3 and 119 cells/mm^3, respectively.[79,80] In this study, 15 individuals in the nonrandomized cohort used the CD4 post-attachment inhibitor IBA in combination with FTR and other ARVs. The virological response rate for these participants by snapshot analysis was 53% at Week 48 and 33% at Week 96.
- **Lenacapavir (LEN)** is a LA HIV capsid inhibitor that can be given by one of two initiation schemes (oral plus subcutaneous [SQ] dosing), followed by SQ injections every 6 months (see Appendix A, Table 10 for dosing details).

  A Phase 3 multicenter trial (CAPELLA) enrolled 72 heavily ART-experienced participants who had multidrug-resistant HIV-1 and experienced virologic failure into two cohorts.[81] Cohort 1 (n = 36) included participants who had a <0.5 $\log_{10}$ HIV-1 RNA decline between screening and baseline (i.e., stable viremia at ≥400 copies/mL, confirming lack of response to the failing therapy). The participants were randomized 2:1 to either oral LEN or placebo (on Days 1, 2, and 8) and continued to receive the failing ARV regimen for 14 days to evaluate the virologic effect of LEN functional monotherapy. Starting on Day 15, all participants began on an OBR; those randomized to oral LEN began SQ LEN every 6 months, whereas participants in the placebo arm received oral LEN on Days 15, 16, and 22 followed by SQ LEN on Day 29 (14 days after the first

oral LEN dose) and then every 6 months. On Day 15, 88% of participants in the LEN arm and 17% in the placebo arm had HIV RNA level reduction of ≥0.5 $\log_{10}$ copies/mL, with least-squares mean change in HIV RNA level of −2.1 $\log_{10}$ copies/mL versus −0.07 $\log_{10}$ copies/mL for the LEN and placebo arms, respectively ($P < 0.001$). At the end of 26 weeks (i.e., after one dose of SQ LEN), 81% of participants had RNA levels <50 copies/mL, and 89% had RNA levels <200 copies/mL, with a mean change in RNA level of −2.58 ± 1.04 $\log_{10}$ copies/mL.[81] At the end of 52 weeks (i.e., after two doses of SQ LEN), 83% of participants had RNA levels <50 copies/mL, with 94% of those with at least two active OBR drugs and 67% with no active OBR drugs. The mean CD4 cell count change at 52 weeks[76] was +82 cells/mm^3.

Cohort 2 (n = 36) was a nonrandomized cohort that included participants who either had a ≥0.5 $\log_{10}$ HIV-1 RNA decline from screening to baseline visit or were enrolled after Cohort 1 reached its planned sample size. All participants were started on an OBR and received oral LEN on Days 1, 2, and 8; on Day 15, SQ LEN was started and given every 6 months. After 26 weeks, 83% of the participants had HIV RNA levels <50 copies/mL, and 86% had HIV RNA levels <200 copies/mL. At Week 52, 72% had RNA levels <50 copies/mL, and the mean CD4 cell count change was +113 cells/mm^3.

Oral lead-in therapy was well tolerated overall, with nausea reported in 13% of participants who received LEN. Injection site reactions, which were generally mild and transient, were reported in 63% of the participants.[81]

Twenty-two of 72 (31%) participants met the criteria for resistance testing at confirmed virologic failure through Week 52.[76] LEN-associated capsid resistance mutations were found in 9 of the 22 (41%) participants with confirmed virologic failure. The M66I mutation was the most common mutation, reported in six participants. Four of the nine participants with LEN-associated capsid resistance mutations had no active agent in the OBR. Four others had low plasma concentrations of the OBR drugs at Week 26, suggesting poor adherence of the self-administered OBR, resulting in an unfavorable LEN functional monotherapy.[82]

Taken together, these data[76,82,83] highlight the importance of selecting a robust OBR to support LEN and counseling about adherence to the OBR. Additionally, LEN is a moderate CYP3A4 inhibitor and may increase concentrations of some coadministered drugs, whereas LEN concentration may be significantly decreased in the presence of a strong CYP3A4 inducer (see Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs for further details). Therefore, people with HIV should be routinely counseled to inform all their health care providers of all medications they are taking, including LEN, even though it is not taken daily. Potential drug–drug interactions should be discussed, particularly before a new drug is started, to minimize the risk of toxicities, nonadherence, and drug resistance.

People with HIV who continue to have detectable viremia and who lack sufficient treatment options to construct a fully suppressive regimen also may be candidates for research studies or expanded access programs, or they may qualify for single-person access to an investigational new drug, as specified in the U.S. Food and Drug Administration's Physician Request for a Single Patient Investigational New Drug for Compassionate or Emergency Use. Information about ARV agents that are in clinical studies can be found in the drug database available on the Clinicalinfo website.

People With HIV on ART With Suspected Drug Resistance Who Present With Limited Information (Incomplete or No Self-Reported ARV History, Medical Records, or Drug-Resistance Test Results)

Every effort should be made to obtain the person's ARV history and prior drug-resistance test results; however, this may not always be possible. One strategy is to restart the most recent ARV regimen and assess drug resistance in 2 to 4 weeks to guide the selection of the next regimen. Another strategy is to start two or three drugs that are predicted to be fully active based on the

person's treatment history. If no ARV history is available, a clinician may consider using agents with a high barrier to resistance—such as twice-daily DTG, BIC (which is available only in a combination pill with FTC/TAF and for which dosage in this setting is unclear), and/or twice-daily boosted DRV—as part of the regimen. Regardless of which strategy is employed, people should be closely monitored for virologic response (e.g., HIV RNA level testing approximately 4 to 8 weeks after reinitiation of therapy), with prompt drug-resistance testing performed if virologic response is inadequate.

People With HIV Who Are Unable to Achieve Viral Suppression Due to Poor Adherence to Oral ART and Who Do Not Have Resistance to Cabotegravir and Rilpivirine

Based on very limited data discussed below, the Panel recommends the use of LA CAB/RPV on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral ART, who have no evidence of resistance to RPV or CAB, and with shared decision-making between providers and people with HIV **(CIII).**

Some people with HIV cannot reach or maintain viral suppression on oral ART despite intensive adherence support. Although a complete LA injectable regimen may overcome some adherence obstacles for people with viremia, long-term clinical efficacy data are limited in these circumstances and the regimen is only approved for people who are virologically suppressed for at least 3 months. No large, published randomized controlled trial has demonstrated the efficacy of a complete regimen of any INSTI plus NNRTI, including LA CAB/RPV, in people with viremia. However, cohort data are emerging, resulting in two possible approaches to use LA CAB/RPV in this population. If achieving viral suppression with oral ART is possible with intensive adherence support to oral ART, switching to LA CAB/RPV after viral suppression can serve as a goal to incentivize the person to adhere to the oral regimen. Data from the Long-Acting Therapy to Improve Treatment Success in Daily Life (LATITUDE) AIDS Clinical Trial Group (ACTG) A5359 study using this strategy is discussed in Approach #1 below.[84] If achieving viral suppression with oral ART is not possible despite intensive adherence support to oral ART, switching to LA CAB/RPV without viral suppression may be an option in certain circumstances, as discussed in Approach #2 below.

Approach #1: Intensive efforts to achieve viral suppression prior to switching to LA CAB/RPV

Because all of the large LA CAB/RPV studies enrolled participants who were adherent to ART with sustained viral suppression, every effort should be made to achieve viral suppression before considering a switch to LA CAB/RPV, even in people with poor adherence. The Phase 3 prospective, randomized, open-label LATITUDE study was designed to assess this strategy in people who faced challenges with ART adherence. Preliminary data have been presented from this study that enrolled individuals without resistance to CAB or RPV from 33 sites in the United States and Puerto Rico.[84] Participants received adherence support and conditional economic incentives to assist in achieving viral suppression on oral ART. Study participants who experienced viral suppression were randomized to continue oral ART or switch to LA CAB/RPV every 4 weeks. At a planned data safety monitoring board (DSMB) interim efficacy analysis, only 294 (68%) of the 434 participants enrolled achieved viral suppression and were eligible for randomization, with 146 assigned LA CAB/RPV and 148 continuing standard of care (SOC) oral ART. At randomization, it was noted that despite the intensive adherence support, 17% in the LA CAB/RPV arm and 7% in the SOC arm had HIV RNA >200 copies/mL. At Week 48 of the randomized phase, 24% in the LA CAB/RPV arm and 39% in the SOC arm met the primary endpoint of earliest confirmed virologic failure or treatment discontinuation, which did not meet the predefined stringent stopping criteria. However, two secondary endpoints—virologic failure alone (7% in LA CAB/RPV vs. 25% in SOC)

and treatment-related failure (defined as first virologic failure or discontinuation due to adverse events) (10% in LA CAB/RPV vs. 26% in SOC)—met the predefined stopping criteria and were statistically significant. Based upon the totality of the data, in February 2024, the DSMB recommended halting randomization and offering all eligible participants LA CAB/RPV. Of the six participants with virologic failure on LA CAB/RPV, two had new drug-resistance mutations (one conferring high-level resistance to CAB and one conferring high-level resistance to both CAB and RPV). The available data suggest that an intensive effort to achieve viral suppression followed by a switch to LA CAB/RPV may be a viable option for individuals who cannot adhere to an oral ARV regimen. Further analyses and formal publication of LATITUDE study results are pending.

Approach #2: Administer LA CAB/RPV in people with viremia who are unable to achieve viral suppression despite intensive adherence support

Emerging data show that select people with HIV who are unable to achieve viral suppression on an oral ARV regimen despite intensive support might benefit from use of LA CAB/RPV, which is currently not approved for use in this population. Available data with this strategy include an initial case report,[85] followed by outcome data from a compassionate use program,[86] showing that 16 of 28 (57%) people with viremia achieved virologic suppression after a median of 5 months with LA CAB/RPV. Among those with virologic failure and for whom resistance data were available, all had new NNRTI mutations conferring RPV resistance and 50% had new integrase mutations, two of which conferred CAB resistance. Since then, three small observational studies have suggested that LA CAB/RPV may achieve viral suppression in select people with viremia and poor adherence to oral ART.[50-52] In these studies, select people with viremia who were unable to adhere to daily oral ART were initiated on monthly or twice-monthly LA CAB/RPV with or without oral lead-in therapy. At up to 10 months of follow-up, 95% achieved HIV RNA <50 copies/mL. Of those with virologic failure for whom genotypes were available, new reverse transcriptase (e.g., L100I, E138K, Y181I) and/or integrase (e.g., G140S, Q148R, R263K) mutations were detected, conferring intermediate to high resistance to RPV and/or CAB, respectively. Various levels of multidisciplinary support and intensive case management were utilized throughout these studies (e.g., provision of injections in field sites, financial incentives, appointment reminders, and transportation assistance). Despite the intensive support, not all injections were given on time.

In the multisite U.S. Observational Pharmacoepidemiology Research and Analysis (OPERA) cohort,[87] clinical data on the use of LA CAB/RPV were prospectively captured from electronic health records from 84 clinics in 18 U.S. states and territories. Among the 36 individuals who had HIV RNA >200 copies/mL before starting LA CAB/RPV and had at least one follow-up HIV RNA test, 94% had an HIV RNA <200 copies/mL at their last follow-up visit.

Taken together, until additional data are available, these approaches may provide alternatives for individuals with viremia and difficulties with adherence to oral ART, especially for those at the highest risk for disease progression or death. If either of the above approaches are employed, close monitoring is recommended with drug-resistance testing performed if virologic response is inadequate. Importantly, beyond conventional and intensive multidisciplinary team involvement, case management and outreach support are needed to ensure adherence and adequate monitoring while on LA CAB/RPV (see the Adherence to the Continuum of Care section for discussion on strategies to improve adherence in these situations). Caution with close monitoring is advised, as data are unavailable for detailed guidance regarding the need for specific adherence or intensive case management services or whether every 4- or every 8-week LA CAB/RPV will yield similar virologic outcomes in people with viremia before switching. Every 4-week dosing was used in the LATITUDE study. In the published case series to date in people with viremia, every 4-week dosing was prescribed for most, with the option of switching to every 8 weeks after achieving viral suppression. Until further data are available, it may be prudent to use similar strategies when LA CAB/RPV is

being considered. People with HIV and providers need to be aware of the significant risk of developing resistance to NNRTIs, and particularly INSTIs if virologic failure occurs on LA CAB/RPV. Such resistance may limit future treatment options and may also lead to its transmission, which should be balanced with the individual's HIV-related risk for disease progression and death.[88] Closely monitoring for viral responses is advised if LA CAB/RPV is used in people with viremia and who have challenges with adherence.

Summary

The goal of treatment for people with HIV and virologic failure is to establish virologic suppression. The management of people with virologic failure often requires expert advice to construct virologically suppressive regimens. Before modifying a regimen, it is critical to carefully evaluate the potential cause(s) of virologic failure, including incomplete adherence, poor tolerability, and drug–drug and drug–food interactions, as well as review HIV RNA and CD4 count changes over time, complete treatment history, and current and previous drug-resistance test results. If HIV RNA suppression is not possible with currently approved agents, consider the use of investigational agents through participation in clinical trials or expanded/single-patient access programs. If virologic suppression is still not achievable, the choice of regimens should focus on minimizing toxicity and preserving treatment options while maintaining CD4 counts to delay clinical progression.

Table 10. Antiretroviral Options for People With HIV and Virologic Failure

Designing a new regimen for people with HIV who are experiencing treatment failure should always be guided by ARV history and results from current and past resistance testing. This table summarizes the text above and displays the most common or likely clinical scenarios seen in people with virologic failure. For more detailed descriptions, please refer to the texts above and/or consult an expert in HIV drug resistance to assist in the design of a new regimen. It is also crucial to provide continuous adherence support before and after regimen changes.

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a]	Goal
First Regimen Failure	NNRTI plus two NRTIs	Most likely resistant to NNRTI +/– 3TC or FTC (i.e., NNRTI mutations +/– M184V/I).[b] Additional NRTI mutations also may be present.	DTG (or possibly BIC) plus two NRTIs (preferably at least one fully active[c]) **(AI);** *or* Boosted PI plus two NRTIs (preferably at least one fully active) **(AI);** *or* Boosted PI plus INSTI (boosted DRV plus DTG **[AI]**; LPV/r plus RAL **[CI]**)	Resuppression
	Boosted PI plus two NRTIs	Most likely no resistance or resistance only to 3TC or FTC (i.e., M184V/I, without resistance to other NRTIs)[b]	DTG, or possibly BIC, plus two NRTIs (preferably at least one fully active; if only one of the NRTIs is fully active[c] or if adherence is a concern, DTG is currently preferred over other INSTIs) **(AIII);** *or* Continue same regimen **(AII);** *or* Boosted PI plus INSTI (boosted DRV plus DTG **[AIII]**; LPV/r plus RAL **[CI]**); *or* Another boosted PI plus two NRTIs (at least one fully active[c]) **(AIII).**	Resuppression
	INSTI plus two NRTIs	If failure with no INSTI resistance	Boosted PI plus two NRTIs (preferably at least one fully active[c]) **(AIII);** *or* DTG, or likely BIC, plus two NRTIs (preferably at least one fully active[c]) **(AIII);** *or* DRV/r plus DTG **(AIII)**	Resuppression

Table 10. Antiretroviral Options for People with HIV and Virologic Failure

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a]	Goal
		If failure on EVG or RAL, often have INSTI resistance, but potentially susceptible to DTG Can have 3TC or FTC resistance.	Boosted PI plus two NRTIs (preferably at least one fully active[c]) **(AIII);** *or* DTG[d] twice daily or possibly BIC (if HIV is sensitive) plus two fully active NRTIs **(BIII);** *or* DTG[d] twice daily or possibly BIC (if HIV is sensitive) plus a boosted PI (preferably DRV/r) **(AIII).**	Resuppression
	INSTI plus NNRTI (DTG/RPV or LA CAB/RPV)	INSTI and/or NNRTI resistance possible	Use ART history and past and current resistance testing to design a new regimen. Consult an expert in drug resistance as needed.	Resuppression
Second Regimen Failure and Beyond	Drug resistance with fully active treatment options—	Use past and current genotypic- +/– phenotypic-resistance testing and ART history when designing new regimen.	New regimen according to original treatment type—	Resuppression
	(i) Boosted PI, but not second-generation INSTI, fully active		(i) Boosted PI with two NRTIs (preferably at least one fully active)	
	(ii) Second-generation INSTI, but not boosted PI, fully active		(ii) DTG or BIC with two NRTIs (preferably at least one fully active)	
	(iii) Both PI and INSTI fully active		(iii) The two options above or boosted PI with INSTI	
	Multiple or extensive drug resistance with few treatment options (e.g., fully active boosted PI or second-generation INSTI unavailable)	Use past and current genotypic- and phenotypic-resistance testing to guide therapy. Confirm with a viral tropism assay when use of MVC is considered.	New regimen should include at least two, and preferably three, fully active agents, including those with novel mechanisms of action (e.g., IBA, FTR, LEN). If fewer than three fully active drugs, include as many fully active drugs as possible, along with	Resuppression if possible; otherwise, keep viral RNA levels as low as possible and CD4 count as high as possible.

Table 10. Antiretroviral Options for People with HIV and Virologic Failure

Clinical Scenario	Type of Failing Regimen	Resistance Considerations	New Regimen Options[a]	Goal
		Consult an expert in drug resistance if needed.	potentially partially active drugs **(BII).** Consider enrollment into clinical trials or expanded access programs for investigational agents if available. Discontinuation of all ARV drugs **is not recommended (AI).**	
People With Suspected Drug Resistance and Limited or Incomplete ARV and Resistance History	Unknown	Obtain medical records if possible. Resistance testing may be helpful in identifying drug-resistance mutations, even if the person has been off ART. Keep in mind that resistance mutations may not be detected in the absence of drug pressure.	Consider restarting the old regimen with careful monitoring of virologic response and early resistance testing if inadequate virologic suppression. If no ARV history is available, consider initiating a regimen with drugs with high genetic barriers to resistance (e.g., DTG, BIC, and/or boosted DRV) with careful monitoring of virologic response and early resistance testing, if inadequate virologic suppression.	Resuppression

[a] When switching an ARV regimen in a person with HBV/HIV coinfection, ARV drugs that are active against HBV and have a high resistance barrier to HBV (i.e., tenofovir) should be continued as part of the new regimen, or another HBV drug (i.e., entecavir) should be started. Discontinuation of these drugs may lead to the reactivation of HBV, which may result in serious hepatocellular damage.

[b] If other NRTI-resistance mutations are present, use resistance test results to guide NRTI usage in the new regimen.

[c] See text for details and additional options in special settings.

[d] Response to DTG depends on the type and number of INSTI mutations.

Key: 3TC = lamivudine; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CD4 = CD4 T lymphocyte; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EVG = elvitegravir; FTC = emtricitabine; FTR = fostemsavir; HBV = hepatitis B virus; IBA = ibalizumab; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; RAL = raltegravir

Isolated Central Nervous System Virologic Failure and Neurologic Symptoms

Cerebrospinal Fluid Viral Escape

Presentation with new-onset central nervous system (CNS) signs and symptoms has been reported as a rare form of "compartmentalized" virologic failure. People experiencing this present with new, usually subacute, neurological symptoms that are associated with a breakthrough of HIV replication within the CNS compartment, despite relative plasma HIV RNA suppression. In this case, cerebrospinal fluid (CSF) HIV RNA shows higher concentrations than in plasma.[89-91] Clinical evaluation frequently shows abnormalities on magnetic resonance imaging (MRI) and abnormal CSF findings with characteristic lymphocytic pleocytosis.[92] In most (though not all) people, drug-resistant CSF virus is evident.[93] Consensus among experts is that this "neurosymptomatic" form of CNS viral escape should be treated through optimization of ARV regimens based on drug-resistance testing results if available **(CIII).**[94] Although drug-resistance testing of HIV in CSF can be used to guide changes in the ARV regimen, according to the principles outlined above for plasma HIV RNA resistance, such testing typically needs to be conducted in a research setting. If CSF HIV drug-resistance testing is not available, the regimen may be changed based on the person's treatment history or on predicted drug penetration into the CNS **(CIII).**[95-98]

This "neurosymptomatic" CNS viral escape should be distinguished from "neuroasymptomatic" escape, defined as—

- The incidental detection of asymptomatic and mild CSF HIV RNA elevation, which is similar to plasma viral blips in that it is usually transient with low levels of CSF HIV RNA and has been associated with PI-based regimens[99-101]; *or*
- A transient increase in CSF HIV RNA that is related to other CNS infections that can induce a brief increase in CSF HIV RNA (e.g., herpes zoster).[102]

There is not clear evidence to support a change in an ARV regimen for incidentally detected "neuroasymptomatic" escape, although careful clinical review and follow-up of each person with this condition are recommended to monitor for the emergence of neurologic symptoms or systemic viremia.[94] There does not appear to be an association between these asymptomatic CSF HIV RNA elevations and the relatively common chronic, usually mild, neurocognitive impairment in people with HIV who show no evidence of CNS viral breakthrough.[103]

Neurological Symptoms in People With HIV on Antiretroviral Therapy

Evidence is currently not available to support empiric intensification or switch of ARV regimens in people on systemically suppressive ART with mild neurological and/or cognitive symptoms who do not have documented CSF escape. Such individuals should be referred for neurological evaluation to determine if further evaluation is indicated. This may include blood laboratory testing, lumbar puncture, neuropsychological testing, and MRI to evaluate for CSF escape, as well as other causes of neurological symptoms. A recent multinational randomized, double-blinded, placebo-controlled trial randomized 191 ART-experienced participants—with cognitive impairment and suppressed plasma HIV RNA level and not taking an INSTI—to one of three arms: dual placebo, addition of DTG plus placebo, or DTG plus MVC. Compared with placebo, ART intensification with DTG or DTG plus MVC did not alter neuropsychological performance or depressive symptoms over time in participants with cognitive impairment.[104]

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Suboptimal CD4 Cell Recovery Despite Viral Suppression

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Key Considerations and Recommendations
• Suboptimal CD4 T lymphocyte (CD4) cell recovery is associated with increased AIDS- and non–AIDS-related morbidity and mortality among individuals with antiretroviral therapy (ART)–mediated viral suppression. • Promptly initiating ART in people diagnosed early with HIV provides the best opportunity for maximal CD4 cell recovery. • Adding antiretroviral (ARV) drugs to a suppressive ART regimen (ART intensification) does not improve CD4 cell recovery and therefore **is not recommended** for this purpose **(AI).** • Switching ARV drugs or drug classes in people with suppressed viral load does not improve CD4 cell recovery substantially and **is not recommended** for this purpose **(AII).** • Interleukin-2 **is not recommended** to increase CD4 counts because clinical trial data demonstrated no clinical benefit **(AI).** • Other interventions to increase CD4 counts **are not recommended** outside of a clinical trial, because no current interventions have been proven to decrease morbidity or mortality during ART-mediated viral suppression **(AII).** • Efforts to decrease morbidity and mortality during ART-mediated viral suppression should focus on preventive care (e.g., opportunistic infection prophylaxis, vaccinations, cancer screening, statin therapy to reduce cardiovascular risk), addressing modifiable risk factors for chronic disease (e.g., tobacco use, alcohol and substance use, unhealthy diet, sedentary lifestyle), and optimizing management of comorbidities (e.g., hypertension, diabetes).
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

Most people with HIV who achieve and maintain antiretroviral therapy (ART)–mediated viral suppression experience increases in peripheral blood CD4 T lymphocyte (CD4) cell counts over time[1-4] and recovery of CD4 counts to within the normal range (>500 cells/mm^3) of people without HIV.[5-7] However, some people who started ART at low CD4 counts do not experience recovery to the desired immunologic goal of >500 cells/mm^3 despite sustained virologic suppression on ART.[2,3,8] Promptly initiating ART in people diagnosed early with HIV provides the best opportunity for maximal CD4 cell recovery.[9,10]

There is no clear consensus on terminology to use or thresholds that define "suboptimal CD4 cell recovery."[11,12] A common threshold used for "suboptimal CD4 cell recovery" is CD4 ≤500 cells/mm^3 after several years of suppressive ART. The term "immunologic nonresponse" also has been used to describe a lack of CD4 cell recovery, with common thresholds of <200 cells/mm^3 or <350 cells/mm^3 after several years of suppressive ART.[12] Some experts consider an increase of <200 cells/mm^3 above baseline after 24 months as an inadequate immunologic response for people with CD4 counts ≤500 cells/mm^3. The relationship between improved clinical outcomes and higher CD4 counts likely spans all ranges of CD4 counts, although incremental benefits are harder to discern once CD4

counts reach moderate-to-high levels,[13] especially beyond 500 cells/mm^3. Rarely, people with HIV may experience substantial declines in CD4 counts while maintaining virologic suppression on ART.[14]

Clinical Consequences

Persistently low CD4 counts despite ART-mediated viral suppression are associated with increased risk of morbidity, hospitalizations, and mortality. Data from two large international cohorts of people with HIV initiating ART as early as 1996 showed that individuals with HIV and CD4 counts ≤200 cells/mm^3 despite at least 3 years of suppressive ART had a 2.6-fold greater risk of mortality than those with higher CD4 counts.[15] A multicenter cohort study from Spain of individuals who started ART with low CD4 counts between 2005 and 2019 found that those whose CD4 counts remained <200 cells/mm^3 after 2 years of ART had a 4.6-fold greater risk of mortality than those with CD4 >500 cells/mm^3.[16]

People with CD4 counts <200 cells/mm^3 despite at least 1 year of suppressive ART are at increased risk of AIDS-related and non–AIDS-related events.[17-23] This population is at risk of severe infections (e.g., pneumonia) and is less likely to mount a robust immune response following vaccination.[24] In addition, these individuals have an increased risk of infection-related cancers (e.g., Epstein-Barr virus-associated lymphoma, human papillomavirus–associated malignancies, hepatocellular carcinoma associated with hepatitis B virus [HBV] or hepatitis C virus [HCV]). A cohort study of people with HIV from 1996 to 2020 demonstrated that people with CD4 <200 cells/mm^3 had a 3.5-fold higher risk of infection-related cancers compared to people with CD4 ≥500 cells/mm^3.[25] Another study found that CD4 count <350 cells/mm^3 was associated with non–AIDS-defining, smoking-related, and other malignancies.[26] People with HIV who receive chemotherapy or radiation therapy can also experience CD4 count decline. One study reported a 27% increase in mortality for every 100 cells/mm^3 decrease in CD4 count.[27] Lastly, cardiovascular disease and other comorbidities have also been observed at increased rates in people with low CD4 recovery.[15,28-35]

Pathogenesis

Suboptimal CD4 recovery after ART-mediated virologic suppression is typically associated with higher levels of inflammation and immune activation[36] and is most frequently observed in people with older age, prior AIDS-defining illness, lower nadir CD4 count,[16,37] and some coinfections (e.g., HCV).[38-40] The association of higher inflammation levels with persistently low CD4 counts is likely multifactorial and, to some extent, may be driven by inadequate immunologic control of other chronic viral infections, based on observed decreases in inflammation after treatment of cytomegalovirus and chronic HCV infection.[41,42] Numerous factors have deleterious effects on T-cell survival and proliferation, such as chronic coinfections, a persistently activated innate immune system (due to stimuli such as microbial translocation and dysbiosis), more severe fibrosis of lymph node tissue with disruption of naive T-cell homeostasis, potential senescence of hematopoietic progenitors, and possibly autoantibodies.[43-46]

CD4 count may occasionally decline despite suppressive ART, which may be due to a new medication, a new underlying malignancy, infection, or autoimmune disorder, including the presence of anti-CD4 autoantibodies,[44,45] and/or dysregulation of interleukin-7 (IL-7)–mediated naive T-cell homeostasis or more accentuated immune senescence.[14,47,48]

Alternative Causes of Suboptimal CD4 Cell Recovery

Evaluation of people with suboptimal CD4 cell recovery should begin with identifying modifiable causes, such as concomitant medications that reduce total white blood cells, particularly lymphocytes and CD4 cells. When possible, these drugs should be discontinued and replaced with

alternatives if necessary. Untreated coinfections (e.g., HCV, *Mycobacterium avium* complex, histoplasmosis) and serious medical conditions (e.g., malignancy, autoimmune disease) may also contribute to CD4 lymphopenia, particularly in people with declining CD4 counts (and percentages) while on suppressive ART and in those with CD4 consistently <100 cells/mm^3. Treating coinfections and optimizing management of contributing conditions should be pursued when feasible.

Interventions Tested to Improve CD4 Cell Recovery

For people with suboptimal CD4 cell recovery despite suppressive ART, effective interventions to increase CD4 counts and improve clinical outcomes have not been identified.[49] Strategies to raise CD4 counts by modifying or intensifying ART regimens have been evaluated in clinical trials. Intensification strategy by adding ARV drugs to a suppressive ART regimen does not improve CD4 cell recovery[50-56] and does not reduce morbidity or mortality. Therefore, ART intensification **is not recommended** as a strategy to improve CD4 cell recovery **(AI).** Similarly, switching ARV drugs or classes has not been shown to improve CD4 cell recovery substantially for individuals with viral suppression and **is not recommended (AII).**[57,58]

Therapies targeting immunomodulatory pathways (e.g., interleukin-2 [IL-2], IL-7, growth hormone, thymosin alpha-1) have also been investigated as a strategy to increase CD4 counts.[59] Two large randomized trials, powered to assess impact on clinical endpoints (AIDS and death), evaluated the role of IL-2 for improving CD4 cell recovery. Although there is strong evidence linking low CD4 cell counts with increased morbidity, IL-2 adjunctive therapy did not decrease the risk of clinical events despite substantial increases in CD4 count.[60] Therefore, IL-2 is **not recommended** as a strategy to improve CD4 recovery **(AI).** Dysregulation in IL-7–mediated naive T-cell homeostasis has been reported among people with suboptimal CD4 recovery.[14,47,48] While several early-phase trials of human recombinant IL-7 treatment have shown an increase in CD4 counts among people with HIV on ART, no clinical trials designed to evaluate whether IL-7 treatment confers benefit on clinical outcomes have been performed.[61]

Additional interventions have been studied in early-phase trials, and some have demonstrated improvements in CD4 counts among people with HIV on ART with suboptimal CD4 cell recovery. These studies were not designed to evaluate clinical endpoints. Examples include the use of novel antivirals,[62] repurposed medications,[63,64] probiotics,[65,66] plants and herbal treatments with medicinal properties,[67-69] and other nutritional supplements,[70] as well as human umbilical cord mesenchymal stem cell infusions[71,72] or allogenic natural killer cell immunotherapy.[73] As demonstrated by the IL-2 clinical trial results, randomized trials with clinical endpoints will be needed to establish clinical benefit. Because of the lack of clinical efficacy data from these alternative interventions, the use of adjunct therapies to improve immune recovery **is not recommended,** except in the context of a clinical trial **(AII).**

Prevention of Clinical Consequences

With continuous ART and viral suppression, life expectancy for people with HIV is approaching that of people without HIV. However, persistently low CD4 counts despite ART-mediated viral suppression are associated with higher rates of both AIDS and non–AIDS-related morbidity and mortality over the long term. Reducing AIDS- and non–AIDS-related morbidity and mortality remains a cornerstone of HIV treatment and is especially important for people with suboptimal CD4 recovery, given the increased risk of such outcomes. Risk for opportunistic infections (OIs) is generally low for people on ART with viral suppression, but some primary or secondary prophylaxis may need to be extended for certain OIs among people who do not experience CD4 recovery above certain thresholds (see the Adult OI Guidelines for specific guidance).

Given the increased risk for severe manifestations and/or poor outcomes from infections such as tuberculosis, HBV, and HCV, guidelines for screening for such infections should be followed closely, and treatments should be initiated promptly when indicated. Clinicians should also be vigilant about ensuring that people with HIV are up to date on vaccinations for preventable infections. It should be noted that live virus vaccines are contraindicated for people with CD4 counts <200 cells/mm^3 (see Immunizations for Preventable Diseases in Adults and Adolescents With HIV in the Adult OI Guidelines for detailed recommendations).

For non-AIDS-related morbidities, providers should offer preventive counseling, evaluate and manage cardiovascular risk factors (see Cardiovascular Complications), ensure that screening for malignancies (e.g., colorectal cancer, anal or cervical cancer, hepatocellular carcinoma, lung cancer, breast cancer) is up to date (see Primary Care Guidance), initiate statin therapy when indicated (see Statin Therapy in People With HIV), and provide prompt care and referrals when appropriate.[74] As for all people with HIV, regardless of CD4 count, preventive counseling should address lifestyle modifiable risk factors, including but not limited to smoking cessation, abstinence from alcohol and substance use, dietary modification, regular exercise, and treatment optimization for comorbidities such as hypertension and diabetes.

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Optimizing Antiretroviral Therapy in the Setting of Viral Suppression

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Key Considerations and Recommendations
• Advances in antiretroviral (ARV) treatment and a better understanding of HIV drug resistance have made it possible to consider switching a person with HIV from an effective ARV regimen to an alternative ARV regimen in some situations. • The fundamental principle of ARV regimen optimization is to maintain viral suppression without jeopardizing future treatment options. • Adverse events, drug–drug or drug–food interactions, pill burden, pregnancy, cost, stigma, inconvenience from taking oral medications, or the desire to simplify a regimen may prompt regimen optimization. • It is critical to review a person's full ARV history, including virologic responses, past ARV-associated toxicities and intolerances, and cumulative resistance test results before selecting a new ARV regimen **(AI).** • People with HIV who have no history of drug-resistance mutations or virologic failure can likely switch to any regimen that has been shown to be highly effective in people who are ARV-naive **(AI)** or to NRTI-sparing options extensively researched in switch studies, such as dolutegravir (DTG) plus rilpivirine (RPV) **(AI)** or long-acting cabotegravir plus rilpivirine (LA CAB/RPV) **(AI).** • For regimen optimization in the setting of existing nucleoside reverse transcriptase inhibitor (NRTI) resistance, if an NRTI is to be included in the new regimen, two NRTIs (tenofovir alafenamide [TAF] or tenofovir disoproxil fumarate [TDF] plus emtricitabine [FTC] or lamivudine [3TC]) should be included, along with a fully active drug with a high resistance barrier, such as DTG **(AII),** bictegravir (BIC) **(BIII),** or boosted darunavir **(BIII).** Alternatively, as noted above, an NRTI-sparing regimen (such as DTG/RPV **[AI]** or LA CAB/RPV **[AI]**) is possible if there is no evidence of prior integrase strand transfer inhibitor (INSTI) or RPV resistance**.** • Monotherapy with either a boosted protease inhibitor or an INSTI has been associated with unacceptable rates of virologic failure and the development of resistance; therefore, monotherapy as a switch strategy **is not recommended (AI).** • When switching an ARV regimen in a person with chronic hepatitis B virus (HBV)/HIV coinfection, HBV-active drugs that are potent and have a high barrier to resistance (i.e., TAF, TDF, or entecavir) should be used **(AII).** Discontinuation of HBV drugs may lead to reactivation of HBV, which may result in serious hepatocellular damage. • Consultation with an HIV specialist is recommended when planning a regimen switch for a person with a history of resistance to two or more drug classes **(AIII).** • Close monitoring to assess tolerability, viral suppression, adherence, and safety is recommended during the first 3 months after a regimen switch **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

With currently available antiretroviral therapy (ART), most people with HIV can achieve and maintain HIV viral suppression. Furthermore, advances in antiretroviral (ARV) treatment and a better understanding of drug resistance have made it possible to consider switching a person with HIV from one effective regimen to another in some situations. When considering optimization—a switch in

therapy to improve certain aspects of therapy—clinicians must keep several key principles in mind to maintain viral suppression while addressing the concerns with the current regimen.

Reasons to Consider Regimen Optimization in the Setting of Viral Suppression

- To simplify a regimen by reducing pill burden and/or dosing frequency
- To enhance tolerability and/or decrease short- or long-term toxicity (see Table 21 in the Adverse Effects of Antiretroviral Agents section for a more in-depth discussion of toxicities)
- To prevent or mitigate drug–drug interactions (see Drug–Drug Interactions)
- To eliminate food requirements
- To switch to a long-acting (LA) injectable regimen for convenience, to relieve pill fatigue, or to decrease potential stigma or disclosure concerns associated with taking daily oral medications
- To allow optimal use of ART during pregnancy or when pregnancy is desired or may occur (see Perinatal Guidelines)
- To reduce costs (see Cost Considerations and Antiretroviral Therapy)

General Principles of Regimen Optimization

Maintain Viral Suppression

The fundamental principle of ARV regimen optimization is to maintain viral suppression without jeopardizing future treatment options. If a regimen switch results in virologic failure with the emergence of new resistance mutations, the person may require a more complex and/or a less tolerated regimen.

Careful Review of Antiretroviral Treatment and Drug-Resistance History Before Optimization

Before switching treatments, it is critical to thoroughly assess a person's full ARV history, including virologic responses, inferred resistance (as discussed below), cumulative resistance test results, and any past ARV-related intolerances, toxicities, or adverse reactions **(AI).**

If a person with pre-ART wild-type HIV achieves and maintains viral suppression after ART initiation, one can safely assume that no new drug-resistance mutations emerged while the person was on the suppressive regimen. In people with a history of virologic failure or pre-treatment drug resistance, a review of cumulative resistance test results and clinical and virologic response to prior regimens is essential when designing a new regimen. Cumulative resistance test results refer to all previous and currently available results from standard genotype, proviral DNA genotype (if available), phenotype, and tropism assays that can be used to guide the selection of a new regimen. Once selected, a drug-resistance mutation—even when it is not detected in the person's most recent drug-resistance test—can be archived in the HIV reservoir and reemerge under the appropriate selective drug pressure. Resistance often can be inferred from the ARV history. For people with documented failure on a regimen that includes drugs with relatively low barriers to resistance—such as a non-nucleoside reverse transcriptase inhibitor (NNRTI), elvitegravir (EVG), raltegravir (RAL), lamivudine (3TC), or emtricitabine (FTC)—a clinician should assume that there is resistance to these drugs, so-called *inferred resistance*. When uncertain about prior resistance, it is generally not advisable to switch from a suppressive ARV regimen, unless the new regimen is likely to be at least as active against potential resistant virus as the current suppressive regimen. This principle is particularly applicable

when switching ARV-experienced individuals from a regimen with a relatively high barrier to resistance—such as those that include pharmacologically boosted protease inhibitors (PIs), dolutegravir (DTG), or bictegravir (BIC)—to one with a lower barrier to resistance.[1] The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends that clinicians consult an HIV specialist when contemplating optimization for a person with a history of resistance to two or more drug classes **(AIII).**

If optimization is considered in people with suppressed viral loads who do not have prior drug resistance data, proviral DNA genotypic resistance testing can be considered. For those who have no prior virologic failures and who are on their first or second regimen, or who have genotypic test results from prior virologic failures, the use of the proviral DNA genotypic test is unlikely to provide valuable information. In individuals with a history of multiple prior failures or multiple prior ARV regimens, the use of proviral DNA genotypic testing may be useful. However, whenever proviral DNA genotypic testing is used, the results must be interpreted with caution because these assays may not detect any or all drug-resistance mutations, especially those that were selected by a previous ARV regimen.[2] In addition, these assays may identify mutations that appear inconsistent with a person's response to treatment, making the clinical relevance of the assay results questionable. Overall, the clinical utility of these assays remains an area of active investigation (see Drug-Resistance Testing).

Considerations for HBV/HIV Coinfection

For People With HBV/HIV Coinfection

When switching an ARV regimen in a person with active hepatitis B virus (HBV)/HIV coinfection (hepatitis B surface antigen [HBsAg] positive), tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) (generally given with 3TC or FTC) should be continued as part of the new regimen. Both TDF and TAF are active against HBV and can be used as HBV monotherapy. Although 3TC and FTC are active against HBV, their use as monotherapy against HBV infection **is not recommended (AII)** because emergent HBV resistance to these drugs is highly likely. If TAF or TDF cannot be used, entecavir—a potent antiviral with a high HBV resistance barrier—should be used to treat HBV alongside a fully suppressive ARV regimen **(AII).** Entecavir should not be used without an active ARV regimen to prevent the development of the HIV M184V resistance mutation. Discontinuation of HBV antivirals may lead to reactivation of HBV, which can result in serious hepatocellular damage and death. Refer to the Hepatitis B Virus/HIV Coinfection section for specific recommendations.

Screening for HBV for People With No History of HBV/HIV Coinfection

People with HIV and unknown or nonimmune HBV status should be screened for HBV infection before switching an ARV regimen to one that does not include TAF or TDF plus 3TC or FTC (e.g., DTG/rilpivirine [RPV], DTG/3TC, LA cabotegravir [CAB]/RPV). If a person with HIV shows no evidence of chronic HBV infection (i.e., negative for HBsAg) and is not immune to HBV (i.e., negative for hepatitis B surface antibody [HBsAb]), vaccination should be initiated while considering the ARV switch (including in those with isolated hepatitis B core antibody [HBcAb]).

People with HIV and prior exposure to HBV infection without evidence of chronic infection (i.e., negative HBsAg, positive HBcAb, and either positive or negative HBsAb) are likely at low risk (<1%) of HBV reactivation and even lower risk of HBV reactivation-associated hepatitis, despite the discontinuation of NRTIs. However, there are no published studies to confidently estimate risk in this population. Within this group, those with positive HBsAb are at the lowest risk for HBV reactivation, although HBV reactivation has been described when HBV active therapy is withdrawn as part of an ART regimen in this situation.[3] See more information in the Hepatitis B Virus Infection section in the

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV.

For people previously exposed to HBV, alanine aminotransferase (ALT) should be monitored for 6 months (e.g., at the time of HIV viral load follow-up visits) after switching from ART that includes tenofovir (TDF or TAF) to one that does not include either of these drugs. An increase in ALT levels should prompt HBV DNA testing to assess for the reactivation of HBV. The presence of HBV reactivation would require the immediate addition of TAF, TDF, or entecavir to the ARV regimen.

Assessment for Potential Drug Interactions

Before switching a regimen, it is important to review each ARV drug in the new regimen and concomitant medications to assess whether any potential drug–drug interactions exist. For example, oral rilpivirine (RPV) and atazanavir (ATV) interact with acid-lowering agents, and many ARV drugs may interact with drug transporters or drugs that are inhibitors, inducers, or substrates of cytochrome P450 (CYP) enzymes (see Drug–Drug Interactions). In addition to new drug interactions, the discontinuation of some ARV drugs also may necessitate adjusting the dosage of concomitant medications. For example, discontinuation of pharmacokinetic (PK) boosters (ritonavir or cobicistat) may reduce the concentrations of some concomitant medications. Concomitant medications, which may have been previously managed with dose adjustments, will need to be reevaluated in the context of the new ARV regimen.

Assessment for Pregnancy or Pregnancy Potential

Women of childbearing potential should have a pregnancy test before switching ART. If a woman with HIV is found to be pregnant or desires pregnancy, clinicians should refer to the Perinatal Guidelines for recommendations on the safety and efficacy of ARV use at the time of conception or during pregnancy. All pregnancies that occur while a woman is receiving ART should be reported to the Antiretroviral Pregnancy Registry.

Monitoring After Switching Antiretroviral Therapy

After a treatment switch, people with HIV should be evaluated closely for 3 months (e.g., a clinic visit or telephone call 1 to 2 weeks after the change and a viral load test to check for rebound viremia 4 to 12 weeks after the switch) **(AIII).** The purpose of this close monitoring is to ensure the person clearly understands their prescribed ART regimen, assess medication tolerance, and conduct targeted laboratory testing when there are preexisting laboratory abnormalities or if there are potential concerns with the new regimen. For example, if lipid abnormality prompted the ARV change or is a concern with the new regimen, fasting cholesterol subsets and triglycerides should be assessed within 3 months after the ART change. In the absence of any new complaints, laboratory abnormalities, or evidence of viral rebound over the first 2 to 3 months, clinical and laboratory monitoring may resume on a regularly scheduled basis (see Laboratory Testing for Initial Assessment and Monitoring).

Specific Regimen Optimization Considerations

As with the recommendation for people who are starting ART, the use of a 2- or 3-drug ARV regimen (as discussed below) is generally recommended when switching ART in people with suppressed viral loads **(AI).** People who have no history of resistance mutations or virologic failure can likely switch to any regimen that has been shown to be highly effective in people who have not been on ART **(AI).** People with prior drug resistance can be switched to a new regimen based on their ARV history and cumulative resistance testing results. Monotherapy with either a boosted PI or an integrase strand transfer inhibitor (INSTI) has been explored in several trials or cohort studies.[4-7]

Both INSTI[8] and boosted PI[9] monotherapy have been associated with higher rates of virologic failure than combination regimens. In addition, INSTI monotherapy has been associated with the development of resistance;[10,11] therefore, ARV monotherapy as a maintenance strategy is **not recommended (AI).**

Optimization Strategies With Good Supporting Evidence for People Without Known Drug Resistance

Many clinical trials have enrolled participants with stable, suppressed viral loads without known underlying drug resistance and switched them to another regimen. Most of these studies demonstrated maintenance of viral suppression, some of which are referenced below. However, some regimen switches have had limited success in clinical trials but have informed optimization strategies. The SWITCHMRK 1 and 2 studies illustrated the importance of considering the possibility of underlying drug resistance before switching therapy in those with virologic suppression, particularly when the switch is to a drug with a low barrier to resistance.[1] In the two SWITCHMRK studies, those with viral suppression on two NRTIs plus lopinavir/ritonavir (LPV/r) were switched to two NRTIs plus RAL. The studies found that individuals with a history of previous virologic failure had a higher risk of failure after switching to the RAL-based regimen. This finding is likely explained by underlying NRTI resistance, a setting where viral suppression can generally be maintained by drugs with a high barrier to resistance, such as boosted PIs, but is less likely to maintain viral suppression when switched to a drug with a low barrier to resistance, such as RAL. The strategies listed below support these observations and principles of optimizing therapy and include a discussion about switching ART regimens in those with underlying resistance.

Three-Drug Regimens

Within-Class Switches

Within-class switches (e.g., switching from one INSTI to another INSTI) may be prompted by adverse events or the availability of ARVs in the same class that offer a better safety profile, reduced dosing frequency, higher barrier to resistance, lower pill burden, or do not require PK boosting. Within-class switches usually maintain viral suppression, provided there is no drug resistance to the new ARV. Below are examples of within-class switch strategies that are proven to be effective in clinical trials or are likely to be effective in those without underlying drug resistance:

- From TDF[12,13] or abacavir (ABC)[14] to TAF
- From RAL or elvitegravir/cobicistat (EVG/c)[15] to BIC or DTG
- From DTG[16-18] to BIC or BIC to DTG
- From efavirenz to RPV,[13,19] doravirine (DOR),[20] or RPV to DOR

Between-Class Switches

Between-class switches (e.g., switching from a boosted PI to an INSTI) generally maintain viral suppression, provided there is no resistance to the other components of the regimen. In general, such switches should be avoided if any doubt exists about the activity of the other agents in the regimen. As noted earlier, prior resistance test results will be very informative in guiding this switch. The following are examples of between-class switches that have been proven to be effective in clinical trials or are likely to be effective in those without underlying drug resistance:

- From a boosted PI to a second-generation INSTI (e.g., DTG,[21] BIC[22])

- From a boosted PI to RPV[23] or DOR[20]
- From an NNRTI to a second-generation INSTI[24,25] or a boosted PI

Two-Drug Regimens

Some two-drug ARV regimens are effective in maintaining HIV virologic control in people who initiated therapy with three-drug regimens and achieved sustained virologic suppression for at least 3 months. However, none of the two-drug regimens are effective as treatment for HBV and are therefore not recommended for people with HBV coinfection. In people with HBV who cannot take TAF or TDF, these regimens can be considered if used with a potent, high barrier-to-resistance anti-HBV active medication (i.e., entecavir) **(AII).** See the section above on HBV considerations during optimization. The following are examples of successful strategies studied in clinical trials for switching from 3- to 2-drug regimens in people with suppressed HIV.

Dolutegravir Plus Rilpivirine

Two Phase 3 trials, SWORD-1 and SWORD-2, demonstrated noninferior efficacy of switching to a 2-drug regimen of DTG with RPV compared to continuing a first or second ARV regimen in individuals with suppressed HIV-RNA without prior virologic failure.[26] Individuals were excluded from the study if they had active HBV infection (unless the person was also on a specific HBV active regimen), resistance to DTG or RPV, or significant drug interactions. DTG/RPV is suitable for use in people with an isolated K103N resistance mutation and in those with NRTI resistance. Individuals with active HBV infection need to be on a potent HBV drug with a high barrier to resistance (i.e., TAF, TDF, or entecavir).

Dolutegravir Plus Lamivudine or Emtricitabine

A switch from a stable 3-drug ARV regimen to DTG plus 3TC or FTC as a maintenance strategy in people with ongoing virologic suppression and no history of prior virologic failure or resistance to these agents was noninferior to continuing a 3-drug therapy in a large randomized clinical trial (TANGO),[27] in smaller clinical trials,[28-30] and in observational studies[31-33] **(AI).** Individuals with active HBV infection need to be on a potent HBV drug with a high barrier to resistance (i.e., TAF, TDF, or entecavir). 3TC or FTC monotherapy is not considered standard of care for HBV treatment because of a high risk of emerging resistance.[34]

Boosted Protease Inhibitor Plus Lamivudine

A boosted PI plus 3TC is a reasonable 2-drug optimization option in individuals without resistance who are suppressed on a current regimen and who do not have active HBV infection. Pill burden and potential drug interactions are limitations compared to the above 2-drug regimens. Several regimens using a boosted PI plus 3TC have been shown to be effective in clinical trials, including darunavir/ritonavir (DRV/r) **(BI),**[35] darunavir/cobicistat (DRV/c) **(BIII),** atazanavir/ritonavir (ATV/r) **(CI),**[36,37] and LPV/r **(CI).**[38] Individuals with active HBV infection need to be on a potent HBV drug with a high barrier to resistance (i.e., TAF, TDF, or entecavir). 3TC or FTC monotherapy is not considered the standard of care for HBV treatment because of a high risk of emerging resistance.[34]

Boosted Darunavir Plus Dolutegravir

An open-label, Phase 3b, noninferiority clinical trial evaluated the continuation of DRV/r plus two NRTIs versus a switch to DRV/r plus DTG; the switched regimen was noninferior.[39] Because of the small sample size of this study, the regimen of DRV/r plus DTG is recommended only in the absence of other alternative options but can be considered in particular for individuals with resistance and/or

intolerance to 3TC (or FTC), ABC, and TDF (or TAF) **(CI).** Similar results were observed in two small observational studies.[40,41] Individuals with active HBV infection need to be on a potent HBV drug with a high barrier to resistance (i.e., TAF, TDF, or entecavir).

Long-Acting Intramuscular Cabotegravir Plus Rilpivirine

Long-acting ARV medications provide the convenience of reduced dosing frequency and may improve quality of life for individuals with pill fatigue or concerns about disclosure of HIV status or stigma associated with daily oral medication. Long-acting (LA) intramuscular (IM) injectable formulations of the INSTI cabotegravir (CAB) and the NNRTI RPV are approved by the U.S. Food and Drug Administration (FDA) to be given once monthly or every 2 months as a complete regimen for individuals ≥12 years old with sustained (e.g., ≥3 months) virologic suppression (HIV-1 RNA <50 copies/mL) on a stable ARV regimen, with no history of treatment failure, and with no known or suspected resistance to either CAB or RPV.[42-44]

Panel's Recommendation

The Panel recommends that monthly or every 2-month LA CAB/RPV can be used to replace an existing oral ARV regimen in people with HIV who fulfill all of the following criteria **(AI)**:

- Sustained viral suppression for at least 3 months
- No history of documented or suspected resistance to either CAB or RPV
- No active HBV infection (unless also receiving TAF, TDF, or entecavir)
- Not pregnant or actively planning pregnancy
- Not receiving medications with significant drug interactions with oral (during lead-in or bridging therapy) or injectable CAB or RPV (see Table 24b and Table 24d)

Oral lead-in therapy with CAB and RPV is optional and can be done based on provider–patient discussion.

Clinical Trial Data

Two Phase 3 clinical trials (ATLAS and FLAIR) randomized almost 1,200 participants with HIV-1 and viral suppression on oral ART to receive once-monthly LA CAB/RPV or to continue their oral ARV regimens.[45,46] Participants could not have prior resistance to INSTIs or NNRTIs (except the K103N mutation), previous virologic failure (ATLAS trial), or active or occult HBV infection. Both studies used a 1-month oral lead-in of once-daily CAB 30 mg with RPV followed by injectable LA CAB/RPV monthly (loading dose x 1 followed by maintenance dosing). In the intention to treat the exposed population, HIV RNA >50 copies/mL at Week 48 occurred in 11 (1.9%) participants in the IM arms and 10 (1.7%) participants in the oral therapy arms (combining data from both studies) demonstrating that long-acting therapy was noninferior to continued oral therapy.[47] Virologic failure was rare; however, when it occurred, resistance to INSTIs, NNRTIs, or both was common.

The ATLAS-2M study compared LA CAB 600 mg/RPV 900 mg every 8 weeks (n = 522) versus LA CAB 400 mg/RPV 600 mg every 4 weeks (n = 523) in ART-experienced adults.[48] At 48 and 96 weeks, every 8-week dosing was noninferior to every 4-week dosing (HIV RNA ≥50 copies/mL; 2% vs. 1% at 48 weeks).[48,49]

In the SOLAR study, 687 individuals who were virologically suppressed on BIC/FTC/TAF were randomized 2:1 to either switch to LA CAB/RPV every 2 months or remain on BIC/FTC/TAF.[50] At 48 weeks LA CAB/RPV was virologically noninferior to continued BIC/FTC/TAF with 1% versus

<1% virologic failure, respectively. There was also no difference in viral suppression with or without oral lead-in when initiating LA CAB/RPV therapy. Based on these data and other existing data, oral lead-in therapy is now considered optional (see the CABENUVA FDA drug label).

Lastly, the Cabotegravir and Rilpivirine Efficacy and Safety (CARES) trial, an open-label trial conducted in Africa, randomized people with HIV and viral suppression to receive LA CAB/RPV every 8 weeks or to continue with their oral ARV regimen. At 48 weeks, 246 of 255 (96%) in the LA CAB/RPV arm and 250 of 257 (97%) in the oral ARV arm maintained HIV RNA <50 copies/mL. Two LA CAB/RPV participants had virologic failure at Week 48 and developed high-level resistance to both CAB and RPV.[51]

Adverse Effects

The most common adverse events associated with LA CAB/RPV are injection site reactions (ISRs) which occurred in more than 80% of participants at least once. ISRs reduce in frequency over time, occurring in about 10% to 30% of participants after the first year. ISRs were generally mild to moderate, with 99% being Grade 1 or 2 and the median duration of symptoms being 3 days. Hypersensitivity reactions, post-injection reactions, hepatotoxicity, and depressive disorders have also been reported.[45,52]

Practical Considerations When Using Long-Acting Injectable Cabotegravir and Rilpivirine

When prescribing LA CAB/RPV, clinicians should refer to the FDA product label[42] for guidance with the following practical considerations:

- Injection techniques, including injection sites and needle length in people with body mass index >30 kg/m^2
- Several drugs, particularly those interacting with CYP3A or uridine diphosphate glucuronosyltransferase 1A1, are contraindicated with CAB and RPV (oral and/or IM) due to significant drug interactions (Drug–Drug Interaction Tables 24b and 24d).
- Management strategies for missed doses of IM injections and use of oral bridging therapy

HIV Viral Load and Drug-Resistance Testing Monitoring

HIV viral load monitoring should be performed 4 to 8 weeks after a switch to LA CAB/RPV. HIV viral load also should be checked in people with unplanned missed visits and delayed dosing of LA CAB/RPV. When viremia develops during LA therapy, resistance testing, including integrase resistance testing, should be performed. Follow-up dosing in people with missed doses should not be delayed while awaiting viral load and resistance test results. In a pooled analysis from FLAIR, ATLAS, and ATLAS-2M, confirmed virologic failure was more common in the setting of baseline, proviral, RPV resistance-associated mutations; HIV-1 subtype A6 (rare in the United States); higher baseline body mass index; and lower week-8 trough RPV concentration.[53] However, some recent studies did not observe worse outcomes in people with a high body mass index (Opera Cohort and CARES Study).[51,54] In the setting of confirmed virologic failure on LA CAB/RPV, resistance to NNRTIs and INSTIs is common.[45,46,55]

Pregnancy Considerations

Initiation of LA CAB/RPV is not recommended during pregnancy. Clinicians should refer to the Perinatal Guidelines for recommendations in managing women who become pregnant or are

planning pregnancy while receiving LA CAB/RPV. Health care providers are strongly encouraged to register women with HIV who become pregnant while receiving LA CAB/RPV in the Antiretroviral Pregnancy Registry.

Considerations Regarding Long-Acting Cabotegravir Plus Rilpivirine Use in People With a History of Adherence Challenges

There are emerging data on the use of LA CAB/RPV in people with a history of adherence challenges. The open-label Long-Acting Therapy to Improve Treatment Success in Daily Life (LATITUDE [ACTG A5359]) Study enrolled people who had HIV viremia, challenges in taking daily oral ART, and no evidence of CAB or RPV resistance.[56] After adherence support and conditional financial incentive, participants who were able to achieve viral suppression were randomized to monthly LA CAB/RPV or to continue on the oral regimen. Study randomization was stopped early by the Data Safety Monitoring Board because of lower rates of virologic failure in individuals randomized to LA CAB/RPV than those staying on oral therapy (see the Virologic Failure section for more discussion).

Optimization Strategies for People With Viral Suppression and a History of NRTI and/or NNRTI Resistance

Some existing data demonstrate the safety and efficacy of select within-class and between-class switches for individuals with underlying drug resistance who are on a stable ARV regimen with suppressed HIV RNA (e.g., for 6 months or longer). These findings are further supported by data extrapolated from those experiencing virologic failure.

Within-Class Switch From Dolutegravir to Bictegravir in the Setting of Limited Resistance

The GS-US-380-4030 study enrolled 565 participants who were stably suppressed on DTG plus two NRTIs. The participants were randomized to either remain on their current regimen or switch to BIC/FTC/TAF. After 48 weeks, the groups had similar rates of sustained suppression. The rates of viral suppression were similar for those with a documented history of NRTI resistance (approximately 25% of participants) and those without a history of NRTI resistance.[57] Results from this trial lend theoretical support to other optimization strategies that include a switch from one high-barrier drug to another in the setting of underlying NRTI genotypic resistance. This study also supports using drugs with a high barrier to resistance when only one, and possibly no NRTIs in the background regimen, need to be fully active. This is further supported by other lines of evidence, some of which are discussed below.

Data of Within and Between Class Switches to Bictegravir in the Setting of Limited Drug Resistance

The BRAAVE study was an open-label, optimization study for Black people with HIV and viral suppression for ≥12 months on a standard regimen of two NRTIs plus a third agent (INSTI, NNRTI, or PI). Individuals were randomized to switch to BIC/FTC/TAF or to remain on current therapy (although individuals on TDF were switched to TAF). Switching to BIC-based therapy was noninferior for maintaining viral suppression compared with continuing current oral therapy. Baseline regimens included 61% INSTI, 31% NNRTI, and 9% PI. Baseline resistance did not affect the outcomes of therapy. In particular, NRTI resistance was present in 14% of participants, with 10% harboring the M184V/I mutation.[58]

Switch From a Boosted Protease Inhibitor to Dolutegravir in Individuals With Viral Suppression and Prior First-Line NNRTI Plus NRTI Failure

The second-line switch to DTG (2SD) study was conducted at four sites in Kenya in a population of people with HIV who had prior first-line NNRTI plus NRTI regimen failure and achieved viral suppression on a current ritonavir-boosted PI-based regimen without undergoing genotypic resistance testing.[59] In this prospective, open-label trial, 795 participants with HIV were randomized 1:1 to switch the boosted PI to DTG or continue the current regimen. NRTIs were not switched, although a switch was allowed if clinically indicated. At Week 48, switching to DTG was noninferior to continuing a boosted PI with about 5% of participants in each arm having viral rebound >50 copies/mL. In the 40 people with virologic rebound, 20 in each arm, no resistance to DTG or PIs was found. Grade 3 or 4 adverse events were similar in the two groups. This study was limited by the absence of genotypic resistance data demonstrating the amount of NRTI resistance present at the time of first-line NNRTI plus NRTI failure. Nevertheless, several related studies in similar settings have demonstrated that extensive NRTI and NNRTI resistance is expected in this situation, often including resistance to tenofovir and 3TC or FTC.[60-62] Accepting that substantial NRTI resistance was likely to be present in this study population, 2SD provided evidence that a person who is suppressed on a boosted PI-based regimen is likely to remain suppressed on a second-generation INSTI-based regimen in the setting of NRTI resistance. This is further supported by data showing that people with virologic failure and NRTI resistance can be successfully treated with second-generation INSTIs plus TAF or TDF and FTC or 3TC.[60]

Data From Virologic Failure Studies Inform Optimization With NRTI Resistance in Clinical Practice

Several studies conducted in resource-limited countries where people with first-line NNRTI-based virologic failure and who have NRTI-resistance support treatment recommendations for optimizing ART in these settings (details in the Virologic Failure section). In the DAWNING study,[63] for individuals who failed first-line NNRTI-based ART, DTG (84%) outperformed LPV/r (70%) for 48-week viral suppression <50 copies/mL. Participants who had one active NRTI in their study regimen had similar virologic responses as those with two active NRTIs. In the NADIA study, participants failing first-line NNRTI-based therapy were randomized to either DTG or DRV/r combined with randomized NRTIs. At enrollment, resistance to NRTIs was common with 86% of participants having an M184V mutation and 50% having a K65R mutation. At 48 weeks, DTG was noninferior to DRV/r, with both groups achieving viral suppression to <400 copies/mL in about 90% of participants. There were no differences in rates of viral suppression between participants with resistance to one or both NRTIs in their regimen compared to those with no NRTI resistance.[60] At Week 96, TDF was superior to zidovudine when combined with 3TC.[64]

Although these were studies of ART use in the setting of initial NNRTI-based virologic failure, we expect that regimens that are effective during viremia would also be effective in the setting of viral suppression in people with similar ARV resistance patterns (NRTI resistance, but no known or suspected PI or INSTI resistance). These studies support that for optimization in the setting of NRTI resistance, two NRTIs (TAF or TDF plus 3TC or FTC) should be included in the regimen with a fully active drug with a high resistance barrier, such as DTG **(AII),** BIC **(BIII),** or boosted DRV (DRV/c or DRV/r) **(BIII).** The use of regimens without any fully active NRTIs **is not routinely recommended** when there are other viable treatment options. However, in some clinical situations—such as when prior resistance testing is not fully available, to avoid major drug–drug interactions, to keep regimens simpler, or for other reasons—a regimen with a fully active drug with a high resistance barrier plus two partially active NRTIs can be considered. Both tenofovir and cytidine analogs may retain partial activity even when resistance is present.

Optimization Strategies for People With Viral Suppression and a History of Complex Underlying Resistance

Before optimizing an ARV regimen of a person with viral suppression who has a history of treatment failure and complex drug resistance, a careful review of the individual's full ARV history and cumulative drug resistance profile should be undertaken. Consultation with a clinician with expertise in HIV drug resistance is recommended **(AIII).**

As described in the Optimization Strategies for People With Viral Suppression and a History of NRTI and/or NNRTI Resistance section above, any regimen that includes a fully active drug with a high barrier to resistance (e.g., DTG, BIC, or boosted DRV) plus two NRTIs (even if resistance is present), is likely to achieve suppression in those experiencing virologic failure and maintain suppression in the setting of optimization.[59,60] Reliably maintaining suppression when there is not a fully active drug with a high resistance barrier is more complicated and requires careful consideration before any switch is made. In people with prior virologic failure(s) and/or limited prior resistance testing, proviral DNA genotypes can be considered. Clinicians should keep in mind that proviral DNA resistance mutations found will be useful, but some archived resistance mutations may not be found with this testing. Previous studies demonstrated that it is best to include at least 2 (preferably 3) fully active drugs in the setting of virologic failure if a fully active drug with a high resistance barrier is not included in the regimen due to resistance and/or intolerance.[65] In this setting, it will often require incorporating active drugs in classes other than NRTIs, NNRTIs, PIs, and INSTIs, such as entry inhibitors (i.e., CCR5 antagonists, post-attachment inhibitors, attachment inhibitors, and fusion inhibitors) or capsid inhibitors (e.g., lenacapavir), recognizing that entry and capsid inhibitors have primarily been studied and are indicated for those with virologic failure.

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Discontinuation or Interruption of Antiretroviral Therapy

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Discontinuation or interruption of antiretroviral therapy (ART) may result in viral rebound, immune decompensation, and/or clinical progression.[1-5] Thus, discontinuation or planned interruption of ART is not recommended outside the context of a clinical trial **(AI).** However, unplanned interruption of ART may occur under certain circumstances as discussed below.

Unanticipated Interruptions of Oral Antiretroviral Drugs

Reasons for short-term interruption (days to weeks) of ART vary and may include intercurrent illnesses that preclude oral intake (e.g., gastroenteritis, pancreatitis), surgical procedures, drug toxicity, or interrupted access to antiretroviral (ARV) drugs. Stopping ART for a short time (i.e., less than 1 day to 2 days) usually can be done by holding all drugs in the regimen. Whether unplanned interruptions occur by accident or by necessity (e.g., because of drug toxicities), all efforts should be made to minimize their duration. Recommendations for some specific scenarios are listed below.

When a Patient Experiences Unexpected Inability to Take Solid Oral Medications

For patients who require tube feeding, some ARV drugs are available in liquid formulations, and some pills may be crushed. The Oral Antiretroviral/HCV DAA Administration[6] provides information on crushing pills and formulating liquid ARV drugs. Additional information also may be available in drug product labels. Clinicians should consult an HIV specialist and/or pharmacist to assess the best way for a patient with a feeding tube to continue an effective ARV regimen.

For patients unable to take medications by any enteral route (e.g., in the context of severe gastrointestinal disease), all components of the oral drug regimen should be stopped simultaneously, regardless of half-lives of the drugs. After resolution, all components of the ARV regimen should be restarted simultaneously.

Several ARV drugs are available as parenteral formulations; these include zidovudine, enfuvirtide, ibalizumab (IBA), and the long-acting (LA) injectable formulations of cabotegravir (CAB LA) and rilpivirine (RPV LA). The combination of CAB LA and RPV LA is approved as a complete regimen for the treatment of HIV. However, this regimen has not been studied as an alternative for patients who cannot take oral medications. Clinicians should consult with an HIV specialist before prescribing any of these agents.

When a Patient Experiences a Severe or Life-Threatening Toxicity to an Antiretroviral Agent

All components of the ARV drug regimen should be stopped simultaneously, regardless of drug half-life. After resolution, a different complete regimen that does not include the offending agent should be started.

Interruption of Long-Acting Antiretroviral Drugs

The combination of CAB LA and RPV LA is approved as a complete regimen for the treatment of HIV. CAB LA and RPV LA are given as intramuscular (IM) injections and have extended half-lives. Therefore, patients who miss doses or discontinue therapy without bridging with an oral ARV regimen are at increased risk of virologic failure with development of drug resistance. Clinicians should refer to prescribing information for CAB LA and RPV LA for the management of missed doses or discontinuations.[7] For planned missed injection doses of CAB LA and RPV LA, oral formulations of CAB and RPV should be made available to patients as a bridging therapy for up to 2 months. Oral formulation of RPV is available by prescription in community pharmacies, but oral formulation of CAB is available only through the manufacturer. When stopping long-acting injectable ART, transition to a suppressive oral ARV regimen should occur within 4 weeks of the last planned IM doses. Patients who have missed or delayed clinic visits repeatedly should be reassessed to determine if resumption of injections is appropriate or if they may need to be transitioned back to an oral regimen. Plasma viral load testing should be performed before the transition, and drug-resistance testing should be considered if plasma viremia is present.

Patients with drug-resistant HIV may receive IBA as part of a salvage regimen. IBA is initiated with a 2,000-mg loading dose given as an intravenous (IV) infusion, then followed by 800 mg given as an IV infusion every 14 days as maintenance therapy. If a dose is missed by ≥3 days, a repeat loading dose of 2,000 mg IV infusion is recommended before resumption of maintenance therapy.

Analytical Treatment Interruption

Several research studies are evaluating approaches to achieve sustained ART-free viral remission or a functional cure for HIV.[8] Viral eradication (i.e., elimination of HIV entirely from an individual) remains a more challenging, longer-term goal. Currently, the only way to reliably test the effectiveness of these strategies is to interrupt ART and closely monitor for viral rebound in the setting of a clinical trial, an approach referred to as “analytical treatment interruption” or ATI.[9] The duration of treatment interruption, the dynamics of viral rebound, and the criteria for restarting ART are part of ATI clinical trial designs with the goal to conduct these clinical trials safely.

Before ART is interrupted, participants of ATI trials should be made aware of and understand the risks of viral rebound,[10] acute retroviral syndrome, increased risk of HIV transmission, decline of CD4 count, HIV disease progression, development of minor HIV-associated manifestations (e.g., oral thrush) or serious non-AIDS complications (e.g., renal, cardiac, hepatic, or neurologic complications), and the development of drug resistance. Patients should be counseled about the need for close clinical and laboratory monitoring during ART interruptions and provided counseling and linkage to pre-exposure prophylaxis services should they wish to refer sexual partners at risk for acquiring HIV.

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CARDIOVASCULAR AND METABOLIC COMPLICATIONS IN PEOPLE WITH HIV

Introduction

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With continuous antiretroviral therapy (ART) and viral suppression, life expectancy for people with HIV is approaching that of people without HIV. Despite a narrowing mortality gap between people with and without HIV, some estimates suggest a gap of up to 10 years, which remains clinically relevant.[1] With prolonged survival, age-related comorbidities have increased at higher rates among people with HIV than among those without HIV, including atherosclerotic cardiovascular disease (ASCVD), metabolic complications (e.g., weight gain, insulin resistance, dyslipidemia, and metabolic syndrome), cancer linked to pro-oncogenic viruses, and other aging-related conditions.[2-8] Three key factors that contribute to this burden of age-related noncommunicable diseases among people with HIV include: (1) an over-representation of traditional risk factors in this population, especially higher rates of smoking, diabetes, and dyslipidemia; (2) possible cardiometabolic toxicities from some antiretroviral drugs; and (3) HIV-associated chronic inflammation and immune activation, which are not completely abated by suppressive ART.[9-18]

In this context, the U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents has developed this section to provide guidance on the prevention and optimal management of cardiovascular disease (CVD) and metabolic complications in people with HIV. This section is divided into four subsections: (1) HIV-associated inflammation and immune activation as a contributor to CVD and metabolic complications, (2) CVD risks among people with HIV, (3) recommendations on the use of statin therapy for the prevention of ASCVD in people with HIV, and (4) weight gain among people with HIV receiving ART. Given the relevance of HIV-associated immune activation and inflammation as a mediating factor across the comorbidities discussed, this topic is also included within this section of the guidelines.[19-24]

Other important CVD manifestations and metabolic complications are not currently covered in detail here, such as insulin resistance and risk for diabetes mellitus, metabolic syndrome, metabolic dysfunction–associated steatotic liver disease, heart failure, sudden cardiac death, and bone disease. At this time, guidance on the management of these conditions remains similar for people with and without HIV infection. Still, these conditions represent areas of active research, and as future evidence arises that informs management specific to people with HIV, this section may be expanded.

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Immune Activation and Inflammation Among People With HIV Receiving Antiretroviral Therapy

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Key Considerations and Recommendations
• HIV-related immune activation and systemic inflammation, despite viral suppression with antiretroviral therapy, are associated with increased risk for cardiovascular disease and metabolic complications, as well as a broad spectrum of comorbidities. • Switching or adding antiretroviral (ARV) drugs solely to reduce immune activation or inflammation **is not recommended,** except in a clinical trial **(AII).** • The use of immunomodulatory or anti-inflammatory therapy to reduce HIV-related immune activation or inflammation **is not recommended,** except in a clinical trial **(AII).** • Routine monitoring of markers of immune activation or inflammation (e.g. high-sensitivity C-reactive protein [CRP] or interleukin-6 [IL-6]) to inform the clinical management of HIV **is not recommended (BII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

The Influence of Immune Activation and Inflammation on Disease Risk in People With HIV

Compared to people without HIV, people with HIV have demonstrated higher overall immune cell activation and higher levels of systemic inflammation (as measured by biomarkers such as interleukin-6 [IL-6]) and acute phase reactants (e.g., high-sensitivity C-reactive protein [hsCRP]).

Although immune activation declines with suppressive antiretroviral therapy (ART), it often persists at elevated levels in virologically suppressed people with HIV.[1,2] Extensive literature over the past decades has demonstrated a link between HIV-related systemic inflammation and an increased risk of age-related comorbidities, as well as mortality from non-AIDS conditions.[3-16] Specifically, blood markers of systemic inflammation among people with HIV have been associated with increased risk for a wide range of chronic conditions, including atherosclerotic cardiovascular disease (ASCVD), diabetes mellitus, obesity, cancer, osteopenia/osteoporosis, and chronic obstructive pulmonary disease.[8-18] Even in individuals with CD4 T lymphocyte (CD4) cell counts >500 cells/mm^3, immune activation and inflammation are associated with increased morbidity and mortality from age-related comorbidities.[19,20]

Antiretroviral Therapy as a Strategy to Reduce Inflammation

Early HIV diagnosis combined with prompt ART initiation can effectively achieve a lower level of persistent immune activation. Most inflammatory markers decline during the first several months of ART and may achieve a stable “setpoint” within 1 to 2 years.[21,22] In observational studies, people with HIV who initiated ART during acute HIV infection appeared to achieve a lower immune activation setpoint during ART-mediated viral suppression than those who started ART at later disease stages.[23] These data reinforce the recommendation to start ART as soon as possible after HIV diagnosis, regardless of CD4 count (see Initiation of Antiretroviral Therapy).

Currently, data do not support intensifying or modifying ART as a strategy to reduce immune activation after viral suppression is already achieved. For example, adding antiretroviral (ARV) drugs to an already suppressive regimen (or ART intensification) does not consistently improve immune activation.[24-28] Although some studies have suggested that switching an ARV regimen to one with a more favorable lipid profile may improve some markers of immune activation and inflammation, these studies have limitations, and results are not consistent across markers or among studies.[29-31] Thus, adding or switching ARVs solely to reduce immune activation or inflammation **is not recommended,** except in a clinical trial **(AII).**

Adjunct Treatments to Reduce Immune Activation and Inflammation

Treatment strategies targeting immune activation and inflammation have been a focus of ongoing investigation. In this context, research strategies to mitigate inflammation among people with HIV on suppressive ART have typically taken one of three approaches: (1) target the root drivers of immune activation specific to HIV disease, (2) downregulate inflammatory pathways broadly, or (3) leverage anti-inflammatory properties of medications targeting traditional risk factors.

The HIV-related mechanisms driving immune activation have been posited to include viral persistence, permanent injury impairing immune recovery (i.e., due to lymphatic tissue fibrosis), presence of copathogens, as well as dysbiosis and microbial translocation.[32-36] Among these mechanisms, investigational approaches have targeted HIV reactivation from latently infected cells, fibrotic pathways, the gut microbiome, and cytomegalovirus coinfection.[27,37-41] However, thus far, none of these strategies have improved clinical outcomes. Therefore, these interventions should be pursued only in the context of clinical trials.

Data have emerged demonstrating the potential clinical benefit of broadly anti-inflammatory and immunosuppressive strategies among people without HIV who are at high risk for ASCVD events. The CANTOS trial (Canakinumab Anti-Inflammatory Thrombosis Outcomes Study) studied canakinumab, a human monoclonal antibody targeting cytokine interleukin-1b, a driver of the IL-6 signaling pathway, as a secondary prevention strategy among people with known ASCVD who do not have HIV. CANTOS demonstrated a treatment effect for reducing inflammation, as well as cardiovascular events and cancer death, in the general population.[42] In people with HIV, canakinumab and tocilizumab, inhibitors of the receptor for IL-6, have been shown to reduce blood levels of markers of inflammation and immune activation.[43,44] However, it is unclear whether the potential risks of these immunomodulatory therapies, including the increased sepsis risk seen in the CANTOS trial,[42] outweigh their possible benefits for people with HIV, particularly with long-term use. Therefore, the clinical use of immunomodulatory or anti-inflammatory therapy solely to reduce HIV-associated immune activation or inflammation **is not recommended** among people with HIV, except in a clinical trial **(AII).**

Finally, beyond the well-established clinical benefit for reducing ASCVD events, hydroxymethylglutaryl coenzyme A (or HMG-CoA) reductase inhibitors, also known as statins, have been shown to improve biomarker levels of inflammation (e.g., hsCRP) and immune activation in the general population.[45,46] In this context, data from REPRIEVE (Randomized Trial to Prevent Vascular Events in HIV) have demonstrated a reduction in cardiovascular events with pitavastatin use among people with HIV (see Statin Therapy in People With HIV). Other commonly used medications with anti-inflammatory properties—such as aspirin, angiotensin-converting enzyme inhibitors, methotrexate, and angiotensin receptor blockers—have failed to consistently reduce biomarkers of immune activation and/or inflammation in people with HIV in randomized controlled trials.[39,47-50]

Monitoring Inflammation

As evidence is insufficient to inform differential screening practices or clinical management strategies (e.g., for ASCVD) based solely on the level of individual blood biomarkers, there is no clear rationale to routinely monitor levels of immune activation and inflammation in people with HIV. Thus, routine monitoring of markers of immune activation or inflammation (e.g., hsCRP, IL-6) to inform the clinical management of HIV **is not currently recommended (BII).**

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Cardiovascular Complications in People With HIV

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Key Considerations and Recommendations

Antiretroviral Management

- All people with HIV should maintain viral suppression with continuous antiretroviral therapy (ART) to reduce the risk of atherosclerotic cardiovascular disease (ASCVD) **(AII).**
- Due to concerns regarding an increased risk of cardiovascular events, alternative antiretroviral (ARV) medications should be considered in place of abacavir and lopinavir/ritonavir in people with higher underlying ASCVD risk or known ASCVD **(AII).**

ASCVD Risk Stratification

- For people with HIV aged 40–75 years, 10-year ASCVD risk score should be calculated using the Pooled Cohort Equations (or PCE) at least annually to inform management, including whenever lipids are measured or in certain clinical scenarios that may affect ASCVD risk* **(BIII)** (see Atherosclerotic Cardiovascular Disease Risk Scores in the text).
- Lipid screening should be performed in people with HIV **(AIII),** with the following suggested frequency: (1) at entry into care or at the time of ART initiation, (2) 3–6 months after ART initiation once viral suppression is achieved, (3) annually for those aged ≥40 years or receiving statin therapy, (4) every 1–3 years for those aged <40 years **and** not on statin therapy, and (5) with changes in cardiovascular disease (CVD) risk factors (see text for additional details on monitoring).
- There is insufficient evidence to support the use of inflammatory biomarkers for ASCVD risk stratification among people with HIV.
- When compared to the general population, women with HIV have both a greater increase in relative risk of ASCVD and a greater underprediction of ASCVD by risk scores than men with HIV. For women with HIV, it is critical to ensure optimal ASCVD risk factor modification regardless of ASCVD risk score, implement ASCVD prevention strategies, and perform diagnostic evaluation if they present with possible cardiac symptoms.

ASCVD Prevention and Risk Factor Management

- Statin therapy is recommended for all people with HIV aged 40–75 years and in additional clinical scenarios for other age groups to reduce the risk of ASCVD and major adverse cardiovascular events. See Statin Therapy in People With HIV for recommendations on statin use.
- The use of immunomodulatory therapy to reduce HIV-associated ASCVD risk **is not recommended** except in a clinical trial **(AII).**
- Some drugs prescribed to prevent or treat CVD may have clinically significant interactions with certain ARV drugs. Before initiating or changing ARV drugs or concomitant medications, clinicians should carefully assess for potential interactions **(AIII).**
- All people with HIV should be counselled about ways to reduce CVD risk through behavioral modifications such as healthy diet, weight control, regular exercise, smoking cessation, and limiting alcohol consumption.
- Optimal management of comorbidities (e.g., hypertension, diabetes, obesity) remains important to further reduce CVD risk among people with HIV.

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

* HIV-related CVD risk-enhancing factors include prolonged duration of HIV infection, delayed ART initiation, long periods of HIV viremia and/or treatment nonadherence, low current or nadir CD4 T

lymphocyte cell count (e.g., <350 cells/mm^3), exposure to some older ARV drugs associated with cardiometabolic toxicity, and/or coinfection with hepatitis C virus.

Overview

Most people with HIV who are using continuous antiretroviral therapy (ART) and achieve viral suppression have a life expectancy that is approaching that of people without HIV.[1] However, a gap in mortality remains due to comorbidities such as atherosclerotic cardiovascular disease (ASCVD). As mortality from AIDS events among people with HIV has declined, the proportion of ASCVD-related deaths has increased. When compared to people without HIV, people with HIV have an approximately twofold higher risk of developing ASCVD, even after accounting for traditional cardiometabolic risk factors.[2] The age at incident ASCVD diagnosis among people with HIV is often younger than that of people without HIV. In this context, the 2018 Multisociety Cholesterol Guidelines identified HIV as an ASCVD risk enhancer.[3] Factors influencing ASCVD risk among people with HIV include a higher prevalence of traditional cardiometabolic risk factors compared with the general population,[4] ongoing systemic inflammation associated with HIV despite viral suppression,[5] and cardiometabolic toxicity associated with certain ARV drugs.[6,7] Data also suggest that excess ASCVD risk relative to the general population is greater among women with HIV than among age-matched men with HIV.[8,9] In addition, differential access to screening and treatment of ASCVD risk factors also contributes to excess ASCVD risk among certain people with HIV in the United States.[10,11]

While there has been extensive focus on the epidemiology and pathogenesis of ASCVD among people with HIV, there are also data demonstrating increased risk of other cardiac and vascular diseases. People with HIV have an increased risk of developing stroke (including ischemic and hemorrhagic), heart failure, arrhythmia or sudden cardiac death, and thrombosis.[12-15] Risk factors for these outcomes are thought to be similar to those for ASCVD, with an etiologic role for both traditional risk factors and HIV-related factors. Currently, this section of the guidelines is focused on primary prevention strategies for people with HIV, with an emphasis on ASCVD. As data emerge concerning primary and secondary prevention strategies for other cardiovascular outcomes specific to people with HIV, this section may be expanded.

HIV-Related Risk Factors for Atherosclerotic Cardiovascular Disease

Factors related to HIV and its treatment have been shown to be important contributors to excess cardiovascular disease (CVD) risk. Specifically, HIV-related inflammation has been associated with elevated CVD risk. This inflammation is increased in the presence of active viremia and decreases with ART, but still remains elevated when compared to those without HIV (see Introduction). Data from the SMART trial demonstrated that continuous ART not only improves HIV-related outcomes but also significantly reduces non-AIDS events, including CVD, an observation thought to be related to the beneficial effects of ART on inflammation.[16] In the large Veterans Aging Cohort Study (VACS), myocardial infarction (MI) risk was independently associated with detectable or increased HIV RNA; compared to people without HIV, MI risk was increased by 39% in those with HIV RNA <500 copies/mL and by 75% in those with HIV RNA ≥500 copies/mL.[17] In REPRIEVE, even low-level HIV viremia (median 62 copies/mL) was linked to increased rates of major adverse cardiac events (MACE), as viremic individuals had a higher risk than those with viral load below the limit of detection (adjusted hazard ratio 1.4; 95% confidence interval, 1.00–1.97)[4,18]; however, another recent study did not show an association between HIV viremia and CVD.[19] Based on these findings, continuous ART is recommended for all people with HIV to maintain viral suppression and reduce ASCVD risk **(AII).** Immunomodulatory therapy as an intervention to reduce HIV-associated ASCVD risk **is not recommended** except in a clinical trial **(AII).** See Immune Activation and Inflammation Among People With HIV Receiving Antiretroviral Therapy for additional details.

Additional factors related to HIV may further impact ASCVD risk. Lower CD4 T lymphocyte (CD4) cell count and nadir CD4 count have been shown to be associated with CVD events independent of traditional CVD risk factors or specific ART,[20,21] with VACS demonstrating CD4 <200 cells/mm^3 as an independent predictor of MI with an increased risk of nearly 90%.[17,22] HIV-related CVD risk-enhancing factors include prolonged duration of HIV infection, delayed ART initiation, long periods of HIV viremia and/or treatment nonadherence, low current or nadir CD4 count (e.g., <350 cells/mm^3), exposure to older antiretroviral (ARV) drugs associated with cardiometabolic toxicity, and coinfection with hepatitis C.[23]

Women with HIV have also been shown to have a greater relative risk of ASCVD compared to men with HIV. Although data indicating the absolute risk of MI is similar between genders—12.71 versus 10.48 per 1,000 person-years for women and men with HIV, respectively—women with HIV have exhibited a nearly 3- to 4-fold increase in relative MI risk versus a 1.5- to 2-fold increase for men compared to sex-specific rates among people without HIV.[9,24-26] A substudy from REPRIEVE demonstrated the absence of an expected protective effect of female sex for the development of a MACE.[4] The presence of HIV-related ASCVD risk-enhancing factors, including female sex, may strengthen the rationale for ASCVD prevention strategies, including statin initiation (see Statin Therapy in People With HIV), and may be used to inform decisions to avoid certain ARV medications that have been associated with increased ASCVD risk.

Antiretroviral Therapy and Cardiometabolic Complications

Specific ARV medications and classes have been associated with potential cardiometabolic toxicity, which has informed the U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel)'s recommendations on ART regimen selection to reduce risk for cardiometabolic complications. See Interactions Between ARV Drugs and Drugs for Treatment or Prevention of Cardiovascular Diseases below and Table 7 of What to Start for more information. Specifically, for individuals with elevated traditional ASCVD risk or known CVD, the selection of an ART regimen should consider options that minimize the introduction of new cardiometabolic adverse effects.

Antiretroviral Therapy and Atherosclerotic Cardiovascular Disease Risk

Individual ARV medications and classes have been linked to increased risk of CVD events. An association between abacavir (ABC) use and MI was first reported in the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study, with the increased risk noted only with recent/current ABC exposure (i.e., within 6 months) and particularly among participants with pre-existing cardiac risk factors.[27] Since the D:A:D report, multiple studies, systematic reviews, and meta-analyses have evaluated the relationship between ABC therapy and cardiovascular events, with some confirming the initially observed association and others failing to identify an association.[27-32] Retrospective analyses from the REPRIEVE study corroborated the D:A:D results, showing an increased hazard of a first MACE with ART regimens, including ABC versus tenofovir-containing regimens,[33] and an increased MACE hazard of 62% in participants with previous use and 41% with current use of ABC compared with participants who were never exposed.[34] An association between ABC and ASCVD risk reported in multiple large studies provides a rationale to consider underlying ASCVD risk when using ABC as a component of ART. Based on these data, the Panel recommends considering alternative ARV medications in place of ABC in people with HIV and higher underlying ASCVD risk or known CVD **(AII).**

An early study from the D:A:D cohort demonstrated a 16% increased risk of MI per year of cumulative protease inhibitor (PI) exposure,[35] specifically with older PIs (e.g., indinavir and ritonavir-boosted lopinavir [LPV/r]). A case-control study within the French HIV ANRS cohort CO4 also found

a 33% increase in MI risk with LPV/r use.[36] A later study from the D:A:D cohort showed a 59% increased risk of CVD per 5 additional years of use with ritonavir-boosted darunavir (DRV/r) but not ritonavir-boosted atazanavir (ATV/r),[37] yet subsequent studies did not observe an association between boosted darunavir and increased CVD risk.[38-40] Based on these data, the Panel recommends considering alternative ARV medications in place of LPV/r in people with HIV and higher underlying ASCVD risk or known CVD **(AII).** If use of DRV/r is indicated, clinicians should weigh the potential benefits of therapy versus the potential cardiovascular risk.

The effect of integrase strand transfer inhibitors (INSTIs) on the risk of CVD is an area of active research, with recent studies showing inconsistent results. In a multicenter observational study of the international RESPOND consortium, INSTI exposure was associated with a nearly twofold greater incidence of a composite CVD endpoint within the first 6 months after exposure compared to no INSTI exposure,[41] and the increased risk persisted throughout the first 24 months. Subsequently, two target trial emulation studies found no association between INSTI use and a composite CVD outcome that included MI, stroke, or invasive cardiovascular procedures, regardless of previous ART experience.[42,43] Based on current data, there is insufficient evidence to recommend modifying suppressive INSTI-based ART regimens in people with weight gain, higher underlying ASCVD risk, or known CVD.

Antiretroviral Therapy and Dyslipidemia

Higher levels of low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), and triglycerides have been observed with tenofovir alafenamide (TAF), efavirenz (EFV), all boosted PIs, and elvitegravir/cobicistat (EVG/c).[44,45] Among the PIs, similar lipid changes have been shown in participants from a randomized trial of ATV/r- and DRV/r-based regimens.[46] Importantly, differences in lipid levels between two ART regimens can be due to a lipid-raising effect of a given medication and/or a lipid-lowering effect of the other medication. For example, levels of total cholesterol, LDL, HDL, and triglycerides are higher in participants who received TAF when compared with those who received tenofovir disoproxil fumarate (TDF) in multiple randomized controlled trials.[47,48] However, data from a placebo-controlled pre-exposure prophylaxis trial support that TDF exposure has an independent lipid-lowering effect (for total cholesterol, LDL, and HDL).[49] Further, data support that total cholesterol to HDL ratios did not differ between participants receiving TAF and those receiving TDF,[50,51] and the clinical significance of CVD risk from increases across all lipid indices without changes in total to HDL ratios is uncertain.

Antiretroviral Therapy and Diabetes/Insulin Resistance

Direct effects on diabetes mellitus (DM) and insulin resistance have been observed with older ARVs, including ZDV and LPV/r.[52] Several studies have demonstrated an increased risk of DM with INSTI use,[53-55] an association that may be mediated in part by weight gain.[56] An association between ART and DM has not been consistently observed with other contemporary ARVs, including those recommended as initial therapy in the guidelines.

Antiretroviral Therapy and Other Cardiac Complications

EFV, as well as higher than recommended doses of fostemsavir and rilpivirine, have been associated with QTc (QT corrected for heart rate) prolongation.[57-59] These ARV drugs should be used with caution in people with pre-existing heart disease, QTc prolongation, or concomitant use of medications that may increase drug concentration or prolong the QTc interval. Both ATV/r and LPV/r have been associated with PR prolongation, particularly among people with risk factors, including pre-existing heart disease and concomitant use of medications that may cause PR prolongation.[60,61]

Strategies for Atherosclerotic Cardiovascular Disease Risk Estimation and Screening For People With HIV

Cardiovascular risk assessment and prevention strategies developed for the general population do not reflect HIV-specific factors, such as inflammation and immune activation or potential contributions from certain ARV drugs, which are key mechanistic contributors to HIV-associated CVD. This section will address ASCVD risk estimation and lipid screening for people with HIV. ASCVD prevention strategies specific to people with HIV are further discussed in the Introduction and Statin Therapy in People With HIV sections.

Lipid Monitoring

Lipid screening should be performed in people with HIV **(AIII),** given the increased risk for ASCVD and the increased rate of dyslipidemia associated with certain ARV drugs. A fasting or random lipid profile should be obtained for all people with HIV at entry into care or at the time of ART initiation or modification. If a random profile is abnormal, a fasting lipid profile should be obtained. Lipid levels should be rechecked 3 to 6 months after starting ART or later if viral suppression is not achieved within 6 months. Lipid levels measured after initiation of ART should then be used to calculate an ASCVD risk score and determine indications for statin therapy (see Statin Therapy in People With HIV). Among people with HIV who are aged 40 years or older or who are any age and are receiving statin therapy, lipid monitoring should be performed annually to reassess ASCVD risk and inform decisions on statin management and/or other risk modification strategies. Further, specific to people on statin therapy, the approach to monitor lipids at least annually to assess adherence and the need for treatment intensification is consistent with recommendations by the *2018 American Heart Association (AHA)/American College of Cardiology (ACC)/Multisociety Guideline on the Management of Blood Cholesterol* among people in the general population.[62] For people with HIV who are under age 40 and not receiving statin therapy, lipid levels should be monitored every 1 to 3 years to reassess ASCVD risk. For all people with HIV, lipid monitoring may occur more frequently based on lifestyle factors or clinical scenarios, including changes in traditional ASCVD risk factors (e.g., weight gain, new diagnosis of hypertension, concomitant medications that affect lipids, or change to an ARV regimen with increased ASCVD risk).

Atherosclerotic Cardiovascular Disease Risk Scores

ASCVD risk prediction algorithms enable clinicians to quantify the risk of a future cardiovascular event and are used in clinical practice to stratify risk and to guide the intensity of ASCVD preventative measures and risk factor management, including statin use and antihypertensive therapy. Yet established ASCVD risk prediction scores validated in the general population typically do not include risk factors specific to HIV, and they have been shown to systematically underestimate risk among people with HIV. Data from multiple studies and a meta-analysis have shown that the ACC/AHA Pooled Cohort Equations (PCE) underpredict ASCVD risk in people with HIV in high-income countries.[63-68] Studies also suggest the accuracy of established ASCVD risk scores for people with HIV may vary by patient demographics and clinical characteristics, with underprediction of ASCVD risk demonstrated among women,[63,66,67] Black or African-American individuals,[63,67] and individuals with low or moderate predicted CVD risk versus high risk.[63,65,66] ASCVD risk score accuracy may also differ by region globally, with a study of REPRIEVE data showing underprediction of risk in high-income countries yet overprediction in low-income and middle-income countries.[67] Additional research is needed to better tailor ASCVD risk scores to people with HIV overall, as well as by geographic region and demographic and clinical characteristics.

In 2023, the AHA developed a new set of ASCVD risk equations for the general population. The Predicting Risk of CVD EVENTs (PREVENT) equations differ from the PCE on several levels,

including the inclusion of a new derivation dataset of more than 6 million individuals, new variables reflecting a broader cardiovascular-kidney-metabolic framework, a new outcome including heart failure, and the removal of race from the models.[69] Because PREVENT was developed for the general population, this updated risk score does not incorporate risk factors specific to HIV or its treatment. Predicted ASCVD risk has been shown to be lower using PREVENT in the general population.[70] For people with HIV,[71] 97% had a lower predicted risk, and 58% fewer would be strongly recommended for statins using the PREVENT (vs. PCE) risk score. Further study is needed to determine if and how the PREVENT risk estimates may inform the clinical management of people with HIV.

The PCE is recommended for predicting ASCVD risk among people with HIV, as it has been more extensively studied in this population and used in the REPRIEVE trial to inform recommendations on the use of statins in people with HIV (see Statin Therapy in People With HIV). For people with HIV aged 40 to 75 years, the 10-year ASCVD risk score should be calculated using the PCE at least annually, including whenever lipids are measured or in certain clinical scenarios that may affect ASCVD risk (e.g., changes in traditional CVD risk factors, such as weight gain, new diagnosis of hypertension, concomitant medications that affect lipids, or change to an ARV regimen with increased ASCVD risk) **(BIII).** Presently, there is insufficient evidence to recommend strategies to account for the underprediction of ASCVD risk by the PCE and other established ASCVD risk scores among people with HIV, including use of inflammatory biomarkers.

Interactions Between Antiretroviral Drugs and Drugs for Treatment or Prevention of Cardiovascular Diseases

People with HIV may receive a statin to prevent ASCVD or medications for the treatment of CVD risk factors or underlying CVD. Some of these drugs may have clinically significant interactions with some ARV drugs. Before initiating or changing these medications, clinicians should carefully assess for potential interactions **(AIII).** Tables 24a to 24g and the Statin Therapy in People With HIV section of the guidelines, as well as the University of Liverpool HIV Drug Interaction site, provide guidance for managing these interactions. Major mechanisms of pharmacokinetic (PK) interaction between ARV drugs and cardiac drugs are noted in the sections below.

Cytochrome P450 Enzymes

Many cardiac drugs (such as certain antiarrhythmics, anticoagulants, beta-blockers, calcium channel blockers, statins, and others) are substrates of cytochrome P450 (CYP) enzymes and may interact with ARV drugs that are inhibitors or inducers of these enzymes. Concomitant use with:

- CYP inhibitors (such as the PK boosters ritonavir and cobicistat, and the capsid inhibitor lenacapavir) may—
    - Increase the systemic exposure and potentially toxicities of cardiac drugs that are CYP substrates
    - Decrease the efficacy of the antiplatelet drug clopidogrel (a prodrug) by inhibiting the formation of its active metabolite
- CYP inducers (such as EFV and etravirine) may—
    - Reduce concentrations and efficacy of the cardiac drugs that are CYP substrates

Drug Transporters

Interactions related to drug transporters may also play a role in drug disposition. For example, the INSTIs bictegravir, dolutegravir, and elvitegravir are inhibitors of organic cation transporter 2 (OCT2)

and may reduce renal elimination of certain antiarrhythmics (such as dofetilide and disopyramide), thereby increasing concentrations of the cardiac drug and the risk for adverse events.

Because some interactions may result in serious toxicities or lack of efficacy, certain drug combinations are not recommended or are contraindicated. In these cases, clinicians should assess if alternative ARV drugs and/or alternative cardiac drugs can be used. In other cases, dosage modification and therapeutic drug monitoring of cardiac drugs may be needed to guide therapy, with close follow-up to assess efficacy and potential toxicity.

Management of Comorbidities and Traditional Cardiovascular Disease Risk Factors

Although HIV-specific factors influence CVD risk, traditional risk factors also play an important role among people with HIV. Although factors such as advancing age and other demographic characteristics cannot be changed, many CVD risk factors are modifiable with behavioral and pharmaceutical interventions. The AHA has outlined eight components of cardiovascular health for everyone: healthy diet; participation in physical activity; avoidance of nicotine; healthy sleep; healthy weight; and healthy levels of blood lipids, blood glucose, and blood pressure.[72]

Traditional CVD risk factors predict incident CVD events and occur at higher rates among people with HIV compared with the general population.[4] A 2025 global meta-analysis assessed common CVD risk factors among people with HIV and found higher odds of CVD incidence associated with DM, hypertension, dyslipidemia, smoking, and a prior history of CVD.[73] A U.S. population-based study among people with HIV found conventional risk factors, such as tobacco use, hypertension, and obesity, to be persistently associated with CVD incidence over follow-up periods for as long as 15 years.[74] Nontraditional risk factors for CVD that are not specific to HIV, including alcohol use disorders, depression, and hepatitis C virus coinfection, are also more common in people with HIV.

The aforementioned data highlight the importance of preventing and managing traditional risk factors among people with HIV. A longitudinal study comparing CVD risk factors among people with and without HIV found that associations between CVD and HIV status were attenuated when dyslipidemia and DM were well controlled.[75] Recommendations for screening and management of CVD risk factors are outlined in the HIVMA/IDSA 2024 update, *Primary Care Guidance for Providers Who Care for Persons With Human Immunodeficiency Virus*.[76] For women with HIV, ensuring optimal CVD risk factor modification regardless of CVD risk score and performing diagnostic evaluation for possible cardiac symptoms is critical given the greater relative risk of ASCVD.

Other Management Considerations and Unanswered Questions

Estrogen, Progestins, or Testosterone Therapy and Cardiovascular Risk

Studies have produced conflicting results on associations between estrogen, progestins, or testosterone therapy and CVD risk, varying by study design, study population, duration and timing of therapy, and other clinical factors.[77-80] Research on relationships between these drugs and CVD among people with HIV is even more limited.[81-84] Data on testosterone use among people with HIV have been limited to the treatment of testosterone deficiency and lack longitudinal information on CVD-related outcomes.[85,86] Studies of estrogen use suggest a potential increase in CVD risk; however, this association may vary by dose, mode of delivery, and underlying physiological stress.[79-81,87] A longitudinal study of combined estrogen and progestin use for oral contraception among people with HIV suggested increased CVD risk, though the association was not statistically significant.[88]

As the population with HIV ages, a growing number of women with HIV are entering menopause. CVD is the leading cause of morbidity and mortality in menopausal women, and this risk is increased in women with HIV.[89,90] Studies of the cardiovascular risk associated with menopausal hormone therapy have led to changes in guidelines over the years.[90] Systemic hormone therapy is not currently recommended for CVD prevention or treatment.[91] However, hormone therapy remains the most effective treatment for vasomotor symptoms.[92] Some research suggests that women with HIV are undertreated for menopausal symptoms.[93] However, data are lacking on menopause and hormone therapy in women with HIV, including whether menopause amplifies the effects of HIV on CVD risk.[94] Current HIV primary care guidelines recommend that menopause-related hormone therapy for women with HIV should not differ from the care of women without HIV.[76]

Cardiovascular Risks of Adults Who Acquired HIV Perinatally or During Adolescence

An increasing number of adults acquired HIV perinatally or during adolescence, but the cardiovascular effects of perinatal or adolescent HIV acquisition and long-term ART use are unclear. For individuals who acquired HIV perinatally, it is hypothesized that exposure to HIV and ART *in utero* while the cardiovascular system is developing, use of older ART drugs with cardiometabolic and mitochondrial toxicity, lifelong duration of infection, and a longer period of chronic inflammation may further exacerbate the already heightened CVD risk observed in people with HIV. Investigation of the cardiovascular complications of perinatal HIV infection has largely focused on youth and adolescents. Abnormalities in cardiac structure and function have been well documented and include systolic and diastolic dysfunction, left ventricular hypertrophy and dilatation, and myocardial fibrosis.[95-99] Studies of perinatally acquired HIV have also demonstrated elevated rates of surrogate markers of atherosclerosis (including carotid intima-media thickness, arterial stiffness, and endothelial dysfunction),[100,101] impaired glucose metabolism and insulin resistance,[102] lipodystrophy and metabolic syndrome,[103] and increased Pathobiological Determinants of Atherosclerosis in Youth (or PDAY) cardiovascular risk scores.[104,105] Adults with perinatally acquired HIV also appear to be at risk for cardiometabolic comorbidities, with a large North American study of young adults aged 18 to 30 years demonstrating a high incidence of DM, hypercholesterolemia, hypertriglyceridemia, hypertension, and chronic kidney disease.[106] Current gaps in knowledge regarding CVD risk among those who acquired HIV perinatally or during adolescence include (1) the clinical significance of cardiac structural and functional abnormalities and surrogate markers of atherosclerosis with respect to coronary plaque and cardiac endpoints; (2) whether the epidemiology and pathophysiology of CVD differ for people with similar durations of perinatally versus horizontally acquired HIV, including HIV acquired during adolescence; (3) whether the epidemiology and pathophysiology of CVD differ for people in low- and middle-income versus high-income countries; (4) the optimal approach to estimate ASCVD risk and frequency of monitoring in adults who acquired HIV perinatally or during adolescence; and (5) whether primary prevention approaches (e.g., statins) for adults with HIV aged 40 and older apply to younger adults who acquired HIV perinatally or during adolescence.

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Statin Therapy as Primary Prevention of Atherosclerotic Cardiovascular Disease in People With HIV

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Panel's Recommendations

For People With HIV Who Have Low-to-Intermediate (<20%) 10-Year Atherosclerotic Cardiovascular Disease (ASCVD) Risk Estimates

Note: Estimates based on the ASCVD Risk Estimator from the American College of Cardiology (ACC).

Aged 40–75 Years

- When 10-year ASCVD risk estimates are 5% to <20%, the Panel for the Use of Antiretroviral Agents in Adults and Adolescents With HIV (the Panel) recommends initiating at least moderate-intensity statin therapy **(AI).**
  - Recommended options for moderate-intensity statin therapy include the following:
    - Pitavastatin 4 mg once daily **(AI)**
    - Atorvastatin 20 mg once daily **(AII)**
    - Rosuvastatin 10 mg once daily **(AII)**
  - When 10-year ASCVD risk estimates are <5%, the Panel favors initiating at least moderate-intensity statin therapy **(CI).** The absolute benefit from statin therapy is modest in this population; therefore, the decision to initiate a statin should take into account the presence or absence of HIV-related factors that can increase ASCVD risk.[a]
    - Same options for moderate-intensity statin therapy as recommended for 10-year ASCVD risk estimates of 5% to <20% (see above)

Aged <40 Years

- Data are insufficient to recommend for or against statin therapy as primary prevention of ASCVD in people with HIV. In the general population, lifestyle modifications are recommended for people aged <40 years, with statin therapy considered only in select populations (see American Heart Association (AHA)/ ACC/Multisociety Guidelines).

Key Recommendations for the General Population (Including People With HIV)

Note: Recommendations based on AHA/ACC/Multisociety Guidelines.

For People Aged 40–75 Years With High (≥20%) 10-Year ASCVD Risk Estimates

- Initiate high-intensity statin therapy (see Table 11b below).

For People Aged 20–75 Years With Low-Density Lipoprotein Cholesterol (LDL-C) ≥190 mg/dL

- Initiate high-intensity statin therapy at the maximum tolerated dose (see Table 11b below).

For People Aged 40–75 Years With Diabetes Mellitus

- Initiate at least moderate-intensity statin therapy (see Table 11b below). Perform further risk assessment to consider using a high-intensity statin.

Key Considerations
• Coadministration of certain statins and antiretroviral drugs may result in significant drug–drug interactions. In some cases, the interaction may require statin dose adjustment, switching to another statin, or increased monitoring for statin-related adverse effects (see the Drug–Drug Interaction section below for details). • As in the general population, initiation of statin therapy should be deferred during pregnancy; statin therapy should be discontinued if pregnancy occurs, and breastfeeding is not recommended while using statin therapy.
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion*
[a] HIV-related factors that may increase ASCVD risk but are not considered in traditional risk estimation tools may strengthen the rationale for initiating statin therapy in this population. Examples include prolonged duration of HIV infection, delayed antiretroviral therapy initiation, long periods of HIV viremia and/or treatment nonadherence, low current or nadir CD4 T lymphocyte cell count (e.g., <350 cells/mm^3), exposure to older antiretroviral drugs associated with cardiometabolic toxicity, and/or hepatitis C coinfection (see text below for rationale of the Panel's recommendations).

The above recommendations inform the use of statin therapy in primary prevention of atherosclerotic cardiovascular disease (ASCVD) in people with HIV receiving care in the United States. These recommendations were developed by the Panel for the Use of Antiretroviral Agents in Adults and Adolescents With HIV (the Panel) in collaboration with representatives from the American College of Cardiology (ACC), American Heart Association (AHA), and the HIV Medicine Association (HIVMA). The recommendations and supporting text have been endorsed by these organizations.

Background

Traditional risk factor modification remains an important component of primary ASCVD prevention strategies for people with HIV, including modifications related to diet, exercise, smoking cessation, blood pressure control, and lipid lowering for those with hyperlipidemia. Hydroxymethylglutaryl-coenzyme A reductase inhibitors (i.e., statins) may offer advantages for people with HIV over other prevention strategies, given that statin therapy is associated with a well-described reduction in ASCVD events, as well as treatment effects on inflammatory pathways.[1-3]

Findings from the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) have provided evidence to support specific recommendations for statin therapy as primary ASCVD prevention in people with HIV aged 40 to 75 years in the United States. The 2018 AHA/ACC/Multisociety Guidelines for the general population recommend statin therapy for all people at high 10-year ASCVD risk (defined as ≥20%). For people at intermediate risk (i.e., ≥7.5% to <20%) or borderline risk (i.e., 5% to <7.5%), it is recommended to prescribe statin therapy based on shared decision-making. These recommendations are based on risk stratification that uses the pooled cohort risk equations to estimate 10-year ASCVD risk, along with clinician–patient discussions about risk, benefits, and patient preference.[4,5] Given that current ASCVD risk prediction tools typically underestimate risk among people with HIV, the AHA/ACC/Multisociety Guidelines identify HIV as a potential "risk enhancer" that should influence discussions on the use of statin therapy among those at borderline or intermediate risk.[5] However, prior to the REPRIEVE trial, no formal recommendations had been issued for people with HIV at low-to-intermediate ASCVD risk (i.e., <20%). Results from REPRIEVE now provide clear evidence to inform the use of statin therapy

as primary prevention among people with HIV who are aged ≥40 years, on continuous antiretroviral therapy (ART), and at low-to-intermediate ASCVD risk.

Primary Study Results From the REPRIEVE Trial

REPRIEVE was a Phase 3 global randomized controlled trial of oral daily pitavastatin 4 mg versus placebo to prevent ASCVD. The study enrolled a total of 7,769 people with HIV who were aged 40 to 75 years and at low-to-intermediate risk based on 10-year ASCVD risk estimates.[6,7] People with known ASCVD were excluded, and further eligibility criteria were based on low-density lipoprotein cholesterol (LDL-C) thresholds that varied based on 10-year risk estimates for ASCVD (up to a risk of 15%). The primary outcome was the occurrence of major adverse cardiovascular events (MACE), defined as a composite of cardiovascular disease death, myocardial infarction, hospitalization for unstable angina, stroke, transient ischemic attack, peripheral arterial ischemia, revascularization of coronary, carotid, or peripheral artery, or death of undetermined cause. Study participants were 31% female, 53% from high-income countries, 41% Black, and 35% White, with a median age of 50 years (interquartile range [IQR] 45–55) and 10-year ASCVD risk of 4.5% (IQR 2.1–7.0). Additionally, median CD4 T lymphocyte (CD4) cell count was 621 cells/mm^3 (IQR 448–827), with prior CD4 nadir <200 cells/mm^3 in 49%, and HIV RNA below quantification in 88%.

Compared to placebo, pitavastatin was associated with a 36% reduction in MACE (hazard ratio 0.64; 95% confidence interval [CI], 0.48–0.84), with event rates of 7.77 and 4.95 per 1,000 person-years, respectively, over a median follow-up of 5.6 years. A similar treatment effect was present across the individual components of MACE. In REPRIEVE, the absolute risk reduction was substantially greater for people with ASCVD risk estimates of ≥5% compared to those with risk of <5%, as discussed in the next section. Median LDL-C levels at baseline and 12 months were 107 mg/dL and 74 mg/dL, respectively, in the pitavastatin group, compared to 106 mg/dL and 105 mg/dL in the placebo group. During the study, a statin was initiated as part of clinical care in 5.7% of the pitavastatin group and 9.6% of the placebo group, leading to discontinuation of the blinded study drug. Incident diabetes (incident rate ratio [IRR] 1.29; 95% CI, 1.07–1.57) and Grade ≥3 or treatment-limiting muscle-related symptoms (IRR 1.58; 95% CI, 1.14–2.19) were also higher in the pitavastatin group.

Rationale for the Panel's Recommendations for People With HIV at Low-to-Intermediate (<20%) 10-Year ASCVD Risk

The overall findings from REPRIEVE, combined with the observation that equations based on traditional risk factors underestimate ASCVD risk among people with HIV, informed the Panel's decision to recommend the use of at least moderate-intensity statin therapy as primary prevention among people with HIV aged 40 to 75 years.[8,9]

To determine whether some participants demonstrated greater benefit from pitavastatin, subgroup analyses were performed in REPRIEVE.[6] Relative risk reductions across subgroups defined by key demographic and clinical characteristics did not demonstrate a clear interaction with the treatment effect. However, when incident MACE was stratified by 10-year ASCVD risk score, the absolute reduction in events was greatest for people with a 10-year ASCVD risk ≥5%. The estimated number needed to treat over 5 years (NNT_5) to avoid incident MACE events with pitavastatin treatment is reported below (Table 11a). Of note, the NNT_5 for people with ASCVD risk ≥5% was one-quarter to one-third that for those with ASCVD risk <5%. These data motivated the Panel's decision to issue a strong recommendation for initiating statin therapy among those with ASCVD risk ≥5%. It should be noted that some of these NNT_5 for subgroups defined by ASCVD risk are estimated based on low numbers of events and should be interpreted with caution.

Table 11a. Estimated NNT_5 for MACE Prevention With Pitavastatin in People With HIV Based on REPRIEVE[a]

10-Year ASCVD Risk Score	N	NNT_5
>10%	563	34
5% to 10%	2,995	53
2.5% to <5.0%	2,055	130
0% to <2.5%	2,156	187
Overall	7,769	100

[a] REPRIEVE[7]

Key: ASCVD = atherosclerotic cardiovascular disease; NNT_5 = number needed to treat over 5 years

The relationship between a higher absolute benefit from statin therapy (i.e., lower NNT_5) with higher baseline ASCVD risk estimates is well described and should be used to inform shared decision-making discussions on the use of statins.[5] These discussions should take into account the benefits along with side effects (see Common Adverse Effects of Statin Therapy below), costs, drug–drug interaction potential, and other patient-centered factors. For people at low (<5%) 10-year ASCVD risk who may experience a more modest absolute benefit from statin therapy, it is particularly important to weigh potential benefits for the individual against risks.

The findings from REPRIEVE reporting higher absolute benefit of statin therapy among people with HIV aged 40 to 75 years with greater ASCVD risk informed the Panel's decision to recommend the use of at least moderate-intensity statin therapy with a strong recommendation for those with a 10-year ASCVD risk score ≥5% to <20% **(AI).** Among participants aged 40 to 75 years with low estimated ASCVD risk (<5%), additional HIV-related factors may be important to consider. Using a large body of observational data, the AHA identified HIV-related ASCVD risk-enhancing factors that include the following: history of prolonged HIV viremia and/or delayed ART initiation, low current or nadir CD4 count (<350 cells/mm^3), HIV treatment failure or nonadherence, and lipodystrophy/lipoatrophy, as well as metabolic syndrome, fatty liver disease, and coinfection with hepatitis C.[10] Additional HIV-related factors associated with greater ASCVD risk that may be considered include, but are not limited to, a longer total duration of HIV infection and prior or current exposure to certain antiretroviral (ARV) drugs with cardiometabolic toxicity (e.g., abacavir, ritonavir-boosted lopinavir, ritonavir-boosted darunavir, and older protease inhibitors [PIs] no longer in use) (see Cardiovascular Complications for more detailed discussion). Conversely, people with HIV who initiated ART with contemporary regimens at higher CD4 counts (e.g., >500 cells/mm^3) are likely to be at lower absolute ASCVD risk. Finally, non-HIV risk factors that may favor initiating statin therapy are discussed within the AHA/ACC/Multisociety Guidelines.[5] In this context, clinician–patient discussions that weigh individual HIV-related factors along with the potential benefits and risks of statins are particularly important for people with HIV at low (<5%) 10-year ASCVD risk, where the NNT_5 for benefit is substantially higher. In summary, the Panel favors initiating at least moderate-intensity statin therapy for those with a 10-year ASCVD risk score <5% **(CI),** and the decision to initiate a statin should take into account the presence or absence of HIV- and non-HIV-related factors that can increase ASCVD risk.

Initiation of statin therapy should be deferred until after pregnancy for those with HIV and low-to-intermediate ASCVD risk, and statin therapy should be discontinued if pregnancy occurs in the context of HIV. As in the general population, breastfeeding is not recommended while taking statin therapy.

REPRIEVE did not enroll people with HIV under 40 years of age. In the general population, lifestyle modifications targeting traditional risk factors (e.g., diet, exercise, smoking cessation, and blood pressure control) are recommended for people under 40 years of age.[5] Still, some of these individuals also may benefit from statin therapy, and recommendations for the general population suggest risk factors such as familial hypercholesterolemia or a family history of premature ASCVD may favor statin therapy. There are insufficient data to inform whether risk enhancers, such as HIV-related factors, would favor statin therapy among people with HIV under 40 years of age. However, some younger people with HIV may be at increased ASCVD risk—particularly those with a very long duration of HIV infection (e.g., due to perinatal exposure); in these cases, decisions on statin therapy should be individualized.

Key Recommendations for the General Population (Including People With HIV) Based on AHA/ACC/Multisociety Guidelines

The 2018 ACC/AHA/Multisociety Guidelines recommend the use of statins as primary prevention for all people at high risk, defined as those aged 40 to 75 years with a 10-year ASCVD risk estimate of ≥20%, as well as those aged 20 to 75 years with an LDL-C ≥190 mg/dL.[5] In this context, an LDL-C reduction of ≥50% should be achieved, which typically requires high-intensity statin therapy (see the Intensity of Statin Therapy table below). For people with diabetes mellitus, the 2018 ACC/AHA/Multisociety Guidelines recommend at least a moderate-intensity statin, with additional risk assessment to inform consideration of initiating a high-intensity statin. These general population guidelines are based on high-quality randomized trial data and should inform the management of people with HIV who meet these criteria.[5]

Rationale for the Panel's Recommendation on Choice and Dose of Statin

In REPRIEVE, pitavastatin was chosen in part due to lower drug–drug interaction potential with certain ARV medications compared with other statins.[11] Although there are no clinical outcome comparative effectiveness trials analyzing different statins among people with HIV, some studies support the treatment effect of other moderate-intensity statins for lipid lowering or reductions in inflammation and immune activation, as well as a treatment effect on surrogate measures of ASCVD. Pitavastatin, atorvastatin, and rosuvastatin are all associated with greater reductions in LDL-C among people with HIV than pravastatin. In addition, pitavastatin (4 mg daily), rosuvastatin (10 mg daily), and high-dose atorvastatin (80 mg daily) have demonstrated reductions in inflammatory, monocyte, and T-cell immune activation biomarkers among people with HIV.[12-14] Finally, in two separate Phase 2 placebo-controlled randomized trials of statin therapy in people with HIV, atorvastatin (initiated at 20 mg daily) was associated with reductions in coronary noncalcified plaque by computed tomography angiography, and rosuvastatin (10 mg daily) was associated with slower progression of common carotid artery intima-media thickness.[15,16] Cumulatively, these data among people with HIV who are aged 40 to 75 years old and with ASCVD risk between 5% and <20% motivated the Panel's recommendation for use of at least moderate-intensity statins to include pitavastatin 4 mg daily **(AI),** atorvastatin 20 mg daily **(AII),** or rosuvastatin 10 mg daily **(AII).**

The recommendation for which statin agent to select and the intensity of therapy is based on the person's overall risk profile. As outlined in the 2018 AHA/ACC/Multisociety Guideline on the Management of Blood Cholesterol, statin intensity consists of three categories—high, moderate, and low—based on the LDL-C lowering effect.[5] Table 11b below outlines the statin agent and dose that qualify for each intensity, as well as the anticipated LDL-C lowering effect. More specifically, for every 39 mg/dL reduction in LDL-C, there is approximately a 20% reduction in ASCVD events and a

10% reduction in all-cause mortality.[17] However, it should also be noted that the magnitude of LDL-C lowering is variable in clinical practice.

Table 11b. Intensity of Statin Therapy

High Intensity (≥50% LDL-C Lowering Effect)	Moderate Intensity (30% to 49% LDL-C Lowering Effect)	Low Intensity (<30% LDL-C Lowering Effect)
Atorvastatin[a] 40–80 mg	**Pitavastatin 4 mg (AI)**[b]	Pravastatin 10–20 mg
Rosuvastatin[a] 20–40 mg	**Atorvastatin 20 mg (AII)**[a,b]	Simvastatin[c] 10 mg
	Rosuvastatin 10 mg (AII)[a,b]	Fluvastatin 20–40 mg
	Fluvastatin XL 80 mg	Lovastatin[c] 20 mg
	Fluvastatin 40 mg twice daily	
	Lovastatin[c] 40–80 mg	
	Pravastatin 40–80 mg	
	Simvastatin[c] 20–40 mg	

[a] Atorvastatin and rosuvastatin have known drug–drug interactions with ritonavir- and cobicistat-boosted antiretrovirals (ARVs); see drug–drug interactions between statin therapies and antiretroviral medications in Table 11c below.

[b] Bolded statins are included in recommendations from the Panel for the Use of Antiretroviral Agents in Adults and Adolescents With HIV; see Rationale for the Panel's Recommendation on Choice and Dose of Statin above.

[c] Simvastatin and lovastatin are contraindicated with ritonavir- and cobicistat-boosted ARVs.

Key: LDL-C = low-density lipoprotein cholesterol; XL = extended-release

Drug–Drug Interactions Between Statin Therapies and Antiretroviral Medications

Drug–drug interaction potential varies among the statins based on susceptibility to cytochrome P450 (CYP) and transporter-mediated interactions. Pitavastatin, pravastatin, and rosuvastatin are not significantly metabolized by CYP enzymes. Atorvastatin, lovastatin, and simvastatin are primarily metabolized by CYP3A4, whereas fluvastatin is a major substrate of CYP2C9. All statins are susceptible to interactions related to drug transporters (e.g., OATP1B1).[18]

Ritonavir (RTV)- and cobicistat (COBI)-boosted ARVs are particularly prone to drug–drug interactions with statins. When RTV- or COBI-boosted ARVs are coadministered with atorvastatin or rosuvastatin, statin dose reduction, a switch to an alternative statin, or increased monitoring for statin-related adverse effects may be required. Lovastatin and simvastatin are **contraindicated** when coadministered with COBI or RTV.

In general, some degree of drug–drug interactions may be expected between certain statins and HIV PIs, COBI-boosted elvitegravir, older non-nucleoside reverse transcriptase inhibitors, fostemsavir, and lenacapavir. The magnitude of the interaction and management strategy vary based on the individual statin and ARV combination. For more information on drug–drug interactions between pitavastatin, atorvastatin, and rosuvastatin with ARV drugs, see Table 11c below. Interactions

between other statins and ARV drugs can be found in the Drug Interaction tables (Tables 23, 24a, 24b, 24c, 24d, 24e, 24f, 24g, 25a, 25b).

Table 11c. Concomitant Use of Antiretroviral Drugs and Statins Recommended by the Panel as Primary ASCVD Prevention

This table includes recommendations for pitavastatin, atorvastatin, and rosuvastatin when used with different ARV drugs based on their drug–drug interaction potential. Because all statins can be used with nucleoside reverse transcriptase inhibitors (NRTIs) without dosage adjustment, NRTIs are not listed in this table. Drug interaction information for statins not listed in this table can be found in Tables 24a, 24b, 24d, 24f, and 24g of the Adult and Adolescent Antiretroviral Guidelines.

Panel Recommended Statins and Doses	ARV Drugs	Recommendations
Pitavastatin 4 mg once daily **(AI)**	INSTI: BIC, CAB, DTG, RAL NNRTI: DOR, EFV, ETR, RPV PI/r: ATV/r, DRV/r Other: LEN, MVC	No dosage adjustment
	INSTI: EVG/c PI/c: ATV/c, DRV/c Other: FTR	No data; use standard dose and monitor for AEs.
Atorvastatin 20 mg once daily **(AII)**	INSTI: BIC, CAB, DTG, RAL NNRTI: DOR, RPV Other: LEN, MVC	No dosage adjustment
	INSTI: EVG/c PI/b: DRV/c, DRV/r	↑ atorvastatin concentrations observed. Do not exceed 20 mg per day[a]; monitor for AEs.
	NNRTI: EFV, ETR	↓ atorvastatin concentrations observed
	PI/c: ATV/c	Do not coadminister.
	PI: ATV, ATV/r Other: FTR	↑ atorvastatin concentrations observed or possible. Monitor for AEs.
Rosuvastatin 10 mg once daily **(AII)**	INSTI: BIC, CAB, DTG, RAL NNRTI: DOR, EFV, ETR, RPV Other: LEN, MVC	No dosage adjustment
	INSTI: EVG/c PI/r: DRV/r Other: FTR	↑ rosuvastatin concentrations observed. Monitor for AEs.

Table 11c. Concomitant Use of Antiretroviral Drugs and Statins Recommended by the Panel as Primary ASCVD Prevention

Panel Recommended Statins and Doses	ARV Drugs	Recommendations
	PI/c: DRV/c	↑ rosuvastatin concentrations observed. Do not exceed 20 mg per day[a]; monitor for AEs.
	PI: ATV, ATV/r, ATV/c	↑ rosuvastatin concentrations observed or expected. Do not exceed 10 mg per day[a]; monitor for AEs.

[a] Based on recommendations from the U.S. Food and Drug Administration product label.

Key: AE = adverse effect; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTR = fostemsavir; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/b = boosted protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; RAL = raltegravir; RPV = rilpivirine

Common Adverse Effects of Statin Therapy

Statin therapy is well tolerated and safe; however, some side effects have been observed. The 2018 AHA/ACC/Multisociety Guidelines introduced the terminology *statin-associated side effects*, as opposed to *statin intolerance*, when these adverse effects occur.[5] The reason for this nomenclature is due to the fact that most people are able to tolerate statin rechallenge with an alternative statin agent or regimen. The most frequent adverse events are statin-associated muscle symptoms, with reported occurrence in 5% to 25% of people who receive statins.[19]

All statins have been implicated in small increases in both relative and absolute risk of diabetes. The increased risk of diabetes with statin use has been associated with older age and the presence of ≥2 risk factors, such as elevated baseline fasting glucose level, elevated fasting triglycerides, elevated body mass index, or history of hypertension.[20,21] Pitavastatin has previously been shown to have a neutral effect on glucose levels among people with metabolic syndrome, and this effect was consistent in REPRIEVE where there was no difference in glucose levels between pitavastatin and placebo groups over follow-up (median levels at Month 84 were 92 mg/dL and 90 mg/dL, respectively).[7,22] However, in REPRIEVE, there was a small increase in new-onset diabetes (6.0% in the pitavastatin group; 4.7% in the placebo group). Data are lacking on the risk of new-onset diabetes with other statins among people with HIV. However, a randomized controlled trial in people with HIV demonstrated increases in insulin resistance and impaired fasting glucose levels with rosuvastatin use.[23]

Mild increases in liver enzymes are seen in some individuals, though these are usually transient without clinical complications. However, the overall clinical benefits of statin use outweigh the overall risks of adverse effects, especially for people with greater estimated 10-year ASCVD risk.[24] Data related to any concerns of cognitive decline have been weak or contradictory and, as such, do not warrant statin avoidance or cessation.[5] Any time statins are initiated, clinicians should perform a comprehensive evaluation of musculoskeletal symptoms, an assessment of risk factors for diabetes, and a clinician–patient shared decision-making discussion focused on indications, benefits, risks, and patient concerns and preferences. When mild adverse events occur, close clinical follow-up is important.

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Weight Gain in People With Treated HIV

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Panel's Recommendations and Key Considerations
• All people with HIV should receive antiretroviral therapy (ART) to reduce morbidity and mortality **(AI)** and to prevent transmission of HIV to others **(AI).** • Weight gain after ART initiation is common. ART initiation should not be delayed because of concerns for weight gain **(AIII),** and ART should not be interrupted or discontinued because of weight gain **(AIII).** • ART selection, whether for initiation or switch, should be based on optimization of virologic suppression. Specific antiretrovirals should not be selected to prevent or reduce weight gain **(AII),** as available evidence suggests this strategy is ineffective. • Providers should include weight monitoring in conjunction with counseling on strategies for weight control as part of comprehensive care for people with HIV.
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

Weight gain is an increasingly recognized and now expected consequence of antiretroviral therapy (ART) initiation in many people with HIV. Although the mechanisms of weight gain after ART initiation remain unclear, the pathogenesis is complex and multifactorial.[1,2]

Historically, weight gain following ART initiation was thought to be related to a "return to health" phenomenon, given that early in the HIV epidemic, many people suffered from AIDS-wasting syndrome before receiving lifesaving ART. Although "return to health" may explain some weight gain for people with advanced HIV, weight gain occurs regardless of the time between HIV acquisition and ART initiation, including among people who initiate ART shortly after HIV seroconversion.[3-5] Similarly, weight gain with ART initiation occurs with most modern regimens and regardless of baseline body mass index (BMI).[6-9]

People with HIV on ART may experience greater weight gain than the expected age-related changes in people without HIV.[10] The greatest weight gain often occurs within the first 2 years after ART initiation. Notably, pooled data from eight randomized controlled trials suggest that approximately 13% of people with HIV experience excessive (>10%) weight gain within the first year of ART initiation.[11] The average weight gain trajectory frequently slows after 2 years on ART.[10,11] Overall, studies differ on the amount of weight gain seen in people with HIV, depending on the ART regimen and study population.

Weight gain among people with HIV is further complicated by the obesity epidemic in the general population in the United States.[10,12] Importantly, some people with HIV experience a differential weight gain after ART initiation, with increased central fat and/or visceral fat gain, generally termed "lipohypertrophy."[2] Generalized weight gain and obesity can obscure the diagnosis of HIV-associated lipohypertrophy, which can carry additional cardiometabolic risk. Yet, no clear definition or consensus exists to distinguish HIV-associated lipohypertrophy from generalized weight gain following ART or from weight gain unrelated to HIV.

Although weight gain after ART initiation is common, the lack of a clear understanding of its pathogenesis has limited the development of HIV-specific prevention and/or treatment guidance. Thus, what follows is a synopsis of contributors to weight gain in people with HIV and general management considerations, based on available data.

Contributors to Weight Gain

Antiretroviral Therapy

Because weight gain is common with almost all ART regimens, antiretrovirals (ARVs) have been implicated as contributors to weight gain in people with HIV, although data on the mechanisms of ART-induced weight gain are limited. The differential effects observed between ART classes, as well as within-class variability, suggest the possibility of multiple mechanisms by which ARVs contribute to weight gain.

Contemporary Antiretroviral Drugs

Weight gain occurs with nearly all ART regimens, although some are associated with more weight gain than others. For example, the least weight gain occurs with some non-nucleotide reverse transcriptase inhibitor (NNRTI)–based and tenofovir disoproxil fumarate (TDF)–based regimens.[6-9] Weight gain is most pronounced with integrase strand transfer inhibitors (INSTIs), especially bictegravir and dolutegravir, and the nucleotide reverse transcriptase inhibitor (NRTI) tenofovir alafenamide (TAF),[11,13] especially when compared to protease inhibitors (PIs) and older NRTIs.[6,11,13-19] The reasons for differential weight gain among ARVs are unknown. Importantly, differences in weight changes between ART regimens that are described in switch studies may be explained either by a weight-gain effect from exposure to a specific ARV (e.g., INSTI or TAF) and/or the removal of a weight-reduction effect from the ARV(s) that was discontinued (e.g., efavirenz or TDF). Some experts have suggested that medication side effects and/or unknown factors limit weight gain with certain older ARVs, when compared to the newer ARVs that have been linked to greater weight gain. Additional details and specific weight changes associated with individual ARVs can be found in the INSTI and NRTI sections of the guidelines.

Legacy Effects of Older Antiretroviral Drugs

The impact of prior ARV toxicity on an individual's current weight should also be considered. People with HIV who received thymidine analog NRTIs (e.g., zidovudine, stavudine) and older PIs (e.g., indinavir) were at risk for developing lipodystrophy. Lipodystrophy encompasses both lipohypertrophy (i.e., accumulation of visceral adipose tissue [VAT] and subcutaneous adipose tissue accumulation in the dorsocervical region, trunk, and/or breasts) and lipoatrophy (i.e., the loss of subcutaneous adipose tissue predominantly from the face, buttocks, and extremities).[2,20] Lipodystrophy can persist despite stopping the implicated ARV drugs. Particularly in individuals with lipoatrophy, subcutaneous adipose tissue fibrosis can persist and limit normal re-expansion of the fat depot when weight gain (from any cause) occurs, promoting VAT accumulation and its sequelae.[21] Thus, weight gain distribution and consideration of its effects on cardiometabolic risk may need to be contextualized by both prior and current ART exposure.

Individual Risk Factors and Population Differences

Although studies are limited, the following populations and clinical characteristics may contribute to greater ART-associated weight gain: female sex, older age, Black race/African descent, greater HIV disease severity (including lower CD4 T lymphocyte cell count and/or higher HIV-1 RNA),[11] and those who switched from a PI- or NNRTI-based ART regimen to an INSTI-based ART regimen while

virologically suppressed.[6,11,22] Data on the influence of weight prior to ART initiation or switch are conflicting, with some studies showing lower and others higher weight as a risk factor for subsequent ART-associated weight gain.[11,22]

Consequences of Weight Gain

Weight gain in people with HIV undoubtedly contributes to obesity-related comorbidities. In two Advancing Clinical Therapeutics Globally (ACTG) network protocols of longitudinal cohorts of people with HIV, individuals who experienced >10% weight gain within a year of ART initiation had an increased risk of type 2 diabetes mellitus (DM), metabolic syndrome, and cardiometabolic events 48 weeks after ART initiation.[23] Moreover, weight gain in people with HIV may confer a greater risk of cardiometabolic disease compared to people without HIV. The Veterans Aging Cohort Study found that each 5-pound weight gain was associated with a 14% greater risk of DM for people with HIV compared to 8% greater risk in people without HIV.[24] The Data Collection on Adverse events of Anti-HIV Drugs (D:A:D) cohort observed an 18% to 20% increased relative risk of cardiovascular disease (CVD) per 1.0 kg/m^2 BMI increase among people with HIV who had a normal weight at ART initiation.[25] In comparison, a cohort of people without HIV from Finland demonstrated a 4% to 5% increase in CVD risk per 1.0 kg/m^2 BMI increase.[26] Thus, even small amounts of weight gain in people with HIV could potentially contribute to increased cardiometabolic risk, and any weight gain >10% from baseline weight has been strongly associated with incident DM, metabolic syndrome, and other cardiometabolic outcomes.[23]

Management of HIV-Associated Weight Gain

General Antiretroviral Therapy Considerations

Data on effective strategies to prevent or reverse ART-associated weight gain remain limited. Although weight gain among people with HIV likely increases risk for multiple cardiometabolic comorbidities and can negatively affect body image and psychosocial functioning, early and sustained ART treatment is critical to optimize short- and long-term clinical outcomes in people with HIV. ART initiation should not be delayed because of concerns for weight gain **(AIII),** and ART should not be interrupted or discontinued because of weight gain **(AIII).** ART selection should be based on optimization of virologic suppression. Specific ARVs should not be selected (for initiation or switch) to prevent or reduce weight gain **(AII),** as available evidence suggests that this strategy is ineffective. Specifically, greater average weight gains associated with INSTI- or TAF-based regimens should not influence decisions on regimen selection, especially in cases when these agents are likely to be the best option for effective virologic suppression, as the reasons for these differential effects on weight among specific ARVs are not clear.

Sustainable Lifestyle Modifications and Behavioral Weight Loss Programs

Lifestyle modification remains the starting point and gold standard weight management intervention. As in the general population, people with HIV should be educated on long-term healthy eating habits and encouraged to exercise regularly. Some individuals may benefit further from consultation with a licensed dietitian, nutritionist, and/or formal behavioral weight loss program, where available. Of note, few studies have evaluated behavioral weight loss programs specifically in people with HIV, although available data suggest they achieve outcomes similar to those seen in the general population.[27-29] Referral to an obesity medicine specialist and/or bariatric surgery center should be considered for select individuals.

Pharmacotherapy Targeting Adipose Tissue and/or Weight in People With HIV

Currently, there is not enough population-specific evidence for the Panel to recommend weight loss pharmacotherapy for people with HIV beyond what is recommended for the general population. Several therapeutic trials have been conducted targeting abnormal adipose tissue accumulation in people with HIV; some of the medications tested in these trials also cause weight loss, as discussed below.

Tesamorelin, a synthetic growth hormone–releasing hormone analog, is the only U.S. Food and Drug Administration–approved therapy to treat excessive abdominal fat in people with HIV. The efficacy and safety of tesamorelin were largely established by two large Phase 3 trials conducted in people with HIV with central obesity. Tesamorelin 2 mg given as a daily subcutaneous injection was associated with a 13.1% reduction in VAT from baseline over 26 weeks, representing a 15.4% relative reduction compared to placebo. Through 52 weeks, the reduction from baseline reached 17.5%, demonstrating that most VAT loss occurred during the first 6 months of treatment.[30] Although the participants enrolled in the initial trials were primarily treated with the older NNRTIs and PIs used at the time, another small randomized controlled trial demonstrated similar results among people with HIV taking INSTI-based regimens.[31] The use of tesamorelin, however, is limited by modest response rates (two-thirds of the participants with clinically significant VAT reduction), the need for weekly reconstitution, daily subcutaneous injections, and reversal of effects with drug discontinuation.

Glucagon-like peptide-1 (GLP-1) and dual GLP-1/glucose-dependent insulinotropic polypeptide (GIP) receptor agonists (RAs) have gained considerable popularity in the general population due to the significant weight loss effects along with reduced risk for multiple CVD outcomes. However, few studies exist among people with HIV. The only randomized controlled trial to date in HIV was conducted in 108 participants with HIV-associated lipohypertrophy and overweight or obese BMI who received subcutaneous semaglutide 1.0 mg or placebo weekly over 24 weeks (plus an 8-week titration phase). People with DM were excluded from study entry. Semaglutide treatment resulted in an estimated weight loss of 10.4%, with significant reductions in total body fat and abdominal total and VAT.[32] In ACTG A5371, a 24-week, open-label, single-arm study of semaglutide 1.0 mg weekly for the treatment of metabolic dysfunction–associated steatotic liver disease in people with HIV who did not have DM, significant improvements in liver fat and other cardiometabolic parameters occurred that strongly correlated with weight loss (average of 8.1%).[33]

Although the few studies conducted in people with HIV showed an adverse event profile similar to the general population, the 1.0-mg dose used is lower than the maximum currently approved 2.0- and 2.4-mg doses for DM and obesity in the general population, respectively. Thus, the safety and side effect profile of GLP-1 and GLP-1/GIP RAs at higher doses or longer duration in people with HIV are currently unknown. Until more data become available, the Panel on Antiretroviral Guidelines for Adults and Adolescents advises prescribing GLP-1 and GLP-1/GIP RAs among people with HIV based on current general population indications and prescribing information.

Other weight loss drugs are available with and without a prescription in the United States and should similarly be used in accordance with general population recommendations. It is important to recognize the potential for known or possible drug–drug interactions with ARV drugs when considering the use of such therapeutic agents. For example, some case reports link orlistat, which promotes weight loss by reversibly inhibiting lipase and reducing dietary fat absorption, to loss of virologic suppression due to decreased ARV drug absorption.[34,35] In another example, the use of naltrexone-bupropion requires increased drug monitoring when coadministered with certain ARVs that may affect expected pharmacokinetic parameters.[36] Thus, it is critical to evaluate for any drug–drug interactions or possible adverse effects that may preferentially affect people with HIV on ARVs.

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CONSIDERATIONS FOR ANTIRETROVIRAL USE IN SPECIAL POPULATIONS

Adolescents and Young Adults With HIV

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Key Considerations and Recommendations
• Adolescents and young adults (AYA) with HIV largely belong to two distinct groups: those who acquired HIV in the first decade of life and who may be heavily antiretroviral therapy (ART)–experienced (early-acquired HIV); and those who acquired HIV in or after the second decade of life who may be mostly ART-naive. • ART is recommended for **all** AYA with HIV **(AI)** to reduce HIV-related morbidity, mortality, and transmission. • For AYA with HIV who are at risk for poor clinical outcomes, it is critically important to assess the behavioral and psychosocial context, and their ability to adhere to ART. Efforts should be made to provide youth-friendly support and infrastructure to reduce barriers to adherence and maximize success in achieving sustained viral suppression **(AIII).** • Pediatric and adolescent care providers should prepare AYA with HIV for the transition into adult care settings. Adult providers should be knowledgeable about this unique patient population and the challenges that frequently accompany the transition into the adult care setting. Consulting and collaborating with pediatric and adolescent HIV care providers is critical to ensure the successful transition of AYA with HIV to adult providers and continued engagement in care **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

Adolescents (13–19 years old) and young adults (20–24 years old) (AYA) with HIV consistently account for about one-fifth of new infections in the United States.[1] AYA with HIV have lower rates of testing, diagnosis, treatment engagement, and viral suppression than adults with HIV. Importantly, unique developmental, psychosocial, behavioral, and infrastructural factors affect this vulnerable population. Without having their specific challenges and needs addressed, AYA with HIV remain at risk for poorer HIV-related outcomes, including persistent viremia, drug resistance, morbidity, mortality, and secondary transmission.

Epidemiology

Globally, approximately 5 million young people aged 15 to 25 years live with HIV.[2] AYA with HIV are mostly individuals who acquired HIV in the first decade of life, mainly perinatally and rarely via blood transfusion or from sexual abuse. During adolescence and young adulthood, most individuals acquire HIV through sexual activity. Among the latter group, the Centers for Disease Control and Prevention (CDC) estimates that consistently one-fifth of the approximately 40,000 individuals newly diagnosed with HIV in the United States annually are adolescents and young adults.[1] The majority of new infections in this age group are among Black/African Americans and Hispanic/Latino men who have sex with men (MSM). For example, in 2018, more than 50% of the infections in this age group

were among young Blacks and African Americans, and 27% were among Hispanics and Latinos. Most (87%) were male, with 92% identifying as MSM. Compared to adults with HIV, AYA with HIV are less likely to have acquired HIV from injection drug use, and trends in HIV and AIDS prevalence indicate that the disproportionate burden of HIV among racial and ethnic minorities is even greater among youths 13 to 24 years of age than among those older than 24. Together, AYAWH account for approximately 34,000 of the individuals being followed at pediatric and adult clinics in the United States.[3]

Heterogeneity of Adolescents and Young Adults With HIV

AYA with HIV represent a diverse population in terms of socio-demographics, mode of HIV acquisition, sexual and substance use history, clinical and immunologic status, psychosocial development, and ability to adhere to medications. These distinctions have implications for HIV treatment, including the best ways to support AYA with HIV to optimize outcomes. AYA with HIV largely belong to two distinct groups:

- ***Adolescents and Young Adults With Early-Acquired HIV:*** These individuals, who acquired HIV in the first decade of life, are more likely to be treatment-experienced and have antiretroviral (ARV) drug resistance that may limit their options for ART regimens. This may be even more relevant for AYA with HIV who emigrated from parts of the world where routine viral load and genotypic resistance testing are not as readily available so that recognition of virologic failure and drug resistance may be delayed or missed. Also, individuals in this group generally have undergone a longer duration of disease chronicity and may have greater disease burden and more complications, less functional autonomy, and higher mortality risks.[4]
- ***Adolescents and Young Adults With HIV Acquired Later in Life:*** Individuals in this group are a more heterogeneous group of mostly young men (especially MSM) and other people who acquired HIV through sexual activities. A minority in this group acquired HIV through injecting drugs. Some of these AYA were victims of sexual abuse. The intersection of adolescence and young adulthood with other key risk populations (e.g., MSM, people who use drugs) magnifies the risk of poor clinical outcomes in this younger population. A statistically higher percentage of individuals in this group reported experiencing an even more extensive number of negative life experiences compared to those who acquired HIV early in life (38.8% versus 16.3%, P<.012).[5]

Unique Characteristics and Considerations for Adolescents and Young Adults With HIV

Although a diverse group, many AYA with HIV share unique characteristics that distinguish them from adults with HIV. Furthermore, AYA with HIV have certain commonalities that, while not necessarily unique to youth, disproportionately affect their chances of successful HIV treatment. Compared to adults 25 years old and older, AYA with HIV have poorer outcomes on each step of the HIV care continuum[6] (i.e., HIV diagnosis, linkage to HIV care, receipt of care, retention in care, achievement of viral suppression, maintenance of viral suppression). Most notably, only 40% of AYA with HIV are aware of their diagnosis and only 6% to 30% are virally suppressed.[7] These numbers are significantly worse than documented in older adults with HIV.[1] In one study of MSM of all ages, the percentage of those linked to HIV care within one month of diagnosis was lowest among AYA with HIV aged 13 to 19 (69%) and 20 to 24 (70%) years.[8] This group also had the lowest rates of retention in care and viral suppression. Older young adults (through age 29), who currently have the highest incidence of HIV infection among all age groups, have similar challenges, with 30% unaware of their infection status. They, too, require focused attention.

There are myriad reasons AYA with HIV do not perform as well on the HIV care continuum and are at greater risk of poorer clinical outcomes than adults with HIV. Perhaps most important, AYA with

HIV often do not have the same developmental capacity or ability to secure resources as their adult counterparts. These key features, discussed below, should be considered carefully because they can negatively affect HIV treatment and may alter clinical decision-making.

Adolescents and Young Adults With HIV as a Developmentally Distinct Patient Population

Developmental maturity in AYA with HIV generally can be grouped into several, often overlapping, areas, including physical, cognitive, communication and language, and social and emotional maturity. Several overarching factors—especially HIV-related stigma, discrimination, and a fear of familial and/or social rejection—can contribute to impaired development in all areas and adversely affect HIV treatment and clinical outcomes for many AYA with HIV. Additional important psychosocial factors discussed below commonly are seen in this population and also can affect development and successful HIV treatment.

Key developmental factors that may impact HIV treatment are highlighted below:

- ***Cognitive development:*** Evolving cognitive processes, which normally continue well into the third decade of life, are particularly relevant to HIV treatment in AYA with HIV. Their developing decision-making capacity often is driven by concrete thinking processes, risk-taking behaviors, preoccupation with self-image, and the need to fit in with their peers, all of which can affect HIV treatment negatively, including medication adherence and long-term clinical outcomes.[4,9,10] Likewise, AYA with HIV are at risk for neurocognitive impairment and mental health comorbidities,[11-14] including psychiatric, behavioral, and substance use disorders, which can further affect cognitive development and compromise effective HIV treatment.
- ***Physical development:*** The rapid physiologic changes (e.g., puberty, rapid growth) that occur in adolescence may result in altered ARV pharmacokinetics, underscoring the importance of adolescent-specific studies.[4] AYA with HIV, particularly those with infection acquired early in life and/or while sexually immature, also are at risk for impaired physical development, especially delayed sexual maturation and impaired normal bone development, which may have long-term consequences like reduced final height and peak bone mass, the latter being a key risk factor for developing osteoporosis.[15] Both delayed maturation and short stature may increase anxiety, depression, and stigma, which may, in turn, affect treatment adherence.[16] AYA with HIV who acquire HIV later in life still may be affected because peak bone mass is not achieved until around age 30. A small study showed lower bone mass in Tanner Stage 5 young men aged 20 to 25 years who acquired HIV during adolescence than in HIV-uninfected age-matched controls.[17]

Thus, developmental maturity should be considered in AYA with HIV, because associated clinical implications may alter HIV treatment decisions, including ARV selection and dosing.

Psychosocial and Related Risk Factors Affecting Adolescents and Young Adults With HIV

Several psychosocial, behavioral, and environmental risk factors affect many AYA with HIV and can undermine successful HIV treatment disproportionately in this population. Common key risk factors are summarized here:

- ***Mental and behavioral health:*** The percentage of AYA with HIV with behavioral and mental health conditions is very high and can undermine engagement in care and medication adherence. The most common conditions include anxiety and behavioral disorders, mood disorders (including depression), and attention deficit hyperactivity disorder. Among adolescents

with early-acquired HIV, nearly 70% meet criteria for a psychiatric disorder at some point in their lives.[12,18-20] Similarly, depression and anxiety were identified by symptom inventory 43% and 31% of the time, respectively, among AYA with HIV presenting for care at treatment sites in the Adolescent Trials Network.[21]

- ***Substance use:*** Substance use is prevalent among AYA with HIV. Among more than 2,000 AYA with HIV (72% acquiring HIV later in life) surveyed by the Adolescent Trials Network, weekly or more frequent use of tobacco (33%), marijuana (28%), alcohol (21%), and other illicit drugs (23%) was reported.[22,23] Young MSM had higher odds of each substance use behavior. Suboptimal ART was associated with increased risk of substance use behaviors,[23] underscoring the need to screen for and address substance use to improve treatment outcomes.
- ***Homelessness and unstable housing:*** Among the 4.2 million homeless adolescents and young adults in the United States (of whom 700,000 are unaccompanied minors),[24] the estimated HIV prevalence ranges from 3% to 16%. Youth who are lesbian, gay, bisexual, or queer; those with mental health concerns; and those who engage in substance use are disproportionately represented among homeless youth.[25] Homeless and unstably housed AYA with HIV have greater difficulties securing and sustaining resources and engaging in and being retained in care and treatment.[26]
- ***Additional social and environmental factors:*** A number of social and environmental factors commonly found among AYA with HIV negatively affect their HIV treatment, including limited familial and/or social support, lack of health insurance and/or experience with health care systems, unstructured and chaotic lifestyles, transportation barriers, food insecurity, limited educational opportunities, limited employment opportunities and/or unstable employment, and a history of trauma and/or sexual abuse.[27]

Optimizing Treatment Effectiveness and Supporting Adherence in Adolescents and Young Adults With HIV

Given the unique physiologic, developmental, and psychosocial characteristics discussed above, AYA with HIV require comprehensive systems of care with culturally competent providers and tailored treatment to serve all their specific medical and psychosocial needs. To maximize their chances of success, it is also imperative to routinely assess each AYA with HIV for individual factors that may need to be addressed or considered in treatment decisions or that may affect adherence.

Table 14 summarizes common adherence barriers among AYA with HIV, along with recommended support strategies. Refer to the Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection and the Adherence to Antiretroviral Therapy in Children and Adolescents with HIV additional approaches. Targeted interventions to improve treatment effectiveness and adherence related to a few key psychosocial factors among AYA with HIV also are highlighted here:

- ***Mental health care:*** Strategies to improve the provision of mental health care for AYA with HIV are critically important for optimizing treatment for co-occurring HIV and mental health problems.[28] These strategies include improving provider education, integrating trauma-informed care practices, increasing access to mental health professionals through collocated services for HIV care, expanding care delivery paradigms like telemedicine, and optimizing treatment approaches. An example of the latter is a combination of tailored psychotherapy and pharmacotherapy.[29,30] Further guidance for providing appropriate mental health care for AYA with HIV can be found in the Pediatric Guidelines.
- ***Substance use disorders:*** Providers should assess and recommend treatment for substance use disorders, with consideration of emerging substance use trends, such as the use of electronic vapor products. Further guidance for providing appropriate substance use screening

and treatment for AYA with HIV can be found in the Pediatric Guidelines and in the Substance Use Disorders and HIV section.

- ***Psychosocial and environmental stressors:*** Multimodal interventions that enhance social support and teach adaptive coping skills may help AYA with HIV manage environmental stressors and improve clinical outcomes.

Specific Antiretroviral Therapy Considerations in Adolescents and Young Adults With HIV

All AYA with HIV should initiate ART as soon as possible and stay on ART indefinitely to maximize viral suppression, reduce morbidity and mortality, and prevent secondary HIV transmission **(AI).** As described below, clinicians should consider simplifying ART regimens and using antiretrovirals with high barriers to resistance whenever possible to support adherence.

Strategies to Improve Medication Adherence

Clinicians selecting ART for AYA with HIV must balance the goal of prescribing a maximally potent regimen with a patient-by-patient assessment of existing and potential adherence barriers and available youth-friendly support strategies to facilitate adherence.[31] Additional considerations and strategies that may affect adherence among AYA with HIV are highlighted below in **Table 12.**

Table 12. Antiretroviral Therapy–Specific Strategies to Improve Medication Adherence

Antiretroviral Therapy-Specific Strategies to Improve Medication Adherence	
Regimen selection	• Simple ART regimens (e.g., fixed-dose, once daily combinations) with high barriers to resistance are preferable, if possible.[32] • Minimal side effects (e.g., gastrointestinal)
Treatment plan	• Develop the plan in partnership with AYA with HIV, considering daily schedule; tolerance of pill number, size, and frequency; issues affecting absorption; and potential adverse effects and interactions with other medications.[31,33] • Design adolescent-friendly reminder systems[34] (e.g., apps, cell phone reminders, pill boxes) for adherence support.[35]
Motivators	• Emphasize personal benefits (e.g., viral suppression, improved health). • Undetectable equals untransmittable (U=U) status disclosure to sexual partners without HIV may act as a particularly strong motivator for reducing stigma and improving adherence among AYA with HIV.

Antiretroviral Therapy Regimens for Adolescents and Young Adults With HIV Without Drug Resistance

The boosted protease inhibitor (PI) darunavir (DRV) and the integrase strand transfer inhibitors (INSTIs) dolutegravir (DTG) and bictegravir (BIC) offer once-daily dosing. When coformulated with a dual nucleoside backbone, they also provide single-tablet regimens with high genetic barriers to resistance.

Clinical trials have demonstrated the superiority of DTG over boosted PI-based regimens. BIC coformulated with tenofovir (TAF) and emtricitabine (FTC) also appears to have a low risk of treatment-emergent resistance and is available as a single-tablet regimen with a small pill size and no food requirements. BIC is currently licensed for use in children or adolescents ≥25kg. Adolescent studies are ongoing with an adult fixed-dose combination of BIC/FTC/TAF from 12 years of age and 35 kg with a favorable interim analysis in a stable adolescent switch study.[36]

A two-drug once-daily single-tablet regimen of DTG/lamivudine is recommended as an initial ART regimen except for individuals with HIV RNA >500,000 copies/mL, hepatitis B virus (HBV) coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.

Long-acting formulation regimens, the first of which (cabotegravir/rilpivirine) was recently FDA-approved in the United States, are considered a viable option for patients who are engaged in care, virologically suppressed on oral therapy, and agreeable to the administration schedule. These agents are being studied for AYA with HIV[37] ages 12 to 17 without relevant antiretroviral drug resistance. Case reports of viral suppression with the use of long-acting rilpivirine (RPV) and cabotegravir (CAB)[38] in AYA with HIV with a history of poor adherence are encouraging (see Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression). Studies to evaluate these modalities among nonadherent AYA with HIV are under development.[39]

Antiretroviral Therapy–Experienced Adolescents and Young Adults With HIV and Drug Resistance

AYA with HIV who acquired HIV early in life often have treatment challenges associated with the long-term use of ART that mirrors those of ART-experienced adults, such as extensive resistance, complex regimens, and adverse drug effects. In ART-experienced adolescents, DTG was safe and well tolerated, and it achieved viral suppression rates of 44% to 66% when combined with an optimized background regimen. Acquired treatment-emergent INSTI resistance may occur.[40] For adolescents with dual-class resistance, the introduction of DRV/cobicistat/FTC/TAF in combination with DTG offers the potential of a potent triple-class regimen with a high genetic barrier to resistance with only two pills once daily[41] (see Virologic Failure and Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression).

Antiretroviral Therapy Considerations in Sexually Immature Adolescents and Young Adults With HIV

The physiologic changes (e.g., puberty, rapid growth) that occur in adolescence may result in altered pharmacokinetics. Therefore, although generally it is appropriate for postpubertal adolescents to be dosed with ARV drugs according to adult guidelines, adolescents in early puberty should be dosed according to the Pediatric Guidelines, which factor in dosages by weight and sexual maturity ratings.

Additional Antiretroviral Therapy Considerations in Adolescents and Young Adults With HIV

Additional considerations include an increased risk of side effects, such as bone and renal toxicity with tenofovir-based drugs in the rapidly growing adolescent. These concerns are magnified in low-weight adolescents for whom appropriate lower-dose formulations are not available. Because AYA with HIV have not yet reached peak bone mass, TAF generally should be used instead of TDF, because of a greater bone loss with the latter ARV.

For a more detailed discussion on ART therapy in AYA with HIV, please see the What to Start section and the Pediatric Guidelines. For additional information on treatment adherence in AYA with HIV, please see Table 18, Adherence to the Continuum of Care, and the Pediatric Guidelines.

Preventive Measures and Supporting Long-Term Health in Adolescents and Young Adults With HIV

People with HIV are at an increased risk of HIV- and ART-related comorbidities, including cardiovascular disease, diabetes, metabolic syndrome, osteoporosis, and neurocognitive impairment. When HIV is acquired at birth or early in life, an individual can live for many decades with the condition. However, engagement in health-risk behaviors (e.g., tobacco smoking, alcohol and drug use, unhealthy diet, physical inactivity) may have greater long-term implications for clinical outcomes in this population.

Preventive health care and promotion of positive health behavior during the critical time of adolescence and young adulthood can shape future habits and clinical outcomes over a lifetime. Incorporating regular screening, preventive health care, and health education is critical for optimizing short- and long-term physical and mental well-being and should be considered part of routine HIV treatment. Careful attention should be paid to modifiable risk factors in these early decades, such as weight gain and obesity, dyslipidemia, vitamin D deficiency, and tobacco use. Aggressive screening and risk factor mitigation early in the life of AYA with HIV not only improves current health but also can decrease their risk of developing comorbidities later in life. See HIV Medicine Association of the Infectious Diseases Society of America HIV primary care guidance for more details.

Transitioning to Adult HIV Care

Given lifelong infection with HIV and the need for treatment throughout the life course, HIV care programs and providers need flexibility to transition care appropriately for AYA with HIV. A successful transition requires an awareness of fundamental differences between many adolescent and adult HIV care models.

In most adolescent HIV clinics, care is more teen-centered and multidisciplinary, with primary care highly integrated into HIV care.[42] Often there is anonymity, with clinics not being devoted specifically to HIV or infectious diseases. Moreover, such services as sexual and reproductive health and mental health care are often found in one clinic setting (i.e., the medical home). Additionally, these clinics are more likely to be “youth-friendly” by including such aspects as waiting areas where AYA with HIV can access computers and other items that may facilitate engagement; flexible schedules that include evening hours or walk-ins; technology like social media and texting to engage patients; staff who are trained specifically in the unique cognitive, developmental, and other psychosocial aspects of AYA with HIV; and lower patient-to-provider ratios. In contrast, some adult HIV clinics may be more HIV-specific and rely more on referral of the patient to separate subspecialty care settings, such as gynecology.[43] Furthermore, adult clinic settings tend to be larger and can easily intimidate younger, less motivated patients.

Transitioning the care of an AYA with HIV must consider such factors as medical insurance; degree of independence, autonomy, and decision-making capacity; patient confidentiality; and informed consent. Nonetheless, given the structural limitations (adolescent clinics not being able to see patients over a certain age), care transitions must occur, usually between the ages of 21 and 25. The period of transition is a highly vulnerable time for attrition from HIV care. Data on transition outcomes are emerging, showing variable rates of successful transition to adult care ranging between 50% and 85%.[44-47]

It is important to recognize that the transition for AYA with HIV with early-acquired HIV versus those who acquired HIV later in life may pose distinct challenges. AYA with HIV who acquired HIV early in life—who often have experienced significant instability and prior loss—may experience the transition to adult HIV care as yet another traumatizing event. Alternatively, those who acquired HIV later in life, given their more recent engagement in the medical system, may be less likely to be effectively engaged in pediatric and adolescent care, which may affect their ability to transition successfully. Factors to date that have been associated with successful transition for those with early-acquired HIV include high self-management and perceived emotional and social support.[48]

To maximize the likelihood of a successful transition, interventions to facilitate transition are best implemented early on.[46,49-51] Strategies and approaches for both the adult and pediatric and adolescent programs are discussed below:

Table 13. Approaches to Optimize Care Transition for AYA With HIV

Pediatric/Adolescent	Adult
Personnel	
• Engage a multidisciplinary team knowledgeable about medical and psychosocial issues of AYA with HIV, including the challenges of transitioning youth to adult care settings. • Utilize combined internal medicine and pediatrics-trained providers if available. • Assign a transition point person and have their contact information readily available. • Educate HIV care teams and staff about transitioning AYA with HIV and their needs.	• Engage a multidisciplinary adult care team knowledgeable about medical and psychosocial issues of AYA with HIV, including the challenges of transitioning youth to adult care settings. • Utilize combined internal medicine and pediatrics providers if available. • Assign a transition point person and have their contact information readily available. • Identify outreach specialists, navigators, social workers, case managers, and providers with a youth-friendly approach. • Educate clinic personnel about AYA with HIV and their challenges to enhance sensitivity and understanding and minimize stigma.
Education and Preparation of AYA With HIV	
• Enhance AYA with HIV health literacy, including understanding of HIV and their medical history. • Address patient and family resistance to transition of care caused by lack of information, concerns about stigma or risk of disclosure, and differences in practice styles. • Help youth develop life skills, including, but not limited to, counseling on appropriate use of a primary care provider and how to manage appointments; the importance of prompt symptom recognition and reporting; and self-efficacy in managing medications, insurance, and assistance benefits.	• Meet AYA with HIV before transition, if possible. • Clearly outline policies and expectations before and during the first visit. • Have an orientation plan to acquaint newly transitioned AYA with HIV to the clinic environment and adult clinical care program. • Implement interventions that may improve outcomes, such as patient navigators, peer support groups, mental health assessment, and inclusion of parents and guardians where available. • Address health literacy and ensure AYA with HIV understand HIV, goals of care, etc.

Table 13. Approaches to Optimize Care Transition for AYA With HIV

Pediatric/Adolescent	Adult
	• Continue to work with AYA with HIV toward developing life skills, etc.
Strategies and Approaches	
• Identify adult care providers able to provide youth-friendly care for adolescents and young adults. • Develop a formal, purposeful individualized transition plan to address comprehensive care needs, including medical, psychosocial, and financial aspects of transitioning to adult HIV care. • Optimize provider communication between adolescent and adult clinics, including a warm multidisciplinary, comprehensive medical history hand-off that includes prior regimens and outcomes (e.g., adherence, virologic failure and resistance).	• Develop a realistic clinic model based on specific needs (e.g., simultaneous transition of mental health and/or case management versus a gradual phase-in) and staffing. • Engage in a warm handoff from the pediatric team, which allows the accepting adult team to learn about and understand the multidisciplinary challenges and goals for the patient. Devise a plan for how to continue building the skills on the adult side. • Build in flexibility (e.g., permissive grace period for appointments, leniency for missed appointments, particularly when first transitioning). • Incorporate other aspects of care beyond HIV management, if possible (e.g., family planning, sexually transmitted infection testing and treatment, mental health, substance use).
Communication	
• Foster regular dialogue between pediatric and adolescent and adult teams before and after transition through regular meetings, case conferences, etc. • Solicit feedback from the AYA with HIV • Use technology (e.g., texting, HIPAA-compliant messaging apps, telemedicine).	
Evaluation	
• Implement ongoing evaluation to measure the success of the selected model (retention in adult care).	

Discussions regarding transition should begin early and before the actual transition process.[52] Attention to the key interventions noted above will be likely to improve adherence to appointments and avoid the potential for youth to fall through the cracks, as this concept is referred to commonly in adolescent medicine. For a more detailed discussion on specific topics related to transitioning care for adolescents and young adults, see Transitioning into Adult HIV Care. Please also refer to the Pediatric Guidelines.

Table 14. AYA With HIV ARV Adherence Barriers and Strategies to Support Adherence

ART Adherence Barrier	Adherence Support Strategy	Rationale for Adherence Support Strategy
Prioritization of short-term goals and socialization with peers over daily HIV treatment adherence	Youth-friendly reminder systems (e.g., text, phone, apps)	• Daily adherence to ARV regimens may not take priority in the lives of AYA with HIV. • AYA with HIV benefit from reminder systems to facilitate adherence.
	Novel ART delivery strategies (e.g., long-acting oral or injectable ARVs)	• AYA with HIV show interest in long-acting alternatives for ART delivery. • Long-acting ARVs are a promising tool to facilitate adherence, once approved for AYA with HIV.
Social concerns related to loss of confidentiality	Simple ARV regimens	• Adolescents do not want to be different from peers; adherence to complex regimens is particularly challenging. • Simple ARV regimens are preferable for AYA with HIV.
	User-friendly and discreet regimens	• Avoidance of HIV-related stigma and of unintentional disclosure of HIV status is a priority for AYA with HIV. • Protect confidentiality with user-friendly and discreet adherence supports (e.g., discreet pill bottles, reminder systems, etc.).
Side effects/fear of side effects	ARV regimens that minimize side effects	• Side effects are associated with nonadherence to ARVs. • Regimens with minimal side effects and medications that manage side effects have utility for AYA with HIV.
Denial or dismissal of HIV diagnosis	Motivational interviewing (MI) and motivational enhancement therapy (MET)	• MI and MET acknowledge AYA with HIV's autonomy and potential ambivalence about treatment adherence. • MI and MET have shown promise for improving adherence to chronic disease treatment, including HIV.
	Positive affirmation messages (e.g., text, app)	• Electronically delivered positive affirmation messages can improve self-esteem and ARV adherence among AYA with HIV.
Lack of health literacy regarding the benefits of ART	Health literacy support and U=U education	• AYA with HIV may not fully understand the importance of taking ARVs daily, particularly when they are asymptomatic. • Increased health literacy is associated with better adherence to ARV regimens. • U=U education holds promise for AYA with HIV.

Table 14. AYA With HIV ARV Adherence Barriers and Strategies to Support Adherence

ART Adherence Barrier	Adherence Support Strategy	Rationale for Adherence Support Strategy
Mistrust of providers and the medical establishment	Empathetic and patient-centered communication	• Communication exploring the needs of AYA with HIV patients can build trust, including exploring needs not directly related to HIV treatment (e.g., school, employment, relationships, etc.).
Mental health and/or substance use	Individualized mental health and substance use services	• Comprehensive mental health and substance use services have shown promise for improving viral suppression among AYA with HIV. • Service should be delivered based on individualized needs assessments.
	Directly observed therapy may be considered	• For some AYA with HIV with difficult adherence problems, directly observed therapy may be considered.
Lack of familial and social support	Family and peer support groups	• Family members and peers are a defense against stigma and social isolation, source of emotional support, and partners in medication management. • Family and peer support groups have utility for AYA with HIV living with HIV.
Provider views of AYA with HIV as “risky” and/or not ready for ART	Promote development of a positive rather than risk-centered identity among AYA with HIV	• Adolescence and young adulthood are periods of identity development where HIV stigma is particularly problematic. • Providers should not conceptualize AYA with HIV as “high risk” to reduce stigma and improve ARV adherence.
Provider implicit biases of AYA with HIV	Implicit bias training	• Consciously changing biased associations and repeated bias self-regulation training can reduce providers’ implicit biases.
Lack of youth-friendly services	Dedicated youth HIV clinic	• Clinic days or hours dedicated to AYA with HIV patients better address unique adherence needs; youth-friendly services include the following: ○ flexible hours, easy scheduling, telephone/telehealth appointments; ○ providers trained in working with AYA with HIV; ○ youth-friendly waiting rooms and physical spaces; ○ supplemental services that comprehensively address psychosocial and health needs of AYA with HIV; and ○ incentives for AYA with HIV care engagement.

Table 14. AYA With HIV ARV Adherence Barriers and Strategies to Support Adherence

ART Adherence Barrier	Adherence Support Strategy	Rationale for Adherence Support Strategy
	Youth-friendly hours, staff, and physical space	• Where dedicated hours and services are not possible, youth-friendly service elements can be integrated into existing clinic structures, e.g.: ○ offering evening hours; ○ staff training on service delivery to AYA with HIV; and ○ youth-friendly waiting rooms and physical spaces.
	Referrals to more youth-friendly HIV providers	• Where youth-friendly services are not possible, referrals to more youth-friendly HIV care providers should be considered. • Referral decisions should be made collaboratively with the patient.
Lack of comprehensive services that address common psychosocial stressors	Supplemental health, behavioral health, and psychosocial support services	• Individualized delivery of comprehensive supplemental services helps address unique needs of AYA with HIV, including the following: ○ primary care and sexual and reproductive health services; ○ behavioral health services; and ○ psychosocial support services (e.g., school support, transportation, support groups, housing and food assistance).
	Collaboration with and referrals to outside support services	• Where delivery of comprehensive supplemental services is not possible, collaborations with and referrals to outside support services should be considered.

Key: ART = antiretroviral treatment; ARV = antiretroviral; AYA = adolescent and young adult; U=U = undetectable equals untransmittable

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Early (Acute and Recent) HIV Infection

Updated: September 12, 2024
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Panel's Recommendations

• Antiretroviral therapy (ART) is recommended for all people with HIV, including those with early[a] HIV infection **(AI).** ART should be initiated as soon as possible after HIV diagnosis **(AII).**
• The goals of ART are to suppress plasma HIV RNA to undetectable levels **(AI),** prevent transmission of HIV **(AI),** and preserve immune function **(AIII).** Monitoring of plasma HIV RNA levels, CD4 T lymphocyte cell counts, and antiretroviral (ARV) drug-related adverse effects should be done as recommended for people with chronic HIV infection **(AII).**
• A blood sample for genotypic resistance testing should be sent to the laboratory before initiating ART **(AIII).**
  ○ Standard genotypic drug-resistance testing should be performed for mutations in the reverse transcriptase and protease genes **(AIII)** for all people with early HIV.
  ○ Genotype testing for integrase strand transfer inhibitor (INSTI) resistance should be performed for those who acquire HIV during or after the use of long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP), if transmitted integrase stand transfer inhibitor (INSTI) resistance is suspected, or if HIV diagnosis occurs after receiving an INSTI-based regimen for post-exposure prophylaxis (PEP) **(AIII).**
• ART can be initiated before drug-resistance test results are available.
  ○ For those without a history of using CAB-LA as PrEP, one of the following ARV regimens is recommended[b] **(AIII):**
  ▪ Bictegravir (BIC)/tenofovir alafenamide (TAF)/emtricitabine (FTC)
  ▪ Dolutegravir (DTG) with (TAF or tenofovir disoproxil fumarate [TDF])[c] plus (FTC or lamivudine [3TC])
  ○ For those with a history of CAB-LA use as PrEP, genotype testing before starting ART should include screening for INSTI-resistance mutations **(AIII).**
  ▪ A regimen of cobicistat- (COBI)[d] or ritonavir-boosted darunavir (DRV) with (TAF or TDF)[b] plus (FTC or 3TC) is recommended while awaiting the results of the genotype testing **(AIII).**
  ▪ Use of an empiric INSTI-containing regimen is not recommended unless genotype testing shows no evidence of INSTI resistance **(AIII).** This is because INSTI resistance may be present in those who acquire HIV during and possibly after the use of CAB-LA as PrEP.
• In people with HIV RNA levels ≥200 copies/mL and who are taking PrEP, immediate initiation of an effective HIV treatment regimen is recommended while awaiting confirmation of HIV diagnosis **(AIII).**
• Pregnancy testing should be performed in women of childbearing potential before initiating ART **(AIII).**
• When the results of drug-resistance tests are available, the treatment regimen can be modified if needed **(AII).**
• Providers should inform individuals starting ART of the importance of adherence in achieving and maintaining viral suppression **(AIII).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed non-randomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

[a] Early infection represents either acute or recent (≤6 months) infection.

[b] Because of the low rates of transmitted INSTI resistance in the United States at present, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started while awaiting the results of the INSTI genotype.

[c] TAF and TDF are two forms of tenofovir that are approved in the United States. TAF has fewer bone and kidney toxicities than TDF, whereas TDF is associated with lower lipid levels. Safety, cost, and accessibility are among the factors to consider when choosing between these drugs.

[d] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters.

Introduction

Acute HIV infection occurs soon after transmission and is typically characterized by the lack of anti-HIV antibodies and the presence of viremia, which can be detected by an HIV RNA test or p24 antigen test. Recent HIV infection is considered the period of ≤6 months after infection during which anti-HIV antibodies become detectable. Throughout this section, the term "early HIV infection" is used to refer to either acute or recent HIV infection. People with acute HIV infection may experience fever, lymphadenopathy, pharyngitis, skin rash, myalgia, arthralgia, and other symptoms; however, illness is generally nonspecific, and people can be asymptomatic or experience relatively mild symptoms.[1-6] Clinicians may fail to recognize acute HIV infection because its manifestations are similar to those of many other viral infections, such as COVID-19, influenza, and infectious mononucleosis. Table 15 below provides clinicians with guidance to recognize, diagnose, and manage acute HIV infection.

Diagnosing Acute HIV Infection

Health care providers should consider a diagnosis of acute HIV infection in a person who has a suggestive clinical syndrome or in asymptomatic individuals who report recent engagement in activities that may put them at high risk of HIV acquisition (see Table 15 below).[7] Individuals may not always disclose high-risk activities or perceive that such activities put them at risk for HIV acquisition. Thus, even in the absence of reported high-risk activities, health care providers should have a low threshold for considering a diagnosis of acute HIV infection. Health care visits to emergency departments provide an opportunity for health care providers to screen for acute or established HIV infection, as well as other sexually transmitted infections. Since 2019, the United States Preventive Services Task Force has recommended routine screening for HIV in adolescents and adults aged 15 to 65 years (Grade A recommendation). Testing of remnant blood specimens from an emergency department identified acute HIV infection in approximately 5 of 499 (1%) people presenting with flu-like symptoms.[8] Acute HIV infection was also diagnosed in 7 of 563 (1.2%) people presenting for evaluation of possible mononucleosis with negative heterophile antibody tests.[9] A study of HIV screening in nine emergency departments in six U.S. cities found that a new HIV diagnosis was made in 0.4% of 214,524 adolescents and adults, of whom 14.5% had acute HIV infection.[10] Current statistics on the prevalence of HIV in geographical areas in the United States can be found on the AIDSVu and Centers for Disease Control and Prevention (CDC) AtlasPlus websites.

The recommended initial laboratory HIV testing algorithm includes combination immunoassays that detect HIV-1 and HIV-2 antibodies, as well as HIV p24 antigen (Ag/Ab assays),[11] primarily due to their enhanced ability to detect acute HIV infection. Specimens that are reactive on an initial Ag/Ab assay should be tested with an immunoassay that differentiates HIV-1 from HIV-2 antibodies. Specimens that are reactive on the initial assay and have either a negative or indeterminate antibody differentiation test result should be tested for quantitative or qualitative HIV RNA; an undetectable HIV RNA test result indicates that the original Ag/Ab test result was a false positive. Detection of HIV RNA in this setting indicates that acute HIV infection is highly likely.[11] People presenting to care during the earliest days following HIV infection may have yet to develop a positive p24 Ag response, which typically occurs with viral load levels of >20,000 to 30,000 copies/mL. In clinical settings with a

high probability of infection, quantitative or qualitative HIV RNA testing should be considered even if the HIV Ag/Ab test result is negative. HIV infection should be confirmed by repeat quantitative HIV RNA testing or subsequent testing to document HIV antibody seroconversion. People who receive antiretroviral therapy (ART) during acute or very early HIV infection may demonstrate weaker reactivity to screening antibody assays or incomplete HIV antibody evolution; may remain non-reactive to confirmatory antibody assays; and in the setting of sustained virologic suppression, may have complete or partial seroreversion.[12-16]

Providers should be aware that even a low-positive quantitative HIV RNA level (e.g., <200 copies/mL but detectable) in the setting of a negative or indeterminate antibody test result is consistent with acute HIV infection. When a low-positive quantitative HIV RNA test result is present at this level, the HIV RNA test should be repeated on a new blood specimen to confirm the diagnosis. Repeated false-positive HIV RNA test results are unlikely.[2] HIV RNA levels in acute infection are generally very high (e.g., >100,000 copies/mL)[1,2,4]; however, levels may be <200 copies/mL in the earliest weeks following infection as viral load continues to rise. In rare cases, however, such low HIV RNA levels also may represent a false-positive result. The previously proposed threshold of <3,000 copies/mL is based on historical data, which used laboratory methods that are now considered obsolete.[17] Improvements in plasma viral load methodology suggest that any positive result on a quantitative plasma HIV RNA test in the setting of a negative or indeterminate antibody test result may be consistent with acute HIV infection. Some health care facilities may still be using HIV testing algorithms that test only for anti-HIV antibodies. In such settings, when acute HIV infection is suspected in a person with a negative or indeterminate HIV antibody test result, a quantitative or qualitative HIV RNA test should be performed. A negative or indeterminate HIV antibody test result and a positive HIV RNA test result (<200 copies/mL)[18] indicate that acute HIV infection is highly likely.

Diagnosing Acute HIV Infection in People Taking Pre-Exposure Prophylaxis

Three antiretroviral (ARV) options—oral emtricitabine (FTC) with either tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF) and intramuscular long-acting cabotegravir (CAB-LA)—are now available for HIV pre-exposure prophylaxis (PrEP). People who acquire HIV while taking PrEP may sometimes have ambiguous HIV test results. A positive HIV Ag/Ab test result or a positive HIV RNA test result in the setting of a negative HIV antibody test result should prompt immediate confirmation of HIV diagnosis. It is important to collect a new blood specimen to verify the HIV diagnosis before initiating ART. Important considerations include the following:

- In people with HIV RNA level ≥200 copies/mL who are taking PrEP, immediate initiation of an effective HIV treatment regimen[18] is recommended while awaiting confirmation of HIV diagnosis **(AIII).**
- In people taking PrEP who have a negative HIV antibody test result and a low-positive quantitative HIV RNA test result (<200 copies/mL), a confirmatory HIV antibody test and repeat quantitative plasma HIV RNA test should be performed, and results should be available before initiating ART.
- In rare cases, particularly when PrEP is transitioned to an ARV regimen and HIV RNA and antibody diagnostic testing are inconclusive, HIV DNA testing may be of value.[19] Options for confirming HIV infection and managing such cases are areas of evolving science summarized by the CDC.[19] Clinicians seeking urgent advice can contact the Clinical Consultation Center's PrEP Service at 1-855-HIV-PREP (or 1-855-448-7737).

Acute HIV Infection in People Taking Long-Acting Cabotegravir for Pre-Exposure Prophylaxis

In the HPTN 083 trial, a pivotal trial of CAB-LA versus TDF/FTC for HIV PrEP with more than 2,000 participants enrolled in each arm, 25 incident cases of HIV were identified in the CAB-LA arm compared to 72 cases in the TDF/FTC arm.[20,21] Selection of a potent ARV regimen in people who develop acute HIV infection while taking CAB-LA for PrEP should consider that injectable cabotegravir (CAB) may remain detectable after treatment discontinuation, for up to 3 years in men and 4 years in women.[22] This long pharmacokinetic tail may contribute to the selection of drug-resistant variants in the setting of incident infection. In an extended analysis of HPTN 083, 34 cases of HIV infection were reported in the CAB-LA arm, with 6 of these cases occurring despite on-time CAB-LA injections.[23,24] Detection of HIV infection was delayed in 15 of 32 cases and was associated with waxing and waning HIV Ag/Ab, HIV antibody, and qualitative and quantitative HIV RNA test results (i.e., fluctuating between reactive/non-reactive, detectable/non-detectable).[23] Major resistance to an integrase strand transfer inhibitor (INSTI) occurred in 10 of the 32 cases evaluated. All 10 participants with INSTI resistance in the CAB-LA arm received their last CAB dose within 6 months of their initial HIV-positive site visit. While the risk of acquired INSTI resistance appears to wane after 6 months, this trend is based on few observations. These data reinforce the importance of screening for INSTI-resistance mutations when acute HIV infection is diagnosed in people taking CAB-LA or with a history of prior CAB-LA PrEP use **(AIII).**

Treating Early HIV Infection

The goals of ART during early HIV infection are to suppress plasma HIV RNA to undetectable levels **(AI),** prevent the transmission of HIV **(AI),** and preserve immune function **(AIII).**[25-27] Importantly, as with chronic HIV infection, an individual's barriers to ART adherence and appointments should be assessed at the time of ART initiation (see Adherence to the Continuum of Care). ART should be initiated as soon as possible after a positive qualitative or quantitative HIV RNA test result **(AII).** Same-day or rapid ART initiation in people with acute HIV has been shown to be safe, acceptable, and effective.[28] It is important to collect a new blood specimen for a confirmatory HIV antibody test and quantitative plasma HIV RNA test to verify the HIV diagnosis. Given the sensitivity of current HIV RNA assays,[29] a positive result by quantitative or qualitative plasma HIV RNA testing in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. HIV treatment does not need to be delayed while awaiting confirmation of HIV diagnosis. Some individuals may not accept their diagnosis or may decline ART initially for other reasons. Individuals who do not begin ART immediately should be maintained in care, and every effort should be made to initiate therapy as soon as they are ready.

Clinical trial data indicate that individuals who are treated during early HIV infection may experience immunologic and virologic benefits.[26,30-41] In addition, early HIV infection is considered a period of high infectivity,[42] and early ART substantially reduces the risk of HIV transmission.[43-46]

Drug-Resistance Testing in the Setting of Early HIV Infection

Prior to the widespread use of INSTIs, data from the United States and Europe demonstrated that transmitted virus strains with resistance to at least one ARV drug were present in up to 16% of people with HIV.[47,48] In one study, 21% of isolates from people with acute HIV infection demonstrated resistance to at least one ARV drug, most commonly non-nucleoside reverse transcriptase inhibitors (NNRTIs).[49-51] The rate of transmitted INSTI resistance was reported to be ≤2.5% of the samples tested, and <0.5% with second-generation INSTIs.[52-55] Before initiating ART in a person with early HIV infection, a blood specimen should be sent for standard genotypic drug-resistance testing for mutations in the reverse transcriptase and protease genes **(AIII).** Genotype

testing for INSTI resistance should be performed for those who acquire HIV during or after the use of CAB-LA as PrEP, if transmitted INSTI resistance is suspected, or if HIV diagnosis occurs after receiving an INSTI-based regimen for post-exposure prophylaxis (PEP) **(AIII).**[22]

Treatment should not be delayed pending resistance-test results. The test results should be used to modify the ARV regimen if necessary **(AII).** In people with no history of CAB-LA use or use of an INSTI-based regimen for PEP, the Panel on Antiretroviral Guidelines for Adults and Adolescents does not currently recommend genotype testing for INSTI resistance given the low rate of transmitted INSTI resistance and the high barrier to resistance of bictegravir (BIC) and dolutegravir (DTG), unless transmitted INSTI resistance is a concern **(AIII).**

Considerations for Preventing HIV Transmission During Early HIV Infection

People with early HIV infection have a higher likelihood of sexual transmission of HIV to others. Prompt initiation of ART and sustained viral suppression to <200 copies/mL can prevent transmission of HIV to sexual partners. Individuals starting ART should use another form of prevention (e.g., condoms, PrEP for partners who are HIV negative, sexual abstinence) for at least the first 6 months of treatment and until they have a documented viral load of <200 copies/mL **(AII).** Many experts would recommend confirming sustained viral suppression before assuming no risk of sexual transmission of HIV **(AIII)** (see Antiretroviral Therapy to Prevent Sexual Transmission of HIV).

Antiretroviral Regimens for Early HIV Infection

ART should be initiated with one of the combination regimens recommended for people with chronic HIV infection **(AIII)** (see What to Start). Providers should inform individuals starting ART of the importance of adherence in achieving and maintaining viral suppression **(AIII).** If available, the results of ARV drug-resistance testing or the resistance pattern of the source person's virus should be used to guide selection of the regimen. All women of childbearing potential should undergo a pregnancy test before initiating ART **(AIII).**

For individuals who have not received CAB-LA as PrEP prior to diagnosis of acute HIV, one of the following INSTI-based regimens is recommended **(AIII):**

- BIC/TAF/FTC
- DTG with (TDF or TAF) plus (3TC or FTC)

DTG and BIC are good treatment options because transmitted resistance to second-generation INSTIs in the United States is rare at present and both BIC and DTG have a high barrier to resistance.

For individuals who acquire HIV during and after the use of CAB-LA as PrEP:

- While awaiting integrase genotype results, the use of an INSTI-based regimen **is not recommended (AIII).** The recommended regimen, until resistance testing confirms the absence of INSTI-resistance mutations, is a cobicistat (COBI)- or ritonavir (RTV)-boosted darunavir (DRV) with (TAF or TDF) plus (FTC or 3TC) **(AIII).**

A pharmacologically boosted protease inhibitor (PI)–based regimen (e.g., boosted DRV) is an option because resistance to PIs emerges slowly, and clinically significant transmitted resistance to PIs is uncommon. Therefore, boosted DRV plus (TAF or TDF) plus (FTC or 3TC) is generally recommended in this setting. Baseline laboratory testing recommended for individuals with chronic

HIV infection should be performed (see Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy). Individuals with hepatitis B virus/HIV coinfection should receive TDF/FTC or TAF/FTC as part of their ARV regimen.

Given the increasing use of TDF/FTC[56-58] and TAF/FTC as PrEP,[59,60] early HIV infection may be diagnosed in some people while they are taking TDF/FTC or TAF/FTC. In this setting, drug-resistance test results are particularly important; however, these regimens remain reasonable treatment options pending drug-resistance test results.

Abacavir/3TC **is not recommended** for treatment of acute HIV infection unless the person is known to be HLA-B*5701-negative, and this information is rarely available in people with acute HIV infection. Additionally, due to relatively high rates of transmitted drug resistance for NNRTIs, agents in this drug class **are not recommended** as a component in the regimen of people initiating ART before the results of drug-resistance tests are available.

Treatment Regimens for Early HIV Infection During Pregnancy

All women of childbearing potential who receive a diagnosis of early HIV infection should have a pregnancy test **(AIII).** Because early HIV infection, especially in the setting of high-level viremia, is associated with a high risk of perinatal transmission, all pregnant women with HIV should start combination ART as soon as possible to prevent perinatal transmission **(AI).** COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters. For more information on the safety and efficacy of ARV use in pregnancy, refer to the Perinatal Guidelines.

Follow-Up After Antiretroviral Therapy Initiation

After ART initiation, monitoring of plasma HIV RNA levels, CD4 T lymphocyte cell counts, and adverse effects should be performed as described in Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy (i.e., HIV RNA testing 2–8 weeks after ART initiation, then every 4–8 weeks until viral suppression and every 3–4 months thereafter) **(AII).**

Table 15. Identifying, Diagnosing, and Treating Acute and Recent HIV Infection

Suspicion of Acute HIV Infection

- Health care providers should consider the possibility of acute HIV infection in people with the signs, symptoms, or laboratory findings described below and in asymptomatic people with a possible acute (within 2–6 weeks) exposure to HIV.[a]
  - Signs, symptoms, or laboratory findings of acute HIV infection may include but are not limited to, one or more of the following: fever, lymphadenopathy, skin rash, myalgia, arthralgia, headache, diarrhea, pharyngitis, oral ulcers, leucopenia, thrombocytopenia, and transaminase elevation.
  - High-risk exposures include sexual contact with someone who has HIV or is at risk of HIV infection, sharing needles, syringes, or equipment for drug preparation or injection, or any situation where a person's mucous membranes or broken skin come into contact with bodily fluids that may carry HIV.

Differential Diagnosis

- The differential diagnosis of acute HIV infection may include but is not limited to, viral illnesses such as COVID-19, EBV and non-EBV (e.g., CMV) infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, or syphilis. Diagnosis of any STI should prompt HIV testing and consideration of acute HIV infection.

Testing to Diagnose or Confirm Acute HIV Infection

- Acute HIV infection is defined as detectable HIV RNA or p24 antigen (the specific antigen used in currently available HIV-1/2 Ag/Ab combination assays) in the setting of a negative or indeterminate HIV antibody test result.
- A reactive HIV antibody test result or Ag/Ab combination test result must be followed by supplemental confirmatory testing.
- A negative or indeterminate HIV antibody test result in a person with a reactive Ag/Ab test result or in whom acute HIV infection is suspected requires plasma HIV RNA testing to diagnose acute HIV infection.
- A positive result on a quantitative or qualitative plasma HIV RNA test in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. In this case, the diagnosis of HIV infection should be confirmed by subsequent documentation of HIV antibody seroconversion.
- A positive HIV Ag/Ab test result or a positive HIV RNA test result in the setting of a negative HIV antibody test result in a person taking PrEP should prompt immediate confirmation of HIV diagnosis. It is important to collect a new blood specimen to verify the HIV diagnosis before initiating HIV treatment.

Antiretroviral Therapy After Diagnosis of Early HIV Infection

- ART is recommended for all people with HIV, including those with early HIV infection **(AI).** ART should be initiated as soon as possible after HIV diagnosis **(AII).**
- Once initiated, the goals of ART are to achieve sustained plasma virologic suppression, prevent HIV transmission **(AII),** and preserve immune function **(AIII).**
- All women of childbearing potential who receive a diagnosis of early HIV infection should have a pregnancy test **(AIII).**
- Pregnant women with early HIV infection should begin ART as soon as possible for their own health and to prevent perinatal transmission of HIV **(AI).**

Table 15. Identifying, Diagnosing, and Treating Acute and Recent HIV Infection

- A blood sample for genotypic drug-resistance testing should be obtained before initiating ART to guide the selection of the regimen **(AIII),** but ART should be initiated as soon as possible, often before resistance-test results are available. If resistance is subsequently identified, treatment should be modified as needed.
- Standard genotypic drug-resistance testing should be performed for mutations in the reverse transcriptase and protease genes **(AIII)** for all people with early HIV**.** Genotype testing for INSTI resistance should be performed for those who acquire HIV during or after the use of CAB-LA as PrEP, if transmitted INSTI resistance is suspected, or if HIV diagnosis is made after receiving an INSTI-based regimen for PEP **(AIII).**
- ART can be initiated before the results of drug-resistance testing are known. For individuals who do not have a history of using CAB-LA as PrEP, one of the following ARV regimens is recommended **(AIII):**
  - BIC/TAF/FTC **(AIII);** or
  - DTG with (TAF or TDF)[b] plus (FTC or 3TC) **(AIII)**
- For individuals with a history of using CAB-LA as PrEP, genotypic resistance testing performed before starting ART should include screening for INSTI-resistance mutations **(AIII).** Recommended regimens include the following:
  - (DRV/c[c] or DRV/r) with (TAF or TDF)[b] plus (FTC or 3TC)—pending the results of the genotype **(AIII).** Empiric INSTI-containing regimens **are not recommended (AIII),** because INSTI resistance may be present in those who acquire HIV during the use of CAB-LA and possibly up to 4 years after.

[a] In some settings, activities that increase the risk of HIV infection may not be recognized or perceived as risky by the health care provider, the person at risk, or both. Thus, even in the absence of reported high-risk activities, symptoms and signs consistent with acute retroviral syndrome should motivate health care providers to consider a diagnosis of acute HIV infection.

[b] TAF and TDF are two forms of tenofovir that are approved in the United States. TAF has fewer bone and kidney toxicities than TDF, whereas TDF is associated with lower lipid levels. Safety, cost, and accessibility are among the factors to consider when choosing between these drugs.

[c] COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters.

Key: 3TC = lamivudine; Ag/Ab = antigen/antibody; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CAB-LA = long-acting cabotegravir; CMV = cytomegalovirus; COBI = cobicistat; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EBV = Epstein-Barr virus; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; PEP = post-exposure prophylaxis; PrEP = pre-exposure prophylaxis; STI = sexually transmitted infection; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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HIV-2 Infection

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Key Considerations and Recommendations
• The clinical course of HIV-2 infection is generally characterized by a longer asymptomatic stage, lower plasma viral loads, and lower mortality rate than HIV-1 infection. However, without treatment, the majority of individuals with HIV-2 will progress to AIDS and death. • No randomized controlled trials have addressed when a person with HIV-2 should start antiretroviral therapy (ART) or which regimens are most effective for initial or second-line ART when treating HIV-2; thus, the optimal treatment strategy is not well defined. • Existing data on the treatment of HIV-2, and extrapolation from data on the treatment of HIV-1, suggest that ART should be started at or soon after HIV-2 diagnosis to prevent disease progression and transmission of HIV-2 to others **(AIII).** • Quantitative plasma HIV-2 RNA viral load testing for clinical care is available and should be performed before initiating ART **(AIII).** • For ART-naive patients who have HIV-2 mono-infection or HIV-1/HIV-2 coinfection, antiretroviral (ARV) regimens should include an integrase strand transfer inhibitor (INSTI) plus two nucleoside reverse transcriptase inhibitors (NRTIs) **(AII).** A recommended alternative regimen is a boosted protease inhibitor (PI) that is active against HIV-2 (darunavir or lopinavir) plus two NRTIs **(BII).** • HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors (NNRTIs); therefore, NNRTI-based regimens, including long-acting injectable rilpivirine (given with the INSTI cabotegravir), **are not recommended** for treatment of HIV-2 **(AIII).** • Patients with hepatitis B virus (HBV)/HIV-2 coinfection should be prescribed ART that contains drugs with activity against both HIV-2 and HBV **(AIII).** • HIV-2 RNA, CD4 T lymphocyte (CD4) cell counts, and clinical status should be used to assess treatment response **(AII).** Unlike people with HIV-1, people with HIV-2 should continue to undergo periodic CD4 testing even if their viral loads are persistently suppressed, because disease progression can occur despite an undetectable viral load **(AIII).** • Resistance-associated viral mutations to INSTIs, PIs, or NRTIs may develop in people with HIV-2 while they are on ART. However, no validated HIV-2 genotypic or phenotypic antiretroviral resistance assays are approved for clinical use. • In the event of virologic, immunologic, or clinical failure, a new ARV regimen should be constructed in consultation with an expert in HIV-2 management. • *In vitro* studies demonstrate that HIV-2 is intrinsically resistant to the fusion inhibitor enfuvirtide, and limited data also show that HIV-2 is intrinsically resistant to fostemsavir); therefore, these drugs **are not recommended** for treatment of people with HIV-2 **(AIII).** • For patients with multidrug-resistant virus, ibalizumab and lenacapavir demonstrate *in vitro* potency against HIV-2 and may be considered **(BIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Overview

HIV-2 infection is endemic in West Africa, with certain countries experiencing a population prevalence of >1%. The possibility of HIV-2 infection should be considered when treating people of West African origin, people who have had sexual contact with or shared needles with people of West African origin, and people who reside in countries with strong socioeconomic ties to West Africa (e.g., France, Spain, Portugal, and former Portuguese colonies, such as Brazil, Angola, Mozambique, and parts of India). Globally, it has been estimated that 1 million to 2 million people have HIV-2—a number that includes people with HIV-1/HIV-2 dual infection. However, current and accurate prevalence data are scarce, and neither the Joint United Nations Programme on HIV and AIDS nor the World Health Organization has formal surveillance systems for HIV-2.[1]

Clinical Course of HIV-2 Infection

The clinical course of HIV-2 infection is generally characterized by a longer asymptomatic stage, lower plasma viral loads, and a lower mortality rate than HIV-1 infection.[2,3] However, without effective antiretroviral therapy (ART), HIV-2 infection will progress to AIDS and death in the majority of individuals.[4] Concomitant infection with HIV-1 and HIV-2 may occur, and the possibility of this coinfection should be considered when treating people from areas with a high prevalence of HIV-2.

Diagnostic and Monitoring Assays for HIV-2 Infection

In the appropriate epidemiologic setting, HIV-2 infection should be suspected in people who have clinical conditions that suggest HIV infection but who have atypical serologic results (e.g., a positive screening assay with an indeterminate HIV-1 Western blot).[5] The possibility of HIV-2 infection should also be considered in the appropriate epidemiologic setting in people who have serologically confirmed HIV infection but low or undetectable HIV-1 RNA levels, or in those who have declining CD4 T lymphocyte (CD4) cell counts despite apparent virologic suppression on ART.

The 2014 Centers for Disease Control and Prevention guidelines for HIV diagnostic testing[6] recommend using an HIV-1/HIV-2 antigen/antibody combination immunoassay for initial testing and using an HIV-1/HIV-2 antibody differentiation immunoassay for subsequent testing. The Geenius HIV 1/2 Supplemental Assay (Bio-Rad Laboratories) is approved by the U.S. Food and Drug Administration (FDA) to differentiate HIV-1 infection from HIV-2 infection. The Multispot HIV-1/HIV-2 Rapid Test is no longer available. Commercially available HIV-1 RNA assays do not reliably detect or quantify HIV-2 RNA.[7] Quantitative HIV-2 RNA testing is available at the University of Washington (UW)[8] and the New York State Department of Health (NYSDOH).[9] HIV-2 nucleic acid amplification test–based (total DNA/RNA) diagnostic testing is now commercially available for clinical care.[10,11] However, it is important to note that up to one-third of people with untreated HIV-2 will have HIV-2 RNA levels below the limits of detection (10 copies/mL for UW testing and 7 IU/mL for NYSDOH testing); some of these people will have clinical progression and CD4 count decline. No validated HIV-2 genotypic or phenotypic antiretroviral (ARV) resistance assays are approved by the FDA for clinical use. HIV-2 genotypic ARV resistance assays are available at UW for research use only.

Treatment of HIV-2 Infection

To date, no randomized controlled trials that address when to start ART or the choice of initial or subsequent ART for HIV-2 have been reported[12]; thus, the optimal treatment strategy has not been defined. Existing data on the treatment of HIV-2 and extrapolation from data on the treatment of HIV-1 suggest that ART should be started at or soon after HIV-2 diagnosis to prevent disease

progression and transmission of HIV-2 to others **(AIII).** However, CD4 cell recovery in people with HIV-2 who are on ART is generally poorer than that observed in people with HIV-1.[13,14]

Data from *in vitro* studies suggest that HIV-2 is sensitive to the currently available nucleoside reverse transcriptase inhibitors (NRTIs); however, HIV-2 is more likely to develop resistance to NRTIs than HIV-1.[15] HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors (NNRTIs)[16]; thus, NNRTI-based regimens, including the long-acting injectable rilpivirine (RPV) (given with the integrase strand transfer inhibitor [INSTI] cabotegravir [CAB]), **are not recommended** for treatment of HIV-2 **(AIII).** Several small studies in individuals with HIV-2 have reported poor responses to dual-NRTI regimens[17,18] or regimens that contain an NNRTI plus two NRTIs.[19,20] Clinical data on the effectiveness of triple-NRTI regimens are conflicting.[21,22]

INSTI-based regimens or protease inhibitor (PI)–based regimens are treatment options for people with HIV-2. As discussed below, three single-arm clinical trials showed favorable outcomes in patients who received INSTI-based regimens. Data regarding the efficacy of PI-based regimens primarily come from observational reports. A randomized controlled trial comparing raltegravir (RAL) plus tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) to lopinavir/ritonavir (LPV/r) plus TDF/FTC is completed, but the results have not been reported (FIT-2; NCT02150993).

Integrase Strand Transfer Inhibitor–Based Regimens

All FDA-approved INSTIs—RAL, elvitegravir (EVG), dolutegravir (DTG), bictegravir, and CAB—have potent activity against HIV-2 *in vitro*.[23-28] INSTI-based regimens have shown favorable treatment responses in observational studies.[29-31] Three small, single-arm, open-label clinical trials have assessed the effectiveness of INSTI-based regimens in ART-naive individuals with HIV-2. These studies evaluated RAL plus TDF/FTC, EVG/cobicistat/TDF/FTC, and DTG plus either abacavir/lamivudine or TDF/FTC. All the studies demonstrated favorable clinical and immuno-virologic results at 48 weeks, providing the best evidence to date for HIV-2 treatment recommendations.[32-34]

Protease Inhibitor–Based Regimens

In general, regimens that contain boosted PIs that are active against HIV-2 (and that also include two NRTIs) have resulted in more favorable virologic and immunologic responses than regimens that consist of only two or three NRTIs.[13,14,22,35] Darunavir (DRV), lopinavir (LPV), and saquinavir are more active against HIV-2 than other approved PIs.[36-38] While LPV/r is more active against HIV-2 than DRV *in vitro*, it is less well tolerated. Some clinicians may use boosted DRV (where available) to enhance adherence. Older unboosted PI-based regimens, including nelfinavir or indinavir plus zidovudine and lamivudine, and atazanavir-based regimens have shown poor clinical success rates.[12,17,18,39,40]

Other Antiretroviral Drugs

Among the entry inhibitors, HIV-2 is intrinsically resistant to enfuvirtide.[41] The CCR5 antagonist maraviroc appears to be active against some HIV-2 isolates[42]; however, there are no FDA-approved assays that can determine HIV-2 co-receptor tropism, and HIV-2 is known to use many other minor co-receptors in addition to CCR5 and CXCR4.[43] The post-attachment inhibitor ibalizumab (IBA) has potent *in vitro* activity against HIV-2 isolates.[44] Limited data suggest HIV-2 is intrinsically resistant to the attachment inhibitor fostemsavir (FTR).[45,46]

The capsid inhibitor lenacapavir (LEN) demonstrates nanomolar potency against HIV-2 *in vitro* but is 11- to 25-fold less active against HIV-2 than HIV-1.[47,48]

Some national and international guidelines have recommended specific preferred and alternative drug regimens for initial and second-line ART for HIV-2 infection[49-52]; however, there are currently no comparative randomized controlled clinical trial data that support the effectiveness of a specific recommended regimen.

The Panel's Recommendations

Until more definitive data on outcomes are available, the Panel on Antiretroviral Guidelines for Adults and Adolescents provides the following recommendations for the management of individuals with HIV-2 mono-infection or HIV-1/HIV-2 dual infection:

- A regimen that contains one INSTI plus two NRTIs is the recommended initial ART for most individuals with HIV-2 **(AII).**
- An alternative regimen is a boosted PI (DRV or LPV) that is active against HIV-2 plus two NRTIs **(BII).**
- HIV-2 is intrinsically resistant to NNRTIs; therefore, NNRTI-based regimens, including long-acting injectable RPV (given with the INSTI CAB), **are not recommended** for treatment of HIV-2 **(AIII).**
- HIV-2 demonstrates intrinsic resistance to the fusion inhibitor enfuvirtide *in vitro*, and limited data show intrinsic resistance to FTR; therefore, these drugs **are not recommended** for treatment of people with HIV-2 **(AIII).**
- For people with multidrug-resistant HIV-2, IBA and LEN may be considered based on *in vitro* data **(BIII).**
- Patients with hepatitis B virus (HBV)/HIV-2 coinfection require ART that contains drugs with activity against both HIV-2 and HBV **(AIII).** See Hepatitis B Virus/HIV Coinfection for more information.
- HIV-2 plasma RNA levels, CD4 counts, and clinical status should be monitored to assess treatment response, as is recommended for HIV-1 **(AII).**
- People who have HIV-2 RNA levels that are below the limits of detection before they initiate ART should still undergo routine HIV-2 plasma RNA monitoring in addition to CD4 count and clinical monitoring. Unlike HIV-1, people with HIV-2 require continued CD4 count monitoring, as disease progression can occur in the setting of undetectable HIV-2 viral load **(AIII).**

Women with HIV-2 who are of childbearing potential require similar considerations when choosing a regimen as women of childbearing potential with HIV-1 (see What to Start). There are no data on HIV-2 treatment as prevention; however, both data from studies of people with HIV-1 and data on the natural history of HIV-2 transmission suggest that effective ART likely provides a reduced risk of transmission to sexual partners.[53-55]

Viral mutations that are associated with resistance to NRTIs, PIs, and/or INSTIs may develop in people with HIV-2 while they are on ART.[38,56,57] Currently, transmitted drug resistance appears to be rare among people with HIV-2.[58,59] In several small studies, twice-daily dosing of DTG was found to have some residual activity as a second-line INSTI in some people with HIV-2 who had extensive ART experience and RAL resistance.[60-63] Genotypic algorithms that are used to predict drug resistance in HIV-1 may not be applicable to HIV-2 because the pathways and mutational patterns that lead to resistance may differ between the HIV types (see the HIV2EU Algorithm and the Stanford University HIV Drug Resistance Database).[64] In the event of virologic, immunologic, or clinical failure, a new ART regimen should be constructed in consultation with an expert in HIV-2 management.

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HIV and the Older Person

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Key Considerations and Recommendations When Caring for Older People With HIV
• Diagnosis of HIV at a later stage of disease is more common among older people. Early diagnosis and treatment of HIV and counseling to prevent secondary HIV transmission remain important in the clinical care of older people with HIV. • Antiretroviral therapy (ART) is recommended for all people with HIV **(AI).** ART is especially important for older individuals because they have a greater risk of serious non-AIDS complications and potentially a blunted immunologic response to ART. • Compared to people without HIV, people with HIV have a twofold higher risk of developing atherosclerotic cardiovascular disease (ASCVD), and their age at incident ASCVD diagnosis is about a decade younger. In addition to current American Heart Association (AHA)/American College of Cardiology (ACC)/ Multisociety Guidelines, the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommends initiating at least a moderate-intensity statin in people with HIV aged 40 to 75 years who have 10-year ASCVD risk estimates of 5% to <20% **(AI).** See Statin Therapy in People With HIV for the Panel's additional recommendations on the use of statin therapy as primary prevention for people with HIV. • Polypharmacy is common in older people with HIV, and all drugs, supplements, and herbal treatments should be assessed regularly for appropriateness, potential for adverse effects, proper dosing, and drug interactions **(AIII).** • Potential for drug–drug interactions between antiretroviral drugs and concomitant medications (including statins, supplements, and herbal medicines) should be assessed regularly, especially before a new ART regimen or concomitant medication is started. In this context, it is also important to inquire and counsel about the use of non-daily medications, including long-acting injectables and as-needed medications. • Adverse drug events from ART and concomitant drugs may occur more frequently in older people with HIV than in younger individuals with HIV. Therefore, the bone, kidney, metabolic, cardiovascular, cognitive, and liver health of older individuals with HIV should be monitored closely. • HIV infection is associated with immunologic aging and systemic inflammation, which may contribute to the development of comorbidities across multiple organ systems as well as aging phenotypes like frailty. HIV experts, primary care providers, and other specialists should work together to optimize the medical care of older people with HIV, including adhering to treatment and prevention guidelines for different medical comorbidities. • Age-related decline in neurocognitive function is faster in people with HIV compared to those without. Cognitive impairment in people with HIV—with manifestations including problems with memory, attention, and executive function—is associated with reduced adherence to therapy and poorer health outcomes, including increased risk of death. For people with progressive cognitive impairment, referral to a specialist (e.g., neurologist, neuropsychologist, geriatrician) for evaluation, testing, and management may be warranted **(BIII).** • Mental health disorders, including an increased risk of anxiety and depression, are a concern among aging people with HIV. Screening for depression and management of mental health issues are important when caring for older people with HIV. • Given that the burden of aging-related diseases is significantly higher among people with HIV than in the general population, additional medical and social services may be required to effectively manage both HIV and comorbid conditions.
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

Effective antiretroviral therapy (ART) has increased survival in people with HIV[1-4], resulting in an increasing number of older people with HIV. In the United States in 2022, the proportion of people newly diagnosed with HIV aged ≥55 years was 9%, according to the Centers for Disease Control and Prevention (CDC). Among people with HIV in 2022, 38% were aged ≥55 years, 13.2% were aged ≥65 years, and these proportions are expected to increase steadily.[5] The difference in life expectancy between people with HIV and the general population has significantly narrowed since the use of effective ART and is now estimated to be 5 years or fewer for those with CD4 T lymphocyte (CD4) cell count >500/μL after initiating ART.[3] However, the difference in mortality rates increases significantly with advancing age. While there has been a large reduction in AIDS-related mortality with effective ART, noninfectious comorbidities and complications, including atherosclerotic cardiovascular diseases (ASCVD) and non-AIDS malignancies, now account for a growing proportion of the causes of death among people with HIV.[2,3,6,7]

The discussion in this section of the guidelines refers to individuals aged ≥50 years as older people with HIV. Many older people with HIV have had HIV for years or decades; therefore, accumulating disease risk associated with longstanding HIV disease itself and/or exposure to antiretroviral (ARV) medications (including prior use of older ART regimens with greater toxicity in some cases) should be considered. Specifically, HIV may affect the biology of aging, possibly resulting in earlier manifestations of morbidities generally associated with more advanced age. As a result, older people with HIV may suffer from aging-related illnesses earlier and at higher rates than those without HIV, and will require more non-ART medications than younger people, which may complicate HIV clinical care.[8,9,10]

It is also important to consider distinct issues for people who are diagnosed with and/or acquire HIV at older ages. For example, older adults may have an increased risk of acquisition and transmission of HIV, in part as a consequence of reduced mucosal and immunologic defenses and changes in risk related-behaviors (e.g., decrease in condom use because of less concern about pregnancy or more high-risk sexual activity with increased use of erectile dysfunction drugs).[11,12] In addition, HIV screening among older adults remains low because they are generally perceived to be at low risk of acquiring HIV. The sections below review important considerations for the diagnosis and treatment of HIV among older people, as well as the potential clinical implications for people now living to older ages with longstanding HIV disease.

HIV Screening and Diagnosis in the Older Person

Older people with HIV (aged ≥55 years) are significantly more likely to meet the case definition of AIDS at HIV diagnosis than people aged <55 years (threshold defined by CDC surveillance data).[13] Also, older adults appear to have lower CD4 counts at seroconversion and steeper CD4 count decline over time[14] and tend to present to care with significantly lower CD4 counts.[15,16] Therefore, education, preventive measures (including pre-exposure prophylaxis or PrEP), and routine screening of asymptomatic older adults for HIV should be emphasized,[17] as well as considering HIV infection in the medical evaluation of older adults.

Antiretroviral Therapy in the Older Person With HIV

Importance of Prompt Initiation of Antiretroviral Therapy After HIV Diagnosis

ART is recommended for all individuals with HIV (**AI;** see Initiation of Antiretroviral Therapy). Early treatment may be particularly important in older adults because of blunted immune recovery and

increased risk of serious non-AIDS events in this population.[18,19] However, ART-associated CD4 cell recovery in older adults is generally slower and lower in magnitude than in younger people,[20-23] suggesting that early diagnosis and treatment may result in better immunologic response and possibly improved clinical outcomes. In a modeling study based on data from an observational cohort, the beneficial effects of early ART were projected to be greatest in the oldest age group (people aged 45 to 65 years).[24] The benefits of early ART initiation were further demonstrated in an analysis of HIV cohorts from Europe and the Americas showing a lower all-cause and non-AIDS mortality with immediate ART initiation in people aged 50 to 70 years.[25] More definitive information was provided by the START study, which randomized ARV treatment–naive participants with CD4 counts >500 cells/mm^3 to either immediate ART or deferred ART until CD4 count dropped below 350 cells/mm^3. The highest absolute risk reduction of serious AIDS and non-AIDS events associated with immediate ART was found in participants aged 50 years or older.[26] All older people with HIV should be informed that maintaining a plasma HIV RNA (viral load) at <200 copies/mL with ART improves overall health and prevents sexual transmission of HIV (see the Treatment as Prevention section).

Choice of Antiretroviral Regimens in the Older Person With HIV

The choice of ARV regimen for an older person with HIV should be informed by a comprehensive review of the person's other medical conditions and medications (including non-prescription drugs, supplements, and herbal treatments), and results from cumulative genotypic resistance testing. The What to Start section (Table 7) of these guidelines provides guidance on selecting an ARV regimen based on a person's characteristics and specific clinical conditions (e.g., kidney disease, elevated risk for cardiovascular disease [CVD], osteoporosis). In older people with HIV and reduced renal function, dosage adjustment of nucleoside reverse transcriptase inhibitors (NRTIs) may be necessary (see Appendix B). In addition, ARV regimen selection may be influenced by potential interactions between ARV medications and drugs used concomitantly to manage comorbidities (see Tables 24a through 25b). Adults aged >50 years should be monitored for ART effectiveness and safety as similarly recommended for other populations with HIV (see Table 3); however, in older people, special attention should be paid to the greater potential for adverse effects of ART on renal, liver, cardiovascular, central nervous system, metabolic, and bone health (see Table 21). A meta-analysis confirmed that people with HIV have a 1.5-fold higher risk of fragility-related fracture and a fourfold higher risk of hip fracture. The increased risk is not completely explained by differences in bone mineral density (BMD) alone, indicating there may be differences due to bone microarchitecture or other HIV-related factors contributing to the marked fracture risk. ART regimens that contain tenofovir disoproxil fumarate (TDF),[27] boosted protease inhibitors (PIs), or both are associated with a significantly greater loss of BMD, with or without osteoporosis, compared to regimens containing other NRTIs and integrase strand transfer inhibitors (INSTIs).[28-31] Abacavir (ABC), NRTI-sparing regimens, and tenofovir alafenamide (TAF) may be considered as alternatives to the use of TDF in older individuals who may be at risk of nephrotoxicity, osteopenia, or osteoporosis; however, with ABC, the benefit should be balanced with its potential for increasing the risk of CVD (see What to Start). The long-acting (LA) injectable combination of cabotegravir (CAB) and rilpivirine (RPV) is also an option for ART among older people with HIV, with the same considerations as for all people with HIV (see Optimizing Antiretroviral Therapy in the Setting of Viral Suppression).

Antiretroviral Efficacy and Safety Considerations in the Older Person With HIV

The efficacy, pharmacokinetics (PK), adverse effects, and drug interaction potentials of ART in older adults have not been studied systematically. Data from clinical trials of second-generation INSTIs (dolutegravir [DTG] and bictegravir),[32] two-drug regimens (DTG/lamivudine),[33] and LA CAB/RPV

have shown similar virologic efficacy, safety, and tolerability between participants >50 years of age and those aged 50 and younger.[34]

Hepatic metabolism and renal elimination are the major routes of drug clearance, including the clearance of ARV drugs. Both liver and kidney functions decrease with age and may result in impaired drug elimination and increased drug exposure.[35] Most clinical trials have included only a small proportion of participants aged >50 years, and current ARV dosing recommendations are based on PK and pharmacodynamic data derived from participants with normal organ function. Because it is not known whether drug accumulation in older people may lead to greater incidence and severity of adverse effects than in younger people, therapy in older people requires close monitoring and heightened awareness of drug-related adverse effects, especially in those with hepatic or renal impairment.

Adherence Concerns

Suboptimal adherence to ART is the most common cause of treatment failure. Although most older people with HIV are able to achieve viral suppression with a single-tablet regimen, some people who have a long history of ART may have acquired drug resistance, thus requiring more complex multiple-pill regimens. Complex dosing requirements, high pill burden, polypharmacy, inability to access medications because of cost or availability, limited health literacy (including misunderstanding of instructions), depression, substance use, frailty, and neurocognitive impairment are among the key reasons for nonadherence and should be regularly assessed and managed (see Adherence to the Continuum of Care).[36-38] Although some of the factors associated with nonadherence may be more prevalent in older people with HIV, older people have demonstrated better adherence to ART than younger people in some studies.[39-41] Severe menopausal symptoms are also associated with reduced adherence to ART, which increases the risk of drug resistance and adverse HIV-related health outcomes in menopausal women, highlighting the importance of managing these symptoms among women with HIV.[42,43] To facilitate ART adherence, it may be useful to discontinue unnecessary non-HIV medications, simplify ART regimens, and apply evidence-based behavioral approaches including the use of adherence aids such as pillboxes or daily calendars, and support from family members and friends (see Adherence to the Continuum of Care). LA dosing options, such as LA CAB/RPV, may ease pill burden and adherence concerns for some older adults (see Optimizing Antiretroviral Therapy).

Optimizing Antiretroviral Therapy in Older People With HIV

Given the greater incidence of comorbidities, non-AIDS complications, and frailty among older people with HIV, switching one or more ARVs in an HIV regimen may be necessary to minimize toxicities, drug–drug interactions, or to reduce pill burden.[38] Expert guidance now recommends bone density monitoring in men aged ≥50 years and postmenopausal women and suggests switching from TDF or boosted PIs to other ARVs (such as TAF or INSTIs, respectively) in older people at high risk for fragility fractures.[44] Given the high prevalence and faster progression of chronic kidney disease (CKD) in aging people with HIV—likely from a combination of HIV, ART, and non-HIV risk factors—development of CKD must be closely monitored in an older person on ART.[45,46] Table 7 provides guidance for ARV drugs to use based on selected clinical scenarios, including comorbidities.

Polypharmacy in Older People With HIV

People with HIV and aging-associated comorbidities may require additional pharmacologic interventions that can complicate therapeutic management.[8] In addition to taking medications to manage HIV and comorbid conditions, many older people with HIV are also taking medications to relieve discomfort (e.g., pain medications, sedatives) or to manage adverse effects of medications

(e.g., anti-emetics). Older individuals may also self-medicate with over-the-counter medicines or supplements.

Polypharmacy is more common in older people with HIV than similarly aged people in the general population.[8,47,48] Among people with HIV aged ≥65 years, it is predicted that the prevalence of comorbidities and polypharmacy rose with increasing age and duration of HIV infection.[49,50] In the Swiss HIV Cohort Study, the prevalence of polypharmacy and inappropriate prescribing in people aged ≥75 was 66% and 67%, respectively.[51]

In people aging with HIV, the effects of polypharmacy, including the use of drugs that affect neurocognitive function, can contribute to serious adverse outcomes, such as serious falls and fractures, delirium, hospitalization (including intensive care unit admissions), and death.[52-57] Polypharmacy may also increase the likelihood of adverse consequences such as medication errors (by prescribers or prescription recipients), medication nonadherence, additive drug toxicities, and drug–drug interactions. Older people with HIV are probably at an even greater risk of polypharmacy-related adverse consequences than younger or similarly aged people without HIV. When evaluating any new clinical concern or laboratory abnormality in people with HIV, especially in older people, clinicians should always consider the possible role of adverse drug reactions from both ARV drugs and other concomitantly administered medications.

Drug–Drug Interaction Concerns

Interactions between ARV drugs and concomitant medications, supplements, and herbal treatments can occur and can be easily overlooked by prescribers.[58] Potential drug–drug interactions can occur between ARV and non-ARV medications, as well as between non-ARV medications.[48,59] The available drug interaction information on ARV agents is derived primarily from PK studies performed in small numbers of relatively young participants with normal organ function who do not have HIV (see Tables 24a–25b). Data from these studies provide clinicians with a basis to assess whether a significant interaction may exist. However, the magnitude of an interaction may be greater in older than in younger people with HIV; therefore, it is important for clinicians to remain vigilant to assess for potential drug–drug interactions given the high prevalence of polypharmacy in older people with HIV. The risk of significant drug–drug interactions appears to be higher with PI-based or non-nucleoside reverse transcriptase inhibitors-based ART than with INSTI-based ART, although there are some important interactions with INSTIs that should be recognized and managed (including with polyvalent cations that are frequently taken as supplements).[60-62]

Hormonal therapies may be taken to alleviate symptoms of menopause or for other medical indications. Although data on drug–drug interactions between hormonal therapies and ART are limited, existing data suggest little to no impact of hormonal therapies on the efficacy of some ART.[63-65]

HIV and Immunologic Aging

Chronic HIV infection is associated with elevated soluble markers of immune activation and inflammation, as well as cellular phenotypes indicative of T cell and myeloid cell activation, even after HIV RNA levels are suppressed with ART.[66] The levels of inflammation and immune activation also increase with age and age-associated diseases.[67] In this context, the combined effects of HIV and advancing age on chronic inflammation have implications for risk from a broad spectrum of diseases.[68,69]

A contributing factor to the early development of aging-related diseases among people with HIV has been posited to be the effect of HIV on immunologic aging. In addition to higher levels of immune activation, aging is associated with a higher frequency of cellular senescence as well as impaired

immune responses and surveillance.[70] HIV infection is associated with higher frequencies of T cell phenotypes characteristic of immunosenescence, as well as phenotypes reflective of highly differentiated or activated states.[71-74] Higher frequencies of senescent T cells are then associated with a greater risk for such comorbidities as CVD. In addition, the degree of CD4 T cell recovery after ART initiation is diminished among people ≥50 years old versus younger people with HIV.[75,76] This impaired T cell recovery with advancing age may then have functional consequences, as people with HIV demonstrate reduced immune responses to vaccination, as well as impaired control of copathogens such as cytomegalovirus (CMV).[77-79] The persistence of impaired or ineffective immune response toward copathogens then contributes to ongoing chronic immune activation (e.g., CMV-specific responses),[78] as well as the increased risk of both AIDS and non-AIDS–defining cancers that are driven by pro-oncogenic viruses (e.g., human papillomavirus [HPV]-and Epstein-Barr virus [EBV]-related cancers).[80]

Immunologic aging in the context of HIV also entails chromosomal and genetic changes. Whether a consequence of untreated HIV viremia, direct toxicity from ARV drugs, or both, people with HIV have been shown to have shorter leukocyte chromosome telomere length, itself a marker of poor health and mortality.[81-83] DNA methylation is an epigenetic alteration that occurs at a predictable rate with advancing age, predicts lifespan, and increases in the setting of chronic HIV disease.[84-87] Finally, a genetic mechanism that may more directly link immunologic aging to comorbid disease risk is clonal hematopoiesis, which entails an age-related expansion of somatic gene mutations among leukocytes (also referred to as age-related clonal hematopoiesis or ARCH). Clonal hematopoiesis is more common among people with HIV, and the degree of difference with people without HIV may be more pronounced with advancing age[88,89] and in people with low nadir CD4 counts.[90,91] Several of the leukocyte gene mutations characteristic of clonal hematopoiesis lead to dysregulation of inflammatory pathways, which is then associated with higher levels of inflammatory markers and ASCVD.[92-94] In summary, clonal hematopoiesis is an example of HIV disease influencing age-related genetic somatic mutations that may contribute to ongoing systemic inflammation and associated disease risk among older people with HIV.

Disease-modifying pharmacologic interventions targeting immunologic aging are an area of active study within geroscience, but none are currently recommended specifically for older people with HIV with the exception of statin therapy as primary prevention of ASCVD risk (see Atherosclerotic Cardiovascular Disease in the Older Person With HIV below and Statin Therapy in People With HIV).

Morbidity, Mortality, and Non-AIDS Complications Among Older People With HIV

The clinical implications of greater immunologic aging and persistent inflammation can manifest in any organ system, diminishing the health span of older people with HIV. The frailty phenotype—defined clinically as a decrease in muscle mass, weight, physical strength, energy, and physical activity—represents an important example of an age-related syndrome that occurs with greater frequency and at earlier ages among people with HIV and is associated with a broad spectrum of adverse effects and disease risk. Specifically, frailty among people with HIV has been associated with incident CVD, diabetes mellitus, recurrent falls and fractures, lower quality of life, cognitive impairment, hospitalization, and mortality.[95-104] The frailty phenotype remains incompletely characterized among older people with HIV and identifying effective treatment strategies is an important priority for clinical management. However, pharmacologic and non-pharmacologic interventions addressing frailty among people with HIV have been proposed and have the potential to significantly impact their quality of life and survival.[105,106]

Although the life expectancy of people with HIV is approaching that of people without HIV, the incidence and prevalence of age-associated comorbidities in people with HIV are increasing.[107,108]

The age-related comorbidity burden is significantly higher in people with HIV compared to the age-matched general population.[8] These predictions differ by comorbidity and by demographic factors—including race, ethnicity, age, sex, and HIV transmission mode—displaying substantial disparities for some populations.

Data from insured adults suggest that people with HIV spend approximately 15 years more of their lifespan with one or more major comorbidities when compared to people without HIV; this difference is reduced but persists (at approximately 10 years) for people who initiate ART at a CD4 count of >500 cells/mm^3.[109] A simulation modeling study projected that by 2030, 45% of people with HIV on ART would be living with two or more physical comorbidities and 64% with at least one mental health comorbidity.[110]

Non-AIDS–Defining Complications and Comorbidities in the Older Person With HIV

Non-AIDS comorbid conditions constitute an increasing proportion of morbidity and mortality among people with HIV.[3,111] Heart disease and cancer are the leading causes of death in older people with HIV in the United States. Similarly, other non-AIDS events, such as cognitive impairment and liver disease, have also emerged as major causes of morbidity and mortality in people with HIV receiving effective ART. The prevalence of multimorbidity among people with HIV has increased in the past decade,[112] with hypertension and hypercholesterolemia being the most common comorbidities.[113]

Three groups of factors likely contribute to this burden of noncommunicable diseases among people with HIV: (1) an over-representation of traditional risk factors in this population, especially higher rates of smoking, diabetes, and dyslipidemia; (2) HIV-associated chronic inflammation and immune activation, which are not completely abated by suppressive ART; and (3) possible cardiometabolic complications of some ARV drugs.[114-122]

As the life expectancy of people with HIV increases with ART, more women with HIV are experiencing menopause. Although menopause may occur earlier in women with HIV than in women in the general population,[123] early menopause may also be a consequence of smoking, depression, substance use disorder, and other psychosocial factors that are disproportionately present in women with HIV.[124] Also, HIV might compound menopause-related metabolic changes. For instance, HIV infection and menopausal stage were independent predictors of lower BMD and had an additive effect on lumbar spine and total hip BMD.[125]

HIV-specific primary care guidelines have been developed and are available for clinicians caring for people with HIV, especially for older people with HIV.[126,127] Additional specific guidelines have also been developed for the evaluation and management of the following specific comorbidities in people with HIV: bone health,[44] kidney disease,[128] and secondary prevention for ASCVD.[129] In addition, the following guidelines recently developed for the general population can be applied to older people with HIV: management of hypertension[130], hyperglycemia[131], and hyperlipidemia.[132] However, it is important to note that the recommendations in many of these guidelines have not all been validated in the context of HIV disease. For instance, cardiovascular risk prediction functions developed for the general population likely underestimate the risk in people with HIV.[129,133] Findings of the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) study have provided significant insight into the potential role of statins in the prevention of major adverse cardiovascular events in people with HIV. See Statin Therapy in People With HIV for recommendations from the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) on statin therapy as primary prevention of ASCVD among people with HIV. Further analyses of the REPRIEVE data will likely yield additional insights into their benefits (and potential risks) in people with HIV, as well as differences in the predictive value of risk equation scores in demographic subsets of study participants.

Atherosclerotic Cardiovascular Disease in the Older Person With HIV

When compared to people without HIV, data from several studies have shown that people with HIV have about a twofold higher risk of developing ASCVD, and their age at incident ASCVD diagnosis is about a decade younger.[108,109,134,135] ASCVD risk prediction tools used for the general population tend to underestimate risk among people with HIV.[133,136] Data also suggest that the relative increase in ASCVD risk is greater among women with HIV than among age-matched men with HIV when compared to people without HIV.[137,138] Factors influencing ASCVD risk among people with HIV include both higher prevalence of traditional cardiometabolic risk factors and ongoing systemic inflammation associated with HIV,[114,137] even in individuals with viral suppression while on ART. In addition, structural barriers and health disparities in screening and treatment of ASCVD risk factors likely also contribute to excess ASCVD risk among people with HIV in the United States.[139,140]

The 2018 American Heart Association (AHA)/American College of Cardiology (ACC)/Multisociety Guidelines provide recommendations on the use of statins as primary prevention based on risk stratification using estimates of 10-year ASCVD risk from the pooled cohort equations.[141,142] In the general population, statin therapy is recommended for all people at high 10-year ASCVD risk (defined as ≥20%). Recent findings from the REPRIEVE trial have provided evidence for the use of statin therapy as primary prevention for people with HIV at low-to-intermediate ASCVD risk (i.e., <20%). REPRIEVE, a large randomized controlled trial among people with HIV aged 40 to 75 years who were receiving ART, showed that when compared to placebo, pitavastatin 4 mg daily was associated with a 35% reduction in major adverse cardiovascular events over a median follow-up duration of 5 years.[143] Results from REPRIEVE informed the Panel's recommendation on the use of at least moderate-intensity statin therapy as primary prevention among people with HIV of age 40 to 75 years, with a stronger recommendation for those with ASCVD risk score ≥5% who will have a higher absolute benefit from statin therapy. See Statin Therapy in People With HIV for the Panel's full recommendations on statin therapy.

Neurocognitive Impairment in the Older Person With HIV

Cognitive impairment in people with HIV can manifest as difficulty with memory, attention, speed of information processing, and executive and motor functions. Studies that use neuropsychological testing to define categories of impaired cognition—termed HIV-associated neurocognitive disorder (HAND)—find that up to 30% of people with HIV on virally suppressive ART meet these research-based criteria[144], although these categories have not been validated for use in clinical practice. Research studies also demonstrate a steeper decline in performance on neuropsychological tests with advancing age in individuals with HIV compared to those without HIV over the same age range.[145] Although viral persistence and chronic brain inflammation can contribute, cognitive impairment is multifactorial in people with HIV. It is not solely HIV-associated, but also influenced by factors related to comorbidities, including polypharmacy, mood disorders, vascular disease, social isolation, stress, and independent neurodegenerative conditions.[146-151] Hormonal shifts that occur with aging may contribute to neurocognitive impairment, and these changes may manifest as unique differences in clinical manifestations by sex.[152] Finally, the risk of neurodegenerative disease rises with increasing age independent of HIV, and diagnosis of Alzheimer's disease or other forms of progressive dementia in older people with HIV is now an important clinical concern.[153]

Cognitive impairment carries potentially detrimental clinical consequences for aging people with HIV. In a prospective observational study, cognitive impairment was predictive of a lower likelihood of retention in care among older people.[154] Cognitive impairment is also associated with reduced adherence to therapy[155] and poorer health outcomes including increased mortality.[156] Given the importance of cognitive health, screening for neurocognitive impairment is important, though optimal primary care-based screening methods remain unclear. Initial screening with questions about

symptoms of memory loss, slowness, and poor attention can help to guide the need for referral to a specialist (e.g., neurologist, neuropsychologist, or geriatrician).[157,158] Though such questions can be useful in identifying cognitive impairment, a positive response to these questions is not necessarily specific to impairment related to HIV.[159] Of note, people with substantial impairment may not have enough insight into their condition to answer the questions, and input from a partner or family member corroborating the impaired person's cognitive history may enhance the validity of the assessment. No brief cognitive screening test has been clearly shown to be sensitive or specific for cognitive impairment in HIV; the frequently used Mini-Mental State Exam does not typically capture executive function impairment, which is the main manifestation of subtle cognitive impairment in people with HIV.[160] The Montreal Cognitive Assessment may be more sensitive but is not specific. A lower threshold than the original cut-off score of 26 on the Montreal Cognitive Assessment is likely more optimal for HAND screening, as it lowers false positive rates and improves diagnostic accuracy.[161] If a person has persistent concerns over time, has symptoms corroborated by an acquaintance, or has progressively worsening symptoms, referral to a neurologist for evaluation and management or to a neuropsychologist for formal neuropsychological testing may be warranted **(BIII).**[160]

Beyond screening and referral to specialists in neurology, neuropsychology, or geriatrics, an approach to cognitive impairment in aging people with HIV should involve assessing and correcting reversible and treatable factors that contribute to cognitive symptoms, as well as directly addressing modifiable risk factors. Reversible and treatable factors that may contribute to cognitive symptoms include hypothyroidism, low vitamin B12 levels, syphilis, sleep apnea, and cerebrovascular disease.[162] Hearing impairment, diabetes, obesity, hypertension, depression, smoking, alcohol or substance use, and limited physical and social activity have been identified as significant modifiable risk factors for dementia in people without HIV.[163] Given the prevalence of many of these risk factors in older people with HIV, careful attention to their prevention or amelioration is an important component of primary care and cognitive care in aging people with HIV. Finally, the U.S. Preventive Service Task Force now recommends screening older adults (>65 years) for depression.[164]

Mental Health Concerns in the Older Person With HIV

Mental health-related problems are a growing concern in aging people with HIV, though little is known about their prevalence and consequences in this population specifically. In a study that compared a cohort of individuals aged >60 years with HIV to a historical control group of healthy older people, a heightened risk of mood disorders including anxiety and depression was noted among people with HIV.[165] Social isolation combined with depression is particularly common among older adults with HIV and, in addition to its direct effects on morbidity and mortality, it may contribute to poor medication adherence and retention in care.[166,167] The risk of suicide remains greater in people with HIV than in the general population, though increasing age might not further heighten the risk.[168] In one analysis of a multicenter observational study in France, suicide emerged as the second-highest cause of death among virologically suppressed people with HIV on ART.[169] Screening for depression and management of mental health issues are critical aspects of HIV primary care; guidelines for people with HIV, as well as for aging individuals without HIV, recommend behavioral approaches including individual psychotherapy, cognitive behavioral therapy, group therapy, and often pharmacological treatment.[169] When resources are available, integrated care models with routine screening by health care support staff, review by primary providers, and referral to on-site mental health specialists are likely to be the most effective approaches in vulnerable aging populations.

Health Care Utilization and Cost Sharing

The substantially increased burden of age-related comorbidities among people aging with HIV, including CVD, CKD, neurocognitive disease, and fractures, can lead to increased healthcare

utilization and higher costs.[170] Out-of-pocket health care expenses (e.g., copayments, deductibles), loss of employment, and other financial-related factors can cause temporary interruptions in treatment, including ART, which should be avoided whenever possible (see Cost Considerations and Antiretroviral Therapy for more information). The increased life expectancy and higher prevalence of chronic complications in aging populations with HIV can place greater demands upon HIV services[171] and require a focused approach to prioritize modifiable health-related problems. Facilitating continued access to health care, including access to insurance-covered care and medications, is essential to minimize treatment interruptions; clinical outcomes can improve with additional multidisciplinary services to manage concomitant chronic disorders and assist with overcoming structural barriers to care. See the Ryan White HIV/AIDS Program's Available Care & Services page for additional information.

End-of-Life Issues, Including Palliative Care and Interruption of ART

As with all aging people, it is important to discuss living wills, advance directives, and long-term care planning. Palliative care and hospice should be discussed with a person-centered approach that incorporates the person's family situation and cultural, religious, and personal values, among other factors.[172,173]

Few data exist on the use of ART in people with debilitating chronic, severe, or non-AIDS terminal conditions.[174,175] Discontinuation of ART usually results in rebound viremia and a decline in CD4 count; an acute retroviral syndrome has also been reported after abrupt ART discontinuation. For these reasons, most clinicians would continue ART if there are no significant adverse reactions to the ARV drugs. In cases where ART negatively affects quality of life, the decision to continue therapy should be made together with the affected person and/or family members after a discussion of the risks and benefits of continuing or stopping ART.

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Key Considerations and Recommendations
• Substance use disorders (SUDs) are prevalent among people with HIV and contribute to poor health outcomes; therefore, screening for SUDs should be a routine part of clinical care **(AII).** • The most commonly used substances among people with HIV include the following (listed in alphabetical order): alcohol, benzodiazepines, cannabinoids, club drugs, opioids, stimulants (cocaine and methamphetamines), and tobacco. • Health care providers should be nonjudgmental when addressing substance use with people with HIV **(AIII).** • People with HIV and SUDs should be screened for additional mental health disorders **(AII).** • People with HIV and SUDs should be offered evidence-based pharmacotherapy (e.g., opioid agonist therapy, tobacco cessation treatment, alcohol use disorder treatment; see Table 16 below) as part of comprehensive HIV care in clinical settings **(AI).** • Ongoing substance use is not a contraindication to antiretroviral therapy (ART). People who use substances can achieve and maintain viral suppression with ART. • Substance use may increase the likelihood of HIV transmission risk behaviors, the potential for drug–drug interactions, and the risk or severity of substance-associated adverse events (e.g., increased hepatotoxicity or an increased risk of overdose). • Selection of antiretroviral (ARV) regimens for individuals who practice unhealthy substance and alcohol use should take into account potential adherence barriers, comorbidities that could impact care (e.g., advanced liver disease from alcohol or hepatitis viruses), potential drug–drug interactions, and possible adverse events associated with the medications **(AII).** • For people with SUDs, ARV regimens with once-daily formulations (ideally as a single-tablet regimen), high barriers to resistance, low hepatotoxicity, and low potential for drug–drug interactions are preferred **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Background on Substance Use Disorders Among People With HIV

Ending the HIV epidemic requires addressing substance use among people with HIV, which poses a barrier to optimal engagement in the HIV care continuum. Ongoing substance use may prevent an individual from being tested for HIV, initiating antiretroviral therapy (ART), or adhering to ART. Substance use may also increase the likelihood of risk-taking behaviors (e.g., sexual transmission risk behaviors, needle sharing, injection of substances), the potential for drug–drug interactions, and the risk or severity of substance-related adverse events (e.g., increased hepatotoxicity and increased risk of overdose). In the United States, the death toll for drug overdose (102,123 deaths as of February 2024)[1] far exceeds the death toll for HIV (4,941 deaths in 2022).[2] As the drug overdose epidemic continues to expand, health care providers need a basic understanding of how to screen for and treat substance use disorders (SUDs) in people with HIV in clinical settings.[3]

Substance use exists on a continuum, from episodic use to an SUD with its concomitant negative consequences. Research on alcohol consumption has defined a threshold at which consumption does not reach a diagnosis of SUD, but where the level of consumption is nonetheless hazardous to the person. This level of consumption has been defined as at-risk or hazardous use. A comparable category does not exist for other substances. The prevalence of substance use and SUDs is higher among people with HIV than among the general public,[4] and polysubstance use is common. This section will focus on the most commonly used substances among people with HIV (listed in alphabetical order): alcohol, benzodiazepines, cannabinoids, club drugs,[5] opioids, stimulants (cocaine and methamphetamines), and tobacco. Additionally, xylazine, a non-opioid veterinary analgesic that is a common substance adulterant—a substance added to another substance that may lead to negative health consequences—is also discussed.

People with HIV may use more than one substance and may not be ready to consider reducing the use of substances or seeking treatment for SUDs. Polysubstance use occurs for multiple reasons, including to improve the euphoria associated with use (e.g., use of cocaine and heroin mixtures called “speedballs”) and to reduce the adverse effects of a particular substance (e.g., the use of alcohol or benzodiazepines to reduce the anxiety caused by cocaine use).

Substance Use and Sexual Risk-Taking

A growing body of literature describes the intersection of substance use and sexual risk-taking, in which drugs are intentionally used to enhance sexual activity (“chemsex”). This research highlights the impact of substance use on sexual transmission risk behaviors; although no precise definition of “chemsex” exists, studies have investigated various substances used to enhance sexual pleasure, decrease inhibitions related to particular sexual acts, and combat low self-esteem. In a retrospective study in a London sexual health clinic, individuals who disclosed substance use (463 of 1,734 participants) had higher odds of acquiring new HIV infection, bacterial sexually transmitted infections (STIs), and/or hepatitis C virus (HCV).[6] A much larger analysis using the European Men Who Have Sex With Men (MSM) Internet Survey, which collected data from 16,065 United Kingdom-based respondents, found that MSM who reported using methamphetamines or gamma-hydroxybutyrate (GHB) during the previous year were more likely to have gonorrhea infection than MSM who did not use these drugs, with odds ratios of 1.92 and 2.23, respectively.[7] Between 2017 and 2020, the American Men’s Internet Survey collected data on chemsex drug use among MSM in the United States over the preceding 12 months. Of 30,294 MSM respondents, 3,113 (10.3%) self-reported chemsex in the past 12 months, with 3,4-methylenedioxymethamphetamine (MDMA or “ecstasy”) (65.1%), methamphetamine (42.5%), and GHB (21.7%) being the top drugs reported for use.[8] A recent study in Spain using an online, self-administered questionnaire found that 81.4% of 2,919 MSM attending four HIV/STI testing sites in Madrid and Barcelona had ever used any drug, and 50% had engaged in chemsex in the past 12 months. Of those engaging in chemsex, half engaged in condomless anal sex.[9] These data emphasize the need to screen people with HIV for substance use and STIs in clinical settings and to discuss strategies with these individuals to reduce potential harm.[10]

Substance Use and Unstable Housing

People with HIV who inject drugs are more likely to be unhoused.[11] Houselessness among people who inject drugs is associated with an increased risk of HIV acquisition.[12]

Among people with HIV and SUD, houselessness confers an increased risk for disruptions in the HIV care continuum independent of ongoing substance use. In a longitudinal study of people with HIV who used drugs, lack of housing was associated with a 44% decrease in the odds of progression through the HIV care continuum.[13] After adjusting for multiple intersecting risks, including unhealthy alcohol use, other substance use, incarceration, unemployment, education, age,

sex, and race/ethnicity, unhoused people with HIV and SUD had significantly decreased odds of ART initiation and, adherence, and of viral suppression.

Interventions supporting housing among people with HIV and SUD can result in improved HIV treatment outcomes. A randomized controlled trial of a rapid rehousing intervention for people with HIV who were houseless (n = 236, 81% with substance use) found that clients in the Enhanced Housing Placement Assistance arm were more likely to be placed and, placed faster, and were twice as likely as the control group to reach or maintain viral suppression (95% confidence interval [CI], 1.1–4.0).[14,15] An observational study of applicants to a supportive housing program for low-income people with HIV and a mental health condition or SUD (n = 958; 86% with SUD) found that people who achieved stable housing were more likely to engage in HIV care and to achieve viral suppression.[16] These data reflect the importance of not only addressing SUD among people with HIV, but also understanding the co-occurring structural determinants that contribute to poorer outcomes among people with HIV and SUD.

Screening for Substance Use Disorders

Screening for SUDs should be incorporated into the routine clinical care of all people with HIV. The following questions can be used to screen for drug or alcohol use: “How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?” and “How many times in the past year have you had X or more drinks in a day?” (X is five for men and four for women).[17] Individuals with liver disease, including active HCV infection, should not consume alcohol.

A positive response to either of the two questions above should prompt additional screening with other short screening tools (see the Screening and Assessment Tools Chart from the National Institute on Drug Abuse). These tools can identify substance use and guide decisions on appropriate treatment interventions. Currently, there are not enough data to determine how often people with HIV should be screened for SUDs; however, given the potential negative impact that SUDs may have on people with HIV, it is advisable to ask these questions during every clinical visit.

Health care providers should be nonjudgmental when discussing substance use with people who have HIV **(AIII).** People with HIV who experience stigma or judgment may lose trust in their health care provider’s advice, avoid future visits, and consequently experience poorer health outcomes.[18] Language is one way in which stigma is communicated, and words such as “addict” and “dirty urine” convey a negative connotation. The Office of National Drug Control Policy (ONDCP), American Medical Association, American Society of Addiction Medicine, International Society of Addiction Journal Editors, and others have recommended the adoption of clinical, nonstigmatizing language for substance use, as described in the *Changing the Language of Addiction* report from ONDCP.

Co-occurring Mental Illness

Many people who use substances have co-occurring mental health disorders, including a history of trauma that may drive or exacerbate their substance use. Conversely, ongoing use of substances can place individuals at risk for trauma, such as sexual assault and sexual exploitation, which may further exacerbate their substance use.[6,19] People with SUDs should undergo evaluation and treatment for concurrent mental health disorders using standardized screening instruments (e.g., the Patient Health Questionnaire-2, or PHQ-2, for depression). Where applicable, clinicians should use available behavioral and pharmacological interventions to address mental health concerns, because recommending that people stop their substance use without providing treatment for underlying mental health conditions has very limited efficacy.[20]

Selecting, Initiating, and Maintaining Antiretroviral Therapy

Ongoing substance use is **not** a contraindication for prescribing ART. ART is recommended for all people with HIV to improve their health and to prevent transmission of HIV to others **(AI),** including sexual partners and individuals who share drug paraphernalia. These clinical, community, and individual benefits should encourage health care providers to initiate ART in all people with HIV who use substances. Although effective ART prevents sexual transmission of HIV, its effectiveness in preventing transmission through shared needles and shared use of other drug paraphernalia remains unknown.

For people actively injecting drugs, engagement in a syringe service program (SSP) can facilitate access and adherence to ART. SSPs primarily provide clean drug preparation and injection supplies to reduce transmission of HIV, HCV, and other bloodborne, skin, and soft tissue pathogens. As a regular point of contact for people with complex health and social challenges, SSPs also provide opportunities to offer other integrated health-related and social support services,[21] including those for treating SUDs.[22] For people with HIV, SSPs can be adapted to provide or link to rapid initiation[23,24] and maintenance of effective ART.[24]

When selecting ART regimens for individuals who use substances, clinicians should consider potential barriers to adherence (see Adherence to the Continuum of Care), comorbidities that could impact care (e.g., advanced liver disease from alcohol or HCV), potential drug–drug interactions, and possible adverse events that are associated with the medications. Providers and people with HIV should discuss adherence during multiple, nonjudgmental evaluations. In general, the use of simplified ART regimens should be considered to aid adherence. Regimens for people with SUDs should be easy to take, such as once-daily formulations, ideally as a single-tablet regimen,[25] and should have a high barrier to resistance and a low risk of hepatotoxicity **(AIII).** Adherence counseling should highlight the benefits of ART use, irrespective of concurrent substance use. While a reduction in substance use may improve adherence to ART,[26,27] ongoing use is not a contraindication to ART.

Long-Acting Antiretroviral Therapy

The development of long-acting (LA) injectable ART provides additional options for treatment. The combination of injectable cabotegravir (CAB) and rilpivirine (RPV) is an optimization option for people with HIV who demonstrate retention in HIV care and who are virologically suppressed on oral therapy (see Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression). Current U.S. Food and Drug Administration (FDA) approval for LA CAB/RPV is limited to individuals with expected good adherence and an ability to achieve virologic suppression on oral therapy prior to starting LA ART. Limited data from a small, ongoing observational study found that LA CAB/RPV leads to high levels of viral suppression in people with HIV who have struggled with adherence to oral ART and those who are viremic at treatment initiation, including people who use stimulants.[28] Of note, the clinic in this study provided a significant amount of social support to ensure adherence to the LA CAB/RPV regimen (see Virologic Failure for additional details). It is not known if similar responses can be seen in clinics without the resources to provide a similar level of adherence support. Missing LA CAB/RPV doses or a delay in receiving scheduled injections may result in emergence of HIV drug resistance.[28]

The following factors should be considered when contemplating the use of LA CAB/RPV in people with HIV and SUDs:

- As with all treatment conversations, providers should discuss adherence with their patients during multiple, nonjudgmental evaluations.

- Providers and people with HIV should consider the impact of using LA CAB/RPV in the context of current or past substance use behaviors. Although some people may welcome or even prefer LA CAB/RPV,[29] one qualitative study highlighted that using a needle for administering LA CAB/RPV could be a trigger for people with a history of injecting illicit substances.[30]
- Studies utilizing LA CAB/RPV have included individuals with good adherence before starting the LA ART, but this should not exclude people with SUDs who are struggling with adherence from being considered for LA CAB/RPV. Rather, the clinical team should consider what additional support may be needed to help people with SUDs be successful with LA CAB/RPV and whether using LA ART without established viral suppression is warranted based on preliminary data (see Virologic Failure and Adherence to the Continuum of Care for additional details). Case management, patient navigators, and/or peer navigators should be considered to help people with HIV return for follow-up injections.
- Given the often unpredictable lifestyles of people with SUDs, clinical care teams should be flexible in scheduling injections or accommodating walk-ins for injections. However, it should be stressed that the doses should be given within the mandatory 7 days before or after the scheduled LA CAB/RPV injection date.
- As for all people with HIV, hepatitis B virus (HBV) status should be evaluated before the initiation of LA CAB/RPV (see HBV/HIV Coinfection and Optimizing Antiretroviral Therapy in the Setting of Virologic Suppression for additional details). If not already immune or infected, HBV vaccination should be initiated while considering LA CAB/RPV, including in those with isolated hepatitis B core antibody (HBcAb).
- LA CAB/RPV is not recommended for people with HBV/HIV coinfection unless HBV-active drugs (i.e., tenofovir, entecavir) are included in the regimen.
- As depressive disorders have been associated with LA CAB/RPV in all populations, people with SUD also should be screened for depressive disorders and treated for depression if indicated.[31] If depressive disorders worsen while on LA CAB/RPV, reevaluation should occur to determine whether continued therapy with this regimen is advisable.

Importantly, despite emerging observational data, multiple knowledge gaps exist regarding the use of LA ARVs among people with HIV and SUDs. The results from the ongoing Long-Acting Therapy to Improve Treatment Success in Daily LifE (LATITUDE) Study (NCT 03635788) will provide clinical trial results to help inform the use of LA CAB/RPV among people with HIV and SUDs who have struggled with ART adherence.[32] Additional research is also needed to determine optimal methods for supporting ART adherence (including to LA ARVs) among people with HIV and SUDs. These research studies will need to take into consideration the combination of various interventions (e.g., peer support, case management, pharmacotherapy for SUDs, housing) and the appropriate individual interventions needed to support overall ART adherence.

Commonly Used Substances and Their Impact on HIV and Antiretroviral Therapy

Health care providers should have a basic understanding of evidence-based pharmacologic and behavioral (e.g., cognitive behavioral therapy, motivational interviewing, motivational enhancement therapy, contingency management) treatments for different substances, including alcohol, benzodiazepines, cannabinoids, club drugs, opioids, stimulants (cocaine and methamphetamines), and tobacco. The sections below discuss the impact of these substances on people with HIV and how these substances affect ART use.

Alcohol

Epidemiology

Alcohol consumption is common among people with HIV. Recent estimates indicate that >50% of people with HIV in the United States consume any amount of alcohol (range, 54% to 67%).[33,34] Among a sample of people with HIV across seven university-based HIV clinics in the United States, 27% of people screened positive for unhealthy alcohol use as determined by the AUDIT-C.[34] Unhealthy alcohol use includes a spectrum of consumption, including at-risk or hazardous use, heavy episodic use (binge drinking), and alcohol use disorder (AUD).[35]

Risk-Taking Behaviors, the HIV Care Continuum, and Comorbidities

Unhealthy alcohol use has been linked to HIV acquisition because it can increase the frequency of behaviors that put a person at risk for sexual transmission of HIV.[36-38] In a meta-analysis of 27 studies, any alcohol use, unhealthy alcohol use, and alcohol use in sexual contexts all were associated with condomless sex among people with HIV.[37]

In addition, unhealthy alcohol use has been associated with interruptions in all steps of the HIV care continuum, including lower adherence to ART.[39,40] Studies have demonstrated both temporal and dose-related relationships between alcohol use and adherence, where ART is more likely to be missed on a given drinking day and the day after drinking, with a stronger association on heavy (binge) drinking days.[41-43] The negative impact of unhealthy alcohol use on ART adherence is likely multifactorial and driven by the effects of intoxication, ARV regimen complexity, and patient perceptions of adverse interactions between alcohol and ARV drugs.[44-46] Studies also have demonstrated an association between unhealthy alcohol use and the loss of durable viral suppression,[47-49] greater time spent with a viral load >1,500 copies/mL after ART initiation,[50] increased risk of viral rebound, lower retention in care,[51,52] and increased mortality.[53-55] Unhealthy alcohol use alone (hazardous or AUD) and in combination with other common comorbidities, including viral hepatitis coinfection, can hasten liver fibrosis progression in people with HIV.[56,57] Finally, in general medical populations, unhealthy alcohol use complicates the management of diabetes mellitus, hypertension, mental health disorders, other substance use, and other chronic diseases, and it increases the risk for pneumonia, osteoporosis, a number of cancers (e.g., liver, head and neck, and breast cancers), and tuberculosis.

Management of Unhealthy Alcohol Use

Ongoing alcohol use is not a contraindication for a person to receive ART. However, treatment for unhealthy alcohol use may improve HIV treatment outcomes. Behavioral treatments for unhealthy alcohol use among people with HIV demonstrate a small but significant reduction in alcohol use[58,59] (see additional resources for alcohol management from the National Institute on Alcohol Abuse and Alcoholism and the Substance Abuse and Mental Health Services Administration [SAMHSA]). Pharmacotherapy also can reduce alcohol use among people with HIV. The FDA has approved three pharmacotherapies for AUD: naltrexone, disulfiram, and acamprosate (see Table 16 below).

Clinical trials have demonstrated the efficacy of naltrexone in reducing the number of heavy drinking days among those with HIV and among the general population. Naltrexone appears to be safe to use in people with HIV,[60,61] and it is not associated with significant drug–drug interactions or irreversible hepatotoxicity. However, it is not recommended for individuals with decompensated liver disease and should be used with caution in individuals with elevated transaminase levels. Use of naltrexone in people with HIV and AUD can improve HIV treatment outcomes.[62] In a randomized placebo-controlled trial of 100 prisoners with HIV who met the criteria for AUD, individuals who were

provided depot naltrexone upon release from prison were more likely to achieve viral suppression at 6 months than the placebo group (56.7% vs. 30.3%).[61]

Data on the use of disulfiram and acamprosate among people with HIV are lacking. Notably, integrating treatment for AUD with treatment for HIV has been shown to increase the number of people who receive alcohol treatment medication, counseling, and formal outpatient alcohol treatment services. Integrating these treatments also may improve the likelihood that a person with HIV will achieve viral suppression on ART. A randomized controlled trial of 128 individuals with HIV and AUD compared an integrated stepped-care model of alcohol treatment in Veterans Administration HIV clinics to treatment as usual. At the end of treatment (24 weeks), integrated stepped-care resulted in more participants receiving pharmacotherapy for AUD and participating in counseling. Although differences in alcohol use and viral suppression were not seen at 24 weeks, at 52 weeks, integrated stepped-care was associated significantly with an increased number of alcohol-abstinent days, a decrease in the number of drinks per drinking day, and a decreased number of heavy drinking episodes. In addition, the participants in the stepped-care group had increased odds of achieving viral suppression (odds ratio [OR] 5.58; 95% CI, 1.11–27.99).[63]

Liver cirrhosis—whether related to chronic heavy alcohol use, viral hepatitis, or metabolic dysfunction–associated steatotic liver disease—can result in altered metabolism of ARV drugs. For those who have hepatic impairment due to alcohol-related liver disease, ART dosing should follow the recommendations in Appendix B, which are based on Child-Pugh classifications.

Benzodiazepines

Epidemiology

While the specific epidemiologic data on the prevalence of benzodiazepine use among people with HIV are limited, benzodiazepine misuse is a growing public health concern due to its impact on both morbidity and mortality.[64] Benzodiazepines cause anterograde amnesia, defined as difficulty recalling events after taking the medication. Individuals do not develop tolerance to this neurocognitive effect, and long-term use of benzodiazepines may result in impairment of neurocognitive functioning.[65]

Risk-Taking Behaviors and the HIV Care Continuum

People who inject drugs and who also use benzodiazepines engage in riskier behaviors than people who inject drugs but do not use benzodiazepines; these behaviors may include paying for sex, sharing injection equipment with more people, and performing more frequent injections.[66] A cohort of 2,802 people who injected drugs was followed from 1996 to 2013. During that time, benzodiazepines were the substances with the greatest association with mortality.[67] In a study of opioid and benzodiazepine use and all-cause mortality among 64,602 veterans (16,989 with HIV and 47,613 without) from the Veterans Aging Cohort Study (VACS) cohort (October 2008 to September 2009), long-term benzodiazepine receipt was associated with increased mortality regardless of long-term opioid receipt.[68] The long-term neurocognitive impact of benzodiazepines on ART adherence among people with HIV is unclear, but prescribing a memory-impairing medication to people with HIV who are prone to neurocognitive impairments from other causes may increase the risk of poor ART adherence.[69] Benzodiazepines also are used illicitly to counteract the negative side effects of stimulants, such as cocaine and methamphetamine.[70]

Management of Benzodiazepine Use

Repeated use of benzodiazepines can result in physiologic dependence and life-threatening withdrawal in some people. When feasible, individuals who chronically use benzodiazepines should

be slowly tapered off the benzodiazepines under the supervision of an experienced clinician. Different benzodiazepines have different potencies (e.g., alprazolam is more potent than diazepam) and, therefore, require different tapers in terms of length and graduated decrease in dosage.

Benzodiazepine and Antiretroviral Drug Interactions

Several pharmacological interactions between benzodiazepines and ARV drugs have also been described. For example, some benzodiazepines are cytochrome P450 (CYP) 3A4 substrates; thus, when these benzodiazepines are used with a ritonavir (RTV)-boosted or cobicistat (COBI)-boosted ARV drug, their half-lives and concentrations can increase significantly, leading to enhanced and prolonged sedating effects. See Drug–Drug Interactions for available data on benzodiazepine-related interactions.[71]

Cannabis and Cannabinoids

Epidemiology

Both medical and recreational cannabis (marijuana) use are prevalent among people with HIV.[72] Cannabis belongs to a class of compounds that activate cannabinoid receptors. This class, known as cannabinoids, also includes synthetic compounds, such as K2. In recent years, cannabinoids have become more popular. In 2009, two cannabinoids were reported to the National Forensic Laboratory Information System. By 2015, 84 compounds had been reported.[73] These compounds most commonly cause tachycardia, agitation, and nausea, but they have a wide range of psychiatric effects, including psychosis and paranoia.[74]

Risk-Taking Behaviors and the HIV Care Continuum

Cannabis has not been shown to negatively impact adherence to ART or a person's ability to achieve viral suppression. In one study, among 874 people with HIV, daily cannabis use did not predict lower odds of ART use or achieving an undetectable HIV RNA level, except when combined with binge drinking.[75] Data from the Multicenter AIDS Cohort Study have supported the idea that marijuana use does not predict problems with adherence to ART or achieving viral suppression.[76] In some cases, however, cannabinoids have been listed as the cause of death in overdoses. While data are lacking among adults with HIV, the nationally representative 2015 Youth Risk Behavior Survey (which includes data from 15,624 adolescent students in Grades 9 to 12) found that students who had ever used synthetic cannabinoids engaged in riskier activities, including sex, than students who only used marijuana.[77] While the available data suggest that the use of marijuana is not associated with decreased adherence to ART,[78] data are lacking on the impact of synthetic cannabinoids on ART adherence. Finally, with the growing use of synthetic cannabinoids, there is concern that fentanyl could be added to these products, which may increase the risk of opioid overdose.

Management of Cannabis and Cannabinoid Use

Because of the aforementioned concerns regarding cannabinoid use, particularly the variety of compounds and neuropsychiatric effects, people with HIV should be discouraged from using cannabinoids until more data are available. No pharmacological treatment exists for cannabinoid use disorder; however, behavioral health treatment may be effective for some people.[79-81]

Club Drugs

Epidemiology

Club drugs are recreational substances that have euphoric or hallucinogenic effects or that are used to enhance sexual experiences.[5] The use of multiple club drugs or other drugs simultaneously is common. Although these substances are used by many different people with HIV, the majority of data come from MSM with HIV. The use of club drugs in this population has been shown to negatively impact HIV treatment.[82] Club drugs include MDMA, GHB, ketamine, benzodiazepines (see the benzodiazepine section above), and other drugs that are used to enhance sexual experiences (e.g., mephedrone, inhaled nitrates [poppers], and phosphodiesterase-5 inhibitors [PDE5] for erectile dysfunction). Survey data from users of club drugs also have revealed that efavirenz is purchased by people without HIV for its intoxicating effects.[83]

Risk-Taking Behaviors and the HIV Care Continuum

Club drugs have disinhibitory effects. Using club drugs increases the likelihood that a person will engage in high-risk sexual practices, which can increase the risk of HIV transmission. In addition, these disinhibitory effects can lead to poor ART adherence.[71,82,84]

Management of Club Drug Use

Treatment strategies for club drug use have not been well studied in controlled trials.[85] No recommended pharmacotherapies exist at this time, and the most common strategy for treating people who use club drugs is to employ the behavioral interventions that are used for other drug use disorders.

Club Drug and Antiretroviral Drug Interactions

MDMA, GHB, ketamine, and methamphetamine all have the potential to interact with ARV drugs because they are metabolized, at least in part, by the CYP450 system.[71,84] Overdoses secondary to interactions between club drugs (i.e., MDMA or GHB) and protease inhibitor–based ART have been reported.[71,86] For instance, using PDE5 or ketamine concurrently with potent CYP3A4 inhibitors, such as RTV or COBI, can potentiate the effects of these substances.[82]

Cocaine

See the discussion in the section on stimulants below.

Opioids

Epidemiology

Opioids remain a significant concern for people with HIV, both for the acquisition of HIV and as major contributors to morbidity and mortality. Overdose involving opioids is the leading cause of accidental death in the United States.[87] The appropriate use of opioids while caring for people with HIV and chronic pain is an important component of combating the opioid epidemic, but this subject is beyond the scope of this section. Please refer to additional resources, such as those from the Centers for Disease Control and Prevention (CDC) and the Infectious Diseases Society of America.[88] To combat the opioid overdose epidemic, health care providers should prescribe naloxone for opioid overdose prevention for all people who are using opioids beyond the short-term treatment of acute pain.[3]

Risk-Taking Behaviors and the HIV Care Continuum

Many people who use opioids start by using opioid tablets (e.g., oxycodone) that are ingested orally or crushed and sniffed. Once tolerance develops, some individuals move from sniffing the crushed tablets to injecting heroin purchased on the streets. This transition from sniffing to injecting dramatically increases the risk of HIV and HCV infection.

Low-cost heroin is often a mix of heroin and higher-potency synthetic opioids, such as fentanyl.[87] Methamphetamines and cocaine also have been combined with fentanyl but at a lower rate than heroin.[89,90] With the growing use of synthetic cannabinoids, there is concern that fentanyl could be added to these as well. In all instances where fentanyl or other high-potency opioids are added to other drugs, the risk of overdose increases.

Although treatment for an opioid use disorder (OUD) can improve HIV treatment outcomes, it is not a prerequisite for treating HIV, as some people with HIV are able to adhere successfully to ART despite ongoing opioid use. Although ART coverage among people with HIV who injected drugs increased from 58% to 71% between 2009 and 2015, additional work is needed to improve ART coverage in this population.[91] Data from the Johns Hopkins HIV Clinical Cohort (2001–2012) demonstrated that in the early years of the cohort, people who injected drugs were less likely to be retained in care; however, this gap in retention had closed by 2012, and people who injected drugs and noninjectors had similar probabilities of being on ART and having a suppressed viral load during the later years of the cohort.[92]

Management of Opioid Use

FDA has approved three medications for the treatment of OUD that can help decrease or eliminate opioid use, reduce the risks of morbidity and mortality that are associated with opioid use, and improve HIV treatment success. These medications—collectively termed medications for opioid use disorder (MOUD)—include buprenorphine, methadone, and naltrexone (see Table 16 below). Buprenorphine and methadone are opioid agonists (the use of these drugs is termed opioid agonist therapy), whereas naltrexone is an opioid antagonist or "blocker." Both buprenorphine and naltrexone can be prescribed in the setting of routine HIV clinical care.[93] Prescribing buprenorphine requires specific training but no longer requires an X waiver (see the SAMHSA website for more information). Methadone must be prescribed through a licensed opioid treatment program (OTP). An OTP directory also can be found on the SAMHSA website.[94]

Use of buprenorphine or methadone can lead to reductions in risky behaviors associated with HIV transmission, psychosocial and medical morbidity related to OUD, and criminal behaviors. People who are receiving treatment for opioid use are already engaging with the health care system; therefore, they are more likely to initiate treatment for HIV and to be adherent to their ARV regimens. Both buprenorphine and methadone are cost-effective interventions at the societal level.[95] Methadone has better retention in SUD treatment than either buprenorphine or naltrexone, and it should be considered for individuals who do not achieve successful outcomes with buprenorphine or naltrexone.[96] Buprenorphine has a lower risk of overdose than methadone. In addition, it can be prescribed in primary care offices. People who are taking buprenorphine have significantly better retention in treatment than those who are taking daily oral naltrexone.[97] Although several randomized, controlled clinical trials have demonstrated efficacy for naltrexone when treating OUD, subsequent study results have been disappointing; one meta-analysis revealed that oral naltrexone was equivalent to placebo.[98] To address the adherence challenges with naltrexone, a depot formulation was created for monthly administration. This preparation has the potential to improve adherence; however, studies that compare opioid agonists (i.e., buprenorphine and methadone) to depot naltrexone as treatments for OUD have not been conducted. In a randomized, placebo-controlled trial in people with both HIV and OUD, participants who received at least three doses of

depot naltrexone before discharge from prison achieved longer periods of continuous abstinence after transitioning from prison to the community than those who received either placebo or two or less doses of depot naltrexone.[61] On the basis of these data, methadone or buprenorphine generally are used as first-line agents for the treatment of OUD. Depot naltrexone is used as an alternative treatment for people who have been released recently from correctional facilities when other options are not available.

Important pharmacokinetic interactions between these medications (particularly methadone) and certain ARV drugs are listed in Drug–Drug Interactions.

Although medications remain the backbone of treatment for OUD, there is growing recognition of the critical importance of the social drivers of health and how they impact the willingness of people to engage in treatment with the medications discussed above. A recent randomized study of 114 people with HIV compared the effectiveness of different medications for the treatment of OUD to achieve viral suppression, finding that stable housing, high school–level education or greater, and income stability were associated with a greater reduction in opioid use.[94]

Xylazine and Opioids

Xylazine—a non-opioid analgesic utilized in veterinary medicine that is a commonly used adulterant in opioids and other substances—has become an emerging drug threat associated with the opioid epidemic.[99] The CDC has documented a 276% increase in the monthly percentage of illicitly manufactured fentanyl (IMF)–involved deaths where xylazine was detected.[100] Between 2020 and 2021, the Drug Enforcement Agency reported that xylazine-associated deaths increased by over 100% in all regions of the United States and over 1,000% in the South.[101] This growing body of data led the ONDCP to formally designate fentanyl adulterated with xylazine as an emerging drug threat.[102]

Xylazine is a substrate of CYP3A4 and, as such, when used with an ARV regimen including a CYP3A4 inhibitor, such as RTV or COBI, may lead to elevated levels and prolonged half-lives of xylazine.[103] For people with HIV who continuously use opioids in areas with high rates of xylazine-adulterated IMF, providers should weigh the risks and benefits of using ARV drugs with CYP3A4 inhibitors, given potential interactions and the increase in xylazine-associated adverse effects.

Opioid adulterants, such as xylazine, increase the risk of overdose. Although naloxone only reverses opioid effects, that alone may be sufficient to reverse the overdose. This highlights the need for universal access to naloxone and the active prescribing of naloxone by health care providers. The CDC maintains information about xylazine and how to reduce its harm on its website.[104]

Stimulants

Epidemiology

Cocaine and methamphetamine are powerful stimulants that have been associated with multiple detrimental effects among people with HIV, including accelerated disease progression, poor ART adherence, and lack of viral suppression. Cocaine powder is snorted or injected, whereas the free-base form (crack) is smoked. Methamphetamines can be taken orally or rectally, injected, or smoked. Cocaine and methamphetamine are commonly used with other substances, including alcohol, and can be combined with fentanyl, which increases the risk of overdose.[89,90] Individuals who use stimulants experience a sense of euphoria and may have heightened sexual desire and arousal. This can lead to disinhibited sexual behaviors, increasing the risk of HIV transmission.

The prevalence of stimulant use among people with HIV has been estimated to be 5% to 15% across multiple studies.[105-107] Methamphetamine use is more common among MSM,[108] and increased rates of cocaine use have been observed among ethnic and racial minorities and persons with a history of incarceration.[109]

Risk-Taking Behaviors and the HIV Care Continuum

People with HIV who use stimulants may experience multiple negative health consequences, including rapid development of dependence and adverse effects on multiple organ systems, particularly the central nervous and cardiovascular systems. Stimulant use is associated with neurocognitive impairment,[110] delirium, seizures, hemorrhagic strokes, and mental health disturbances, including anxiety, psychosis, and paranoia.

Stimulant use may independently lead to HIV disease progression even among people who are taking ART and have achieved viral suppression. Research to identify the cellular mechanisms responsible for this is ongoing, but increased viral replication, direct effects on the immune system that lead to declines in CD4 T lymphocyte cell count, enhanced immune activation, and disruption of the blood-brain barrier, facilitating HIV entry into the brain, have been implicated.[111-115] Stimulant use has been associated with poor HIV continuum of care outcomes, including suboptimal rates of ART adherence,[116] retention in care, and viral suppression.[117-119] Lack of viral suppression, combined with the increased likelihood of risky sexual behaviors that occur under the influence of stimulants, poses a threat to the HIV treatment-as-prevention paradigm.[120]

Management of Stimulant Use

Several pharmacologic and behavioral interventions for stimulant dependence have been investigated, and some trials have included people with HIV. The results of pharmacologic interventions generally have been disappointing. No FDA-approved pharmacotherapy for cocaine use disorder currently exists, despite research on multiple drug classes, including antidepressants, antipsychotics, anticonvulsants, and dopaminergic medications (e.g., disulfiram).[121,122] Among people with HIV who use crack and opioids, medication-assisted treatment for OUD may improve ART adherence and viral suppression.[123,124] Limited evidence indicates that some pharmacologic interventions (e.g., methylphenidate, modafinil, bupropion, naltrexone)[125] can reduce methamphetamine use or cravings. A double-blind, placebo-controlled trial of extended-release injectable naltrexone plus oral extended-release bupropion in adults with moderate or severe methamphetamine use disorder demonstrated a higher response of methamphetamine-free urine samples compared to placebo; however, the overall response rate was low.[126] A double-blind randomized clinical trial on people with methamphetamine use disorder evaluated daily mirtazapine versus placebo in individuals who have sex with men. Over 36 weeks of follow-up, daily mirtazapine use led to reduced methamphetamine-positive urine drug tests and concurrent reductions in sexual risk behaviors.[127] No specific recommended pharmacotherapy exists to treat stimulant use disorder in people with HIV.

Several behavioral interventions have shown promise in randomized trials. People with HIV who received motivational interviewing sessions, cognitive behavioral therapy, or a combination of the two experienced decreased stimulant use, improved ART adherence, and were less likely to engage in sexual transmission risk behaviors.[128] Contingency management has been shown to be effective in decreasing stimulant use among people with HIV, but the sustained effects on the reduction of stimulant use and improvements in ART adherence are less clear.[106,129,130] The addition of a positive affect intervention to contingency management, compared with an attention control condition, decreased HIV viral load among gay, bisexual, and other MSM with HIV.[131] Technology-based interventions, such as text messaging, may have a role in supporting ART adherence and decreasing methamphetamine use among people with HIV, but further research is needed.[132]

People with HIV who use stimulants benefit most from multidimensional interventions that target substance use, ART adherence, and risky sexual behaviors.[128]

Despite the challenges discussed above, people with HIV who use stimulants can achieve viral suppression with ART[119] and should be prescribed ART even if stimulant use is ongoing.

Tobacco

Epidemiology

The prevalence of tobacco smoking among people with HIV in the United States is approximately twice that of the general population (33.6% vs. 16.8%).[133] Prevalence is even higher among specific subgroups, including those who use alcohol and/or other drugs, those who have concurrent mental health disorders, and those of a lower socioeconomic status. Although smoking rates are declining overall in the United States, people with HIV are less likely to quit smoking than people in the general population.[133]

Associated Risks of Tobacco Use and HIV Infection

With respect to substance use and HIV, tobacco smoking is the biggest threat to health-related gains achieved through ART. Among individuals with viral suppression on ART, more years of life may be lost from continued smoking than from HIV infection itself.[134,135] Tobacco smoking among people with HIV is associated with an increased risk of numerous health conditions, including lung cancer and other smoking-related cancers, cardiovascular disease, and pulmonary disease. In a sample of 17,995 people with HIV on ART in Europe and North America, individuals who smoked had nearly twice the mortality of those who did not (mortality rate ratio 1.94; 95% CI, 1.56–2.41) with significant mortality attributed to cardiovascular disease and non-AIDS-related malignancy.[134] Importantly, tobacco cessation reduces the incidence of cardiovascular disease and smoking-related cancers (although definitive data on lung cancer are not available) and improves quality of life.[136-138]

Managing Tobacco Use

To maximize the survival benefits of ART, clinicians should consider using evidence-based behavioral and pharmacological[139-141] cessation strategies when treating people with HIV who smoke tobacco (see the tools and recommendations provided by the CDC and the U.S. Preventive Services Task Force and recent review).[142] These include (but are not limited to) advising the individual to quit smoking, using the five A's, employing motivational interviewing, and referring them to a tobacco quitline. Pharmacotherapies for smoking cessation (nicotine replacement therapy, bupropion, and varenicline) have few clinically significant interactions with ARV drugs and can lead to enormous reductions in morbidity and mortality if the person is able to stop smoking. Nicotine replacement is efficacious[143]; however, bupropion doubles rates of smoking cessation compared with nicotine replacement therapy.[144] Varenicline is a partial nicotine receptor agonist. In comparative studies, varenicline was more effective than bupropion in smoking cessation.[144,145] Clinical trials among people with HIV have found varenicline to be both effective and safe.[139,141] In a randomized controlled trial among 179 individuals with HIV who were assigned to receive 12 weeks of behavioral counseling and either varenicline or placebo, varenicline use led to an increase in the percentage of participants who achieved a 7-day abstinence period at 12 weeks (28.1% vs. 12.1%, OR 4.5; 95% CI, 1.83–11.2) and produced higher continuous abstinence between Weeks 9 and 12 (23.6% vs. 10%, OR 4.65; 95% CI, 1.71–12.67) compared to placebo.[141] Although significant between-group differences were not observed after 24 weeks, these data support the use of varenicline among people with HIV. Varenicline should be used in combination with relapse prevention strategies and other measures for long-term tobacco cessation.

Table 16. Medications for Treatment of Substance Use Disorders

Medication	Dose and Recommendations	Potential Interaction With ARV Drugs	Comments
Alcohol Use Disorder			
Acamprosate	666 mg PO three times a day *or* 333 mg PO three times a day for people with CrCl 30–50 mL/min	No significant interaction with ARV drugs expected.	**Contraindicated** in people with CrCl <30 mL/min
Disulfiram	250 mg PO once daily	Use with caution when prescribing an ARV oral solution that contains ethanol and/or propylene glycol (e.g., FPV, LPV/r, RTV).	Counsel people regarding disulfiram reaction when taken with alcohol; symptoms for the reaction may include flushing, tachycardia, nausea, vomiting, or hypotension.
Naltrexone	50–100 mg PO once daily Depot formulation is a fixed-dose monthly injection.	No significant interaction with ARV drugs expected.	Has the greatest efficacy of all FDA-approved medications for AUD.
Opioid Use Disorder			
Buprenorphine	Individualize buprenorphine dosing based on the person's opioid use. The dose range is 4–24 mg sublingually. Dosing is once daily or twice daily.	Potential interaction with ARV drugs that are CYP inhibitors or inducers. See Drug–Drug Interactions for further recommendations.	Buprenorphine has 90% first-pass hepatic metabolism. Verify that the person is using the appropriate technique for sublingual administration before adjusting the dose, because improper administration will result in poor absorption and low drug levels.
Methadone	Individualize the dose. People who receive higher doses (>100 mg) are more likely to remain in treatment.	Potential interaction with ARV drugs that are CYP inhibitors or inducers. See Drug–Drug Interactions for further recommendations.	QTc prolongation is a concern at higher doses. Methadone can be prescribed for OUD only by a licensed OTP.
Naltrexone	50–100 mg PO once daily Depot formulation is a fixed-dose monthly injection.	No significant interaction with ARV drugs expected.	Longer time of continuous abstinence in those who received depot formulation naltrexone compared with placebo after transition from prison to community.

Table 16. Medications for Treatment of Substance Use Disorders

Medication	Dose and Recommendations	Potential Interaction With ARV Drugs	Comments
Nicotine Use Disorder			
Nicotine Replacement Therapy	The FDA has approved a wide variety of nicotine replacement products. All formulations are effective.	No significant interaction with ARV drugs expected.	Work with the person to identify the route of delivery that they will use and find most helpful.
Bupropion	Start at 150 mg PO daily for 3 days, then increase to either 150 mg twice daily or 300 mg once daily (use only formulations that are approved for once-daily dosing).	Concentration may be reduced when used with ARV drugs that are CYP2D6 inducers. See Drug–Drug Interactions for further recommendations.	For optimal results, tobacco quit date should occur 1 week after starting therapy.
Varenicline	Titrate the dose based on tolerability until the desired effect is achieved. The goal is to reach a dose of 1 mg PO twice daily. Requires dose adjustment in people with CrCl <30 mL/min.	No significant interaction with ARV drugs expected.	For optimal results, tobacco quit date should occur 1 week after starting therapy.

Key: ARV = antiretroviral; AUD = alcohol use disorder; CrCl = creatinine clearance; CYP = cytochrome P450; FDA = U.S. Food and Drug Administration; FPV = fosamprenavir; LPV/r = lopinavir/ritonavir; OTP = opioid treatment program; OUD = opioid use disorder; PO = orally; QTc = QT corrected for heart rate; RTV = ritonavir

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Transplantation in People With HIV

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Panel's Recommendations and Key Considerations
• People with HIV who are eligible for solid organ transplant (SOT) or hematopoietic cell transplant (HCT) should have equitable access to transplant **(AII).** • People with HIV should be managed by a multidisciplinary team before, during, and after transplant **(AIII).** • Transplant candidates with HIV should be up-to-date on their vaccination schedule **(AIII).**
Antiretroviral Drug Considerations Before Transplant

• In preparation for transplant, HIV providers should review the transplant candidate's antiretroviral (ARV) history, efficacy of the current ARV regimen, prior HIV drug resistance results, ARV adherence, and the potential for drug–drug interactions **(AIII).**
• All ARV regimen changes should be guided by ARV history, along with current and prior HIV drug resistance testing results **(AIII).**
• If switching to an alternative ARV regimen is necessary, changes should be completed several weeks before the transplant whenever possible to minimize drug–drug interactions in the post-transplant period and to assure tolerability and efficacy of the new regimen before transplant **(BIII).**
• Tenofovir alafenamide (TAF) is preferred over tenofovir disoproxil fumarate (TDF) in transplant candidates and recipients due to the lower risk of affecting renal function and bone mineral density **(AII).**
• To avoid significant drug–drug interactions between ARV drugs and anticipated immunosuppressive therapies, chemotherapies (for HCT), and prophylactic regimens for opportunistic infections, the following should be considered:
  ○ Unboosted second-generation oral integrase strand transfer inhibitor (INSTI)–based regimens (i.e., with bictegravir or dolutegravir) are preferred in most people with HIV needing transplant **(AII).**
  ○ In general, potent cytochrome P450 (CYP) 3A4 inhibitors—including pharmacokinetic boosters, such as ritonavir (RTV) or cobicistat (COBI), and protease inhibitor (PI)-containing regimens—should be avoided **(AII).**
  ○ In general, non-nucleoside reverse transcriptase inhibitors (NNRTIs) such as nevirapine (NVP), efavirenz (EFV), and etravirine (ETR), which are CYP3A4 inducers, should be avoided **(AII).**

Maintenance of Viral Suppression
• HIV viral suppression should be maintained before and after transplant **(AIII).*** • HIV providers with appropriate expertise should design alternative ARV regimen(s) that are likely to achieve viral suppression if post-transplant regimen changes are necessary **(AIII).**
Immediately Post-Transplant
• Immediately post-transplant, renal or hepatic function may fluctuate; close monitoring of these organ functions is recommended to ensure appropriate dosing of ARV drugs and other concomitant medications to avoid potential drug toxicities **(AIII).** • Interruption of antiretroviral therapy (ART) post-transplant should be avoided **(AIII).** • If interruption is necessary, all components of an oral ART regimen should be stopped simultaneously to avoid exposure to an incomplete regimen. The period of interruption should be kept to a minimal duration **(AIII).** • If a person cannot swallow pills, providers should consider using oral liquid formulation if available; alternatively, some pills can be crushed or dissolved for administration orally or via an enteral tube **(AIII).**

Post-Transplant
• Therapeutic drug monitoring for immunosuppressive drugs should be performed to guide dosing adjustments, especially before, during, and after the start or switch of ARV drugs that may interact with immunosuppressive drugs **(AII).** • The burden of medication increases significantly post-transplant. Providers should continue to evaluate for potential drug–drug interactions and overlapping toxicities with the addition of new medications **(AIII).**   ○ When feasible, providers should consider consolidating ART using fixed-dose combination tablets and/or single-tablet regimens to minimize pill burden and bolster adherence **(AIII).**
Hepatitis B Virus or Hepatitis C Virus Coinfection
• All donors and recipients should be screened for hepatitis B virus (HBV) and hepatitis C virus (HCV) with a serological and/or nucleic acid amplification test, according to transplant guidelines **(AIII).** • Transplant candidates and recipients who are nonimmune to HBV (as measured by HBV surface antibody [HBsAb]) should be vaccinated, ideally before transplant **(AIII).** • HBV serology should be monitored after transplant for loss of HBsAb in order to guide the need for revaccination per professional society and transplant center guidelines **(AIII).** • Transplant recipients with active HBV infection should be treated with ARV regimens with anti-HBV activity before transplant and indefinitely after transplant **(AIII).** Use of nucleos(t)ide reverse transcriptase inhibitors (NRTIs) with activities against both HIV and HBV is strongly recommended unless contraindicated or not tolerated **(AIII).** • For management of recipients with HIV without HBV who receive an organ from a donor with markers of HBV infection, see guidance in the HBV-Positive and HCV-Positive Donors section below and follow appropriate institutional protocols. • All transplant candidates and/or recipients with HCV infection should be treated with direct-acting antivirals against HCV **(AII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*
* In some cases, it may be necessary to interrupt ART due to intolerance of or inability to administer ARV drugs pre-transplant, such as in end-stage liver disease or when enteral access is limited. In these situations, the HIV provider should design a regimen that will result in viral suppression after transplant and resume therapy as soon as feasible.

General Principles When Managing People With HIV Before and After Transplant

Below are some key principles to follow when caring for people with HIV before and after transplant.

- Ensure that people with HIV have equitable access to transplant.
- Utilize a multidisciplinary approach.
- Maintain HIV viral suppression.
- Select or maintain an antiretroviral (ARV) regimen to minimize drug–drug interactions.
- Be aware of changes in renal or liver function.
- Perform therapeutic drug monitoring (TDM) of immunosuppressants for all transplant recipients.
- Consider pill burden.

- Consider and address hepatitis B virus (HBV) and hepatitis C virus (HCV) coinfection.
- Prevent infectious complications post-transplant with updated vaccination and antimicrobial prophylaxis.

Outcomes of Transplant in People With HIV and the Importance of Equitable Access to Transplant

Before the introduction of potent antiretroviral therapy (ART), people with HIV were systematically denied solid organ transplantation (SOT).[1] When performed, SOT was linked to unfavorable outcomes,[2] partly attributed to the use of older antiretroviral (ARV) regimens that included protease inhibitors (PI), which interact with immunosuppressive medications, such as calcineurin inhibitors or mTOR inhibitors.[3] SOT also had unfavorable outcomes in people with HIV and HCV coinfection before the era of direct-acting antivirals (DAAs) for HCV treatment.[4] The use of PIs also affects the choice of DAAs for HCV treatment. In the era of integrase strand transfer inhibitors (INSTIs) with fewer drug–drug interactions and the widespread availability of DAAs for HCV, recent cohorts have shown a reduction in the disparity of transplant outcomes between people with and without HIV.[5-7]

In people with end-stage renal disease (ESRD), those with HIV are less likely to be referred for kidney transplant than those without HIV. With the use of potent ART, kidney transplant in people with HIV is associated with a survival benefit over chronic hemodialysis, with high rates of recipient and graft survival at both 1 and 3 years post-transplant.[8] Lower but acceptable rates of recipient and graft survival have been reported with long-term (between 5 and 15 years) follow-up when comparing kidney and liver transplantation outcomes in people with HIV compared with recipients without HIV. This difference was primarily driven by lower rates of survival in people with HIV/HCV coinfection before the use of DAAs for HCV treatment.[6,9] In retrospective studies conducted in the post-DAA era, rates of recipient and graft survival in liver transplant recipients with HIV/HCV appear to be similar to people with HIV without HCV.[5,6] Acute rejection rates for kidney transplant recipients are higher in people with HIV than in recipients without HIV.[10]

Hematopoietic cell transplants (HCTs) in people with HIV are now the standard of care in people with hematologic malignancies for which HCT is indicated.[11] In most reported prospective and retrospective studies in the combination ART era, HIV status does not appear to impact the outcome of autologous or allogeneic HCT with respect to nonrelapse mortality. Allogeneic HCT is particularly intriguing due to its potential to significantly reduce HIV reservoirs or even achieve a cure, particularly when complete chimerism is achieved and the donor is CCR5delta32 homozygous. It is important to note that acute and even life-threatening viral rebound can occur if ART is discontinued after HCT. Planned ARV interruptions should only be attempted in the setting of a clinical trial.[11-16]

Given the improved outcomes and benefits to quality of life and other measures associated with transplantation, transplant eligibility should be equitable between people with and people without HIV **(AII).** Infectious complications and malignancy risk remain a concern post-transplant. For discussion of transplantation from donors with HIV to recipients with HIV, see Solid Organ Transplant Considerations From Donors With HIV below.

Multidisciplinary Approach

With the complexity of care required before, during, and after transplant in people with HIV, a multidisciplinary team approach is recommended, including transplant-specific specialists such as nephrologists, hepatologists, hematologists, infectious disease and HIV specialists, transplant surgeons, pharmacists, nurses, and social workers **(AIII).** This approach is to ensure favorable outcomes and to effectively prevent and manage adverse events.

Antiretroviral Therapy Before, During, and After Transplant

This section of the guidelines will focus on special considerations for ART use before, during, and after SOT or HCT in people with HIV.

Maintain HIV Viral Suppression

Before and after a transplant, it is crucial to ensure that HIV suppression is maintained **(AIII).** This involves continuing ART as prescribed and closely monitoring viral load. Consistent adherence to ART is essential to prevent HIV viral rebound and maintain overall immune health. However, interruption of ART may be necessary in certain situations, such as intolerance of or inability to take oral ARV drugs pre-transplant, which may occur in some people with end-stage liver disease or when enteral access is limited post-transplant. In these situations, an ART regimen that will result in viral suppression after transplant should be resumed as soon as feasible**.**

Antiretroviral History and Review of Drug Resistance Testing Results

Before transplant and before starting, stopping, or changing any ARV drug, it is essential to review the person's ART history and any current and previous drug resistance testing results. This review guides the selection of an appropriate ARV regimen that will maintain or result in viral suppression.

If a person with wild-type HIV achieves and maintains viral suppression after starting ART, it is generally safe to assume that no drug resistance mutations have developed during that time. However, for people who have experienced virologic failure in the past, it is important to thoroughly review their resistance test results and their clinical and virologic responses to previous regimens when designing a new treatment plan.

Cumulative resistance test results encompass all previous and current test results, including genotypic, proviral DNA genotypic (if available), phenotypic, and tropism assays. Proviral DNA genotypic resistance testing can be considered in people with HIV who have suppressed viral loads and no prior drug resistance or unknown ART history information. In individuals with multiple treatment failures, proviral DNA genotypic testing may be useful but should be interpreted with caution. For additional information on proviral DNA assays, refer to the Drug Resistance Testing section.

Using the ART history and resistance results, one should be able to design at least one future suppressive regimen if changes are necessary.

Minimize Drug–Drug Interactions

Transplant recipients require multiple medications to prevent organ rejection, graft versus host disease (GVHD), and opportunistic infections, and to manage post-transplant complications. Polypharmacy can result in a complex array of drug–drug interactions. Consultation with a pharmacist with expertise in transplant, oncology, and/or HIV is recommended to aid with assessing and managing these challenging drug interactions.

Transplant-related drug interactions are commonly mediated by the cytochrome P450 (CYP) enzyme system. Below are some key principles for managing these drug–drug interactions.

- Use an ARV regimen with the lowest potential for drug interactions with medications used post-transplant, such as immunosuppressants, certain chemotherapeutic agents (for HCT recipients), azoles, corticosteroids, and acid-reducing drugs.

- Unboosted, oral, second-generation INSTI-based regimens (i.e., bictegravir or dolutegravir [DTG]) are preferred for most people with HIV needing transplantation **(AII).**
- In general, potent CYP3A4 inhibitors, including pharmacokinetic (PK) boosters such as ritonavir or cobicistat and PI-containing regimens, should be avoided **(AII).**
- In general, non-nucleoside reverse transcriptase inhibitors (NNRTIs) (e.g., efavirenz, etravirine, nevirapine), which are CYP3A inducers, should be avoided **(AII).** Among NNRTIs, doravirine (DOR) has fewer drug–drug interactions; however, experience with DOR in the transplant setting is limited.
- To minimize interactions in the post-transplant period and to assure tolerability and efficacy of the new regimen before transplant, whenever possible, any necessary ARV switches should be completed several weeks before the transplant **(BIII).**
- Therapeutic drug monitoring (TDM) of immunosuppressants is recommended for all transplant recipients; this is particularly important when drug–drug interactions with ARVs are expected **(AII).** Consultation with a pharmacist is recommended.

Drug Interactions Between Antiretroviral Drugs and Immunosuppressants

Immunosuppressants such as cyclosporine, sirolimus, and tacrolimus are mainstays of therapy post-transplant to prevent organ rejection or GVHD and are metabolized by CYP3A4.[17] These immunosuppressants have a narrow therapeutic window for efficacy and toxicity, and their drug concentrations may be impacted by ARV drugs that are CYP3A4 inhibitors or inducers because significant changes in their exposure may occur. There are limited data and experience evaluating interactions between newer ARV drugs and immunosuppressants, including a lack of published studies or case reports.[18-20] Immunosuppressant dose and target drug levels depend on the type of transplant, time since transplant, transplant center-specific protocols, transplant recipients' medical conditions, and other factors. Table 17 provides information regarding expected interactions based on available data and theoretical estimates. Safe and effective use of immunosuppressants should be guided by TDM.

Table 17. Drug Interactions Between Antiretroviral Drugs and Immunosuppressants Used Post-Transplant

	Overview of Interaction Potential	Tacrolimus	Sirolimus	Cyclosporine
NRTI	↔ NRTI ↔ Immunosuppressant	Initiate standard doses. Monitor renal function if used with TDF.	Initiate standard doses. Monitor renal function if used with TDF.	Initiate standard doses. Monitor renal function if used with TDF.
NNRTI	↔ NNRTI **With EFV, ETR, and NVP** • ↓ Immunosuppressant expected	Initiate standard doses and adjust based on TDM. **With EFV, ETR, and NVP** • May need higher doses	Initiate standard doses and adjust based on TDM. **With EFV, ETR, and NVP** • May need higher doses	Initiate standard doses and adjust based on TDM. **With EFV, ETR, and NVP** • May need higher doses.

Table 17. Drug Interactions Between Antiretroviral Drugs and Immunosuppressants Used Post-Transplant

	Overview of Interaction Potential	Tacrolimus	Sirolimus	Cyclosporine
	With DOR (A Weak Inducer) • ↓ Immunosuppressant possible **With RPV** • ↔ Immunosuppressant	**With RPV** • Monitor QTc with RPV.	**With RPV** • Monitor QTc with RPV.	**With RPV** • Monitor QTc with RPV.
PI (With COBI or RTV as PK Booster)	↔ PI ↑ Immunosuppressant requiring dose reduction and/or extending dosing interval	↑ ↑ Tacrolimus Switch to a non-PI/c or PI/r-based regimen. If not possible, consider initiating tacrolimus 0.5 mg PO every 5–7 days. Adjust based on TDM.	↑ ↑ Sirolimus Switch to a non-PI/c or PI/r-based regimen. If not possible, consider initiating sirolimus 1–1.5 mg PO once weekly. Adjust based on TDM.	↑ CsA Consider initiating reduced dose of CsA at 5% to 20% of standard daily dose. Adjust based on TDM.
INSTI	↔ INSTI **For BIC, CAB, DTG, or RAL** • ↔ Immunosuppressant **With EVG/c** • ↑ Immunosuppressant with EVG/c	**For BIC, CAB, DTG, or RAL** • Initiate standard doses and adjust based on TDM. **With EVG/c** • ↑ ↑ Tacrolimus expected • Switch to a non–EVG/c-based regimen. If not possible, consider initiating tacrolimus 0.5 mg PO every 5–7 days. Adjust based on TDM.	**For BIC, CAB, DTG, or RAL** • Initiate standard doses and adjust based on TDM. **With EVG/c** • ↑ ↑ Sirolimus expected • Switch to a non–EVG/c-based regimen. If not possible, consider initiating sirolimus 1–1.5 mg PO once weekly. Adjust based on TDM.	**For BIC, CAB, DTG, or RAL** • Initiate standard doses and adjust based on TDM. **With EVG/c** • ↑ CsA expected • Consider initiating reduced CsA at 10% to 20% of total standard daily dose. Adjust based on TDM.

Table 17. Drug Interactions Between Antiretroviral Drugs and Immunosuppressants Used Post-Transplant

	Overview of Interaction Potential	Tacrolimus	Sirolimus	Cyclosporine
Capsid Inhibitors	↔ LEN expected ↑ Immunosuppressant expected	No data to guide dosing Adjust based on TDM.	No data to guide dosing Adjust based on TDM.	No data to guide dosing Adjust based on TDM.
CCR5 Antagonist, Fusion, Attachment, and Post-Attachment Inhibitors	↔ ARV drugs expected ↔ Immunosuppressant expected	Initiate standard doses. Adjust based on TDM.	Initiate standard doses. Adjust based on TDM.	Initiate standard doses. Adjust based on TDM.

Key: ↔ = No clinically significant change; ↓ = decreased; ↑ = increased; ↑ ↑ = greatly increased; ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; CCR5 = chemokine co-receptor 5; COBI = cobicistat; CsA = cyclosporine; DOR = doravirine; DTG = dolutegravir; EFV= efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; NRTI = nucleos(t)ide reverse transcriptase inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PI/c = cobicistat-boosted protease inhibitor; PI/r = ritonavir-boosted protease inhibitor; PO = orally; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TDF = tenofovir disoproxil fumarate; TDM = therapeutic drug monitoring

Drug Interactions Between Antiretroviral Drugs and Other Transplant-Related Medications

Transplant recipients often require other medications that may interact with ARV drugs via the CYP450 system or through decreased oral absorption due to altered gastric pH. These include azole antifungals, chemotherapy drugs, corticosteroids, and acid-reducing agents. A summary of these commonly encountered interactions can be found in Tables 24a to 24g. The table below is not comprehensive and is meant to highlight commonly used drug classes in transplant recipients with HIV.

Table 18. Drug Interactions Between Antiretroviral Drugs and Medications Commonly Used in Transplant Recipients

Drug Class	Examples	Effects of Interactions
Azole Antifungals	Isavuconazole Itraconazole Posaconazole Voriconazole	**CYP Inhibition (e.g., With RTV or COBI as PK Booster, Azoles)[a]** • ↑ Azole concentration, ↑ toxicities • ↑ ARV concentration possible, ↑ toxicities **CYP or Glucuronidation Induction (e.g., EFV, NVP)** • ↓ Azole concentration, ↓ efficacy

Table 18. Drug Interactions Between Antiretroviral Drugs and Medications Commonly Used in Transplant Recipients

Drug Class	Examples	Effects of Interactions
Chemotherapy	Busulfan Cyclophosphamide Etoposide[b]	**CYP Inhibition or Induction (e.g., With RTV or COBI as PK Booster)** • ↑ or ↓ Chemotherapy concentration with RTV, ↑ toxicities, or ↓ efficacy • ↑ Chemotherapy concentration with COBI, ↑ toxicities **CYP Induction (e.g., EFV, ETR, NVP)** • ↓ Chemotherapy concentration, ↓ efficacy
Corticosteroids	Dexamethasone	**Dose-Dependent CYP3A4 Induction** • ↓ ARVs that are metabolized by CYP3A4
	High-dose Prolonged Use Prednisone/Prednisolone	**CYP3A4 Inhibition (e.g., With RTV or COBI as PK booster)** • ↑ Steroid concentration, ↑ toxicities
Acid-Reducing Medications	PPI, H2 Antagonists	**Increase in Gastric pH** • ↓ Absorption of certain ARVs, including ATV or RPV. See Table 24a and 24b for recommended timing of administration if concomitant therapy is needed.

Key: ARV = antiretroviral, ATV = atazanavir; COBI = cobicistat; CYP = cytochrome P450; CYP3A4 = cytochrome P3A4; EFV = efavirenz; ETR = etravirine; H2 = histamine 2; NVP = nevirapine; PK = pharmacokinetic; PPI = proton pump inhibitor; RPV = rilpivirine; RTV = ritonavir

[a] CYP inhibition by azoles can ↑ concentrations of immunosuppressants and certain cancer chemotherapy drugs.

[b] The listed are frequently used conditioning therapy pre-hematopoietic transplants that have potential interactions with ART. For other chemotherapeutic agents, consult a clinical pharmacist with expertise in transplant-related drug–drug interactions.

Considerations When Switching Antiretroviral Drugs Due to Drug–Drug Interactions

To minimize immediate interactions in the post-transplant period, whenever possible, any necessary ARV drug switches should be completed several weeks before the transplant **(BIII).** Waiting at least five half-lives would allow for adequate elimination of any interacting ARV drugs and/or PK booster prior to transplant. Switching ART by at least several weeks before transplant also allows clinicians to assess the tolerability and efficacy of the new regimen. Clinicians should be aware that

discontinuation of certain ARV drugs may reverse previously stable drug interactions, therefore other comedications may need to be adjusted. For example, a person's immunosuppressant dose may need to be increased if the clinician is discontinuing a PI-based ARV regimen or the dose may need to be decreased if the clinician is discontinuing certain NNRTI-based regimens.

Changes in Renal or Hepatic Function

Following a kidney or liver transplant or after HCT, there may be abrupt changes in renal or hepatic function that may require dose adjustments of one or more drugs, including certain ARV drugs. All NRTIs except for abacavir (ABC) primarily undergo renal elimination and should be adjusted for dynamic changes in renal function. During the post-transplant period, it may be necessary to use individual components of ARV drugs instead of single-tablet regimens or fixed-dose combinations to allow for appropriate dose adjustments. Tenofovir alafenamide (TAF) is preferred over tenofovir disoproxil fumarate (TDF) because it has a lower risk of affecting renal function **(AII).** Because the rate of renal or hepatic function recovery can differ among recipients and immediate fluctuations may occur post-transplant, regular monitoring of organ function is important to ensure appropriate dosing of ARV drugs and minimize adverse effects or reduced efficacy (refer to Appendix B for ARV dosing in renal and hepatic insufficiency).

Alternative Methods for Antiretroviral Drug Delivery Post-Transplant

Interruption of ART post-transplant should be avoided **(AIII).** If interruption is necessary, all components in an oral ART regimen should be stopped simultaneously to avoid exposure to an incomplete regimen. The period of interruption should be kept to a minimal duration **(AIII).** If an ARV regimen includes both oral and long-acting injectable drugs (e.g., lenacapavir [LEN] or ibalizumab [IBA]) and interruption of the oral drugs is necessary, the oral ARV drugs should be resumed as soon as feasible to avoid monotherapy with the injectable agent.

If a transplant recipient cannot swallow pills immediately post-transplant, providers should consider using oral liquid formulation if available, or crushing and administering ARV drugs (if possible) to administer orally or via an enteral tube **(AIII).** Only a few ARV drugs are available in liquid formulations (Appendix A, Tables 1–10). Although PK data are limited, some ARVs can be temporarily crushed or dissolved and immediately administered orally or via an enteral tube until the recipients are able to swallow whole tablets (see more on Crushing and Liquid Antiretroviral Formulations). For people who require administration of crushed ARVs over an extended period of time, more frequent HIV viral load monitoring is recommended. If adequate oral absorption is a concern, TDM of certain ARV drugs may be considered.

Pill Burden and Post-Transplant Medication Management

Medications required for preventing graft rejection or opportunistic infections following SOT or HCT add significant pill burden and potential cost through medication copays. The complex medication schedule may also lead to medication errors and increased risk for suboptimal adherence. When renal and liver function are more stable, switching to single-tablet regimens or a fixed-dose combination ARV regimen (e.g., TAF or TDF with lamivudine [3TC] or emtricitabine [FTC]), dosed separately pre-transplant, can help reduce pill burden. Assisting transplant recipients with medication coordination, such as using a single pharmacy for dispensing all medications; attempting to synchronize refills to minimize trips to the pharmacy; and utilizing services such as adherence packaging, medication delivery, and refill reminders can also facilitate adherence. Medication and adherence counseling for transplant recipients and caregivers at each medical encounter is essential to ensure safe and effective therapy.

Impact of Medications on Adverse Effects and Comorbid Conditions

Close monitoring and prompt management of drug-associated adverse events is critical for all transplant recipients. Transplant medications, ARV drugs, and other medications may have some overlapping effects that can increase the risk or severity of toxicity. This overlap may have both short-term and long-term effects. Electrolyte disturbances may occur with sirolimus, tacrolimus, and cyclosporine. Of note, TDF may cause Fanconi syndrome, which could exacerbate the electrolyte disturbances. Similarly, nephrotoxicity associated with tacrolimus may also increase with concomitant TDF use.[21] All immunosuppressants are associated with side effects, such as nausea, vomiting, and diarrhea. These gastrointestinal side effects may be worsened when combined with ARV drugs, particularly PIs. While some of these adverse effects may be mitigated with symptomatic treatment, risk can be lowered pre-emptively by avoiding PIs and using TAF over TDF whenever possible.

In the long-term, people undergoing transplant are at high risk of developing new cardiovascular disease, diabetes, or osteoporosis.[22-24] If those conditions were present before transplant, they may worsen post-transplant. ARVs and/or transplant medications may play a role in the worsening of these conditions. Dyslipidemias associated with sirolimus or tacrolimus may be compounded by lipid disturbances associated with PIs or NNRTIs, such as efavirenz.[25,26] Cardiovascular events have been associated with ABC in some studies.[27] Fracture risk may be increased if corticosteroids are used in combination with TDF.[28] Since TDF may negatively impact bone mineral density,[28] TAF is preferred over TDF **(AII).** Management of comorbid conditions in transplant recipients is highly individualized. Clinicians must consider the risks and benefits of adjusting stable ARV regimens versus using other medications to manage complications. If ARV regimens are adjusted post-transplant, selecting agents that have minimal impact on transplant-related comorbidities is helpful in optimizing therapy.

Considerations for Long-Acting Antiretroviral Drugs

Several important factors should be considered when making decisions to initiate or continue transplant candidates on long-acting (LA) injectable ARV drugs, including cabotegravir (CAB) and rilpivirine (RPV) (typically used together as a complete ART regimen), IBA, and LEN. Experience with these LA ARV drugs in transplant candidates is limited, and these agents have not been studied in the setting of severe hepatic disease, ESRD, or post-transplant. The impact of fluctuations in renal function, hepatic function, and fluid shifts that may occur around the time of transplant on the PK of these LA ARVs is largely unknown. Additionally, it should be noted that because LA ARVs may be difficult to obtain in the hospital, administration must be carefully timed to avoid any medication access issues and treatment interruptions.

The benefits of initiating LA CAB/RPV pre-transplant should be weighed against potential risks. People who are stable on LA CAB/RPV prior to transplant may be maintained on their regimen and monitored closely. For individuals with very low platelet counts or who require anticoagulation, intramuscular (IM) injections of LA CAB/RPV may need to be postponed. In these cases, initiation of a bridging regimen with oral CAB and oral RPV until IM injections can be resumed may need to be considered. If oral CAB is not available, DTG may be used in its place.

Although there are occasions when a transplant recipient may not be able to take oral medications immediately post-transplant, in general, this should be resolved within a few days. There are no data on temporarily switching to LA CAB/RPV as a bridging strategy in this instance and, therefore, this strategy is not advised.

IBA and LEN are two LA ARV drugs approved for use in people with multiple drug-resistant HIV. IBA is given as an intravenous infusion every 2 weeks, whereas LEN is given as a

subcutaneous injection every 6 months. These drugs should not be started post-transplant just to reduce pill burden without other indications for their use. Transplant candidates on ARV regimens containing LEN or IBA likely have very limited alternative treatment options and should continue these LA ARV drugs as scheduled, in combination with any oral ARVs that are part of their complete regimen.

Because LA ARV drugs have very long half-lives, abruptly stopping any oral ARVs can lead to functional monotherapy with the LA ARV drugs, which may result in viral rebound and resistance. Therefore, the oral background regimen should be continued. People undergoing transplant who are maintained on these medications should be monitored closely for adverse events, drug interactions, and HIV viral load suppression. Drug interactions are an especially important consideration with LEN, which is a moderate CYP3A4 inhibitor (see Table 17). There is a prolonged period of drug interaction risk due to the extended presence of LEN in the body. Clinicians may inadvertently miss these interactions if they are unaware that LEN is part of the ARV regimen, as clinic-administered injectable LA ARV drugs are often listed separately from other ambulatory prescription medications in electronic health records.

Prevention of Infectious Complications Post-Transplant

Vaccination

Vaccination is a critical tool for preventing infections in all transplant recipients; however, the timing and some aspects of the approach to vaccination differ between SOT and allogeneic bone marrow transplant (BMT) candidates.

Timing of Vaccination

After registering as a transplant candidate and before SOT, there is typically a waiting period that provides an opportunity to assess vaccination status and update the vaccination record. It is important to consult the Centers for Disease Control and Prevention for up-to-date and specific vaccination recommendations, which include those for individuals with end-stage organ disease or immunocompromising conditions. Following an allogeneic BMT, vaccination plays a crucial role in restoring immune function and protecting against infectious diseases. Notably, the goal of vaccination in allogeneic BMT is to induce immune responses by the new engrafted donor immune system, not the pre-existing (recipient) one. However, vaccination strategies can vary based on the recipient's specific condition, transplant protocols, and recommendations from the transplant center. After allogeneic BMT, vaccination schedules are typically planned in phases, starting after the initial recovery period. Following that, vaccines are usually administered sequentially based on the transplant recipient's immune reconstitution status.

General principles for both SOT and allogenic BMT include the following:

- Vaccine recommendations for both SOT and BMT candidates and recipients should follow the same guidance as those recommended for those without HIV.
- In addition to reviewing standard pre- and post-transplant vaccine strategies described by the American Society of Transplantation Infectious Diseases Community of Practice, the need for additional vaccines based on HIV status (e.g., meningococcus) and/or exposure-related risk factors (e.g., mpox) should be assessed (see Immunization section of the *Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV*).
- For people without HBV infection, HBV vaccination is important to maximize options for ARV simplification strategies that may involve tenofovir-sparing regimens.

- Inactivated vaccines, which do not contain live pathogens, are generally considered safe after BMT. These include vaccines such as influenza, COVID-19, pneumococcal, HBV, tetanus, and diphtheria, as well as the new recombinant zoster vaccine.
- Live vaccines—including the varicella-zoster virus (VZV) and measles, mumps, and rubella (MMR) vaccines—should be avoided in SOT recipients while on immunosuppressants and may not be recommended immediately after BMT due to the recipient's weakened immune system. The decision to administer live vaccines is based on the individual's clinical condition and time since transplantation.

Pre-transplant Screening for Infection Risk and Antimicrobial Prophylaxis

Prior to transplant, transplant candidates should undergo a detailed assessment for infection risk, including history of prior infections, travel history, and environmental exposures. Due to the increased risk of reactivation of latent infections (e.g., tuberculosis, Strongyloides), transplant candidates with HIV who are at risk for these latent infections should undergo screening to guide pre-transplant treatment to prevent reactivation and disease post-transplant. Active opportunistic infections are a contraindication for transplantation. Additionally, both HIV and the immunosuppression associated with transplant are risk factors for anogenital or cervical human papillomavirus-related malignancies.[29] Prophylaxis against bacterial, fungal, and viral diseases is a standard of care at transplant centers and is tailored to factors such as serostatus (e.g., cytomegalovirus) or geographic risk (e.g., coccidioidomycosis). Clinicians should also be aware of the risk for donor-derived infections, especially in the early transplant period.

For more information regarding the prevention and treatment of opportunistic infections and donor-derived infections, refer to the *Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV* and center-specific protocols.

Recipient Considerations

HBV and HCV Coinfection

Due to overlapping risk factors, HBV and HCV coinfection is common in people with HIV. Both HBV and HCV are causes of cirrhosis that may lead to the need for liver transplant, and are also associated with extrahepatic manifestations such as diabetes mellitus, polyarteritis nodosa, membranoproliferative glomerulonephritis, and cryoglobulinemic vasculitis, which may contribute to ESRD.[30,31] Immunosuppression and chemotherapy (in cases of HCT) associated with transplant may result in loss of control of either HBV or HCV. Flares of active HBV or HCV following liver transplant begin with rises in HBV or HCV viral load, often followed by elevations in liver transaminases,[32,33] and can result in shortened graft survival. In those with only markers of prior HBV infection (core antibody [HBcAb] positive) and without evidence of active replication, HBV may reactivate from a latent state. Rarely, fibrosing cholestatic hepatitis results in rapidly progressive liver disease in transplant recipients.[34-38]

Assessment for HBV and HCV coinfection should occur at entry into HIV care and periodically for those at risk; status should be updated during the pre-transplant period. Transplant candidates or recipients who lack immunity to HBV (as indicated by negative HBV surface antibody [HBsAb]), including those with HBsAb loss, should receive vaccination regardless of HBcAb status and ideally before SOT.[39] Despite repeated attempts at vaccination, some people with end-stage organ disease or immunosuppression do not respond serologically and thus may be at risk for flares. Those undergoing allogeneic HCT generally undergo vaccination after the procedure.[40] For additional

information regarding ARV drugs for people with HIV/HBV coinfection, refer to the Hepatitis B Virus/HIV Coinfection section.

Candidate/Recipient Considerations

Candidate/recipient is HBsAg positive. In people with active HBV (HBV surface antigen [HBsAg]–positive) coinfection, it is important to include either TAF or TDF as part of the ARV regimen, with the goal of suppressing both viruses. Both TAF and TDF are active against HBV, and either can serve as the only active agent for HBV, although they are often used in combination with 3TC or FTC in people with both HIV and HBV. If TAF or TDF cannot be included, another potent anti-HBV drug—entecavir—should be initiated. Entecavir has weak anti-HIV activity and is not considered part of the ARV regimen but can induce nucleoside resistance mutation (M184V) and thus should never be used without a fully active ARV regimen.[41] Due to the low barrier to resistance and high likelihood for viral rebound, the use of 3TC or FTC as the only anti-HBV drug in individuals with HBV/HIV coinfection **is not recommended.**

Maintaining regimens with anti-HBV activity before transplant and indefinitely after transplant is recommended for transplant recipients with HIV and active HBV infection due to the risk of HBV reactivation and the potential for severe liver damage, including fulminant liver failure.

Candidate/recipient is HBcAb positive, HBsAg negative, and HBsAb negative or positive. The risk of HBV reactivation in the transplant recipient depends on the type of transplant, the depth of immunosuppression, and the presence of HBsAb. For liver transplant recipients who are HBcAb positive without evidence of active HBV (negative serum HBsAg and HBV DNA), reactivation risks are considered negligible due to removal of the potential liver reservoir. By contrast, in non-hepatic transplant recipients with markers of past infection, reactivation may occur in up to approximately 5%, usually during the first year, when immunosuppression is most intense and in the absence of protective levels of HBsAb.[42] This risk can be further abrogated if anti-HBV agents are already part of the ART regimen and by boosting HBsAb levels with vaccination. For non-hepatic transplant recipients not already on agents with anti-HBV activity, periodic prophylaxis or monitoring (regular measurements of transaminases and if newly elevated, rapid HBV DNA) strategies may be deployed to the highest-risk recipients per institutional protocol.[43,44]

Candidate/recipient is HCV RNA positive. All transplant candidates and/or recipients with HCV infection should be treated with DAAs against HCV **(AII),** preferably prior to transplant. Exceptions to this principle might include select candidates awaiting liver transplant, with a short waiting time for transplant (e.g., high Model for End-Stage Liver Disease, or MELD, score),[45] or select candidates for non-liver transplants who elect to defer treatment to remain eligible for donor organs from HCV viremic donors,[46-48] per discretion of the transplant providers. For those deferring treatment for HCV before transplant, treatment should be initiated early in the post-transplant period.[49-51] Additional considerations for the care of people with HIV and HCV, including fibrosis assessment, are found in the Hepatitis C Virus/HIV Coinfection section.

Donor-Related Considerations

HBV-Positive and HCV-Positive Donors

Organs from donors with serologic or virologic markers of HBV or HCV infection may be considered when recipients have given informed consent and providers have determined that benefits outweigh potential risks.[52,53] Antiviral treatment for recipients prior to transplantation can help prevent or manage post-transplant infection. Additionally, monitoring for donor-derived transmission and close follow-up of the recipient post-transplantation are necessary to detect and manage any potential infection.

Donor is HBcAb and/or HBsAg positive. To expand the size of the donor pool, use of HBcAb positive/HBsAg negative organs has become common practice.[54] More rarely, donors who are HBsAg positive are also utilized.[55] Without prophylaxis or recipient immunity (presence of surface antibody), the risk of HBV transmission from such donors is present for non-hepatic organs and is extraordinarily high for liver transplants. Strategies to mitigate the risk of donor-derived HBV include pre-transplant vaccination, nucleos(t)ide therapy, and—particularly for liver transplant recipients who receive HBsAg-positive organs—hepatitis B immunoglobulin.[56] Anti-HBV agent prophylaxis may be deployed for moderate to high-risk recipients, with the highest risk (liver transplant recipients) receiving lifelong nucleos(t)ide analogues. Organ recipients with HIV may continue on regimens that already include tenofovir; those on tenofovir-sparing regimens pre-transplant may require the addition of anti-HBV agents such as tenofovir or entecavir. 3TC or FTC alone is not preferred for this indication.

Donor is HCV antibody or HCV RNA positive. The safety of using organs from HCV antibody-positive donors in both HCV viremic and aviremic recipients has been established, especially with early initiation of antivirals in the post-transplant setting.[45-48,51,57-62] Although untreated chronic HCV infection may have an accelerated course in people with HIV and SOT, early and effective treatment abrogates this risk substantially. Transplant candidates with HIV without current HCV infection should consider accepting HCV viremic organs if prompt DAA therapy is available at their center (see the Hepatitis C Virus section for more information).

Solid Organ Transplant Considerations From Donors With HIV

Kidney transplantation demonstrates survival benefit compared to dialysis for people with HIV and ESRD.[63] Previously, the use of organs from donors with HIV was banned. After a successful study of transplanting kidneys from donors with HIV into recipients with HIV in South Africa, the U.S. HIV Organ Policy Equity (HOPE) Act was approved in 2013, amending the law to allow transplantation of organs from donors with HIV into recipients with HIV (HIV D+/R+) under research protocols.[64]

For transplant candidates, eligibility criteria for HIV D+/R+ transplantation are the same as standard transplant criteria. For donors, federally mandated research criteria require that donors do not have active opportunistic infections.[65] Organs from donors with any CD4 lymphocyte cell count or viral load are allowed; however, transplant teams need to consider the likelihood of any ART resistance in the donors and justify whether an ART regimen in the recipient will be effective and tolerated.[65] To date, INSTI resistance has been rare in deceased donors with HIV.[66]

Early studies have shown excellent outcomes of HIV D+/R+ kidney and liver transplantation.[64,67] Based on this, the federal Advisory Committee on Blood and Tissue Safety and Availability has recommended to the U.S. Department of Health and Human Services that HIV D+/R+ kidney and liver transplantation be moved outside of research and into clinical care.[68] Due to the paucity of outcome data, HIV D+/R+ heart or lung transplantation remains under research protocols for now.[68] HIV D+/R+ kidney transplantation has been shown to decrease wait times for transplant.[69] SOT candidates with HIV may therefore consider being listed at a center currently offering organs from donors with HIV, if feasible.

As organ allocation in the United States occurs at a national level, all people with HIV may register as organ donors regardless of their distance from these centers, as their organs would only be directed to transplant candidates with HIV.[70] In addition, people with HIV may be living organ donors under HOPE Act research protocols.[68,71]

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Women With HIV

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Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all people with HIV to improve their health and to reduce the risk of HIV transmission to sexual partners without HIV **(AI).** • When prescribing antiretroviral (ARV) drugs for women with HIV, clinicians should consider that some ARV drugs have significant pharmacokinetic (PK) interactions with hormonal contraceptives **(AII)** and hormone replacement therapy **(BIII).** Consult Tables 24a, 24b, 24d, 24e, 24f, and 24g for detailed recommendations and a summary of available data when selecting ARV and hormone combination therapy **(AIII).** • Clinicians should discuss with women the possibility of weight gain after initiating or changing ART. Some women in general, and Black women in particular, experience greater weight gain with ART over time than men. Concerns for weight gain should not be a reason for deferring ART. • A pregnancy test should be performed for women of childbearing potential before initiation of ART **(AIII).** • When selecting or evaluating an ARV regimen for women with HIV of childbearing potential, clinicians should consider the regimen's effectiveness, the woman's hepatitis B status, the teratogenic potential of the drugs in the ARV regimen, and the possible adverse outcomes for the mother and the fetus if the woman becomes pregnant while receiving the regimen **(AII).** • During pregnancy, an additional goal of ART is to maintain a viral load below the limit of detection throughout pregnancy in order to reduce the risk of HIV transmission to the fetus and newborn **(AI).** • When selecting an ARV regimen for a pregnant woman, clinicians should consider the available safety, efficacy, and PK data on the use of each agent during pregnancy. The risks and benefits of ARV use during pregnancy should be discussed with all pregnant women **(AIII),** and clinicians should consult the Perinatal Guidelines when designing a regimen **(AIII).** • Achieving and maintaining viral suppression with ART while breastfeeding does not completely eliminate HIV transmission risk but does reduce it to less than 1% **(AI).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

This section focuses on some unique clinical and therapeutic issues to consider and basic principles to follow when caring for women with HIV. Clinicians who care for pregnant women with HIV should consult the Perinatal Guidelines for a more in-depth discussion.

Sex Difference Considerations in Antiretroviral Therapy

In general, studies to date have not shown sex differences in virologic responses to antiretroviral therapy (ART).[1-6] However, limited data show that pharmacokinetics (PK) for some ARV drugs may differ between men and women, possibly because of variations in factors such as body weight, plasma volume, gastric emptying time, plasma protein levels, cytochrome P450 activity, drug transporter function, and excretion activity.[6-10]

Adverse Effects

Several studies with older ARV drugs have suggested that sex may influence the frequency, presentation, and severity of some ARV-related adverse events.[11-13] In the ICONA cohort, people

with HIV treated with dolutegravir (DTG)-based regimens were followed for up to 4 years. There was a higher risk of DTG discontinuation due to toxicity in both ART-naive and ART-experienced women compared with men.[14]

Some studies have investigated how metabolic complications that are associated with the use of ARV drugs differ between women and men. Women have an increased risk of osteopenia, osteoporosis, and fractures, particularly after menopause, and this risk is exacerbated by HIV and some ARV drugs.[15-18] ARV regimens that contain tenofovir disoproxil fumarate (TDF), ritonavir-boosted protease inhibitors (PI/r), or both are associated with a significantly greater loss of bone mineral density (BMD) than regimens that contain other nucleoside reverse transcriptase inhibitors (NRTIs) and raltegravir (RAL).[19-22] Abacavir (ABC), NRTI-sparing regimens, and tenofovir alafenamide (TAF) may be considered as alternatives to TDF for patients who are at risk of osteopenia or osteoporosis. Recommendations for the management of bone disease in people with HIV have been published.[23]

Weight Gain and Antiretroviral Therapy

Weight gain after initiation of ART, especially in people with advanced HIV, can be a sign of a return to better health. However, data from clinical trials and longitudinal cohort studies suggest sex differences in ARV-associated weight gain across all classes of ART among treatment-naive individuals, particularly with the use of certain integrase strand transfer inhibitor (INSTI)–based regimens (DTG and bictegravir [BIC]). In a pooled analysis of eight randomized controlled trials with ARV-naive people initiating HIV treatment, female sex was associated with 1.5 times the odds of a ≥10% weight gain compared with male sex (17.4% vs. 12.2%), with Black females significantly more likely to experience a ≥10% weight gain than non-Black females (19.7% vs. 12.4%).[24] At 144 weeks of follow-up in the ADVANCE study, a 12.3-kg weight gain was recorded among women receiving TAF/emtricitabine (FTC)/DTG compared with 7.4 kg and 5.5 kg among women receiving TDF/FTC/DTG and TDF/FTC/efavirenz (EFV), respectively.[25] In addition to women being more likely to experience weight gain with ARV initiation, the pattern of weight gain differs between men and women. In the ADVANCE study, at 96 weeks of follow-up, women gained more fat than lean body mass than men, with weight gain concentrated in the limbs and trunk. ARV-associated weight gain similarly has been observed among virologically suppressed women switching to an INSTI-based regimen.[26-28] In the Women's Interagency HIV Study, virologically suppressed women who switched to INSTI-based ART or had an INSTI added to their regimen (n = 234) gained an average of 4.2 kg in body weight at the 2-year follow-up compared with 0.2 kg in women remaining on non-INSTI ART (n = 884).[27] Mean change in percent body fat (1.7% vs. 0.3%) and body circumference measures were also greater in the INSTI group than in the non-INSTI group. Investigators did not detect a difference in weight gain by individual INSTI.

It should be noted that, although randomized controlled trials and observational studies suggest that individuals receiving INSTI-based regimens experience greater weight gain than those receiving comparator regimens, significant uncertainty continues as to whether INSTIs are causing weight gain or whether the comparator drugs are suppressing weight gain. For example, an analysis in the ADVANCE trial demonstrated that the greater weight gain observed in DTG- versus EFV-treated participants was dependent primarily on CYP2B6 polymorphisms, which are associated with slow EFV metabolism (and presumably higher EFV levels). Among those with rapid EFV metabolism genotypes, no evidence was found for a weight difference between DTG- and EFV-treated participants.[29] The underlying mechanisms for weight gain in people receiving an INSTI-based regimen, and their impact on cardiovascular diseases, diabetes, pregnancy-related outcomes, and age-related comorbidities among women with HIV are currently unknown.

Switching from TDF to TAF, regardless of whether participants took INSTI, non-nucleoside reverse transcriptase inhibitor (NNRTI), or PI combinations, was found to be associated with weight gain,

particularly in women and people of African descent.[30] The extent of TAF-associated weight gain may be affected by baseline body mass index (BMI). Among participants of the Women's Interagency HIV Study (WIHS) cohort, weight and BMI rose among women with baseline BMI below 30kg/m^3 when transitioning to INSTI, TAF, or INSTI and TAF together.[31]

All these data indicate that ARV-associated weight gain should be a factor to consider when initiating or changing ART, particularly in Black women. Because some ART regimens are more likely to cause weight gain in women, clinicians should weigh the benefits and risks of a particular regimen when initiating or changing ART. However, concerns about weight gain should not be a reason for deferring ART.

Adherence to Antiretroviral Therapy

Some observational studies have found that women are more likely than men to have suboptimal adherence to ART. Defining adherence as missing no dose of ART in the prior 3 days, the Centers for Disease Control and Prevention analyzed data from the nationally representative Medical Monitoring Project (n = 12,394) by race and sex.[32] Race comparisons by sex indicated that women had consistently lower ART adherence than men of the same race. Adherence rates were 94% for White men compared with 88% for White women, 93% for Latino men compared with 88% for Latina women, and 89% for Black men compared with 87% for Black women. A Canadian study followed 4,534 individuals (including 904 women) for a median of 65.9 months and found that a significantly lower proportion of women relative to men were optimally adherent (57.0% vs. 77.1%).[33] In the analysis adjusted for ethnicity and injection drug use, female sex remained associated independently with suboptimal adherence. Women with HIV face multifactorial barriers to adherence. Increasing access to social services—such as food, housing, and transportation—has been associated with improved ART adherence, as have social support and good patient–provider relationships.[34,35] Another analysis of 6,186 women from the Medical Monitoring Project found that women aged 50 and older were more likely to be adherent to ART than women younger than 50.[36] However, menopausal symptoms have been associated significantly with suboptimal ART adherence in cross-sectional[37] and longitudinal studies[38] of older women with HIV. It also was noted that 68.8% of older women with HIV experienced symptoms of menopause, but only 17% received treatment for these symptoms. It is plausible that treating menopausal symptoms may improve ART adherence among older women with HIV.[38,39]

Antiretroviral Therapy Considerations in Women With HIV Who Are of Childbearing Potential

All women with HIV who are of childbearing potential should be offered comprehensive reproductive and sexual health counseling and care as part of routine primary medical care. Topics for discussion should include safe sex practices, reproductive desires and options for conception, the HIV status of sexual partner(s), the use of effective contraception to prevent unplanned pregnancy, and maintaining viral suppression to optimize health in preparation for pregnancy. Counseling also should include discussion of special considerations pertaining to ARV use when using hormonal contraceptives, when trying to conceive, and during pregnancy (see the Perinatal Guidelines). Clinicians should discuss intentions regarding pregnancy with all women of childbearing potential, and a pregnancy test should be performed before initiating ART **(AIII).**

Antiretroviral Regimen Considerations for Individuals Who Are Trying to Conceive

ART should be initiated and viral suppression achieved prior to pregnancy whenever possible. People should be given information about the benefits and risks of initiating specific ARV regimens

when trying to conceive so they can make informed decisions about their care (see Appendix C: Antiretroviral Counseling Guide for Health Care Providers).

Earlier data from the birth outcomes surveillance study in Botswana raised concern about an increased risk of neural tube defects (NTDs) (0.9%) in infants born to women who were receiving DTG at the time of conception.[40,41] At the time of the study, folate fortification of grains in Botswana was uncommon. Folate prescribed before conception was low (0.1% to 0.2%) among the study participants.[42] Updated results from the same study showed that the prevalence of NTDs in infants born to women on DTG at the time of conception was not significantly different from those on non-DTG regimens at the time of conception.[43] Because folic acid is known to prevent NTDs in the general population, all pregnant women and women who might conceive should take at least 400 mcg of folic acid daily **(AI).** In a small cohort of 69 U.S. women who had periconceptional or early-pregnancy DTG exposure and access to folic acid fortification of food and/or received folate supplementation, there was no increased risk of NTDs in exposed infants.[44]

EFV is teratogenic in nonhuman primates.[45] However, in humans, no increase in teratogenicity has been reported with the use of EFV. Based on drug-specific risk assessments by the Antiretroviral Pregnancy Registry, sufficient numbers of first-trimester exposures to EFV have been monitored with no detected increase in the risk of overall birth defects, including in cardiovascular and genitourinary systems. Women who become pregnant while on EFV-containing regimens should continue their current regimens **(BIII).**

Before initiating ART in a woman of childbearing potential, clinicians should review the What to Start: Initial Combination Regimens for People With HIV section and the Perinatal Guidelines for information to consider when choosing an ARV regimen. The key recommendations are listed below:

For individuals who are trying to conceive, the Panel on Antiretroviral Guidelines for Adults and Adolescents recommends initiating one of the following regimens, which are designated as *Preferred* regimens during pregnancy in the Perinatal Guidelines: DTG plus a dual NRTI combination (TAF/FTC, TDF/FTC, or TDF/3TC) or BIC/TAF/FTC. DTG-based regimens are associated with rapid, durable viral load suppression, which is important for maternal health and the prevention of perinatal HIV transmission. Data on the use of long-acting (LA) injectable cabotegravir (CAB) with rilpivirine (RPV) in pregnancy are limited.

For individuals who are not planning to conceive but who are at risk for pregnancy, consider a regimen's effectiveness and tolerability the available data on potential teratogenicity, and the person's preferences (e.g., pill burden) when choosing between regimens that are recommended for initial therapy (see Tables 6a and 6b in the Initial Combination Antiretroviral Regimens for People With HIV section). Clinicians should refer to the Perinatal Guidelines for recommendations.

Reproductive Options for Couples With Differing HIV Status

Couples with differing HIV status should be informed of options to prevent sexual transmission of HIV while attempting conception. If the partner with HIV is on ART and has achieved sustained viral suppression, sexual intercourse without a condom allows conception with effectively no risk of sexual HIV transmission to the partner without HIV (see Antiretroviral Therapy to Prevent Sexual Transmission of HIV).[46-48] People with HIV who intend to prevent transmission by using ART need to maintain high levels of ART adherence and should be informed that transmission is possible during periods of poor adherence, treatment interruption, and viremia. Both partners should be screened for sexually transmitted infections (STIs) and receive appropriate treatment if STIs are diagnosed.

Hormonal Contraception

Safe and effective reproductive health and family planning services to prevent unplanned pregnancies and perinatal transmission of HIV are essential components of care for women with HIV of childbearing potential. These women should receive ongoing counseling on reproductive issues. Individuals who do not desire pregnancy currently but are sexually active or considering initiating sexual activity should be offered effective and appropriate contraceptive methods to reduce the likelihood of unintended pregnancy. Women with HIV can use all available contraceptive methods (e.g., pill, patch, ring, injection, implant) and intrauterine devices (IUDs),[49] after consideration of potential drug–drug interactions as discussed in the next section (also see the Perinatal Guidelines).

Drug–Drug Interactions Between Hormonal Contraceptives and ARV Drugs

Interactions between some ARV drugs and hormonal contraceptives may reduce contraceptive efficacy. However, most data are generated from healthy-volunteer, short-duration PK studies, and clinical data regarding interactions between ARV drugs and hormonal contraceptives in women with HIV are limited. The magnitude of change in drug concentrations that may reduce contraceptive efficacy or increase the risk of adverse effects is not known for all forms of contraceptives, making the clinical implications of some ARV-hormone drug interactions challenging to predict.

Concerns about PK interactions between hormonal contraceptives and ARV drugs should not prevent clinicians from prescribing hormonal contraceptives for individuals on ART. However, an alternative or additional effective contraceptive method is recommended if significant interactions may occur between hormonal contraceptives and ARV drugs (see Tables 24a, 24b, 24d, 24e, 24f, and 24g). A summary of ARVs with known interactions with hormonal contraceptives is described below:

Combination contraceptives containing ethinyl estradiol and progestins, including combined oral contraceptives (COCs), transdermal patches, and intravaginal rings:[50,51]

- EFV significantly decreases progestin concentrations from both COCs and intravaginal rings, which may increase the risk of contraceptive failure. EFV did not reduce oral ethinyl estradiol exposure in one small study, but it reduced exposure when combined with an intravaginal ring, which may increase the risk of intermenstrual bleeding (spotting), particularly with ultra-low and low-dose estrogen-containing contraceptives.
- Elvitegravir boosted with cobicistat (EVG/c), and cobicistat-boosted PIs or PI/r decrease ethinyl estradiol levels, which may increase the risk of spotting, particularly with ultra-low and low-dose estrogen-containing contraceptives. However, these ARV regimens also increase progestin exposure, which preserves contraceptive effectiveness.
- Cobicistat- and ritonavir-containing regimens should be avoided with drosperinone-containing products because of an increased risk of hyperkalemia.
- Fostemsavir (FTR) increases ethinyl estradiol exposure, which may increase risk of thromboembolic events. Product labeling recommends a maximum dose of ethinyl estradiol of 30 mcg per day when combined with FTR.[52]

Progestin-only pills:[50,51]

- EFV significantly decreases concentrations of oral progestin pills, including emergency contraception, which may increase the risk of contraceptive failure.

- Cobicistat- or ritonavir-boosted ARV regimens may increase progestin exposure. The combination may be used without dose adjustment; monitor for progestin-related adverse effects.

Injectable contraceptives (depot-medroxyprogesterone):

- One study of EFV-based ART plus depo-medroxyprogesterone acetate (DMPA) did not find a significant reduction in medroxyprogesterone acetate (MPA) exposure. No change in DMPA dose or frequency is necessary.[53]
- For women receiving both rifampin and EFV for the treatment of tuberculosis and HIV, some experts suggest administering DMPA every 8 to 10 weeks instead of every 12 weeks.[54]

Progestin-releasing contraceptive implants:[50,51]

- EFV significantly decreases progestin concentrations released from a contraceptive implant. Cohort studies have found that women receiving EFV-based ART and contraceptive implants have a higher rate of unintended pregnancies than women receiving other ART combinations.[55,56]
- Cobicistat- or ritonavir-boosted ARV regimens may increase progestin exposure, but the combination may be used without dose adjustment.

Pregnancy

All women with HIV should receive ART early in pregnancy, regardless of their viral load or CD4 T lymphocyte (CD4) cell count, for their own health and for the prevention of perinatal HIV transmission and transmission of HIV to sexual partners **(AI).** ARV drugs reduce the risk of perinatal HIV transmission by decreasing maternal viral load in blood and genital secretions.[57-59] Clinicians who are caring for pregnant adults and adolescents with HIV should review the Perinatal Guidelines.

Antiretroviral Regimen Considerations

In general, the recommendations for the use of ART in pregnant women are the same as those for women who are not pregnant. As in nonpregnant individuals, genotypic drug-resistance testing is recommended for all pregnant women before initiating ARV drugs **(AIII)** and for those with detectable HIV viral load while on ART **(AI).** However, if not yet on ART, ART initiation should not be delayed pending genotypic drug-resistance test results. The ARV regimen can be modified, if necessary, once the resistance test results are available **(BIII).** Unique considerations that influence recommendations on the ARV drugs to use during pregnancy include the following:

- Potential ARV-associated adverse effects for pregnant women, fetuses, and infants
- Need for strict adherence to the prescribed ARV regimen to avoid viremia and drug resistance, optimize health outcomes, and minimize the risk of perinatal transmission
- Limited long-term outcome data for infants who were exposed to ARV drugs *in utero*, especially for newer ARV drugs

Clinicians should review the Perinatal Guidelines for ARV drug recommendations for individuals who recently have received an HIV diagnosis or those who become pregnant while on ART. Selection of ARV drugs for pregnant women should be individualized according to specific ARV history, the results of drug-resistance assays, and the presence of comorbidities, as well as the individual's preferences for balancing known and unknown risks and benefits of an ARV regimen.

Because of data suggesting decreased drug levels during pregnancy and associated loss of virologic suppression, cobicistat-containing regimens, including EVG/c, ATV/c, or DRV/c, are not recommended for initiation during pregnancy.[60] A pregnant woman who has a suppressed plasma viral load on one of these regimens could continue the regimen with frequent (e.g., monthly) viral load monitoring. Alternatively, another regimen that is predicted to maintain viral suppression can be used for the duration of the pregnancy.

The use of LA CAB with RPV has not been studied in pregnancy. In clinical trials, participants who became pregnant were switched from LA CAB and RPV to an alternative oral ARV regimen throughout the remainder of their pregnancies. Based on the pharmaceutical company's clinical trials and compassionate program through March 2021, 25 pregnancies were reported (20 LA CAB/RPV and 5 during oral lead-in phase); in 4 cases, conception occurred during the washout period after treatment discontinuation. There were 8 elective abortions, 6 miscarriages, and 1 ectopic pregnancy. Among the 10 livebirths (9 LA CAB/RPV and 1 oral), 1 infant had congenital ptosis.[61] Women who become pregnant while on ART will need close monitoring, and their pregnancy outcomes should be reported to the Antiretroviral Pregnancy Registry.

If maternal HIV viral load is ≥1,000 copies/mL (or unknown) near delivery, intravenous infusion of zidovudine during labor is recommended, regardless of the mother's antepartum regimen and resistance profile and the mode of infant delivery **(AI).** Administration of combination ART should continue during labor and before a cesarean delivery (oral medications can be administered with sips of water during this time).

Clinicians who are treating pregnant women with HIV are strongly encouraged to report cases of prenatal exposure to ARV drugs (either administered alone or in combination) to the Antiretroviral Pregnancy Registry.

Postpartum Management

Following delivery, clinical, immunologic, and virologic follow-up should continue as recommended for nonpregnant adults and adolescents. Maternal ART should be continued after delivery. For more information regarding postpartum management of HIV, refer to the Perinatal Guidelines.

Some studies have demonstrated that adherence to ART may decline during the postpartum period.[62-64] Clinicians should address ART adherence at each postpartum clinic visit, including an evaluation of specific factors that facilitate adherence or present as a barrier to adherence. Clinicians may recommend an intervention to improve adherence (see Adherence to the Continuum of Care).

Clinicians should discuss future reproductive plans and timing, the risks and benefits of conceiving on specific ARV medications, and the use of appropriate contraceptive options to prevent unintended pregnancy. If an LA reversible contraceptive—such as an implant or IUD—is desired by the person, it should be inserted before hospital discharge or during the postpartum visit if possible.

Infant Feeding

Clinicians should refer to the Perinatal Guidelines for detailed recommendations regarding initiation or modification of infant feeding. Women with HIV should receive evidence-based, patient-centered counseling to support shared decision-making about their desire for infant feeding. Replacement feeding with properly prepared formula or pasteurized donor human milk eliminates the risk of postnatal HIV transmission to the infant.

Breastfeeding is **not recommended** for women who are not virally suppressed or for those who develop a detectable viral load while breastfeeding because of concern for increased risk of HIV

transmission through breast milk.[65] If viremia occurs during breastfeeding, the woman should be advised to replace breastfeeding with another mode of feeding. Viral load testing should be repeated and plasma genotypic resistance testing should be performed if the level of viremia allows for a test to be done.

HIV and Menopause

The population of people with HIV is aging; thus, the number of women with HIV who are experiencing menopause is increasing. The median age of menopause in the general U.S. population is 52.5 years.[66] Evidence suggests that women with HIV are reaching menopause at earlier ages than those who do not have HIV.[67,68] The WIHS, which included 3,059 participants, demonstrated that approximately 1% (n = 35) experienced premature menopause before age 41, 3% (n = 101) between ages 41 and 45, and 21% (n = 442) between ages 46 and 50. These participants self-reported low ranges of hormone replacement therapy (14%, 16%, and 7%, respectively).[39] However, other confounding factors may affect age of menopause in women with HIV, such as sociodemographic factors, illicit drug use, hepatitis C coinfection, smoking, and possibly ART.

A Canadian study of 229 women with HIV reported that the average age of menopause was 48 years, which was 3 years younger than the general Canadian population. Lower level of education and hepatitis C coinfection were associated independently with menopause at <45 years of age.[69] In another study of 667 women with HIV in Rio de Janeiro, Brazil, 24% reached menopause during the observational period and 27% had early menopause (<45 years of age). The median age of menopause was 48 years of age. Age at menarche <11 years, cigarette smoking, chronic hepatitis C, and CD4 count <50 cell/mm^3 were associated significantly with an earlier age of natural menopause.[70]

Menopause is a high-risk period for osteoporosis, which may be exacerbated by HIV and/or ART. A small, randomized international multicenter study demonstrated a trend of increased BMD at the lumbar spine after a switch from TDF to TAF in peri- and early postmenopausal women with HIV.[71]

Defining the relationship between HIV and menopausal symptoms, mental health, and depression is complicated because of overlapping symptoms from HIV itself, effects of ART, other comorbidities, and substance use. Some studies suggest that women with HIV experience a greater burden of menopausal symptoms, including vasomotor symptoms, sexual dysfunction, and mood changes.[67,68,72] Other studies did not find differences between women with HIV and those without HIV.[73,74] Menopausal symptoms also have been associated with reduced adherence to ART and poor cognitive performance.[37,38,75,76]

No studies have shown evidence of estrogen deficiency (i.e., menopause) affecting CD4 count, plasma HIV viral loads, or response to ART.[77,78] Two small studies showed no difference in plasma levels of tenofovir and RAL between pre- and postmenopausal women.[79,80]

The use of hormone replacement therapy (HRT) is low among women with HIV.[38] Data are limited on drug–drug interactions between ART and estradiol as part of HRT, and drug interaction data with ethinyl estradiol cannot be extrapolated to the estrogens used for HRT because of differences in metabolism. Drug interactions between HRT and ART are possible, particularly regimens containing cobicistat, ritonavir, PIs, or some NNRTIs. See the drug–drug interaction Tables 24a, 24b, 24c, 24d, 24e, 24f, and 24g for predicted interactions and clinical recommendations.

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CONSIDERATIONS FOR ANTIRETROVIRAL USE IN PEOPLE WITH COINFECTIONS

Hepatitis B Virus/HIV Coinfection

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Panel's Recommendations
• Hepatitis A, B, and C virus serologies should be performed for all people with HIV **(AIII).** • Before initiating or switching antiretroviral therapy (ART), all people who test positive for hepatitis B surface antigen (HBsAg) should be tested for hepatitis B virus (HBV) DNA using a quantitative assay to determine the level of HBV replication **(AIII).** • Because tenofovir alafenamide (TAF), tenofovir disoproxil fumarate (TDF), emtricitabine (FTC), and lamivudine (3TC) are active against both HIV and HBV, an antiretroviral (ARV) regimen for people with both HIV and HBV should include (TAF or TDF) plus (3TC or FTC) as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of a fully suppressive ARV regimen **(AI).** • In people with HBV/HIV coinfection, using 3TC or FTC as the only drug in a regimen with HBV activity **is not recommended (AII),** because HBV resistance to these drugs can emerge. • If TAF or TDF cannot be safely used, or if there is a desire to use a tenofovir-sparing ART regimen, entecavir should be used as the alternative HBV therapy **(BI).** Entecavir has weak activity against HIV. Using entecavir for HBV treatment without ART may result in selection of the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, entecavir must be used in addition to a fully suppressive ARV regimen when given to people with HBV/HIV coinfection **(AII).** • Adefovir **(AI)** or pegylated interferon alfa **(AIII) are not recommended** for people with HBV/HIV coinfection. • In people with HBV/HIV coinfection, the discontinuation of agents with anti-HBV activity may cause serious hepatocellular injury resulting from HBV reactivation hepatitis; people with HBV/HIV coinfection should be advised against stopping these medications and should be carefully monitored during interruptions of HBV-active treatment **(AII).** • When switching or modifying an ARV regimen in a person with HBV/HIV coinfection, including switching to long-acting injectables, ARV drugs that are active against HBV should be continued **(AII)** or specific anti-HBV drugs, such as entecavir, should be initiated **(AII).** • HBV reactivation has been reported in people with HIV and prior exposure to HBV (positive hepatitis B core antibody, negative HBsAg) when HBV-active agents are withdrawn as part of an ART regimen. Regardless of hepatitis B surface antibody level, people with HIV and prior HBV exposure are at low risk for reactivation and the associated hepatitis, which can result in serious hepatocellular injury. A monitoring strategy is considered a safe and effective way to assess HBV reactivation in low-risk people **(BIII).** • HBV reactivation has been observed in people with HBV/hepatitis C virus (HCV) coinfection while receiving interferon-free HCV treatment. For this reason, all people initiating HCV therapy should be tested for HBV. People with HCV/HIV coinfection and active HBV infection (determined by a positive HBsAg test) should receive ART that includes two agents with anti-HBV activity before initiating HCV therapy **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Approximately 5% to 15% of people with HIV in the United States also have chronic hepatitis B virus (HBV) infection, defined as positive HBV surface antigen (HBsAg).[1-3] The progression of chronic HBV to cirrhosis, end-stage liver disease, or hepatocellular carcinoma is more rapid in people with HBV/HIV coinfection than in people with chronic HBV mono-infection.[4] Conversely, chronic HBV does not substantially alter the progression of HIV infection and does not influence HIV suppression or CD4 T lymphocyte cell responses following the initiation of antiretroviral therapy (ART).[5,6] Liver-associated complications may occur due to immune reconstitution after initiation,[7,8] or HBV reactivation after discontinuation of antiretroviral (ARV) drugs that are active against both HIV and HBV.[9-14]

Recommendations for People With HBV/HIV

- All people with HIV should be tested for viral hepatitis, including hepatitis A virus (HAV), HBV, and hepatitis C virus (HCV). People without immunity to HAV or HBV should receive a full vaccination series **(AIII).**
- A survey of people with HIV/HBV coinfection in the United States revealed that 4.0% had a positive hepatitis D virus (HDV) serologic test, of which 41.7% had detectable HDV RNA.[15] Because HBV/HDV coinfection has been associated with serious liver complications, many experts recommend that people with HIV and chronic HBV be tested for HDV infection.[16,17] The recommended initial serologic test is an HDV antibody test, which, if positive, should be followed by HDV RNA testing. People with HIV and HBV/HDV coinfection should be referred to an expert in the management of viral hepatitis.
- All people with chronic HBV should be evaluated to assess the severity of HBV infection (see Hepatitis B Virus in the Adult and Adolescent Opportunistic Infections Guidelines). In addition, people with chronic HBV should be advised to abstain from alcohol, be screened for alcohol use disorder,[18] and be counseled on prevention methods that protect against both HBV and HIV transmission.[19]
- Before ART is initiated, all persons who test positive for HBsAg should be tested for HBV DNA by using a quantitative assay to determine the level of HBV DNA **(AIII),** and the test should be repeated every 3 to 6 months to ensure effective HBV suppression. The goal of HBV therapy with nucleos(t)ide reverse transcriptase inhibitors (NRTIs) is to prevent liver disease complications by sustaining the suppression of HBV replication. A large cohort study found that persistent HBV viremia while taking ART and high HBV DNA levels were associated with a higher risk of hepatocellular carcinoma (HCC), even if HIV was suppressed; whereas sustained HBV DNA suppression for ≥1 year was associated with a 58% reduction in HCC risk.[20] The most common reason for persistent HBV viremia in people with HBV/HIV coinfection on tenofovir alafenamide (TAF)– or tenofovir disoproxil fumarate (TDF)–containing ART is suboptimal adherence; thus, the primary focus in this setting should be on improving adherence.[21]
- Because HBV reactivation has been observed in people with HBV infection during interferon-free HCV treatment,[22,23] people with HCV/HIV coinfection and chronic HBV infection should receive ART that includes two agents with anti-HBV activity (such as TAF or TDF plus emtricitabine [FTC] or lamivudine [3TC]) prior to initiating HCV therapy **(AIII).** The diagnosis of HBV reactivation should be considered in people with current HBV infection who experience elevated liver transaminases during or immediately after HCV therapy.

Antiretroviral Drugs With Dual Activities Against HBV and HIV

The NRTIs TAF, TDF, FTC, and 3TC are active against HBV. Entecavir is an HBV nucleoside analog that has weak HIV activity. TAF is a tenofovir prodrug with HBV activity and potentially less

renal and bone toxicity than TDF,[24,25] although weight gain has been observed more frequently with TAF than TDF.[26,27]

The efficacy of TAF versus TDF in hepatitis B e antigen (HBeAg)–negative patients with HBV mono-infection was evaluated through a randomized controlled trial, involving both treatment-naive and treatment-experienced participants. In this study, TAF was non-inferior to TDF, based on the percentage of participants with HBV DNA levels <29 IU/mL at 48 weeks of therapy (94% for TAF vs. 93% for TDF; *P* = 0.47).[28] In another study, TAF was also non-inferior to TDF in HBeAg-positive people with chronic HBV mono-infection, with a similar percentage of participants achieving HBV DNA levels <29 IU/mL at 48 weeks of therapy (64% for TAF vs. 67% for TDF; *P* = 0.25).[29] In both studies, people on TAF experienced significantly smaller mean percentage decreases from baseline in hip and spine bone mineral density at 48 weeks than participants receiving TDF. The median change in estimated glomerular filtration rate (eGFR) from baseline to 48 weeks also favored TAF.[28,29]

In people with HBV/HIV coinfection, (TAF or TDF) plus (3TC or FTC) can be considered part of the ARV regimen; entecavir has weak anti-HIV activity and must not be considered part of an ARV regimen. In addition, TDF is fully active for the treatment of people with known or suspected 3TC-resistant HBV infection, whereas 3TC resistance compromises the activity of entecavir against HBV.

Recommended Therapy

The combination of (TAF or TDF) plus (3TC or FTC) should be used as the NRTI backbone of an ARV regimen and for the treatment of both HIV and HBV infection **(AI).**[30-32] The decision whether to use a TAF- or TDF-containing regimen should be based on an assessment of risk for nephrotoxicity and the acceleration of bone loss. In a switch study in people with HBV/HIV coinfection, study participants who switched from a primarily TDF-based ARV regimen to the fixed-dose combination elvitegravir/cobicistat (EVG/c)/TAF/FTC maintained or achieved HBV suppression with improved eGFR and bone turnover markers.[33] See Appendix B for guidance on renal dosing of NRTIs. Although data on switching from a TDF-based to a TAF-based ARV regimen are limited, the data from the EVG/c/TAF/FTC switch study suggest that people with HBV/HIV coinfection can switch to TAF/FTC-containing regimens with a potential reduction in renal and bone toxicity while maintaining HBV suppression.

Alternative Therapy

If TDF or TAF cannot be safely used or if there is a desire to use a TAF- or TDF-sparing ART regimen**,** entecavir can be used as an alternative HBV therapy in addition to a fully suppressive ARV regimen **(BI).** Entecavir has weak activity against HIV; its use for HBV treatment without ART may result in the selection of the M184V mutation that confers HIV resistance to 3TC and FTC.[34,35] Therefore, entecavir must be used in addition to a fully suppressive ARV regimen when given to people with HBV/HIV coinfection **(AII).** Because entecavir and 3TC share a partially overlapping pathway to HBV resistance, it is unknown whether the combination of entecavir plus 3TC or FTC will provide greater virologic or clinical benefit than entecavir alone. In people with known or suspected 3TC-resistant HBV infection, the entecavir dose should be increased from 0.5 mg/day to 1 mg/day.[36] However, entecavir resistance may emerge rapidly in people with 3TC-resistant HBV infection. Therefore, entecavir should be used with caution in such people, with frequent monitoring (approximately every 3 months) of the HBV DNA level to detect viral breakthroughs.[35]

Important Considerations

- Discontinuation of HBV-active NRTI drugs may potentially cause serious hepatocellular injury resulting from the reactivation of HBV.[37]

- Entecavir has activity against HIV. However, when entecavir is used to treat HBV in people with HBV/HIV coinfection who are not on ART, the drug may select for the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, when used in people with HBV/HIV coinfection, entecavir must be used in addition to a fully suppressive ARV regimen **(AII).**[38]
- When 3TC is the only active drug used to treat chronic HBV in people with HBV/HIV coinfection, 3TC-resistant HBV emerges in approximately 40% and 90% of people after 2 years and 4 years on 3TC, respectively. Given the similarities between FTC and 3TC, these drugs should only be used in combination with other anti-HBV drugs **(AII).**[39]
- In people with HBV/HIV coinfection, immune reconstitution following the initiation of treatment for HIV and HBV can be associated with elevated liver transaminase levels, possibly because HBV-induced liver injury is primarily an immune-mediated disease.[40]
- Some ARV agents (especially older drugs, such as nevirapine, tipranavir, and high-dose ritonavir) can increase liver transaminase levels. The incidence and magnitude of these increases were higher with HBV/HIV coinfection than with HIV mono-infection.[41-43] The etiology and consequences of these changes in transaminases are unclear because the changes may resolve with continued ART. Nevertheless, some experts suspend the suspected agent(s) when the serum alanine transferase (ALT) level increases to 5 to 10 times the upper limit of normal, or at a lower threshold if the person has symptoms of hepatitis and/or new elevations in bilirubin. However, increased transaminase levels in people with HBV/HIV coinfection may indicate HBeAg seroconversion due to immune reconstitution; thus, the cause of the elevations should be investigated before medications are discontinued. In people with increases in transaminase, HBeAg seroconversion should be evaluated by testing for HBeAg and anti-HBe, as well as HBV DNA levels, which should decrease in the setting of immune reconstitution. Other causes of ALT elevation—such as HCV or HDV infection, alcohol use, metabolic dysfunction-associated steatotic liver disease, and hepatotoxicity from non-ARV agents—should also be considered.

HBV Drugs Not Recommended

Adefovir in combination with 3TC or FTC with a fully suppressive ARV regimen was studied in people with HIV/HBV coinfection.[30,44,45] Adefovir was associated with high rates of HBV treatment failure and a high incidence of renal toxicity. Therefore, the Panel **does not recommend** adefovir for people with HBV/HIV coinfection **(AI).** Pegylated interferon alfa monotherapy is a potential therapy for the treatment of HBV mono-infection; however, data on its use in people with HBV/HIV coinfection are limited, and tolerance of the therapy in people with HIV is a significant limitation to its use. As a result, the Panel **does not recommend** pegylated interferon alfa for people with HBV/HIV coinfection **(AIII).** Pegylated interferon alfa can remain a treatment option in rare cases and with the consultation of an expert.

Changing Antiretroviral Therapy

- **When switching or modifying an ARV regimen in a person with HBV/HIV coinfection:** ARV drugs that are active against HBV (TDF or TAF in combination with 3TC or FTC) should be continued **(AII)** or a specific anti-HBV drug such as entecavir should be initiated **(AII).**
- **When ARV medications that are active against HBV in people with HBV/HIV coinfection must be discontinued:** Withdrawal of HBV-active treatment in a person with chronic HBV infection **is not recommended (AII).** If TAF or TDF cannot be continued due to concern for safety or if there is a desire to use a TAF- or TDF-sparing regimen and entecavir cannot be used or if there is concern for entecavir resistance, the person's clinical course should be monitored with monthly testing of liver transaminases. The risk of HBV flare in this setting is highest in people with positive HBeAg and those with active HBV. If no anti-HBV ARV drug can be used,

entecavir should be added to a fully suppressive ARV regimen to prevent HBV flare **(AII)**, especially in people with marginal hepatic reserve, such as those with compensated or decompensated cirrhosis.[37]

Screening for HBV Before Initiating NRTI-Sparing or NRTI-Limited Antiretroviral Regimens

HBV status should be evaluated in all people with HIV who are not known to have chronic HBV before the initiation of an NRTI-sparing or NRTI-limited ARV regimen (such as long-acting cabotegravir plus rilpivirine [LA CAB/RPV], dolutegravir [DTG]/rilpivirine [RPV], or DTG/3TC). Considerations for screening include the following:

- People with HIV should be screened for HBV infection, and if not already immune or infected (including those with isolated hepatitis B core antibody [HBcAb]), vaccination should be initiated while considering these new ARV regimens (see Hepatitis B Virus Infection in the Adult and Adolescent Opportunistic Infections Guidelines).
- People with HBV/HIV coinfection were not included in clinical trials that evaluated NRTI-sparing or NRTI-limited regimens. If LA CAB/RPV, DTG/RPV, or DTG/3TC are used in people with HBV coinfection, TAF, TDF, or entecavir should also be prescribed **(AII).** In people with prior exposure to 3TC monotherapy, TAF or TDF is preferred due to the risk of HBV resistance to 3TC; thus, there is a lower barrier of resistance for entecavir.
- People with HIV and prior exposure to HBV infection (negative HBsAg, positive HBcAb, and either positive or negative hepatitis B surface antibody [HBsAb]) are likely at low risk (<1%) of HBV reactivation and even lower risk of HBV reactivation hepatitis,[14] although there are insufficient studies to confidently estimate the risk in this population. Of people with HIV and prior exposure to HBV infection, those with positive HBsAb are at the lowest risk for HBV reactivation, although HBV reactivation has been described when HBV-active therapy is withdrawn as part of an ART regimen.[14]
- For individuals with prior HBV exposure, it is reasonable and feasible to incorporate ALT monitoring into the frequent laboratory testing already recommended after switching from ART with HBV NRTI therapy (TDF, TAF, or entecavir) to LA CAB/RPV, DTG/RPV, or DTG/3TC. An increase in ALT would warrant HBV DNA testing to assess for HBV reactivation hepatitis and immediate initiation of HBV therapy once reactivation is confirmed. A monitoring strategy is considered a safe and effective way to assess for HBV reactivation in low-risk people **(BIII).**[46,47] The timeline for reactivation is not clear in this population. Monitoring every 1 to 3 months for 6 months after switching from HBV-active ART is consistent with current recommendations for low-risk people without HIV.

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Hepatitis C Virus/HIV Coinfection

Updated: March 23, 2023
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Panel's Recommendations
• All people with HIV should be screened for hepatitis C virus (HCV) infection **(AIII).** Patients at high risk of HCV infection should be screened annually and whenever incident HCV infection is suspected **(AIII).** • Antiretroviral therapy (ART) may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation. For most patients with HCV/HIV coinfection, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury. Therefore, ART should be initiated in all patients with HCV/HIV coinfection, regardless of CD4 T lymphocyte cell count **(AI).** • Initial antiretroviral (ARV) regimens that are recommended for most patients with HCV/HIV coinfection are the same as those recommended for people with HIV who do not have HCV infection. However, when treatment for both HIV and HCV is indicated, the ARV and HCV treatment regimens should be selected with special consideration for potential drug–drug interactions and overlapping toxicities **(AIII)** (see discussion in the text below and in Table 19). • All patients with HCV/HIV coinfection should be evaluated for HCV therapy, which includes assessing their liver fibrosis stage to guide the duration of therapy and to predict subsequent risk of hepatocellular carcinoma and liver disease complications **(AIII).** • Patients with chronic HCV/HIV coinfection should be screened for active and prior hepatitis B virus (HBV) infection by testing for the presence of hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B surface (HBsAb) and hepatitis B core (HBcAb; total or Immunoglobulin G). Persons who are not immune to HBV infection (HBsAb negative) should receive anti-HBV vaccination **(AIII).** • HBV reactivation has been observed in people with HBV infection during HCV treatment with direct-acting antivirals. Accordingly, before initiating HCV therapy, patients with HCV/HIV coinfection and active HBV infection (HBsAg positive) should receive ART that includes two agents with anti-HBV activity **(AIII).**
Rating of Recommendations: *A = Strong; B = Moderate; C = Weak* ***Rating of Evidence:*** *I = Data from randomized controlled trials; II = Data from well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

The treatment of hepatitis C virus (HCV) infection is rapidly evolving. Patients with HCV/HIV coinfection treated with all-oral, direct-acting antiviral (DAA) HCV regimens can achieve sustained virologic response (HCV cure) at rates comparable to those in patients with HCV mono-infection.[1-3] This section of the guidelines focuses on hepatic safety and drug–drug interaction issues related to HCV/HIV coinfection and the concomitant use of antiretroviral (ARV) agents and HCV drugs. For specific guidance on HCV treatment, clinicians should refer to the HCV Guidance from the American Association for the Study of Liver Diseases and the Infectious Diseases Society of America.

Approximately one-third of patients with chronic HCV infection progress to cirrhosis at a median time of <20 years.[4,5] The rate of progression increases with older age, alcoholism, male sex, and HIV infection.[6-9] A meta-analysis found that patients with HCV/HIV coinfection had a threefold greater risk of progression to cirrhosis or decompensated liver disease than patients with HCV mono-infection.[8] The risk of progression is even greater in patients with HCV/HIV coinfection who have low CD4 T lymphocyte cell counts. Although antiretroviral therapy (ART) appears to slow the rate of HCV disease progression in patients with HCV/HIV coinfection, several studies have demonstrated that the rate of disease progression continues to exceed that observed in patients without HIV.[10,11] Whether HCV infection accelerates HIV progression, as measured by the occurrence of AIDS-

related opportunistic infections or death,[12] is unclear. With older ARV drugs, people with HIV and HCV coinfection experienced higher rates of hepatotoxicity than those seen in people with HIV but not HCV.[13,14] These higher rates have not been observed with the newer ARV agents that are currently in use.

Assessment of HCV/HIV Coinfection

All people with HIV should be screened for HCV infection using sensitive immunoassays licensed for the detection of antibodies to HCV in blood.[15] Patients who are HCV-seronegative but at risk for HCV infection should undergo repeat testing annually or as clinically indicated. Patients who are HCV-seropositive should be tested for HCV RNA using a sensitive quantitative assay to confirm the presence of active infection. Patients who test HCV RNA positive should undergo HCV genotyping and liver disease staging as recommended by the HCV Guidance.

- Patients with HCV/HIV coinfection should be counseled to avoid consuming alcohol.
- Patients with HCV/HIV coinfection also should be counseled about appropriate precautions to prevent transmission of HIV and/or HCV to others.
- Patients with chronic HCV/HIV coinfection should be screened for active and prior hepatitis B virus (HBV) infection by testing for the presence of hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B surface (HBsAb) and hepatitis B core (HBcAb; total or Immunoglobulin G).
    - Patients with evidence of active HBV infection (HBsAg positive) should be further evaluated and treated with ART that includes agents with anti-HIV and anti-HBV activities **(AIII).**
    - Those who are not immune to HBV infection (HBsAb negative) should receive anti-HBV vaccination.
- Patients with HCV/HIV coinfection who are susceptible to hepatitis A virus (HAV) should be vaccinated against HAV.
- All patients with HCV/HIV coinfection are candidates for curative HCV treatment.

Antiretroviral Therapy in HCV/HIV Coinfection

When to Start Antiretroviral Therapy

Initiation of ART for patients with HCV/HIV coinfection should follow the recommendations for all persons with HIV infection, considering the need for concurrent HCV treatment with oral DAA regimens, the potential for drug–drug interactions, and the individual's HBV status.

Considerations When Starting Antiretroviral Therapy

The same regimens that are recommended for initial treatment of HIV in most ART-naive persons also are recommended for patients with HCV/HIV coinfection. Special considerations for ARV selection in patients with HCV/HIV coinfection include the following:

- When both HIV and HCV treatments are indicated, the ARV regimen should be selected with careful consideration of potential drug–drug interactions with the HCV treatment regimen (see Table 19 below).
- In patients with HCV/HBV coinfection, HBV reactivation has been observed during HCV treatment with DAAs.[16,17] Therefore, before initiating HCV therapy, patients with HCV/HIV coinfection and active HBV infection (HBsAg positive) should receive ART that includes agents

with anti-HBV activity (such as tenofovir disoproxil fumarate [TDF] or tenofovir alafenamide plus emtricitabine or lamivudine) **(AIII).**

- Patients with cirrhosis should be evaluated for signs of liver decompensation according to the Child-Turcotte-Pugh classification system. All patients with Child-Pugh class B or C disease should be evaluated by an expert in advanced liver disease and considered for liver transplantation. Furthermore, hepatically metabolized ARV and HCV DAA drugs may be contraindicated or require dose modification in patients with Child-Pugh class B and C disease (see Appendix B).

Hepatotoxicity

Drug-induced liver injury (DILI) following the initiation of ART is more common in patients with HCV/HIV coinfection than in those with HIV mono-infection. Individuals with HCV/HIV coinfection who have advanced liver disease (e.g., cirrhosis, end-stage liver disease) are at greatest risk for DILI.[18] Eradicating HCV infection with treatment may decrease the likelihood of ARV-associated DILI.[19] Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels should be monitored 4 to 8 weeks after initiation of ART and at least every 6 to 12 months thereafter, and more often if clinically indicated. Mild to moderate fluctuations in ALT and/or AST levels (<5 times upper limit of normal [ULN]) are typical in individuals with chronic HCV infection. In the absence of signs or symptoms of liver disease or increases in bilirubin, these fluctuations do not warrant interruption of ART, but they do warrant monitoring to ensure a return to baseline. Patients with significant elevations in ALT or AST levels (>5 times ULN), concomitant increase in total bilirubin, or concomitant symptoms (weakness, nausea, vomiting) should be evaluated carefully for signs and symptoms of liver insufficiency and for alternative causes of liver injury (e.g., acute HAV or HBV infection, hepatobiliary disease, alcoholic hepatitis). If these signs and symptoms do not resolve, ART should be discontinued.

Concurrent Treatment of HIV and HCV Infections

Guidance on the treatment and management of HCV in adults with and without HIV can be found in the HCV Guidance. Several ARV drugs and HCV DAAs have the potential for clinically significant pharmacokinetic drug–drug interactions when used in combination. Before starting HCV therapy, the ART regimen may need to be modified to reduce the drug–drug interaction potential. Table 19 below provides recommendations on the concomitant use of selected drugs for the treatment of HCV and HIV infection. In patients receiving ART that has been modified to accommodate HCV treatment, HIV RNA should be measured within 2 to 8 weeks after changing HIV therapy to confirm the effectiveness of the new regimen. After ART modification, initiation of an HCV DAA regimen should be delayed for ≥2 weeks. Resumption of the original ARV regimen also should be delayed until ≥2 weeks after the HCV DAA regimen is completed. The prolonged half-life of some HIV and HCV drugs poses a potential risk of drug–drug interactions if a regimen is resumed soon after ART modification or HCV treatment completion.

Table 19. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

The recommendations in this table for concomitant use of select HIV drugs with U.S. Food and Drug Administration (FDA)–approved HCV DAA drugs are based on available pharmacokinetic (PK) interaction data or are predictions based on the known metabolic pathways of the agents. (Instances where PK interaction data are limited or not available are indicated in the table.) Whenever HIV and HCV drugs are used concomitantly, patients should be closely monitored for HIV and HCV virologic efficacy and potential toxicities. Because the field of HCV therapy is rapidly evolving, readers also should refer to the latest drug product labels and the HCV Guidance for updated information.

Note: Interactions with fosamprenavir (FPV) and nelfinavir (NFV) are **not** included in this table. Please refer to the FDA product labels for information regarding drug interactions with these HIV protease inhibitors (PIs).

ARV Drugs	Individual Drug	Coformulated				
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT **(Cirrhosis classified as Child-Pugh class B or C)**		
	Sofosbuvir	**Ledipasvir/ Sofosbuvir**	**Sofosbuvir/ Velpatasvir**	**Sofosbuvir/ Velpatasvir/ Voxilaprevir**	**Glecaprevir/ Pibrentasvir**	**Elbasvir/ Grazoprevir**
3TC	✓	✓	✓	✓	✓	✓
ABC	✓	✓	✓	✓	✓	✓
FTC	✓	✓	✓	✓	✓	✓
TAF	✓	✓	✓	✓	✓	✓
TDF	✓	✓ Monitor for TDF-associated adverse events.	✓ Monitor for TDF-associated adverse events.	✓ Monitor for TDF-associated adverse events.	✓	✓

Table 19. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

ARV Drugs	Individual Drug	Coformulated				
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT **(Cirrhosis classified as Child-Pugh class B or C)**		
	Sofosbuvir	**Ledipasvir/ Sofosbuvir**	**Sofosbuvir/ Velpatasvir**	**Sofosbuvir/ Velpatasvir/ Voxilaprevir**	**Glecaprevir/ Pibrentasvir**	**Elbasvir/ Grazoprevir**
Unboosted ATV	✓	✓	✓	✖	✖	✖
ATV/r or ATV/c	✓	✓ If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated adverse events.[a]	✓ If a PI/r or PI/c is used with TDF, ↑ TDF concentrations are expected. If coadministration is necessary, monitor for TDF-associated adverse events.[a]	✖	✖	✖
DRV/r or DRV/c	✓			✓ If a PI/r is used with TDF, ↑ TDF concentrations are expected. Monitor for TDF-associated adverse events.[a] Consider monitoring for hepatotoxicity.[b]	✖	✖
LPV/r	✓			✖	✖	✖
TPV/r	✖	✖	✖	✖	✖	✖
DOR	✓	✓ If used with TDF, monitor for TDF-associated adverse events.	✓	✓	✓	✓
EFV	✓		✖	✖	✖	✖
ETR	✓		✖	✖	✖	✖
NVP	✓		✖	✖	✖	✖
RPV PO and IM	✓		✓	✓	✓	✓
BIC/TAF/FTC	✓	✓	✓	✓	✓	✓
CAB PO and IM	✓	✓	✓	✓	✓	✓

Table 19. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

ARV Drugs	Individual Drug	Coformulated				
				SHOULD NOT BE USED IN THOSE WITH MODERATE TO SEVERE HEPATIC IMPAIRMENT (Cirrhosis classified as Child-Pugh class B or C)		
	Sofosbuvir	**Ledipasvir/ Sofosbuvir**	**Sofosbuvir/ Velpatasvir**	**Sofosbuvir/ Velpatasvir/ Voxilaprevir**	**Glecaprevir/ Pibrentasvir**	**Elbasvir/ Grazoprevir**
DTG	✓	✓ If used with TDF, monitor for TDF-associated adverse events.	✓	✓	✓	✓
EVG/c/TDF/FTC	✓	✖	✓ If used with TDF, monitor for TDF-associated adverse events.	✓ If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity.[b]	✓ If used with TDF, monitor for TDF-associated adverse events. Consider monitoring for hepatotoxicity.[c]	✖
EVG/c/TAF/FTC	✓	✓	✓	✓ Consider monitoring for hepatotoxicity.[e]	✓ Consider monitoring for hepatotoxicity.[f]	✖
RAL	✓	✓	✓	✓	✓	✓
MVC	✓	✓	✓	✓	✓	✓
FTR	✓	✓	✓	✖ Use alternative HCV regimen if possible.	✓	✖ Use alternative HCV regimen if possible.
LEN	✓	✓	✓	✓	✓	✓

[a] Consider using an alternative HCV treatment or ARV regimen to avoid increases in TDF exposure. If coadministration is necessary, monitor patient for TDF-associated adverse events.

[b] Voxilaprevir exposures can increase when it is coadministered with pharmacologically boosted DRV or EVG. Until more safety data in clinical settings become available, patients who are receiving voxilaprevir and pharmacologically boosted DRV or EVG should be monitored for hepatotoxicity.

Table 19. Concomitant Use of Selected Antiretroviral Drugs and Hepatitis C Virus Direct-Acting Antiviral Drugs for Treatment of Hepatitis C Virus in Adults With HIV

[c] Glecaprevir exposures can increase when it is coadministered with EVG/c. Until more safety data in clinical settings become available, patients who are receiving glecaprevir and EVG/c should be monitored for hepatotoxicity.

Key to Symbols:

✓ = ARV agents that can be used concomitantly
✖ = ARV agents not recommended
? = Data on PK interactions with ARV drug are limited or not available
↑ = Increase
↓ = Decrease

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; DAA = direct-acting antiviral; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; FTR = fostemsavir; HCV = hepatitis C virus; IM = intramuscular; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; MVC = maraviroc; NVP = nevirapine; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PO = oral; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir

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Tuberculosis/HIV Coinfection

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Key Considerations and Recommendations

- Treatment for latent tuberculosis infection (LTBI) in people with HIV should take into consideration the individual's antiretroviral (ARV) regimen as noted below.
  - General recommendations for **once-weekly** isoniazid plus rifapentine for 3 months (3HP) and **once-daily** isoniazid plus rifapentine for 1 month (1HP):
    - These regimens **are not recommended** for people who require twice-daily dolutegravir (DTG) therapy (e.g., those with certain integrase strand transfer inhibitor [INSTI]–associated resistance substitutions or clinically suspected INSTI resistance) **(AIII).**
    - Tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) **(AIII),** tenofovir alafenamide (TAF)/FTC **(BIII),** or abacavir (ABC)/lamivudine (3TC) **(BIII)** can be used as the nucleoside reverse transcriptase inhibitor (NRTI) backbone. Rifapentine may lower concentrations of TAF. If used, monitor for virologic response.
  - For 3HP
    - Efavirenz (EFV) 600 mg once daily or raltegravir 400 mg twice daily can be used **(AII).**
    - DTG 50 mg once daily may be used for those in whom once-daily DTG is appropriate **(BII).**
  - For 1HP
    - EFV 600 mg once daily can be used without dose adjustment **(AI).**
    - For a person with virologic suppression while on a DTG 50 mg once-daily regimen, the DTG dose should be increased to 50 mg twice daily throughout the course of 1HP, continuing DTG 50 mg twice daily for 14 days after 1HP completion before switching back to once-daily DTG dosing **(AII).**
  - With daily isoniazid alone for 6 or 9 months, any ARV regimen can be used **(AIII).**
  - If rifampin is used to treat LTBI, clinicians should review Tables 24a through 24g to assess the potential for drug–drug interactions between rifampin and different ARV drugs **(AII).**
- All people with HIV and active tuberculosis (TB) who are not on antiretroviral therapy (ART) should be started on ART **(AI)** as described below.
  - **CD4 T lymphocyte (CD4) cell counts <50 cells/mm^3:** Initiate ART as soon as possible, but within 2 weeks of starting TB treatment **(AI).**
  - **CD4 counts ≥50 cells/mm^3:** Initiate ART within 2 to 8 weeks of starting TB treatment **(AI).**
  - **During pregnancy, regardless of CD4 count:** Initiate ART as early as feasible for treatment of the person with HIV and prevention of HIV transmission to the infant **(AIII).**
  - **With TB meningitis:** Initiate ART after TB meningitis is under control and after at least 2 weeks of anti-TB treatment to reduce the risk of life-threatening inflammation in a closed space as a result of immune reconstitution **(AIII).**
- For people with active TB who are receiving ART, the ARV regimen should be assessed with particular attention to potential drug–drug interactions between ARVs and TB drugs. Rifamycin antibiotics (rifabutin, rifampin, and rifapentine), in particular, have considerable potential for drug–drug interactions. The ARV regimen may need to be modified to permit use of the optimal TB treatment regimen (see Tables 24a through 24g for drug interaction data and dosing recommendations) **(AII).**

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Managing Latent Tuberculosis Infection in People With HIV

Approximately one-quarter of the world's population has tuberculosis (TB) infection, with a 5% to 10% lifetime risk of progressing to active disease.[1] Among individuals with latent TB infection (LTBI), the risk of developing active TB is much higher among those who also have HIV, and this risk increases as immune deficiency worsens.[2]

Tuberculosis Preventive Treatment

After active TB has been excluded, the Centers for Disease Control and Prevention preferentially recommends one of the following short-course regimens for LTBI treatment (see Treatment Regimens for Latent TB Infection):

- 3 months of once-weekly isoniazid plus rifapentine (3HP)
- 4 months of daily rifampin (4R)
- 3 months of daily isoniazid plus rifampin (3HR)

The World Health Organization (WHO)[3] and the Panel on Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents With HIV also recommend 1 month of daily isoniazid with rifapentine (1HP) as an alternative short-course regimen.

For more than 30 years, isoniazid had been the cornerstone of treatment for LTBI to prevent active TB. Randomized controlled clinical trials have demonstrated that treatment with isoniazid for 6 or 9 months for LTBI in people with HIV reduces the risk of active TB, especially in those with a positive tuberculin skin test.[4] Isoniazid given daily or twice weekly for 6 or 9 months can be coadministered with any antiretroviral (ARV) regimen and remains an alternative option, especially for people in whom rifamycin antibiotics cannot be used **(AIII).**

In the PREVENT TB study, the combination of isoniazid and rifapentine administered once a week for 3 months (3HP), as directly observed therapy, was as safe and effective as 9 months of isoniazid in preventing TB in people with HIV who were not on antiretroviral therapy (ART).[5] Another study randomized 1,148 South African adults with HIV who were not on ART to one of four treatment groups: 3 months of isoniazid and rifapentine, 3 months of isoniazid and rifampin, 6 months of isoniazid, or isoniazid continued for the duration of the trial. TB incidence did not differ among the groups.[6] The Panel for the Use of Antiretroviral Agents in Adults and Adolescents With HIV (the Panel) recommends dolutegravir (DTG) 50 mg once daily with 3 months of once-weekly isoniazid and rifapentine in people with virologic suppression and for whom once-daily DTG is appropriate **(BII).** More importantly, this 3-month regimen **is not recommended** for people who require twice-daily DTG therapy (e.g., those with certain integrase strand transfer inhibitors [INSTI]–associated resistance substitutions or clinically suspected INSTI resistance) **(AIII).** Isoniazid given daily for 6 or 9 months should be used in this setting.

A study of 6,000 people that compared completion rates, safety, and effectiveness of 4 months of daily rifampin (4R) versus 9 months of isoniazid found that 4R was non-inferior to isoniazid for 9 months for the prevention of TB disease, and that safety and completion rates were superior for 4R.[7] However, this trial included only 242 (4%) participants with HIV. While 4R may also be considered for TB-preventive treatment, clinicians should pay careful attention to potential drug–drug interactions with specific ARV drugs (see Tables 24a through 24g).

In 3,000 people with HIV infection in the BRIEF TB study, no difference was observed in TB incidence between those who received 1HP and those who received 9 months of isoniazid.[8] Approximately half of the participants were on ART (either efavirenz [EFV] or nevirapine-based

regimens) while receiving the 1-month regimen. Fewer adverse events and a higher treatment completion rate occurred with the 1HP regimen than with 9 months of isoniazid.

Although rifapentine induces cytochrome P450 (CYP) isoenzymes and can potentially cause significant drug–drug interactions with ARVs, pharmacokinetic (PK) data support its use daily **(AI)** or once weekly **(AII)** with EFV 600 mg daily,[9,10] and once weekly with raltegravir (RAL) 400 mg twice daily **(AII).**[11] In a Phase 1/2 study of 60 adults with HIV and virologic suppression on once-daily dolutegravir (DTG)-based ART and weekly rifapentine with isoniazid,[12] DTG trough concentrations were reduced by 50% to 60%; all but one participant's trough concentration remained above the DTG protein-adjusted 90% inhibitory concentration (IC_{90}), and all HIV viral loads remained suppressed. In a multicenter PK study (A5372), 32 adults with HIV and virologic suppression on DTG-containing ART received DTG 50 mg twice daily throughout the course of 1HP and for 14 days after.[13] DTG trough concentrations were comparable with standard-dose DTG once daily without 1HP, and 31 (96.9%) of 32 participants maintained virologic suppression. One participant had an HIV RNA of 160 copies/mL at Day 28, with HIV RNA <50 copies/mL upon repeat testing on Day 42. Based on these data, the Panel recommends DTG 50 mg twice daily when given with 1HP in people with virologic suppression, continuing DTG 50 mg twice daily for 14 days after 1HP completion before switching back to once-daily DTG dosing **(AII).**

When prescribing either 1HP or 3HP, tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) **(AIII),** tenofovir alafenamide (TAF)/FTC **(BIII),** or abacavir (ABC)/lamivudine (3TC) **(BIII)** can be used as the nucleoside reverse transcriptase inhibitor (NRTI) backbone. The drug concentrations for ABC, TDF, 3TC, and FTC are not expected to be affected by rifapentine. Rifapentine may lower concentrations of TAF; if TAF is used, monitor for virologic response.

If a person with HIV has been in close contact with a person with drug-resistant TB, the options for LTBI treatment should be modified, taking into consideration drug-susceptibility test results from the source patient. In this setting, consultation with a TB expert is advised.

Isoniazid Preventive Therapy Plus Antiretroviral Therapy in Pregnant Women With HIV

A randomized trial of isoniazid preventive therapy (IPT) compared isoniazid initiated during pregnancy (immediate IPT) to isoniazid delayed until 12 weeks postpartum (deferred IPT) in 956 women with HIV on ART. A greater number of adverse pregnancy outcomes were seen in women on immediate IPT, suggesting that IPT should be delayed until after delivery.[14] Treatment-related maternal adverse events were higher than expected in both arms. In the BRIEF TB study, first-trimester IPT exposure was associated with a nearly twofold increased risk of fetal demise—mostly spontaneous abortion—though the association was attenuated when adjusted for covariates proximal to pregnancy outcome, including ART use.[15] However, two observational studies from South Africa showed better pregnancy outcomes and no increase in hepatotoxicity in pregnant women on ART receiving antenatal IPT.[16,17] The WHO continues to recommend IPT for individuals with HIV.[3]

Impact of Antiretroviral Therapy in Preventing Active Tuberculosis

Effective ART can prevent active TB in areas with high TB prevalence. The TEMPRANO study conducted in Côte d'Ivoire randomized 2,056 participants with HIV to one of four study arms: deferred ART, deferred ART plus IPT, early ART, or early ART plus IPT. The initial results demonstrated that IPT and early ART each independently reduced the risk of a serious HIV-related event, many of which were TB, and that IPT with early ART provided the best protection from serious HIV events and death.[18] Data from longer follow-up (median 4.9 years) showed that 6 months of IPT given early in the course of HIV infection provided a durable survival benefit, with a 37% reduction in the risk of death that was independent of ART.[19] In the START study,

4,685 participants with CD4 T lymphocyte (CD4) cell counts >500 cells/mm^3 were randomized to receive immediate ART or deferred ART. For participants in the deferred ART arm, ART was started when their CD4 count dropped to 350 cells/mm^3 or if they developed a clinical condition that required ART. TB was one of the three most common clinical events, occurring in 14% of participants in the immediate ART group and 20% of participants in the deferred ART group.[20] Collectively, these two large randomized studies showed that early initiation of ART (with or without IPT) reduced active TB, particularly in countries with a high prevalence of TB/HIV coinfection.

Antiretroviral Therapy for People With HIV and Active Tuberculosis

All people with HIV/TB disease should be treated with ART **(AI)**, although the timing of ART initiation may vary as discussed below. Important considerations related to the use of ART in people with active TB disease include the following:

- When to start ART in the setting of drug-resistant TB and in people with TB meningitis,
- Significant PK drug–drug interactions between anti-TB and ARV drugs, *and*
- The development of TB-associated immune reconstitution inflammatory syndrome (IRIS) after ART initiation.

Active pulmonary or extrapulmonary TB disease requires prompt initiation of TB treatment. The treatment of active TB disease in people with HIV should follow the general principles guiding treatment for people without HIV. The Adult and Adolescent Opportunistic Infection Guidelines include a more complete discussion of the diagnosis and treatment of TB disease in people with HIV.

The TB Trials Consortium Study 31/ AIDS Clinical Trials Group (ACTG) A5349 demonstrated success with a shorter, 4-month regimen.[21] This randomized, open-label, controlled Phase 3 trial compared two 4-month rifapentine-containing regimens to the standard 6-month control regimen of isoniazid plus rifampin. In 2,516 participants, including 193 (8%) with HIV, the rifapentine-moxifloxacin regimen was non-inferior to the control regimen, with 11.6% versus 9.6% unfavorable outcomes, respectively (difference 2.0%; 95% confidence interval, −1.1% to +5.1%), and it was safe and well tolerated. Participants with HIV were either already on an EFV-based ART or initiating an EFV-based ART.[22] In both groups, EFV concentrations were decreased slightly, but most maintained EFV concentrations of >1 mg/L and undetectable viremia.[23] This 4-month TB regimen with DTG-based ART is currently under investigation in the ACTG A5406 trial (NCT05630872).

Tuberculosis Diagnosed While a Person Is Receiving Antiretroviral Therapy

ART should be continued when TB is diagnosed in a person receiving ART, but the ARV regimen should be assessed with particular attention to potential drug interactions between ARVs and TB drugs (discussed below). The person's ARV regimen may need to be modified to permit use of the optimal TB treatment regimen **(AII)** (see Tables 24a through 24g for dosing recommendations).

Tuberculosis Diagnosed in a Person With HIV Not Yet Receiving Antiretroviral Therapy

ART should not be delayed until TB treatment is completed, because this strategy was associated with higher mortality rates in the SAPiT-1 study.[24] The timing of ART in specific populations is discussed below.

People with HIV and CD4 counts <50 cells/mm^3: Three large randomized clinical trials in people with HIV/TB disease, conducted in Africa and Asia, all convincingly showed that early ART in those with CD4 counts <50 cell/mm^3 significantly reduced AIDS events or deaths.[25-27] In these studies, early ART was defined as either ≤2 weeks[26] or ≤4 weeks[25] after initiation of TB therapy.

Collectively these three trials support the initiation of ART within the first 2 weeks of TB treatment in people with CD4 counts <50 cells/mm^3 **(AI).**

People with HIV and CD4 counts ≥50 cells/mm^3: In two of the three studies mentioned above,[26,27] no survival benefit was seen for people with CD4 counts ≥50 cells/mm^3 who initiated ART at <2 weeks versus later (8–12 weeks), after beginning TB treatment. Importantly, none of the studies demonstrated harm from earlier ART initiation, and many benefits of ART in people with HIV are well documented, regardless of TB coinfection. It is unlikely that more trials will be conducted to specifically inform the decision on when to start ART in people with TB and CD4 counts ≥50 cells/mm^3.

However, given the growing body of evidence supporting early ART in general and the lack of data showing any harm in people with TB coinfection, the Panel recommends ART initiation within 2 to 8 weeks after starting TB treatment for people with CD4 counts ≥50 cells/mm^3 **(AI).**

People with HIV and drug-resistant TB: People may have single-drug-resistant TB, multidrug-resistant TB (MDR-TB) (defined as strains with resistance to both isoniazid and rifampin); pre-extensively drug-resistant (pre-XDR) TB (defined as MDR-TB plus resistance to any fluoroquinolone), or extensively drug-resistant TB (XDR-TB) (defined as MDR-TB plus resistance to any fluoroquinolone and at least one additional Group A drug listed in the WHO guidelines).[28] Historically, mortality rates in people with MDR-TB or XDR-TB and HIV have been high,[29] but more recent data suggest that treatment outcomes are similar for people with MDR-TB with and without HIV infection. In the Nix-TB study of an all-oral, 6-month regimen of bedaquiline, pretomanid, and linezolid for MDR-TB and XDR-TB, 51% of the 109 participants also had HIV. Rates of cure, serious adverse events, and mortality were similar among those with and without HIV.[30]

Although randomized clinical trial data to guide the optimal timing for ART initiation are lacking, the WHO guidelines recommend ART for all people with HIV and drug-resistant TB, irrespective of CD4 count, as early as possible (within the first 8 weeks), following the initiation of TB treatment.

Management of people with HIV and drug-resistant TB is complex, and expert consultation is advised **(AIII).**

People with TB meningitis: TB meningitis is often associated with severe complications and a high mortality rate. In a study conducted in Vietnam, people with HIV-associated TB meningitis were randomized to immediate ART or to ART deferred until 2 months after initiation of TB treatment. A significantly higher rate of severe (Grade 4) adverse events was seen in people who received immediate ART than in those who received deferred ART (80.3% vs. 69.1% for immediate and deferred ART, respectively; $P = 0.04$).[31]

Despite these study results, in the setting of TB meningitis, many experts would recommend initiating ART early in settings where close monitoring of drug-related toxicities and central nervous system adverse events is feasible (see Adult and Adolescent Opportunistic Infection Guidelines) **(BIII).** ART should be started after TB meningitis is under control and after at least 2 weeks of anti-TB treatment to reduce the risk of life-threatening inflammation in a closed space as a result of immune reconstitution **(AIII).**

Managing people with HIV and TB meningitis is complex, and expert consultation is advised **(AIII).**

Pregnant women: All women with HIV and active TB who are pregnant should be started on ART as early as feasible, both for the treatment of the person with HIV and prevention of HIV transmission to the infant **(AIII).** The choice of ART should be based on efficacy and safety in pregnancy and should take into account potential drug–drug interactions between ARVs and rifamycins (see Perinatal Guidelines for more detailed discussions).

Drug Interaction Considerations

Rifamycin antibiotics (rifabutin, rifampin, and rifapentine) are an important component of TB treatment regimens because of their sterilizing ability. However, they are associated with a considerable potential for drug interactions due to their ability to affect various drug-metabolizing enzymes and transporters. Rifampin is a potent inducer of the CYP (mostly 3A and 2C subfamilies) enzyme system, P-glycoprotein (P-gp), and uridine diphosphate glucuronosyltransferase 1A1 (UGT1A1). Rifabutin and rifapentine are both substrates and inducers of CYP3A4. As potent inducers of metabolic enzymes and drug transporters, rifamycin-related drug interactions may result in significant reduction in ARV drug exposure. The ARV drugs most affected include all protease inhibitors (PIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), INSTIs, the CCR5 antagonist maraviroc (MVC), the gp120 attachment inhibitor fostemsavir, and the capsid inhibitor lenacapavir. Coadministration of rifamycins with long-acting injectable cabotegravir with rilpivirine or lenacapavir is contraindicated.[32] Most NRTIs, the fusion inhibitor enfuvirtide, and the CD4 post-attachment inhibitor ibalizumab are not expected to have significant drug interactions with the rifamycins. Tables 24a through 24g outline the magnitude of these interactions and provide dosing recommendations when rifamycin antibiotics and selected ARV drugs are used concomitantly.

Because TAF is a P-gp substrate, its plasma concentrations may be reduced by rifamycin antibiotics. Current labeling does not recommend concomitant administration of TAF and any rifamycin antibiotic.[33] However, in a healthy volunteer study, following administration of TAF/FTC with rifampin, intracellular tenofovir-diphosphate concentrations were still 4.2-fold higher than those achieved by TDF.[34] TAF can be used with rifampin with caution and close monitoring of virologic response.

Several ARV drugs are not recommended for use with rifampin; clinicians should refer to Tables 24a through 24g before prescribing these drugs in combination. When DTG, RAL, or MVC are used with rifampin for TB treatment, the ARV doses must be increased. In contrast to its effect on other ARV drugs, rifampin leads to only a modest reduction in EFV concentrations.[35,36] Even though the current EFV label recommends increasing the EFV dose from 600 mg once daily to 800 mg once daily in people weighing >50 kg,[37] this dosage increase is generally not necessary. The Panel recommends EFV 600 mg for individuals receiving rifampin therapy. High-dose (up to 35 mg/kg/day) rifampin is currently being evaluated for treatment of TB meningitis. The data on the magnitude and extent of interactions between high-dose rifampin and ARV drugs are limited.[38-40]

Rifabutin, a weaker CYP3A4 enzyme inducer, is an alternative to rifampin for TB treatment, especially in people taking PI- or INSTI-based ARV regimens. Because rifabutin is a substrate of the CYP450 enzyme system, its metabolism may be affected by NNRTIs or PIs. Therefore, rifabutin dosage adjustment is generally recommended (see Tables 24a through 24g for dosing recommendations).

Rifapentine is a long-acting rifamycin that may be given once weekly or once daily. When given daily, it is a more potent inducer than rifampin.[41] Once-daily rifapentine did not affect the oral clearance of EFV 600 mg in individuals with HIV in the BRIEF TB study,[42] and once-weekly rifapentine has demonstrated minimal impact on EFV 600 mg exposure.[9] Once-weekly rifapentine led to an increase, rather than a decrease, in RAL drug exposure in healthy volunteers.[11] A PK study conducted in South Africa found that once-weekly isoniazid-rifapentine plus once-daily DTG was well tolerated in participants with HIV, with only 3 of 60 participants experiencing a Grade 3 adverse effect (two with

elevated creatinine and one with hypertension). The extent of the interaction varied by day, with a 23% reduction on Day 1, 64% reduction on Day 2, and 56% reduction on Days 5 and 6 after isoniazid-rifapentine dose.[12] In a multicenter PK study (A5372), 32 adults with HIV and virologic suppression on DTG-containing ART received DTG 50 mg twice daily during 1HP and for 14 days after.[13] DTG trough concentrations were comparable with standard-dose DTG once daily without 1HP.

Tuberculosis-Associated Immune Reconstitution Inflammatory Syndrome

Immune reconstitution inflammatory syndrome (IRIS) is a clinical condition caused by ART-induced restoration of pathogen-specific immune responses to opportunistic infections, such as TB, resulting in either the deterioration of a treated infection (paradoxical IRIS) or a new presentation of a previously subclinical infection (unmasking IRIS). Manifestations of unmasking TB-associated IRIS (TB-IRIS) are characterized by their marked inflammatory nature, such as high fever, respiratory distress, lymphadenitis, abscesses, and sepsis syndrome. Manifestations of paradoxical TB-IRIS include fevers, new or worsening lymphadenopathy, new or worsening pulmonary infiltrates, enlarging pleural effusions, and new or enlarging tuberculomas.

TB-IRIS has been reported in 8% to more than 40% of people who start ART after being diagnosed with TB, although the incidence depends on the definition of IRIS and the intensity of monitoring.[43,44] IRIS is infrequently associated with mortality.

Predictors of IRIS include a baseline CD4 count <50 cells/mm^3; higher on-ART CD4 counts; high pre-ART and lower on-ART HIV viral loads; severity of TB disease, especially high pathogen burden; and <30-day interval between initiation of TB and HIV treatments.[45] Most IRIS in HIV/TB disease occurs ≤3 months from the start of ART.

In general, the Panel recommends continuing ART without interruption during IRIS **(AIII).**

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LIMITATIONS TO TREATMENT SAFETY AND EFFICACY

Adherence to the Continuum of Care

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Key Considerations and Recommendations

• Linkage to HIV care and adherence to both antiretroviral therapy (ART) and clinic appointments should be regularly assessed.
• An individual's barriers to ART and clinic appointment adherence should be assessed before or shortly after the initiation of ART and regularly thereafter.
• Rapid access to ART is one of the pillars of the United States' plan to end the HIV epidemic; therefore, delays in access to ART should be addressed and treatment initiated as soon as possible.
• People with HIV having ART adherence problems should be placed on regimens with high genetic barriers to resistance, such as dolutegravir, bictegravir, or boosted darunavir. Side effects, out-of-pocket costs, convenience, and individual preferences should also be considered.
• People with HIV having difficulties with adherence to appointments or ART should be provided additional adherence support using a constructive, collaborative, nonjudgmental, and problem-solving approach.
• The approach taken to improve adherence should be tailored to each person's needs and barriers to care. Approaches could include, but are not limited to—
  ○ Changing ART to simplify dosing or to reduce side effects
  ○ Allowing flexible appointment scheduling
  ○ Finding resources to assist with treatment costs to maintain uninterrupted access to both ART and appointments
  ○ Linkage to resources to assist with unmet social and economic needs, such as transportation, food, housing, and other support services
  ○ Linkage to services to overcome stigma, substance use, or mental illness
• A multidisciplinary approach—including collaborations with nursing, pharmacy, social work, and case management (to the extent available—is often necessary to identify solutions to ART and appointment adherence. The clinician's role is to help people with HIV understand the importance of adherence to the continuum of care, identify the barriers to adherence and address those that are within their purview, and link them to resources to overcome other barriers.
• Single-tablet ART regimens are generally recommended when clinically appropriate, but high-quality evidence to definitively recommend them is lacking and shared decision-making between clinicians and people with HIV is essential **(BIII).**
• At this time, evidence does not support the use of financial incentives to engage people with HIV in ongoing routine care.
• Methods to estimate adherence based on drug levels measured in plasma, dried blood spots, urine, and hair samples are available. Measuring adherence with these methods has not been shown in randomized studies to improve outcomes. However, these methods should be used in a collaborative manner to avoid an adversarial relationship between the provider and people with HIV.

- Because delayed administration of long-acting cabotegravir plus rilpivirine (LA CAB/RPV) may lead to the emergence of drug resistance, LA CAB/RPV is not generally recommended as a complete regimen in people with viremia due to suboptimal adherence to ART, or in people who have ongoing challenges with retention in HIV care. However, based on very limited data, the Panel for the Use of Antiretroviral Agents in Adults and Adolescents With HIV recommends the use of LA CAB/RPV on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral ART, and who have no evidence of resistance to rilpivirine RPV or CAB and, with shared decision-making between providers and people with HIV **(CIII).** See Virologic Failure for a more detailed discussion.
- A summary of best practice interventions to improve linkage, retention, and adherence can be found in the Centers for Disease Control and Prevention's Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention.

Rating of Recommendations: *A = Strong; B = Moderate; C = Weak*

Rating of Evidence: *I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

Introduction

HIV treatment adherence includes initiating care with an HIV provider (linkage to care), regularly engaging in appointments (retention in care), and adhering to antiretroviral therapy (ART). The concept of a "continuum of care" has been used to describe the process of HIV testing, linkage to HIV care, initiation of ART, adherence to ART, retention in care, and virologic suppression.[1-3] The Centers for Disease Control and Prevention (CDC) estimates that about 13% of people with HIV are undiagnosed in the United States.[4] Based on 2022 data, about 82% of individuals were linked to care within 30 days of receiving an HIV diagnosis.[5,6] However, only 54% of people with diagnosed HIV were retained in HIV care. It is estimated that only approximately 69% of people with complete data were virologically suppressed within 6 months of diagnosis. This low rate of viral suppression is primarily due to poor adherence to clinic appointments and ART.[5,7] Outcomes along the continuum of care also vary by geographic region and other population characteristics, such as sex, race and ethnicity, and HIV risk factors.[7] To achieve optimal clinical outcomes and to realize the potential public health benefit of treatment as prevention, adherence to each step in the continuum of care is critical.[8] It is important to note that retention and adherence may fluctuate as a result of life events, changes in insurance status, comorbid conditions, and health system changes, causing people with HIV to shift back and forth on the continuum. Knowledgeable providers and high-quality system processes are vital in promoting rapid linkage and sustained retention in care and adherence to ART. Finally, clinicians should recognize that adherence is a complex behavior requiring knowledge, motivation, memory, behavior change, external resources, and successful and persistent interaction with complex and, sometimes, challenging health care systems.[9-11] The patient–provider relationship is central to improving HIV care engagement and adherence to treatment. Providers must recognize that adherence is a collaborative effort between clinicians and people with HIV.

Addressing social determinants of health (SDOH) is critical to adherence along the HIV continuum of care. The CDC defines SDOH as "the conditions in which people are born, grow, work, live, and age" and "that influence health outcomes."[12] SDOH include access to education, income, nutritious food, transportation, stable housing, and health insurance coverage, as well as policies that may lead to structural racism, HIV criminalization, stigmatization, or immigration status. There are several commonly used screening tools for health-related social needs, including the Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences (PRAPARE),[13] the American Academy of Family Physicians Social Needs Screening Tool (long and short forms),[14,15] and the Centers for Medicare & Medicaid Services (CMS) Accountable Health Communities Health-Related Social Needs (AHC-HRSN) Screening Tool.[16] The CMS Accountable Health Communities Model conducted a randomized trial connecting beneficiaries to community resources for five core health-related social needs compared with a referral-only group. Individuals in the community resources

group received an in-depth assessment of social needs, planning, referral to community services, and follow-up until the needs were resolved or determined unresolvable. The beneficiaries who received community service navigation experienced reduced emergency department visits and a trend toward lower expenditures and improved hospital-based utilization outcomes compared with the referral-only group.[17] Any unmet social and economic needs identified via screening should be addressed, either through direct service provision or by community referrals.

This section provides guidance on linking people with HIV to care, assessing and improving retention in care, and assessing and improving adherence to ART. The CDC maintains a Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention to improve linkage, retention, and adherence, and the Health Resources and Services Administration (HRSA) has multiple tools to assist clinics housed in the Ryan White HIV/AIDS Program (RWHAP) Best Practices Compilation. In addition, a number of other groups and organizations have provided guidance for improving adherence to the steps in the care continuum.[8,18]

Linkage to Care

Receiving an HIV diagnosis can be traumatic, and linkage to care efforts must be delivered with compassion and persistence. The time from diagnosis to linkage to care can be affected by many factors, including insufficient socioeconomic resources, active substance use, mental health problems, stigma, and disease severity (symptomatic HIV is associated with more successful linkage).[19-23] In the United States, youth, people who use injection drugs, and Black/African American people have lower rates of linkage to care.[7] Some health system factors have also been associated with linkage success or failure. Co-location of testing and treatment services[22] and active linkage services (e.g., assistance in setting up HIV care appointments, maintaining an active relationship with individuals until linkage is completed, providing linkage case management services)[24-26] bolster linkage to care. Conversely, passive linkage (e.g., only providing names and contact information for treatment centers) is associated with lower linkage to care.

Monitoring Linkage to Care

Linking to HIV care after a new HIV diagnosis is defined as completing an outpatient appointment with a clinical provider who has the skills and ability to treat HIV, including prescribing ART. People with HIV should be linked to care as soon as possible after HIV diagnosis, preferably within 30 days. Monitoring linkage is critical to ensure that interventions can effectively reach people who are not linked to care. If the facilities that diagnose and treat an individual are the same or share the same electronic medical record system, it is relatively straightforward to monitor linkage to care. Monitoring linkage for people whose HIV is diagnosed outside the treatment provider's health care system is difficult and generally is the responsibility of the diagnosing provider or entity and the public health authority. However, once people with HIV make contact with the treating clinical system, they should be engaged in linkage efforts. The referring entity should monitor for successful linkage to and retention in HIV care.

Improving Linkage to Care

Strategies to improve linkage to care are summarized in Table 20 below. Linkage efforts should include immediate referral to care at diagnosis, appointment reminders, and outreach efforts if needed.[24] The only intervention shown to increase linkage to care in a randomized trial conducted in the United States is the Anti-Retroviral Treatment and Access to Services (ARTAS) intervention.[25] In this study, participants randomized to the control arm received information about HIV and care resources and a referral to a local HIV medical provider, whereas participants in the intervention arm worked with an ARTAS interventionist for five sessions, 90 days, or until linkage—whichever came first. The interventionist helped participants to identify and use their strengths, abilities, and skills to

link to HIV care; participants were also linked to community resources. Linkage to care, defined in this study as completing at least one visit with an HIV clinician within the first 6 months, was greater among the ARTAS participants than the control participants (78% vs. 60%, adjusted risk ratio = 1.36, $P < 0.001$). Furthermore, a greater percentage of ARTAS participants were retained in care, defined as visiting an HIV clinician at least once in each of the first two 6-month blocks after enrollment (64% vs. 49% for ARTAS and control participants, respectively; adjusted risk ratio = 1.41, $P = 0.006$). The results from the ARTAS intervention have been replicated in a community-based study.[26] The CDC supports free training in the ARTAS intervention. Other studies support the importance of post-test counseling to educate, motivate, and present positive messages about HIV,[27] peer support,[28] and engaging people with HIV at the clinic in advance of the visit with the provider.[29] Financial incentives did not increase linkage to care within 90 days in a large randomized trial.[30]

Retention in Care

Poor retention in HIV care is associated with a greater risk of death.[31,32] Poor retention is more common in people who use substances, have serious mental health problems, have unmet socioeconomic needs (e.g., housing, food, transportation), lack financial resources or health insurance, have schedules that complicate adherence, have been recently incarcerated, or face stigma.[33-36] At the provider and health system level, low trust in providers and a poor relationship between providers and people with HIV have been associated with lower retention, as has lower satisfaction with the clinic experience.[37-39] Availability of appointments and timeliness of appointments (i.e., long delay between the appointment request and the appointment date) and scheduling convenience are also factors.

Monitoring Retention in Care

Retention in care should be routinely monitored.[8] There are various ways to measure retention, including measures based on attended visits over a defined period of time (constancy measures) and measures based on missed visits.[40] Both approaches are valid and independently predict survival.[41] Missed visits and a prolonged time since the last visit are relatively easy to measure and should trigger efforts to retain or reengage a person in care. Constancy measures (e.g., at least two visits that are at least 90 days apart over 1 year, or at least one visit every 6 months over the last 2 years) can be used as clinic quality assurance measures.

Improving Retention in Care

Strategies to improve retention in care are summarized in Table 20 below. The Retention through Enhanced Personal Contact (REPC) intervention was tested in a randomized trial in six clinics in the United States. The study enrolled people with HIV who had a history of inconsistent clinic attendance. The intervention relied on personal contact and included a brief face-to-face meeting upon returning to care and at each subsequent clinic visit, plus three types of phone calls (check-ins between visits, to provide appointment reminders just before visits, and to attempt to reschedule missed visits). REPC resulted in small but significant improvements in retention in care, including in racial/ethnic minority populations and people with detectable plasma HIV RNA.[42] When necessary, in-clinic opioid replacement therapy helps opioid users remain in care.[43] An intervention using the electronic medical record to alert providers when people had suboptimal follow-up or high viral loads also improved retention in care.[44]

Telehealth has emerged as an important modality for retention in HIV care during the COVID-19 pandemic. A cluster-randomized study conducted in the U.S. Department of Veterans Affairs health facilities before the pandemic showed that the availability of telehealth resulted in improvements in viral suppression and the number of completed visits.[45] Reengaging and retaining people who are out of care remains particularly challenging.

Navigation services for out-of-care individuals with HIV in a New York City Medicaid health plan resulted in faster re-linkage to care but did not improve retention in care.[46] In two randomized trials involving out-of-care, hospitalized people with HIV, peer counselors and patient navigators did not improve re-linkage to care after hospital discharge.[47,48] Two randomized studies tested a Data to Care intervention, which uses clinic and public health data to reach and reengage out-of-care people with HIV.[49] One trial conducted in Seattle found that the intervention did not result in significantly faster time to re-linkage or viral suppression.[50] However, only people with unsuppressed viremia and CD4 T lymphocyte (CD4) cell counts <350 cells/mm^3 or people with no laboratory values in the preceding 12 months were included, reflecting the HIV treatment guidelines at the time. The Cooperative Re-Engagement Controlled Trial (CoRECT) was more recently conducted in the Northeast United States (Connecticut, Massachusetts, Philadelphia) and included people with HIV with no evidence of a clinic visit or laboratory measurement in the preceding 6 months, regardless of their most recent laboratory results. The proportion of people re-linked to care within 90 days and retained in care at 12 months was significantly higher in the intervention group, but no differences were observed in the proportion who achieved viral suppression in 12 months. Time to viral suppression among those who achieved viral suppression in 12 months was shorter for participants who were randomized to the Data to Care arm compared with the standard of care. Using the Data to Care approach requires substantial resources and notable privacy concerns; although short-term re-linkage may be improved, there is no evidence of an impact on long-term re-linkage or time to viral suppression.

Data from nonrandomized studies are less conclusive, but many interventions bear mentioning. Clinic-wide marketing (e.g., posters, brochures) and customer service training of staff to promote attending scheduled visits and provide people with a welcoming and courteous experience have improved retention.[51] People with HIV who rated their experience with their doctor more highly were more likely to stay in care.[52] Stepped-case management and social and outreach services,[53] including mobile health applications that enhance communication and provide support, are beneficial, although the applications that have been developed and studied are not available for widespread public use. Differentiated care approaches reduce the need for appointments and other expectations for people doing well and allow extra resources to be devoted to people not achieving optimal health outcomes. The evidence to support the use of differentiated care is strongest in low-resource settings, whereas in the United States, the evidence is limited to observational data, which suggests the approach has a beneficial impact.[54]

Overall, these data support the concept that all clinic personnel, from the facilities' staff to nurses to providers, play important roles in supporting retention in care by providing the optimal care experiences, constructively affirming attendance rather than criticizing non-attendance, and collaboratively solving problems with people to overcome barriers to care.[38,42,51] Flexible appointment schedules, expanded clinic hours, and copay or other financial or insurance assistance—such as that provided by the RWHAP—also facilitate uninterrupted access to clinical care. Navigation services, telehealth, and engaging with people through mobile health applications are likely to improve outcomes, although the evidence is not sufficient to support their use unequivocally.

The use of financial incentives or rewards to promote retention in care has been studied. A large study randomized clinic sites to financial incentives or standard of care. At baseline, 45% of the participants were retained in care in these clinics. The relative increase in the proportion of participants retained in care was 9% higher in clinics offering incentives than in standard-of-care clinics. Viral suppression also improved by 4% at financial incentive clinics, from a baseline of 62%.[30] Evidence from a *post hoc* analysis of a subset of the sites involved in that trial shows a reduced but persistent improvement in retention in care after the withdrawal of the incentives without a persistent effect on viral suppression.[55] In another large, randomized study of people who were out of care and hospitalized, financial incentives plus patient navigation did not lead to sustained

improvement in retention or viral load suppression compared to standard care.[47] At this time, financial incentives remain experimental in the context of improved retention due to a lack of data supporting their use in routine care.

Adherence to Antiretroviral Therapy

Adherence to ART can be influenced by several factors, including a person's social situation, clinical condition, the prescribed regimen, and the patient–provider relationship.[56] Poor adherence is often a consequence of one or more behavioral, structural, and psychosocial barriers (e.g., depression and other mental illnesses, neurocognitive impairment, low health literacy, low levels of social support, stressful life events, busy or unstructured daily routines, active substance use, homelessness, poverty, nondisclosure of HIV serostatus, denial, stigma, inconsistent access to medications due to financial and insurance status).[57-60]

Characteristics of one or more components of the prescribed regimen can affect adherence. Once-daily regimens,[61] including those with low pill burden (even if not one pill once daily), no food requirement, and few side effects or toxicities, are associated with higher levels of adherence.[62,63] Single-tablet regimens (STRs) that include all antiretroviral (ARV) drugs in one pill taken once daily are easier for people to use. However, data to support or refute the superiority of an STR versus a once-daily multi-tablet regimen (MTR), as might be required for the use of some generic-based ARV regimens, are limited. Comparisons of these regimens are hampered because not all drugs and classes are available as STRs. There are demonstrated beneficial effects on virologic suppression in a meta-analysis of MTRs versus STRs.[64,65] Whether an STR is beneficial in people with HIV who are ART-naive is not known, with observational cohort studies showing the benefit of a once-daily STR versus a once-daily MTR.[63,66-69] On the other hand, observational data from Spain showed that co-formulated dolutegravir (DTG)/abacavir (ABC)/lamivudine (3TC) resulted in similar viral suppression compared to DTG plus ABC/3TC when used both at treatment initiation and when people with viral suppression on STR were switched to the two-pill formulation as a cost-saving strategy.[70] Given these findings and their wide availability, STRs are generally recommended when clinically appropriate, but high-quality evidence to definitively recommend them is lacking, and shared decision-making is essential **(BIII).**

Characteristics of the clinical setting can also have important structural influences on the success or failure of medication adherence. Settings that provide comprehensive multidisciplinary care (e.g., by case managers, pharmacists, social workers, mental health and substance use providers) support the complex needs of individuals, including those related to medication adherence. Treatment programs for substance use may offer services that promote adherence, such as directly observed therapy (DOT) (see Substance Use Disorders and HIV).

Monitoring Adherence to Antiretroviral Therapy

Adherence to ART should be assessed and addressed in a constructive and nonjudgmental manner at every clinic visit. Given the potency of contemporary ART, a detectable viral load identified during chronic care for a person with stable access to ART is most likely the result of poor adherence. Self-report, the most frequently used method for evaluating medication adherence, remains a useful tool. Carefully assessed self-report of high-level adherence to ART has been associated with favorable viral load responses,[71-73] whereas admission of suboptimal adherence is highly correlated with poor therapeutic response. The reliability of self-reporting often depends on how the clinician elicits the information. It is most reliable when ascertained in a simple, nonjudgmental, routine, and structured format that normalizes less-than-perfect adherence and minimizes socially desirable responses. To allow people to disclose lapses in adherence, some experts suggest inquiring about the number of missed doses during a defined period. For example, for a person with a detectable viral load, a provider might state, "I know it is difficult to take medicine every day. Most people miss doses at

least sometimes. Thinking about the last 2 weeks, how many times have you missed doses? Please give me a rough estimate so I can help you take the best care of yourself." Other research supports simply asking people to rate their adherence during the last 4 weeks on a 5- or 6-point Likert scale[74,75] or using qualitative response categories.[73]

Other measures of adherence include pharmacy records and pill counts. Pharmacy records can be valuable when medications are obtained exclusively from a single source. Because pill counts can be altered, are labor intensive, and can be perceived as confrontational, they are generally not used in routine care. Electronic measurement devices are costly and are generally reserved for research settings. Finally, methods to estimate adherence based on drug levels measured in plasma, dried blood spots, urine, and hair samples are available.[76] Some of these are commercially available, but none have been shown in randomized studies to improve outcomes. However, if these methods are used, they should be implemented collaboratively between the provider and the person with HIV to avoid an adversarial relationship.

Improving Adherence to Antiretroviral Therapy

Strategies to improve adherence to ART are summarized in Table 20 below. Just as they support retention in care, all health care team members play integral roles in successful ART adherence programs.[72,77-79] An increasing number of interventions have proven effective in improving adherence to ART (for descriptions of the interventions, see the CDC's Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention). These interventions can be customized to suit a range of needs and settings. Many interventions that are efficacious in randomized trials require specialized training and resources before they can be implemented in routine care, and this has limited their impact. Nonetheless, these interventions have contributed to our knowledge in developing general principles of improving and maintaining adherence.

Every person with HIV must receive and understand basic information about HIV infection, including the goals of therapy (achieving and maintaining viral suppression, which will decrease HIV-associated complications and prevent transmission), the prescribed regimen (including dosing schedule and potential side effects), the importance of adherence to ART, and the potential for the development of drug resistance as a consequence of suboptimal adherence. People with HIV must also be positively motivated to initiate therapy, which can be assessed by simply asking people if they want to start treatment for HIV. Clinicians should assist people with HIV in identifying facilitating factors and potential barriers to adherence and develop multidisciplinary plans to attempt to overcome those barriers. Processes for obtaining medications and refills should be clearly described. Transportation to pharmacy and clinic visits should be assessed with linkage to appropriate services as needed. Plans to ensure uninterrupted access to ART via insurance, copay assistance, pharmaceutical company assistance programs, or AIDS Drug Assistance Programs (ADAP), for example, should be made and reviewed with each person with HIV. Much of this effort to inform, motivate, and reduce barriers can be achieved by nonphysician members of the multidisciplinary team and can be accomplished concomitantly with, or even after, starting therapy.[80-83]

While delaying the initiation of ART is rarely indicated, some people may not be comfortable starting treatment right away. People expressing reluctance to initiate ART should be engaged to understand and overcome barriers to ART initiation. Although homelessness, substance use, and mental health problems are associated with poorer adherence, they are not predictive enough at the individual level to warrant withholding or delaying therapy given the simplicity, potency, and tolerability of contemporary ART. Rapid ART initiation at the time of HIV diagnosis has been pursued as a strategy to increase viral load suppression and retention in care, but safety data, data on intermediate or long-term outcomes, and data from randomized controlled trials conducted in high-resource settings are currently lacking.[80-86] In low-resource settings, data from randomized trials

suggest that rapid ART probably increases ART use and viral suppression at 12 months, but data on other important outcomes—such as retention in care, regimen switching, and mortality—are not sufficient to draw conclusions.[87,88] Rapid access to ART has become a pillar of the United States' plan to end the HIV epidemic, and delays in access to ART should be addressed.[89] For more details, see Initiation of Antiretroviral Therapy.

Successful treatment requires a regimen that the individual can adhere to,[90,91] considering their daily schedule, tolerance of pills (number, size, and frequency), and any issues affecting absorption (e.g., use of acid-suppressing therapy, food requirements). As reviewed above, STRs have been associated with high rates of adherence. People with risk factors for poor adherence or a history of poor adherence should be offered regimens with high genetic barriers to resistance (e.g., a second-generation integrase strand transfer inhibitor [INSTI] or a boosted protease inhibitor), if clinically appropriate. Using shared decision-making, a medication choice and administration schedule should be tailored to each person's daily activities. Clinicians should explain to people that their first regimen is usually the best option for a simple regimen, which affords long-term treatment success. Establishing a trusting patient–provider relationship and maintaining good communication will help to improve adherence and long-term outcomes. Medication adherence can also be enhanced using medication reminder aids. The evidence is strongest for text messaging, although pillbox monitors, pill boxes, and alarms may also improve adherence.[92-96]

Positive reinforcement, such as informing people of their low or suppressed viral load and increased CD4 counts, can greatly help maintain high levels of adherence. Motivational interviewing has also been used with some success.[97-99] Other effective interventions include nurse home visits, a five-session group intervention, and couples- or family-based interventions. Interventions involving several approaches are generally more successful than single-strategy interventions, and interventions based on cognitive behavioral therapy and supporter interventions have been shown to improve viral suppression.[100] Problem-solving approaches that vary in intensity and culturally tailored approaches are also promising.[99,101,102] Providing additional therapy (e.g., for substance use or mental health) and social support may be important to maintain high levels of adherence. DOT has been effective in providing ART to people actively using drugs[103] but not to people in a general clinic population[104] or in home-based settings with partners responsible for DOT.[105,106] The use of incentives or rewards to promote adherence has been studied, demonstrating improved adherence in one study conducted by the HIV Prevention Trials Network (HPTN)[30] and reduce viral load in another study that required very frequent viral load measurement and incentives.[107] Although the durability and feasibility of financial incentives are limited, and behavior change is generally not sustained after the incentives are withdrawn, the HPTN study did find some evidence of sustained adherence after 9 months.[55] Data are too limited to support the use of financial rewards for adherence to routine care.[47,108,109]

Transitions of Care

Transitions of HIV care are critical periods during which people may be more likely to fall out of care. Some important examples of transitions of care are discussed in further detail below.

Transition From Pediatric to Adult HIV Care

The transition from pediatric to adult HIV care requires proactive attention to the medical and psychosocial needs of adolescents as they move from a child-focused to an adult-focused health care system, with the goal of preventing disruption in care and ensuring ART adherence.[110] Recommendations for transition planning from pediatric to adult HIV care can be found in the Adolescents and Young Adults With HIV section of these guidelines and the Pediatric Antiretroviral Guidelines.

Transition From Obstetric to Primary HIV Care Postpartum

Pregnancy and the postpartum period offer a unique opportunity to engage in HIV care, both for people newly diagnosed with HIV during pregnancy and for people with HIV prior to pregnancy. Childcare responsibilities and postpartum depression can contribute to decreased adherence to HIV care in the postpartum period, thus requiring additional support services. Guidance on postpartum follow-up for people with HIV can be found in the Perinatal Guidelines.

Transitions Between Health Care Providers or Settings

Transitions in health care providers or settings can occur between hospitals, primary HIV care practices, ambulatory specialty care practices, long-term care facilities, home health, and rehabilitation facilities.[111] Safe transitions in HIV care can be supported by coordinating with HIV care providers and educating people with HIV and their support systems. In the setting of a health care facility discharge, bedside medication delivery or "Meds to Beds" programs may enhance post-discharge medication adherence by eliminating the need to visit a pharmacy to fill post-discharge medications.[112,113] In the setting of a residential move from one geographic area to another, a new HIV care provider would ideally be identified ahead of the move so that communication and transfer of medical records occur in a timely manner. This is particularly important for people with HIV who are receiving RWHAP services because not all HIV care providers receive RWHAP funding. HRSA provides an online resource for identifying RWHAP providers nationally. Provision of at least a 30-day ART supply at the time of a residential move may mitigate gaps in adherence due to delays in health care access in a new geographic area.

Reengagement in HIV Care After Loss to Follow-up

Adherence along the HIV care continuum is fluid and can change depending on an individual's life circumstances. In general, guidance around reengagement in care is similar to the guidance for individuals who are newly diagnosed with HIV. However, specific attention should be paid to understanding the reasons for previous disengagement from care, and shared decision-making should be used to identify strategies to address these barriers using a multidisciplinary approach. Hospitalization can provide an important opportunity for reengagement when an acute illness may increase an individual's motivation for behavior change. As noted above, bedside medication delivery or "Meds to Beds" programs have the potential to enhance post-discharge medication adherence.[112,113]

Individuals in Custody Released From Jails and Prisons

HIV continues to disproportionately affect individuals who are incarcerated at a rate three times that of the general population. Approximately 1.1% of individuals in custody have HIV, compared with 0.4% of the general population.[114,115] Incarceration presents an opportunity to identify and treat previously undiagnosed people with HIV, reengage those who had fallen out of HIV care in the community before incarceration, and stabilize HIV treatment among those who struggled with adherence and retention in care in the community. HIV treatment inside carceral facilities should mirror treatment in the community with respect to ART selection. Treatment interruptions should be avoided when people enter and leave such facilities. HIV treatment outcomes can be improved by having HIV specialty care teams within carceral facilities to communicate and coordinate care with community-based providers. There are unique considerations when treating HIV inside prisons and jails, given a lack of individual privacy, restricted movement to the health care unit, HIV stigma, and solitary confinement—all of which can negatively impact ART adherence while in custody. Conversely, this setting can allow the individual in custody to focus on adherence and allow the health care team to assess the safety, tolerability, and effectiveness of an ART regimen.

Adherence challenges can increase exponentially upon release from custody and include lapses in medical and prescription benefits (including for mental health and substance use disorders), housing instability, lack of transportation, lack of identification and other important documents (e.g., birth certificate, social security card) needed to secure medical benefits, relapse to substance use, and risk of overdose. Interventions to reduce barriers to HIV treatment should be assessed during the prerelease discharge planning process when feasible and can be enhanced by accessing assistance through community-based organizations that provide post-release services.[116] Factors that promote treatment adherence post-release include registering for health insurance and completing an ADAP application prior to release,[117] coordinating follow-up HIV care with community providers, and providing a 30-day supply of ART at the time of release.[118] Various interventions to improve post-release treatment adherence have demonstrated the efficacy of an interdisciplinary medical team, including case management and patient navigation resources.[119-124]

Long-Acting Antiretroviral Therapy

An ART regimen of long-acting intramuscular cabotegravir and rilpivirine (LA CAB/RPV) given monthly or every 2 months has been studied and approved for use in populations with viral suppression. In addition, preliminary data from a randomized clinical trial suggest that LA CAB/RPV may be safe and effective among people without viral suppression despite intensive adherence support on oral ART; however, final data and long-term outcomes are not yet available.[125] The long pharmacologic tail of LA CAB/RPV after the last dose raises concerns about the emergence of drug-resistance mutations in people who discontinue therapy without rapidly transitioning to oral therapy. Further, efficacy data from randomized clinical trials do not always translate to effectiveness in real-world settings.

The use of the LA CAB/RPV as a complete regimen is generally not recommended in people with viremia due to suboptimal adherence to ART, or in people who have ongoing challenges with retention in HIV care. However, limited data from small observational studies found that LA CAB/RPV can lead to high levels of viral suppression in people who have struggled with adherence to oral ART and who are viremic at treatment initiation.[126-128] It should be noted that these studies were conducted in settings where LA CAB/RPV was available on Medicaid and ADAP formularies. Further, significant social and case management support, including full-time dedicated staff, was provided to ensure adherence to the regimen. This support was provided by multidisciplinary teams involving clinicians, pharmacists, and case managers and included appointment reminders, assistance with transportation, financial incentives, and assistance with rescheduling missed injection appointments. Additionally, injections were offered in people's homes, at harm-reduction sites, and via street medicine. It is unknown whether similar responses can be achieved in clinics without the resources to provide the level of adherence support seen in previous studies.

Based on these limited data, the Panel recommends the use of LA CAB/RPV on a case-by-case basis in select individuals with persistent virologic failure despite intensive adherence support on oral ART, who have no evidence of resistance to RPV or CAB, and with shared decision-making between providers and people with HIV **(CIII)**.

This approach may provide alternatives for individuals with viremia and difficulties with adherence to oral ART, especially for those at the highest risk for disease progression or death. If LA CAB/RPV is used, close monitoring is recommended, with drug-resistance testing performed if virologic response is inadequate. Importantly, conventional adherence support is likely inadequate, and expanded, intensive, multidisciplinary case management and outreach support are needed when using this strategy to assure adherence and adequate monitoring for people while on LA CAB/RPV. People with HIV and providers need to be aware of the significant risk of developing resistance to non-nucleoside reverse transcriptase inhibitors and particularly INSTIs if virologic failure occurs on LA CAB/RPV, which may limit future treatment options and may also lead to

transmission of HIV; these concerns should be balanced with the given individual's HIV-related risk for disease progression and death. See Virologic Failure for a more detailed discussion.

Conclusion

Clinicians should obtain accurate information about a person's adherence and barriers to ART and appointment adherence, followed by meaningful discussions on solutions, rather than simply instructing adherence and warning about potential consequences of poor adherence. The latter approach fails to acknowledge a person's barriers to adherence, fails to provide actionable information, erodes rather than builds the patient–provider relationship, and has been demonstrated to not improve adherence.[129,130] At the same time, however, many of the interventions shown to improve adherence are difficult to implement in routine care. Nonetheless, effective lessons from this body of research can be applied to routine care to improve linkage to care, adherence to ART, and adherence to appointments. These lessons include the following:

- Regularly assess adherence to ART and appointments.
- Engage people struggling with adherence at any step on the care continuum with a constructive, collaborative, nonjudgmental, and problem-solving approach rather than reprimanding them or lecturing them on the importance of adherence.
- Elicit an individual's barriers to adherence, which may include personal, behavioral, medical, or structural barriers (e.g., substance use, housing instability, stigma, lack of transportation), clinic barriers (e.g., limited clinic hours, processes that make it more difficult to obtain prescriptions or schedule appointments), and system barriers (e.g., copays, prior approvals, processes that complicate maintaining pharmacy benefits or obtaining refills).
- Tailor approaches to improve adherence to an individual's specific needs and barriers, for example, by changing ART to simplify dosing or reduce side effects, finding resources to assist with copays or other out-of-pocket costs (see Table 20 below), to maintain an uninterrupted supply of ART, and to assure access to clinicians, or linking people to counseling to overcome stigma, substance use, or mental illness.
- Utilize ART regimens with high genetic barriers to resistance—such as DTG, bictegravir, or boosted darunavir regimens—for people with adherence problems. When selecting the regimen, consider possible side effects, out-of-pocket costs, convenience, and individual preferences, because the only regimen that will work is the one that people can obtain and are willing and able to take.
- Recognize the need for multidisciplinary approaches to identify and address barriers. Clinicians should help people with HIV understand the importance of adherence to the continuum of care, identify and address immediate barriers, and link them to resources for overcoming other obstacles.

Table 20. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy

Strategies	Examples
Provide an accessible, trustworthy, nonjudgmental multidisciplinary health care team.	• Include care providers, nurses, social workers, case managers, pharmacists, medication managers, and administrative staff on the care team; train all members on providing compassionate and person-centered care.
Strengthen early linkage to care and retention in care.	• Encourage health care team participation in linkage to and retention in care. • Use ARTAS training (if available). • Actively support linkage to care with assistance in making appointments and linkage to services to overcome barriers to care. • Streamline Ryan White HIV/AIDS Program eligibility verification processes for uninsured and underinsured clients.
Evaluate an individual's knowledge about HIV, HIV prevention, and HIV treatment and provide information based on this assessment.	• Keeping the current knowledge base in mind, provide information about HIV, including the natural history of the disease, HIV viral load and CD4 count and expected clinical outcomes according to these parameters, therapeutic and prevention consequences of poor adherence, and the importance of staying in HIV care.
Identify facilitators, potential barriers to adherence, and necessary medication management skills both when starting ART and thereafter.	• Assess each individual's cognitive competence and impairment. • Assess behavioral and psychosocial challenges, including mental illnesses, trauma, social support levels, alcohol consumption, substance use, nondisclosure of HIV serostatus, and stigma. • Identify and address language and literacy barriers. • Assess beliefs, perceptions, and expectations about taking ART (e.g., impact on health, side effects, disclosure issues, consequences of poor adherence). • Ask about medication-taking skills and foreseeable challenges with adherence (e.g., past difficulty keeping appointments, adverse effects from previous medications, issues managing other chronic medications, need for medication reminders and organizers). • Assess structural issues, including unstable housing, lack of income, unpredictable daily schedule, lack of prescription drug coverage, lack of continuous access to medications, and transportation problems.
Provide needed resources.	• Provide or refer for mental health and/or substance use treatment. • Provide resources to obtain prescription drug coverage (e.g., AIDS Drug Assistance Programs, Pharmaceutical Company HIV Patient Assistance Programs and Cost-Sharing Assistance Programs). • Assist people during insurance enrollment periods to facilitate enrollment in plans that cover antiretrovirals. • Provide resources about stable housing, social support, transportation assistance, income, and food security.

Table 20. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy

Strategies	Examples
Involve people with HIV in ARV regimen selection.	• Review potential side effects, dosing frequency, pill burden, storage requirements, food requirements, and consequences of poor adherence. • Assess daily activities and tailor a regimen to predictable and routine daily events. • Consider preferential use of ART regimen with a high barrier to resistance, such as BIC-, DTG-, or boosted DRV-based ART if poor adherence is anticipated. • Consider the use of STR or fixed-dose-combination formulations to reduce pill burden and/or dosing frequency. • Consider the use of LA CAB/RPV if clinically appropriate (see the Long-Acting Antiretroviral Therapy section above for further discussion). • Assess if the cost or copayment for drugs will affect adherence and access to medications.
Assess adherence at every clinic visit.	• Monitor viral load as a strong biological measure of adherence. • Use a simple behavioral rating scale or self-reported assessment. • Employ a structured format that normalizes or assumes less-than-perfect adherence and minimizes socially desirable or “white-coat adherence” responses. • Ensure that other members of the health care team also assess and support adherence.
Use positive reinforcement to foster adherence success.	• Inform people of the benefits of low or nondetectable levels of HIV viral load (e.g., “Undetectable = Untransmittable”) and increases in CD4 counts. • Thank people for attending their appointments.
Identify the type of and reasons for poor adherence and target ways to improve adherence.	Identify if any of the following have contributed to poor adherence: • Failure to understand dosing instructions. • Complexity of regimen (e.g., pill burden, size, dosing schedule, food requirements, polypharmacy). • Pill aversion or pill fatigue. • Adverse effects. • Inadequate understanding of drug resistance and its relationship to adherence. • Appointment reminders and incorporation of input from people with HIV in appointment scheduling. • Cost-related issues (e.g., copays for medications or visits, missed work time). • Mental illness, drug and alcohol use, homelessness, or poverty. • Stigma of taking pills or attending HIV-related appointments. • Nondisclosure of status or privacy concerns leading to missed doses, refills, or appointments.

Table 20. Strategies to Improve Linkage to Care, Retention in Care, Adherence to Appointments, and Adherence to Antiretroviral Therapy

Strategies	Examples
Select from among available effective adherence and retention interventions.	• See the CDC's Compendium of Evidence-Based Interventions and Best Practices for HIV Prevention for a summary of best practice interventions to improve linkage, retention, and adherence. • Use adherence-related tools to complement education and counseling interventions (e.g., text messaging, pill box monitors, pill boxes, alarms). • Use community resources to support adherence (e.g., visiting nurses, community workers, family, peer advocates, transportation assistance, pharmacy delivery). • Use prescription assistance programs (see "Provide needed resources" above in this table). • Use motivational interviews. • Provide outreach for people who drop out of care. • Use peer or paraprofessional treatment navigators. • Recognize positive clinical outcomes resulting from better adherence. • Arrange for DOT for people in substance use treatment (if feasible). • Enhance clinic support and structures to promote linkage and retention (e.g., reminder calls, flexible scheduling, assessment of clinic service satisfaction). • Offer telehealth services for primary care, as well as supportive services when appropriate.
Systematically monitor retention in care.	• Record and follow up on missed visits.

Key: ART = antiretroviral therapy; ARTAS = Anti-Retroviral Treatment and Access to Services; ARV = antiretroviral; BIC = bictegravir; CD4 = CD4 T lymphocyte; CDC = Centers for Disease Control and Prevention; DOT = directly observed therapy; DRV = darunavir; DTG = dolutegravir; LA CAB/RPV = long-acting cabotegravir/rilpivirine; STR = single-tablet regimen

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Adverse Effects of Antiretroviral Medications

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Adverse effects have been reported with all antiretroviral (ARV) medications. Commonly reported reasons for switching or discontinuing oral or injectable therapy were due to adverse effects, especially with the initiation of antiretroviral therapy (ART) regimens in the late 1990s and early 2000s.[1] Fortunately, newer ART regimens are associated with fewer serious and intolerable adverse effects. Generally, <10% of participants who are ART-naive and who enrolled in randomized trials of newer agents experience treatment-limiting adverse events.[2,3] However, the short-term and long-term complications of ART may be underestimated because most clinical trials use specific inclusion criteria that exclude individuals with certain underlying medical conditions, and the duration of participant follow-up is relatively short (generally 2–4 years).

ART is recommended for all people with HIV regardless of CD4 T lymphocyte cell count, and with current treatments and approaches/strategies, therapy must be continued indefinitely. To achieve and sustain viral suppression over a lifetime, both long-term and short-term ART adverse effects must be anticipated and managed. From a safety and tolerability standpoint, the focus of management has evolved from identifying and managing toxicities related to early ARVs to individualizing therapy to avoid or mitigate long-term adverse effects, such as atherosclerotic cardiovascular disease, diabetes and other metabolic complications, kidney dysfunction, neuropsychiatric events, and accelerated declines in bone mineral density.

Antiretroviral Regimen Selection

When selecting an ARV regimen, clinicians must consider potential adverse effects and any prior history of drug intolerance. Additionally, several factors may predispose people with HIV to adverse effects of ARV medications. These factors include:

- Concomitant use of medications with overlapping and additive toxicities.
- Comorbid conditions that increase the risk of adverse effects. For example, underlying liver disease from alcohol use, coinfection with viral hepatitis, and/or liver steatosis[4,5] may increase the risk of hepatotoxicity when some protease inhibitors are used; and borderline or mild renal dysfunction increases the risk of nephrotoxicity from tenofovir disoproxil fumarate (TDF).[6]
- Certain ARVs that may exacerbate pre-existing conditions. For example, psychiatric disorders may be exacerbated by efavirenz (EFV), rilpivirine, and, infrequently, by integrase strand transfer inhibitors.[7,8]
- Drug–drug interactions that may increase the toxicities of ARV medications or concomitant medications. For example, when pharmacokinetic boosters such as ritonavir or cobicistat are used.[9]
- Genetic factors that predispose people with HIV to some adverse effects of medications that are no longer commonly used in clinical practice, such as abacavir (ABC) hypersensitivity reaction,[10,11] EFV neuropsychiatric toxicity[9,12] or QTc (QT corrected for heart rate) prolongation,[13,14] and atazanavir (ATV)-associated hyperbilirubinemia.[15]
- Dosing errors, which can predispose people with HIV to adverse effects when medications are administered at incorrect doses—whether at doses that are too high or at inappropriate intervals—and can increase the likelihood of adverse effects.

Management of Adverse Effects

ART-associated adverse effects can range from acute and potentially life-threatening to chronic and insidious. When people with HIV experience treatment-limiting toxicities associated with ART, selecting new ART regimens that pose either no or a lower risk of exacerbating the condition or contributing to further complications is warranted. Serious life-threatening effects (e.g., hypersensitivity reaction due to ABC, symptomatic hepatotoxicity, severe cutaneous reactions) require the immediate discontinuation of all ARV medications and re-initiation of an alternative regimen without overlapping toxicity. Toxicities that are not life-threatening (e.g., urolithiasis with ATV, renal tubulopathy with TDF) can usually be managed by substituting another ARV medication for the presumed causative medication without interrupting ART. Chronic, non–life-threatening adverse effects (e.g., dyslipidemia) can be addressed either by switching the potentially causative medication for another medication or by managing the adverse effect with nonpharmacological interventions or pharmacologic interventions such as statins. Management strategies must be individualized for each person with HIV. When adverse effects occur during the use of long-acting injectable ARV drugs, management may be challenging due to the persistence of drug in the body over the course of many months to years. Oral lead-in regimens for cabotegravir plus rilpivirine are available to assess short-term tolerability.

Switching from an effective ARV agent or regimen to a new agent or regimen must be done carefully and only when the potential benefits of the change outweigh the potential risks of altering treatment. The fundamental principle of regimen switching is to maintain viral suppression. When selecting a new agent or regimen, providers should be aware that drug-resistant viruses previously acquired or selected, even those not detected by past genotypic resistance testing, are archived in HIV reservoirs. The resistant virus, even if absent from subsequent resistance test results, may reappear under selective drug pressure. See Optimizing Antiretroviral Therapy in the Setting of Viral Suppression for further discussion. It is critical that providers review the following information before implementing any treatment switch:

- Medical and complete ARV history, including prior virologic responses to ART
- All previous drug resistance test results
- Viral tropism (if maraviroc is being considered)
- HLA-B*5701 status (if ABC is being considered)
- Comorbidities
- Pregnancy status and the desire and/or ability to become pregnant or use contraceptives
- Hepatitis B virus (HBV) status. People with evidence of chronic HBV infection should not discontinue ARVs active against HBV (e.g., TDF, tenofovir alafenamide, lamivudine, emtricitabine). If discontinuation is necessary due to adverse effects, consult the HBV/HIV Coinfection section for guidance.
- Adherence history
- Prior intolerances to any ARVs
- Concomitant medications and supplements, considering any potential drug interactions with ARVs
- Cost to people with HIV and options for patient assistance programs if needed (see Cost Considerations and Antiretroviral Therapy)

For the first few months after an ART switch, the person should be closely monitored for any new adverse effects, and HIV viral load should be monitored to ensure continued viral suppression.

Information on the adverse effects of ARVs is outlined in several tables in these Guidelines. Table 21 provides clinicians with a list of the most common and/or severe ARV-associated adverse events for each drug class. The most common adverse effects of individual ARV agents are summarized in Appendix A, Tables 3, 4, 5, 6, 7, 8, 9, and 10.

Table 21. Common and/or Severe Adverse Effects Associated With Antiretroviral Medications

This table focuses on antiretroviral (ARV)-associated adverse effects that a person may experience as a result of taking an ARV regimen. The attribution of adverse effects to individual ARVs is inherently limited by the absence of long-term monotherapy trials, making it difficult to delineate the specific contribution of each medication within the combination regimens. These limitations should be considered carefully when assessing causality, as adverse effects may be related to the ARV regimen as a whole rather than to any single component.

Adverse effects for ARV medications that are no longer on the market or are not commonly used in clinical practice (didanosine [ddI], fosamprenavir/ritonavir, indinavir, lopinavir/ritonavir, nelfinavir, nevirapine, saquinavir/ritonavir, stavudine [d4T], tipranavir/ritonavir, zidovudine [ZDV]), with few exceptions, have been removed from this table. Clinicians should refer to the product labels or to the archived July 10, 2019, version of the Guidelines for information regarding the adverse effects associated with select older ARVs. Because some adverse effects may persist long after discontinuation of the older ARVs—such as d4T, ddI, zalcitabine, and ZDV—and people with HIV may still present with these long-lasting toxicities, these medications remain listed among the ARVs associated with adverse effects such as lipodystrophy and peripheral neuropathy.

For information regarding potential adverse effects of ARVs on fetuses and newborns when certain ARVs are taken around the time of conception or during pregnancy, refer to the Perinatal Guidelines.

This table highlights the common and/or severe adverse effects by ARV class and for individual ARVs, when appropriate. For ARV class–specific adverse effects, the table provides relative comparisons among individual ARVs for each class effect. In some cases, the terms “no known effect,” “rarely observed” (for select severe effects), “not common or severe,” or “no or limited data” are used, especially for the entry inhibitor and capsid inhibitor classes, where the evaluation of safety is based mostly on uncontrolled and nonrandomized clinical trials. See Appendix A, Tables 3, 4, 5, 6, 7, 8, 9, and 10 for additional information listed by ARV medication.

Adverse Effect Type	Adverse Effect	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Cardiovascular Effects	Cardiac Conduction Effects	No known effect	**RPV and EFV:** QTc prolongation **RPV:** QTc prolongation occurred at 3 and 12 times the recommended dose. Consider alternatives when coadministered with drugs with known risk of Torsade de Pointes.	**ATV:** PR prolongation. Risk factors include pre-existing heart disease and concomitant use of medications that may cause PR prolongation.	No known effect	**FTR:** QTc prolongation was seen at 4 times the recommended dose. Consider alternatives when coadministered with drugs with a known risk of Torsade de Pointes.	No known effect

Table 21. Common and/or Severe Adverse Effects Associated With Antiretroviral Medications

Adverse Effect Type	Adverse Effect	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
	Cardiovascular Disease	**ABC:** Associated with an increased risk of MI in some cohort studies. Absolute risk greatest in people with traditional CVD risk factors.	No known effect	**DRV/r:** Associated with cardiovascular events in some cohorts.	Not common or severe	No or limited data	No or limited data
Dermatologic Effects, Not Including Systemic Hypersensitivity Reaction	Rash	**FTC:** Skin hyperpigmentation	All NNRTIs	ATV, DRV	All INSTIs	MVC, IBA, FTR	Not common or severe
	Stevens-Johnson Syndrome/Toxic Epidermal Necrosis	No known effect	EFV, ETR > DOR, RPV	Rarely observed with DRV and ATV	Rarely observed with BIC, CAB, and RAL	No or limited data	Not common or severe
Gastrointestinal Effects	Cholelithiasis	No known effect	No or limited data	**ATV:** Cholelithiasis and kidney stones may present concurrently. Median onset is 42 months after ARV initiation.	No known effect	No known effect	No known effect
	Gastrointestinal Effects	**ZDV > other NRTIs:** Nausea and vomiting	Not common or severe	GI intolerance (e.g., diarrhea, nausea, vomiting)	**EVG/c:** Nausea and diarrhea	No known effect	Not common or severe

Table 21. Common and/or Severe Adverse Effects Associated With Antiretroviral Medications

Adverse Effect Type	Adverse Effect	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Hepatic Effects	Hepatic Effects	**When TAF, TDF, 3TC, and FTC are withdrawn in people with HBV/HIV coinfection or when HBV resistance develops:** People with HBV/HIV coinfection may develop severe hepatic flares.	**EFV:** Most cases relate to an increase in transaminases. Fulminant hepatitis leading to death or hepatic failure requiring transplantation have been reported. **RPV:** Risk may be further increased in people with HBV or HCV coinfection.	**All PIs:** Drug-induced hepatitis and hepatic decompensation have been reported. **ATV:** Jaundice due to indirect hyperbilirubinemia	**DTG:** Rarely observed, but risk may be further increased in people with HBV or HCV coinfection. **BIC, CAB, EVG/c, RAL:** Not common or severe	**MVC:** Hepatotoxicity with or without rash or HSRs has been reported. **FTR:** Transaminase elevation was seen more commonly in patients with HBV/HCV. Transient elevation of bilirubin observed in clinical trials.	Not common or severe
Hypersensitivity Reactions, Not Including Rash Alone or Stevens-Johnson Syndrome	Hypersensitivity Reaction	**ABC: Contraindicated** if person is HLA-B*5701 positive. Median onset for HSR is 9 days after treatment initiation; 90% of reactions occur within 6 weeks.	Rarely observed	No known effect	Rarely observed	**MVC:** HSR reported as part of a syndrome related to hepatotoxicity. **IBA:** HSR, including infusion-related reactions and anaphylactic reactions, were reported.	No known effect

Table 21. Common and/or Severe Adverse Effects Associated With Antiretroviral Medications

Adverse Effect Type	Adverse Effect	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
		HSR symptoms (in order of descending frequency): Fever, rash, malaise, nausea, headache, myalgia, chills, diarrhea, vomiting, abdominal pain, dyspnea, arthralgia, and respiratory symptoms Symptoms worsen with continuation of ABC. People should not be rechallenged with ABC if HSR is suspected, regardless of their HLA-B*5701 status.					
Injection Site Reactions	Injection Site Reaction	Not applicable	**RPV IM injection:** Reported in >80% of patients; reactions may include localized pain/discomfort (most common), nodules, induration, swelling, erythema, hematoma. **When given with CAB IM, injection site pain:** RPV > CAB.	Not applicable	**CAB IM injection:** Reported in >80% of patients; reactions may include localized pain/discomfort (most common), nodules, induration, swelling, erythema, hematoma. **When given with RPV IM, injection site pain:** RPV > CAB.	Not applicable	**LEN SQ injection:** Reported in 47–65% of people; reactions may include swelling, erythema, pain, nodules, inflammation, and induration. Nodules and induration may persist for months in some people. Injection site necrosis has been reported.

Table 21. Common and/or Severe Adverse Effects Associated With Antiretroviral Medications

Adverse Effect Type	Adverse Effect	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Metabolic Effects	Bone Density Effects	**TDF:** Associated with greater loss of BMD than other NRTIs, especially when given with a PK booster. Osteomalacia may be associated with proximal tubulopathy and urine phosphate wasting. **TAF:** Associated with smaller declines in BMD than those seen with TDF.	No known effect	No known effect	Not common or severe	No known effect	No known effect
	Diabetes Mellitus and Insulin Resistance	**ZDV**	No known effect	Rarely observed	No known effect	No or limited data	No or limited data
	Dyslipidemia	**ABC:** ↑ TG and ↑ LDL **TAF:** ↑ TG, ↑ LDL, and ↑ HDL (no change in TC:HDL ratio) **TDF:** Associated with lower lipid levels than ABC or TAF.	**EFV:** ↑ TG, ↑ LDL, ↑ HDL	**All RTV- or COBI-boosted PIs:** ↑ TG, ↑ LDL, ↑ HDL	**EVG/c:** ↑ TG, ↑ LDL, ↑ HDL	No known effect	No known effect
	Lactic Acidosis	Reported with older NRTIs (e.g., d4T, ZDV, ddI), but not with ABC, 3TC, FTC, TAF, or TDF.	No known effect	No known effect	No known effect	No known effect	No known effect

Table 21. Common and/or Severe Adverse Effects Associated With Antiretroviral Medications

Adverse Effect Type	Adverse Effect	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
	Lipodystrophy	**Lipoatrophy:** Associated with history of exposure to d4T or ZDV (d4T > ZDV). Not reported with ABC, 3TC or FTC, or TAF or TDF.	**Lipohypertrophy:** Trunk fat increase is observed with EFV-containing regimens; however, a causal relationship has not been established.	**Lipohypertrophy:** Trunk fat increase is observed with PI-containing regimens; however, a causal relationship has not been established.	**Lipohypertrophy:** Trunk fat increase is observed with RAL-containing regimens; however, a causal relationship has not been established.	No known effect	No known effect
	Weight Gain	Weight gain has been associated with initiation of ART and subsequent viral suppression. The increase appears to be greater with INSTIs, especially BIC and DTG, than with other drug classes. Greater weight increase has also been reported with TAF than with TDF and with DOR than with EFV.				No known effect	No known effect
Musculoskeletal Effects	Myopathy/ Rhabdomyolysis	ddI, D4T Rarely observed with ABC, TAF, or TDF.	No known effect	No known effect	Rarely observed	No known effect	No known effect

Table 21. Common and/or Severe Adverse Effects Associated With Antiretroviral Medications

Adverse Effect Type	Adverse Effect	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Neuropsychiatric Effects	Nervous System/ Psychiatric Effects	**Peripheral neuropathy (can be irreversible):** Associated with history of exposure to ddI, ddC, or d4T.	**Neuropsychiatric events:** EFV > DOR, RPV > ETR **EFV:** Somnolence, insomnia, abnormal dreams, dizziness, impaired concentration, depression, psychosis, suicidal ideation, ataxia, encephalopathy. Some symptoms may subside or diminish after 2–4 weeks. Bedtime dosing and taking without food may reduce symptoms. **RPV:** Depression, suicidality, sleep disturbances **DOR:** Sleep disorders and disturbances, dizziness, altered sensorium; depression, suicidality, and self-harm	No known effect	Insomnia, depression, and suicidality have been reported with INSTI use, primarily in people with pre-existing psychiatric conditions.	Not common or severe	Not common or severe

Table 21. Common and/or Severe Adverse Effects Associated With Antiretroviral Medications

Adverse Effect Type	Adverse Effect	NRTIs	NNRTIs	PIs	INSTIs	EIs	CI
Renal Effects	Renal Effects/ Nephrolithiasis/ Urolithiasis	**TDF:** ↑ SCr, proteinuria, hypophosphatemia, urinary phosphate wasting, glycosuria, hypokalemia, and non-anion gap metabolic acidosis. Concurrent use of TDF with COBI- or RTV-containing regimens appears to increase risk. **TAF:** Less renal effect than TDF.	**RPV:** Inhibits Cr secretion without reducing renal glomerular function	**ATV:** Associated with increased risk of chronic kidney disease in a large cohort study. **ATV:** Stone or crystal formation; adequate hydration may reduce risk **COBI (as a pharmacokinetic booster for DRV or ATV):** Inhibits Cr secretion without reducing renal glomerular function	**DTG, COBI (as a pharmacokinetic booster for EVG), and BIC:** Inhibits Cr secretion without reducing renal glomerular function	No or limited data	No or limited data

Key: 3TC = lamivudine; ABC = abacavir; ART= antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; BIC = bictegravir; BMD = bone mineral density; CAB = cabotegravir; CI = capsid inhibitor; COBI = cobicistat; Cr = creatinine; CVD = cardiovascular disease; d4T = stavudine; ddC = zalcitabine; ddI = didanosine; DOR = doravirine; DRV = darunavir; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EI = entry inhibitor; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; FTR = fostemsavir; GI = gastrointestinal; HBV = hepatitis B virus; HCV = hepatitis C virus; HDL = high-density lipoprotein; HSR = hypersensitivity reaction; IBA = ibalizumab; IDV = indinavir; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LDL = low-density lipoprotein; LEN = lenacapavir; MI = myocardial infarction; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SCr = serum creatinine; SQ = subcutaneous; TAF = tenofovir alafenamide; TC = total cholesterol; TDF = tenofovir disoproxil fumarate; TG = triglycerides; ZDV = zidovudine

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Cost Considerations and Antiretroviral Therapy

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Key Considerations
• The complexities of the U.S. health care system may require that the costs for antiretroviral therapy (ART), especially out-of-pocket costs for the person with HIV, be one of the considerations in regimen selection, because such expenditures can directly affect affordability and adherence.
• Health insurance and prescription drug coverage can directly affect clinical outcomes for people with HIV; changes to coverage can result in lapses in viral suppression and should be anticipated as best possible.
• The Ryan White HIV/AIDS Program offers opportunities to access essential HIV medical and support services, including medication assistance, to minimize cost as a barrier to care for people with HIV and lower incomes.
• Both medical and nonmedical case management services can be used to identify and address cost-related barriers to ART by linking individuals to private and public funding sources.
• Disengagement from care occurs more frequently during transitions in care and coverage (e.g., transitioning from pediatric to adult care; changing employment status; moving from one state to another; being released from incarceration; switching insurance, including to Medicare).

Introduction

The clinical benefits, public health impact, and cost-effectiveness of HIV treatment are well established,[1-6] and increased uptake and utilization of antiretroviral therapy (ART) is one of the four pillars of the *Ending the HIV Epidemic in the U.S.* initiative.[7,8] However, HIV treatment with ART is costly. A 2023 study estimated that the net Medicaid spending from 2007 through 2019 was $25 billion for 17 million 30-day supplies of antiretroviral (ARV) drugs.[9] Estimated annual spending—inclusive of statutorily required manufacturer rebates to offset federal and state costs of most outpatient prescription drugs dispensed to Medicaid beneficiaries—increased 178%, from $1.1 billion to $3.0 billion during this 12-year period. According to a study of risk-adjusted 2016 Medicare claims, total spending for Medicare beneficiaries with HIV receiving ART was 221% greater than for beneficiaries without HIV, largely driven by ARV drug expenses.[10] Since the initial inclusion of an ARV cost table in these guidelines in 2012, the cost of brand-name, first-line ARV regimens has increased by more than 30% from 2012 to 2018,[11] which is 3.5 times the rate of inflation for that same time period.

This section provides guidance on cost considerations related to HIV clinical care. Ideally, ART costs do not influence regimen selection. However, the complexities of the U.S. health care system, including those related to out-of-pocket costs to people with HIV, may necessitate their consideration in regimen selection, because expenditures may directly or indirectly affect adherence and virologic outcomes. Additionally, health insurance and prescription drug coverage determinations, based in part on ART costs, can directly affect clinical outcomes for people with HIV; the clinical impact of changes to insurance coverage is also discussed in this section. Overall costs to the health care system, insurers, and society are also important, especially given the increasing number of people with HIV, rising drug costs, and increasing multimorbidity among people aging with HIV. Providers should make every effort to understand cost considerations that may limit HIV care and the support services available to mitigate cost as a barrier to effective HIV treatment.

Health Care Coverage to Maximize Access to ART

Health care access in the United States can vary, depending on factors such as location and income, among others. Although the Patient Protection and Affordable Care Act (ACA) has substantially improved access to HIV clinical services in many regions of the United States since 2010, an estimated 35% of people with HIV in the United States live in the 10 states—including Florida, Georgia, and Texas—that had not expanded Medicaid in accordance with the ACA as of November 2024.[12]

The ACA and its Medicaid expansion have greatly improved insurance coverage among people with HIV.[13] Before the ACA, many individuals with HIV were denied insurance due to pre-existing condition exclusions and high costs. Medicaid eligibility was also restricted to specific categories, such as disability, which excluded many low-income individuals from coverage.[14,15] Soon after implementation of the ACA and Medicaid expansion in a growing number of states, HIV testing and diagnoses increased, more individuals started ART and achieved viral suppression, uninsured hospitalizations among people with HIV decreased, and fewer people were unaware of their HIV status.[16-19]

A retrospective analysis of NA-ACCORD data examined the associations between state Medicaid expansion associated with the ACA and HIV outcomes in the United States.[20] The study found a beneficial effect of Medicaid expansion on higher CD4 T lymphocyte (CD4) cell counts at the point of enrollment in care. However, no evidence was observed indicating either a positive or negative impact on additional continuum of care outcomes. The authors suggest the null effect on downstream HIV measures for individuals with HIV may be due to the Ryan White HIV/AIDS Program (RWHAP), the highly cost-effective federal safety net program, potentially concealing HIV outcome deficits that might otherwise be apparent in states foregoing Medicaid expansion.[21] At the population level, Medicaid expansion could have a greater effect on reducing HIV incidence by increasing diagnoses and improving linkage to care.[22]

Changes or lapses in health insurance are common and can result in interruptions in clinical care and virologic suppression. Frequent recertification requirements for AIDS Drug Assistance Programs (ADAPs) or Medicaid can lead to lapses in ART use.[23,24] Providers should be aware of the certification needs for the states in which they provide care. Both ADAPs and Medicaid are administered at the state level; therefore, eligibility criteria and medication formularies differ from state to state. When people with HIV receiving Medicaid or ADAP ARV drug coverage move from one state to another, advanced planning is required to ensure uninterrupted access to ART. For example, specific antivirals covered by Medicaid may not be covered by the state ADAP (e.g., long-acting cabotegravir/rilpivirine [LA CAB/RPV]), potentially resulting in the need for regimen changes if a change from Medicaid to an ADAP is required.

Interruptions in health insurance and prescription drug coverage access are also common for people with HIV involved with the criminal justice system. While incarcerated, some people with HIV may be disenrolled from their healthcare insurance and prescription drug coverage. However, in 2023, the Centers for Medicare & Medicaid Services (CMS) released guidance for states when applying for a partial waiver of this policy, enabling coverage for services provided 30 to 90 days before release.[25] With approval of this waiver, states are expected to suspend (not terminate) Medicaid coverage during incarceration and must collaborate with correctional facilities to assist incarcerated individuals who are not currently enrolled in Medicaid with submitting applications during incarceration using presumptive eligibility. Minimum benefits expected by CMS in state waiver proposals include case management services for pre- and post-release (including linkage to outpatient HIV care), medication-assisted therapy for substance use disorders, and at least a 30-day supply of medications at release. Additionally, although federal RWHAP and ADAP funds cannot cover care

and treatment for individuals in state or federal prison systems, they can provide short-term, transitional support to people with HIV in local correctional facilities (e.g., city or county jails).[26]

Cost Sharing in the United States

Prescription drug pricing in the United States involves complex systems with varying requirements for mandatory and voluntary discounts, rebates, and reimbursement rates, and much of the pricing information is confidential. Prices can vary depending on the state, purchaser, type of public or private insurance coverage in use, and number of generic competitors to branded drugs (see Table 22b below). Therefore, providers may find it difficult to navigate payer cost-containment practices, including formulary restrictions, prior authorization requirements, and cost-sharing arrangements, such as copayments (a fixed dollar amount per prescription), coinsurance (a fixed percentage of the prescription cost), and insurance deductible payments.

Out-of-pocket costs for people with HIV can be prohibitive, creating a barrier to the initiation and continuation of ART. Cost sharing results in higher rates of people not initiating ART, prescription abandonment at the pharmacy, decreased adherence, and more frequent drug discontinuation. In turn, out-of-pocket costs may indirectly lead to worse health outcomes and an increased use of the medical system, especially among people with chronic diseases.[27-32] In 2022, the Centers for Disease Control and Prevention (CDC) Medication Monitoring Project (MMP) reported that less than 5% of people with HIV previously taking ART had stopped; however, among people in the MMP who were no longer taking ART, 34% reported that money or insurance problems were contributors to stopping ART.[33]

Conversely, reducing out-of-pocket costs (e.g., through RWHAP or ADAP cost-sharing assistance, manufacturer copayment-assistance programs, or by prescribing generic drugs instead of more costly brand-name products) has been associated with improved adherence.[34] Given the clear association between out-of-pocket costs and the ability to pay for and adhere to medications, clinicians should minimize out-of-pocket drug-related expenses for people with HIV whenever possible. However, many of the cost-sharing arrangements that determine out-of-pocket costs are not transparent to clinicians or people with HIV at the time decisions on ART are made. Asking people with HIV about their copays and working with case management specialists can help to identify and overcome this structural barrier to improving clinical care.

Maximum allowable copayments are statutorily capped at $4 for preferred drugs; in some states, maximum allowable copayments can increase to up to $8 for certain non-preferred drugs for beneficiaries with income <150% of the federal poverty level. For commercial insurers, cost sharing generally is subject to maximum payment rules under the ACA, which increase annually. Manufacturer cost-sharing assistance programs are available for most brand-name ARV products but may be restricted by pharmacy and by state. Manufacturer copay assistance also may be subject to copay accumulator programs implemented by insurers' pharmacy benefit managers, whereby manufacturer payments do not count toward a person's deductible or out-of-pocket maximum.

ADAPs make ARVs and other prescription drugs accessible to people with HIV who are underinsured and have limited financial resources, particularly during lapses in insurance coverage.[35,36] Furthermore, many ADAPs provide premium and/or cost-sharing assistance to eligible clients covered by Medicaid, commercial insurance plans, employer-sponsored insurance plans, or Medicare.[13]

Medicare Beneficiaries With HIV

ARV cost considerations associated with Medicare coverage are increasingly important as more people with HIV age into Medicare. According to CDC HIV prevalence data, 15% of all people with diagnosed HIV in the United States were aged 65 or older in 2022; an additional 27% were aged 55 to 64, with the vast majority expected to age into Medicare over the next 10 years.[37] Enrollment into Medicare can change out-of-pocket costs, which can cause unexpected changes to ART affordability and, ultimately, adherence.[38,39]

Medicare Part D prescription drug cost sharing includes deductibles and copayments or coinsurance, including out-of-pocket payments of up to 25%. However, beginning in 2025, as required under the Inflation Reduction Act, there will be a $2,000 out-of-pocket spending cap.[40]

Medicare Part B cost sharing is not subject to out-of-pocket caps. Where provider-administered drugs—such as long-acting injectable CAB/RPV, ibalizumab-uiyk (IBA) infusions, or subcutaneously (SQ) administered lenacapavir (LEN)—are covered under Medicare Part B, beneficiary cost sharing can be up to 20% of all medication costs.[41]

Low-income beneficiaries may qualify for subsidies to defray Part D cost-sharing payments or the Qualified Medicare Beneficiary program to defray Part B cost-sharing payments. Medicare Advantage and Part D plans are now required to offer beneficiaries an option to enroll in a Medicare Prescription Payment Plan[42] authorized under the Inflation Reduction Act, which will allow beneficiaries to pay cost sharing associated with high-cost prescription drugs in capped monthly payments instead of a single pharmacy payment. Manufacturer copay assistance programs may not be applied toward Medicare plan cost sharing, but assistance from state/territorial ADAPs, other State Pharmaceutical Assistance Programs, and independent foundations (e.g., Patient Access Network Foundation, Patient Advocate Foundation) may provide cost-sharing support if financial eligibility criteria are met.

In addition to its Medicare Part D cost-sharing provisions intended to lower out-of-pocket costs for beneficiaries, the Inflation Reduction Act also requires the Secretary of the U.S. Department of Health and Human Services to negotiate prices with manufacturers for certain drugs with the highest total Part D and Part B spending. Ten Part D drugs were selected for price negotiation in 2026 (2026 pricing was finalized in 2024), with another 15 Part D drugs selected for 2027, 15 Part D and Part B drugs for 2028, and 20 Part D and Part B drugs selected for 2029 and thereafter. The selected drugs will come from the 50 with the highest total Medicare Part D spending and the 50 with the highest total Medicare Part B spending. Although ARV drugs did not qualify for negotiated pricing during the 2026 and 2027 cycles, several ARV drugs are potentially subject to negotiated pricing going into effect in 2028.[43]

Generic Antiretrovirals and Multi-Tablet Regimens

In 2023, savings to the U.S. health care system generated from the use of generic drugs and biosimilar products totaled $445 billion, including $137 billion and $206 billion in savings to Medicare and commercial insurers, respectively.[42,44] Total generic and biosimilar savings for the past 10 years are estimated to be $3.1 trillion.

With substantial improvements in the long-term safety and effectiveness of contemporary ART, a number of regimens and regimen components in Tables 6a and 6b in the Initial Combination Antiretroviral Regimens for People With HIV section remain listed beyond their patent protection date and are or will be available as lower-cost generic options. Keen interest exists in assessing the economic value of using newer, more expensive drugs compared with older, less expensive generic drugs that have established clinical safety and efficacy, such as generic tenofovir disoproxil

fumarate (TDF), which has been available since 2018. A nationwide cross-sectional analysis of 2019 Medicare Part D formulary and pricing data investigated the cost-effectiveness of generic TDF-based regimens versus branded tenofovir alafenamide (TAF)–based regimens.[45] The study demonstrated that the similar efficacy—but slightly improved toxicity profile—of the TAF-based regimens would justify no more than a $1,000 higher annual premium for the TAF-based regimens than generically available TDF-based regimens. A cost-containment analysis evaluated the use of branded dolutegravir (DTG) plus generic lamivudine (3TC) as a two-pill regimen compared with a branded single-tablet regimen (STR).[46] Model findings supported that if 50% of people with newly diagnosed HIV initiated a two-pill regimen consisting of branded DTG plus generic 3TC, the cost savings would reach $550 million to $800 million over a 5-year period; similarly, if 25% of people with sustained viral suppression switched to branded DTG plus generic 3TC maintenance therapy, the cost savings would exceed $3 billion in 5 years.[46]

Because all commercially available STRs listed among the *Recommended Initial Regimens for Most People With HIV* (Table 6a) and *Other Initial Antiretroviral Regimens for Certain Clinical Scenarios* (Table 6b) are branded products, including STRs that contain ARV components that are no longer patent protected, use of generics in the United States may necessitate modest increases in pill burden, but without changes in drug frequency. One study of Medicare Part D spending, which included expenditures for one ARV fixed-dose combination tablet (abacavir [ABC]/3TC), demonstrated that splitting up brand-name coformulated products into their generic components could have saved Medicare an estimated $2.7 billion from 2011 through 2016, and it highlighted this approach as a critical cost-containment measure.[47]

However, to the extent that pill burden, rather than drug frequency, results in reduced adherence, generic ART could lead to decreased costs but at the potential expense of worsening virologic suppression rates and poorer clinical outcomes.[29,30] An additional benefit of STRs is that they eliminate the risk that one drug in the regimen will be temporarily or permanently discontinued because of prescribing error, unsynchronized refill schedules, or prohibitive out-of-pocket costs. Data to support or refute the superiority of once-daily STRs versus once-daily multi-tablet regimens, particularly based on virologic outcomes and especially following viral suppression, remain limited. One large observational cohort study demonstrated a small but statistically significant virologic efficacy benefit associated with STRs.[46] In this study, the time to treatment discontinuation was shorter for non-STRs than for once-daily STR regimens; however, this difference disappeared when modifications for regimen simplification were included in the analysis. On the other hand, observational data from Spain showed that coformulated DTG/ABC/3TC resulted in similar viral suppression compared with DTG plus ABC/3TC, both when used as an initial ARV regimen and when people with viral suppression on the STR were switched to the two-pill formulation as a cost-saving strategy.[48]

Importantly, when the costs of brand-name drug products and generic ARV drugs are compared, savings associated with generic ARV drugs may vary when branded drugs are subject to discounts or rebates across public and private payer systems. Although generic drug products may be associated with societal cost savings and, specifically, savings for public payers, commercial insurers, and people with HIV with significant out-of-pocket pharmacy expenses, manufacturer copay assistance is not generally available to commercially insured individuals. In cases where manufacturer copay assistance may be available for a brand-name ARV product but not for an equivalent generic ARV product, the generic drug prescription paradoxically may result in higher out-of-pocket costs.

Long-Acting Injectable ART

CAB/RPV, IBA, and LEN are ARVs with unique formulations and pharmacokinetic characteristics that allow for long-acting administration via intramuscular (IM) injection, intravenous (IV) infusion,

and SQ injection, respectively. IBA and LEN are approved for use among highly treatment-experienced people, typically in combination with an optimized background regimen consisting of at least one daily oral ARV drug product, and are associated with unique cost considerations. Conversely, monthly or bimonthly LA CAB/RPV injections can be prescribed and administered as a complete regimen replacement for daily oral ARV regimens.

Wholesale Acquisition Cost (WAC) prices for the LA CAB/RPV formulations are comparable to those of commonly prescribed oral regimens on an annual basis. However, long-acting HIV treatment options requiring administration by a licensed medical provider may be associated with costs not typically associated with oral ART, including clinic visit and administration fees, medical benefit determinations and prior authorization requirements, patient scheduling and follow-up to ensure adherence, upfront medication purchasing costs incurred by clinics, and inadequate "buy-and-bill" insurance reimbursements.

Cost-effectiveness modeling indicates that long-acting ART may be particularly advantageous for people struggling with adherence to daily oral regimens.[49-51] Studies have demonstrated that long-acting ART can achieve similar or better clinical outcomes than oral ART, particularly when adherence is factored into the equation. In cost terms, LA CAB/RPV may lead to lifetime savings, given lower health care expenditures associated with improved viral suppression and reduced risk of HIV transmission.

Costs and Cost-Effectiveness of ARV Regimens for Highly Treatment-Experienced People With Multidrug-Resistant HIV

For people with multidrug-resistant (MDR) HIV, an ARV regimen that includes IV IBA, SQ LEN, or oral fostemsavir can be effective in achieving viral suppression, though costly. Two cost-effectiveness analyses using independent simulation models have demonstrated that IBA-containing ARV regimens would substantially improve survival for people with MDR HIV, but at a high cost per quality-adjusted life years, given the high cost of IBA. However, the overall budget impact of such regimens would be relatively small, given the limited number of people for whom IBA would be necessary.[52,53]

340B Drug Pricing Program, Prescription Drug Affordability, and Program Savings for People With HIV

Created by Congress in 1992, the 340B Drug Discount Program requires pharmaceutical manufacturers to sell drugs at a discount to certain hospitals and federally funded clinics providing safety net care, including RWHAP providers and state/territorial ADAPs. 340B discounts help to ensure the affordability of outpatient prescription drugs for uninsured and underinsured people with HIV and to retain any revenue associated with discounted sales. This revenue, or program savings, is generated when 340B-covered entities are able to purchase discounted drugs but are reimbursed by third-party payers at usual and customary rates that do not account for discounted purchases. Although potentially incentivizing providers to prescribe higher-cost brand-name drugs that yield substantially greater revenue than generic alternatives, 340B savings can be used to "stretch scarce federal resources as far as possible, reaching more eligible patients and providing more comprehensive services."[54]

By purchasing ARV drugs and other essential medicines at significantly reduced prices, covered entities can reinvest savings into essential HIV care and support services, including case management, behavioral health care, offsetting uncompensated care, transportation, adherence support, and outreach efforts. These services can help improve HIV care retention, medication adherence, and viral suppression rates.[13]

Costs and Cost-Effectiveness of Routine Laboratory Services for People With HIV on ART

In the context of lifelong ART, the amount of money to be saved by reducing the frequency of expensive tests (e.g., genotypes, serologies) is modest. Even so, judicious use of laboratory testing, without compromising patient care, can still be an important way to reduce costs. For people with deductibles for laboratory tests, decreasing the use of tests with limited clinical value could reduce costs and improve adherence to a care plan. Several studies have examined the value of laboratory services in HIV care. One cost analysis study suggested that there may be no clinical benefit to continuing CD4 monitoring in people with suppressed viral loads and CD4 counts >200 cells/mm^3 after 48 weeks of therapy.[31] In the United States, reducing biannual CD4 monitoring to annual monitoring could save approximately $10 million per year.[55] Another study reviewed the records of 429 hospitalizations for 274 people with HIV during a 6-month period. The inpatient chart review demonstrated that 45% of ordered laboratory tests were not indicated, including hepatitis serologies, other serologies, and cytomegalovirus polymerase chain reaction. During this 6-month period at this single site, the estimated cost of excess and inappropriate laboratory testing totaled $14,000 to $92,000.[56]

Cost-effectiveness analyses from 2001 and 2005 demonstrated the value of genotypic resistance testing in people who are ART-experienced and ART-naive and supported the Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) recommendation to perform resistance testing before ART initiation and at the time of virologic failure.[57,58] More recent cost-effectiveness analyses have revisited the value of baseline, pre-treatment genotype testing in the setting of integrase strand transfer inhibitor (INSTI) plus two–nucleoside reverse transcriptase inhibitor (NRTI) regimens. One modeling study suggested that INSTI-specific genotype testing before initiation of a DTG plus two-NRTI regimen is not cost-effective and may lead to underutilization of INSTIs; the results highlighted that some people with minor INSTI resistance mutations would still become virologically suppressed on a DTG-based regimen.[59] A second modeling study found that standard (NRTI, non-nucleoside reverse transcriptase inhibitor, protease inhibitor) genotype testing before ART initiation also is not cost-effective because it may have little impact on outcomes, given the use of an INSTI plus two NRTIs in first-line treatment.[60] Both modeling studies assessed the use of genotype testing only for decision-making for initial ART and presumed that genotype testing would be available for use at the time of first-line failure. The results of these modeling studies suggest that additional clinical research is needed to define the role of genotypic resistance testing before initiation of an INSTI plus two-NRTI regimen. Importantly, these modeling data do not apply to the initiation of two-drug ARV regimens (e.g., DTG plus 3TC) or to people who have received oral (TDF or TAF) plus (3TC or FTC) or IM cabotegravir (CAB) as pre-exposure prophylaxis (PrEP), which are being prescribed increasingly in clinical practice. It should be noted that the Panel continues to recommend baseline testing for clinically relevant protease and reverse transcriptase mutations for most people, with additional genotypic resistance testing for integrase mutations for individuals with a history of CAB use for PrEP or an INSTI-based regimen for post-exposure prophylaxis (see Drug-Resistance Testing).

Costs and Cost-Effectiveness of Comprehensive HIV Care

Comprehensive person-centered HIV care offers substantial clinical benefits.[61] Such programs include the integration of social service needs and services for mental health, substance use disorders, sexual health, and age-associated multimorbidity (see Substance Use Disorders and HIV, Adherence to the Continuum of Care, and HIV and the Older Person). Integrated services can improve engagement in care and virologic suppression among people with HIV, but they require investment and resources. Several cost-effectiveness analyses have demonstrated that integrated

care programs can offer excellent value, especially if delivered to people at increased risk of disengagement in care.[62-64]

RWHAP provides a critical source of outpatient HIV clinical care for people with HIV who have low incomes and remain uninsured or underinsured under the ACA or who require wraparound support.[26] A recent cost-effectiveness analysis underscored the value of this safety net program and projected its clinical and cost impact over 50 years. Given higher rates of virologic suppression among people with HIV attending RWHAP clinics (compared with estimated virologic suppression in the absence of such supports), the analysis projects fewer HIV incident infections and longer life expectancy and demonstrates the cost-effectiveness of RWHAP.[21] RWHAP funds can be used to provide eligible individuals with services related to the delivery of HIV care, the treatment of related conditions, and support, as well as to address identified barriers to care. However, RWHAP funds cannot be used for inpatient care and services.[65]

Comprehensive HIV care and treatment often requires navigating a complex, dynamic patchwork of service delivery and both payer and financing mechanisms. Provider awareness of this patchwork, including the array of services available to people with HIV eligible for RWHAP, is therefore essential to maximizing clinical outcomes.

Conclusion

Ideally, costs should not drive clinical care, yet they are a factor in contemporary health care. Because regimen costs may affect people's ability to afford and adhere to therapy, understanding ART-related costs in the United States is increasingly important. Providers play a key role in ensuring optimal care while working to both (1) minimize costs for ARV drugs and avoid or minimize unnecessary laboratory monitoring and (2) retain excellent clinical outcomes in an environment of cost-containment strategies, including formulary restrictions, utilization management (e.g., prior authorization), and cost sharing. Providers should, therefore, remain informed of current insurance and payment structures, ART costs (see Table 22b below for estimates of average drug prices), out-of-pocket expenditure requirements, and available generic ARV options. Providers should work with people with HIV and pharmacists, social workers, case managers, financial service providers, and peer navigators to understand their clients' medication benefits and any potential financial hurdles to prescription fulfillment and full adherence. This information will help providers identify treatment options that are safe, effective, and affordable. Engaging people with HIV in discussions about cost constraints during regimen selection will likely facilitate adherence. Additionally, providers should familiarize themselves with ARV affordability resources (such as ADAPs and pharmaceutical company assistance programs for people who qualify) and refer them to such assistance if needed. Similarly, providers should help people with HIV to find comprehensive clinical care coverage when available and consider opportunities to integrate care when feasible.

Table 22a. Insurance and Health Program Prescription Drug Pricing and Access

Insurance/Health Program	Prescription Drug Pricing and Access
Medicaid	Drug manufacturers must participate in the MDRP for their drugs to be covered by Medicaid and Medicare Part B. Manufacturers are required to pay Medicaid programs a rebate of at least 23.1% of the AMP for most brand-name drugs (13% for generics) sold to retail pharmacies or outpatient care providers (notably infused, injected, implanted, inhaled, or instilled drugs). Manufacturers pay additional rebates if this confidential AMP increases faster than the CPI-U rate of inflation. Additionally, many states negotiate with manufacturers for supplemental rebates. States are permitted to require "nominal" cost sharing for medical and pharmacy benefits for some beneficiaries, although many elect not to do so. States can obtain a waiver to allow them to apply higher cost sharing.
Medicare	ARVs are one of six "protected drug classes" under Medicare Part D. Part D plans must provide access to all, or substantially all, FDA-approved ARVs. Part D plan sponsors, or PBMs on their behalf, negotiate rebates on outpatient drugs with manufacturers; the extent of rebating is unclear. Most physician-administered drugs and biologics are covered under Medicare Part B at a set cost: ASP plus 6%. This pricing mechanism controls spending by narrowing the spread between what is actually paid for the drug and what is actually billed to Medicare. Premiums and cost-sharing payments may be significant for both services and prescription drugs, though caps on out-of-pocket spending for drugs covered by Medicare Part D went into effect in 2024; Part A (hospital care) and Part B place no cap on out-of-pocket spending. Some subsidies and supplemental coverage are offered for low-income beneficiaries. Manufacturer copay assistance programs cannot be applied to Part B or Part D cost sharing; cost-sharing support is available from ADAPs, foundations, and other sources and is based on financial eligibility criteria.
Commercial Insurance	Private insurance plans, or PBMs on their behalf, negotiate rebates on inpatient and outpatient drugs with manufacturers; the extent of rebating is unclear. Formulary restrictions and utilization management (prior authorization, step therapy, higher cost sharing) involving drugs and biologics covered under plans' pharmacy benefit or medical benefit (e.g., infused or injected ARVs) are possible cost-containment measures. Cost sharing can be highly variable. Manufacturer copay assistance programs can be applied in most cases but may not count toward annual ACA cost-sharing limits; cost-sharing support is also available from ADAPs, foundations, and other sources and is based on financial eligibility criteria.

Table 22a. Insurance and Health Program Prescription Drug Pricing and Access

Insurance/Health Program	Prescription Drug Pricing and Access
ADAPs	Significant discounting on most ARVs negotiated by the ADAP Crisis Task Force is allowed under the 340B Drug Pricing Program. There is usually no cost sharing for ADAP clients who are uninsured. ADAP can assist with commercial or public insurance out-of-pocket costs.
Veterans Affairs	The FCP is the maximum price manufacturers may charge the four largest federal purchasers of pharmaceuticals (the "Big Four"): the U.S. Department of Veterans Affairs, U.S. Department of Defense, U.S. Public Health Service (including the Indian Health Service), and U.S. Coast Guard. The FCP of a drug includes a 24% discount on a drug's average price paid by nonfederal purchasers. Additional discounts may be applied if nonfederal purchase prices increase faster than the CPI-U inflation rate. Big Four prices may be 40% to 50% below list prices. Veterans Affairs may negotiate further price reductions. Prescription drug cost sharing is generally nominal; medications are not withheld from those who cannot afford cost-sharing expenses.
Community Health Centers	Many community health centers are enrolled in the 340B Drug Pricing Program, which allows discounted drug purchasing using the MDRP formula. Discounts start at 23.1% off AMP, with additional discounts if the AMP increases faster than the CPI-U rate of inflation. Cost sharing in community health centers is first driven by payer source. For clients who are uninsured, cost sharing, if required, is typically based on a sliding fee scale.
Jails and Prisons	Under the U.S. Constitution, correctional facilities have a legal obligation to provide necessary medical care, including prescription drugs, to incarcerated individuals.[a] Jails and prisons generally do not have access to discounted drugs available to government programs, such as Medicaid or "Big Four" purchasers (see Veterans Affairs above), but may benefit from centralized municipal or state purchasing mechanisms. Jails and prisons also may be able to purchase discounted ARV drugs and other medications under the 340B Drug Pricing Program, either as a recipient of certain federal funds associated with STI, HIV, and viral hepatitis prevention, or in partnership with other 340B-covered entities contracted to provide health care services to jailed or incarcerated individuals (e.g., disproportionate share hospital programs, community health centers). RWHAP programs and ADAPs also may provide time-limited HIV care and prescription drug access support for people with HIV in local prisons and jails.

Table 22a. Insurance and Health Program Prescription Drug Pricing and Access

Insurance/Health Program	Prescription Drug Pricing and Access
Manufacturer and Charitable Prescription Drug Assistance Programs	Manufacturer PAPs are run by, or in association with, pharmaceutical companies to provide free or low-cost medications to people who meet certain eligibility requirements, including FPL-based income limits. A CAP is operated by manufacturers to provide assistance with cost-sharing requirements (including deductibles, copayments, and coinsurance) associated with prescription drug fills/refills for individuals with private health insurance. Pharmaceutical company CAPs cannot be used by individuals covered by Medicaid, Medicare, or other state and federal programs. Charitable third-party assistance programs, such as Patient Advocate Foundation Co-pay Relief, provide cost-sharing assistance to people who meet financial eligibility requirements. NASTAD maintains a number of PAP and CAP resources for use in clinical practice.

[a] *Estelle v. Gamble* [66]

Key: ACA = Affordable Care Act; ADAP = AIDS Drug Assistance Program; AMP = average manufacturer price; ARV = antiretroviral; ASP = average sales price; CAP = cost-sharing assistance program; CPI-U = consumer price index-urban; FCP = federal ceiling price; FDA = U.S. Food and Drug Administration; FPL = federal poverty level; NASTAD = National Alliance of State & Territorial AIDS Directors; MDRP= Medicaid Drug Rebate Program; PAP = patient assistance program; PBM = pharmacy benefits manager; RWHAP = Ryan White HIV/AIDS Program; STI = sexually transmitted infection

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

Table 22b includes three benchmark prices, rounded to the nearest dollar, for commonly used antiretroviral (ARV) drugs[a] as a general reference for health care providers when considering the cost of HIV treatment. Health care providers should contact pharmacies or payers regarding actual prices, comparative cost savings, formulary restrictions, and cost-sharing requirements. The **wholesale acquisition cost (WAC)** is the list price published by manufacturers for prescription drugs or biologics sold to wholesalers. The WAC price approximates what retail pharmacies pay wholesalers for single-source (e.g., brand-name) drugs. There is a range of WAC prices for generic ARV drugs, because these are multiple-source products with variable list prices. With increasing competition, actual transactional prices of generic drugs decrease substantially among wholesalers and pharmacies. **Average wholesale price (AWP)** has historically been used as the basis for setting public (e.g., Medicaid) and private (e.g., commercial insurer) reimbursement rates for pharmacies. Neither WAC nor AWP includes variable price concessions along supply and payment chains, including discounts and rebates to wholesalers, pharmacies, federal purchasers (e.g., the U.S. Department of Veterans Affairs), pharmacy benefit managers, commercial insurers, Medicaid, 340B pharmacies, and AIDS Drug Assistance Programs. The availability of these discounts and rebates depends on product demand, market competition, and WAC price increases set by manufacturers. Maximum Medicaid payment rates are assigned to generic products with three or more therapeutically and pharmaceutically equivalent products, as determined by the U.S. Food and Drug Administration. This federally established pharmacy reimbursement limit is the **federal upper limit (FUL).** Federal Medicaid will reimburse state Medicaid programs up to this limit for multiple-source drugs (plus the dispensing fee); states may set their own **state maximum allowable costs (SMACs)** and commercial insurers set their own reimbursement upper limits with pharmacies. Whereas WACs and AWPs are generally set annually, FULs are adjusted on a monthly basis, particularly for multiple-source drugs with fluctuating pharmacy acquisition costs. In this table, the FUL for a drug is described as “pending” if a generic drug currently lacks the competition required to trigger a FUL.

ARV Drug (Generic and Brand Names)	**Strength, Formulation**	**Tablets, Capsules, Vials, or mLs** (Monthly, Unless Otherwise Noted)	**WAC** (Monthly, Unless Otherwise Noted)[b]	**AWP** (Monthly, Unless Otherwise Noted)[b]	**FUL** (As of April 30, 2025)[c]
NRTIs					
Abacavir Generic	300-mg tablet	60 tablets	$100 to $150	$578 to $603	$22
Emtricitabine • Generic, *or* • Emtriva	200-mg capsule	30 capsules	*Generic* • $390 to $536 *Emtriva* • $537	*Generic* • $482 to $644 *Emtriva* • $644	Pending

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	**Strength, Formulation**	**Tablets, Capsules, Vials, or mLs** (Monthly, Unless Otherwise Noted)	**WAC** (Monthly, Unless Otherwise Noted)[b]	**AWP** (Monthly, Unless Otherwise Noted)[b]	**FUL** (As of April 30, 2025)[c]
Lamivudine • Generic, *or* • Epivir	300-mg tablet	30 tablets	*Generic* • $40 to $415 *Epivir* • $416	*Generic* • $429 *Epivir* • $499	*Generic* • $72 *Epivir* • N/A
Tenofovir Disoproxil Fumarate • Generic, *or* • Viread	300-mg tablet	30 tablets	*Generic* • $27 to $300 *Viread* • $1,254	*Generic* • $167 to $1,216 *Viread* • $1,504	*Generic* • $23 *Viread* • N/A
Zidovudine Generic	300-mg tablet	60 tablets	$36 to $54	$54 to $365	$13
NRTI Combination Products					
Abacavir + Lamivudine Generic	600-mg/300-mg tablet	30 tablets	$100 to $302	$1,393 to $1,395	$51
Tenofovir Alafenamide + Emtricitabine Descovy	25-mg/200-mg tablet	30 tablets	$2,202	$2,643	N/A
Tenofovir Disoproxil Fumarate + Emtricitabine • Generic, *or* • Truvada	300-mg/200-mg tablet	30 tablets	*Generic* • $25 to $853 *Truvada* • $1,842	*Generic* • $70 to $2,100 *Truvada* • $2,211	*Generic* • $67 *Truvada* • N/A
Tenofovir Disoproxil Fumarate + Lamivudine Cimduo	300-mg/300-mg tablet	30 tablets	$1,185	$1,422	N/A
Zidovudine + Lamivudine Generic	300-mg/150-mg tablet	60 tablets	$125 to $578	$265 to $932	$36

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	**Strength, Formulation**	**Tablets, Capsules, Vials, or mLs** (Monthly, Unless Otherwise Noted)	**WAC** (Monthly, Unless Otherwise Noted)[b]	**AWP** (Monthly, Unless Otherwise Noted)[b]	**FUL** (As of April 30, 2025)[c]
NNRTIs					
Efavirenz Generic	600-mg tablet	30 tablets	$80 to $894	$1,043 to $1,118	$40
Doravirine Pifeltro	100-mg tablet	30 tablets	$1,840	$2,208	N/A
Etravirine • Generic, *or* • Intelence	200-mg tablet	60 tablets	*Generic* • $1,287 *Intelence* • $1,498	*Generic* • $1,609 *Intelence* • $1,797	*Generic* • $842 *Intelence* • N/A
Nevirapine • Generic, *or* • Generic XR	*Generic* • 200-mg tablet *Generic XR* • 400-mg tablet	*Generic* • 60 tablets *Generic XR* • 30 tablets	*Generic* • $10 to $45 *Generic XR* • $135 to $565	*Generic* • $648 to $651 *Generic XR* • $595 to $706	*Generic* • $7 *Generic XR* • $149
Rilpivirine Edurant	25-mg tablet	30 tablets	$1,483	$1,780	N/A
PIs					
Atazanavir • Generic, *or* • Reyataz	200-mg capsule, *or* 300-mg capsule	*200-mg capsule* • 60 capsules *300-mg capsule* • 30 capsules	*Generic 200 mg* • $178 to $316 *Reyataz 200 mg* • $1,463 *Generic 300 mg* • $178 to $316 *Reyataz 300 mg* • $1,449	*Generic 200 mg* • $1,502 to $1,668 *Reyataz 200 mg* • $1,756 *Generic 300 mg* • $1,502 to $1,652 *Reyataz 300 mg* • $1,739	*Generic 200 mg* • $146 *Generic 300 mg* • $192 *Reyataz* • N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	**Strength, Formulation**	**Tablets, Capsules, Vials, or mLs** (Monthly, Unless Otherwise Noted)	**WAC** (Monthly, Unless Otherwise Noted)[b]	**AWP** (Monthly, Unless Otherwise Noted)[b]	**FUL** (As of April 30, 2025)[c]
Atazanavir + Cobicistat Evotaz	300-mg/150-mg tablet	30 tablets	$1,605	$1,927	N/A
Darunavir • Generic, *or* • Prezista	*Generic* • 600-mg tablet • 800-mg tablet *Prezista* • 600-mg tablet • 800-mg tablet • 100-mg/mL suspension	*600-mg tablets* • 60 tablets *800-mg tablets* • 30 tablets *100-mg/mL suspension* • 200 mL	*Generic 600 mg* • $60 to $1,145 *Prezista 600 mg* • $2,158 *Generic 800 mg* • $60 to $1,153 *Prezista 800 mg* • $2,158 *Prezista suspension* • $1,199	*Generic 600 mg* • $1,373 to $2,388 *Prezista 600 mg* • $2,590 *Generic 800 mg* • $1,384 to $2,388 *Prezista 800 mg* • $2,590 *Prezista suspension* • $1,439	*Generic 600 mg* • Pending *Generic 800 mg* • Pending *Prezista* • N/A
Darunavir + Cobicistat Prezcobix	800-mg/150-mg tablet	30 tablets	$2,467	$2,960	N/A
Lopinavir + Ritonavir • Generic, *or* • Kaletra	200-mg/50-mg tablet	120 tablets	*Generic* • $885 *Kaletra* • $1,024	*Generic* • $1,106 *Kaletra* • $1,229	*Generic* • $747 *Kaletra* • N/A
Tipranavir Aptivus	250-mg capsule	120 capsules	$2,054	$2,466	N/A
INSTIs					
Dolutegravir Tivicay	50-mg tablet	30 tablets, *or* 60 tablets	*30 tablets* • $2,325 *60 tablets* • $4,650	*30 tablets* • $2,790 *60 tablets* • $5,580	N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	**Strength, Formulation**	**Tablets, Capsules, Vials, or mLs** (Monthly, Unless Otherwise Noted)	**WAC** (Monthly, Unless Otherwise Noted)[b]	**AWP** (Monthly, Unless Otherwise Noted)[b]	**FUL** (As of April 30, 2025)[c]
Raltegravir • Isentress, *or* • Isentress HD	*Isentress* • 400-mg tablet *Isentress HD* • 600-mg tablet	60 tablets	*Isentress* • $2,083 *Isentress HD* • $2,083	*Isentress* • $2,500 *Isentress HD* • $2,500	N/A
Capsid Inhibitor					
Lenacapavir Sunlenca	300-mg tablet, *or* 927-mg injection kit	*300-mg tablet* • 4 tablets • 5 tablets *Injection kit* • 2 vials (1 kit every 6 months)	*Four 300-mg tablets* • $3,250 *Five 300-mg tablets* • $4,063 *Injection kit* • $19,500 (every 6 months)	*Four 300-mg tablets* • $3,900 *Five 300-mg tablets* • $4,875 *Injection kit* • $23,400 (every 6 months)	N/A
CCR5 Antagonist					
Maraviroc • Generic, *or* • Selzentry	150-mg tablet, *or* 300-mg tablet	*Generic* • 60 tablets *Selzentry* • 60 tablets • 120 tablets (300 mg)	*Generic 150 mg* • $700 *Selzentry 150 mg* • $1,730 *Generic 300 mg* • $700 *Selzentry 300 mg (60 tablets)* • $1,730 *Selzentry 300 mg (120 tablets)* • $3,460	*Generic 150 mg* • $1,764 *Selzentry 150 mg* • $2,076 *Generic 300 mg* • $1,764 *Selzentry 300 mg (60 tablets)* • $2,076 *Selzentry 300 mg (120 tablets)* • $4,152	*Generic 150 mg* • $1,382 *Generic 300 mg* • $1,148 *Selzentry* • N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	**Strength, Formulation**	**Tablets, Capsules, Vials, or mLs** (Monthly, Unless Otherwise Noted)	**WAC** (Monthly, Unless Otherwise Noted)[b]	**AWP** (Monthly, Unless Otherwise Noted)[b]	**FUL** (As of April 30, 2025)[c]
CD4-Directed Post-Attachment Inhibitor					
Ibalizumab-uiyk Trogarzo	200-mg vial	8 vials	$12,196	$14,635	N/A
gp120-Directed Attachment Inhibitor					
Fostemsavir Rukobia	600-mg tablet	60 tablets	$9,280	$11,136	N/A
Coformulated Combination Products as Single-Tablet Regimens					
Bictegravir + Tenofovir Alafenamide + Emtricitabine Biktarvy	50-mg/25-mg/200-mg tablet	30 tablets	$4,216	$5,059	N/A
Darunavir + Cobicistat + Tenofovir Alafenamide + Emtricitabine Symtuza	800-mg/150-mg/10-mg/200-mg tablet	30 tablets	$4,717	$5,660	N/A
Dolutegravir + Abacavir + Lamivudine Triumeq	50-mg/600-mg/300-mg tablet	30 tablets	$3,897	$4,677	N/A
Dolutegravir + Lamivudine Dovato	50-mg/300-mg tablet	30 tablets	$3,096	$3,715	N/A
Dolutegravir + Rilpivirine Juluca	50-mg/25-mg tablet	30 tablets	$3,653	$4,383	N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	**Strength, Formulation**	**Tablets, Capsules, Vials, or mLs** (Monthly, Unless Otherwise Noted)	**WAC** (Monthly, Unless Otherwise Noted)[b]	**AWP** (Monthly, Unless Otherwise Noted)[b]	**FUL** (As of April 30, 2025)[c]
Doravirine + Tenofovir Disoproxil Fumarate + Lamivudine Delstrigo	100-mg/300-mg/300-mg tablet	30 tablets	$2,800	$3,361	N/A
Efavirenz + Tenofovir Disoproxil Fumarate + Emtricitabine Generic	600-mg/300-mg/200-mg tablet	30 tablets	$82 to $252	$302 to $3,414	$51
Efavirenz + Tenofovir Disoproxil Fumarate + Lamivudine Symfi	*Symfi* • 600-mg/300-mg/150-mg tablet	30 tablets	$1,926	$2,312	N/A
Elvitegravir + Cobicistat + Tenofovir Alafenamide + Emtricitabine Genvoya	150-mg/150-mg/10-mg/200-mg tablet	30 tablets	$4,216	$5,059	N/A
Elvitegravir + Cobicistat + Tenofovir Disoproxil Fumarate + Emtricitabine Stribild	150-mg/150-mg/300-mg/200-mg tablet	30 tablets	$4,423	$5,307	N/A
Rilpivirine + Tenofovir Alafenamide + Emtricitabine Odefsey	25-mg/25-mg/200-mg tablet	30 tablets	$3,840	$4,604	N/A
Rilpivirine + Tenofovir Disoproxil Fumarate + Emtricitabine Complera	25-mg/300-mg/200-mg tablet	30 tablets	$3,837	$4,604	N/A

Table 22b. Monthly Average Prices of Commonly Used Antiretroviral Drugs

ARV Drug (Generic and Brand Names)	**Strength, Formulation**	**Tablets, Capsules, Vials, or mLs** (Monthly, Unless Otherwise Noted)	**WAC** (Monthly, Unless Otherwise Noted)[b]	**AWP** (Monthly, Unless Otherwise Noted)[b]	**FUL** (As of April 30, 2025)[c]
Copackaged Combination Products as Injectable Regimens					
Cabotegravir + Rilpivirine Cabenuva	*3 mL* • 600 mg • 900 mg *2 mL* • 400 mg • 600 mg	*3 mL* • 2 vials (every other month) *2 mL* • 2 vials	*3 mL* • $6,789 (every other month) *2 mL* • $4,526	*3 mL* • $8,147 (every other month) *2 mL* • $5,431	N/A
PK Enhancers (Boosters)					
Cobicistat Tybost	150-mg tablet	30 tablets	$315	$378	N/A
Ritonavir • Generic, *or* • Norvir	100-mg tablet	30 tablets	*Generic* • $80 to $160 *Norvir* • $257	*Generic* • $278 *Norvir* • $309	*Generic* • $51 *Norvir* • N/A

[a] The following less commonly used ARV drugs are not included in this table: fosamprenavir and nelfinavir.
[b] **Source:** Micromedex Red Book [database]. Merative. 2025. Available at: https://www.micromedexsolutions.com.
[c] **Source:** Federal Upper Limits–May 2025 [database]. Centers for Medicare & Medicaid Services. 2025. Available at: https://www.medicaid.gov/medicaid/prescription-drugs/pharmacy-pricing/index.html.

Key: ARV = antiretroviral; AWP = average wholesale price; CD4 = CD4 T lymphocyte; FUL = federal upper limit; HD = high dose; INSTI = integrase strand transfer inhibitor; N/A = not applicable; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; WAC = wholesale acquisition cost; XR = extended release

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DRUG–DRUG INTERACTIONS

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Overview

Pharmacokinetic (PK) drug–drug interactions between antiretroviral (ARV) drugs and concomitant medications are common and may lead to increased or decreased drug exposure. In some instances, changes in drug exposure may increase the frequency and/or severity of toxicities or affect therapeutic responses. When prescribing or switching one or more drugs in an ARV regimen, clinicians must consider the potential for drug–drug interactions—both those affecting ARVs and those affecting concomitant drugs. A thorough review of concomitant medications in consultation with an expert in ARV pharmacology can help in designing a regimen that minimizes undesirable interactions. Recommendations for managing a specific drug interaction may differ depending on whether a new ARV is being initiated in a patient on a stable concomitant medication or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of interactions are difficult to predict when several drugs with competing metabolic pathways and drug transporter systems are prescribed concomitantly. When it is necessary to prescribe interacting drugs, clinicians should be vigilant in monitoring for therapeutic efficacy and/or concentration-related toxicities. Tables 24a through 25b provide information on known or suspected drug interactions between ARV agents and commonly prescribed medications based on published PK data or information from product labels. The tables provide general guidance on drugs that should not be coadministered and recommendations for dose modification of ARVs or concomitant medicines or for alternative therapy.

Mechanisms of Pharmacokinetic Interactions

PK interactions may occur during absorption, metabolism, or elimination of the ARV and/or the interacting drugs. The most common drug interaction mechanisms are described and listed for individual ARV drugs in Table 23 below.

Pharmacokinetic Interactions Affecting Drug Absorption

The extent of oral absorption of drugs can be affected by the following mechanisms:

- Acid-reducing agents—such as proton pump inhibitors, H2 antagonists, or antacids—can reduce the absorption of ARV drugs that require gastric acidity for optimal absorption (i.e., atazanavir and rilpivirine).
- Products that contain polyvalent cations—such as supplements, iron products, or antacids that contain aluminum, calcium, or magnesium—can bind to integrase strand transfer inhibitors (INSTIs) and reduce absorption of these ARV agents.
- Drugs that induce or inhibit the enzyme cytochrome P450 (CYP) 3A4 or efflux transporter P-glycoprotein in the intestines may reduce or promote the absorption of other drugs.

Pharmacokinetic Interactions Affecting Hepatic Metabolism

Two major enzyme systems are most frequently responsible for clinically significant drug interactions:

- The CYP enzyme system is responsible for the metabolism of many drugs, including non-nucleoside reverse transcriptase inhibitors, protease inhibitors, the CCR5 antagonist maraviroc, and the INSTI elvitegravir. CYP3A4 is the most common enzyme responsible for drug metabolism, though multiple enzymes may be involved in the metabolism of a drug. ARV drugs and concomitant medications may be inducers, inhibitors, and/or substrates of these enzymes.
- The uridine diphosphate glucuronosyltransferase (UGT) 1A1 enzyme is the primary enzyme responsible for the metabolism of the INSTIs cabotegravir and raltegravir. Drugs that induce or inhibit the UGT enzyme can affect the PK of these INSTIs.
- The INSTIs bictegravir and dolutegravir (DTG) and the capsid inhibitor lenacapavir have mixed metabolic pathways, including both CYP3A4 and UGT1A1. Drugs that induce or inhibit these enzymes may have variable impact on the PK of these ARVs.

Pharmacokinetic Enhancers (Boosters)

PK enhancing is a strategy used to increase exposure of an ARV by concomitantly administering a drug that inhibits the enzymes that metabolize the ARV. Currently, two agents are used as PK enhancers: ritonavir (RTV) and cobicistat (COBI). Both drugs are potent inhibitors of the CYP3A4 enzyme and, thus, when coadministered with ARVs metabolized by the CYP3A4 pathway, the resultant systemic exposure of the ARVs is higher. Importantly, RTV and COBI have different effects on other CYP- or UGT-metabolizing enzymes and drug transporters. Complex or unknown mechanisms of PK-based interactions preclude extrapolation of RTV drug interactions to certain COBI interactions, such as interactions with warfarin, direct oral anticoagulants, phenytoin, voriconazole, oral contraceptives, and certain hydroxy-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (or statins).

Other Mechanisms of Pharmacokinetic Interactions

Drug transporters are expressed in various tissues, and they play an important role in drug disposition. Knowledge of drug transporters is evolving, elucidating additional drug interaction mechanisms. For example, DTG decreases the renal clearance of metformin by inhibiting organic cation transporters in renal tubular cells. Similar transporters aid hepatic, renal, and biliary clearance of drugs and may be susceptible to drug interactions. ARVs and concomitant medications may be inducers, inhibitors, and/or substrates of these drug transporters. The influence of drug transporters on drug–drug interactions is complex, and the clinical significance of these interactions is unclear but is under investigation. Further research is needed to better understand these pathways and the clinical significance of this drug interaction mechanism.

Role of Therapeutic Drug Monitoring in Managing Drug–Drug Interactions

Therapeutic drug monitoring (TDM) can guide the dosing of certain medications by using measured drug concentrations to improve the likelihood of desired therapeutic and safety outcomes. Drugs suitable for TDM are characterized by a known exposure-response relationship and a therapeutic range of concentrations. The “therapeutic range” is a range of concentrations established through clinical investigations that are associated with a greater likelihood of achieving the desired therapeutic response and/or reducing the frequency of drug-associated adverse reactions.

When concomitant use of an ARV drug and another medication is likely to result in a clinically important drug–drug interaction, the first step is to assess whether other, equally effective treatment options can be used to avoid the interaction. If that is not possible, TDM may be useful in assessing whether a dose adjustment is needed.

Drug concentration assays for some ARV drugs are commercially available; however, result reporting may take 1 week or longer. When interpreting assay results, clinicians should consider the patient's medication adherence, the timing of the patient's last ARV dose and blood draw, and the time elapsed since coadministration of the interacting drug combination. If needed, a specialist in ARV clinical pharmacology should be consulted when interpreting the results and deciding what actions to take. If a dose adjustment is needed, TDM must be repeated after the dose-adjusted drug reaches steady state to ensure appropriate dosing.

TDM information should not be used alone; it must be considered in conjunction with other clinical information—including virologic response, medication adherence, and signs and symptoms of drug toxicities—to assure safe and effective therapy.

Table 23. Mechanisms of Antiretroviral-Associated Drug Interactions

Pharmacokinetic interactions may occur during absorption, metabolism, or elimination of the antiretroviral (ARV) drug and/or the interacting drug. This table does not include a comprehensive list of all possible mechanisms of interactions for individual ARV drugs (e.g., transporters); however, the table lists the most common mechanisms of known interactions and focuses on absorption and cytochrome P450 (CYP)– and uridine diphosphate glucuronosyltransferase (UGT) 1A1–mediated interactions.

Note: N/A indicates that there are no clinically relevant interactions by the mechanism. Identified mechanisms are specific to the ARV drugs described in the row and may not be reflective of complete ARV regimens. Some older ARVs—unboosted atazanavir, fosamprenavir, nelfinavir, nevirapine, tipranavir, and zidovudine—are not commonly used in clinical practice and are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions for these ARVs.

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or Are Induced or Inhibited by ARV Drugs			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
INSTIs							
BIC	N/A	Concentrations of PO INSTIs are decreased by-products that contain polyvalent cations (e.g., Ca, Mg, Al, Fe, Zn).	Substrate	3A4	N/A	N/A	Substrate
CAB	N/A		Substrate	N/A	N/A	N/A	Substrate
DTG	N/A		Substrate	3A4 (minor)	N/A	N/A	Substrate
EVG/c	N/A		Inhibitor	3A4	3A4, 2D6	2C9	Substrate
RAL	N/A		N/A	N/A	N/A	N/A	Substrate
PIs							
ATV/c	Concentration decreased	N/A	Substrate, inhibitor	3A4	3A4, 2D6, 2C8	N/A	Inhibitor
ATV/r	Concentration decreased	N/A	Substrate, inhibitor	3A4, 2D6	3A4, 2D6, 2C8	1A2, 2B6, 2C8, 2C9, 2C19	**ATV:** Inhibitor **RTV:** Inducer
DRV/c	N/A	N/A	Substrate, inhibitor	3A4	3A4, 2D6	N/A	No data

Table 23. Mechanisms of Antiretroviral-Associated Drug Interactions

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or Are Induced or Inhibited by ARV Drugs			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
DRV/r	N/A	N/A	Substrate, inhibitor	3A4, 2D6	3A4, 2D6	1A2, 2B6, 2C8, 2C9, 2C19	Inducer
LPV/r	N/A	N/A	Substrate	3A4, 2D6	3A4	1A2, 2B6, 2C8, 2C9, 2C19	Inducer
NNRTIs							
DOR	N/A	N/A	N/A	3A4, 3A5	N/A	N/A	N/A
EFV	N/A	N/A	N/A	2B6 (primary), 2A6, 3A4	3A4	3A4, 2B6, 2C19	N/A
ETR	N/A	N/A	N/A	3A4, 2C9, 2C19	2C9, 2C19	3A4	N/A
RPV	**Only RPV PO:** Concentration decreased	N/A	N/A	3A4	N/A	N/A	N/A
NRTIs							
ABC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
FTC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
3TC	N/A	N/A	N/A	N/A	N/A	N/A	N/A
TAF	N/A	N/A	Substrate	N/A	N/A	N/A	N/A
TDF	N/A	N/A	Substrate	N/A	N/A	N/A	N/A

Table 23. Mechanisms of Antiretroviral-Associated Drug Interactions

ARV Drugs by Drug Class	Mechanisms That May Affect Oral Absorption of ARV Drugs			Enzymes That Metabolize or Are Induced or Inhibited by ARV Drugs			
	Increasing Gastric pH	Cationic Chelation	P-gp	CYP Substrate	CYP Inhibitor	CYP Inducer	UGT1A1
Capsid Inhibitor							
LEN (SQ and PO)	N/A	N/A	Substrate	3A4	3A4	N/A	Substrate
CCR5 Antagonist							
MVC	N/A	N/A	Substrate	3A4	N/A	N/A	N/A
gp120-Directed Attachment Inhibitor							
FTR	N/A	N/A	Substrate	3A4	N/A	N/A	N/A
Fusion Inhibitor							
T-20	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Post-Attachment Inhibitor							
IBA	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Key: 3TC = lamivudine; ABC = abacavir; Al = aluminum; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; Ca = calcium; CAB = cabotegravir; CCR5 = C-C chemokine receptor type 5; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; FTR = fostemsavir; gp120 = glycoprotein 120; IBA = ibalizumab; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; LPV/r = lopinavir/ritonavir; Mg = magnesium; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitors; NRTI = nucleoside reverse transcriptase inhibitors; P-gp = P-glycoprotein; PI = protease inhibitor; PO = oral; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; T-20 = enfuvirtide; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT = uridine diphosphate glucuronosyltransferase; Zn = zinc

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between protease inhibitors (PIs) and non-antiretroviral (ARV) drugs. The term "PI" refers to atazanavir (ATV) or darunavir (DRV) boosted with either ritonavir (RTV or r) or cobicistat (COBI or c). This table does not include interactions for unboosted ATV, fosamprenavir (FPV), lopinavir (LPV), nelfinavir (NFV), or tipranavir (TPV). For information regarding interactions between PIs and other ARV drugs, including dosing recommendations, refer to Tables 24c, 25a, and 25b.

Recommendations for managing particular drug interactions may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Note: Unboosted ATV, FPV, LPV/r, NFV, and TPV are no longer commonly used in clinical practice in the United States and are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between these PIs and concomitant medications. Information regarding these agents may also be found in archived versions of this guideline.

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	ATV/c, ATV/r	**When Given Simultaneously** • ↓ ATV expected	Administer ATV at least 2 hours before or 2 hours after antacids or buffered medications.
H2 Receptor Antagonists	ATV/c, ATV/r	↓ ATV expected	H2RA dose should not exceed a dose equivalent to famotidine 40 mg twice daily in ART-naive patients or famotidine 20 mg twice daily in ART-experienced patients. Give ATV 300 mg (plus COBI 150 mg **or** RTV 100 mg) with food simultaneously with and/or ≥10 hours after the dose of H2RA.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			If using TDF and H2RA in ART-experienced patients, administer ATV 400 mg plus RTV 100 mg with food simultaneously with and/or ≥10 hours after the dose of H2RA. **Do not coadminister** ATV/c with TDF and H2RA in ART-experienced patients.
	DRV/c, DRV/r	**With Ranitidine** • ↔ DRV/r	No dose adjustment needed
Proton Pump Inhibitors	ATV/c, ATV/r	**With Omeprazole 40 mg** • ATV AUC ↓ 76% **When Omeprazole 20 mg Is Given 12 Hours Before ATV/c or ATV/r** • ATV AUC ↓ 42%	PPI dose should not exceed a dose equivalent to omeprazole 20 mg daily in PI-naive patients. PPIs should be administered at least 12 hours before ATV/c or ATV/r. **Do not coadminister** in PI-experienced patients.
	DRV/c	↔ PI expected	No dose adjustment needed
	DRV/r	↔ DRV/r Omeprazole AUC ↓ 42%	Consider alternative ARV or acid reducer. If coadministered, monitor for omeprazole effectiveness. If the patient does not experience symptomatic relief, increase the dose to no more than omeprazole 40 mg daily.
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ alfuzosin expected	**Contraindicated**
Doxazosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ doxazosin possible	Initiate doxazosin at lowest dose and titrate. Monitor blood pressure. Dose reduction may be necessary.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Tamsulosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ tamsulosin expected	**Do not coadminister** unless benefits outweigh risks. If coadministered, monitor blood pressure.
Terazosin	ATV/c, ATV/r, DRV/c, DRV/r	↔ or ↑ terazosin possible	Initiate terazosin at lowest dose and titrate. Monitor blood pressure. Dose reduction may be necessary.
Silodosin	ATV/c, ATV/r, DRV/c, DRV/r	↑ silodosin expected	**Contraindicated**
Antibacterials—Antimycobacterials			
Bedaquiline	ATV/c, ATV/r, DRV/c, DRV/r	• ↑ bedaquiline possible	**Do not coadminister** unless benefits outweigh risks. If coadministered, consider therapeutic drug monitoring and monitor for bedaquiline-related adverse effects, including hepatotoxicity and QTc prolongation.
Rifabutin	ATV/r	**Compared With Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Once Daily) Plus ATV/r** • Rifabutin AUC ↑ 110% and metabolite AUC ↑ 2,101%	Recommended dose is rifabutin 150 mg once daily. Monitor for antimycobacterial activity and consider therapeutic drug monitoring. Monitor for rifabutin-related adverse events, including neutropenia and uveitis. PK data in this table are results from healthy volunteer studies. Lower rifabutin exposure has been reported in patients with HIV than in healthy study participants.
	DRV/r	**Compared With Rifabutin (300 mg Once Daily) Alone, Rifabutin (150 mg Every Other Day) Plus DRV/r** • ↔ rifabutin AUC and metabolite AUC ↑ 881%	
	ATV/c, DRV/c	↑ rifabutin expected ↓ COBI expected	**Do not coadminister.**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rifampin	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI concentration by >75%	**Contraindicated.** Increasing the dose of RTV does not overcome this interaction and may increase hepatotoxicity. Increasing the COBI dose **is not recommended.** Consider rifabutin if a rifamycin is indicated.
Rifapentine	ATV/c, ATV/r, DRV/c, DRV/r	**Daily and Weekly Dosing** • ↓ PI expected	**Do not coadminister.**
Antibacterials—Macrolides			
Azithromycin	ATV/c, ATV/r	↑ azithromycin possible	No dose adjustment needed
	DRV/c, DRV/r	↔ azithromycin expected	No dose adjustment needed
Clarithromycin	ATV/c, ATV/r, DRV/c	↑ clarithromycin expected ↑ ATV/r and PI/c expected	Consider alternative ARV or azithromycin.
	DRV/r	DRV/r ↑ clarithromycin AUC 57% RTV 500 mg twice daily ↑ clarithromycin 77%	Consider alternative ARV or azithromycin. If use of clarithromycin is necessary in a patient with impaired renal function, reduce clarithromycin dose by 50% in patients with CrCl 30 to 60 mL/min. In patients with CrCl <30 mL/min, reduce clarithromycin dose by 75%. Monitor for clarithromycin-related adverse events, including QTc prolongation.
Erythromycin	ATV/c, ATV/r, DRV/c, DRV/r	↑ erythromycin expected ↑ PI expected	Consider alternative ARV or use azithromycin.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants			
Apixaban	ATV/c, ATV/r, DRV/c, DRV/r	↑ apixaban expected	**Do not coadminister** in patients who require apixaban 2.5 mg twice daily. **In Patients Requiring Apixaban 5 mg or 10 mg Twice Daily** • Reduce apixaban dose by 50%.
Dabigatran	ATV/c, ATV/r	**With COBI 150 mg Alone** • Dabigatran AUC ↑ 110% to 127% **With ATV/r** • ↑ dabigatran expected	**Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation in Adult Patients** • CrCl >30 mL/min: no dose adjustment needed • CrCl ≤30 mL/min: do not coadminister. **Treatment and Reduction in the Risk of Recurrence of DVT and PE or Prophylaxis of DVT and PE Following Hip Replacement Surgery in Adult Patients** • CrCl ≥50 mL/min: no dose adjustment needed • CrCl <50 mL/min: do not coadminister.
	DRV/c, DRV/r	**With DRV/c** • Single dose DRV/c: dabigatran AUC ↑ 164% • After 14 days of DRV/c: dabigatran AUC ↑ 88% **With DRV/r** • Single dose DRV/r: dabigatran AUC ↑ 72% • After 14 days of daily DRV/r: dabigatran AUC ↑ 18%	
Edoxaban	ATV/c, ATV/r, DRV/c	↑ edoxaban expected	**Treatment of Nonvalvular Atrial Fibrillation** • No dose adjustment needed **Treatment of DVT and PE** • Reduce edoxaban dose to 30 mg once daily.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DRV/r	↑ edoxaban expected	**Treatment of Nonvalvular Atrial Fibrillation** • No dose adjustment needed **Treatment of DVT and PE** • No dose adjustment needed
Rivaroxaban	ATV/c, ATV/r, DRV/c, DRV/r	↑ rivaroxaban expected	**Do not coadminister.**
Warfarin	ATV/c, DRV/c	↑ warfarin possible	Monitor INR closely when stopping or starting PI/c or PI/r and adjust warfarin dose accordingly. If switching between RTV and COBI, the effect of COBI on warfarin is not expected to be equivalent to RTV's effect on warfarin.
	ATV/r, DRV/r	↓ warfarin possible	
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
Antidepressants, Anxiolytics			
Bupropion	ATV/r, DRV/r	↓ bupropion possible	Titrate bupropion dose based on clinical response.
	ATV/c, DRV/c	↔ bupropion expected	No dose adjustment needed
Buspirone	ATV/c, ATV/r, DRV/c, DRV/r	↑ buspirone expected	Administer lowest dose of buspirone with caution and titrate buspirone dose based on clinical response. Dose reduction may be necessary. Monitor for buspirone-related adverse events.
Desvenlafaxine	ATV/c, ATV/r, DRV/c, DRV/r	↑ desvenlafaxine possible	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Duloxetine	ATV/c, DRV/c	↑ duloxetine possible	No dose adjustment needed
	ATV/r, DRV/r	↑ or ↓ duloxetine possible	
Mirtazapine	ATV/c, ATV/r, DRV/c, DRV/r	↑ mirtazapine possible	Monitor for mirtazapine-related adverse events. Mirtazapine dose reduction may be necessary.
Nefazodone	ATV/c, ATV/r, DRV/c, DRV/r	↑ nefazodone expected ↑ PI possible	Monitor for nefazodone-related adverse events and PI tolerability.
Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	DRV/r	Paroxetine AUC ↓ 39% Sertraline AUC ↓ 49%	Titrate SSRI dose based on clinical response.
	ATV/c, ATV/r, DRV/c	↑ or ↓ SSRI possible	Titrate SSRI dose using the lowest available initial or maintenance dose.
Trazodone	ATV/c, ATV/r, DRV/c, DRV/r	**RTV 200 mg Twice Daily (For 2 Days)** • Trazodone ↑ AUC 240%	Administer lowest dose of trazodone and titrate dose based on clinical response. Monitor for trazodone-related adverse events, including CNS and CV adverse events.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	ATV/c, ATV/r, DRV/c, DRV/r	↑ TCA expected	Administer lowest possible TCA dose and titrate based on clinical assessment and/or drug concentrations. Monitor for TCA-related adverse events.
Venlafaxine	ATV/c, ATV/r, DRV/c, DRV/r	↑ venlafaxine and O-desmethylvenlafaxine expected	Monitor for venlafaxine-related adverse events. Consider venlafaxine dose reduction.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antipsychotics			
Aripiprazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate dose based on clinical monitoring for effectiveness/adverse events. Refer to aripiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6-poor metabolizers.
Brexpiprazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate the dose based on clinical monitoring for effectiveness/adverse events. Refer to brexpiprazole label for doses to use in patients who have major depressive disorder or who are known to be CYP2D6-poor metabolizers.
Cariprazine	ATV/c, ATV/r, DRV/c, DRV/r	↑ cariprazine expected	**Starting Cariprazine in a Patient Who Is Already Receiving a PI** • Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum of cariprazine 3 mg daily. If the PI is withdrawn, cariprazine dose may need to be increased. **Starting a PI in a Patient Who Is Already Receiving Cariprazine** • For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce the dose by half. For patients taking cariprazine 4.5 mg daily, the dose should be reduced to cariprazine 1.5 mg or cariprazine 3 mg daily. For patients taking cariprazine 1.5 mg daily, change to cariprazine 1.5 mg every other day. If PI is withdrawn, the cariprazine dose may need to be increased.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Iloperidone	ATV/c, ATV/r, DRV/c, DRV/r	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lumateperone	ATV/c, ATV/r, DRV/c, DRV/r	↑ lumateperone expected	**Do not coadminister.**
Lurasidone	ATV/c, ATV/r, DRV/c, DRV/r	↑ lurasidone expected	**Contraindicated**
Olanzapine, Olanzapine/Samidorphan	ATV/c, DRV/c	↔ olanzapine expected ↑ samidorphan possible	No dose adjustment needed
	ATV/r, DRV/r	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Other Antipsychotics **CYP3A4 and/or CYP2D6 substrates** (e.g., clozapine, perphenazine, risperidone, thioridazine)	ATV/c, ATV/r, DRV/c, DRV/r	↑ antipsychotic possible	Titrate the antipsychotic dose using the lowest initial dose or adjust the maintenance dose accordingly. Monitor for adverse events, including QTc prolongation.
Pimavanserin	ATV/c, ATV/r, DRV/c, DRV/r	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg once daily.
Pimozide	ATV/c, ATV/r, DRV/c, DRV/r	↑ pimozide expected	**Contraindicated**
Quetiapine	ATV/c, ATV/r, DRV/c, DRV/r	↑ quetiapine expected	**Starting Quetiapine in a Patient Receiving a PI** • Initiate quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine effectiveness and adverse events, including QTc prolongation.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			Starting a PI in a Patient Receiving a Stable Dose of Quetiapine • Consider alternative ARV. If coadministered, reduce quetiapine dose to 1/6 of the current dose. Closely monitor for quetiapine effectiveness and adverse events, including QTc prolongation.
Ziprasidone	ATV/c, ATV/r, DRV/c, DRV/r	↑ ziprasidone expected	Monitor for ziprasidone-related adverse events, including QTc prolongation.
Antifungals			
Fluconazole	ATV/c, ATV/r, DRV/c, DRV/r	↔ PI expected ↔ fluconazole expected	No dose adjustment needed
Isavuconazole	ATV/c, DRV/c	↑ isavuconazole expected ↓ PI possible	**Contraindicated**
	ATV/r, DRV/r	↑ isavuconazole expected ↓ PI possible	If coadministered, monitor isavuconazole concentrations and monitor for isavuconazole-related adverse events. Monitor for PI tolerability.
Ibrexafungerp	ATV/c, ATV/r, DRV/c, DRV/r	↑ ibrexafungerp expected	Reduce ibrexafungerp dose to 150 mg twice daily.
Itraconazole	ATV/c, ATV/r, DRV/c, DRV/r	↑ itraconazole expected ↑ PI expected	Itraconazole doses >200 mg/day **are not recommended** unless dosing is guided by itraconazole concentrations.
Posaconazole	ATV/r	ATV AUC ↑ 146% ↔ posaconazole possible	If coadministered, monitor for PI-related adverse events.
	ATV/c, DRV/c, DRV/r	↑ PI expected ↔ posaconazole possible	

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Voriconazole	ATV/c, DRV/c	No data	**Do not coadminister** voriconazole and RTV or COBI unless benefits outweigh risks. If coadministered, monitor voriconazole concentration and adjust dose accordingly.
	ATV/r, DRV/r	RTV 100 mg twice daily ↓ voriconazole AUC 39%	
Antimalarials			
Artemether/Lumefantrine	ATV/c, DRV/c	↑ lumefantrine expected ↑ artemether possible	Clinical significance is unknown. If coadministered, monitor closely for antimalarial effectiveness and lumefantrine-related adverse events, including QTc prolongation.
	DRV/r	↔ artemether expected ↔ DHA[a] expected Lumefantrine AUC ↑ 175% ↔ DRV	
Artesunate	ATV/c	↑ DHA[a] possible	Monitor for artesunate-related adverse effects.
	DRV/c	↔ DHA[a] expected	No dose adjustment needed
	ATV/r, DRV/r	↓ DHA[a] possible	Monitor for clinical response to artesunate.
Atovaquone/Proguanil	ATV/r, DRV/r	**With ATV/r** • Atovaquone AUC ↓ 46% • Proguanil AUC ↓ 41% **With DRV/r** • ↓ atovaquone/proguanil possible	Clinical significance is unknown. Consider alternative ARV or malaria prophylaxis.
	ATV/c, DRV/c	↔ atovaquone/proguanil expected	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Mefloquine	ATV/c, ATV/r, DRV/c, DRV/r	**With RTV 200 mg Twice Daily** • RTV AUC ↓ 31% and C_{min} ↓ 43% • ↔ mefloquine **With ATV (Unboosted), PI/c, or PI/r** • ↑ mefloquine possible	Clinical significance is unknown. Consider alternative ARV or antimalarial drug. If coadministered, monitor for mefloquine-related adverse events, including psychiatric symptoms and QTc prolongation. Monitor virologic response.
Antimigraine			
Ergot Derivatives	ATV/c, ATV/r, DRV/c, DRV/r	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Contraindicated**
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ atogepant expected	Chronic migraine: **Do not coadminister.** Episodic migraine: Administer atogepant at a dose of 10 mg once daily.
Rimegepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ rimegepant expected	**Do not coadminister.**
Ubrogepant	ATV/c, ATV/r, DRV/c, DRV/r	↑ ubrogepant expected	**Contraindicated**
Zavegepant	ATV/r, ATV/c, DRV/c	↑ zavegepant expected	**Do not coadminister.**
	DRV/r	↔ zavegepant expected	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Serotonin 5-HT1B, 1D Receptor Agonists			
Almotriptan	ATV/c, ATV/r, DRV/c, DRV/r	↑ almotriptan expected	Administer single dose of almotriptan 6.25 mg. Maximum dose should not exceed 12.5 mg in a 24-hour period.
Eletriptan	ATV/c, ATV/r, DRV/c, DRV/r	↑ eletriptan expected	**Contraindicated**
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan, Zolmitriptan	ATV/c, ATV/r, DRV/c, DRV/r	↔ triptan expected	No dose adjustment needed
Antiplatelets			
Clopidogrel	ATV/c, ATV/r, DRV/c, DRV/r	Clopidogrel active metabolite AUC ↓ 69% in people with HIV on RTV or COBI-boosted regimens compared with healthy volunteers without HIV. Impaired platelet inhibition observed in people with HIV.	**Do not coadminister.**
Prasugrel	ATV/c, ATV/r, DRV/c, DRV/r	Prasugrel active metabolite AUC ↓ 52% in people with HIV on RTV or COBI-boosted regimens compared to healthy volunteers without HIV. Adequate platelet inhibition observed in people with HIV.	No dose adjustment needed
Ticagrelor	ATV/c, ATV/r, DRV/c, DRV/r	↑ ticagrelor expected	**Do not coadminister.**
Vorapaxar	ATV/c, ATV/r, DRV/c, DRV/r	↑ vorapaxar expected	**Do not coadminister.**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antipneumocystis and Antitoxoplasmosis			
Atovaquone Oral suspension	ATV/r	↔ atovaquone	No dose adjustment needed
	ATV/c, DRV/c, DRV/r	↔ atovaquone expected	No dose adjustment needed
Antiseizure			
Carbamazepine	ATV/r	↑ carbamazepine possible May ↓ PI concentrations substantially	Consider alternative ARV or anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assess virologic response. Carbamazepine dose reduction may be necessary.
	DRV/r	Carbamazepine AUC ↑ 45% ↔ DRV	Monitor anticonvulsant concentration and adjust dose accordingly.
	ATV/c, DRV/c	↑ carbamazepine possible ↓ COBI expected ↓ PI expected	**Contraindicated**
Eslicarbazepine	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Ethosuximide	ATV/c, ATV/r, DRV/c, DRV/r	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lamotrigine	ATV/r	Lamotrigine AUC ↓ 32%	A dose increase of lamotrigine may be needed; monitor lamotrigine concentration or consider alternative ARV or anticonvulsant.
	DRV/r	↓ lamotrigine possible	
	ATV/c	No data	Monitor anticonvulsant concentration and adjust dose accordingly.
	DRV/c	↔ lamotrigine expected	No dose adjustment needed.
Oxcarbazepine	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI possible	Consider alternative ARV or anticonvulsant. If coadministration is necessary, monitor for virologic response. Consider monitoring anticonvulsant and PI concentrations.
Phenobarbital	ATV/r, DRV/r	↓ phenobarbital possible ↓ PI possible	Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	ATV/c, DRV/c	↓ COBI expected ↓ PI expected	**Contraindicated**
Phenytoin	ATV/r, DRV/r	↓ phenytoin possible ↓ PI possible	Consider alternative anticonvulsant. If coadministration is necessary, consider monitoring concentrations of both drugs and assessing virologic response.
	ATV/c, DRV/c	↓ COBI expected ↓ PI expected	**Contraindicated**
Primidone	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI expected	**Do not coadminister.**
Valproic Acid	ATV/c, ATV/r, DRV/c, DRV/r	↓ or ↔ VPA possible	Monitor VPA concentrations and monitor for PI tolerability.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antivirals—Hepatitis C			
Elbasvir/Grazoprevir	ATV/r	Elbasvir AUC ↑ 4.8-fold Grazoprevir AUC ↑ 10.6-fold Elbasvir ↔ ATV Grazoprevir ↑ ATV AUC 43%	**Contraindicated** May increase the risk of ALT elevations due to a significant increase in grazoprevir plasma concentrations caused by OATP1B1/3 inhibition.
	DRV/r	Elbasvir AUC ↑ 66% Grazoprevir AUC ↑ 7.5-fold ↔ DRV	
	ATV/c, DRV/c	↑ grazoprevir expected	
Glecaprevir/Pibrentasvir	ATV/c, ATV/r	**With (ATV 300 mg Plus RTV 100 mg) Once Daily** • Glecaprevir AUC ↑ 6.5-fold • Pibrentasvir AUC ↑ 64%	**Contraindicated**
	DRV/c, DRV/r	**With (DRV 800 mg Plus RTV 100 mg) Once Daily** • Glecaprevir AUC ↑ fivefold • ↔ pibrentasvir	**Do not coadminister.**
Ledipasvir/Sofosbuvir	ATV/r	ATV AUC ↑ 33% Ledipasvir AUC ↑ 113% ↔ sofosbuvir	No dose adjustment needed Coadministration of ledipasvir/sofosbuvir with TDF and a PI/r results in increased exposure to TDF. The safety of the increased TDF exposure has not been established. Consider alternative HCV or ARV drugs to avoid increased risk of TDF toxicities. If coadministration is necessary, monitor for TDF-related adverse events.
	ATV/c, DRV/c, DRV/r	↔ PI expected ↔ ledipasvir and sofosbuvir	

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sofosbuvir/Velpatasvir	ATV/r	↔ ATV/r ↔ sofosbuvir Velpatasvir AUC ↑ 2.4-fold	No dose adjustment needed
	DRV/r	↔ DRV/r Sofosbuvir AUC ↓ 28% ↔ velpatasvir	No dose adjustment needed
	ATV/c, DRV/c	↔ sofosbuvir and velpatasvir expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/ Voxilaprevir	ATV/c, ATV/r	**With ATV/r** • Voxilaprevir AUC ↑ 4.3-fold • Velpatasvir AUC ↑ 93% • Sofosbuvir AUC ↑ 40%	**Do not coadminister.**
	DRV/c, DRV/r	**With DRV/r** • Voxilaprevir AUC ↑ 2.4-fold • ↔ DRV/r, velpatasvir, and sofosbuvir	No dose adjustment needed
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	ATV/c, ATV/r, DRV/c, DRV/r	↑ brincidofovir possible	Give PI dose at least 3 hours after administering brincidofovir and monitor for brincidofovir-related adverse events (i.e., elevations in ALT/AST and bilirubin and GI adverse events).
Cidofovir	ATV/c, ATV/r, DRV/c, DRV/r	↔ cidofovir	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Tecovirimat	ATV/c, ATV/r, DRV/c, DRV/r	↔ tecovirimat	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	ATV/c, ATV/r, DRV/c, DRV/r	↔ molnupiravir	No dose adjustment needed
Remdesivir	ATV/c, ATV/r, DRV/c, DRV/r	↔ remdesivir	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	ATV/r, ATV/c, DRV/c, DRV/r	↑ PI expected ↑ ritonavir-boosted nirmatrelvir expected	No dose adjustment needed. Monitor for increased ritonavir-boosted nirmatrelvir and PI-related adverse events.
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	ATV/c, ATV/r	↑ arformoterol possible	No dose adjustment needed
	DRV/c, DRV/r	↔ arformoterol expected	No dose adjustment needed
Indacaterol	ATV/c, ATV/r, DRV/c, DRV/r	**With RTV 300 mg Twice Daily** • Indacaterol AUC ↑ 1.7-fold	No dose adjustment needed in patients receiving indacaterol 75 mcg daily.
Olodaterol	ATV/c, ATV/r, DRV/c, DRV/r	↑ olodaterol expected	No dose adjustment needed
Salmeterol	ATV/c, ATV/r, DRV/c, DRV/r	↑ salmeterol possible	**Do not coadminister,** due to potential increased risk of salmeterol-related CV events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cardiac Medications			
Antiarrhythmics			
Amiodarone	ATV/r	↑ amiodarone possible ↑ PI possible	**Contraindicated**
	ATV/c, DRV/c, DRV/r	↑ amiodarone possible ↑ PI possible	**Do not coadminister** unless the benefits outweigh the risks. If coadministered, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone drug concentration.
Digoxin	ATV/c, ATV/r, DRV/c, DRV/r	RTV 200 mg twice daily ↑ digoxin AUC 29% and ↑ half-life 43% DRV/r ↑ digoxin AUC 36% COBI ↑ digoxin C_{max} 41% and ↔ AUC	Monitor digoxin concentrations. Digoxin dose may need to be decreased. Titrate initial digoxin dose.
Disopyramide	ATV/c, ATV/r, DRV/c, DRV/r	↑ disopyramide possible	**Do not coadminister.**
Dofetilide	ATV/c, ATV/r, DRV/c, DRV/r	↑ dofetilide possible	**Do not coadminister.**
Dronedarone	ATV/c, ATV/r, DRV/c, DRV/r	↑ dronedarone expected	**Contraindicated**
Flecainide	ATV/c, ATV/r, DRV/c, DRV/r	↑ flecainide possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor flecainide concentrations and for antiarrhythmic-related adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lidocaine	ATV/c, ATV/r, DRV/c, DRV/r	↑ lidocaine possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor lidocaine concentrations and for antiarrhythmic-related adverse events.
Mexiletine	ATV/c, ATV/r, DRV/c, DRV/r	↑ mexiletine possible	Consider alternative ARV or antiarrhythmic. If coadministered, monitor mexiletine concentrations and for antiarrhythmic-related adverse events.
Propafenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ propafenone possible	**Do not coadminister.**
Quinidine	ATV/r	↑ quinidine expected	**Contraindicated**
	ATV/c, DRV/c, DRV/r	↑ quinidine possible	**Do not coadminister.**
Sotalol	ATV/c, ATV/r, DRV/c, DRV/r	↔ sotalol expected	No dose adjustment needed
Beta-Blockers			
Atenolol, Labetalol	ATV/c, ATV/r, DRV/c, DRV/r	↑ beta-blockers possible	No dose adjustment needed
Bisoprolol, Carvedilol, Metoprolol, Nebivolol	ATV/c, ATV/r, DRV/c, DRV/r	↑ beta-blockers possible	May need to decrease beta-blocker dose; adjust dose based on clinical response. Consider using beta-blockers that are not metabolized by CYP2D6 enzymes (e.g., atenolol, labetalol, nadolol).
Calcium Channel Blockers			
Amlodipine, Diltiazem, Felodipine, Nifedipine, Verapamil	ATV/c, ATV/r, DRV/c, DRV/r	↑ dihydropyridine possible ↑ verapamil possible	Titrate CCB dose and monitor closely. ECG monitoring is recommended when CCB is used with ATV.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Diltiazem	ATV/c, ATV/r	Unboosted ATV ↑ diltiazem AUC 125% Greater ↑ of diltiazem AUC is likely with ATV/c or ATV/r	Decrease diltiazem dose by at least 50%. If starting diltiazem, start with the lowest dose and titrate according to clinical response and adverse events. ECG monitoring is recommended.
	DRV/c, DRV/r	↑ diltiazem possible	Titrate diltiazem dose according to clinical response and adverse events.
Cardiac—Other			
Bosentan	ATV/c, ATV/r, DRV/c, DRV/r	**With ATV (Unboosted)** • ↓ ATV expected **With PI/r or PI/c** • ↑ bosentan expected	**Do not coadminister** bosentan and unboosted ATV. **In Patients on a PI (Other Than Unboosted ATV) >10 Days** • Start bosentan at 62.5 mg once daily or every other day. **In Patients on Bosentan Who Require a PI (Other Than Unboosted ATV)** • Stop bosentan ≥36 hours before PI initiation and restart bosentan 10 days after PI initiation at 62.5 mg once daily or every other day. **When Switching Between COBI and RTV** • Maintain same bosentan dose.
Eplerenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ eplerenone expected	**Contraindicated**
Ivabradine	ATV/c, ATV/r, DRV/c, DRV/r	↑ ivabradine expected	**Contraindicated**
Mavacamten	ATV/c, ATV/r, DRV/c, DRV/r	↑ mavacamten expected	**Contraindicated**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ranolazine	ATV/c, ATV/r, DRV/c, DRV/r	↑ ranolazine expected	**Contraindicated**
Corticosteroids			
Beclomethasone Inhaled or intranasal	DRV/r	↔ 17-BMP (active metabolite) AUC RTV 100 mg twice daily ↑ 17-BMP AUC 2-fold	No dose adjustment needed
	ATV/c, ATV/r, DRV/c	↔ 17-BMP expected	No dose adjustment needed
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids possible RTV 100 mg twice daily ↑ fluticasone AUC 350-fold	**Do not coadminister** unless the potential benefits of inhaled or intranasal corticosteroid outweigh the risks of adverse events associated with corticosteroids. Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider alternative inhaled/intranasal corticosteroid (e.g., beclomethasone).
Betamethasone, Budesonide Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids possible ↓ PI possible	**Do not coadminister** unless the potential benefits of systemic corticosteroid outweigh the risks of adverse events associated with systemic corticosteroids. Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Dexamethasone Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids possible ↓ PI possible	Consider alternative corticosteroid for long-term use. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	ATV/c, ATV/r, DRV/c, DRV/r	↑ prednisolone possible	Coadministration may be considered if the potential benefits outweigh the risks of adverse events associated with systemic corticosteroids. If coadministered, monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Betamethasone, Methylprednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	ATV/c, ATV/r, DRV/c, DRV/r	↑ glucocorticoids expected	**Do not coadminister.** Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Glucose-Lowering			
Canagliflozin	ATV/c, DRV/c	↔ canagliflozin	No dose adjustment needed
	ATV/r, DRV/r	↓ canagliflozin expected	If a patient is already tolerating canagliflozin 100 mg daily, increase canagliflozin dose to 200 mg daily. If a patient is already tolerating canagliflozin 200 mg daily and requires additional glycemic control, management strategy is based on renal function. **In Patients With eGFR ≥60 mL/min/1.73 m^2** • Canagliflozin dose may be increased to 300 mg daily. **In Patients With eGFR <60 mL/min/1.73 m^2** • Consider adding another antihyperglycemic agent.
Saxagliptin	ATV/c, ATV/r, DRV/c, DRV/r	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/Saxagliptin	ATV/c, ATV/r, DRV/c, DRV/r	↑ saxagliptin expected	**Do not coadminister.** Dapagliflozin is only available as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination **is not recommended.**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Herbal Products			
St. John's Wort	ATV/c, ATV/r, DRV/c, DRV/r	↓ PI expected	**Contraindicated**
Hormonal Therapies—Contraceptives			
Injectable Contraceptives Depot MPA	ATV/c, ATV/r, DRV/c, DRV/r	↔ expected	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate, norethindrone)	ATV/c	Drospirenone AUC ↑ 130% Ethinyl estradiol AUC ↓ 22%	**Contraindicated** with drospirenone-containing hormonal contraceptive due to potential for hyperkalemia. Use alternative ARV or alternative contraceptive methods.
		↔ ethinyl estradiol AUC and C_{min} ↓ 25% ↔ levonorgestrel	No dose adjustment needed
	ATV/r	Ethinyl estradiol AUC ↓ 19% and C_{min} ↓ 37% Norgestimate AUC ↑ 85% Norethindrone AUC ↑ 51% and C_{min} ↑ 67%	Oral contraceptive should contain at least 35 mcg of ethinyl estradiol.[c]
		↑ drospirenone expected ↔ estetrol	Clinical monitoring is recommended due to the potential for hyperkalemia. Use alternative ARV or contraceptive methods.
	DRV/c	Drospirenone AUC ↑ 58% Ethinyl estradiol AUC ↓ 30%	Clinical monitoring is recommended due to the potential for hyperkalemia. Use alternative ARV or contraceptive methods.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DRV/r	Ethinyl estradiol AUC ↓ 44% and C_{min} ↓ 62% Norethindrone AUC ↓ 14% and C_{min} ↓ 30%	**When Used for Contraception** • Consider alternative ARV or contraceptive methods. If combined, consider using an oral contraceptive with at least 35 mcg of ethinyl estradiol. **When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation)** • Monitor for clinical effectiveness of hormonal therapy.
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	ATV/c, ATV/r, DRV/c, DRV/r	↑ etonogestrel, levonorgestrel expected	No dose adjustment needed
Transdermal Contraceptives (e.g., ethinyl estradiol/norelgestromin, ethinyl estradiol/levonorgestrel)	ATV/c, ATV/r, DRV/c, DRV/r	↓ ethinyl estradiol possible with ritonavir ↑ ethinyl estradiol possible with cobicistat ↑ norelgestromin, levonorgestrel possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	ATV/r	Ethinyl estradiol AUC ↓ 26% Etonogestrel AUC ↑ 79%	No dose adjustment needed with etonogestrel/ethinyl estradiol vaginal rings. Use alternative ARV or contraceptive methods with segesterone/ethinyl estradiol vaginal rings.
	ATV/c, DRV/c, DRV/r	↓ ethinyl estradiol possible with ritonavir ↑ ethinyl estradiol possible with cobicistat	
Emergency Contraceptives Levonorgestrel (oral)	ATV/c, ATV/r, DRV/c, DRV/r	↑ levonorgestrel expected	No dose adjustment needed

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies—Miscellaneous			
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	ATV/c, ATV/r, DRV/c, DRV/r	↑ dutasteride possible ↑ finasteride possible	Adjust dutasteride dose as needed based on clinical effects. No dose adjustment needed for finasteride.
Estradiol	ATV/c, DRV/c	↓ or ↑ estradiol possible	Adjust estradiol dose as needed based on clinical effects.
	ATV/r, DRV/r	↓ estradiol possible	
Goserelin, Leuprolide Acetate, Spironolactone	ATV/c, ATV/r, DRV/c, DRV/r	↔ goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment needed
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, MPA, progesterone)	ATV/c, ATV/r, DRV/c, DRV/r	↓ or ↑ estrogen possible with estradiol or conjugated estrogen (equine and synthetic)	Adjust estrogen dose as needed based on clinical effects.
	ATV/c, ATV/r, DRV/c, DRV/r	↑ drospirenone possible ↑ MPA ↑ micronized progesterone See the Hormonal Therapies—Contraceptives section for other progestin-PI interactions.	Adjust progestin/progesterone dose as needed based on clinical effects. Drospirenone is not contraindicated with ATV/c products because it is prescribed at a lower dose for menopausal HRT than products used for hormonal contraceptives.
Testosterone	ATV/c, ATV/r, DRV/c, DRV/r	↑ testosterone possible	Adjust testosterone dose as needed based on clinical effects.
Immunosuppressants			
Cyclosporine, Sirolimus, Tacrolimus	ATV/c, ATV/r, DRV/c, DRV/r	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Everolimus	DRV/c, DRV/r	↑ immunosuppressant expected	**Do not coadminister.**
	ATV/c, ATV/r	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.
Lipid-Modifying			
Atorvastatin	ATV/r	↑ atorvastatin possible	Administer the lowest effective atorvastatin dose while monitoring for adverse events.
	ATV/c	Atorvastatin AUC ↑ 9.2-fold and C_{max} ↑ 18.9-fold	**Do not coadminister.**
	DRV/c	Atorvastatin AUC ↑ 3.9-fold and C_{max} ↑ 4.2-fold	Administer the lowest effective atorvastatin dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
	DRV/r	DRV/r plus atorvastatin 10 mg similar to atorvastatin 40 mg administered alone	Administer the lowest effective atorvastatin dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
Fluvastatin	ATV/c, DRV/c	↑ fluvastatin expected	Administer the lowest effective fluvastatin dose while monitoring for adverse events.
	ATV/r, DRV/r	↑ or ↓ fluvastatin possible	
Lomitapide	ATV/c, ATV/r, DRV/c, DRV/r	↑ lomitapide expected	**Contraindicated**
Lovastatin	ATV/c, ATV/r, DRV/c, DRV/r	Significant ↑ lovastatin expected	**Contraindicated**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Pitavastatin	ATV/c, DRV/c	No data	No dose adjustment needed. Monitor for pitavastatin-related adverse events.
	ATV/r, DRV/r	**With ATV/r** • ↔ pitavastatin expected • ↔ ATV/r expected **With DRV/r** • ↓ pitavastatin AUC 26% • ↔ DRV/r	No dose adjustment needed
Pravastatin	ATV/c, ATV/r	No data	Administer the lowest effective pravastatin dose while monitoring for adverse events.
	DRV/c, DRV/r	**With DRV/r** • Pravastatin AUC ↑ 81% following single dose of pravastatin • Pravastatin AUC ↑ 23% at steady state	Administer the lowest effective pravastatin dose while monitoring for adverse events.
Rosuvastatin	ATV/r	Rosuvastatin AUC ↑ 3-fold and C_{max} ↑ 7-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events. Do not exceed rosuvastatin 10 mg daily.
	ATV/c	Rosuvastatin AUC ↑ 3.4-fold and C_{max} ↑ 10.6-fold	
	DRV/c	Rosuvastatin AUC ↑ 1.9-fold and C_{max} ↑ 3.8-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events. Do not exceed rosuvastatin 20 mg daily.
	DRV/r	Rosuvastatin AUC ↑ 48% and C_{max} ↑ 2.4-fold	Administer the lowest effective rosuvastatin dose while monitoring for adverse events.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Simvastatin	ATV/c, ATV/r, DRV/c, DRV/r	Significant ↑ simvastatin expected	**Contraindicated**
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	ATV/r	Buprenorphine AUC ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 105%	Monitor for sedation and other signs or symptoms of overmedication. Buprenorphine dose reduction may be necessary. It may be necessary to remove implant and treat with a formulation that permits dose adjustments.
	DRV/r	↔ buprenorphine Norbuprenorphine (active metabolite) AUC ↑ 46% and C_{min} ↑ 71%	No dose adjustment needed. Monitor for buprenorphine-related adverse events. When transferring buprenorphine from transmucosal delivery to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	ATV/c, DRV/c	↑ buprenorphine possible	Titrate buprenorphine dose using the lowest initial dose. Dose adjustment of buprenorphine may be needed. It may be necessary to remove implant and treat with a formulation that permits dose adjustments. Monitor for buprenorphine-related adverse events.
Fentanyl	ATV/c, ATV/r, DRV/c, DRV/r	↑ fentanyl possible	Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression.
Lofexidine	ATV/c, ATV/r, DRV/c, DRV/r	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	ATV/c, DRV/c	No data	Titrate methadone dose using the lowest feasible initial dose. Dose adjustment of methadone may be needed. Monitor for methadone-related adverse events.
	ATV/r, DRV/r	ATV/r and DRV/r ↓ R-methadone[d] AUC 16% to 18%	Opioid withdrawal is unlikely but may occur. Monitor for opioid withdrawal and increase methadone dose as clinically indicated.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Oxycodone	ATV/c, ATV/r, DRV/c, DRV/r	↑ oxycodone expected	Monitor for opioid-related adverse events, including potentially fatal respiratory depression. Oxycodone dose reduction may be necessary.
Tramadol	ATV/c, ATV/r, DRV/c, DRV/r	↑ tramadol expected ↓ M1 (active metabolite) possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors			
Avanafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 600 mg twice daily (for 5 days) ↑ avanafil AUC 13-fold and ↑ C_{max} 2.4-fold	**Do not coadminister.**
Sildenafil	ATV/c, ATV/r, DRV/c, DRV/r	DRV/r plus sildenafil 25 mg similar to sildenafil 100 mg alone RTV 500 mg twice daily ↑ sildenafil AUC 1,000%	**For Treatment of Erectile Dysfunction** • Start with sildenafil 25 mg every 48 hours and monitor for sildenafil-related adverse events. **Contraindicated** for treatment of PAH.
Tadalafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 200 mg twice daily ↑ tadalafil AUC 124%	**For Treatment of Erectile Dysfunction** *As-Needed Use* • Start with tadalafil 5 mg and do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for tadalafil-related adverse events. *Once-Daily Use* • Do not exceed tadalafil 2.5 mg once daily. Monitor for tadalafil-related adverse events. **For Treatment of PAH** *In Patients on a PI >7 Days* • Start with tadalafil 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
			In Patients on Tadalafil Who Require a PI • Stop tadalafil ≥24 hours before PI initiation. Seven days after PI initiation, restart tadalafil at 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability. *In Patients Switching Between COBI and RTV* • Maintain tadalafil dose. **For Treatment of Benign Prostatic Hyperplasia** • Maximum recommended daily dose is tadalafil 2.5 mg per day. Monitor for tadalafil-related adverse events.
Vardenafil	ATV/c, ATV/r, DRV/c, DRV/r	RTV 600 mg twice daily ↑ vardenafil AUC 49-fold	Start with vardenafil 2.5 mg every 72 hours and monitor for vardenafil-related adverse events.
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Clonazepam, Diazepam	ATV/c, ATV/r, DRV/c, DRV/r	↑ benzodiazepine possible RTV 200 mg twice daily (for 2 days) ↑ alprazolam half-life 222% and ↑ AUC 248%	Consider alternative benzodiazepines, such as lorazepam, oxazepam, or temazepam.
Lorazepam, Oxazepam, Temazepam	ATV/c, ATV/r, DRV/c, DRV/r	No data	These benzodiazepines are metabolized via non-CYP450 pathways and, therefore, have less interaction potential than other benzodiazepines.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Midazolam	ATV/c, ATV/r, DRV/c, DRV/r	↑ midazolam expected	Oral midazolam is **contraindicated** with PIs. Parenteral midazolam can be used with caution when given in a monitored situation with appropriate medical management available in case of respiratory sedation and/or prolonged sedation. Consider dose reduction, especially if more than a single dose of midazolam is administered.
Triazolam	ATV/c, ATV/r, DRV/c, DRV/r	↑ triazolam expected RTV 200 mg twice daily ↑ triazolam half-life 1,200% and ↑ AUC 2,000%	**Contraindicated**
Orexin Receptor Antagonist			
Daridorexant, Lemborexant, Suvorexant	ATV/c, ATV/r, DRV/c, DRV/r	↑ daridorexant, lemborexant, suvorexant expected	**Do not coadminister.**
Other Sedatives			
Eszopiclone	ATV/c, ATV/r, DRV/c, DRV/r	↑ eszopiclone expected	Start with lowest dose and increase to a maximum of 2 daily; monitor for eszopiclone-related adverse events.
Zolpidem	ATV/c, ATV/r, DRV/c, DRV/r	↑ zolpidem possible	Initiate zolpidem at a low dose and monitor for zolpidem-related adverse events. Dose reduction may be necessary.

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Miscellaneous			
Calcifediol	ATV/c, ATV/r, DRV/c, DRV/r	↑ calcifediol possible	Dose adjustment of calcifediol may be required, and serum 25-hydroxyvitamin D, intact PTH, and serum calcium concentrations should be closely monitored.
Cisapride	ATV/c, ATV/r, DRV/c, DRV/r	↑ cisapride expected	**Contraindicated**
Colchicine	ATV/c, ATV/r, DRV/c, DRV/r	RTV 100 mg twice daily ↑ colchicine AUC 296% and C_{max} ↑ 184% Significant ↑ colchicine expected with all PIs, with or without COBI or RTV	**For Treatment of Gout Flares** • Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. **For Prophylaxis of Gout Flares** • If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day. **For Treatment of Familial Mediterranean Fever** • Do not exceed colchicine 0.6 mg once daily or colchicine 0.3 mg twice daily. **Contraindicated** in patients with hepatic (Child-Pugh Score A, B, or C) or renal impairment (CrCl <60 mL/min)
Dronabinol	ATV/c, ATV/r, DRV/c, DRV/r	↑ dronabinol possible	Monitor for dronabinol-related adverse events.
Eluxadoline	ATV/c, ATV/r, DRV/c, DRV/r	↑ eluxadoline expected	Administer eluxadoline at a dose of 75 mg twice daily and monitor for eluxadoline-related adverse events.
Finerenone	ATV/c, ATV/r, DRV/c, DRV/r	↑ finerenone expected	**Contraindicated**

Table 24a. Drug Interactions Between Protease Inhibitors and Other Drugs

Concomitant Drug	PI	Effect on PI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Flibanserin	ATV/c, ATV/r, DRV/c, DRV/r	↑ flibanserin expected	**Contraindicated**
Naloxegol	ATV/c, ATV/r, DRV/c, DRV/r	↑ naloxegol expected	**Contraindicated**
Praziquantel	ATV/c, ATV/r, DRV/c, DRV/r	↑ praziquantel possible	Consider alternative ARV. If coadministration is necessary, monitor for praziquantel-related adverse events.

[a] DHA is an active metabolite of artemether and artesunate.

[b] The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Lo Minastrin Fe; Lo Loestrin Fe; Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Minastrin 24 Fe; Ortho Tri-Cyclen Lo. Generic formulations also may be available.

[c] The following products contain at least 35 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Brevicon; Femcon Fe; Modicon; Norinyl 1/35; Ortho-Cyclen; Ortho-Novum 1/35, 7/7/7; Ortho Tri-Cyclen; Ovcon 35; Tri-Norinyl. Generic formulations also may be available.

[d] R-methadone is the active form of methadone.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 17-BMP = beclomethasone 17-monopropionate; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CCB = calcium channel blocker; CNS = central nervous system; COBI = cobicistat; CrCl = creatinine clearance; CMV = cytomegalovirus; CV = cardiovascular; CYP = cytochrome P; DHA = dihydroartemisinin; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DVT = deep vein thrombosis; ECG = electrocardiogram; eGFR = estimated glomerular filtration rate; EVG/c = elvitegravir/cobicistat; GI = gastrointestinal; H2RA = H2 receptor antagonist; HCV = hepatitis C virus; HRT = hormone replacement therapy; INR = international normalized ratio; LPV = lopinavir; LPV/r = lopinavir/ritonavir; MPA = medroxyprogesterone acetate; OATP = organic anion-transporting polypeptide; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PE = pulmonary embolism; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PK = pharmacokinetic; PPI = proton pump inhibitor; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RTV = ritonavir; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; TDF = tenofovir disoproxil fumarate; VPA = valproic acid

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between non-nucleoside reverse transcriptase inhibitors (NNRTIs) and non-antiretroviral drugs. Cabotegravir (CAB) intramuscular (IM) plus rilpivirine (RPV) IM are co-packaged into a single product and are coadministered as a complete regimen; therefore, the dosing recommendations and clinical comments reflect the combination of CAB IM and RPV IM treatments. Drug interaction studies were not conducted with either CAB IM or RPV IM. Drug interaction studies with oral CAB and RPV were leveraged to make the dosing recommendations for CAB IM and RPV IM. For information regarding interactions between NNRTIs and other antiretroviral (ARV) drugs, including dosing recommendations, refer to Tables 24c, 24e, 24f, 25a, and 25b.

Recommendations for managing a particular drug interaction may differ, depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or if a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. When an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Oral doses of RPV at 75 mg and 300 mg once daily (equivalent to 3 and 12 times the recommended dose) were associated with prolonged QTc (or QT corrected for heart rate) interval. Known and expected/theoretical pharmacokinetic interactions, resulting in increased RPV exposures, are included in this table due to the safety concern of QTc prolongation. There is limited information about the potential for pharmacodynamic interactions between RPV (in the absence of increased RPV exposures) and drugs that prolong the QTc interval; therefore, these are not included in this table.

Nevirapine (NVP) is no longer commonly used in clinical practice in the United States and is not included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between NVP and concomitant medications. Information may also be found in archived versions of this guideline.

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Antacids	DOR, EFV	↔ NNRTI AUC	No dose adjustment needed
	ETR	↔ ETR expected	No dose adjustment needed
	RPV IM	↔ RPV expected	No dose adjustment needed
	RPV PO	↓ RPV expected when given simultaneously	Give antacids at least 2 hours before or at least 4 hours after RPV.
H2 Receptor Antagonists	DOR	↔ DOR expected	No dose adjustment needed
	EFV	↔ EFV AUC	No dose adjustment needed
	ETR	↔ ETR AUC	No dose adjustment needed
	RPV IM	↔ RPV expected	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV PO	RPV AUC ↓ 76% when famotidine 40 mg is taken 2 hours prior	Give H2 receptor antagonists at least 12 hours before or at least 4 hours after RPV.
Proton Pump Inhibitors	DOR	↔ DOR AUC and C_{min}	No dose adjustment needed
	EFV	↔ EFV expected	
	ETR	**With Omeprazole 40 mg Daily** • ETR AUC ↑ 41%	
	RPV IM	↔ RPV expected	No dose adjustment needed
	RPV PO	**With Omeprazole 20 mg Daily** • RPV AUC ↓ 40% to 65% and C_{min} ↓ 33%	**Contraindicated**
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin, Doxazosin, Silodosin, Terazosin	DOR, RPV IM, RPV PO	↔ alpha-adrenergic antagonists expected	No dose adjustment needed
	EFV, ETR	↓ alpha-adrenergic antagonists expected	Consider alternative ARV or alpha-antagonist therapy. If coadministration is necessary, monitor for therapeutic effectiveness of alpha antagonist.
Tamsulosin	DOR, RPV IM, RPV PO	↔ tamsulosin expected	No dose adjustment needed
	EFV, ETR	↓ tamsulosin expected	Monitor for therapeutic effectiveness of tamsulosin after 2–4 weeks. May need to increase dose to tamsulosin 0.8 mg once daily for patients who fail to respond to the 0.4-mg dose.
Antibacterials—Antimycobacterials			
Bedaquiline	DOR, RPV IM, RPV PO	↔ bedaquiline expected	No dose adjustment needed
	EFV, ETR	↓ bedaquiline possible	**Do not coadminister.**
Rifabutin	DOR	DOR AUC ↓ 50%	Increase DOR dose to 100 mg twice daily. No dose adjustment is needed for rifabutin.
	EFV	Rifabutin ↓ 38%	Increase rifabutin dose to 450–600 mg per day.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	ETR	↔ rifabutin and metabolite AUC ETR AUC ↓ 37%	**Do not coadminister** ETR plus PI/r with rifabutin. Use rifabutin 300 mg once daily if ETR is administered without PI/r.
	RPV IM	↓ RPV expected	**Contraindicated**
	RPV PO	**Rifabutin Plus RPV 50 mg PO Once Daily Compared to RPV 25 mg Once Daily Alone** • ↔ RPV AUC and C_{min}	Increase RPV dose to 50 mg PO once daily during coadministration. No dose adjustment for rifabutin is needed.
Rifampin	DOR	DOR AUC ↓ 88%	**Contraindicated.** After stopping rifampin, wait 4 weeks before initiating DOR.
	EFV	EFV AUC ↓ 26%	**Do not use** EFV 400 mg with rifampin. Maintain EFV dose at 600 mg once daily and monitor for virologic response.
	ETR	Significant ↓ ETR possible	**Do not coadminister.**
	RPV IM	↓ RPV possible	**Contraindicated**
	RPV PO	RPV AUC ↓ 80%	**Contraindicated**
Rifapentine	DOR	**Once-Weekly Rifapentine Plus Isoniazid and DOR 100 mg Twice Daily Compared to DOR 100 mg Twice Daily Alone** • DOR AUC ↓ 29%, C_{min} ↓ 31%	**Contraindicated.** After stopping rifapentine, wait 4 weeks before initiating DOR.
	EFV	**Daily Rifapentine (Max 600 mg) With EFV** • ↔ EFV **Weekly Rifapentine (Max 900 mg) With EFV** • ↔ EFV	No dose adjustment needed
	ETR	↓ ETR possible	**Do not coadminister.**
	RPV IM, RPV PO	↓ RPV possible	**Contraindicated**
Antibacterials—Macrolides			
Azithromycin	DOR, EFV, ETR, RPV IM, RPV PO	↔ azithromycin expected	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Clarithromycin	DOR	↔ clarithromycin expected ↑ DOR possible	Monitor for ARV tolerability if used in combination.
	EFV	Clarithromycin AUC ↓ 39%	Monitor for effectiveness, or consider alternative agent (e.g., azithromycin) for MAC prophylaxis and treatment.
	ETR	Clarithromycin AUC ↓ 39% ETR AUC ↑ 42%	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment.
	RPV IM, RPV PO	↔ clarithromycin expected ↑ RPV possible	Consider alternative macrolide (e.g., azithromycin) for MAC prophylaxis and treatment. If coadministered, monitor for QTc prolongation.
Erythromycin	DOR	↑ DOR possible	Monitor for ARV tolerability if used in combination.
	EFV, ETR	↑ EFV and ETR possible ↓ erythromycin possible	Monitor for ARV tolerability and antibiotic efficacy if used in combination.
	RPV IM, RPV PO	↑ RPV possible	Consider alternative macrolide (e.g., azithromycin). If coadministered, monitor for QTc prolongation.
Anticoagulants			
Apixaban	DOR, RPV IM, RPV PO	↔ apixaban expected	No dose adjustment needed
	EFV, ETR	↓ apixaban possible	Consider alternative ARV or anticoagulant therapy.
Dabigatran, Edoxaban	DOR, EFV, ETR, RPV IM, RPV PO	↔ DOAC expected	No dose adjustment needed
Rivaroxaban	DOR, RPV IM, RPV PO	↔ rivaroxaban expected	No dose adjustment needed
	EFV, ETR	↓ rivaroxaban possible	Consider alternative ARV or anticoagulant therapy.
Warfarin	DOR, RPV IM, RPV PO	↔ warfarin expected	No dose adjustment needed
	EFV, ETR	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below.			
Antidepressants and Anxiolytics			
Bupropion	DOR, ETR, RPV IM, RPV PO	↔ bupropion expected	No dose adjustment needed
	EFV	Bupropion AUC ↓ 55%	Titrate bupropion dose based on clinical response.
Citalopram, Escitalopram	DOR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
	EFV, ETR	↓ antidepressant possible	Titrate antidepressant dose based on clinical response.
Desvenlafaxine, Venlafaxine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Duloxetine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Fluoxetine, Fluvoxamine	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Mirtazapine	DOR, RPV IM, RPV PO	↔ mirtazapine expected	No dose adjustment needed
	EFV, ETR	↓ mirtazapine possible	Monitor antidepressant effect. Titrate dose as necessary based on clinical response.
Nefazodone	DOR, RPV IM, RPV PO	↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ nefazodone expected ↑ NNRTI possible	Monitor antidepressant effect. Titrate dose as necessary based on clinical response.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Paroxetine	DOR, ETR, RPV IM, RPV PO	↔ paroxetine expected	No dose adjustment needed
	EFV	↔ EFV and paroxetine	No dose adjustment needed
Sertraline	DOR, RPV IM, RPV PO	↔ sertraline expected	No dose adjustment needed
	EFV	Sertraline AUC ↓ 39%	Monitor the antidepressant effect. Titrate dose as necessary based on clinical response.
	ETR	↓ sertraline possible	
Trazodone	DOR, RPV IM, RPV PO	↔ trazodone expected	No dose adjustment needed
	EFV, ETR	↓ trazodone possible	Monitor for therapeutic effectiveness of trazodone and titrate dose as necessary.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	DOR, EFV, ETR, RPV IM, RPV PO	↔ antidepressant expected	No dose adjustment needed
Antipsychotics			
Aripiprazole	DOR, RPV IM, RPV PO	↔ aripiprazole expected	No dose adjustment needed
	EFV, ETR	↓ aripiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling usual dose of aripiprazole over 1–2 weeks. Refer to aripiprazole prescribing information for dose recommendations.
Brexpiprazole	DOR, RPV IM, RPV PO	↔ brexpiprazole expected	No dose adjustment needed
	EFV, ETR	↓ brexpiprazole expected	Monitor for therapeutic effectiveness of antipsychotic. Consider doubling the usual dose of brexpiprazole and making further adjustments based on clinical response. Refer to brexpiprazole prescribing information.
Cariprazine	DOR, RPV IM, RPV PO	↔ cariprazine expected	No dose adjustment needed
	EFV, ETR	↓ cariprazine and ↑ or ↓ active metabolite possible	**Do not coadminister.**

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Iloperidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Lumateperone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	**Do not coadminister.**
Lurasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Olanzapine, Olanzapine/ Samidorphan	DOR, ETR, RPV IM, RPV PO	↔ olanzapine expected	No dose adjustment needed
	EFV	↓ olanzapine possible	Monitor for therapeutic effectiveness of olanzapine.
Other Antipsychotics CYP3A4 Substrates (e.g., clozapine, haloperidol, perphenazine, risperidone, thioridazine)	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Pimavanserin	DOR, RPV IM, RPV PO	↔ pimavanserin expected	No dose adjustment needed
	EFV, ETR	↓ pimavanserin expected	**Do not coadminister.**
Pimozide	DOR, RPV IM, RPV PO	↔ pimozide expected	No dose adjustment needed
	EFV, ETR	↓ pimozide possible	Monitor for therapeutic effectiveness of pimozide.
Quetiapine	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ziprasidone	DOR, RPV IM, RPV PO	↔ antipsychotic expected	No dose adjustment needed
	EFV, ETR	↓ antipsychotic possible	Monitor for therapeutic effectiveness of antipsychotic.
Antifungals			
Fluconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV	↔ fluconazole expected ↔ EFV AUC	No dose adjustment needed
	ETR	ETR AUC ↑ 86%	No dose adjustment needed
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Ibrexafungerp	DOR, RPV PO	↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ ibrexafungerp expected ↑ NNRTI possible	**Do not coadminister.**
	RPV IM	↔ ibrexafungerp expected ↔ RPV IM expected	No dose adjustment needed
Isavuconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV, ETR	↓ isavuconazole possible	Monitor isavuconazole concentration and antifungal response. Dose adjustments for isavuconazole may be necessary.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Itraconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV	**EFV With Itraconazole Solution** • Itraconazole and OH-itraconazole AUC, C_{max}, and C_{min} ↓ 37% to 44% **EFV With Itraconazole Capsules** • Itraconazole AUC ↓ 86% and OH-itraconazole AUC 84%	**Do not coadminister** unless potential benefits outweigh the risks. Failure to achieve therapeutic itraconazole concentrations has been reported. If coadministration is necessary, closely monitor itraconazole concentration and adjust dose accordingly.
	ETR	↓ itraconazole possible ↑ ETR possible	Dose adjustments for itraconazole may be necessary. Monitor itraconazole concentration and antifungal response.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Posaconazole	DOR, ETR	↑ NNRTI possible	No dose adjustment needed
	EFV	Posaconazole AUC ↓ 50% ↔ EFV AUC	**Do not coadminister** unless potential benefits outweigh the risks. If coadministration is necessary, monitor posaconazole concentration and adjust dose accordingly.
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Voriconazole	DOR	↑ DOR possible	No dose adjustment needed
	EFV	Voriconazole AUC ↓ 77% EFV AUC ↑ 44%	**Contraindicated at standard doses** Adjust dose to voriconazole 400 mg twice daily plus EFV 300 mg daily.
	ETR	↔ voriconazole AUC ETR AUC ↑ 36%	No dose adjustment needed
	RPV IM, RPV PO	↑ RPV possible	No dose adjustment needed. If coadministered, consider monitoring for QTc prolongation.
Antimalarials			
Artemether/ Lumefantrine	DOR, RPV IM, RPV PO	↔ antimalarial expected	No dose adjustment needed
	EFV	Artemether AUC ↓ 79% DHA AUC ↓ 75% Lumefantrine AUC ↓ 30% to 56%	Consider alternative ARV or antimalarial drug. If used in combination, monitor closely for antimalarial efficacy.
	ETR	Artemether AUC ↓ 38% ↔ DHA AUC ↔ lumefantrine AUC ↔ ETR AUC	Clinical significance of the reduced antimalarial drug concentrations is unknown. If used in combination with ETR, monitor for antimalarial efficacy.
Atovaquone/Proguanil	DOR, ETR, RPV IM, RPV PO	No data	Monitor for antimalarial efficacy.
	EFV	Atovaquone AUC ↓ 75% Proguanil AUC ↓ 43%	No dose recommendation. Consider alternative drug for malaria prophylaxis, if possible.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimigraine			
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	DOR RPV IM, RPV PO	↔ atogepant expected	No dose adjustment needed
	EFV, ETR,	↓ atogepant possible	Episodic migraine: Increase atogepant dose to 30–60 mg once daily. Chronic migraine: **Do not coadminister.**
Rimegepant	DOR, RPV IM, RPV PO	↔ rimegepant expected	No dose adjustment needed
	EFV, ETR,	↓ rimegepant possible	Consider alternative ARV or migraine medication.
Ubrogepant	DOR, RPV IM, RPV PO	↔ ubrogepant expected	No dose adjustment needed
	EFV, ETR	↓ ubrogepant expected	Use initial dose of 100 mg, followed by second dose of 100 mg if needed.
Zavegepant	DOR, RPV IM, RPV PO	↔ zavegepant expected	No dose adjustment needed
	EFV, ETR,	↓ zavegepant possible	
Serotonin 5-HT1B, 1D Receptor Agonists			
Almotriptan, Eletriptan	DOR RPV IM, RPV PO	↔ almotriptan expected	No dose adjustment needed
	EFV, ETR,	↓ almotriptan possible	
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan, Zolmitriptan	DOR, EFV, ETR, RPV IM, RPV PO	↔ migraine medication expected	No dose adjustment needed
Antiplatelets			
Clopidogrel	DOR, RPV IM, RPV PO	↔ clopidogrel expected	No dose adjustment needed
	EFV, ETR	↓ activation of clopidogrel possible	Consider alternative ARV or antiplatelet. ETR may prevent metabolism of clopidogrel to its active metabolite.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Prasugrel	All NNRTIs	↔ prasugrel expected	No dose adjustment needed
Ticagrelor	DOR, RPV IM, RPV PO	↔ ticagrelor expected	No dose adjustment needed
	EFV, ETR	↓ ticagrelor expected	Consider alternative ARV or anticoagulant therapy.
Vorapaxar	DOR, RPV IM, RPV PO	↔ vorapaxar expected	No dose adjustment needed
	EFV, ETR	↓ vorapaxar expected	Insufficient data to make a dose recommendation.
Antipneumocystis and Antitoxoplasmosis			
Atovaquone (oral solution)	DOR, ETR, RPV IM, RPV PO	No data	Monitor for therapeutic effectiveness of atovaquone.
	EFV	Atovaquone AUC ↓ 44% to 47%	Consider alternative ARV or agent for PCP or toxoplasmosis treatment or prophylaxis. If coadministration is necessary, monitor for therapeutic effectiveness of atovaquone.
Antiseizure			
Carbamazepine, Phenobarbital, Phenytoin, Primidone	DOR	↓ DOR possible	**Contraindicated.** After stopping antiseizure medication, wait 4 weeks before initiating DOR.
	EFV	**Carbamazepine Plus EFV** • Carbamazepine AUC ↓ 27% • EFV AUC ↓ 36% **Phenytoin Plus EFV** • ↓ EFV • ↑ or ↓ phenytoin possible **Phenobarbital or Primidone Plus EFV** • ↓ EFV and antiseizure agent possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor antiseizure drug and EFV concentrations.
	ETR	↓ antiseizure agent and ETR possible	**Do not coadminister.**
	RPV IM, RPV PO	↓ RPV possible	**Contraindicated**

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Eslicarbazepine	DOR, EFV, ETR, RPV IM, RPV PO	↓ NNRTI possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Oxcarbazepine	DOR, RPV IM, RPV PO	↓ NNRTI possible	**Contraindicated**
	EFV, ETR	↓ NNRTI possible	Consider alternative ARV or antiseizure medication. If coadministration is necessary, monitor virologic response and consider monitoring plasma concentrations of ARVs.
Ethosuximide, Lacosamide, Tiagabine, Zonisamide	DOR, RPV IM, RPV PO	↔ antiseizure agent expected	No dose adjustment needed
	EFV, ETR	↓ antiseizure agent possible	Monitor seizure control. Consider anticonvulsant therapeutic drug monitoring.
Lamotrigine	DOR, ETR, RPV IM, RPV PO	↔ lamotrigine expected	No dose adjustment needed
	EFV	↓ lamotrigine possible	Monitor seizure control and plasma concentrations of lamotrigine.
Antivirals—Hepatitis C			
Elbasvir/Grazoprevir	DOR	↔ elbasvir and grazoprevir DOR AUC ↑ 56% and C_{min} ↑ 41%	No dose adjustment needed
	EFV	Elbasvir AUC ↓ 54% Grazoprevir AUC ↓ 83% ↔ EFV	**Contraindicated**
	ETR	↓ elbasvir and grazoprevir expected	**Do not coadminister.**
	RPV IM	↔ elbasvir and grazoprevir expected ↔ RPV expected	No dose adjustment needed
	RPV PO	↔ elbasvir and grazoprevir ↔ RPV AUC and C_{min}	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Glecaprevir/ Pibrentasvir	DOR	↑ DOR expected	No dose adjustment needed
	EFV	↓ glecaprevir and pibrentasvir expected	**Do not coadminister.**
	ETR	↓ glecaprevir and pibrentasvir possible	**Do not coadminister.**
	RPV IM	↔ glecaprevir and pibrentasvir expected ↑ RPV expected	No dose adjustment needed
	RPV PO	↔ glecaprevir and pibrentasvir RPV AUC ↑ 84%	No dose adjustment needed
Ledipasvir/Sofosbuvir	DOR	↔ ledipasvir and sofosbuvir ↔ DOR	No dose adjustment needed
	EFV	Ledipasvir AUC, C_{min}, and C_{max} ↓ 34% ↔ sofosbuvir	
	ETR	No significant effect expected	
	RPV IM	↔ ledipasvir, sofosbuvir, and RPV expected	
	RPV PO	↔ ledipasvir and sofosbuvir ↔ RPV	
Sofosbuvir/ Velpatasvir	DOR, RPV IM, RPV PO	No significant effect expected	No dose adjustment needed
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47%	**Do not coadminister.**
	ETR	↓ velpatasvir expected	**Do not coadminister.**
Sofosbuvir/ Velpatasvir/ Voxilaprevir	DOR, RPV IM, RPV PO	No significant effect expected	No dose adjustment needed.
	EFV	Velpatasvir AUC ↓ 43%, C_{max} ↓ 37%, and C_{min} ↓ 47% ↓ voxilaprevir expected	**Do not coadminister.**
	ETR	↓ voxilaprevir expected ↓ velpatasvir expected	**Do not coadminister.**

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	All NNRTIs	↔ brincidofovir expected	No dose adjustment needed
Cidofovir	All NNRTIs	↔ cidofovir expected	No dose adjustment needed
Maribavir	DOR, RPV IM, RPV PO	↔ maribavir expected	No dose adjustment needed
	EFV, ETR	↓ maribavir possible	
Tecovirimat	DOR, RPV PO	↓ DOR or RPV expected but not likely to be clinically relevant	No dose adjustment needed
	EFV, ETR	↔ EFV or ETR expected	No dose adjustment needed
	RPV IM	↓ RPV expected but not likely to be clinically relevant	No dose adjustment needed. If there is a concern for suboptimal RPV exposure, seek expert consultation. Do not initiate CAB/RPV IM during or within 2 weeks after tecovirimat treatment. (Refer to Table 24d for interaction with CAB.)
Antivirals—SARS-CoV-2			
Molnupiravir	All NNRTIs	↔ expected	No dose adjustment needed
Remdesivir	All NNRTIs	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	DOR	**With Ritonavir 100 mg Twice Daily** • DOR AUC ↑ 254%	No dose adjustment needed
	EFV, ETR, RPV PO, RPV IM	↔ expected	No dose adjustment needed
Cardiac Medications			
Beta-Blockers			
Atenolol, Metoprolol, Nebivolol	DOR, EFV, ETR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Bisoprolol, Carvedilol	DOR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed
	EFV, ETR	↓ beta-blocker possible	No dose adjustment needed. Monitor blood pressure and heart rate and titrate to clinical effect.
Labetalol	DOR, RPV IM, RPV PO	↔ beta-blocker expected	No dose adjustment needed
	EFV, ETR	↑ beta-blocker possible	No dose adjustment needed. Monitor blood pressure and heart rate and adjust dose to achieve desired clinical effect.
Calcium Channel Blockers			
Dihydropyridine Calcium Channel Blockers (e.g., amlodipine, nifedipine)	DOR, RPV IM, RPV PO	↔ CCBs expected	No dose adjustment needed
	EFV, ETR	↓ CCBs possible	Titrate CCB dose based on clinical response.
Non-Dihydropyridine Calcium Channel Blockers (e.g., diltiazem, verapamil)	DOR, RPV IM, RPV PO	↔ CCBs expected ↑ NNRTI possible	No dose adjustment needed
	EFV	Diltiazem AUC ↓ 69% ↓ verapamil possible	Titrate diltiazem or verapamil dose based on clinical response.
	ETR	↓ diltiazem or verapamil possible	
Cardiac—Other			
Bosentan	DOR	↓ DOR possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
	EFV, ETR	↓ NNRTI possible ↓ bosentan possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor bosentan efficacy and virologic response.
	RPV IM, RPV PO	↓ RPV possible	Consider alternative ARV or alternative to bosentan. If coadministration is necessary, monitor virologic response.
Eplerenone	DOR, RPV IM, RPV PO	↔ eplerenone expected	No dose adjustment needed
	EFV, ETR	↓ eplerenone possible	Titrate eplerenone dose based on clinical response.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ivabradine	DOR, RPV IM, RPV PO	↔ ivabradine expected	No dose adjustment needed
	EFV, ETR	↓ ivabradine expected	**Contraindicated**
Mavacamten	DOR, RPV IM, RPV PO	↔ mavacamten expected ↓ NNRTI possible	Consider alternative ARV or alternative to mavacamten. If coadministration is necessary, monitor virologic response.
	EFV, ETR	↓ mavacamten expected ↓ NNRTI possible	**Contraindicated**
Ranolazine	DOR, RPV IM, RPV PO	↔ ranolazine expected	No dose adjustment needed
	EFV, ETR	↓ ranolazine expected	**Contraindicated**
Corticosteroids			
Beclomethasone, Ciclesonide	DOR, EFV, ETR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
Budesonide, Fluticasone, Mometasone	DOR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
	EFV, ETR,	↓ corticosteroid possible	Monitor corticosteroid efficacy and titrate as needed. May consider alternative corticosteroid for long-term use.
Dexamethasone	DOR, EFV, ETR	↓ NNRTI possible	Consider alternative corticosteroid for long-term use. If dexamethasone is used with NNRTI, monitor virologic response.
	RPV IM, RPV PO	Significant ↓ RPV possible	**Contraindicated** with more than a single dose of dexamethasone.
Prednisone, Prednisolone	DOR, RPV IM, RPV PO	↔ corticosteroid expected	No dose adjustment needed
	EFV, ETR,	↓ corticosteroid possible	Monitor corticosteroid efficacy and titrate as needed. May consider alternative corticosteroid for long-term use.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Glucose-Lowering			
Linagliptin, Sitagliptin	DOR, RPV IM, RPV PO	↔ antihyperglycemic expected	No dose adjustment needed
	EFV, ETR	↓ antihyperglycemic possible	Monitor glycemic control.
Metformin	DOR	↔ metformin AUC DOR AUC ↓ 26% and C_{max} ↓ 24%	No dose adjustment needed
	EFV, ETR, RPV IM	↔ metformin expected	No dose adjustment needed
	RPV PO	↔ metformin AUC	No dose adjustment needed
Sodium-Glucose Cotransporter-2 Inhibitors (e.g., canagliflozin, dapagliflozin, empagliflozin)	DOR, EFV, ETR, RPV IM, RPV PO	↔ antihyperglycemic expected	No dose adjustment needed
Herbal Products			
St. John's Wort	DOR	↓ DOR expected	**Contraindicated.** After stopping St. John's Wort, wait 4 weeks before initiating DOR.
	EFV, ETR	↓ EFV or ETR expected	**Do not coadminister.**
	RPV IM, RPV PO	↓ RPV expected	**Contraindicated**
Hormonal Therapies—Contraceptives			
Injectable Contraceptives **Depot MPA**	DOR, ETR, RPV IM, RPV PO	↔ MPA expected	No dose adjustment needed
	EFV	↔ MPA	No dose adjustment needed. Refer to Women With HIV section for people on EFV and RIF.
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate)	DOR	↔ ethinyl estradiol ↔ levonorgestrel ↔ drospirenone expected	No dose adjustment needed
	EFV	↔ ethinyl estradiol Etonogestrel (metabolite of oral desogestrel) C_{min} ↓ 61%	**When Used for Contraception** Use alternative ARV or contraceptive methods.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		Levonorgestrel (metabolite of oral norgestimate) AUC ↓ 83% Norelgestromin (metabolite of oral norgestimate) AUC ↓ 64% ↓ drospirenone possible	**When Used for Other Clinical Indications (e.g., Acne, Menstrual Cycle Regulation)** Monitor for clinical effectiveness of hormonal therapy.
	ETR	Ethinyl estradiol AUC ↑ 22% ↔ norethindrone ↓ drospirenone possible	No dose adjustment needed for regimens that do not contain drospirenone For drospirenone-containing regimens used for contraception, use alternative ARV or alternative contraceptive method. If using drospirenone for other clinical indications, monitor for clinical effectiveness of hormonal therapy.
	RPV IM	↔ ethinyl estradiol expected ↔ norethindrone expected ↔ drospirenone expected	No dose adjustment needed
	RPV PO	↔ ethinyl estradiol ↔ norethindrone ↔ drospirenone expected	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	DOR, RPV IM, RPV PO	↔ etonogestrel expected ↔ levonorgestrel expected	No dose adjustment needed
	EFV	Etonogestrel AUC ↓ 63% to 82% Levonorgestrel AUC ↓ 42% to 47% **Levonorgestrel 300 mg Implant With 600 mg EFV Compared to Levonorgestrel 150 mg Implant** • Levonorgestrel AUC ↓ 34%	Use alternative ARV or contraceptive methods. Unintended pregnancies were observed in women who used EFV and levonorgestrel implant concomitantly.
	ETR	↓ etonogestrel possible ↓ levonorgestrel possible	Consider using alternative ARV or contraceptive methods.
Transdermal Contraceptives (e.g., ethinyl estradiol/ norelgestromin, ethinyl estradiol/levonorgestrel)	DOR, RPV IM, RPV PO	↔ ethinyl estradiol or norelgestromin expected	No dose adjustment needed
	EFV	↓ ethinyl estradiol or norelgestromin possible	Consider alternative ARV or contraceptive method.
	ETR	↓ ethinyl estradiol or norelgestromin possible	Consider alternative ARV or contraceptive method.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	DOR, RPV IM, RPV PO	↔ etonogestrel and ethinyl estradiol expected ↔ segesterone and ethinyl estradiol expected	No dose adjustment needed
	EFV	Ethinyl estradiol (intravaginal ring) AUC ↓ 56% Etonogestrel (intravaginal ring) AUC ↓ 81%	Use alternative ARV or contraceptive method.
		↓ segesterone and ethinyl estradiol possible	Consider alternative ARV or contraceptive method.
	ETR	↓ etonogestrel and ethinyl estradiol possible ↓ segesterone and ethinyl estradiol possible	Consider alternative ARV or contraceptive method.
Emergency Contraceptives Levonorgestrel (oral)	DOR, RPV IM, RPV PO	↔ levonorgestrel expected	No dose adjustment needed.
	EFV	**Levonorgestrel 1.5 mg Plus 600 mg EFV** • Levonorgestrel AUC ↓ 58% **Levonorgestrel 3 mg Plus 600 mg EFV Compared to Levonorgestrel 1.5 mg Alone** • ↔ levonorgestrel AUC	Increase dose of levonorgestrel to 3 mg when used for emergency postcoital contraception.
	ETR	↓ levonorgestrel possible	Consider alternative ARV or contraceptive method.
Hormonal Therapies—Miscellaneous			
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	DOR, RPV IM, RPV PO	↔ dutasteride and finasteride expected	No dose adjustment needed
	EFV, ETR	↓ dutasteride and finasteride possible	Monitor effects of testosterone. Titrate testosterone dose as necessary to achieve therapeutic goals.
Cyproterone, Goserelin Acetate, Leuprolide, Progestogens, Spironolactone	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed
	EFV, ETR	↓ cyproterone and progestogens possible ↔ goserelin, leuprolide acetate, and spironolactone expected	Monitor effects of estrogen and antiandrogen therapy. Titrate dose as necessary to achieve therapeutic goals.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Estradiol	DOR, RPV IM, RPV PO	↔ estradiol expected	No dose adjustment needed
	EFV	Estradiol AUC ↓ 28% ↔ EFV AUC	Monitor effects of estrogen and therapy. Titrate dose as necessary to achieve therapeutic goals
	ETR	↓ estradiol possible	
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	DOR, RPV IM, RPV PO	↔ hormonal concentrations expected	No dose adjustment needed
	EFV, ETR	↓ estrogen possible with estradiol or conjugated estrogen (equine and synthetic) ↓ medroxyprogesterone possible ↓ micronized progesterone possible ↓ drospirenone possible See Contraceptives—Oral above for other progestin-NNRTI interactions	Monitor menopausal symptoms. Titrate to the dose of hormonal therapy that achieves menopausal symptom relief.
Testosterone	DOR, RPV IM, RPV PO	↔ testosterone expected	No dose adjustment needed
	EFV, ETR	↓ testosterone possible	Monitor effects of testosterone. Titrate testosterone dose as necessary to achieve therapeutic goals.
Immunosuppressants			
Cyclosporine	DOR, RPV IM, RPV PO	↔ cyclosporine expected ↑ NNRTI possible	No dose adjustment needed
	EFV, ETR	↓ cyclosporine possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.
Everolimus, Sirolimus, Tacrolimus	DOR, RPV IM, RPV PO	↔ immunosuppressant expected	No dose adjustment needed
	EFV, ETR	↓ immunosuppressant possible	Increase in immunosuppressant dose may be necessary. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with specialist as necessary.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lipid-Modifying			
Atorvastatin	DOR	↔ atorvastatin AUC	No dose adjustment needed
	EFV, ETR	Atorvastatin AUC ↓ 32% to 43%	Adjust atorvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	RPV IM	↔ atorvastatin expected	No dose adjustment needed
	RPV PO	↔ atorvastatin AUC	No dose adjustment needed
Fluvastatin	DOR, RPV IM, RPV PO	↔ fluvastatin expected	No dose adjustment needed
	EFV, ETR	↑ fluvastatin possible	Dose adjustments for fluvastatin may be necessary. Monitor for fluvastatin toxicity.
Lovastatin, Simvastatin	DOR, RPV IM, RPV PO	↔ lovastatin and simvastatin expected	No dose adjustment needed
	EFV	Simvastatin AUC ↓ 60% to 68% Simvastatin active metabolite AUC ↓ 60%	Adjust simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
	ETR	↓ lovastatin possible ↓ simvastatin possible	Adjust lovastatin or simvastatin dose according to lipid response, but do not exceed the maximum recommended dose.
Pitavastatin	DOR, ETR, RPV IM, RPV PO	↔ pitavastatin expected	No dose adjustment needed
	EFV	↔ pitavastatin AUC	No dose adjustment needed
Pravastatin	DOR, RPV IM, RPV PO	↔ pravastatin expected	No dose adjustment needed
	EFV	Pravastatin AUC ↓ 44%	Adjust statin dose according to lipid responses, but do not exceed the maximum recommended dose.
	ETR	↓ pravastatin possible	
Rosuvastatin	DOR, EFV, ETR, RPV IM, RPV PO	↔ rosuvastatin expected	No dose adjustment needed

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Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual or buccal	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed
	EFV	Buprenorphine AUC ↓ 50% Norbuprenorphine (active metabolite) AUC ↓ 71%	No dose adjustment needed, monitor for withdrawal symptoms.
	ETR	Buprenorphine AUC ↓ 25%	No dose adjustment needed
Buprenorphine Implant	DOR, RPV IM, RPV PO	↔ buprenorphine expected	No dose adjustment needed
	EFV, ETR	No data	Clinical monitoring is recommended when NNRTI is initiated after insertion of buprenorphine implant.
Lofexidine	DOR, EFV, ETR, RPV IM, RPV PO	↔ lofexidine expected	No dose adjustment needed
Methadone	DOR	↔ methadone AUC DOR AUC ↓ 26%	No dose adjustment needed
	EFV	Methadone AUC ↓ 52%	Opioid withdrawal common; monitor and increase methadone dose as necessary.
	ETR	↔ methadone AUC	No dose adjustment needed
	RPV IM	↓ methadone AUC expected	No dose adjustment needed; monitor for withdrawal symptoms.
	RPV PO	↔ R-methadone[a] AUC	No dose adjustment needed; monitor for withdrawal symptoms.
PDE5 Inhibitors			
Avanafil, Tadalafil, Vardenafil	DOR, RPV IM, RPV PO	↔ PDE5 inhibitor expected	No dose adjustment needed
	EFV, ETR	↓ PDE5 inhibitor possible	May need to titrate dose based on clinical effect.

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sildenafil	DOR	↔ sildenafil expected	No dose adjustment needed
	EFV	↓ sildenafil possible	May need to titrate sildenafil dose based on clinical effect.
	ETR	Sildenafil AUC ↓ 57%	May need to titrate sildenafil dose based on clinical effect.
	RPV IM	↔ sildenafil expected	No dose adjustment needed
	RPV PO	↔ sildenafil AUC and C_{max}	No dose adjustment needed
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Triazolam	DOR, RPV IM, RPV PO	↔ alprazolam or triazolam expected	No dose adjustment needed
	EFV, ETR	↓ alprazolam or triazolam possible	Monitor for therapeutic effectiveness of benzodiazepine.
Diazepam	DOR, RPV IM, RPV PO	↔ diazepam expected	No dose adjustment needed
	EFV	↓ diazepam possible	Monitor for therapeutic effectiveness of diazepam.
	ETR	↑ diazepam possible	Decreased dose of diazepam may be necessary. Monitor for diazepam toxicity.
Lorazepam	DOR, ETR, RPV IM, RPV PO	↔ lorazepam expected	No dose adjustment needed
	EFV	↔ lorazepam AUC	No dose adjustment needed
Midazolam	DOR	↔ midazolam AUC	No dose adjustment needed
	EFV	↑ or ↓ midazolam possible	Monitor for therapeutic effectiveness and toxicity of midazolam.
	ETR	Midazolam AUC ↓ 31% Midazolam active metabolite C_{max} ↑ 57%	Monitor for therapeutic effectiveness of midazolam.
	RPV IM, RPV PO	↔ midazolam expected	No dose adjustment needed
Orexin Receptor Antagonists			
Daridorexant	DOR, RPV IM, RPV PO	↔ daridorexant expected	No dose adjustment needed
	EFV	Daridorexant AUC ↓ 61%	**Do not coadminister.**
	ETR	↓ daridorexant possible	

Table 24b. Drug Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Other Drugs

Concomitant Drug	NNRTI	Effect on NNRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lemborexant, Suvorexant	DOR, RPV IM, RPV PO	↔ lemborexant expected	No dose adjustment needed
	EFV, ETR	↓ lemborexant possible	**Do not coadminister.**
Other Sedatives			
Eszopiclone, Zolpidem	DOR, RPV IM, RPV PO	↔ eszopiclone or zolpidem expected	No dose adjustment needed
	EFV, ETR	↓ eszopiclone or zolpidem possible	Monitor for therapeutic effectiveness of sedative and titrate to clinical effect.
Miscellaneous			
Finerenone	DOR, RPV IM, RPV PO	↔ finerenone expected	No dose adjustment needed
	EFV, ETR	↓ finerenone expected	Consider alternative ARV or alternative to finerenone. If coadministration is necessary, monitor finerenone efficacy.
Praziquantel	DOR, RPV IM, RPV PO	↔ praziquantel expected	No dose adjustment needed
	EFV	R-praziquantel and S-praziquantel AUC ↓ 74% to 75%	**Do not coadminister**. If coadministration is necessary, consider alternative ARVs.
	ETR	↓ praziquantel possible	**Do not coadminister.** If coadministration is necessary, consider alternative ARVs.

[a] R-methadone is the active form of methadone.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ARV = antiretroviral; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CAB = cabotegravir; CCB = calcium channel blocker; DAA = direct-acting antiviral; DHA = dihydroartemisinin; DOAC = direct oral anticoagulants; DOR = doravirine; EFV = efavirenz; ETR = etravirine; IM = intramuscular; INR = international normalized ratio; isoniazid = isonicotinic acid hydrazide; MAC = *Mycobacterium avium* complex; MPA = medroxyprogesterone acetate; CMV = cytomegalovirus; NNRTI = non-nucleoside reverse transcriptase inhibitor; OH-itraconazole = active metabolite of itraconazole; PCP = *Pneumocystis jirovecii* pneumonia; PDE5 = phosphodiesterase type 5; PI/r = protease inhibitor/ritonavir; PO = orally; QTc = QT corrected for heart rate; RPV = rilpivirine

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between nucleoside reverse transcriptase inhibitors (NRTIs) and non-antiretroviral drugs.

Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

This table focuses on interactions with pharmacokinetic study data and interactions without study data but where there is a clinical recommendation. Interactions associated with zidovudine (ZDV) are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding drug interactions between ZDV and other drugs.

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Antimycobacterials			
Rifabutin	3TC, ABC, FTC,	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	**Use with caution.** If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed
Rifampin	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF With Rifampin Compared With TDF Alone** • TFV-DP AUC ↑ 4.2-fold **TAF With Rifampin Compared With TAF Alone** • TAF AUC ↓ 55% • TFV-DP AUC ↓ 36% **TAF 25 mg Twice Daily With Rifampin Compared With TAF Once Daily Alone** • TAF AUC ↓ 14% • TFV-DP AUC ↓ 24%	**Use with caution.** If coadministered, monitor virologic response. Intracellular TFV-DP levels are higher when TAF is coadministered with rifampin than when TDF is administered alone, but clinical outcomes have not been studied.
	TDF	↔ AUC TFV	No dose adjustment needed

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rifapentine	3TC, ABC, FTC,	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	**Use with caution.** If coadministered, monitor virologic response.
	TDF	↔ AUC TFV	No dose adjustment needed
Antiretrovirals			
Capsid Inhibitor			
LEN (SQ and PO)	3TC, ABC, FTC	↔ 3TC, ABC, FTC, LEN expected	No dose adjustment needed
	TAF	TAF AUC ↑ 32% ↔ LEN	No dose adjustment needed
	TDF	TDF AUC ↑ 47% ↔ LEN	No dose adjustment needed
INSTIs			
DTG	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↔ TAF AUC	No dose adjustment needed
	TDF	↔ TDF AUC ↔ DTG AUC	No dose adjustment needed
RAL	3TC, ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	RAL AUC ↑ 49%	No dose adjustment needed
PIs			
ATV/c, ATV/r	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF 10 mg With ATV/r** • TAF AUC ↑ 91% **TAF 10 mg With ATV/c** • TAF AUC ↑ 75%	No dose adjustment needed (use TAF 25 mg)
	TDF	**With ATV (Unboosted)** • ATV AUC ↓ 25% and C_{min} ↓ 23% to 40% (higher C_{min} with RTV than without RTV) • TFV AUC ↑ 24% to 37%	Use ATV 300 mg plus (RTV 100 mg or COBI 150 mg) daily when coadministering TDF 300 mg daily. If using TDF and an H2 receptor antagonist in an ART-experienced patient, use ATV 400 mg plus (RTV 100 mg or COBI 150 mg) daily. Monitor for TDF-associated toxicities.

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
DRV/c	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF 25 mg With DRV/c** • ↔ TAF	No dose adjustment needed
	TDF	TFV ↑ possible	Monitor for TDF-associated toxicities.
DRV/r	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	**TAF 10 mg With DRV/r** • ↔ TAF AUC	No dose adjustment needed
	TDF	TFV AUC ↑ 22% and C_{min} ↑ 37%	Clinical significance is unknown. If coadministered, monitor for TDF-associated toxicities.
Antiseizure			
Carbamazepine, Oxcarbazepine, Phenobarbital, Phenytoin	ABC	↑ carbamazepine possible ↓ ABC possible with oxcarbazepine, phenobarbital, phenytoin	No dose adjustment needed
	3TC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	**With Carbamazepine** • TAF AUC ↓ 55% • ↓ TAF possible with other anticonvulsants	**Do not coadminister.**
Antivirals—Hepatitis C			
Glecaprevir/Pibrentasvir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↔ TFV AUC	No dose adjustment needed
	TDF	TFV AUC ↑ 29%	No dose adjustment needed
Ledipasvir/Sofosbuvir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	TFV AUC ↑ 27%	No dose adjustment needed
	TDF	Ledipasvir ↑ TFV AUC 35% to 98% when TDF is given with various PIs and NNRTIs. Ledipasvir ↑ TFV C_{min} 55% to 80% when TDF is given with various PIs, NNRTIs, or INSTIs.	**Do not coadminister** with EVG/c, TDF, or FTC. If TDF is used, monitor for TDF toxicities. Consider using TAF in patients at risk of TDF-associated adverse events.

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		Further ↑ TFV AUC and C_{max} possible when TDF, ledipasvir/sofosbuvir, and PIs are coadministered.	Consider using TAF or alternative HCV therapy in patients on TDF plus a PI/r or PI/c. The safety of increased TFV exposure with this combination has not been established.
Ribavirin	3TC	↔ 3TC AUC	No dose adjustment needed
	ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	**Ribavirin With Sofosbuvir 400 mg** • ↔ TFV AUC	No dose adjustment needed
Sofosbuvir/Velpatasvir	3TC, ABC, FTC, TAF	↔ expected	No dose adjustment needed
	TDF	TFV C_{max} ↑ 44% to 46% and AUC ↑ 40% when coadministered with various ARV combinations.	If TDF is used in these patients, monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Sofosbuvir/Velpatasvir/ Voxilaprevir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	TAF AUC ↑ 52% to 57%	No dose adjustment needed
	TDF	TFV C_{max} ↑ 48% and AUC ↑ 39% when coadministered with various ARV combinations.	Monitor for TDF-related toxicities. Consider using TAF in patients at risk of TDF-related adverse events.
Antivirals—Miscellaneous (e.g., for Herpesvirus, CMV, HBV, Mpox)			
Adefovir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF	↑ TFV possible	**Do not coadminister.** Serum concentrations of TDF and/or other renally eliminated drugs may increase.
	TDF	↔ TFV	**Do not coadminister.**
Brincidofovir	3TC, ABC, FTC, TAF, TDF	↔ brincidofovir expected	No dose adjustment needed
Cidofovir	3TC, ABC, FTC, TAF	↔ cidofovir expected	No dose adjustment needed
	TDF	↑ TDF and cidofovir possible	Potential for renal toxicity when TDF is given with a nephrotoxic agent, such as cidofovir. If concomitant use is necessary, closely monitor renal function.

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Famciclovir	3TC, ABC, TAF, TDF	↔ expected	No dose adjustment needed
	FTC	↔ AUC FTC, famciclovir	No dose adjustment needed
Ganciclovir, Valganciclovir	3TC, ABC, FTC	↔ expected	No dose adjustment needed
	TAF, TDF	↑ ganciclovir or TFV possible	Monitor for dose-related toxicities.
Tecovirimat	3TC, ABC, FTC, TAF, TDF	↔ tecovirimat expected	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
Remdesivir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	3TC, ABC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
Hormonal Therapies—Contraceptives			
Injectable Contraceptives Depot MPA	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC, TDF	↔ FTC AUC ↔ TFV AUC	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norelgestromin, norgestimate, norgestrel)	3TC, ABC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	↔ ethinyl estradiol AUC ↔ norelgestromin AUC ↔ norgestrel AUC	No dose adjustment needed
Hormonal Therapies—Menopause			
17-β-estradiol	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC	FTC AUC ↓ 14% to 24%	
	TDF	TFV AUC ↓ 12% to 27%	

Table 24c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug	NRTI	Effect on NRTI and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Estradiol Valerate	3TC, ABC, TAF	↔ expected	No dose adjustment needed
	FTC	↔ FTC AUC ↔ estradiol AUC	
	TDF	↔ TFV AUC ↔ estradiol	
Narcotics and Treatment for Opioid Dependence			
Buprenorphine	ABC, FTC	↔ expected	No dose adjustment needed
	3TC, TDF	↔ 3TC, TDF, and buprenorphine	No dose adjustment needed
	TAF	↔ TAF expected	No dose adjustment needed
Methadone	3TC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
	ABC	Methadone clearance ↑ 22%	No dose adjustment needed
Miscellaneous			
Ethanol	ABC	ABC AUC ↑ 41%	No dose adjustment needed
Riociguat	3TC, FTC, TAF, TDF	↔ expected	No dose adjustment needed
	ABC	Riociguat AUC ↑ 200%	If coadministered, initiate riociguat at 0.5 mg three times daily and monitor for riociguat-related adverse effects (e.g., hypotension).
St. John's Wort	3TC, ABC, FTC, TDF	↔ expected	No dose adjustment needed
	TAF	↓ TAF possible	**Do not coadminister.**

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; COBI = cobicistat; CMV = cytomegalovirus; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; HBV = hepatitis B virus; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MPA = medroxyprogesterone acetate; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; PO: oral; RAL = raltegravir; RTV = ritonavir; SQ = subcutaneous; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; TFV-DP = tenofovir diphosphate

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between integrase strand transfer inhibitors (INSTIs) (bictegravir [BIC], dolutegravir [DTG], elvitegravir [EVG], or raltegravir [RAL]) and non-antiretroviral drugs. EVG is always coadministered with cobicistat (COBI or c). Cabotegravir (CAB) intramuscular (IM) plus rilpivirine (RPV) IM are co-packaged into a single product and are coadministered as a complete regimen; therefore, the dosing recommendations and clinical comments reflect the combination of CAB IM and RPV IM treatments. Because drug interaction studies were not conducted with either IM CAB or RPV, dosing recommendations for the IM formulations are based on drug interaction studies using oral CAB and RPV. For information regarding interactions between INSTIs and other antiretroviral (ARV) drugs, including dosing recommendations, refer to Tables 24c, 24e, 24f, and 25b.

Recommendations for managing a particular drug interaction may differ, depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers			
Al, Mg **+/–** **Ca-Containing Antacids** Please refer to the Miscellaneous Drugs section of this table for recommendations on use with other polyvalent cation products (e.g., Fe and Ca supplements, multivitamins).	BIC	**Al/Mg Hydroxide Antacid** • ↔ BIC AUC if antacid is administered 2 hours after BIC and under fasting conditions • BIC AUC ↓ 52% if antacid is administered 2 hours before BIC • BIC AUC ↓ 47% to 79% if administered simultaneously with antacid **$CaCO_3$ Antacid** • ↔ BIC AUC if administered with food • BIC AUC ↓ 33% if administered under fasting conditions	**With Antacids That Contain Al/Mg** • Administer antacids that contain Al/Mg at least 2 hours after or 6 hours before BIC. **With Antacids That Contain Ca** • Administer BIC and antacids that contain Ca together with food. • **Do not coadminister** BIC simultaneously with antacids that contain Ca on an empty stomach.
	CAB PO	CAB PO ↓ expected	**With Antacids That Contain Polyvalent Cations (Al, Mg, or Ca)** • Administer antacid products at least 2 hours before or 4 hours after taking CAB PO.
	CAB IM	↔ CAB IM expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DTG	DTG AUC ↓ 74% if administered simultaneously with antacid DTG AUC ↓ 26% if administered 2 hours before antacid	Administer DTG at least 2 hours before or at least 6 hours after antacids that contain polyvalent cations.
	EVG/c	EVG AUC ↓ 40% to 50% if administered simultaneously with antacid EVG AUC ↓ 15% to 20% if administered 2 hours before or after antacid; ↔ with a 4-hour interval	Separate EVG/c and antacid administration by more than 2 hours.
	RAL	**Al/Mg Hydroxide Antacid** • RAL C_{min} ↓ 49% to 63% **$CaCO_3$ Antacid** • RAL 400 mg twice daily: C_{min} ↓ 32% • RAL 1,200 mg once daily: C_{min} ↓ 48% to 57%	**Do not coadminister** RAL and Al/Mg hydroxide antacids. Use alternative acid-reducing agent. **With $CaCO_3$ Antacids** • RAL 1,200 mg once daily: **Do not coadminister.** • RAL 400 mg twice daily: No dose adjustment or separation needed
H2-Receptor Antagonists	BIC, CAB (PO and IM), DTG, EVG/c	↔ INSTI	No dose adjustment needed
	RAL	RAL AUC ↑ 44% and C_{max} ↑ 60%	No dose adjustment needed
Proton Pump Inhibitors	BIC, CAB (PO and IM), DTG, EVG/c	↔ INSTI	No dose adjustment needed
	RAL	RAL AUC ↑ 37% and C_{min} ↑ 24%	No dose adjustment needed
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia			
Alfuzosin	BIC, CAB (PO and IM), DTG, RAL	↔ alfuzosin expected	No dose adjustment needed
	EVG/c	↑ alfuzosin expected	**Contraindicated**
Doxazosin	BIC, CAB (PO and IM), DTG, RAL	↔ doxazosin expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ doxazosin possible	Initiate doxazosin at lowest dose. Titrate based on doxazosin efficacy. Monitor blood pressure. Doxazosin dose reduction may be needed.
Tamsulosin	BIC, CAB (PO and IM), DTG, RAL	↔ tamsulosin expected	No dose adjustment needed
	EVG/c	↑ tamsulosin expected	**Do not coadminister** unless the benefits outweigh the risks. If coadministered, monitor blood pressure.
Terazosin	BIC, CAB (PO and IM), DTG, RAL	↔ terazosin expected	No dose adjustment needed
	EVG/c	↑ terazosin possible	Initiate terazosin at lowest dose. Titrate based on terazosin efficacy. Monitor blood pressure. Terazosin dose reduction may be necessary.
Silodosin	BIC, CAB (PO and IM), DTG, RAL	↔ silodosin expected	No dose adjustment needed
	EVG/c	↑ silodosin expected	**Contraindicated**
Antibacterials—Antimycobacterials			
Bedaquiline	BIC, CAB (PO and IM), DTG, RAL	↔ bedaquiline	No dosage adjustment needed
	EVG/c	↑ bedaquiline possible	**Do not coadminister** unless benefits outweigh risks. If coadministered, consider therapeutic drug monitoring and monitor for bedaquiline-related adverse effects, including hepatotoxicity and QTc prolongation.
Rifabutin	BIC	**Rifabutin 300 mg Once Daily** • BIC AUC ↓ 38% and C_{min} ↓ 56%	**Do not coadminister.**
	CAB PO	CAB PO AUC ↓ 23% and C_{min} ↓ 26% ↔ rifabutin	No dose adjustment needed
	CAB IM	↓ CAB IM and RPV expected ↔ rifabutin expected	**Contraindicated** due to ↓ RPV, which is co-packaged and coadministered with CAB IM.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DTG	**Rifabutin 300 mg Once Daily** • ↔ DTG AUC and C_{min} ↓ 30%	No dose adjustment needed
	EVG/c	**Rifabutin 150 mg Every Other Day With EVG/c Once Daily Compared to Rifabutin 300 mg Once Daily Alone** • ↔ rifabutin AUC • 25-O-desacetyl-rifabutin AUC ↑ 625% • EVG AUC ↓ 21% and C_{min} ↓ 67%	**Do not coadminister.**
	RAL	↔ RAL AUC and C_{min} ↓ 20%	No dose adjustment needed
Rifampin	BIC	BIC AUC ↓ 75%	**Contraindicated**
	CAB PO	CAB PO AUC ↓ 59% and C_{min} ↓ 50%	**Contraindicated**
	CAB IM	CAB IM ↓ expected	**Contraindicated**
	DTG	**Rifampin With DTG 50 mg Twice Daily Compared to DTG 50 mg Twice Daily Alone** • DTG AUC ↓ 54% and C_{min} ↓ 72% **Rifampin With DTG 50 mg Twice Daily Compared to DTG 50 mg Once Daily Alone** • DTG AUC ↑ 33% and C_{min} ↑ 22%	Use DTG 50 mg twice daily (instead of DTG 50 mg once daily) in patients without suspected or documented INSTI-associated resistance mutations. Consider an alternative to rifampin, such as rifabutin, in patients with certain suspected or documented INSTI-associated resistance mutations.
	EVG/c	Significant ↓ EVG and COBI expected	**Contraindicated**
	RAL	**RAL 400 mg** • RAL AUC ↓ 40% and C_{min} ↓ 61% **Rifampin With RAL 800 mg Twice Daily Compared to RAL 400 mg Twice Daily Alone** • RAL AUC ↑ 27% and C_{min} ↓ 53%	Use RAL 800 mg twice daily instead of 400 mg twice daily. **Do not coadminister** RAL 1,200 mg once daily with rifampin. Monitor closely for virologic response or consider using rifabutin as an alternative rifamycin.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Rifapentine	BIC, EVG/c	Significant ↓ BIC, EVG, and COBI expected	**Do not coadminister.**
	CAB (PO and IM)	Significant ↓ CAB (PO and IM) expected	**Contraindicated**
	DTG	**Rifapentine 900 mg Once Weekly** • DTG AUC ↓ 26% and C_{min} ↓ 47% **Rifapentine 600 mg Once Daily With DTG 50 mg Twice Daily vs DTG 50 mg Once Daily Alone** • ↔ DTG AUC and C_{min}	With **once-weekly** rifapentine, DTG 50 mg daily may be used in patients with viral suppression on daily DTG. Monitor for virologic efficacy. **Do not coadminister** in patients who require twice-daily DTG. With **once-daily** rifapentine for 4 weeks (1HP), use DTG 50 mg twice daily. See Tuberculosis/HIV Coinfection for more on rifapentine and DTG use.
	RAL	**Rifapentine 900 mg Once Weekly** • RAL AUC ↑ 71% and C_{min} ↓ 12% **Rifapentine 600 mg Once Daily** • RAL C_{min} ↓ 41%	For once-weekly rifapentine and RAL 400 mg twice daily, no dose adjustment is needed. **Do not coadminister** with once-daily rifapentine.
Antibacterials—Macrolides			
Azithromycin	All INSTIs	↔ azithromycin expected	No dose adjustment needed
Clarithromycin	BIC	↑ BIC possible	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ clarithromycin expected	No dose adjustment needed
	EVG/c	↑ clarithromycin expected ↑ COBI possible	Reduce clarithromycin dose by 50% in patients with CrCl 50 to 60 mL/min. **Do not coadminister** in patients with CrCl <50 mL/min. Consider alternative ARV or use azithromycin.
Erythromycin	BIC	↑ BIC possible	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ erythromycin expected	No dose adjustment needed
	EVG/c	↑ erythromycin expected ↑ COBI possible	No data available for dose recommendation. Consider alternative ARV or use azithromycin.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Anticoagulants			
Apixaban	BIC, CAB (PO and IM), DTG, RAL	↔ apixaban expected	No dose adjustment needed
	EVG/c	↑ apixaban expected	**Do not coadminister** in patients who require apixaban 2.5 mg twice daily. Reduce apixaban dose by 50% in patients who require apixaban 5 mg or 10 mg twice daily.
Dabigatran	BIC, CAB (PO and IM), DTG, RAL	↔ dabigatran expected	No dose adjustment needed
	EVG/c	↑ dabigatran expected **With COBI 150 mg Alone** • Dabigatran AUC ↑ 110% to 127%	**Reduction of Risk of Stroke and Systemic Embolism in Nonvalvular Atrial Fibrillation in Adult Patients** • CrCl >30 mL/min: no dose adjustment needed • CrCl ≤30 mL/min: **do not coadminister.** **Treatment and Reduction in the Risk of Recurrence of DVT and PE or Prophylaxis of DVT and PE Following Hip Replacement Surgery in Adult Patients** • CrCl ≥50 mL/min: no dose adjustment needed • CrCl <50 mL/min: **do not coadminister.**
Edoxaban	BIC, CAB (PO and IM), DTG, RAL	↔ edoxaban expected	No dose adjustment needed
	EVG/c	↑ edoxaban expected	**Stroke Prevention in Nonvalvular Atrial Fibrillation** • No dose adjustment needed **DVT and PE** • Administer edoxaban 30 mg once daily.
Rivaroxaban	BIC, CAB (PO and IM), DTG, RAL	↔ rivaroxaban expected	No dose adjustment needed
	EVG/c	↑ rivaroxaban expected	**Do not coadminister.**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Warfarin	BIC, CAB (PO and IM), DTG, RAL	↔ warfarin expected	No dose adjustment needed
	EVG/c	↑ or ↓ warfarin possible	Monitor INR and adjust warfarin dose accordingly.
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below			
Antidepressants, Anxiolytics			
Bupropion	BIC, CAB (PO and IM), DTG, RAL	↔ bupropion expected	No dose adjustment needed
	EVG/c	↑ bupropion possible	Titrate bupropion dose based on clinical response.
Buspirone	BIC, CAB (PO and IM), DTG, RAL	↔ buspirone expected	No dose adjustment needed
	EVG/c	↑ buspirone possible	Initiate buspirone at a low dose. Buspirone dose reduction may be needed.
Desvenlafaxine	All INSTIs	↔ desvenlafaxine expected	No dose adjustment needed
Duloxetine	BIC, CAB (PO and IM), DTG, RAL	↔ duloxetine expected	No dose adjustment needed
	EVG/c	↑ duloxetine possible	No dose adjustment needed
Mirtazapine	BIC, CAB (PO and IM), DTG, RAL	↔ mirtazapine expected	No dose adjustment needed
	EVG/c	↑ mirtazapine possible	Monitor for mirtazapine-related adverse events. Mirtazapine dose reduction may be necessary.
Nefazodone	BIC, CAB (PO and IM), DTG, RAL	↔ nefazodone expected	No dose adjustment needed
	EVG/c	↑ nefazodone expected	Consider alternative ARV or antidepressant.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Trazodone	BIC, CAB (PO and IM), DTG, RAL	↔ trazodone expected	No dose adjustment needed
	EVG/c	↑ trazodone possible	Titrate dose based on antidepressant response and monitor for trazodone-related adverse events.
Tricyclic Antidepressants (e.g., amitriptyline, desipramine, doxepin, imipramine, nortriptyline)	BIC, CAB (PO and IM), DTG, RAL	↔ TCA expected	No dose adjustment needed
	EVG/c	Desipramine AUC ↑ 65%	Initiate with lowest dose of TCA and titrate dose carefully.
		↑ TCA expected	Initiate with lowest dose of TCA. Titrate dose carefully based on antidepressant response and/or drug concentrations.
Selective Serotonin Reuptake Inhibitors (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	EVG/c	↔ sertraline	No dose adjustment needed
	EVG/c	↑ other SSRIs possible	Initiate with lowest dose of SSRI. Titrate dose carefully based on antidepressant response.
	BIC, CAB (PO and IM), DTG, RAL	↔ SSRI expected	No dose adjustment needed
Venlafaxine	BIC, CAB (PO and IM), DTG, RAL	↔ venlafaxine expected	No dose adjustment needed
	EVG/c	↑ venlafaxine possible	Monitor for venlafaxine-related adverse events.
Antipsychotics			
Aripiprazole	BIC, CAB (PO and IM), DTG, RAL	↔ aripiprazole expected	No dose adjustment needed
	EVG/c	↑ aripiprazole expected	Administer 25% of the usual aripiprazole dose. Titrate based on aripiprazole effectiveness and adverse events. Refer to aripiprazole label for dosing recommendations in patients who are known to be CYP2D6-poor metabolizers or who have major depressive disorder.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Brexpiprazole	BIC, CAB (PO and IM), DTG, RAL	↔ brexpiprazole expected	No dose adjustment needed
	EVG/c	↑ brexpiprazole expected	Administer 25% of the usual brexpiprazole dose. Titrate based on brexpiprazole effectiveness and adverse events. Refer to brexpiprazole label for dosing recommendations in patients who are known to be CYP2D6-poor metabolizers or who have major depressive disorder.
Cariprazine	BIC, CAB (PO and IM), DTG, RAL	↔ cariprazine expected	No dose adjustment needed
	EVG/c	↑ cariprazine expected	**Starting Cariprazine in a Patient Who Is Already Receiving EVG/c** • Administer cariprazine 1.5 mg on Day 1 and Day 3, with no dose given on Day 2. From Day 4 onward, administer cariprazine 1.5 mg daily. Dose can be increased to a maximum of cariprazine 3 mg daily. If EVG/c is withdrawn, cariprazine dose may need to be increased. **Starting EVG/c in a Patient Who Is Already Receiving Cariprazine** • For patients receiving cariprazine 3 mg or cariprazine 6 mg daily, reduce the dose by half. For patients receiving cariprazine 4.5 mg daily, reduce dose to cariprazine 1.5 mg or cariprazine 3 mg daily. For patients receiving cariprazine 1.5 mg daily, change to cariprazine 1.5 mg every other day. If EVG/c is withdrawn, cariprazine dose may need to be increased.
Iloperidone	BIC, CAB (PO and IM), DTG, RAL	↔ iloperidone expected	No dose adjustment needed
	EVG/c	↑ iloperidone expected	Decrease iloperidone dose by 50%.
Lumateperone	BIC, CAB (PO and IM), DTG, RAL	↔ lumateperone expected	No dose adjustment needed
	EVG/c	↑ lumateperone expected	**Do not coadminister.**
Lurasidone	BIC, CAB (PO and IM), DTG, RAL	↔ lurasidone expected	No dose adjustment needed
	EVG/c	↑ lurasidone expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Olanzapine, Olanzapine/ Samidorphan	All INSTIs	↔ olanzapine expected	No dose adjustment needed
	EVG/c	↔ olanzapine expected ↑ samidorphan possible	No dose adjustment needed
Other Antipsychotics CYP3A4 and/or CYP2D6 substrates (e.g., perphenazine, risperidone, thioridazine)	EVG/c	↑ antipsychotic possible	Initiate antipsychotic at a low dose. Antipsychotic dose reduction may be needed.
Pimavanserin	BIC, CAB (PO and IM), DTG, RAL	↔ pimavanserin expected	No dose adjustment needed
	EVG/c	↑ pimavanserin expected	Reduce pimavanserin dose to 10 mg.
Pimozide	BIC, CAB (PO and IM), DTG, RAL	↔ pimozide expected	No dose adjustment needed
	EVG/c	↑ pimozide expected	**Contraindicated**
Quetiapine	BIC, CAB (PO and IM), DTG, RAL	↔ quetiapine expected	No dose adjustment needed
	EVG/c	↑ quetiapine AUC expected	**Starting Quetiapine in a Patient Receiving EVG/c** • Start quetiapine at the lowest dose and titrate up as needed. Monitor for quetiapine efficacy and adverse events. **Starting EVG/c in a Patient Receiving a Stable Dose of Quetiapine** • Reduce quetiapine dose to 1/6 of the current dose. Closely monitor for quetiapine efficacy and adverse events.
Ziprasidone	BIC, CAB (PO and IM), DTG, RAL	↔ ziprasidone expected	No dose adjustment needed
	EVG/c	↑ ziprasidone possible	Monitor for ziprasidone-related adverse events.
Antifungals			
Ibrexafungerp	BIC, CAB (PO and IM), DTG, RAL	↔ ibrexafungerp expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ ibrexafungerp expected	Reduce ibrexafungerp dose to 150 mg twice daily.
Isavuconazole	BIC, CAB (PO and IM), DTG, RAL	↑ INSTI possible	No dose adjustment needed
	EVG/c	↑ isavuconazole expected ↑ or ↓ EVG and COBI possible	**Contraindicated**
Itraconazole	BIC	↑ BIC expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ itraconazole expected	No dose adjustment needed
	EVG/c	↑ itraconazole expected ↑ EVG and COBI possible	Consider monitoring itraconazole concentrations to guide dose adjustments. **Do not coadminister** with high itraconazole doses (>200 mg/day) unless guided by itraconazole concentrations.
Posaconazole	BIC	↑ BIC expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ posaconazole expected	No dose adjustment needed
	EVG/c	↑ EVG and COBI possible ↑ posaconazole possible	If coadministered, monitor posaconazole concentrations.
Voriconazole	BIC	↑ BIC possible	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ voriconazole expected	No dose adjustment needed
	EVG/c	↑ voriconazole expected ↑ EVG and COBI possible	**Do not coadminister** voriconazole and COBI, unless the benefit outweighs the risk. If coadministered, consider monitoring voriconazole concentrations and adjust dose accordingly.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimalarials			
Artemether/ Lumefantrine	BIC	↔ antimalarial expected	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ antimalarial expected	No dose adjustment needed
	EVG/c	↑ artemether and lumefantrine possible	Monitor for artemether and lumefantrine-related adverse events, including QTc prolongation.
Artesunate	All INSTIs	↔ dihydroartemisinin expected	No dose adjustment needed
Atovaquone/ Proguanil	All INSTIs	↔ atovaquone/proguanil expected	No dose adjustment needed
Mefloquine	CAB (PO and IM), DTG, RAL	↔ mefloquine expected	No dose adjustment needed
	EVG/c	↑ mefloquine possible	Monitor for mefloquine-related adverse events, including psychiatric symptoms and QTc prolongation.
Antimigraine			
Ergot Derivatives	BIC, CAB (PO and IM), DTG, RAL	↔ dihydroergotamine, ergotamine, and methylergonovine expected	No dose adjustment needed
	EVG/c	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Contraindicated**
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists			
Atogepant	BIC, CAB (PO and IM), DTG, RAL	↔ atogepant expected ↑ atogepant expected	No dose adjustment needed
	EVG/c	↑ atogepant expected	Chronic migraine: **Do not coadminister.** Episodic migraine: Administer atogepant at a dose of 10 mg once daily.
Rimegepant	BIC, CAB (PO and IM), DTG, RAL	↔ rimegepant expected	No dose adjustment needed
	EVG/c	↑ rimegepant expected	**Do not coadminister.**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ubrogepant	BIC, CAB (PO and IM), DTG, RAL	↔ ubrogepant expected	No dose adjustment needed
	EVG/c	↑ ubrogepant expected	**Contraindicated**
Zavegepant	BIC, CAB (PO and IM), DTG, RAL	↔ zavegepant expected	No dose adjustment needed
	EVG/c	↑ zavegepant expected	**Do not coadminister.**
Serotonin 5-HT1B, 1D Receptor Agonist			
Almotriptan	BIC, CAB (PO and IM), DTG, RAL	↔ almotriptan expected	No dose adjustment needed
	EVG/c	↑ almotriptan expected	Administer single dose of almotriptan 6.25 mg. Maximum dose should not exceed 12.5 mg in a 24-hour period.
Eletriptan	BIC, CAB (PO and IM), DTG, RAL	↔ eletriptan expected	No dose adjustment needed
	EVG/c	↑ eletriptan expected	**Contraindicated**
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan Zolmitriptan	All INSTIs	↔ triptan expected	No dose adjustment needed
Antiplatelets			
Clopidogrel	BIC, CAB (PO and IM), DTG, RAL	↔ clopidogrel expected	No dose adjustment needed
	EVG/c	↓ clopidogrel active metabolite, with impaired platelet inhibition expected	**Do not coadminister.**
Prasugrel	BIC, CAB (PO and IM), DTG, RAL	↔ prasugrel expected	No dose adjustment needed
	EVG/c	↓ prasugrel active metabolite, with no impairment of platelet inhibition expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ticagrelor	BIC, CAB (PO and IM), DTG, RAL	↔ ticagrelor expected	No dose adjustment needed
	EVG/c	↑ ticagrelor expected	**Do not coadminister.**
Vorapaxar	BIC, CAB (PO and IM) DTG, RAL	↔ vorapaxar expected	No dose adjustment needed
	EVG/c	↑ vorapaxar expected	**Do not coadminister.**
Antipneumocystis and Antitoxoplasmosis			
Atovaquone	All INSTIs	↔ atovaquone expected	No dose adjustment needed
Antiseizure			
Carbamazepine	BIC	↓ BIC possible	**Do not coadminister.**
	CAB (PO and IM)	↓ CAB expected	**Contraindicated**
	DTG	DTG AUC ↓ 49%	Increase DTG dose to 50 mg twice daily in ART-naive or ART-experienced (but INSTI-naive) patients. **Do not coadminister** in INSTI-experienced patients with known or suspected INSTI resistance.
	EVG/c	Carbamazepine AUC ↑ 43% EVG AUC ↓ 69% and C_{min} ↓ >99% ↓ COBI expected	**Contraindicated**
	RAL	↓ or ↔ RAL possible	**Do not coadminister.**
Eslicarbazepine	All INSTIs	↓ INSTI possible ↓ COBI possible	Consider alternative ARV or anticonvulsant.
Ethosuximide	BIC, CAB (PO and IM), DTG, RAL	↔ ethosuximide expected	No dose adjustment needed
	EVG/c	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events.
Lamotrigine	BIC, CAB (PO and IM), DTG, RAL	↔ lamotrigine expected	No dose adjustment needed
	EVG/c	No data	Monitor anticonvulsant concentrations and adjust dose accordingly.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Oxcarbazepine	BIC, DTG	↓ BIC and DTG possible	**Do not coadminister.**
	CAB (PO and IM)	↓ CAB expected	**Contraindicated**
	EVG/c, RAL	↓ EVG/c and RAL possible	Consider alternative ARV or anticonvulsant.
Phenobarbital, Phenytoin, Primidone	BIC, DTG, RAL	↓ BIC and DTG possible ↓ or ↔ RAL possible	**Do not coadminister.**
	CAB (PO and IM), EVG/c	↓ CAB and EVG/c expected	**Contraindicated**
Valproic Acid	DTG	DTG ↓ possible	No dose adjustment needed. Take with food and monitor virologic response.
	BIC, CAB (PO and IM), RAL	No data	No dose adjustment needed. Monitor virologic response.
Antivirals—Hepatitis C			
Elbasvir/ Grazoprevir	BIC	↔ BIC expected	No dose adjustment needed
	CAB (PO and IM)	↔ CAB, elbasvir, and grazoprevir expected	No dose adjustment needed
	DTG	↔ DTG ↔ elbasvir ↔ grazoprevir	No dose adjustment needed
	EVG/c	↑ elbasvir expected ↑ grazoprevir expected	**Do not coadminister.**
	RAL	↔ RAL with elbasvir RAL AUC ↑ 43% with grazoprevir ↔ elbasvir ↔ grazoprevir	No dose adjustment needed
Glecaprevir/ Pibrentasvir	BIC, CAB (PO and IM)	↔ BIC or CAB expected	No dose adjustment needed
	DTG	↔ DTG and glecaprevir/ pibrentasvir	No dose adjustment needed
	RAL	No significant effect RAL AUC ↑ 47%	

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	Glecaprevir AUC ↑ 3-fold Pibrentasvir AUC ↑ 57% EVG AUC ↑ 47%	No dose adjustment needed If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.
Ledipasvir/ Sofosbuvir	BIC, DTG, RAL	↔ BIC, DTG, and RAL	No dose adjustment needed
	CAB (PO and IM)	↔ CAB expected	No dose adjustment needed
	EVG/c/ TDF/FTC	↑ TDF expected ↑ ledipasvir expected	**Do not coadminister.**
	EVG/c/ TAF/FTC	↔ EVG/c/TAF/FTC expected	No dose adjustment needed
Sofosbuvir	BIC, CAB (PO and IM), DTG, EVG/C	↔ INSTI expected ↔ sofosbuvir expected	No dose adjustment needed
	RAL	↔ RAL and sofosbuvir	No dose adjustment needed
Sofosbuvir/ Velpatasvir	BIC, DTG, RAL	↔ sofosbuvir and velpatasvir	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events.
	CAB (PO and IM)	↔ CAB expected ↔ sofosbuvir and velpatasvir expected	
	EVG/c	↔ EVG/c/TAF/FTC Velpatasvir AUC ↑ 50%	
Sofosbuvir/ Velpatasvir/ Voxilaprevir	BIC	**When Administered With Sofosbuvir/Velpatasvir/ Voxilaprevir (400 mg/ 100 mg/100 mg) Plus Voxilaprevir 100 mg** • ↔ BIC, sofosbuvir, velpatasvir, voxilaprevir	No dose adjustment needed
	EVG/c	**When Administered With Sofosbuvir/Velpatasvir/ Voxilaprevir (400 mg/ 100 mg/100 mg) Plus Voxilaprevir 100 mg** • Sofosbuvir AUC ↑ 22% • ↔ velpatasvir • Voxilaprevir AUC ↑ 2-fold	No dose adjustment needed. If coadministered with TDF, monitor for TDF-related adverse events. Consider monitoring for hepatotoxicity if coadministered with TDF or TAF.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ sofosbuvir, velpatasvir, and voxilaprevir expected	No dose adjustment needed
Antivirals—Miscellaneous (e.g., for CMV, Mpox)			
Brincidofovir	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected	No dose adjustment needed
	EVG/c	↑ brincidofovir possible ↑ EVG possible	Administer EVG/c dose at least 3 hours after administering brincidofovir and monitor for brincidofovir-related adverse events, including elevations in ALT/AST and bilirubin and GI adverse events.
Cidofovir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI expected ↔ cidofovir expected	No dose adjustment needed
Tecovirimat	CAB (IM)	↔ CAB expected	No dose adjustment needed Do not initiate CAB/RPV IM during or within 2 weeks after tecovirimat treatment. (Refer to Table 24b for interaction with RPV.)
	BIC, CAB (PO), DTG, EVG/c, RAL	↔ INSTI expected	No dose adjustment needed
Antivirals—SARS-CoV-2			
Molnupiravir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI and molnupiravir expected	No dose adjustment needed
Ritonavir-boosted Nirmatrelvir	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI and ritonavir-boosted nirmatrelvir expected	No dose adjustment needed.
	EVG/c/ FTC/TAF	↑ TAF possible ↔ ritonavir-boosted nirmatrelvir expected	No dose adjustment needed
Remdesivir	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ INSTI and remdesivir expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Beta-Agonists, Long-Acting Inhaled			
Arformoterol, Formoterol	All INSTIs	↔ arformoterol or formoterol expected	No dose adjustment needed
Indacaterol	BIC, CAB (PO and IM), DTG, RAL	↔ indacaterol expected	No dose adjustment needed
	EVG/c	↑ indacaterol expected	
Olodaterol	BIC, CAB (PO and IM), DTG, RAL	↔ olodaterol expected	No dose adjustment needed
	EVG/c	↑ olodaterol expected	
Salmeterol	BIC, CAB (PO and IM), DTG, RAL	↔ salmeterol expected	No dose adjustment needed
	EVG/c	↑ salmeterol possible	**Do not coadminister** due to the potential for increased risk of salmeterol-associated cardiovascular events.
Cardiac Medications			
Antiarrhythmics			
Amiodarone	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ amiodarone expected	No dose adjustment needed
	EVG/c	↑ amiodarone expected	**Do not coadminister** unless the benefits outweigh the risks. If coadministration is necessary, monitor for amiodarone-related adverse events and consider monitoring ECG and amiodarone concentrations.
Digoxin	BIC, CAB (PO and IM), RAL	↔ digoxin expected	No dose adjustment needed
	EVG/c	Digoxin C_{max} ↑ 41% and ↔ AUC	Therapeutic drug monitoring for digoxin is recommended if available.
Dofetilide	CAB (PO and IM)	↔ dofetilide expected	No dose adjustment needed
	BIC, DTG	↑ dofetilide expected	**Contraindicated**
	EVG/c	↑ dofetilide possible	**Do not coadminister.**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Disopyramide	BIC, CAB (PO and IM), RAL	↔ disopyramide expected	No dose adjustment needed
	DTG	↑ disopyramide possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor disopyramide concentrations and for antiarrhythmic-related adverse events.
	EVG/c	↑ disopyramide expected	**Do not coadminister.**
Dronedarone	BIC, CAB (PO and IM), DTG, RAL	↔ dronedarone expected	No dose adjustment needed
	EVG/c	↑ dronedarone expected	**Contraindicated**
Flecainide	BIC, CAB (PO and IM), DTG, RAL	↔ flecainide expected	No dose adjustment needed
	EVG/c	↑ flecainide possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor flecainide concentrations and for antiarrhythmic-related adverse events.
Propafenone	BIC, CAB (PO and IM), DTG, RAL	↔ propafenone expected	No dose adjustment needed
	EVG/c	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor propafenone concentrations and for antiarrhythmic-related adverse events.
Mexiletine	BIC, CAB (PO and IM), DTG, RAL	↔ mexiletine expected	No dose adjustment needed
	EVG/c	↑ mexiletine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor mexiletine concentrations and for antiarrhythmic-related adverse events.
Systemic Lidocaine	BIC, CAB (PO and IM), DTG, RAL	↔ lidocaine expected	No dose adjustment needed
	EVG/c	↑ lidocaine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor lidocaine concentrations and for antiarrhythmic-related adverse events.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Quinidine	BIC, CAB (PO and IM), DTG, RAL	↔ quinidine expected	No dose adjustment needed
	EVG/c	↑ quinidine possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor quinidine concentrations and for antiarrhythmic-related adverse events.
Beta-Blockers			
Atenolol, Bisoprolol, Carvedilol, Metoprolol, Nadolol, Nebivolol, Sotalol	CAB (PO and IM), RAL	↔ beta-blocker expected	No dose adjustment needed
	BIC, DTG, EVG/c	↑ beta-blocker possible	Beta-blocker dose may need to be decreased; adjust dose based on clinical response.
Calcium Channel Blockers			
Calcium Channel Blockers	BIC	↑ BIC possible with diltiazem ↔ expected for all other CCBs	No dose adjustment needed
	CAB (PO and IM), DTG, RAL	↔ CCB expected	No dose adjustment needed
	EVG/c	↑ CCB possible	Titrate CCB dose and monitor for CCB efficacy and adverse events.
Cardiac—Other			
Bosentan	BIC, DTG	↓ BIC and DTG possible	No dose adjustment needed
	CAB (PO and IM)	↔ bosentan expected	Consider using alternative ARV or an alternative to bosentan because bosentan may ↓ RPV, which is co-packaged and coadministered with CAB IM. If bosentan is used with RPV, monitor virologic response to ART.
	RAL	↔ bosentan expected	No dose adjustment needed
	EVG/c	↑ bosentan possible	**In Patients on EVG/c ≥10 Days** • Start bosentan at 62.5 mg once daily or every other day based on individual tolerability. **In Patients on Bosentan Who Require EVG/c** • Stop bosentan ≥36 hours before EVG/c initiation. At least 10 days after initiation of EVG/c, resume bosentan at 62.5 mg once daily or every other day based on individual tolerability.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Eplerenone	BIC, CAB (PO and IM), DTG, RAL	↔ eplerenone expected	No dose adjustment needed
	EVG/c	↑ eplerenone expected	**Contraindicated**
Ivabradine	BIC, CAB (PO and IM), DTG, RAL	↔ ivabradine expected	No dose adjustment needed
	EVG/c	↑ ivabradine expected	**Contraindicated**
Mavacamten	BIC, CAB (PO and IM), DTG, RAL	↔ mavacamten expected	No dose adjustment needed
	EVG/c	↑ mavacamten expected	**Contraindicated**
Ranolazine	BIC, CAB (PO and IM), DTG, RAL	↔ ranolazine expected	No dose adjustment needed
	EVG/c	↑ ranolazine expected	**Contraindicated**
Corticosteroids			
Beclomethasone Inhaled or intranasal	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ glucocorticoid expected	No dose adjustment needed
Budesonide, Ciclesonide, Fluticasone, Mometasone Inhaled or intranasal	BIC, CAB (PO and IM), DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed
	EVG/c	↑ glucocorticoid possible	**Do not coadminister** unless the potential benefits of inhaled or intranasal corticosteroid outweigh the risks of systemic corticosteroid adverse effects. Coadministration can result in adrenal insufficiency and Cushing's syndrome. Consider using an alternative corticosteroid (e.g., beclomethasone).
Betamethasone, Budesonide Systemic	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI expected ↔ glucocorticoid expected	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	EVG/c	↑ glucocorticoid possible ↓ EVG possible	**Do not coadminister** unless the potential benefits of systemic budesonide outweigh the risks of systemic corticosteroid adverse effects. Coadministration can result in adrenal insufficiency and Cushing's syndrome.
Dexamethasone Systemic	BIC	↓ BIC possible	Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART.
	CAB (PO and IM), DTG, RAL	↔ INSTI expected	No dose adjustment needed
	EVG/c	↓ EVG and COBI possible	Consider alternative corticosteroid for long-term use or alternative ARV. If coadministration is necessary, monitor virologic response to ART.
Prednisone, Prednisolone Systemic	BIC, CAB (PO and IM), DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed
	EVG/c	↑ prednisolone possible	Coadministration may be considered if the potential benefits outweigh the risks of systemic corticosteroid adverse effects. If coadministration is necessary, monitor for adrenal insufficiency and Cushing's syndrome.
Betamethasone, Methylprednisolone, Prednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	BIC, CAB (PO and IM), DTG, RAL	↔ glucocorticoid expected	No dose adjustment needed
	EVG/c	↑ glucocorticoid expected	**Do not coadminister.** Coadministration may result in adrenal insufficiency and Cushing's syndrome.
Glucose-Lowering			
Metformin	BIC	Metformin AUC ↑ 39%	Monitor for adverse events of metformin.
	CAB (PO and IM), RAL	↔ metformin expected	No dose adjustment needed
	DTG	**DTG 50 mg Once Daily Plus Metformin 500 mg Twice Daily** • Metformin AUC ↑ 79% and C_{max} ↑ 66%	Start metformin at the lowest dose and titrate based on glycemic control. Monitor for adverse events of metformin. When starting/stopping DTG in patients on metformin, dose adjustment of metformin may be necessary to maintain optimal glycemic control and/or minimize adverse events of metformin.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		DTG 50 mg Twice Daily Plus Metformin 500 mg Twice Daily • Metformin AUC ↑ 2.4-fold and C_{max} ↑ 2-fold	
	EVG/c	↑ metformin possible	No dose adjustment needed
Saxagliptin	BIC, CAB (PO and IM), DTG, RAL	↔ saxagliptin expected	No dose adjustment needed
	EVG/c	↑ saxagliptin expected	Limit saxagliptin dose to 2.5 mg once daily.
Dapagliflozin/ Saxagliptin	BIC, CAB (PO and IM), DTG, RAL	↔ dapagliflozin or saxagliptin expected	No dose adjustment needed
	EVG/c	↑ saxagliptin expected	**Do not coadminister.** Dapagliflozin is available only as a coformulated drug that contains 5 mg of saxagliptin. When coadministered with EVG/c, the dose of saxagliptin should not exceed 2.5 mg once daily; thus, this combination **is not recommended.**
Herbal Products			
St. John's Wort	BIC, CAB (PO and IM), DTG	↓ BIC and DTG possible	**Do not coadminister.**
	EVG/c	↓ EVG and COBI expected	**Contraindicated**
Hormonal Therapies			
Injectable Contraceptives **Depot MPA**	BIC, CAB (PO and IM), DTG, RAL	↔ INSTI and injectable contraceptive expected	No dose adjustment needed
	EVG/c	↑ MPA possible	No dose adjustment needed
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norethindrone, norgestimate)	BIC, CAB (PO, IM), DTG, RAL	↔ ethinyl estradiol and norgestimate with DTG ↔ ethinyl estradiol and levonorgestrel with CAB PO ↔ ethinyl estradiol and norgestimate expected with BIC, RAL ↔ norgestimate expected with CAB PO and IM	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		↔ levonorgestrel expected ↔ drospirenone expected ↔ norethindrone expected	
	EVG/c	Norgestimate AUC, C_{max}, and C_{min} ↑ > 2-fold Ethinyl estradiol AUC ↓ 25% and C_{min} ↓ 44%	The effects of increases in progestin (norgestimate) are not fully known and may include insulin resistance, dyslipidemia, acne, and venous thrombosis. Decreased ethinyl estradiol may lead to more intermenstrual bleeding. Weigh the risks and benefits of using the drug and consider using an alternative ARV or contraceptive method.
		↑ drospirenone possible	Clinical monitoring is recommended due to the potential for hyperkalemia. Consider using alternative ARV or contraceptive method.
		↑ levonorgestrel possible ↑ norethindrone expected	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	BIC, CAB (PO and IM), DTG, RAL	Etonogestrel ↑ 27% with DTG ↔ etonogestrel or levonorgestrel expected with BIC, CAB, RAL	No dose adjustment needed
	EVG/c	↑ etonogestrel expected ↑ levonorgestrel expected	No dose adjustment needed
Transdermal Contraceptives (e.g., ethinyl estradiol/ norelgestromin, ethinyl estradiol/ levonorgestrel)	BIC, CAB (PO, IM), DTG, RAL	↔ contraceptive expected	No dose adjustment needed
	EVG/c	↑ progestin possible ↓ ethinyl estradiol possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ ethinyl estradiol, segesterone/ethinyl estradiol)	BIC, CAB (PO, IM), DTG, RAL	↔ contraceptive expected	No dose adjustment needed
	EVG/c	↑ progestin possible ↓ ethinyl estradiol possible	For segesterone/ethinyl estradiol vaginal rings, use alternative ARV or contraceptive methods.
Emergency Contraceptives **Levonorgestrel (PO)**	BIC, CAB (PO, IM), DTG, RAL	↔ levonorgestrel expected	No dose adjustment needed
	EVG/c	↑ levonorgestrel possible	No dose adjustment needed

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Hormonal Therapies—Miscellaneous			
Menopausal Replacement Therapy	BIC, CAB (PO and IM), DTG, RAL	↔ estrogen expected with estradiol or conjugated estrogen (equine and synthetic) ↔ drospirenone, MPA, and micronized progesterone expected	No dose adjustment needed
	EVG/c	↓ or ↑ estrogen possible ↑ drospirenone possible ↑ oral MPA possible ↑ oral micronized progesterone possible	Adjust estrogen and progestin dose as needed based on clinical effects.
Miscellaneous	BIC, CAB (PO and IM), DTG, EVG/c, RAL	↔ goserelin, leuprolide acetate, and spironolactone expected	No dose adjustment needed
	BIC, CAB (PO and IM), DTG, RAL	↔ estrogen expected	No dose adjustment needed
		↔ testosterone expected	No dose adjustment needed
	EVG/c	↑ or ↓ estradiol possible ↑ cyproterone, dutasteride, and finasteride possible	Adjust dutasteride dose as needed based on clinical effects.
		↑ testosterone possible	Monitor effects of testosterone and monitor for adverse effects. Adjust testosterone dose as necessary.
Immunosuppressants			
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	BIC, CAB (PO and IM), DTG, RAL	↔ immunosuppressant expected	No dose adjustment needed
	EVG/c	↑ immunosuppressant possible	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant. Monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lipid-Modifying			
Atorvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ atorvastatin expected	No dose adjustment needed
	EVG/c	Atorvastatin AUC ↑ 2.6-fold and C_{max} ↑ 2.3-fold	Administer the lowest effective dose while monitoring for adverse events. Do not exceed 20 mg atorvastatin daily.
Fluvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ fluvastatin expected	No dose adjustment needed
	EVG/c	↑ fluvastatin possible	Administer the lowest effective fluvastatin dose while monitoring for adverse events.
Lomitapide	BIC, CAB (PO and IM), DTG, RAL	↔ lomitapide expected	No dose adjustment needed
	EVG/c	↑ lomitapide expected	**Contraindicated**
Lovastatin	BIC, CAB (PO and IM), DTG, RAL	↔ lovastatin expected	No dose adjustment needed
	EVG/c	Significant ↑ lovastatin expected	**Contraindicated**
Pitavastatin, Pravastatin	BIC, CAB (PO and IM), DTG, RAL	↔ statin expected	No dose adjustment needed
	EVG/c	No data	No dose adjustment needed. Monitor for adverse events.
Rosuvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ rosuvastatin expected	No dose adjustment needed
	EVG/c	Rosuvastatin AUC ↑ 38% and C_{max} ↑ 89%	Administer the lowest effective dose while monitoring for adverse events.
Simvastatin	BIC, CAB (PO and IM), DTG, RAL	↔ simvastatin expected	No dose adjustment needed
	EVG/c	Significant ↑ simvastatin expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics and Treatment for Opioid Dependence			
Buprenorphine Sublingual, buccal, or implant	BIC, CAB (PO and IM), DTG	↔ buprenorphine and norbuprenorphine (active metabolite) expected	No dose adjustment needed
	EVG/c	Buprenorphine AUC ↑ 35% and C_{min} ↑ 66% Norbuprenorphine (active metabolite) AUC ↑ 42% and C_{min} ↑ 57%	No dose adjustment needed. Monitor for adverse events of buprenorphine. When transferring buprenorphine from transmucosal administration to implantation, monitor to ensure buprenorphine effect is adequate and not excessive.
	RAL	↔ buprenorphine and norbuprenorphine (active metabolite) (sublingual) ↔ buprenorphine or norbuprenorphine (active metabolite) expected (implant)	No dose adjustment needed
Fentanyl	BIC, CAB (PO and IM), DTG, RAL	↔ fentanyl expected	No dose adjustment needed
	EVG/c	↑ fentanyl	Monitor for fentanyl efficacy and adverse events, including potentially fatal respiratory depression.
Lofexidine	BIC, CAB (PO and IM), DTG, RAL	↔ lofexidine expected	No dose adjustment needed
	EVG/c	↑ lofexidine possible	Monitor for lofexidine-related adverse events, including symptoms of orthostasis and bradycardia.
Methadone	All INSTIs	↔ methadone	No dose adjustment needed
Tramadol	BIC, CAB (PO and IM), DTG, RAL	↔ tramadol and M1 (active metabolite) expected	No dose adjustment needed
	EVG/c	↑ tramadol expected ↓ M1 (active metabolite) possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors			
Avanafil	BIC, CAB (PO and IM), DTG, RAL	↔ avanafil expected	No dose adjustment needed
	EVG/c	No data	**Do not coadminister.**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Sildenafil	BIC, CAB (PO and IM), DTG, RAL	↔ sildenafil expected	No dose adjustment needed
	EVG/c	↑ sildenafil expected	**For Treatment of Erectile Dysfunction** • Start with sildenafil 25 mg every 48 hours and monitor for sildenafil-related adverse events. **Contraindicated** for treatment of PAH.
Tadalafil	BIC, CAB (PO and IM), DTG, RAL	↔ tadalafil expected	No dose adjustment needed
	EVG/c	↑ tadalafil expected	**For Treatment of Erectile Dysfunction** • Start with tadalafil 5 mg. Do not exceed a single dose of tadalafil 10 mg every 72 hours. Monitor for tadalafil-related adverse events. **For Treatment of PAH** *In Patients on EVG/c >7 Days* • Start with tadalafil 20 mg once daily. Increase to tadalafil 40 mg once daily based on tolerability. *In Patients on Tadalafil who Require EVG/c* • Stop tadalafil ≥24 hours before EVG/c initiation. Seven days after EVG/c initiation, restart tadalafil at 20 mg once daily and increase to tadalafil 40 mg once daily based on tolerability.
Vardenafil	BIC, CAB (PO and IM), DTG, RAL	↔ vardenafil expected	No dose adjustment needed
	EVG/c	↑ vardenafil expected	Start with vardenafil 2.5 mg every 72 hours and monitor for vardenafil-related adverse events.
Sedative/Hypnotics			
Benzodiazepines			
Alprazolam, Clonazepam, Clorazepate, Diazepam, Estazolam, Flurazepam	BIC, CAB (PO and IM), DTG, RAL	↔ benzodiazepine expected	No dose adjustment needed
	EVG/c	↑ benzodiazepine possible	Dose reduction of benzodiazepine may be necessary. Initiate with a low dose and monitor for benzodiazepine-related adverse events. Consider using an alternative benzodiazepine, such as lorazepam, oxazepam, or temazepam.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Midazolam, Triazolam	BIC, CAB (PO and IM), RAL	↔ benzodiazepine expected	No dose adjustment needed
	DTG	**With DTG 25 mg** • ↔ midazolam AUC	No dose adjustment needed
	EVG/c	↑ midazolam expected ↑ triazolam expected	**Contraindicated** **Do not coadminister** triazolam or oral midazolam and EVG/c. Parenteral midazolam can be administered in a closely monitored setting. Consider dose reduction, especially if >1 dose is administered.
Orexin Receptor Antagonists			
Daridorexant, Lemborexant, Suvorexant	BIC, CAB (PO and IM), DTG, RAL	↔ daridorexant, lemborexant, suvorexant expected	No dose adjustment needed
	EVG/c	↑ daridorexant, lemborexant, suvorexant expected	**Do not coadminister.**
Other Sedatives			
Eszopiclone	BIC, CAB (PO and IM), DTG, RAL	↔ eszopiclone expected	No dose adjustment needed
	EVG/c	↑ eszopiclone expected	Start with lowest dose and increase to a max of 2 mg daily. Monitor for eszopiclone-related adverse events.
Zolpidem	BIC, CAB (PO and IM), DTG, RAL	↔ zolpidem expected	No dose adjustment needed
	EVG/c	↑ zolpidem expected	Initiate zolpidem at a low dose. Dose reduction of zolpidem may be necessary.
Miscellaneous Drugs			
Calcifediol	BIC, CAB (PO and IM), DTG, RAL	↔ calcifediol expected	No dose adjustment needed
	EVG/c	↑ calcifediol possible	Dose adjustment of calcifediol may be required. Monitor serum 25-hydroxyvitamin D, intact PTH, and serum Ca concentrations.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cisapride	BIC, CAB (PO and IM), DTG, RAL	↔ cisapride expected	No dose adjustment needed
	EVG/c	↑ cisapride expected	**Contraindicated**
Colchicine	BIC, CAB (PO and IM), DTG, RAL	↔ colchicine expected	No dose adjustment needed
	EVG/c	↑ colchicine expected	**Do not coadminister** in patients with hepatic or renal impairment. **For Treatment of Gout Flares** • Administer a single dose of colchicine 0.6 mg, followed by colchicine 0.3 mg 1 hour later. Do not repeat dose for at least 3 days. **For Prophylaxis of Gout Flares** • If original dose was colchicine 0.6 mg twice daily, decrease to colchicine 0.3 mg once daily. If dose was 0.6 mg once daily, decrease to 0.3 mg every other day. **For Treatment of Familial Mediterranean Fever** • Do not exceed colchicine 0.6 mg once daily or 0.3 mg twice daily.
Dronabinol	BIC, CAB (PO and IM), DTG, RAL	↔ dronabinol expected	No dose adjustment needed
	EVG/c	↑ dronabinol possible	Monitor for dronabinol-related adverse events.
Eluxadoline	BIC, CAB (PO and IM), DTG, RAL	↔ eluxadoline expected	No dose adjustment needed
	EVG/c	↑ eluxadoline possible	Monitor for eluxadoline-related adverse events.
Ergot Derivatives	BIC, CAB (PO and IM), DTG, RAL	↔ dihydroergotamine, ergotamine, and methylergonovine expected	No dose adjustment needed
	EVG/c	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Contraindicated**

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Finerenone	BIC, CAB (PO and IM), DTG, RAL	↔ finerenone expected	No dose adjustment needed
	EVG/c	↑ finerenone expected	**Contraindicated**
Flibanserin	BIC, CAB (PO and IM), DTG, RAL	↔ flibanserin expected	No dose adjustment needed
	EVG/c	↑ flibanserin expected	**Contraindicated**
Naloxegol	BIC, CAB (PO and IM), DTG, RAL	↔ naloxegol expected	No dosage adjustment needed
	EVG/c	↑ naloxegol expected	**Contraindicated**
Polyvalent Cation Supplements Mg, Al, Fe, Ca, Zn, including multivitamins with minerals. **Note:** Please refer to the Acid Reducers section in this table for recommendations on use with Al-, Mg-, and Ca-containing antacids.	BIC	↔ BIC AUC if administered simultaneously with Fe or Ca and food BIC AUC ↓ 33% if administered simultaneously with $CaCO_3$ under fasting conditions BIC AUC ↓ 63% if administered simultaneously with Fe under fasting conditions	**With Supplements That Contain Ca or Fe** • Administer BIC and supplements that contain Ca or Fe together with food. **Do not coadminister** BIC under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.
	CAB	↓ INSTI possible	If coadministration is necessary, administer INSTI at least 2 hours before or at least 4 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.

Table 24d. Drug Interactions Between Integrase Strand Transfer Inhibitors and Other Drugs

Concomitant Drug	INSTI	Effect on INSTI or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
	DTG	DTG AUC ↓ 39% if administered simultaneously with $CaCO_3$ under fasting conditions DTG AUC ↓ 54% if administered simultaneously with Fe under fasting conditions ↔ DTG when administered with Ca or Fe supplement simultaneously with food	**With Supplements That Contain Ca or Fe** • Administer DTG and supplements that contain Ca or Fe together with food, or administer DTG at least 2 hours before or at least 6 hours after supplement. **Do not coadminister** DTG under fasting conditions simultaneously with, or 2 hours after, supplements that contain Ca or Fe.
	EVG/c, RAL	↓ INSTI possible	If coadministration is necessary, administer INSTI at least 2 hours before or at least 6 hours after supplements that contain polyvalent cations, including but not limited to the following products: cation-containing laxatives; Fe, Ca, or Mg supplements; and sucralfate. Monitor for virologic response. Many oral multivitamins also contain varying amounts of polyvalent cations; the extent and significance of chelation is unknown.
Praziquantel	BIC, CAB (PO and IM), DTG, RAL	↔ praziquantel and INSTI expected	No dose adjustment needed
	EVG/c	↑ praziquantel possible	Consider alternative ARV. If coadministration is necessary, monitor for praziquantel-related adverse events.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: Al = aluminum; ALT = alanine aminotransferase; ART = antiretroviral therapy; ARV = antiretroviral; AST = aspartate aminotransferase; AUC = area under the curve; BIC = bictegravir; Ca = calcium; CAB = cabotegravir; $CaCO_3$ = calcium carbonate; CCB = calcium channel blocker; C_{max} = maximum plasma concentration; C_{min} = minimum plasma concentration; CMV = cytomegalovirus; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P450; DTG = dolutegravir; DVT = deep vein thrombosis; ECG = electrocardiogram; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; Fe = iron; FTC = emtricitabine; GI = gastrointestinal; IM = intramuscular; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; Mg = magnesium; MPA = medroxyprogesterone acetate; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PE = pulmonary embolism; PO = orally; PTH = parathyroid hormone; QTc = QT corrected for heart rate; RAL = raltegravir; RPV = rilpivirine; SSRI = selective serotonin reuptake inhibitors; TAF = tenofovir alafenamide; TCA = tricyclic antidepressants; TDF = tenofovir disoproxil fumarate; Zn = zinc

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Updated: September 12, 2024
Reviewed: September 12, 2024

In the table below, "no dose adjustment needed" indicates that the U.S. Food and Drug Administration–approved dose of maraviroc (MVC) 300 mg twice daily should be used. Recommendations for managing a particular drug interaction may differ, depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgment to select the most appropriate alternative medication.

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Macrolides		
Azithromycin	↔ MVC expected	No dose adjustment needed
Clarithromycin	↑ MVC possible	MVC 150 mg twice daily
Erythromycin	↑ MVC possible	No dose adjustment needed
Antifungals		
Fluconazole	↑ MVC possible	No dose adjustment needed
Isavuconazole	↑ MVC possible	No dose adjustment needed
Itraconazole	↑ MVC possible	MVC 150 mg twice daily
Posaconazole	↑ MVC possible	MVC 150 mg twice daily
Voriconazole	↑ MVC possible	MVC 150 mg twice daily
Antimycobacterials		
Rifabutin	MVC AUC ↔ and C_{min} ↓ 30%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 300 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
Rifampin	MVC AUC ↓ 63%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • Consider alternative ARV or antimycobacterial
Rifapentine	**Rifapentine Weekly and Daily** ↓ MVC expected	Do not coadminister.

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiretroviral Drugs		
Attachment Inhibitor		
FTR[a]	MVC AUC ↑ 25% ↔ TMR[a]	No dose adjustment needed
Capsid Inhibitor		
LEN (SQ and PO)	↑ MVC possible	No dose adjustment needed
INSTIs		
BIC, CAB (IM and PO), DTG	↔ MVC expected	No dose adjustment needed
EVG/c	↑ MVC possible	MVC 150 mg twice daily.
RAL	MVC AUC ↓ 21% RAL AUC ↓ 37%	No dose adjustment needed
NNRTIs		
DOR, RPV (IM and PO)	↔ MVC expected	No dose adjustment needed
EFV	MVC AUC ↓ 45%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
ETR	MVC AUC ↓ 53%	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
PIs		
ATV/c, ATV/r	**With (ATV/r 300 mg/100 mg) Once Daily** • MVC AUC ↑ 388%	MVC 150 mg twice daily
DRV/c, DRV/r	**With (DRV/r 600 mg/100 mg) Twice Daily** • MVC AUC ↑ 305% **With (DRV/r 600 mg/100 mg) Twice Daily and ETR** • MVC AUC ↑ 210%	MVC 150 mg twice daily

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiseizure		
Carbamazepine, Phenobarbital, Phenytoin	↓ MVC possible	**If Used *Without* a Strong CYP3A Inhibitor** • MVC 600 mg twice daily **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily
Eslicarbazepine	↓ MVC possible	Consider alternative ARV or anticonvulsant.
Oxcarbazepine	↓ MVC possible	Consider alternative ARV or anticonvulsant.
Antivirals—Hepatitis C Direct-Acting Antivirals		
Elbasvir/Grazoprevir	↔ MVC expected	No dose adjustment needed
Ledipasvir/Sofosbuvir	↔ MVC expected	No dose adjustment needed
Glecaprevir/Pibrentasvir	↔ MVC expected	No dose adjustment needed
Simeprevir	↔ MVC expected	No dose adjustment needed
Sofosbuvir	↔ MVC expected	No dose adjustment needed
Sofosbuvir/Velpatasvir	↔ MVC expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/Voxilaprevir	↔ MVC expected	No dose adjustment needed
Antivirals—Miscellaneous (e.g., for CMV, Mpox)		
Brincidofovir	↔ MVC expected	No dose adjustment needed
Cidofovir	↔ MVC expected	No dose adjustment needed
Tecovirimat	**When Given With MVC Without a Boosted PI or Other Potent CYP3A4 Inhibitors** • ↓ MVC possible but not expected to be clinically relevant **When Given With MVC Plus a Boosted PI or Other Potent CYP3A4 Inhibitors** • ↑ MVC expected	**If Used *Without* a Strong CYP3A Inhibitor** • No dose adjustment needed **If Used *With* a Strong CYP3A Inhibitor** • MVC 150 mg twice daily

Table 24e. Drug Interactions Between the CCR5 Antagonist Maraviroc and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on CCR5 Antagonist and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antivirals—SARS-CoV-2		
Molnupiravir	↔ MVC expected	No dose adjustment needed
Remdesivir	↔ MVC expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	**MVC With Ritonavir 100 mg Twice Daily** • MVC AUC ↑ 161%	MVC 150 mg twice daily
Herbal Products		
St. John's Wort	↓ MVC expected	**Do not coadminister.**
Hormonal Therapies		
Hormonal Contraceptives	↔ ethinyl estradiol or levonorgestrel	No dose adjustment needed
Menopausal Hormone Replacement Therapy	↔ MVC or hormone replacement therapies expected	No dose adjustment needed

[a] FTR is a prodrug metabolized to its active moiety, TMR. Therefore, the effect on gp120-directed attachment inhibitor in the table refers to TMR concentrations.

Key to Symbols

↑ = increase
↓ = decrease
↔ = no change

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; CAB = cabotegravir; C_{min} = minimum plasma concentration; CMV = cytomegalovirus; CYP = cytochrome P; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTR = fostemsavir; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; ; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; TMR = temsavir

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Updated: September 12, 2024
Reviewed: September 12, 2024

Fostemsavir (FTR), an HIV-1 gp120-directed attachment inhibitor, is a prodrug of temsavir (TMR). In this table, the effect on gp120-directed attachment inhibitor refers to TMR concentrations. Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. Providers should exercise their clinical judgment to select the most appropriate alternative medication to use in cases where an interacting drug needs to be replaced with an alternative.

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers		
H2 Receptor Antagonists	↔ TMR	No dose adjustment needed
Antibacterials—Antimycobacterials		
Rifabutin	**With Rifabutin 300 mg Once Daily and Without RTV** • TMR AUC ↓ 30% **With Rifabutin 150 mg Once Daily and With RTV 100 mg Once Daily** • TMR AUC ↑ 66%	**If Used *Without* PI/r** • No dose adjustment needed **If Used *With* PI/r** • Recommended dose is rifabutin 150 mg once daily. • No dose adjustment of FTR
Rifampin	TMR AUC ↓ 82%	**Contraindicated**
Rifapentine	**Daily and Weekly Dosing** ↓ TMR expected	**Do not coadminister.**
Antiretroviral Drugs		
Capsid Inhibitor		
LEN (SQ and PO)	↔ TMR expected ↔ LEN expected	No dose adjustment needed

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
CCR5 Antagonist		
MVC	↔ TMR MVC AUC ↑ 25%	No dose adjustment needed
CD4 Post-Attachment Inhibitor		
IBA	↔ expected	No dose adjustment needed
INSTIs		
BIC, CAB (IM and PO), DTG, EVG/c	↔ TMR expected	No dose adjustment needed
RAL plus TDF	↔ TMR	No dose adjustment needed
NRTIs		
TDF	↔ TMR ↔ TDF	No dose adjustment needed
NNRTIs		
DOR, RPV (IM and PO)	↔ TMR expected	No dose adjustment needed
EFV	↓ TMR possible ↔ EFV expected	No dose adjustment needed
ETR	TMR AUC ↓ 50% ↔ ETR	No dose adjustment needed
ETR plus DRV/r	TMR C_{max} and AUC ↑ 34% to 53% ↔ DRV, RTV ETR AUC ↑ 28%	No dose adjustment needed

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
PIs		
ATV/c	↑ TMR expected ↔ ATV expected	No dose adjustment needed
ATV/r	TMR C_{max} and AUC ↑ 54% to 58% ↔ ATV, RTV	No dose adjustment needed
DRV/c	TMR C_{max} and AUC ↑ 79% to 97% ↔ DRV, RTV expected	No dose adjustment needed
DRV/r	TMR C_{max} and AUC ↑ 52% to 63% ↔ DRV, RTV	No dose adjustment needed
Antiseizure		
Carbamazepine, Phenobarbital, Phenytoin	↓ TMR expected	**Contraindicated**
Antivirals—Hepatitis C Direct-Acting Antivirals		
Elbasvir/Grazoprevir	↑ grazoprevir expected	Increased grazoprevir exposures may increase the risk of ALT elevations. **Use an alternative** HCV regimen.
Ledipasvir/Sofosbuvir	↔ expected	No dose adjustment needed
Glecaprevir/Pibrentasvir	↔ expected	No dose adjustment needed
Sofosbuvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/Voxilaprevir	↑ voxilaprevir expected	**Use an alternative** HCV regimen if possible.
Antivirals—Miscellaneous (e.g., for CMV, Mpox)		
Brincidofovir	↑ brincidofovir possible	Give FTR dose at least 3 hours after administering brincidofovir, and monitor for brincidofovir-related adverse events (i.e., elevations in ALT/AST and bilirubin and GI adverse events).

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cidofovir	↔ TMR expected	No dose adjustment needed
Tecovirimat	↔ TMR expected	No dose adjustment needed
Antivirals—SARS-CoV-2		
Molnupiravir	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	TMR AUC ↑ 45%	No dose adjustment needed
Remdesivir	↔ expected	No dose adjustment needed
Herbal Products		
St. John's Wort	↓ TMR expected	**Contraindicated**
Hormonal Therapies		
Hormonal Contraceptives	Ethinyl estradiol AUC ↑ 40% ↔ norethindrone	Prescribe oral contraceptive that contains no more than 30 mcg of ethinyl estradiol[a] or use alternative ARV or contraceptive methods.
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	↑ estrogens, estradiol possible	Use lowest effective dose for estrogen-containing regimens.
Lipid-Modifying Agents		
Atorvastatin, Fluvastatin, Pitavastatin, Simvastatin	↑ statin possible ↔ expected	Increased statin concentration may not be clinically relevant. Follow clinical guidelines. Administer the lowest effective statin dose while monitoring for adverse events.
Rosuvastatin	Rosuvastatin AUC ↑ 69%	Increased rosuvastatin concentration may not be clinically relevant. Follow clinical guidelines. Administer the lowest effective dose while monitoring for adverse events.

Table 24f. Drug Interactions Between HIV-1 gp120-Directed Attachment Inhibitors and Other Drugs (Including Antiretroviral Agents)

Concomitant Drug Class/ Name	Effect on gp120-Directed Attachment Inhibitor and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Narcotics and Treatment for Opioid Dependence		
Buprenorphine/Naloxone	Buprenorphine AUC ↑ 30% Norbuprenorphine (active metabolite) AUC ↑ 39%	No dose adjustment needed
Methadone	↔ Total methadone ↔ R(−) methadone (active metabolite) ↔ S(+) methadone	No dose adjustment needed

[a] The following products contain no more than 30 mcg of ethinyl estradiol combined with norethindrone or norgestimate: Lo Minastrin Fe; Lo Loestrin Fe; Loestrin 1/20, 1.5/30; Loestrin Fe 1/20, 1.5/30; Loestrin 24 Fe; Minastrin 24 Fe; Ortho Tri-Cyclen Lo. Generic formulations also may be available.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ALT = alanine aminotransferase; ARV = antiretroviral; AST = aspartate aminotransferase; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{max} = maximum plasma concentration; CAB = cabotegravir; CCR5 = C-C chemokine receptor type 5; CMV = cytomegalovirus; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTR = fostemsavir; GI = gastrointestinal; gp120 = glycoprotein 120; HCV = hepatitis C virus; IBA = ibalizumab; IM = intramuscular; INSTI = integrase strand transfer inhibitor; LEN = lenacapavir; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/r = ritonavir-boosted PI; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; TDF = tenofovir disoproxil fumarate; TMR = temsavir

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Updated: September 12, 2024
Reviewed: September 12, 2024

This table provides information on the known or predicted interactions between lenacapavir (LEN), an HIV capsid inhibitor, and other drugs, including antiretroviral (ARV) drugs.

LEN is available as an oral tablet (to be used only as initial therapy) and a long-acting injectable formulation that is administered every 6 months. LEN is a moderate cytochrome P450 (CYP) 3A4 inhibitor and may increase the concentration of drugs metabolized by CYP3A4. Due to the long half-life of the injectable formulation, this inhibitory effect may persist, and clinicians should continue to assess for drug interactions for up to 9 months after the last LEN injection. Recommendations for managing a particular drug interaction may differ depending on whether LEN is being initiated in a patient on a stable concomitant medication or whether a new medication is being initiated in a patient on a stable LEN-containing ARV regimen.

The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. Providers should exercise their clinical judgment to select the most appropriate alternative medication to use in cases where an interacting drug needs to be replaced with an alternative. People with HIV should be counseled about the importance of informing all their health care providers about their HIV regimen prior to starting any new concomitant medications (e.g., prescription, over-the-counter, and herbal or dietary supplements) to minimize the risk of drug–drug interactions.

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Acid Reducers		
Antacids, H2 Receptor Antagonists, Proton Pump Inhibitors	↔ expected	No dose adjustment needed
Alpha-Adrenergic Antagonists for Benign Prostatic Hyperplasia		
Alfuzosin	↑ alfuzosin expected	Consider an alternative to alfuzosin or an alternative ARV. If coadministered, monitor blood pressure.
Doxazosin	↑ doxazosin possible	No dose adjustment needed. Monitor blood pressure.
Tamsulosin	↑ tamsulosin possible	Initiate tamsulosin at 0.4 mg/day. Monitor blood pressure.
Terazosin	↔ expected	No dose adjustment needed
Silodosin	↑ silodosin possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antibacterials—Antimycobacterials		
Bedaquiline	↑ bedaquiline expected	Consider alternatives unless benefits outweigh risks. Monitor liver function and ECG for QTc prolongation.
Rifabutin	↓ LEN expected	**Do not coadminister.**
Rifampin	LEN AUC ↓ 84%	**Contraindicated**
Rifapentine	**Daily and Weekly Dosing** • ↓ LEN expected	**Do not coadminister.**
Antibacterials—Macrolides		
Azithromycin	↔ expected	No dose adjustment needed
Clarithromycin	↑ LEN possible	No dose adjustment needed
Erythromycin	↑ LEN possible	No dose adjustment needed
Anticoagulants		
Apixaban	↑ apixaban possible	No dose adjustment needed Monitor for apixaban-related adverse events, such as increased bleeding.
Dabigatran	↑ dabigatran possible	No dose adjustment needed Monitor for dabigatran-related adverse events, such as increased bleeding.
Edoxaban	↑ edoxaban possible	No dose adjustment needed Monitor for edoxaban-related adverse events, such as increased bleeding.
Rivaroxaban	↑ rivaroxaban possible	Monitor for rivaroxaban-related adverse events, such as increased bleeding, and adjust rivaroxaban dose accordingly.
Warfarin	↑ warfarin possible	Monitor INR and adjust warfarin dose accordingly.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antidepressants, Anxiolytics, and Antipsychotics Also see the Sedative/Hypnotics section below.		
Bupropion	↔ expected	No dose adjustment needed
Buspirone	↑ buspirone expected	Administer lowest dose of buspirone with caution and titrate buspirone dose based on clinical response. Dose reduction may be necessary. Monitor for buspirone-related adverse events.
Desvenlafaxine	↔ expected	No dose adjustment needed
Duloxetine	↔ expected	No dose adjustment needed
Mirtazapine	↑ mirtazapine possible	No dose adjustment needed. Monitor for mirtazapine-related adverse events.
Nefazodone	↑ LEN possible	No dose adjustment needed
Selective Serotonin Reuptake Inhibitor (e.g., citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, vortioxetine)	↑ paroxetine possible ↔ citalopram, escitalopram, fluoxetine, fluvoxamine, sertraline, vortioxetine expected	Dose reduction may be necessary with paroxetine. No dose adjustment needed
Trazodone	↑ trazodone expected	Administer lowest dose of trazodone and monitor for CNS and CV adverse events.
Tricyclic Antidepressants (e.g., amitriptyline, doxepin, nortriptyline)	↔ expected	No dose adjustment needed
Venlafaxine	↔ expected	No dose adjustment needed
Antipsychotics		
Aripiprazole	↑ aripiprazole possible	No dose adjustment needed
Brexpiprazole	↑ brexpiprazole expected	If patient is a known CYP2D6 poor metabolizer, then administer one-quarter of usual brexpiprazole dose.
Cariprazine	↑ cariprazine possible	No dose adjustment needed
Iloperidone	↑ iloperidone possible	No dose adjustment needed or consider dose reduction. Monitor for iloperidone-related adverse events.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lumateperone	↑ lumateperone expected	Reduce dose of lumateperone to 21 mg once daily.
Lurasidone	↑ lurasidone expected	If LEN is added to lurasidone therapy, administer half of lurasidone dose. If lurasidone is added to LEN therapy, the recommended starting dose of lurasidone is 20 mg daily, and the maximum recommended dose is 80 mg daily.
Olanzapine **Olanzapine/Samidorphan**	↔ LEN olanzapine expected ↑ samidorphan possible	No dose adjustment needed
Other Antipsychotics (e.g., clozapine, risperidone, thioridazine)	↑ clozapine possible	No dose adjustment needed. Monitor for clozapine-related adverse events.
	↑ risperidone possible	No dose adjustment needed
	↑ thioridazine possible ↓ LEN possible	**Do not coadminister.**
Pimavanserin	↑ pimavanserin possible	No dose adjustment needed. Monitor ECG for QTc prolongation.
Pimozide	↑ pimozide expected	**Contraindicated**
Quetiapine	↑ quetiapine expected	Consider alternatives unless benefits outweigh risks. Monitor ECG for QTc prolongation and consider dose reduction accordingly.
Ziprasidone	↔ expected	No dose adjustment needed
Antifungals		
Fluconazole	↑ LEN possible	No dose adjustment needed
Ibrexafungerp	↑ ibrexafungerp possible	No dose adjustment needed
Isavuconazole	↔ expected	No dose adjustment needed
Itraconazole	↑ LEN possible	No dose adjustment needed
Posaconazole	↑ LEN possible	No dose adjustment needed
Voriconazole	↑ LEN AUC 41%	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antimalarials		
Artemether/Lumefantrine	↑ artemether and lumefantrine possible	Monitor for lumefantrine-related adverse events, including QTc prolongation.
Artesunate	↔ expected	No dose adjustment needed
Atovaquone/Proguanil	↔ expected	No dose adjustment needed
Mefloquine	↑ mefloquine possible	Monitor for mefloquine-related adverse events, including QTc prolongation.
Antimigraine		
Ergot Derivatives	↑ dihydroergotamine, ergotamine, and methylergonovine expected	**Do not coadminister.**
Calcitonin Gene-Related Peptide (CGRP) Receptor Antagonists		
Atogepant	↑ atogepant expected	No dose adjustment needed
Rimegepant	↑ rimegepant expected	Avoid a second dose of rimegepant within 48 hours.
Ubrogepant	↑ ubrogepant expected	Avoid a second dose of ubrogepant within 24 hours.
Zavegepant	↔ expected	No dose adjustment needed
Serotonin 5-HT1B, 1D Receptor Agonist		
Almotriptan	↔ expected	No dose adjustment needed
Eletriptan	↑ eletriptan expected	No dose adjustment needed. Monitor for eletriptan-related adverse events.
Frovatriptan, Naratriptan, Rizatriptan, Sumatriptan, Zolmitriptan	↔ expected	No dose adjustment needed
Antiplatelets		
Clopidogrel	↓ clopidogrel active metabolite possible	Consider alternative ARV or antiplatelet drug. If coadministered, monitor for clopidogrel-related adverse events.
Prasugrel	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Ticagrelor	↑ ticagrelor possible	No dose adjustment needed. Monitor for ticagrelor-related adverse events.
Vorapaxar	↑ vorapaxar possible	No dose adjustment needed
Antipneumocystis and Antitoxoplasmosis		
Atovaquone Oral suspension	↔ expected	No dose adjustment needed
Antiretroviral Drugs		
CCR5 Antagonist		
MVC	↔ expected	No dose adjustment needed
CD4 Post-attachment Inhibitor		
IBA	↔ expected	No dose adjustment needed
gp120 Attachment Inhibitor		
FTR	↔ expected	No dose adjustment needed
INSTIs		
BIC, CAB (IM or PO), DTG, EVG/c, RAL	↔ expected	No dose adjustment needed
NRTIs		
ABC, 3TC, FTC	↔ expected	No dose adjustment needed
TAF	TAF AUC ↑ 32%	No dose adjustment needed
TDF	TDF AUC ↑ 47%	No dose adjustment needed
NNRTIs		
EFV	LEN AUC↓ 56%	**Do not coadminister.**
ETR	↓ LEN expected	**Do not coadminister.**
DOR	↑ DOR possible	No dose adjustment needed
RPV (IM or PO)	↑ RPV possible	No dose adjustment needed
PIs		
ATV/r	↑ LEN expected	**Do not coadminister.**
ATV/c	LEN AUC ↑ 4-fold	**Do not coadminister.**
DRV/c	DRV/c AUC ↑ 94%	No dose adjustment needed
DRV/r	↑ LEN expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Antiseizure		
Carbamazepine	↓ LEN expected	**Contraindicated**
Eslicarbazepine	↓ LEN expected	**Do not coadminister.**
Ethosuximide	↑ ethosuximide possible	Monitor for ethosuximide-related adverse events and adjust ethosuximide dose accordingly.
Lamotrigine	↔ expected	No dose adjustment needed
Oxcarbazepine	↓ LEN expected	**Do not coadminister.**
Phenobarbital	↓ LEN expected	**Do not coadminister.**
Phenytoin	↓ LEN expected	**Contraindicated**
Primidone	↓ LEN expected	**Do not coadminister.**
Valproic Acid	↔ expected	No dose adjustment needed
Antivirals—Hepatitis C		
Elbasvir/Grazoprevir	↔ expected	No dose adjustment needed
Glecaprevir/Pibrentasvir	↔ expected	No dose adjustment needed
Ledipasvir/Sofosbuvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir	↔ expected	No dose adjustment needed
Sofosbuvir/Velpatasvir/Voxilaprevir	↔ expected	No dose adjustment needed
Antivirals—Miscellaneous (e.g., for CMV, Mpox)		
Brincidofovir	↔ expected	No dose adjustment needed
Cidofovir	↔ expected	No dose adjustment needed
Maribavir	↔ expected	No dose adjustment needed
Tecovirimat	↓ LEN possible	No dose adjustment needed
Valganciclovir	↔ expected	No dose adjustment needed
Antivirals—SARS-CoV-2		
Molnupiravir	↔ expected	No dose adjustment needed
Ritonavir-Boosted Nirmatrelvir	↑ LEN possible	No dose adjustment needed
Remdesivir	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Beta-Agonists, Long-Acting Inhaled		
Arformoterol, Formoterol, Indacaterol, Olodaterol, Salmeterol	↔ expected	No dose adjustment needed
Cardiac Medications		
Antiarrhythmics		
Amiodarone	↑ amiodarone expected ↑ LEN possible	**Do not coadminister.**
Digoxin	↑ digoxin expected	Consider alternative ARV or antiarrhythmic. If coadministered, monitor digoxin therapeutic concentration.
Disopyramide	↑ disopyramide expected	**Do not coadminister.**
Dofetilide	↔ expected	No dose adjustment needed
Dronedarone	↑ dronedarone possible ↑ LEN possible	Consider alternative ARV or cardiac medication. If coadministered, monitor for dronedarone-related adverse events.
Flecainide	↔ expected	No dose adjustment needed
Lidocaine	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events and monitor concentrations, if available.
Mexiletine	↔ expected	No dose adjustment needed
Propafenone	↑ propafenone possible	Consider alternative ARV or antiarrhythmics. If coadministered, monitor for antiarrhythmic-related adverse events and monitor concentrations, if available.
Quinidine	↑ quinidine expected	**Do not coadminister.**
Sotalol	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Beta-Blockers		
Atenolol, Bisoprolol, Carvedilol, Labetalol, Metoprolol, Nebivolol, Timolol	↔ expected	No dose adjustment needed
Calcium Channel Blockers		
Amlodipine, Felodipine, Nifedipine	↑ amlodipine, felodipine expected ↑ nifedipine possible	Monitor and dose adjust according to clinical response and adverse events.
Diltiazem, Verapamil	↑ diltiazem possible ↔ verapamil expected	No dose adjustment needed
Cardiac – Other		
Bosentan	↓ LEN expected	**Do not coadminister.**
Eplerenone	↑ eplerenone expected	**For Post-MI CHF** • Dosing of eplerenone should not exceed 25 mg daily. **For Hypertension** • Initiate at 25 mg once daily. Dosing may be increased to a maximum of 25 mg twice daily.
Ivabradine	↑ ivabradine expected	**Do not coadminister.**
Mavacamten	↓ LEN possible ↑ mavacamten expected	Initiate mavacamten at the recommended starting dose of 5 mg daily in patients who are on stable therapy with LEN. Reduce dose of mavacamten by one level (i.e., 15 to 10 mg, 10 to 5 mg, or 5 to 2.5 mg) in patients who are on mavacamten treatment and intend to initiate LEN.
Ranolazine	↑ ranolazine expected	Limit ranolazine to 500 mg twice daily.
Corticosteroids		
Beclomethasone Inhaled or intranasal **Ciclesonide** Inhaled	↔ expected	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Budesonide, Fluticasone, Mometasone Inhaled or intranasal	↑ glucocorticoids possible	Initiate with the lowest starting dose and titrate carefully and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Betamethasone Systemic	↑ betamethasone possible ↓ LEN possible	**Do not coadminister.**
Budesonide, Prednisone, Prednisolone Systemic	↑ glucocorticoids expected	Initiate with the lowest starting dose, titrate carefully, and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Dexamethasone Systemic	↑ dexamethasone expected ↓ LEN expected if used with dexamethasone >16 mg/day	Initiate with the lowest starting dose, titrate carefully, and monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events. **Do not coadminister** with dexamethasone >16 mg/day**.**
Betamethasone, Methylprednisolone, Triamcinolone Local injections, including intra-articular, epidural, or intra-orbital	↑ glucocorticoids possible	Monitor for adrenal insufficiency, Cushing's syndrome, and other corticosteroid-related adverse events.
Glucose-Lowering		
Canagliflozin	↔ expected	No dose adjustment needed
Saxagliptin	↑ saxagliptin possible	No dose adjustment needed
Dapagliflozin/Saxagliptin	↑ saxagliptin possible	No dose adjustment needed
Herbal Products		
St. John's Wort	↓ LEN expected	**Contraindicated**
Hormonal Therapies—Contraceptives		
Injectable Contraceptives Depot MPA	↑ MPA possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Oral Contraceptives (e.g., desogestrel, drospirenone, ethinyl estradiol, levonorgestrel, norgestimate)	↑ contraceptive exposures possible	No dose adjustment needed
Subdermal Implant Contraceptives (e.g., etonogestrel, levonorgestrel)	↑ contraceptive exposures possible	No dose adjustment needed
Transdermal Contraceptives (e.g., ethinyl estradiol/norelgestromin, ethinyl estradiol/levonorgestrel)	↑ contraceptive exposures possible	No dose adjustment needed
Vaginal Ring Contraceptives (e.g., etonogestrel/ethinyl estradiol, segesterone/ethinyl estradiol)	↑ contraceptive exposures possible	No dose adjustment needed
Emergency Contraceptives Levonorgestrel (oral)	↑ levonorgestrel possible	No dose adjustment needed
Hormonal Therapies—Miscellaneous		
5-Alpha Reductase Inhibitors (e.g., dutasteride, finasteride)	↑ dutasteride and finasteride possible	No dose adjustment needed
Estradiol	↔ expected	No dose adjustment needed
Goserelin, Leuprolide Acetate	↔ expected	No dose adjustment needed
Menopausal Hormone Replacement Therapy (e.g., conjugated estrogens, drospirenone, estradiol, medroxyprogesterone, progesterone)	↑ estrogen and progesterone possible ↑ drospirenone possible	No dose adjustment needed
Testosterone	↑ testosterone possible	No dose adjustment needed
Immunosuppressants		
Cyclosporine, Everolimus, Sirolimus, Tacrolimus	↑ immunosuppressant expected	Initiate with an adjusted dose of immunosuppressant to account for potential increased concentrations of the immunosuppressant and monitor for immunosuppressant-related adverse events. Therapeutic drug monitoring of immunosuppressant is recommended. Consult with a specialist as necessary.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Lipid-Modifying		
Atorvastatin	↑ atorvastatin possible	No dose adjustment needed
Fluvastatin	↔ expected	No dose adjustment needed
Lomitapide	↑ lomitapide expected	**Contraindicated**
Lovastatin	↑ lovastatin expected	Administer the lowest effective lovastatin dose while monitoring for adverse events.
Pitavastatin	↔ expected	No dose adjustment needed
Pravastatin	↔ expected	No dose adjustment needed
Rosuvastatin	↑ rosuvastatin possible	No dose adjustment needed
Simvastatin	↑ simvastatin expected	Administer the lowest effective simvastatin dose while monitoring for adverse events.
Narcotics and Treatment for Opioid Dependence		
Buprenorphine Sublingual, buccal, or implant	↑ buprenorphine possible	**Initiation of Buprenorphine in Patients Taking LEN** • Titrate buprenorphine dose to desired effect and use the lowest feasible initial dose. **Initiation of LEN in Patients Taking Buprenorphine** • Dose adjustment for buprenorphine may be needed. Monitor for buprenorphine-related adverse events.
Fentanyl	↑ fentanyl possible	Monitor for fentanyl-related adverse events, including potentially fatal respiratory depression. Fentanyl dose reduction may be necessary.
Lofexidine	↔ expected	No dose adjustment needed
Methadone	↑ methadone possible	**Initiation of Methadone in Patients Taking LEN** • Titrate methadone dose to desired effect and use the lowest feasible initial dose.

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		Initiation of LEN in Patients Taking Methadone • Dose adjustment for methadone may be needed. Monitor for buprenorphine-related adverse events.
Oxycodone	↑ oxycodone possible	Monitor for opioid-related adverse events, including potentially fatal respiratory depression. Oxycodone dose reduction may be necessary.
Tramadol	↑ tramadol possible	Tramadol dose adjustments may be necessary. Monitor for clinical response and tramadol-related adverse events.
PDE5 Inhibitors		
Avanafil	↑ avanafil expected	Avanafil dose should not exceed 50 mg once every 24 hours.
Sildenafil	↑ sildenafil expected	**For Treatment of Erectile Dysfunction** • Start with sildenafil 25 mg and monitor for sildenafil-related adverse events. **For Treatment of PAH** • Reduce the dose of sildenafil to 20 mg three times a day when discontinuing treatment with LEN.
Tadalafil	↑ tadalafil expected	**For Treatment of Erectile Dysfunction** • For once-daily use: Consider maximum dose of 2.5 mg daily. If higher dose is needed, consider alternative PDE5 inhibitor. • For use as needed: Consider maximum dose of 10 mg every 72 hours. If higher dosing is needed, consider alternative PDE5 inhibitor. **For Treatment of PAH** • **Do not coadminister.**

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
		For Treatment of Benign Prostatic Hyperplasia • Consider maximum dose of 2.5 mg daily. Use caution and monitor for AEs if dose increases to 5 mg.
Vardenafil	↑ vardenafil expected	Vardenafil dose should not exceed 5 mg once every 24 hours.
Sedative/Hypnotics		
Benzodiazepines		
Alprazolam, Diazepam, Triazolam	↑ benzodiazepine expected	Consider lowest dose and monitor for benzodiazepine-related adverse events.
Clonazepam	↑ clonazepam possible	Use with caution and consider alternative benzodiazepines.
Lorazepam, Oxazepam, Temazepam	↔ expected	No dose adjustment needed
Midazolam (Oral)	↑ midazolam AUC 259–308%	Use with caution and consider alternative benzodiazepine.
Orexin Receptor Antagonist		
Daridorexant, Lemborexant, Suvorexant	↑ daridorexant expected ↑ lemborexant expected ↑ suvorexant expected	Maximum recommended daridorexant dose is 25 mg. **Do not coadminister** with lemborexant. Initiate suvorexant dose at 5 mg daily. Suvorexant dose can be increased to 10 mg once per night if the 5 mg dose is not effective. **Do not exceed** 10 mg per night.
Other Sedatives		
Eszopiclone	↑ eszopiclone expected	Consider lowest dose and monitor for eszopiclone-related adverse events.
Zolpidem	↑ zolpidem possible	Consider initiating zolpidem at a low dose.
Miscellaneous Drugs		
Calcifediol	↑ calcifediol possible	No dose adjustment needed

Table 24g. Drug Interactions Between the Capsid Inhibitor Lenacapavir and Other Drugs (Including Antiretroviral Drugs)

Concomitant Drug Class/ Name	Effect on LEN and/or Concomitant Drug Concentrations	Dosing Recommendations and Clinical Comments
Cisapride	↑ cisapride expected	**Do not coadminister.**
Colchicine	↑ colchicine expected	**For Treatment of Gout Flares** • Administer single colchicine dose of 1.2 mg. Do not repeat dose for at least 3 days. **For Treatment of Familial Mediterranean Fever** • Colchicine dose should not exceed 1.2 mg daily (may be given as 0.6 mg twice a day).
Dronabinol	↔ expected	No dose adjustment needed
Eluxadoline	↔ expected	No dose adjustment needed
Finerenone	↑ finerenone expected	Monitor serum potassium at initiation and during therapy according to finerenone product labeling.
Flibanserin	↑ flibanserin expected	**Contraindicated**
Naloxegol	↑ naloxegol expected	Avoid use; if coadministration is necessary, decrease dosage of naloxegol and monitor for naloxegol-related adverse events.
Praziquantel	↑ praziquantel possible	Consider alternative antiretroviral. If coadministration is necessary, monitor for praziquantel-related adverse events.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse event; AUC = area under the curve; ARV = antiretroviral; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; CD4 = CD4 T lymphocyte; CHF = congestive heart failure; CMV = cytomegalovirus; CNS = central nervous system; CV = cardiovascular; CYP = cytochrome P450; DOR = doravirine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; ECG = electrocardiogram; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; FTR = fostemsavir; IBA = ibalizumab; IM = intramuscular; INR = international normalized ratio; INSTI = integrase strand transfer inhibitor; QTc = QT corrected for heart rate; LEN = lenacapavir; MI = myocardial infarction; MPA = medroxyprogesterone acetate; MVC = maraviroc; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PAH = pulmonary arterial hypertension; PDE5 = phosphodiesterase type 5; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

Updated: September 12, 2024
Reviewed: September 12, 2024

Note: Interactions associated with unboosted atazanavir (ATV), delavirdine (DLV), fosamprenavir (FPV), indinavir (IDV), lopinavir (LPV), nelfinavir (NFV), nevirapine (NVP), saquinavir (SQV), and tipranavir (TPV) are **not** included in this table. Please refer to the U.S. Food and Drug Administration product labels for information regarding interactions between these drugs and other concomitant drugs.

Rilpivirine (RPV) intramuscular (IM) is not included in this table, because the combination of cabotegravir (CAB) IM plus RPV IM is a two-drug co-packaged product. Therefore, RPV IM is not expected to be used with a protease inhibitor.

PIs		NNRTIs			
		DOR	**EFV**	**ETR**	**RPV**
ATV/c	**PK Data**	↑ DOR expected ↔ ATV expected	↔ EFV expected ↓ ATV possible ↓ COBI possible	↑ ETR possible ↓ ATV possible ↓ COBI possible	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed	**ATV/c in ART-Naive Patients** • ATV 400 mg plus COBI 150 mg once daily • **Do not use** coformulated ATV 300 mg/COBI 150 mg. **ATV/c in ART-Experienced Patients** • **Do not coadminister.** No dose adjustment needed for EFV.	**Do not coadminister.**	No dose adjustment needed

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

PIs		NNRTIs			
		DOR	**EFV**	**ETR**	**RPV**
ATV/r	**PK Data**	↑ DOR expected ↔ ATV expected	↔ EFV expected **(ATV 400 mg Plus RTV 100 mg) Once Daily** • ATV concentrations similar to (ATV 300 mg plus RTV 100 mg) without EFV	**(ATV 300 mg Plus RTV 100 mg) Once Daily** • ETR AUC and C_{min} both ↑ ~30% • ↔ ATV AUC and C_{min}	↑ RPV PO possible ↔ ATV expected
	Dose	No dose adjustment needed	**ATV/r in ART-Naive Patients** • (ATV 400 mg plus RTV 100 mg) once daily **ATV/r in ART-Experienced Patients** • **Do not coadminister.** No dose adjustment needed for EFV	No dose adjustment needed	No dose adjustment needed
DRV/c	**PK Data**	↑ DOR expected ↔ DRV expected	↔ EFV expected ↓ DRV possible ↓ COBI possible	**ETR 400 mg Once Daily With (DRV 800 mg Plus COBI 150 mg) Once Daily** • ↔ ETR AUC and C_{min} • ↔ DRV AUC and C_{min} ↓ 56% • COBI AUC ↓ 30% and C_{min} ↓ 66%	↔ DRV expected ↑ RPV PO possible
	Dose	No dose adjustment needed	**Do not coadminister.**	**Do not coadminister.**	No dose adjustment needed

Table 25a. Interactions Between Non-Nucleoside Reverse Transcriptase Inhibitors and Protease Inhibitors

PIs		NNRTIs			
		DOR	**EFV**	**ETR**	**RPV**
DRV/r	**PK Data**	↑ DOR expected ↔ DRV expected	**With (DRV 300 mg Plus RTV 100 mg) Twice Daily** • EFV AUC ↑ 21% • ↔ DRV AUC and C_{min} ↓ 31%	**ETR 100 mg Twice Daily With (DRV 600 mg Plus RTV 100 mg) Twice Daily** • ETR AUC ↓ 37% and C_{min} ↓ 49% • ↔ DRV	**RPV 150 mg PO Once Daily With (DRV 800 mg Plus RTV 100 mg) Once Daily** • RPV PO AUC ↑ 130% and C_{min} ↑ 178% • ↔ DRV
	Dose	No dose adjustment needed	Clinical significance unknown. Use standard doses and monitor patient closely. Consider monitoring drug levels.	No dose adjustment needed Despite reduced ETR concentration, safety and efficacy of this combination have been established in a clinical trial.	No dose adjustment needed

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ART = antiretroviral therapy; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; C_{min} = minimum plasma concentration; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; EFV = efavirenz; ETR = etravirine; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PO = oral; PK = pharmacokinetic; RPV = rilpivirine; RTV = ritonavir

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

Updated: September 12, 2024
Reviewed: September 12, 2024

Recommendations for managing a particular drug interaction may differ depending on whether a new antiretroviral (ARV) drug is being initiated in a patient on a stable concomitant medication, or a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly.

Information on drug interactions with oral (PO) cabotegravir (CAB) is not included in this table. The CAB PO tablet is not available in retail pharmacies and will be provided directly to people with HIV for short-term use only (PO lead-in and to bridge if intramuscular [IM] administration is delayed).

CAB IM and rilpivirine (RPV) IM are not included in this table because the combination is a two-drug, co-packaged product. Therefore, it is not anticipated that they will be used with PO non-nucleoside reverse transcriptase inhibitors (NNRTIs) or protease inhibitors (PIs).

ARV Drugs by Drug Class		INSTIs			
		BIC	**DTG**	**EVG/c**	**RAL**
NNRTIs					
DOR	**PK Data**	↔ DOR and BIC expected	↔ DOR DTG AUC ↑ 36% and C_{min} ↑ 27%	↑ DOR expected ↔ EVG	↔ DOR and RAL expected
	Dose	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.	No dose adjustment needed.
EFV	**PK Data**	↓ BIC expected	**With DTG 50 mg Once Daily** • DTG AUC ↓ 57% and C_{min} ↓ 75%	↑ or ↓ EVG, COBI, and EFV possible	**With RAL 400 mg Twice Daily** • RAL AUC ↓ 36% and C_{min} ↓ 21% **With RAL 1,200 mg Once Daily** • ↔ RAL AUC and C_{min}

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
	Dose	**Do not coadminister.**	**In Patients Without INSTI Resistance** • DTG 50 mg twice daily **In Patients With Certain INSTI-Associated Resistance[a] or Clinically Suspected INSTI Resistance** • Consider alternative combination	**Do not coadminister.**	No dose adjustment needed.
ETR	**PK Data**	↓ BIC expected	**ETR 200 mg Twice Daily Plus DTG 50 mg Once Daily** • DTG AUC ↓ 71% and C_{min} ↓ 88% **ETR 200 mg Twice Daily With (DRV 600 mg Plus RTV 100 mg) Twice Daily and DTG 50 mg Once Daily** • DTG AUC ↓ 25% and C_{min} ↓ 37%	↑ or ↓ EVG, COBI, and ETR possible	**ETR 200 mg Twice Daily Plus RAL 400 mg Twice Daily** • ETR C_{min} ↑ 17% • RAL C_{min} ↓ 34%
	Dose	**Do not coadminister.**	**Do not coadminister** ETR and DTG without concurrently administering ATV/r or DRV/r. **In Patients Without INSTI Resistance** • DTG 50 mg once daily with ETR (concurrently with ATV/r or DRV/r)	**Do not coadminister.**	RAL 400 mg twice daily Coadministration with RAL 1,200 mg once daily **is not recommended.**

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	DTG	EVG/c	RAL
			In Patients With Certain INSTI-Associated Resistance[a] or Clinically Suspected INSTI Resistance • DTG 50 mg twice daily with ETR (concurrently with ATV/r or DRV/r)		
RPV	**PK Data**	No data	**With DTG 50 mg Once Daily** • ↔ DTG AUC and C_{min} ↑ 22% • ↔ RPV PO AUC and C_{min} ↑ 21%	↑ RPV PO possible	↔ RPV PO RAL C_{min} ↑ 27%
	Dose	No dose adjustment needed.	No dose adjustment needed.	**Do not coadminister.**	No dose adjustment needed.
PIs					
ATV/c	**PK Data**	BIC AUC ↑ 306%	No data	Not applicable	No data
	Dose	**Do not coadminister.**	No dose adjustment needed.	**Do not coadminister** two COBI-containing products.	No dose adjustment needed.
ATV/r	**PK Data**	↑ BIC expected	**(ATV 300 mg Plus RTV 100 mg) Once Daily Plus DTG 30 mg Once Daily** • DTG AUC ↑ 62% and C_{min} ↑ 121%	Not applicable	**With (ATV 300 mg Plus RTV 100 mg) Once Daily** • RAL AUC ↑ 41%
	Dose	**Do not coadminister.**	No dose adjustment needed.	Do not coadminister RTV and COBI.	No dose adjustment needed.

Table 25b. Interactions Between Integrase Strand Transfer Inhibitors and Non-Nucleoside Reverse Transcriptase Inhibitors or Protease Inhibitors

ARV Drugs by Drug Class		INSTIs			
		BIC	**DTG**	**EVG/c**	**RAL**
DRV	**PK Data**	Not applicable	Not applicable	↔ DRV or EVG expected	Not applicable
	Dose	**Do not administer** DRV without RTV or COBI.	**Do not administer** DRV without RTV or COBI.	No dose adjustment needed.	**Do not administer** DRV without RTV or COBI.
DRV/c	**PK Data**	BIC AUC ↑ 74%	**DRV/c Plus DTG Once Daily** • ↔ DTG, DRV, and COBI **DTG 50 mg Once Daily and DRV/r Once Daily Switched to DRV/c** • DTG C_{min} ↑ 100%	Not applicable	No data
	Dose	No dose adjustment needed.	No dose adjustment needed.	**Do not coadminister** two COBI-containing products.	No dose adjustment needed.
DRV/r	**PK Data**	No data	**(DRV 600 mg Plus RTV 100 mg) Twice Daily With DTG 30 mg Once Daily** • DTG AUC ↓ 22% and C_{min} ↓ 38%	Not applicable	**With (DRV 600 mg Plus RTV 100 mg) Twice Daily** • RAL AUC ↓ 29% and Cmin ↑ 38%
	Dose	No dose adjustment needed.	No dose adjustment needed.	**Do not coadminister** RTV and COBI.	No dose adjustment needed.

[a] Refer to DTG product label for details.

Key to Symbols

↑ = increase
↓ = decrease
↔ = less than 20% change in AUC

Key: ARV = antiretroviral; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; BIC = bictegravir; C_{min} = minimum plasma concentration; COBI = cobicistat; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PK = pharmacokinetic; PO = oral; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir

APPENDIX A. DRUG CHARACTERISTICS TABLES

Appendix A, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Updated: September 12, 2024
Reviewed: September 25, 2025

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved coformulated and copackaged antiretroviral regimens for adults with HIV. Not all products are FDA approved for adolescents with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines. Please see the class-specific drug characteristics tables (Appendix A, Tables 3, 4, 5, and 6) for details about the individual drugs included in these products, including information on elimination and metabolic pathways, serum and intracellular half-lives, and adverse effects. The products in this table are listed by drug class and arranged **in alphabetical order** by generic name within each class.

Generic Name (Abbreviation) *Trade Name*	**ARV Drugs Included in the Regimen**	**Dosing Recommendation**[a]
INSTI Plus Two NRTIs		
Bictegravir/Tenofovir Alafenamide/Emtricitabine (BIC/TAF/FTC) *Biktarvy*	BIC 50 mg/TAF 25 mg/FTC 200 mg	One tablet PO once daily
Dolutegravir/Abacavir/Lamivudine (DTG/ABC/3TC) *Triumeq*	DTG 50 mg/ABC 600 mg/3TC 300 mg	One tablet PO once daily
Elvitegravir/Cobicistat/Tenofovir Alafenamide/Emtricitabine (EVG/c/TAF/FTC) *Genvoya*	EVG 150 mg/COBI 150 mg/TAF 10 mg/FTC 200 mg	One tablet PO once daily with food
Elvitegravir/Cobicistat/Tenofovir Disoproxil Fumarate/Emtricitabine (EVG/c/TDF/FTC) *Stribild*	EVG 150 mg/COBI 150 mg/TDF 300 mg/FTC 200 mg	One tablet PO once daily with food

Appendix A, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Generic Name (Abbreviation) *Trade Name*	**ARV Drugs Included in the Regimen**	**Dosing Recommendation**[a]
INSTI Plus One NRTI		
Dolutegravir/Lamivudine (DTG/3TC) *Dovato*	DTG 50 mg/3TC 300 mg	One tablet PO once daily
INSTI Plus One NNRTI		
Cabotegravir/Rilpivirine (CAB/RPV) *Cabenuva*	**Cabenuva 600-mg/900-mg Kit:** • CAB 600-mg/3-mL vial and RPV 900-mg/3-mL vial **Cabenuva 400-mg/600-mg Kit:** • CAB 400-mg/2-mL vial and RPV 600-mg/2-mL vial	**Optional Lead-In With Oral CAB and RPV** • CAB 30 mg PO and RPV 25 mg PO once daily with food for 4 weeks **Monthly IM CAB and RPV** • Loading dose: CAB 600 mg/3 mL IM for 1 dose and RPV 900 mg/3 mL IM for 1 dose • Continuation phase: CAB 400 mg/2 mL IM every 4 weeks and RPV 600 mg/2 mL IM every 4 weeks **Every 2-Month IM CAB and RPV** • Loading dose: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM **once monthly** for 2 doses • Continuation phase: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM every 2 months
Dolutegravir/Rilpivirine (DTG/RPV) *Juluca*	DTG 50 mg/RPV 25 mg	One tablet PO once daily with food
NNRTI Plus Two NRTIs		
Doravirine/Tenofovir Disoproxil Fumarate/Lamivudine (DOR/TDF/3TC) *Delstrigo*	DOR 100 mg/TDF 300 mg/3TC 300 mg	One tablet PO once daily

Appendix A, Table 1. Coformulated and Copackaged Antiretroviral Regimens

Generic Name (Abbreviation) *Trade Name*	**ARV Drugs Included in the Regimen**	**Dosing Recommendation**[a]
Efavirenz/Tenofovir Disoproxil Fumarate/Emtricitabine (EFV/TDF/FTC) *Generic Only*	EFV 600 mg/TDF 300 mg/FTC 200 mg	One tablet PO once daily on an empty stomach, preferably at bedtime
Efavirenz/Tenofovir Disoproxil Fumarate/Lamivudine (EFV/TDF/3TC) *Symfi*	EFV 600 mg/TDF 300 mg/3TC 300 mg	One tablet PO once daily on an empty stomach, preferably at bedtime
Rilpivirine/Tenofovir Alafenamide/Emtricitabine (RPV/TAF/FTC) *Odefsey*	RPV 25 mg/TAF 25 mg/FTC 200 mg	One tablet PO once daily with food
Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine (RPV/TDF/FTC) *Complera*	RPV 25 mg/TDF 300 mg/FTC 200 mg	One tablet PO once daily with food
PI Plus Two NRTIs		
Darunavir/Cobicistat/Tenofovir Alafenamide/Emtricitabine (DRV/c/TAF/FTC) *Symtuza*	DRV 800 mg/COBI 150 mg/TAF 10 mg/FTC 200 mg	One tablet PO once daily with food

[a] For dose adjustments in people with renal or hepatic insufficiency, see Appendix B. When no food restriction is listed, the product can be taken with or without food.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; BIC = bictegravir; c or COBI = cobicistat; CAB = cabotegravir; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FTC = emtricitabine; IM = intramuscularly; INSTI = integrase strand transfer inhibitor; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PO = orally; RPV = rilpivirine; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix A, Table 2. Nucleoside Reverse Transcriptase Inhibitor–Based, Fixed-Dose Combination Tablets for Use as Part of an Antiretroviral Regimen

Updated: September 25, 2025
Reviewed: September 25, 2025

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved dual nucleoside reverse transcriptase inhibitor fixed-dose combination (FDC) products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines. These FDC tablets are not complete regimens and must be administered in combination with other antiretroviral drugs. FDC products that contain zidovudine (ZDV) have been removed from this table. Please refer to the FDA product labels for information regarding ZDV-containing FDCs. Please see the class-specific drug characteristics tables (Appendix A, Tables 3, 4, 5, and 6) for details about the individual drugs contained in these FDC products, including information on elimination and metabolic pathways, serum and intracellular half-lives, and adverse effects. The FDC tablets in this table are listed by generic name.

Generic Name (Abbreviation) *Trade Name*	**ARV Drugs Included in the FDC Tablet**	**Dosing Recommendation**[a]
Abacavir/Lamivudine (ABC/3TC) *Generic Only*	ABC 600 mg/3TC 300 mg	One tablet PO once daily
Tenofovir Alafenamide/Emtricitabine (TAF/FTC) *Descovy*	TAF 25 mg/FTC 200 mg	One tablet PO once daily
Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC) *Truvada* **Note:** Generic product available.	TDF 300 mg/FTC 200 mg	One tablet PO once daily
Tenofovir Disoproxil Fumarate/Lamivudine (TDF/3TC) *Cimduo*	TDF 300 mg/3TC 300 mg	One tablet PO once daily

[a] For dose adjustments in people with renal or hepatic insufficiency, see Appendix B. All FDC tablets listed in this table can be taken without regard to food.

Key: 3TC = lamivudine; ABC = abacavir; ARV = antiretroviral; FDC = fixed-dose combination; FTC = emtricitabine; NRTI = nucleoside reverse transcriptase inhibitor; PO = orally; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix A, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

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Reviewed: September 25, 2025

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved nucleoside reverse transcriptase inhibitor products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines. The older nucleoside reverse transcriptase inhibitors didanosine (ddI) and stavudine (d4T) have been discontinued in the United States. Zidovudine (ZDV) is no longer used commonly in clinical practice. Therefore, these antiretrovirals have been removed from this table. Please refer to the FDA product label for ZDV for information regarding this drug.

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum/ Intracellular Half-Lives**	**Adverse Events**[b]
Abacavir (ABC) *Ziagen* **Note:** Generic products are available.	**Ziagen** • 20-mg/mL oral solution **Generic** • 300-mg tablet • Also available as FDC with 3TC **FDC Tablets That Contain ABC**[c] • ABC/3TC **STRs That Contain ABC**[d] • Triumeq (DTG/ABC/3TC)	• ABC 600 mg PO once daily, *or* • ABC 300 mg PO twice daily See Appendix A, Tables 1 and 2 for dosing information for FDC tablets that contain ABC.	Metabolized by alcohol dehydrogenase and glucuronyl transferase 82% of ABC dose is excreted in the urine as metabolites of ABC. Dose adjustment is recommended in people with hepatic insufficiency (see Appendix B).	1.5 hours/ 12–26 hours	People who test positive for HLA-B*5701 are at the highest risk of experiencing HSRs. HLA screening should be done before initiating ABC. For people with a history of HSRs, rechallenge **is not recommended.** Symptoms of HSRs may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, fatigue, or respiratory symptoms (e.g., sore throat, cough, or shortness of breath). Some cohort studies suggest an increased risk of MI with recent or current use of ABC, but this risk is not substantiated in other studies.

Appendix A, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum/ Intracellular Half-Lives**	**Adverse Events**[b]
Emtricitabine (FTC) *Emtriva* **Note:** Generic products are available.	**Emtriva** • 200-mg hard gelatin capsule • 10-mg/mL oral solution **Generic** • 200-mg capsule • Also available as FDC with TDF **FDC Tablets That Contain FTC**[c] • Descovy (TAF/FTC) • Truvada (TDF/FTC) **STRs That Contain FTC**[d] • Biktarvy (BIC/TAF/FTC) • Complera (RPV/TDF/FTC) • EFV/TDF/FTC (generic) • Genvoya (EVG/c/TAF/FTC) • Odefsey (RPV/TAF/FTC) • Stribild (EVG/c/TDF/FTC) • Symtuza (DRV/c/TAF/FTC)	*Capsule* • FTC 200 mg PO once daily *Oral Solution* • FTC 240 mg (24 mL) PO once daily See Appendix A, Tables 1 and 2 for dosing information for FDC tablets that contain FTC.	86% of FTC dose is excreted renally. See Appendix B for dosing recommendations in people with renal insufficiency.	10 hours/ >20 hours	Minimal toxicity Hyperpigmentation/skin discoloration Severe acute exacerbation of hepatitis may occur in people with HBV/HIV coinfection who discontinue FTC.
Lamivudine (3TC) *Epivir* **Note:** Generic products are available.	**Epivir** • 150-mg and 300-mg tablets • 10-mg/mL oral solution **Generic** • 100-mg, 150-mg, and 300-mg tablets • 10-mg/mL oral solution • Also available as FDC with ABC	• 3TC 300 mg PO once daily, *or* • 3TC 150 mg PO twice daily See Appendix A, Tables 1 and 2 for dosing information for FDC tablets that contain 3TC.	70% of 3TC dose is excreted renally. See Appendix B for dose recommendations in people with renal insufficiency.	5–7 hours/ 18–22 hours	Minimal toxicity Severe acute exacerbation of hepatitis may occur in people with HBV/HIV coinfection who discontinue 3TC.

Appendix A, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum/ Intracellular Half-Lives**	**Adverse Events**[b]
	FDC Tablets That Contain 3TC[c] • ABC/3TC (generic) • Cimduo (TDF/3TC) **STRs That Contain 3TC**[d] • Delstrigo (DOR/TDF/3TC) • Dovato (DTG/3TC) • Symfi (EFV/TDF/3TC) • Triumeq (DTG/ABC/3TC)				
Tenofovir Alafenamide (TAF) *Vemlidy* **Note:** Vemlidy is available as a 25-mg tablet for the treatment of HBV.	**FDC Tablets That Contain TAF**[c] • Descovy (TAF/FTC) **STRs That Contain TAF**[d] • Biktarvy (BIC/TAF/FTC) • Genvoya (EVG/c/TAF/FTC) • Odefsey (RPV/TAF/FTC) • Symtuza (DRV/c/TAF/FTC)	See Appendix A, Tables 1 and 2 for dosing information for FDC tablets that contain TAF.	Metabolized by cathepsin A See Appendix B for dosing recommendations in people with renal insufficiency.	0.5 hour/ 150–180 hours	Renal insufficiency, Fanconi syndrome, and proximal renal tubulopathy are less likely to occur with TAF than with TDF. Osteomalacia and decreases in BMD are less likely to occur with TAF than with TDF. Severe acute exacerbation of hepatitis may occur in people with HBV/HIV coinfection who discontinue TAF. Diarrhea, nausea, headache Greater weight increase has been reported with TAF than with TDF.

Appendix A, Table 3. Characteristics of Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum/ Intracellular Half-Lives**	**Adverse Events**[b]
Tenofovir Disoproxil Fumarate (TDF) *Viread* **Note:** Generic products are available.	**Viread** • 300-mg tablet • 40-mg/g oral powder **Generic** • 300-mg tablet • Also available as FDC with FTC **FDC Tablets That Contain TDF**[c] • Cimduo (TDF/3TC) • Truvada (TDF/FTC) **STRs That Contain TDF**[d] • Complera (RPV/TDF/FTC) • Delstrigo (DOR/TDF/3TC) • EFV/TDF/FTC (generic) • Stribild (EVG/c/TDF/FTC) • Symfi (EFV/TDF/3TC)	• TDF 300 mg PO once daily, *or* • 7.5 level scoops of oral powder PO once daily (dosing scoop dispensed with each bottle; one level scoop contains 1 g of oral powder). Mix oral powder with 2–4 ounces of a soft food that does not require chewing (e.g., applesauce, yogurt). **Do not mix oral powder with liquid.** See Appendix A, Tables 1 and 2 for dosing information for FDC tablets that contain TDF.	Renal excretion is the primary route of elimination. See Appendix B for dose recommendations in people with renal insufficiency.	17 hours/ >60 hours	Renal insufficiency, Fanconi syndrome, proximal renal tubulopathy Osteomalacia, decrease in BMD Asthenia, headache, diarrhea, nausea, vomiting, flatulence Severe acute exacerbation of hepatitis may occur in people with HBV/HIV coinfection who discontinue TDF.

[a] For dose adjustments in people with renal or hepatic insufficiency, see Appendix B. When no food restriction is listed, the antiretroviral drug can be taken with or without food.

[b] Also see Table 21.

[c] See Appendix A, Table 2 for information about these formulations.

[d] See Appendix A, Table 1 for information about these formulations.

Key: 3TC = lamivudine; ABC = abacavir; BIC = bictegravir; BMD = bone mineral density; DOR = doravirine; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; EVG/c = elvitegravir/cobicistat; FDC = fixed-dose combination; FTC = emtricitabine; HBV = hepatitis B virus; HLA = human leukocyte antigen; HSR = hypersensitivity reaction; MI = myocardial infarction; PO = orally; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix A, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors

Updated: September 25, 2025
Reviewed: September 25, 2025

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved non-nucleoside reverse transcriptase inhibitor (NNRTI) products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines. The older NNRTIs delavirdine (DLV) and nevirapine (NVP) are **not** listed in this table; DLV has been discontinued and NVP is no longer commonly used in clinical practice in the United States.

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum Half-Life**	**Adverse Events**[b]
Doravirine (DOR) *Pifeltro*	**Pifeltro** • 100-mg tablet **STRs That Contain DOR**[c] • Delstrigo (DOR/TDF/3TC)	• DOR 100 mg PO once daily See Appendix A, Table 1 for dosing information for Delstrigo.	CYP3A4/5 substrate	15 hours	Rash, including Stevens-Johnson syndrome Nausea Dizziness Abnormal dreams
Efavirenz (EFV) **Note:** Generic only	**Efavirenz** (generic) • 600-mg tablet **STRs That Contain EFV**[c] • EFV/TDF/FTC (generic) • Symfi (EFV/TDF/3TC)	• EFV 600 mg PO once daily on an empty stomach, preferably at or before bedtime See Appendix A, Table 1 for dosing information for STRs that contain EFV.	Metabolized by CYP2B6 (primary), 3A4, and 2A6 CYP3A4 mixed inducer/inhibitor (more an inducer than an inhibitor) CYP2B6 and 2C19 inducer	40–55 hours	Rash, including Stevens-Johnson syndrome Neuropsychiatric symptoms[d] Serum transaminase elevations Hyperlipidemia QT interval prolongation Use of EFV may lead to false-positive results with some cannabinoid and benzodiazepine screening assays.
Etravirine (ETR) *Intelence* **Note:** Generic products are available.	**Intelence** • 100-mg and 200-mg tablets **Generic** • 100-mg and 200-mg tablets	• ETR 200 mg PO twice daily following a meal.	CYP3A4, 2C9, and 2C19 substrate CYP3A4 inducer CYP2C9 and 2C19 inhibitor	41 hours	Rash, including Stevens-Johnson syndrome HSRs, characterized by rash, constitutional findings, and sometimes organ dysfunction (including hepatic failure), have been reported. Nausea

Appendix A, Table 4. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum Half-Life**	**Adverse Events**[b]
Rilpivirine (RPV) *Edurant*	**Edurant** • 25-mg tablet **STRs That Contain RPV**[c] • Complera (RPV/TDF/FTC) • Juluca (DTG/RPV) • Odefsey (RPV/TAF/FTC) **Copackaged IM Regimen** • Cabenuva (CAB plus RPV)	• RPV 25 mg PO once daily with food See Appendix A, Table 1 for dosing information for coformulated and copackaged regimens that contain RPV.	CYP3A4 substrate	PO: 50 hours IM: 13–28 weeks	Rash, including Stevens-Johnson syndrome Depressive disorders, insomnia, headache Hepatotoxicity QT interval prolongation **IM Formulation Only** • Injection site reactions (pain, induration, swelling, nodules) • Rare postinjection reaction (dyspnea, agitation, abdominal cramps, flushing) occurring within a few minutes after RPV IM injection; possibly associated with inadvertent IV administration.

[a] For dose adjustments in people with renal or hepatic insufficiency, see Appendix B. When no food restriction is listed, the antiretroviral drug can be taken with or without food.

[b] Also see Table 21.

[c] See Appendix A, Table 1 for information about these formulations.

[d] Adverse events can include dizziness, somnolence, insomnia, abnormal dreams, depression, suicidality (e.g., suicide, suicide attempt or ideation), confusion, abnormal thinking, impaired concentration, amnesia, agitation, depersonalization, hallucinations, and euphoria. Approximately 50% of people who are receiving EFV may experience any of these symptoms. Symptoms usually subside spontaneously after 2–4 weeks, but discontinuation of EFV may be necessary in a small percentage of people. Late-onset neurotoxicities, including ataxia and encephalopathy, have been reported.

Key: 3TC = lamivudine; ARV = antiretroviral; CAB = cabotegravir; CD4 = CD4 T lymphocyte; CYP = cytochrome P; DOR = doravirine; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; FTC = emtricitabine; HSR = hypersensitivity reaction; IM = intramuscular; IV = intravenous; NNRTI = non-nucleoside reverse transcriptase inhibitor; PO = orally; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Appendix A, Table 5. Characteristics of Protease Inhibitors

Updated: September 25, 2025
Reviewed: September 25, 2025

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved protease inhibitor products for adults with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines. The older protease inhibitors indinavir (IDV) and saquinavir (SQV) have been discontinued in the United States; fosamprenavir (FPV), lopinavir/ritonavir (LPV/r), nelfinavir (NFV), and tipranavir (TPV) are no longer used commonly in clinical practice. These agents have been removed from this table. Please refer to the July 10, 2019, version of the guidelines (found in the Adult and Adolescent Antiretroviral Archived Guidelines section of the Archived Guidelines webpage on the Clinicalinfo website) or to the FDA product labels for information regarding these drugs.

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum Half-Life**	**Adverse Events**[b]
Atazanavir (ATV) *Reyataz* **Note:** Generic products are available.	**Reyataz** • 200-mg and 300-mg capsules • 50-mg oral powder/packet **Generic** • 200-mg and 300-mg capsules **FDCs That Contain ATV** • Evotaz (ATV 300mg/COBI 150mg)	**Reyataz** *In People Without Prior ARV Treatment* • (ATV 300 mg plus RTV 100 mg) PO once daily with food; *or* • ATV 400 mg PO once daily with food. *With TDF or in ARV-Experienced People* • (ATV 300 mg plus RTV 100 mg) PO once daily with food. • Unboosted ATV is not recommended. *With EFV in People Without Prior ARV Treatment* • (ATV 400 mg plus RTV 100 mg) PO once daily with food. **Evotaz** • One tablet PO once daily with food.	**ATV** • CYP3A4 inhibitor and substrate • Weak CYP2C8 inhibitor • UGT1A1 inhibitor **COBI** • CYP3A inhibitor and substrate • CYP2D6 inhibitor Dose adjustment is recommended in people with hepatic insufficiency (see Appendix B).	7 hours	Indirect hyperbilirubinemia Cholelithiasis Nephrolithiasis Renal insufficiency Serum transaminase elevations Hyperlipidemia (especially with RTV boosting) Skin rash Hyperglycemia Lipodystrophy An increase in serum creatinine may occur when ATV is administered with COBI. PR interval prolongation: First-degree symptomatic AV block has been reported. Use with caution in people who have underlying conduction defects or who are on concomitant medications that can cause PR prolongation.

Appendix A, Table 5. Characteristics of Protease Inhibitors

Generic Name (Abbreviation) *Trade Name*	Formulations	Dosing Recommendations[a]	Elimination/ Metabolic Pathway	Serum Half-Life	Adverse Events[b]
		• The use of ATV/c **is not recommended** for people who are taking TDF and who have baseline CrCl <70 mL/min (see Appendix B for the equation for calculating CrCl). For dosing recommendations for people who also are receiving H2 antagonists and PPIs, refer to Table 24a.			
Darunavir (DRV) *Prezista* **Note:** Generic products are available.	**Prezista** • 600-mg and 800-mg tablets • 100-mg/mL oral suspension **Generic** • 600-mg and 800-mg tablets **FDCs That Contain DRV** • Prezcobix (DRV 800mg/COBI 150mg) **STRs That Contain DRV** • Symtuza (DRV/c/TAF/FTC)	**Prezista** *In People Without Prior ARV Treatment or ARV-Experienced Treatment With No DRV Mutations* • (DRV 800 mg plus RTV 100 mg) PO once daily with food *In ARV-Experienced People With One or More DRV Resistance Mutations* • (DRV 600 mg plus RTV 100 mg) PO twice daily with food DRV is not available as an FDC tablet with RTV. Unboosted DRV **is not recommended.** **Prezcobix** • One tablet PO once daily with food. • **Not recommended** for people with one or more DRV resistance-associated mutations. • Coadministering Prezcobix and TDF **is not recommended** for people with baseline CrCl <70 mL/min (see Appendix B for the equation for calculating CrCl). See Appendix A, Table 1 for dosing information for Symtuza.	**DRV** • CYP3A4 inhibitor and substrate • CYP2C9 inducer **COBI** • CYP3A inhibitor and substrate • CYP2D6 inhibitor	15 hours when combined with RTV 7 hours when combined with COBI	Hepatotoxicity Diarrhea, nausea Headache Hyperlipidemia Serum transaminase elevation Hyperglycemia Lipodystrophy An increase in serum creatinine may occur when DRV is administered with COBI. Skin rash: DRV has a sulfonamide moiety; however, incidence and severity of rash are similar in those with or without a sulfonamide allergy—Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalized exanthematous pustulosis, and erythema multiforme have been reported.

Appendix A, Table 5. Characteristics of Protease Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathway**	**Serum Half-Life**	**Adverse Events**[b]
Ritonavir (RTV) *Norvir* **Note:** Generic product available. RTV was initially developed as a PI for HIV treatment but is now used at a lower dose of 100 mg once or twice daily as a PK enhancer to increase the concentrations of other PIs.	**Norvir** • 100-mg tablet • 100-mg single packet oral powder **Generic** • 100-mg tablet Also available as an FDC tablet of LPV/r in both brand (Kaletra) and generic versions	**As a PK Booster (or Enhancer) for Other PIs** • RTV 100–200 mg PO per day in one or two divided doses (refer to other PIs for specific dosing recommendations) with food	CYP3A4 > 2D6 substrate Potent CYP3A4 and 2D6 inhibitor Inducer of UGT1A1 and CYPs 1A2, 2C8, 2C9, and 2C19	3–5 hours	GI intolerance, nausea, vomiting, diarrhea Paresthesia (circumoral and extremities) Hyperlipidemia (especially hypertriglyceridemia) Hepatitis Asthenia Dysgeusia Hyperglycemia Fat maldistribution

[a] For dose adjustments in people with hepatic insufficiency, see Appendix B.

[b] Also see Table 21.

Key: ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; AV = atrioventricular; COBI = cobicistat; CrCl = creatinine clearance; CYP = cytochrome P; DRV = darunavir; DRV/c = darunavir/cobicistat; EFV = efavirenz; FDC = fixed-dose combination; FTC = emtricitabine; GI = gastrointestinal; H2 = histamine H2 receptor; LPV/r = lopinavir/ritonavir; PI = protease inhibitor; PK = pharmacokinetic; PO = orally; PPI = proton pump inhibitor; RTV = ritonavir; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; UGT1 = uridine diphosphate glucuronyl transferase 1 family

Appendix A, Table 6. Characteristics of Integrase Strand Transfer Inhibitors

Updated: September 12, 2024
Reviewed: September 25, 2025

The following table includes dose recommendations for U.S. Food and Drug Administration (FDA)–approved integrase strand transfer inhibitor products for adults with HIV. Not all formulations are FDA approved for adolescents with HIV. For information regarding the use of these medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines.

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathways**	**Serum Half-Life**	**Adverse Events**[b]
Bictegravir (BIC)	BIC is available only as a component of the STR Biktarvy (BIC/TAF/FTC).[c]	• One tablet PO once daily	CYP3A4 substrate UGT1A1-mediated glucuronidation	~17 hours	Diarrhea Nausea Headache Weight gain
Cabotegravir (CAB)	**Available as part of the copackaged IM long-acting regimen Cabenuva (CAB IM and RPV IM)** • 400-mg/2-mL vial • 600-mg/3-mL vial **Also available in oral tablet formulation Vocabria (CAB PO)** • 30-mg tablet • Must be obtained from manufacturer for oral lead-in and oral bridging during administration of Cabenuva (CAB IM/RPV IM)	See Appendix A, Table 1 for dosing information for coformulated and copackaged regimens that contain CAB.	UGT1A1 and UGT1A9-mediated glucuronidation	PO: 41 hours IM: 6–12 weeks	**CAB Plus RPV** • Headache • Nausea • Abnormal dreams • Anxiety • Insomnia • Depressive disorders • Hepatotoxicity **IM Formulation Only** • Injection site reactions (e.g., pain, induration, swelling, nodules)

Appendix A, Table 6. Characteristics of Integrase Strand Transfer Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathways**	**Serum Half-Life**	**Adverse Events**[b]
Dolutegravir (DTG) *Tivicay*	**Tivicay** • 50-mg tablet **STRs That Contain DTG**[c] • Dovato (DTG/3TC) • Juluca (DTG/RPV) • Triumeq (DTG/ABC/3TC)	**In People Without Prior ARV Treatment or ARV-Experienced People Who Had Never Received INSTIs** • DTG 50 mg PO once daily **In People Without Prior ARV Treatment or ARV-Experienced People Who Had Never Received INSTIs When Coadministered With EFV, FPV/r, TPV/r, or Rifampin** • DTG 50 PO mg twice daily **In INSTI-Experienced People With Certain INSTI Mutations (See Product Label) or With Clinically Suspected INSTI Resistance** • DTG 50 mg PO twice daily See Appendix A, Table 1 for dosing information for STRs that contain DTG.	UGT1A1-mediated glucuronidation Minor substrate of CYP3A4	~14 hours	Insomnia Headache Depressive disorders and suicidal ideation (rare; usually occurs in people with preexisting psychiatric conditions) Weight gain Hepatotoxicity HSRs, including rash, constitutional symptoms, and organ dysfunction (including liver injury), have been reported.
Elvitegravir (EVG)	EVG is only available as a component of an STR tablet that also contains COBI, FTC, and either TDF or TAF. **STRs That Contain EVG**[c] • Genvoya (EVG/c/TAF/FTC) • Stribild (EVG/c/TDF/FTC)	**Genvoya** • One tablet PO once daily with food. • See Appendix B for recommendations on dosing in persons with renal insufficiency. **Stribild** • One tablet PO once daily with food. • **Not recommended** for people with baseline CrCl <70 mL/min (see Appendix B for the CrCl calculation equation).	**EVG** • CYP3A and UGT1A1/3 substrate **COBI** • CYP3A inhibitor and substrate • CYP2D6 inhibitor	EVG/c: ~13 hours	Nausea Diarrhea Depression and suicidal ideation (rare; usually occurs in people with preexisting psychiatric conditions)

Appendix A, Table 6. Characteristics of Integrase Strand Transfer Inhibitors

Generic Name (Abbreviation) *Trade Name*	**Formulations**	**Dosing Recommendations**[a]	**Elimination/ Metabolic Pathways**	**Serum Half-Life**	**Adverse Events**[b]
Raltegravir (RAL) *Isentress* *Isentress HD*	**Isentress** • 400-mg tablet • 100-mg single-use packet for oral suspension **Isentress HD** • 600-mg tablet	**Isentress** • 400 mg PO twice daily *With Rifampin* • 800 mg PO twice daily **Isentress HD** *In People Without Prior ARV Treatment or ARV-Experienced People With Virologic Suppression on a Regimen Containing RAL 400 mg Twice Daily* • 1,200 mg (two 600-mg tablets) PO once daily *With Rifampin* • Not recommended	UGT1A1-mediated glucuronidation	~9 hours	Rash, including Stevens-Johnson syndrome, HSR, and toxic epidermal necrolysis Nausea Headache Diarrhea Pyrexia CPK elevation, muscle weakness, and rhabdomyolysis Weight gain Insomnia Depression and suicidal ideation (rare; usually occurs in people with preexisting psychiatric conditions)

[a] For dose adjustments in people with hepatic insufficiency, see Appendix B. When no food restriction is listed, the antiretroviral drug can be taken with or without food.

[b] Also see Table 21.

[c] See Appendix A, Table 1 for information about these formulations.

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse event; ARV = antiretroviral; BIC = bictegravir; CAB = cabotegravir; COBI = cobicistat; CPK = creatine phosphokinase; CrCl = creatinine clearance; CYP = cytochrome P; DTG = dolutegravir; EFV = efavirenz; EVG = elvitegravir; EVG/c = elvitegravir/cobicistat; FPV/r = fosamprenavir/ritonavir; FTC = emtricitabine; HSR = hypersensitivity reaction; IM = intramuscular; INSTI = integrase strand transfer inhibitor; NTD = neural tube defect; PO = orally; RAL = raltegravir; RPV = rilpivirine; STR = single-tablet regimen; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TPV/r = tipranavir/ritonavir; UGT1 = uridine diphosphate glucuronyl transferase 1 family

Appendix A, Table 7. Characteristics of the CCR5 Antagonist

Updated: September 25, 2025
Reviewed: September 25, 2025

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved CCR5 antagonist. For additional information regarding the use of this medication in adolescents with HIV, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines.

Generic Name (Abbreviation) *Trade Name*	**Formulation**	**Dosing Recommendations**[a]	**Serum Half-Life**	**Elimination/ Metabolic Pathway**	**Adverse Events**[b]
Maraviroc (MVC) *Selzentry* **Note:** Generic products are available.	**Selzentry** • 150-mg and 300-mg tablets • 20-mg/1-mL oral solution **Generic** • 150-mg and 300-mg tablets	• MVC 150 mg PO twice daily when given with drugs that are strong CYP3A inhibitors (with or without CYP3A inducers), including PIs (except TPV/r) • MVC 300 mg PO twice daily when given with NRTIs, TPV/r, NVP, RAL, and other drugs that are not strong CYP3A inhibitors or inducers • MVC 600 mg PO twice daily when given with drugs that are CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor) Take MVC without regard to food.	14–18 hours	CYP3A4 substrate	Abdominal pain Cough Dizziness Musculoskeletal symptoms Pyrexia Rash Upper respiratory tract infections Hepatotoxicity, which may be preceded by severe rash or other signs of systemic allergic reactions Orthostatic hypotension, especially in people with severe renal insufficiency

[a] For dose adjustments in people with hepatic insufficiency, see Appendix B.

[b] Also see Table 21.

Key: CYP = cytochrome P; EFV = efavirenz; ETR = etravirine; MVC = maraviroc; NRTI = nucleoside reverse transcriptase inhibitor; NVP = nevirapine; PI = protease inhibitor; PO = orally; RAL = raltegravir; TPV/r = tipranavir/ritonavir

Appendix A, Table 8. Characteristics of the CD4 Post-Attachment Inhibitor

Updated: May 26, 2023
Reviewed: September 25, 2025

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved CD4 post-attachment inhibitor. Ibalizumab is not FDA approved for use in adolescents with HIV.

Generic Name (Abbreviation) *Trade Name*	**Formulation**	**Dosing Recommendations**	**Serum Half-Life**	**Elimination/ Metabolic Pathway**	**Adverse Events**[a]
Ibalizumab (IBA) *Trogarzo*	• Single-dose 2-mL vial containing 200 mg/1.33 mL (150 mg/mL) of ibalizumab	• Administer a single loading dose of IBA 2,000-mg IV infusion over 30 minutes, followed by a maintenance dose of IBA 800-mg IV infusion over 15 minutes or IV push over 30 seconds every 2 weeks. • See prescribing information for additional instructions for preparing, storing, and administering IBA, and for monitoring people who are receiving IBA.	~64 hours	Not well defined	Diarrhea Dizziness Nausea Rash HSRs, including anaphylaxis and infusion-related reactions, have been reported.

[a] Also see Table 21.

Key: HSR = hypersensitivity reaction; IBA = ibalizumab; IV = intravenous

Appendix A, Table 9. Characteristics of the gp120 Attachment Inhibitor

Updated: May 26, 2023
Reviewed: September 25, 2025

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved gp120 attachment inhibitor. Fostemsavir is not FDA approved for use in adolescents with HIV.

Generic Name (Abbreviation) *Trade Name*	**Formulation**	**Dosing Recommendations**	**Serum Half-Life**	**Elimination/ Metabolic Pathway**	**Adverse Events**[a]
Fostemsavir (FTR) *Rukobia*	• 600-mg extended-release tablets	• FTR 600 mg PO twice daily	11 hours	Hydrolysis (esterases), CYP3A4	Nausea Transaminase elevation; transient bilirubin elevation Sleep disturbance, dizziness QTc prolongation was seen at four times the recommended dose. Use with caution in people with preexisting heart disease, QTc prolongation, or concomitant use of medications that may prolong QTc interval.

[a] Also see Table 21.

Key: CYP = cytochrome P; FTR = fostemsavir; PO = orally; QTc = corrected QT interval

Appendix A, Table 10. Characteristics of the Capsid Inhibitor

Updated: September 25, 2025
Reviewed: September 25, 2025

The following table includes dose recommendations for the U.S. Food and Drug Administration (FDA)–approved capsid inhibitor. Lenacapavir is not FDA approved for use in adolescents with HIV.

Generic Name (Abbreviation) *Trade Name*	**Formulation**	**Dosing Recommendations**	**Serum Half-Life**	**Elimination/ Metabolic Pathway**	**Adverse Events**[a]
Lenacapavir (LEN) *Sunlenca*	• 300-mg tablet • Single-dose 463.5-mg/1.5-mL vial for injection	**Initiation Option 1** • Day 1: 927 mg SQ x 1 dose + 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose **Initiation Option 2** • Day 1: 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose • Day 8: 300 mg PO x 1 dose • Day 15: 927 mg SQ x 1 dose **Maintenance Dosing** • 927 mg by SQ injection every 6 months from the date of the last injection (+/-2 weeks) **Note:** Each SQ dose requires two injections.	PO: 10–12 days SQ: 8–12 weeks	Substrate of P-glycoprotein, CYP3A (minor), UGT1A1 (minor) CYP3A4 inhibitor (moderate)	Injection site reactions, including nodules, induration, and necrosis Serious injection site reactions (e.g., necrosis and ulcer) may occur when LEN is improperly administered intradermally instead of subcutaneously. Nausea, diarrhea, headache

[a] Also see Table 21.

Key: CYP = cytochrome P; LEN = lenacapavir; PO = orally; SQ = subcutaneous

APPENDIX B. ANTIRETROVIRAL DOSING RECOMMENDATIONS IN ADULTS WITH RENAL OR HEPATIC INSUFFICIENCY

Updated: September 25, 2025
Reviewed: September 25, 2025

These tables include antiretroviral (ARV) products that are not approved by the U.S. Food and Drug Administration (FDA) for use in adolescents with HIV. For information regarding the use of ARV medications in adolescents with HIV, including weight limitations and additional dosage forms, please consult FDA product labeling or Appendix A in the Pediatric Antiretroviral Guidelines.

Renal dosing information for fixed-dose combination products, as well as coformulated and copackaged antiretroviral regimens, is included in the tables below. The older antiretroviral drugs fosamprenavir (FPV), lopinavir/ritonavir (LPV/r), nelfinavir (NFV), nevirapine (NVP), tipranavir (TPV), and zidovudine (ZDV) have been removed from this table. Please refer to the FDA product labels for these drugs for recommendations on dosing in adults and adolescents with renal or hepatic insufficiency.

Please refer to the National Institute of Diabetes and Digestive and Kidney Diseases Determining Drug Dosing in Adults With Chronic Kidney Disease webpage for a discussion on using estimated creatinine clearance (CrCl) versus estimated glomerular filtration rate (eGFR) in determining renal function. eGFR based on the 2021 Chronic Kidney Disease Epidemiology Collaboration (or CKD-EPI) equation can be determined using this eGFR calculator. In FDA prescribing information, renal dosing recommendations for most ARVs are based on CrCl using the Cockroft-Gault formula.

See the section at the end of this table for criteria for Child-Pugh Classifications.

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Nucleoside Reverse Transcriptase Inhibitors			
Abacavir (ABC) *Ziagen*	ABC 300 mg PO twice daily *or* ABC 600 mg PO once daily	No dose adjustment.	*Child-Pugh Class A:* ABC 200 mg PO twice daily (use oral solution) *Child-Pugh Class B or C:* **Contraindicated**

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Abacavir/Lamivudine (ABC/3TC)	One tablet PO once daily	Not FDA recommended if CrCl <30 mL/min due to the 3TC component. **Note:** There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose 3TC. See the 3TC entry for more information.	*Child-Pugh Class A:* People with mild hepatic impairment require a dose reduction of ABC (as noted above). Use the individual drugs instead of the FDC tablet in these people. *Child-Pugh Class B or C:* **Contraindicated** due to the ABC component
Emtricitabine (FTC) *Emtriva*	FTC 200-mg oral capsule once daily *or* FTC 240-mg (24-mL) oral solution once daily **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min who are not on HD. To allow people to remain on TAF-containing FDC products, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min who are not on HD.	**Dose by Formulation** **CrCl (mL/min)** / **Capsule** / **Solution** 30–49[b] — No dose adjustment. 15–29 (see **Note**) — 200 mg every 72 hours — 80 mg every 24 hours <15 (not on HD) (see **Note**) — 200 mg every 96 hours — 60 mg every 24 hours On HD[b] — No dose adjustment. On HD days, administer after dialysis.	No dose recommendation

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**			**Dosing in Adults With Hepatic Impairment**
Lamivudine (3TC) *Epivir*	3TC 300 mg PO once daily *or* 3TC 150 mg PO twice daily **Note:** PK and safety data are limited on the use of 3TC doses higher than those recommended by the FDA in people with CrCl <30 mL/min. Clinicians may consider using the nearest available tablet strength (100 mg or 150 mg), as outlined in the "Alternative Dose" column **(BIII)** (see rationale[d]). There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. To allow people to remain on certain ABC and/or DTG-containing FDC products, some Panel members use full-dose 3TC.	**CrCl (mL/min)**	**Epivir Label Dose**	**Alternative Dose**[d]	No dose adjustment
		30–49[c]	No dose adjustment.		
		15–29 (see **Note**)	1 × 150 mg, then 100 mg every 24 hours	100–150 mg every 24 hours	
		5–14 (see **Note**)	1 × 150 mg, then 50 mg every 24 hours	100–150 mg every 24 hours	
		<5 or on HD (see **Note**)	1 × 50 mg, then 25 mg every 24 hours	100–150 mg every 24 hours	
Tenofovir Alafenamide (TAF) *Vemlidy*	Vemlidy is available as a 25-mg tablet given PO once daily for the treatment of HBV.	**CrCl (mL/min)**	**Dose**		*Child-Pugh Class A:* No dose adjustment *Child-Pugh Class B or C:* **Not recommended**
		<15 (not on HD)	**Not recommended**		
		On HD	No dose adjustment. On HD days, administer after dialysis.		

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**		**Dosing in Adults With Hepatic Impairment**
Tenofovir Alafenamide/ Emtricitabine (TAF/FTC) *Descovy*	TAF for HIV treatment is only available as a component of FDC tablets (i.e., in Biktarvy, Descovy, Genvoya, Odefsey, and Symtuza). • TAF 10 mg PO once daily with EVG/c (Genvoya) or DRV/c (Symtuza) • TAF 25 mg PO once daily in other FDC tablets	**CrCl (mL/min)**	**Dose**	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C*: No dose recommendation
		15–29	**Not recommended** **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose FTC in people with CrCl 15–29 mL/min.	
		<15 (not on HD)	**Not recommended**	
		On HD	No dose adjustment. On HD days, administer after dialysis.	
Tenofovir Disoproxil Fumarate (TDF) *Viread*	TDF 300 mg PO once daily	**CrCl (mL/min)**	**Dose**	No dose adjustment
		30–49	300 mg every 48 hours	
		10–29	300 mg twice weekly (every 72–96 hours)	
		<10 (not on HD)	No dose recommendation	
		On HD	300 mg every 7 days (administer after completion of HD)	
Tenofovir Disoproxil Fumarate/Emtricitabine (TDF/FTC) *Truvada*	One tablet PO once daily	**CrCl (mL/min)**	**Dose**	No dose recommendation
		30–49	One tablet every 48 hours	
		<30 or on HD	FDC of TDF/FTC **not recommended**	

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**		**Dosing in Adults With Hepatic Impairment**
Tenofovir Disoproxil Fumarate/Lamivudine (TDF/3TC) *Cimduo*	One tablet PO once daily	**CrCl (mL/min)**	**Dose**	No dose recommendation
		<50 or on HD	FDC of TDF/3TC **not recommended**	
Non-Nucleoside Reverse Transcriptase Inhibitors				
Doravirine (DOR) *Pifeltro*	DOR 100 mg PO once daily	No dose adjustment		*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Doravirine/Tenofovir Disoproxil Fumarate/ Lamivudine (DOR/TDF/3TC) *Delstrigo*	One tablet PO once daily	FDC of DOR/TDF/3TC **not recommended** if CrCl <50 mL/min or on HD		*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Efavirenz (EFV)	EFV 600 mg PO once daily on an empty stomach, preferably at bedtime	No dose adjustment		No dose recommendation; use with caution in people with hepatic impairment.
Efavirenz/Tenofovir Disoproxil Fumarate/ Emtricitabine (EFV/TDF/FTC)	One tablet PO once daily on an empty stomach, preferably at bedtime	FDC of EFV/TDF/FTC **not recommended** if CrCl <50 mL/min or on HD		No dose recommendation; use with caution in people with hepatic impairment.
Efavirenz/ Tenofovir Disoproxil Fumarate/ Lamivudine (EFV/TDF/3TC) *Symfi*	One tablet PO once daily on an empty stomach, preferably at bedtime	FDC of EFV/TDF/3TC **not recommended** if CrCl <50 mL/min or on HD		*Child-Pugh Class A:* Use with caution *Child-Pugh Class B or C:* **Not recommended**
Etravirine (ETR) *Intelence*	ETR 200 mg PO twice daily	No dose adjustment		*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Rilpivirine (RPV PO) *Edurant*	RPV 25 mg PO once daily with food	No dose adjustment	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Rilpivirine IM Plus Cabotegravir IM (RPV IM and CAB IM) *Cabenuva*	**Monthly Dosing** • Loading dose: RPV 900 mg/3 mL IM × 1 dose and CAB 600 mg/3 mL IM × 1 dose • Continuation phase: RPV 600 mg/ 2 mL IM every 4 weeks and CAB 400 mg/2 mL IM every 4 weeks **Every-2-Months Dosing** • Loading dose: RPV 900 mg/3 mL IM and CAB 600 mg/3 mL IM monthly for 2 doses • Continuation phase: RPV 900 mg/ 3 mL IM and CAB 600 mg/3 mL IM every 2 months	No dose adjustment CrCl <30 or on HD: No dose adjustment; increase monitoring for adverse events.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Rilpivirine/Tenofovir Alafenamide/ Emtricitabine (RPV/TAF/FTC) *Odefsey*	One tablet PO once daily with food	**In People With CrCl 15–29 mL/min** • **Not recommended** • **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. **In People With CrCl <15 mL/min (not on HD)** • **Not recommended** **In People on Chronic HD** • No dose adjustment. On HD days, administer after dialysis.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Rilpivirine/Tenofovir Disoproxil Fumarate/ Emtricitabine (RPV/TDF/FTC) *Complera*	One tablet PO once daily with food	FDC of RPV/TDF/FTC **not recommended** if CrCl <50 mL/min or on HD	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Rilpivirine/Dolutegravir (RPV/DTG) *Juluca*	One tablet PO once daily with food	No dose adjustment In people with CrCl <30 mL/min: No dose adjustment, monitor closely for adverse effects.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Protease Inhibitors			
Atazanavir (ATV) *Reyataz*	ATV 400 mg PO once daily with food *or* (ATV 300 mg plus RTV 100 mg) PO once daily with food	**In People Without Prior ARV Treatment on HD** • (ATV 300 mg plus RTV 100 mg) once daily with food. **In ARV-Experienced People on HD** • ATV and ATV/r **are not recommended.**	**For Boosted ATV** • RTV boosting **is not recommended** in people with any degree of hepatic impairment. **For Unboosted ATV** • *Child-Pugh Class A:* No dose adjustment • *Child-Pugh Class B:* ATV 300 mg once daily (unboosted) for people without prior ARV treatment • *Child-Pugh Class C:* **Not recommended**
Atazanavir/Cobicistat (ATV/c) *Evotaz*	One tablet PO once daily with food	**If Used With TDF** • **Not recommended** if CrCl <70 mL/min	**Not recommended** in people with any degree of hepatic impairment.

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Darunavir (DRV) *Prezista*	**In People Without Prior ARV Treatment or ARV-Experienced Treatment With No DRV Mutations** • (DRV 800 mg plus RTV 100 mg) PO once daily with food. **In ARV-Experienced People With at Least One DRV Resistance Mutation** • (DRV 600 mg plus RTV 100 mg) PO twice daily with food.	No dose adjustment	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Darunavir/Cobicistat (DRV/c) *Prezcobix*	One tablet PO once daily with food	**If Used With TDF** • **Not recommended** if CrCl <70 mL/min	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Darunavir/Cobicistat/ Tenofovir Alafenamide/ Emtricitabine (DRV/c/TAF/FTC) *Symtuza*	One tablet PO once daily with food	**In People With CrCl 15–29 mL/min** • **Not recommended** • **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. **In People With CrCl <15 mL/min (not on HD)** • **Not recommended** **In People on Chronic HD** • No dose adjustment. On HD days, administer after dialysis.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Ritonavir (RTV) *Norvir*	**As a PI-Boosting Agent** • RTV 100–400 mg PO per day with food.	No dose adjustment	Refer to recommendations for the primary (i.e., boosted) PI.

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Integrase Strand Transfer Inhibitors			
Bictegravir/Tenofovir Alafenamide/ Emtricitabine (BIC/TAF/FTC) *Biktarvy*	One tablet PO once daily	**In People With CrCl 15–29 mL/min** • **Not recommended** • **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. **In People With CrCl <15 mL/min (not on HD)** • **Not recommended** **In People on Chronic HD** • No dose adjustment. On HD days, administer after dialysis.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Cabotegravir (CAB PO) *Vocabria*	**Treatment (As Optional Oral Lead-In or As Oral Bridging)** • CAB 30 mg PO once daily, given with RPV 25 mg PO, with food before switching to CAB IM and RPV IM	No dose adjustment	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Cabotegravir IM Plus Rilpivirine IM (CAB IM plus RPV IM) *Cabenuva*	**Monthly Dosing** • Loading dose: CAB 600 mg/3 mL IM × 1 dose and RPV 900 mg/3 mL IM × 1 dose • Continuation phase: CAB 400 mg/2 mL IM every 4 weeks and RPV 600 mg/2 mL IM every 4 weeks **Every-2-Months Dosing** • Loading dose: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM monthly for 2 doses • Continuation phase: CAB 600 mg/3 mL IM and RPV 900 mg/3 mL IM every 2 months	No dose adjustment CrCl <30 or on HD: No dose adjustment; increase monitoring for adverse events.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Dolutegravir (DTG) *Tivicay*	DTG 50 mg PO once daily *or* DTG 50 mg PO twice daily	No dose adjustment	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Dolutegravir/Abacavir/ Lamivudine (DTG/ABC/3TC) *Triumeq*	One tablet PO once daily	Not FDA recommended if CrCl <30 mL/min due to the 3TC component **Note:** There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose 3TC.[d]	*Child-Pugh Class A:* People with mild hepatic impairment require a dose reduction of ABC. Use the individual drugs instead of the FDC tablet in these people. *Child-Pugh Class B or C:* **Contraindicated** due to the ABC component

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Dolutegravir/ Lamivudine (DTG/3TC) *Dovato*	One tablet PO once daily	Not FDA recommended if CrCl <30 mL/min due to 3TC component **Note:** There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose 3TC.[d]	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Dolutegravir/ Rilpivirine (DTG/RPV) *Juluca*	One tablet PO once daily with food	No dose adjustment CrCl <30 or on HD: No dose adjustment; increase monitoring for adverse events.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation
Elvitegravir/Cobicistat/ Tenofovir Alafenamide/ Emtricitabine (EVG/c/TAF/FTC) *Genvoya*	One tablet PO once daily with food	**In People With CrCl 15–29 mL/min** • **Not recommended** • **Note:** There is insufficient evidence to recommend for or against the use of full-dose, daily FTC in people with CrCl <30 mL/min. To allow people to remain on the FDC product, some Panel members use full-dose, daily FTC in people with CrCl 15–29 mL/min. **In People With CrCl <15 mL/min (not on HD)** • **Not recommended** **In People on Chronic HD** • No dose adjustment. On HD days, administer after dialysis.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**
Elvitegravir/Cobicistat/ Tenofovir Disoproxil Fumarate/Emtricitabine (EVG/c/TDF/FTC) *Stribild*	One tablet PO once daily with food	EVG/c/TDF/FTC **should not be initiated** in people with CrCl <70 mL/min. Discontinue EVG/c/TDF/FTC if CrCl declines to <50 mL/min while on therapy.	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* **Not recommended**

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Raltegravir (RAL) *Isentress* *Isentress HD*	RAL 400 mg PO twice daily (using Isentress formulation) *or* RAL 1,200 mg PO once daily (using Isentress HD formulation only)	No dose adjustment	**For Isentress** • *Child-Pugh Class A or B:* No dose adjustment • *Child-Pugh Class C:* No dose recommendation **For Isentress HD** • **Not recommended** for people with hepatic impairment.
CCR5 Antagonist			
Maraviroc (MVC) *Selzentry*	The recommended dose differs based on concomitant medications and potential for drug–drug interactions. See Appendix A, Table 7 for detailed dosing information.	**In People With CrCl <30 mL/min or People Who Are on HD** *Without Potent CYP3A Inhibitors or Inducers* • MVC 300 mg twice daily; if postural hypotension occurs, reduce to MVC 150 mg twice daily *With Potent CYP3A Inducers or Inhibitors* • **Not recommended**	No dose recommendations. MVC concentrations will likely be increased in people with hepatic impairment.
CD4 Post-Attachment Inhibitor			
Ibalizumab (IBA) *Trogarzo*	Loading dose: IBA 2,000 mg IV Maintenance dose: IBA 800 mg IV every 2 weeks	No dose adjustment	No dose recommendation
gp-120 Attachment Inhibitor			
Fostemsavir (FTR) *Rukobia*	FTR 600 mg PO twice daily	No dose adjustment	No dose adjustment

Appendix B. Antiretroviral Dosing Recommendations in Adults With Renal or Hepatic Insufficiency

Generic Name (Abbreviation) *Trade Name*	**Usual Dose**[a]	**Dosing in Adults With Renal Insufficiency**	**Dosing in Adults With Hepatic Impairment**
Capsid Inhibitor			
Lenacapavir (LEN) *Sunlenca*	**Initiation Option 1** • Day 1: 927 mg SQ x 1 dose plus 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose **Initiation Option 2** • Day 1: 600 mg PO x 1 dose • Day 2: 600 mg PO x 1 dose • Day 8: 300 mg PO x 1 dose • Day 15: 927 mg SQ x 1 dose **Maintenance Dosing** • 927 mg by SQ injection every 6 months from the date of the last injection (+/-2 weeks)	No dose adjustment	*Child-Pugh Class A or B:* No dose adjustment *Child-Pugh Class C:* No dose recommendation

[a] Refer to Appendix A, Tables 1–10 for additional dosing information.

[b] The prescribing information for FTC (Emtriva) recommends adjusted doses for people with CrCl 30–49 mL/min and people on hemodialysis. However, the prescribing information for several FDC products that contain FTC (including Descovy, Biktarvy, Genvoya, and Odefsey) recommends that the standard dose (FTC 200 mg) can be given once daily in these people. The recommendations in this table incorporate the dosing guidance from the FDC products.

[c] The prescribing information for 3TC (Epivir) recommends dosage adjustment from 300 mg once daily to 150 mg once daily for people with CrCl 30–49 mL/min. However, the prescribing information for several FDC products that contain 3TC (including ABC plus 3TC, Dovato, and Triumeq) recommends no dose adjustment for CrCl 30–49 mL/min. The recommendation in this table incorporates the dosing guidance from the FDC products.

[d] Use of 3TC doses higher than those recommended by the FDA for people with CrCl <30 mL/min has been reported in clinical practice[1-4] and endorsed in the *Guidelines for Chronic Kidney Disease in People With HIV* for many years[5]; limited published literature has supported the safety of this practice.[2,3] 3TC has a wide therapeutic index with no established correlation between elevated concentrations and adverse events. Serious adverse events, such as lactic acidosis and severe hematologic toxicities, have been reported in rare cases; however, these effects typically occurred when 3TC was used in combination with older nucleoside reverse transcriptase inhibitors (such as didanosine, stavudine, zidovudine). Clinicians may consider using the nearest available tablet strength (100 mg or 150 mg) to avoid the need for 3TC oral solution, thereby simplifying ARV regimens and facilitating adherence **(BIII).** See the Alternative Dose column in 3TC table entry. There is insufficient evidence to recommend for or against the use of full-dose 3TC in people with CrCl <30 mL/min. To allow people to remain on certain FDC products, some Panel members use full-dose 3TC.

Key: 3TC = lamivudine; ABC = abacavir; AE = adverse effect; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; BIC = bictegravir; CAB = cabotegravir; CrCl = creatinine clearance; CYP = cytochrome P450; DOR = doravirine; DRV = darunavir; DRV/c = darunavir/cobicistat; DTG = dolutegravir; EFV = efavirenz; ETR = etravirine; EVG/c = elvitegravir/cobicistat; FDA = U.S. Food and Drug Administration; FDC = fixed-dose combination; FTC = emtricitabine; FTR = fostemsavir; HBV = hepatitis B virus; HD = hemodialysis; IBA = ibalizumab; IM = intramuscular; IV = intravenous; LEN = lenacapavir; MVC = maraviroc; the Panel = Panel on Antiretroviral Guidelines for Adults and Adolescents; PK = pharmacokinetic; PI = protease inhibitor; PO = orally; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; SQ = subcutaneous; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

Child-Pugh Classifications

Child-Pugh Score			
Component	**Points Scored**		
	1	**2**	**3**
Encephalopathy[a]	None	Grade 1–2	Grade 3–4
Ascites	None	Mild or controlled by diuretics	Moderate or refractory despite diuretics
Albumin	>3.5 g/dL	2.8–3.5 g/dL	<2.8 g/dL
Total Bilirubin, *or*	<2 mg/dL (<34 μmol/L)	2–3 mg/dL (34–50 μmol/L)	>3 mg/dL (>50 μmol/L)
Modified Total Bilirubin[b]	<4 mg/dL	4–7 mg/dL	>7 mg/dL
Prothrombin Time (Seconds Prolonged), *or*	<4	4–6	>6
International Normalized Ratio (INR)	<1.7	1.7–2.3	>2.3

[a] Encephalopathy Grades

Grade 1: Mild confusion, anxiety, restlessness, fine tremor, slowed coordination

Grade 2: Drowsiness, disorientation, asterixis

Grade 3: Somnolent but rousable, marked confusion, incomprehensible speech, incontinence, hyperventilation

Grade 4: Coma, decerebrate posturing, flaccidity

[b] Modified total bilirubin is used for people who have Gilbert's syndrome or who are taking atazanavir.

Child-Pugh Classification	Total Child-Pugh Score[a]
Class A (Mild)	5–6 points
Class B (Moderate)	7–9 points
Class C (Severe)	>9 points

[a] Sum of points for each component of the Child-Pugh Score.

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APPENDIX C. KEY TO ACRONYMS

Updated: September 25, 2025
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Drug Name Abbreviations

Abbreviation	Definition
3TC	lamivudine
ABC	abacavir
ATV	atazanavir
ATV/c	atazanavir/cobicistat
ATV/r	atazanavir/ritonavir
BIC	bictegravir
CAB	cabotegravir
CAB-LA	long-acting cabotegravir
COBI or c	cobicistat
d4T	stavudine
ddC	zalcitabine
ddI	didanosine
DLV	delavirdine
DOR	doravirine
DRV	darunavir
DRV/c	darunavir/cobicistat
DRV/r	darunavir/ritonavir
DTG	dolutegravir
EFV	efavirenz
ETR	etravirine
EVG	elvitegravir
EVG/c	elvitegravir/cobicistat
FPV	fosamprenavir
FPV/r	fosamprenavir/ritonavir
FTC	emtricitabine
FTR	fostemsavir
IBA	ibalizumab or ibalizumab-uiyk

Abbreviation	Definition
IDV	indinavir
LA CAB/RPV	long-acting cabotegravir plus rilpivirine
LEN	lenacapavir
LPV	lopinavir
LPV/r	lopinavir/ritonavir
MVC	maraviroc
NFV	nelfinavir
NVP	nevirapine
RAL	raltegravir
RPV	rilpivirine
RTV or r	ritonavir
SQV	saquinavir
T-20	enfuvirtide
TAF	tenofovir alafenamide
TDF	tenofovir disoproxil fumarate
TFV	tenofovir
TFV-DP	tenofovir-diphosphate
TMP-SMX	trimethoprim-sulfamethoxazole
TMR	temsavir
TPV	tipranavir
TPV/r	tipranavir/ritonavir
ZDV	zidovudine

General Terms

Abbreviation	Definition
17-BMP	beclomethasone 17-monopropionate
ACA	Affordable Care Act
ACC	American College of Cardiology
ADAP	AIDS Drug Assistance Program
AE	adverse event
Ag/Ab	antigen/antibody
AHA	American Heart Association
AHC-HRSN	Accountable Health Communities Health-Related Social Needs
Al	aluminum
ALT	alanine aminotransferase
AMP	average manufacturer price
ART	antiretroviral therapy
ARTAS	Anti-Retroviral Treatment and Access to Services
ARV	antiretroviral
ASP	average sales price
ASCVD	atherosclerotic cardiovascular disease
AST	aspartate aminotransferase
AUC	area under the curve
AUD	alcohol use disorder
AUDIT-C	Alcohol Use Disorders Identification Test-Consumption
AV	atrioventricular
AWP	average wholesale price
AYA	adolescents and young adults
BMD	bone mineral density
BMI	body mass index
BMT	bone marrow transplant
BUN	blood urea nitrogen
Ca	calcium
$CaCO_3$	calcium carbonate
CAP	cost-sharing assistance program

Abbreviation	Definition
CBC	complete blood count
CCB	calcium channel blocker
CD4	CD4 T lymphocyte
CDC	Centers for Disease Control and Prevention
CGRP	calcitonin gene-related peptide
CHF	congestive heart failure
CI	confidence interval capsid inhibitor
CKD	chronic kidney disease
Cl	chloride
C_{max}	maximum plasma concentration
C_{min}	minimum plasma concentration
CMS	Centers for Medicare & Medicaid Services
CMV	cytomegalovirus
CNS	central nervous system
COC	combined oral contraceptive
CPI-U	consumer price index-urban
CPK	creatine phosphokinase
Cr	creatinine
CrCl	creatinine clearance
CsA	cyclosporine
CSF	cerebrospinal fluid
CV	cardiovascular
CVD	cardiovascular disease
CYP	cytochrome P450
D/M	dual/mixed
DAA	direct-acting antiviral
DDI	drug–drug interaction
DHA	dihydroartemisinin
DILI	drug-induced liver injury
DM	diabetes mellitus
DMPA	depo-medroxyprogesterone acetate

Abbreviation	Definition
DOAC	direct oral anticoagulant
DOT	directly observed therapy
DSMB	Data Safety Monitoring Board
DVT	deep vein thrombosis
EBV	Epstein-Barr virus
ECG	electrocardiogram
eGFR	estimated glomerular filtration rate
EI	entry inhibitor
ESRD	end-stage renal disease
FCP	federal ceiling price
FDA	U.S. Food and Drug Administration
FDC	fixed-dose combination
Fe	iron
FPL	federal poverty level
FUL	federal upper limit
GHB	gamma-hydroxybutyrate
GI	gastrointestinal
GIP	glucose-dependent insulinotropic polypeptide
GLP-1	glucagon-like peptide-1
GVHD	graft versus host disease
H2	histamine type 2
H2RA	H2 receptor antagonist
HAND	HIV-associated neurocognitive disorder
HAV	hepatitis A virus
HbA1C	hemoglobin A1c
HBcAb	hepatitis B core antibody
HBeAg	hepatitis B e antigen
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCO_3	bicarbonate

Abbreviation	Definition
HCT	hematopoietic cell transplant
HCV	hepatitis C virus
HD	hemodialysis high-dose
HDL	high-density lipoprotein
HDV	hepatitis D virus
HHS	U.S. Department of Health and Human Services
HIV	human immunodeficiency virus
HIV RNA	HIV viral load
HIV-1	human immunodeficiency virus type 1
HIV-2	human immunodeficiency virus type 2
HIVMA/IDSA	HIV Medicine Association of the Infectious Diseases Society of America
HLA	human leukocyte antigen
HMG-CoA	hydroxy-methylglutaryl-coenzyme A
HPTN	HIV Prevention Trials Network
HR	hazard ratio
HRSA	Health Resources and Services Administration
HRT	hormone replacement therapy
hs-CRP	high-sensitivity C-reactive protein
HSR	hypersensitivity reaction
HTLV-1	human T-lymphotropic virus-1 type I
IC_{50}	median inhibitory concentration
IL	interleukin
IL-2	Interleukin-2
IL-6	Interleukin-6
IL-7	Interleukin-7
IM	intramuscular
IMF	illicitly manufactured fentanyl
IN	integrase
INR	international normalized ratio
INSTI	integrase strand transfer inhibitor
IPT	isoniazid preventive therapy

Abbreviation	Definition
IQR	interquartile range
IRIS	immune reconstitution inflammatory syndrome
IRR	incident rate ratio
ISR	injection site reactions
IUD	intrauterine device
IV	intravenous
K	potassium
LA	long-acting
LDL	low-density lipoprotein
LDL-C	low-density lipoprotein cholesterol
LLOD	lower limits of detection
LTBI	latent tuberculosis infection
MAC	*Mycobacterium avium* complex
MACE	major adverse cardiovascular events
MDMA	methylenedioxymethamphetamine
MDR	multidrug resistant
MDR-TB	multidrug-resistant tuberculosis
MDRP	Medicaid Drug Rebate Program
MET	motivational enhancement therapy
Mg	magnesium
MHC	major histocompatibility complex
MI	motivational interviewing myocardial infarction
MMP	Medication Monitoring Project
MPA	medroxyprogesterone acetate
MRI	magnetic resonance imaging
MSM	men who have sex with men
MTR	multi-tablet regimen
N/A	not applicable
Na	sodium
NASTAD	National Alliance of State & Territorial AIDS Directors
NIH	National Institutes of Health

Abbreviation	Definition
NNRTI	non-nucleoside reverse transcriptase inhibitor
NNT_5	number needed to treat over 5 years
NRTI	nucleoside/nucleotide reverse transcriptase inhibitor
NTD	neural tube defect
OARAC	Office of AIDS Research Advisory Council
OATP	organic anion-transporting polypeptide
OBR	optimized background regimen
OCT2	organic cation transporter 2
OH-itraconazole	active metabolite of itraconazole
OI	opportunistic infection
ONDCP	Office of National Drug Control Policy
OR	odds ratio
OTP	opioid treatment program
OUD	opioid use disorder
P	phosphorus
P-gp	p-glycoprotein
PAH	pulmonary arterial hypertension
PAP	patient assistance program
PBM	pharmacy benefit manager
PCE	Pooled Cohort Equations
PCP	*Pneumocystis jirovecii* pneumonia
PCR	polymerase chain reaction
PDAY	Pathobiological Determinants of Atherosclerosis in Youth
PDE5	phosphodiesterase type 5
PEP	post-exposure prophylaxis
PI	protease inhibitor
PI/b	boosted protease inhibitor
PI/c	cobicistat-boosted protease inhibitor
PI/r	ritonavir-boosted protease inhibitor
PK	pharmacokinetic
PO	orally
PPI	proton pump inhibitor

Abbreviation	Definition
PR	protease
PRAPARE	Protocol for Responding to and Assessing Patients' Assets, Risks, and Experiences
PrEP	pre-exposure prophylaxis
PREVENT	Predicting Risk of CVD EVENTs
PTH	parathyroid hormone
QTc	QT corrected for heart rate
RA	receptor agonist
REPC	Retention through Enhanced Personal Contact
RNA	ribonucleic acid
RT	reverse transcriptase
RWHAP	Ryan White HIV/AIDS Program
SAMHSA	Substance Abuse and Mental Health Services Administration
SCr	serum creatinine
SDOH	social determinants of health
SMAC	state maximum allowable cost
SMR	sexual maturity rating
SOT	solid organ transplantation
SPT	skin patch test
SQ	subcutaneous
SSP	syringe service program
SSRI	selective serotonin reuptake inhibitor
STI	sexually transmitted infection
STR	single-tablet regimen
SUD	substance use disorder
TasP	treatment as prevention
TB	tuberculosis
TC	total cholesterol
TCA	tricyclic antidepressant
TDM	therapeutic drug monitoring
TDR	transmitted drug resistance
TG	triglyceride

Abbreviation	Definition
The Panel	The Panel on Antiretroviral Guidelines for Adults and Adolescents
U=U	Undetectable = Untransmittable
UGT	uridine diphosphate glucuronosyltransferase
UGT1	uridine diphosphate glucuronosyltransferase 1 family
UGT1A1	uridine diphosphate glucuronosyltransferase 1A1
ULN	upper limit of normal
USPSTF	U.S. Preventive Services Task Force
UW	University of Washington
VAT	visceral adipose tissue
VL	viral load
VPA	valproic acid
WAC	wholesale acquisition cost
WBC	white blood cell
WHO	World Health Organization
XDR	extensively drug-resistant
XR	extended release
Zn	zinc

Study and Trial Names

Acronym/Abbreviation	Name
ACTG	Advancing Clinical Therapeutics Globally or AIDS Clinical Trials Group
ADVANCE	Assessing Donor Variability And New Concepts in Eligibility
ANRS	National Agency for AIDS Research (France)
ARDENT	ACTG A5257 trial
ARTEMIS	Affordability and Real-World Antiplatelet Treatment Effectiveness After Myocardial Infarction Study
ATLAS	Antiretroviral Therapy as Long-Acting Suppression
CANTOS	Canakinumab Anti-Inflammatory Thrombosis Outcomes Study
CARES	Cabotegravir and Rilpivirine Efficacy and Safety
CoRECT	Cooperative Re-Engagement Controlled Trial
D:A:D	Data Collection on Adverse Events of Anti-HIV Drugs
D^2EFT	Dolutegravir and Darunavir Evaluation in Adults Failing Therapy
ECHO	Evidence for Contraceptive Options in HIV
ENCORE	Evaluation of Novel Concepts in Optimization of antiRetroviral Efficacy
FLAIR	First Long-Acting Injectable Regimen
HPTN	HIV Prevention Trials Network
LATITUDE	Long-Acting Therapy to Improve Treatment Success in Daily LifE
NA-ACCORD	North American AIDS Cohort Collaboration on Research and Design
NADIA	Nucleosides And Darunavir/Dolutegravir In Africa
PARTNER	Partners of People on ART: a New Evaluation of the Risks
RAPID	Rapid ART Program Initiative for HIV Diagnoses
RESPOND	International Cohort Consortium of Infectious Disease
REPRIEVE	Randomized Trial to Prevent Vascular Events in HIV
SMART	Strategies for Management of Antiretroviral Therapy
STaR	Study of Treatment and Reproductive Outcomes
START	Strategic Timing of AntiRetroviral Treatment
TEMPRANO	Early Antiretroviral Treatment and/or Early Isoniazid Prophylaxis Against Tuberculosis in HIV-infected Adults
THRIVE	Targeting HIV Retention and Improved Viral Load Through Engagement
VACS	Veterans Aging Cohort Study
WIHS	Women's Interagency HIV Study

Weddle Declaration
Exhibit H

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REVIEW

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Drug Interactions with Gender-Affirming Hormone Therapy: Focus on Antiretrovirals and Direct Acting Antivirals

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ABSTRACT

Introduction: Gender-affirming care may include hormonal therapy to attain desired health outcomes in transgender (trans) individuals. To provide safe, affirming medical care for trans patients, health care providers must identify and manage drug-drug interactions (DDIs) between gender affirming hormonal therapy (GAHT) and other medication therapies.

Areas covered: This review summarizes available data on DDIs between GAHT and antiretrovirals (ARVs) or hepatitis C direct acting antivirals (DAAs). Potential pharmacokinetic and pharmacodynamic DDIs are predicted based on GAHT, ARV, and DAA pharmacology and adverse event profiles. Clinical management strategies are discussed.

Expert opinion: GAHT may be involved in pharmacokinetic and/or pharmacodynamic DDIs. Certain ARV classes (non-nucleoside reverse transcriptase inhibitors, protease inhibitors) may alter GAHT disposition, whereas selected ARVs (unboosted integrase inhibitors, doravirine, or rilpivirine) may have less impact on GAHT. DAAs may interact with GAHT, but the clinical relevance is unclear. ARV- and/or DAA-associated side effects (including depression, cardiovascular disease, hyperlipidemia) are important to consider in the clinical management of trans patients. Clinicians must evaluate potential DDIs and overlapping side effects between ARVs, DAAs and GAHT when providing care for trans patients.

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Androgen blockers; antiretrovirals; direct acting antivirals; drug interactions; estradiol; gender-affirming therapy; transgender care; hiv; hepatitis C; testosterone

1. Introduction

Transgender (trans) persons are those whose gender identity differs from the sex that was assigned at birth. Approximately 25 million people are estimated to be trans worldwide [1], yet this population remains medically underserved. Gender-affirming care involves a multi-disciplinary treatment approach, and often includes the use of hormones to develop physical characteristics of the individual's affirmed gender [2]. Hormonal agents include estrogens with or without an androgen blocker, oral 5α-reductase inhibitors and/or oral progestogens in trans women and testosterone in trans men to support development of identified sex characteristics. Medication therapy used to affirm the individual's gender will be referred to as gender affirming hormone therapy (GAHT).

Recent literature demonstrates that trans persons face a disproportionately high rate of HIV infection, in part due to the intersection of factors such as stigmatization, discrimination, ethnicity, social class, economic barriers, and power differences as well as transgender rights, policies and attitudes, which may differ between countries [3]. Globally, trans women have 49-fold greater HIV prevalence compared with cis-gender (cis) adults [4], but HIV prevalence estimates for trans men, who also are at risk for HIV acquisition, are unavailable. In the United States, laboratory-confirmed HIV prevalence estimates are 14% among trans women and 3.2% among trans men (ages 16–66 years) [5], compared to a 0.3% prevalence estimate in the U.S. population [6]. In addition, HCV infection is increasingly recognized as an emerging public health issue in trans persons [7]. In a retrospective review of 145 sexually active trans youth, the overall prevalence of HCV infection was 2.8% (3.2% in trans women and 2.4% in trans men) [8]. In a recent cross-sectional survey among trans women in San Francisco, hepatitis C prevalence was 23.8%, which is nine-fold higher than that of the general population in San Francisco [9]. Population-based estimates among trans men are lacking; similar risk factors that increase HCV acquisition may exist [10].

The HIV and HCV care continua involve engaging patients in care and providing antiretroviral therapy (ART) or HCV treatment to prevent viral transmission and decrease morbidity and mortality. Combination ART traditionally consists of two nucleoside analogues plus an agent from a third ARV class (integrase inhibitors, protease inhibitors, or non-nucleoside reverse transcriptase inhibitors). Dual regimens including an integrase inhibitor plus a nucleoside or non-nucleoside analogue are emerging [11].

For hepatitis C, treatment with a combination of direct acting antivirals (DAAs), usually for a duration of 8 to 12 weeks, is recommended to prevent spread of infection, reduce the extent of liver damage, and to obtain a sustained virologic response (SVR). Fixed-dose formulations consisting of

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Article highlights

- Antiretrovirals including nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors rilpivirine or doravirine, and unboosted integrase inhibitors, are not expected to have clinically significant effects on gender-affirming hormonal therapy concentrations.
- Non-nucleoside reverse transcriptase inhibitors efavirenz, etravirine, and nevirapine may decrease plasma concentrations of estradiol, cyproterone, 5α-reductase inhibitors, progestogens and testosterone.
- Cobicistat-containing regimens may increase plasma exposure to estradiol, while ritonavir-containing regimens may either increase or decrease exposure to estradiol, and both cobicistat and ritonavir are expected to increase exposure to cyproterone, 5α-reductase inhibitors, progestogens and testosterone.
- Direct acting antiviral therapies for the treatment of hepatitis C virus, including glecaprevir/pibrentasvir, sofosbuvir/velpatasvir, and sofobuvir/velpatasvir/voxilaprevir may theoretically increase estradiol concentrations via inhibition of organic anion transport protein 1B1, but it is unclear whether this occurs to a clinically relevant extent.
- Trans individuals taking GAHT may have an elevated risk for depression, cardiovascular disease, hyperlipidemia, and altered bone mineral density; therefore, ARVs or direct acting antiviral agents with minimal influence on these conditions are recommended.
- Tenofovir disoproxil fumarate is associated with decreased bone mineral density and nephrotoxicity, boosted regimens may increase lipids and abacavir should be avoided in trans patients with other cardiac risk factors.
- Integrase inhibitors and tenofovir alafenamide can cause unwanted weight gain, and efavirenz and some integrase inhibitors may have psychiatric effects.

This box summarizes key points contained in the article.

an NS5A inhibitor plus an NS5B inhibitor and/or an NS3/4A protease inhibitor are available [12].

Due to their route of metabolism and concurrent impact on both cytochrome P450 (CYP) enzymes and drug transporters, both ARVs and DAAs are associated with a high risk of clinically significant drug-drug interactions with co-prescribed medications [13–16]. For ARVs, retrospective analyses identify at least one potential drug-drug interaction in 53–63% of persons receiving ART, with 1–16% of regimens associated with contraindicated drug combination, and the highest incidence of drug-drug interactions occurring in patients receiving protease inhibitors [13–15]. For DAAs, the rate of clinically significant drug-drug interactions was 76% in an analysis of U.S. veterans initiating hepatitis C therapy [16].

Interactions between ARVs and GAHT are a commonly cited concern among the transgender population. In a cross-sectional survey of trans women living with HIV, 40% reported not taking either ART, GAHT, or both due to concerns about drug-drug interactions; however, only 49% of participants had discussed ART-GAHT drug-drug interactions with their provider [17]. These concerns may contribute to treatment interruptions or detectable viral loads that may occur more frequently in trans patients compared with cis individuals [18,19]. Data regarding barriers to ART adherence in trans men are limited, but similar challenges may exist.

Given the improved health and quality of life outcomes associated with GAHT [20], the high rate of HIV infection among trans persons, and the risk of HIV-HCV co-infection, clinicians must be able to identify and manage potential drug-drug interactions with GAHT [21]. This review evaluates the potential for drug-drug interactions between GAHT and either ART or DAAs. For this review, we focus on treatment, not prevention, of both HIV and HCV.

2. Methods

A literature search was completed using the PubMed electronic database for English language literature from 1996 published up to February 2020. Search terms included the following: transgender persons (transsexualism, transgender, gender dysphoria, gender identity disorder, trans*), HIV, Hepatitis C, drug interactions, gender affirming therapy, feminizing hormones, masculinizing hormones, names of individual hormone agents (bicalutamide, conjugated equine estrogens, cyproterone, dutasteride, estradiol, finasteride, goserelin, leuprolide, medroxyprogesterone, progesterone, spironolactone, testosterone), generic names of commonly used individual antiretrovirals (abacavir, atazanavir, bictegravir, cabotegravir, cobicistat, darunavir, dolutegravir, doravirine, efavirenz, elvitegravir, emtricitabine, etravirine, lamivudine, lopinavir, nevirapine, raltegravir, rilpivirine, ritonavir, tenofovir) and generic names of commonly used direct acting antivirals (elbasvir, glecaprevir, grazoprevir, ledipasvir, pibrentasvir, sofosbuvir, velpatasvir, voxilaprevir). Abstracts from international HIV and viral hepatitis conferences were also searched for relevant literature. Randomized, non-randomized and observational studies as well as case reports were included.

3. Pharmacology of gender affirming hormones

Pharmacokinetic interactions may be predicted by the drug metabolism and transport pathways of each agent. A summary of metabolism and transporter characteristics of all GAHT agents is provided in Table 1.

3.1. Feminizing hormonal therapy

For many trans women, GAHT is an important part of gender-affirming care. GAHT supports the development of secondary sex characteristics, including breast development, decreased muscle mass, body fat redistribution, and softening of the skin. Estrogen (as 17β-estradiol) is the mainstay of GAHT. It is available as oral, transdermal, or injectable (intramuscular, subcutaneous) preparations [2]. Adjunctive agents may include an oral antiandrogen: spironolactone, cyproterone acetate, 5α-reductase inhibitors (dutasteride or finasteride), progestogens (medroxyprogesterone or micronized progesterone) or bicalutamide. Gonadotropin releasing hormone analogues (GnRH, leuprolide or goserelin) are also available. During GAHT, desired serum estradiol and total testosterone concentrations are between 367–734 pmol/L and <1.7 nmol/L, respectively [2].

Ethinyl estradiol and conjugated estrogens are not recommended for GAHT due to the potential for elevated venous thromboembolism risk [2]. Conjugated estrogens contain multiple estrogens that are rapidly conjugated to estradiol, estrone, and estriol; therefore, if used for GAHT, their interaction potential is expected to be similar to 17β-estradiol (Table 1 and Figure 1). In contrast, synthetic ethinyl estradiol (EE) metabolism differs from oral estradiol metabolism (Figure 1). Despite this difference,

Table 1. Metabolic pathways and major drug transport of estrogens, anti-androgens, progestogens, and testosterone.

	Drug (Route)	Metabolizing Enzymes	Drug Transporters	References
Estrogens	17β-estradiol (PO/SL, TD); estradiol valerate (PO); Estradiol valerate or cypionate (IM/SC); Conjugated estrogens (PO)[a]	Substrate: CYP3A4 (primary), CYP1A2 (secondary), 2A6, 1B1, 2B6, 2C19, 2C9, 2D6, 2E1, UGT1A1 Inhibition: CYP1A2 Induction: CYP2A6, 2B6, 3A4 (not clinically relevant)	Substrate: OATP1B1, OATP1B3	[22,32,27]
	Ethinyl estradiol[a]	Substrate: CYP3A4 (primary), CYP2C9 (secondary), UGT1A1	None.	[34]
Antiandrogens	Bicalutamide (PO)	Inhibition: CYP3A4 (weak)	None.	[23]
	Cyproterone acetate (PO)	Substrate: CYP3A4 Inhibition: CYP2C8, 2C9, 2C19, 3A4 and 2D6 Induction: CYP1A2, 2E1	None.	[37]
	Dutasteride (PO)	Substrate: CYP3A4	None.	[78]
	Finasteride (PO)	Substrate: CYP3A4	None.	[78]
	Goserelin (SC)	None.	None.	[25]
	Leuprolide (IM/SC)	None.	None.	[24]
	Spironolactone (PO)	None.	None.	[35]
Progestogens	Medroxyprogesterone acetate (PO)	Substrate: CYP3A4	…	[26]
	Progesterone (PO)	Substrate: CYP3A4	…	[134]
Testosterone	Cypionate, enanthate, undecanoate (IM/SC), undecanoate (PO)	Substrate: CYP2B6, 2C19, 2C9, 3A4	…	[41]

[a]Note that conjugated estrogens and ethinyl estradiol are included in this table to highlight pharmacokinetic similarities and differences with estradiol. Ethinyl estradiol and conjugated estrogens are NOT recommended as an estrogen agent for gender affirming therapy.

most estrogen-related drug-drug interaction data are derived from studies with oral EE, which is used in oral contraceptive pills. Herein, we highlight similarities and differences between ethinyl estradiol and estradiol pharmacology to inform the application of these data across products.

3.1.1. Metabolism and elimination

Most GAHT agents are extensively metabolized. To improve bioavailability, oral and injectable estradiol preparations are formulated as ester prodrugs (valerate or cypionate), which are hydrolyzed to the parent drug, 17β-estradiol (Figure 1).

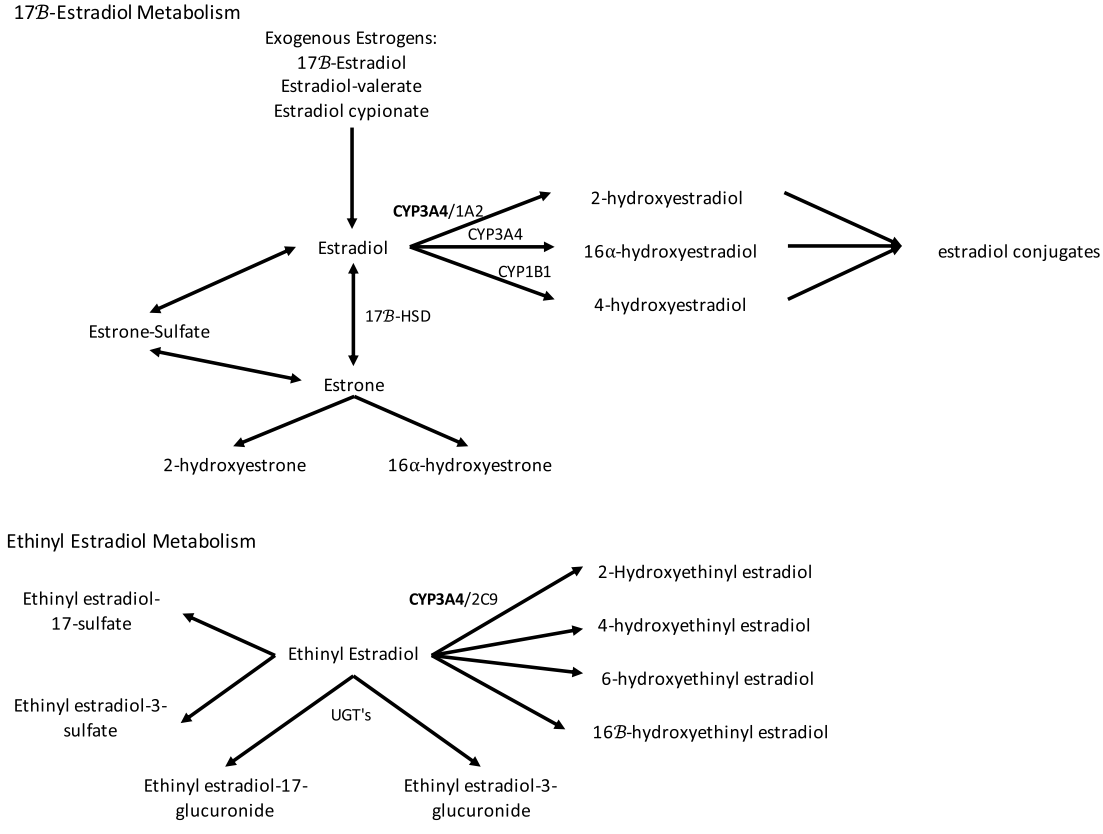


Figure 1. Metabolic pathways of exogenous 17β-estradiol and ethinyl estradiol. Estradiol ester prodrug preparations are cleaved to 17β-estradiol which is metabolized via 17β-hydroxysteroid dehydrogenase to estrone. Estrone is primarily sulfated in the liver and estrone-sulfate may be converted back to estradiol. Estradiol may also be metabolized via cytochrome P450 enzymes to less active catechol estrogens. The main metabolic pathways for ethinyl estradiol include hydroxylation by cytochrome P450 enzymes and glucuronide conjugation. Ethinyl estradiol is not a substrate for 17β-hydroxysteroid dehydrogenase [33–35].

Oral 17β-estradiol tablets are also available as a non-prodrug preparation (micronized estradiol, Estrace®). Estradiol is highly protein-bound in plasma (~98%) [28]. Oral estradiol undergoes extensive first-pass metabolism and is rapidly converted to its active metabolite (estrone) by 17β-hydroxysteroid dehydrogenase (17β-HSD) (Table 1). Estrone is conjugated and excreted in the bile [28] where it undergoes enterohepatic recirculation [29–31]. Estradiol and estrone are extensively hydroxylated by cytochrome P450 (CYP) enzymes (primary: CYP3A4; secondary: CYP1A2). Estradiol and its metabolites are also conjugated by uridine 5′-diphosphoglucuronosyltransferase (UGT) isoenzymes, including UGT1A1 [32]. Drug-drug interaction data specific to 17β-estradiol are limited. *In vitro*, estradiol induces CYP2A6, 2B6, and 3A4 expression at supraphysiologic concentrations [33]. For trans women, desired estradiol concentrations are within physiologic ranges for premenopausal cis women [2]; therefore, estradiol is not expected to induce or inhibit CYP isoenzymes when used as GAHT.

Ethinyl estradiol has higher oral bioavailability than estradiol. Ethinyl estradiol is not metabolized to estrone by 17β-HSD; rather it is directly conjugated (UGT) and hydroxylated (primary: CYP3A4; secondary: CYP2C9) to 2-hydroxy-ethinyl estradiol (Figure 1) [34]. While the clinical implications of these different metabolic pathways are incompletely understood, it is important to consider this difference when predicting drug-drug interactions for GAHT extrapolated from oral contraceptive data. For instance, estradiol may be less susceptible to CYP3A4 or UGT mediated interactions than ethinyl estradiol, as estradiol has an alternative metabolic route via 17β-HSD. Conversely, estradiol may be susceptible to transporter-mediated drug interactions when compared to ethinyl estradiol, as estradiol and estrone conjugates are substrates for organic-anion transporting polypeptide (OATP) as discussed below.

Most antiandrogens are hepatically metabolized. Spironolactone is rapidly and extensively metabolized to active metabolites by hepatic esterases and transferase [35]. No significant drug-drug interactions are expected between spironolactone and CYP inducers or inhibitors [36]. Cyproterone is excreted unchanged in feces and urine (60% and 33%, respectively); it is hydroxylated to 15-hydroxycyproterone, an active metabolite, by CYP3A4 [37]. Cytochrome P450 3A4 inducers or inhibitors may alter the 15-hydroxycyproterone concentration in plasma, although clinical data are limited. At doses used for GAHT (25 to 50 mg daily) cyproterone is not expected to alter CYP isoenzyme activity. The 5α-reductase inhibitors (dutasteride and finasteride) and progestogens (medroxyprogesterone and progesterone) are extensively metabolized by CYP3A isoenzymes, but they do not induce or inhibit CYP isoenzymes. Bicalutamide, a racemic mixture, is predominantly metabolized by conjugation. Its active R-bicalutamide isomer inhibits and it may increase the concentration of CYP3A4 substrates, although this may only be clinically relevant for drugs with a narrow therapeutic range. GnRH analogues (leuprolide, goserelin) are neither metabolized via CYP isoenzyme nor expected to have significant drug-drug interactions.

3.1.2. Drug transporters

Limited *in vitro* data describe the influence of feminizing sex hormones on drug transporter protein expression (mRNA and protein levels). Two efflux drug transporter proteins – breast cancer resistance protein (BCRP) and p-glycoprotein – are either decreased (BCRP: 17β-estradiol) and/or increased (BCRP: progesterone; p-glycoprotein: estrone metabolite) by sex hormones [38,39]. Estradiol (as its glucuronidated form) is a substrate OATP 1B1/1B3, a hepatic uptake transporter [40]. Clinical implications of these *in vitro* findings for GAHT are incompletely understood.

3.2. Masculinizing hormonal therapy

The goal of GAHT in trans men include increasing secondary sex characteristics such as muscle mass and facial hair, while minimizing other secondary sex characteristics. For trans men, testosterone is the mainstay of GAHT. Testosterone is available as several preparations: intramuscular or subcutaneous injection (cypionate, enanthate, undecanoate), transdermal preparations (gel, patch), oral tablet (undecanoate), nasal spray, or implantable pellet. During GAHT, desired serum total testosterone concentrations are between 11.1–34.7 nmol/L [2].

3.2.1. Metabolism and elimination

Testosterone is primarily metabolized to two major metabolites: dihydrotestosterone (DHT) and estradiol. Metabolism to DHT, a potent metabolite, occurs via steroid 5α-reductase in the skin, liver, and urogenital tract. Testosterone is metabolized to estradiol by CYP19 (aromatase) in the brain, fat, and testes [41]. Testosterone is a CYP3A4/5 substrate, and CYP3A4/5 induction or inhibition may alter testosterone concentrations [40].

3.2.2. Drug transporters

Based on available data, neither testosterone nor its active metabolite DHT are expected to induce or inhibit drug transporters during GAHT. *In vitro* data indicates that testosterone and DHT may be substrates of p-glycoprotein but the clinical relevance is unknown [42].

4. Pharmacology of antiretrovirals and direct acting antivirals

ARV and DAA metabolism and transport pathways are summarized in Table 2.

4.1. Antiretrovirals

Antiretroviral therapy includes two or three ARVs selected from different ARV classes. Clinicians must consider the pharmacokinetic properties of each class when predicting potential drug-drug interactions. Based on U.S. guidelines, nucleoside reverse transcriptase inhibitors (NRTIs) combined with an unboosted integrase strand transfer inhibitor (INSTI) are recommended for treatment-naïve individuals [11]. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) are recommended for certain treatment-naïve individuals in US

Table 2. Antiretroviral and hepatitis C direct acting antivirals and major drug transport and metabolic pathways[a].

Agent	Main route(s) of metabolism and drug transport	CYP and UGT Effects: Inhibitor	CYP and UGT Effects: Inducer	Transporters (Inhibitor)
A) Antiretroviral Agents				
Integrase Strand Transfer Inhibitors (INSTIs)				
Bictegravir	UGT1A1, CYP3A4 (similar contribution)	No known effects.	No known effects.	OCT2, MATE1
Cabotegravir	UGT1A1, UGT1A9	No known effects.	No known effects.	OCT1, OCT3
Dolutegravir	UGT1A1, CYP3A4 (10–15%); UGT1A3, UGT1A9 P-gp and BCRP in vitro		No known effects.	OCT2, MATE1
Elvitegravir	CYP3A4		CYP2C9 (modest)	
Raltegravir	UGT1A1	No known effects.	No known effects.	
Protease Inhibitors (PIs)				
Atazanavir	CYP3A4 P-gp, MRP1	3A4, UGT1A1 ≫2C8 (weak)		P-gp, MRP1, OATP1B1, OATP1B3, BCRP
Darunavir	CYP3A P-gp	CYP3A4		BCRP, OATP1B1
Lopinavir/ ritonavir	CYP3A4 P-gp, MRP1	CYP3A4		P-gp, OATP1B1, OATP1B3
Pharmacokinetic Enhancers				
Ritonavir	CYP3A4 P-gp, MRP1	CYP3A4 (potent)> >2D6* *negligible effect at boosting doses	UGT, CYP1A2, 2B6, 2C8, 2C9, 2C19	P-gp, OATP1B1, OATP1B3, BCRP, OATP2B1, OCT2, MATE1
Cobicistat	CYP3A, 2D6 (minor)	CYP3A, CYP2D6		P-gp, BCRP, OATP1B1 and OATP1B3, MATE1
Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs)				
Doravirine	CYP3A4/5	No known effects.	No known effects.	No known effects.
Efavirenz	CYP3A4, 2B6 (minor)	2C9, 2C19 (? Clinical significance).	3A4 (potent), 2B6, UGT1A1	***Inducer***: OATP1B1, MRP2
Etravirine	CYP3A4, CYP2C9, and CYP2C19	CYP2C9 (weak), CYP2C19 (moderate), p-gp (weak)	3A4 (weak)	
Nevirapine	CYP3A4, 2B6 (minor)		3A4, 2B6 (potent)	
Rilpivirine	CYP3A4 (major)	No known effects.	2C19 (moderate)	OCT2
Nucleotide Reverse Transcriptase Inhibitor (NRTI)				
Tenofovir alafenamide	Minimal metabolism via 3A4 P-gp, BCRP	No known effects.	No known effects.	
CCR5 Inhibitors				
Maraviroc	CYP3A4 P-gp	Does not inhibit major CYP isozymes at clinically relevant concentrations.		P-gp (in gut; systemic effects unlikely).
B) DIRECT ACTING ANTIVIRALS FOR HEPATITIS C				
NS5B Inhibitor				
Sofosbuvir	P-gp, BCRP GS-331,007 (primary systemic nucleoside metabolite, accounts for >90% of systemic drug exposure), which is not a P-gp substrate	No known effects.	No known effects.	No known effects.
NS5A Inhibitors				
Elbasvir	CYP3A4 P-gp and OATP in vitro.	No known effects.	No known effects.	BCRP (intestinal)
Ledipasvir	P-gp, BCRP	No known effects.	No known effects.	Weak inhibitor of P-gp and BRCP (intestinal, not systemic). Inhibitor of OATP1B1/1B3 only at concentrations exceeding those achieved in clinic.
Pibrentasvir	P-gp and/or BCRP	CYP1A2, 3A4 and UGT1A1 (weak)		P-gp, BCRP, OATP1B1/3.
Velpatasvir	CYP3A4, 2C8, 2B6 OATP1B1, OATP1B3, P-gp, BCRP	No known effects.	No known effects.	P-gp, OATP1B1, OATP1B3, BCRP (limited to intestinal efflux and hepatic uptake – clinically relevant interactions in systemic circulation not expected).
NS3/4A Protease Inhibitor				
Glecaprevir	P-gp and/or BCRP; OATP1B1, OATP1B3 CYP3A4 (secondary role)	CYP1A2, 3A4 and UGT1A1 (weak)		P-gp, BCRP, OATP1B1/3.
Grazoprevir	CYP3A4 P-gp and OATP1B1	3A4 (weak), UGT1A1 (weak)	No known effects.	BCRP (intestinal)
Voxilaprevir	CYP3A4≫CYP1A2, 2C8 P-gp, BCRP, OATP1B1, OAT1B3	No known effects.		P-gp, BCRP, OATP1B1, OATP1B3.

[a]Key: Substrate = route of hepatic elimination of that specific drug (specified by a specific cytochrome P450 isoenzyme); inducer = leads to more rapid clearance of substrates of a specific hepatic isoenzyme (lowers serum concentrations of the respective drug and may lead to decreased efficacy); inhibitor = leads to decreased clearance of substrates of a specific hepatic isoenzyme (increases serum concentrations of a respective drug and may lead to toxicity).

Adapted with permission from Tseng AL. Interactive case: HIV and HCV Drug Interactions. In: Dodds Ashley ES, Gross AE, eds. Infectious Diseases Self-Assessment Program, 2019 Book 1. HIV and Hepatitis. Lenexa, KS: American College of Clinical Pharmacy, 2019:pp 141–3.

guidelines, but are widely used globally. Finally, protease inhibitors are commonly reserved for individuals with some ARV resistance.

4.1.1. ARV metabolism and elimination

Most NRTIs are eliminated via the kidneys as unchanged parent drug, and none are expected to inhibit or induce major CYP or UGT isozymes. INSTIs are substrates of either CYP3A4 or UGT1A1, (Table 2) [43–46], but most INSTIs have insignificant induction or inhibitory effects on CYP enzymes. The exception is elvitegravir, which is co-formulated with the potent CYP3A4 inhibitor cobicistat, resulting in a high potential for drug-drug interactions [43]. Additionally, elvitegravir may induce CYP2C9 [43].

Protease inhibitors and NNRTIs are CYP3A4 substrates and often cause drug-drug interactions but are also susceptible to drug-drug interactions. Most protease inhibitors are known for CYP inhibition, particularly of CYP3A4 [47–49], and atazanavir also inhibits UGT1A1 (Table 2) [47]. Ritonavir and cobicistat are used as pharmacokinetic enhancers to prevent CYP-mediated metabolism and to improve bioavailability of protease inhibitors or elvitegravir. Ritonavir has mixed inhibition and induction effects on CYP and UGT enzymes in vivo (Table 2) [50]. Some NNRTIs, including efavirenz, nevirapine and etravirine are significant inducers of CYP3A4 and other CYP enzymes [51–53]. Efavirenz and etravirine also inhibit CYP2C9 and 2C19. Other NNRTIs, including rilpivirine and doravirine, do not cause significant hepatic enzyme-mediated interactions, but are highly susceptible to interactions mediated by CYP3A4 [54,55].

4.1.2. ARV drug transporters

Most INSTIs and protease inhibitors are p-glycoprotein substrates. Certain INSTIs (bictegravir, dolutegravir) inhibit drug transporter proteins, specifically organic cation transporter 2 (OCT2) and/or MATE1 – transporters in the renal proximal tubule cell [44,46]. Ritonavir and cobicistat inhibit p-glycoprotein, BCRP, OATP1B1, and OATP1B3. NNRTIs influence several transporter proteins: OCT2 inhibition (rilpivirine), MRP2 induction (efavirenz) [56]; p-gp inhibition (etravirine) [57]; OATP1B1 induction (efavirenz) [56]. Tenofovir alafenamide (TAF) and tenofovir disoproxil fumarate (TDF) are p-glycoprotein and BCRP substrates but do not inhibit or induce either transporter. Parent tenofovir is not a substrate of these transporters. Interactions with p-glycoprotein inducers or inhibitors are primarily clinically significant with the TAF prodrug [11,58].

4.2. Direct acting antivirals

DAA classes include non-structural protein 5A (NS5A) and 5B (NS5B) inhibitors, which reduce viral replication and packaging, and NS3/4A protease inhibitors, which inhibit post-translational processing of HCV proteins. In combination, these agents dramatically improve HCV outcomes in patients, with 95–99% of patients achieving SVR after 8–12 weeks of therapy.

Commonly used DAA regimens include fixed dose formulations of glecaprevir/pibrentasvir, velpatasvir or ledipasvir with sofosbuvir, or elbasvir/grazoprevir. Regimens including voxilaprevir may be considered for patients who have not responded to previous DAA treatment [12]. Clinicians should review a patient's medication history upon DAA initiation to reduce adverse outcomes related to complex drug-drug interactions with these agents [12].

4.2.1. DAA metabolism and elimination

Many DAAs, including elbasvir, velpatasvir, glecaprevir, grazoprevir, and voxilaprevir are metabolized via CYP3A isoenzymes. Velpatasvir is also metabolized via CYP2B6 and CYP2C8. Ledipasvir and pibrentasvir are primarily excreted unchanged in feces. Sofosbuvir is extensively metabolized via non-CYP/UGT isoenzymes and renally eliminated as an inactive metabolite, GS-33,100.

The NS5A and 5B inhibitors velpatasvir, ledipasvir, elbasvir, and sofosbuvir do not induce or inhibit CYP enzymes [59–61]. Pibrentasvir weakly inhibits CYP1A2, 3A4 and UGT 1A1 [62]. The HCV protease inhibitors glecaprevir and grazoprevir have weak inhibitory properties on CYP and/or UGT isoenzymes (27% and 34%, respectively, increase in midazolam area under the curve (AUC), a probe substrate of CYP3A4). Voxilaprevir does not inhibit CYP or UGT enzymes [59].

4.2.2. DAA drug transporters

Drug transporters are common routes of potential drug-drug interactions for DAAs. All of the DAAs currently used in clinical practice are substrates of p-glycoprotein. In addition, elbasvir, glecaprevir, ledipasvir, pibrentasvir, velpatasvir and voxilaprevir are inhibitors of p-glycoprotein. Glecaprevir, ledipasvir, pibrentasvir, velpatasvir, voxilaprevir are both substrates and inhibitors of BCRP. Elbasvir and grazoprevir are intestinal inhibitors of BCRP, and sofosbuvir is a substrate of BCRP. Grazoprevir is a substrate of OATP1B1/1B3. Glecaprevir, velpatasvir and voxilaprevir are OATP1B1/1B3 substrates and inhibitors while pibrentasvir is an inhibitor but not a substrate [63].

5. Pharmacokinetic interactions

A summary of potential pharmacokinetic interactions between ARVs, DAAs and GAHT is provided in Table 3.

5.1. Feminizing hormonal therapy

5.1.1. Estradiol and antiretrovirals

One published case series and one pharmacokinetic study concerning the interaction potential between feminizing hormones and ART were identified during this review. The case series reviewed three transwomen who were taking estradiol plus an efavirenz-based ART regimen [64]. Two of the patients took oral 17β-estradiol, both of whom had subtherapeutic serum estradiol concentrations (<367 pmol/L) and elevated serum testosterone concentrations (>3.47 nmol/L). One patient was switched to rilpivirine-based ART and concurrently switched from oral estradiol (8 mg daily) to conjugated equine estrogen (5 mg daily). Testosterone was suppressed following these modifications (<3.47 nmol/L), but the influence of ART, GAHT, or both changes is unclear. The second patient underwent gender-affirming surgery (orchiectomy and vaginoplasty) and

Table 3. Potential pharmacokinetic interactions between GAHT and ARVs and DAAs.

	Feminizing GAHT					Masculinizing GAHT
	17β-estradiol	Androgen blockers and adjunctive therapies				Testosterone
		cyproterone	dutasteride, finasteride	Progestogens (oral medroxyprogesterone, micronized progesterone)	Spironolactone. Bicalutamide, leuprolide, goserelin	
ARVs						
May coadminister	Bictegravir, cabotegravir, dolutegravir, raltegravir, doravirine, rilpivirine	Bictegravir, cabotegravir, dolutegravir, raltegravir, doravirine, rilpivirine	Bictegravir, cabotegravir, dolutegravir, raltegravir, doravirine, rilpivirine	Bictegravir, cabotegravir, dolutegravir, raltegravir, doravirine, rilpivirine	All ARVs	Bictegravir, cabotegravir, dolutegravir, raltegravir, doravirine, rilpivirine
Caution	Nevirapine, etravirine (↓ estradiol) PIc, EVGc (↑estradiol) PIr (↑/↓estradiol)	Efavirenz, etravirine, nevirapine (↓ cyproterone) PIr, PIc, EVGc (↑cyproterone)	Efavirenz, etravirine, nevirapine (↓dutasteride, finasteride) PIr, PIc, EVGc (↑dutasteride, finasteride)	Efavirenz, etravirine, nevirapine (↓progestogens) PIr, PIc, EVGc (↑progestogens)		Efavirenz, etravirine, nevirapine (↓testosterone) PIr, PIc, EVGc (↑testosterone)
Avoid (if possible)	Efavirenz (↓estradiol)					
DAAs						
May coadminister	ELB/GZR, LDV/SOF	All DAAs	All DAAs	All DAAs	All DAAs	All DAAs
Caution	G/P, SOF/VEL, SOF/VEL/VOX (↑estradiol)					

achieved desired estradiol concentrations during EFV-based ART after switching from oral 17β-estradiol (8 mg daily) to transdermal patches (0.1 mg/24 h weekly). The third patient also underwent gender-affirming surgery and achieved estradiol concentrations similar to other trans women taking the same dose of transdermal estradiol (0.05 mg/24 h weekly). While there is high inter-patient variability in these outcomes, these cases suggest a potential interaction between efavirenz and oral 17β-estradiol, possibly by efavirenz-mediated CYP3A4 induction [64]. Transdermal estradiol may avoid potential drug-drug interactions that occur via first-pass metabolism, although minimization of metabolism-related drug-drug interaction potential has not been observed in studies with non-oral routes of hormone administration. For example, the extent of the interaction between ethinyl estradiol and efavirenz was greater when administered intravaginally compared to orally [65,66] and the observed interaction between lopinavir/ritonavir plus transdermal ethinyl estradiol was similar to oral ethinyl estradiol [67].

The iFACT study, a prospective study among 40 ART-naïve Thai trans women living with HIV, enrolled participants into a single-arm, three-phase pharmacokinetic study: GAHT alone (oral estradiol valerate 2 mg daily plus oral cyproterone 25 mg daily); GAHT plus ART (TDF/emtricitabine/efavirenz); and ART alone [68]. The estradiol AUC, maximum concentration (C_{max}), and concentration at 24 hours (C_{24}) were decreased by 28%, 19%, and 36%, respectively (all $P< 0.01$) in the presence of TDF/emtricitabine/efavirenz. The geometric mean ratios (GMR) of tenofovir AUC and C_{24} (with versus without GAHT) were 0.86 (90% CI: 0.8, 0.93) and 0.83 (90% CI: 0.75, 0.93), respectively. Plasma efavirenz pharmacokinetic parameters were not significantly altered by GAHT, although the C_{24} of efavirenz was decreased by 9% ($P= 0.02$) which is unlikely to be clinically significant. Despite altered tenofovir pharmacokinetics, the majority of participants (90%) achieved viral suppression 12 weeks after initiating ART. Another arm of the iFACT study investigated GAHT with and without TDF/emtricitabine in 20 HIV-negative trans women [69]. Investigators observed decreased tenofovir AUC and C_{24} with GAHT (versus without: 12%, $P< 0.001$; 18%, $P= 0.03$, respectively). Estradiol concentrations were unaltered by TDF/emtricitabine. These findings suggest that the efavirenz component of the iFACT ART regimen decreased estradiol concentrations. Further studies are needed to determine whether estradiol concentrations are consistently decreased by other CYP-inducing ARVs.

Recent PK studies suggest TDF/emtricitabine disposition (either alone or as part of suppressive ART) may be altered in trans women taking GAHT. In a small sample (n = 4) of trans women living with HIV and taking GAHT, no difference was observed in plasma tenofovir and emtricitabine concentrations compared with cis adults [70]; intracellular tenofovir-diphosphate and emtricitabine-triphosphate concentrations (from peripheral blood mononuclear cells) were similar to cis adults. Investigators noted altered ratios of tenofovir-diphosphate to endogenous triphosphate in trans women, but larger studies are needed to fully understand these findings. PK studies investigating TDF/emtricitabine in HIV-negative trans women taking GAHT are reviewed extensively elsewhere [71]. Plasma tenofovir and emtricitabine exposure are modestly decreased in trans women taking GAHT (non-standardized regimens) compared with cis controls (plasma tenofovir AUC: ↓24 to 27%, $P< 0.065$; emtricitabine AUC: ↓14-24%, $P< 0.07$) [72,73]. Overall, these studies were small, and none included trans men. Further studies are needed to

understand potential drug-drug interactions between GAHT and NRTIs.

Clinical data on potential drug-drug interactions between 17β-estradiol and other ARVs are not yet available. Based on the pharmacology of each agent (Tables 1 and 2), unboosted INSTIs and the non-inducing NNRTIs, doravirine and rilpivirine, are not anticipated to interact with estradiol. When possible, it may be preferable to avoid NNRTIs that induce estradiol metabolizing pathways, such as efavirenz, etravirine, and nevirapine, due to risk of decreased estradiol concentrations. In contrast, cobicistat-boosted regimens may increase estradiol via inhibition of CYP3A4 and OATP1B1/3. While ritonavir also inhibits CYP3A4 and OATP transporters, it also induces certain CYP enzymes (Table 2); the net effect of ritonavir on estradiol concentrations is unknown. When ART that is not expected to interact with estradiol is not available or not indicated for trans individuals, drug-drug interactions may be managed through therapeutic drug monitoring guided dosage adjustment and clinical monitoring for estradiol efficacy as well as toxicity.

5.1.2. Estradiol and direct acting antivirals

No literature evaluating direct acting antivirals with 17β-estradiol in trans persons was identified. Theoretically, glecaprevir, pibrentasvir, velpatasvir and voxilaprevir may increase estradiol exposures via inhibition of OATP1B1/1B3, but these combinations have not been studied, and the clinical significance of this theoretical interaction is unclear. Additional discussion on hepatic safety of these DAAs and estradiol is included in section 6.2.8 below, but are not thought to be related to DAA or estradiol pharmacokinetics.

5.1.3. Adjunctive feminizing therapies and antiretrovirals or direct acting antivirals

We identified no drug-drug interaction studies between oral progestogens and either ART or DAAs. However, several investigators have studied potential drug-drug interactions between ART and intramuscular depot-medroxyprogesterone (DMPA) for contraception, which may inform our understanding of the potential for drug-drug interactions. In cis women living with HIV and receiving either lopinavir/ritonavir-, nelfinavir-, or nevirapine-based ART, medroxyprogesterone concentrations were compared with cis women living with HIV who were either not on ART or receiving ART that was not expected to cause a drug-drug interaction [74,75]. Medroxyprogesterone concentrations were similar between participants receiving either nelfinavir- or nevirapine-based ART compared with the control group [75], while the medroxyprogesterone AUC over 12 weeks was higher in women receiving lopinavir/ritonavir-based ART compared to the control group [geometric mean (IQR) 18.08 (16.22, 24.10) versus 12.38 (8.88, 13.88) ng•wk/mL, respectively] [76]. Three studies evaluated DMPA in combination with efavirenz-based ART with variable results. Two studies reported no change in medroxyprogesterone exposure over 12 weeks [74,75], while one study in Malawian cis women found lower medroxyprogesterone exposure at week 13 in participants receiving efavirenz-based ART compared to HIV-negative cis women [mean (SD) 603 (296) vs 1146 (850) pg/mL, P= 0.03] [77]. Mngqibisa *et al* evaluated cis women receiving both efavirenz-based ART and rifampicin/isoniazid for TB therapy and found that the combination of CYP3A inducers efavirenz and rifampin increased the clearance of medroxyprogesterone compared with historical controls (19,681 L/week versus 12,118 L/week, respectively) [78]. Given that oral medroxyprogesterone may be more susceptible to drug-drug interactions than DMPA, drugs that induce or inhibit CYP3A are expected to impact the systemic exposure of this progestogen.

We identified no pharmacokinetic studies evaluating drug-drug interactions between adjunctive antiandrogens (spironolactone, cyproterone, 5α-reductase inhibitors, GnRH analogues, or bicalutamide), or testosterone and either ART or DAAs. Participants in the iFACT study (described in section *5.1.1: Estradiol and Antiretrovirals*) took oral cyproterone 25 mg daily; investigators measured bioavailable testosterone (as a surrogate marker of cyproterone efficacy) before and during TDF/emtricitabine/efavirenz therapy. While cyproterone and efavirenz plasma concentrations were not measured, the bioavailable testosterone serum trough concentrations did not increase during ART. This may suggest that cyproterone concentrations are unaltered by efavirenz-based ART, but further studies are needed [68].

Antiretrovirals that inhibit CYP3A4, such as ritonavir or cobicistat, may inhibit metabolism of CYP3A substrates, including cyproterone, 5α-reductase inhibitors, progestogens, and testosterone, potentially increase systemic concentrations of these agents [79]. Close monitoring of GAHT, including clinical efficacy/toxicity profiles and serum measurement of estradiol and total testosterone, is suggested when coadministered with ART that inhibit CYP3A isoenzymes. GAHT dosage reduction of cyproterone or testosterone may be considered if toxicity occurs. Among DAAs, the NS3/4A protease inhibitors glecaprevir and grazoprevir are weak inhibitors of CYP3A4 and are not anticipated to inhibit metabolism of cyproterone, 5α-reductase inhibitors, and progestogens to a clinically relevant extent.

Conversely, CYP3A4 inducers like efavirenz, etravirine and nevirapine may induce metabolism of these GAHT that are CYP3A substrates, potentially leading to decreased circulating concentrations of these agents. In a cisgender volunteer study, the AUC of finasteride was reduced by over 50% when coadministered with St. John's wort [80]. Monitoring of clinical efficacy and serum hormone concentrations with potential increase in GAHT doses may be required. Unboosted INSTIs, doravirine, or rilpivirine are not anticipated to alter the metabolism of CYP3A substrates.

Given the lack of overlapping CYP isoenzyme involvement in the metabolism of spironolactone with ARVs or DAAs, no pharmacokinetic interactions are expected when these agents are used in combination.

5.2. Masculinizing hormonal therapy

We identified no clinical pharmacokinetic studies evaluating drug-drug interactions between testosterone and either ART or DAAs. Since testosterone is a substrate of CYP3A4/5,

concentrations can be increased by potent inhibitors such as ritonavir or cobicistat. Conversely, testosterone concentrations may be decreased by efavirenz, etravirine and nevirapine. The clinical relevance of these postulated interactions is not clear. Close monitoring of clinical efficacy and toxicity and measurement of total serum testosterone is suggested when using testosterone with enzyme inhibiting or inducing antiretrovirals. Dose reduction of testosterone with ritonavir or cobicistat, or dose increases with enzyme-inducing NNRTIs efavirenz, etravirine or nevirapine may be required. ARV regimens including unboosted INSTIs, doravirine or rilpivirine are not anticipated to alter the metabolism of testosterone.

The NS3/4A protease inhibitors glecaprevir and grazoprevir are weak inhibitors of CYP3A4; as such, significant interactions with testosterone are not anticipated. No other DAAs are expected to interact with testosterone.

6. Pharmacodynamic interactions

Pharmacodynamic drug-drug interactions may alter ARV, DAA, and/or GAHT efficacy and safety by additive, synergistic, or antagonistic mechanisms. Pharmacodynamic interactions between GAHT and ART or DAA regimens are poorly characterized. A summary of potential pharmacodynamic interactions between ARVs, DAAs and GAHT is provided in Table 4. Further details are discussed below.

6.1. Antiretroviral and DAA efficacy

No pharmacologic studies have investigated the influence of GAHT on ARV or DAA efficacy. In a respondent-driven sampling study of trans women living with HIV in San Francisco, 65% of respondents reported taking ART, yet less than half of respondents were virologically suppressed (HIV-RNA ≤200 copies/mL) [81]. Barriers in the HIV treatment cascade may be responsible for decreased virologic suppression rates rather than pharmacologic interactions between GAHT and ART.

In vitro data suggests estradiol inhibits the HCV replication cycle [82], but the clinical significance of these findings is unknown.

6.2. Antiretroviral and DAA toxicities

We identified no studies that investigated ART or DAA pharmacodynamic interactions in trans persons taking GAHT. We predicted overlapping toxicities between GAHT, ART, and DAAs based on data extrapolated from cis adults.

6.2.1. Bone density effects

Recently, the first study investigating fracture outcomes in trans adults was published [83]. This was a retrospective cohort study of trans adults in the Netherlands taking GAHT. Investigators observed 1.9 times higher odds of fracture among trans women (≥50 years) compared with age-matched cis men (95% CI: 1.32, 2.74). No difference in fracture odds was observed compared with cis women. Among trans men, no difference in fracture odds was observed compared with cis men or women [83]. This study suggests that GAHT may adequately maintain bone health in trans adults in the Netherlands, but GAHT regimens used across clinical settings differ – including dosing variations, different routes of administration, variable durations of use. The influence of different GAHT regimens on skeletal health remains incompletely understood [84]. In trans women, a systematic review and meta-analysis observed increased lumbar spine bone mineral density (BMD) from baseline through 24 months of GAHT (0.06 g/cm2; 95% CI: 0.04, 0.08 g/cm^2) [85]. Among trans men taking GAHT, no change was observed in BMD at any skeletal site through 24 months compared with baseline [85]. A prospective study by the same investigators observed that bone turnover markers were decreased following 12 months

Table 4. Potential pharmacodynamic interactions between GAHT and ART and DAAs.

	ARV or DAAs of concern	Potential therapeutic options	Other comments
Bone density	TDF may↓bone mineral density	TAF or other NRTIs	T-scores: use female reference range for both trans women & men; Z-score: use reference range for affirmed gender (trans women and trans men)
Cardiovascular concerns	Abacavir, PK-enhanced darunavir, lopinavir/ritonavir:↑CVD risk	TAF, TDF, INSTIs, doravirine, rilpivirine	Determine cardiovascular risk score using affirmed gender.
Weight gain	INSTIs, TAF	Use alternative ARV from another class	Regular monitoring of body mass index, waist circumference.
Cholelithiasis	Atazanavir	Use alternative PI or ARV from another class	Atazanavir no longer first-line option
Dyslipidemia	TAF, boosted regimens	TDF may have a beneficial effect on lipids. Unboosted INSTIs are lipid neutral.	Regular monitoring of lipid panel.
Psychiatric effects	Efavirenz, bictegravir, dolutegravir	NNRTIs: doravirine, rilpivirine INSTIs: RAL, EVG/c PIs	Monitor for changes in mood or sleep.
QT interval prolongation	Rilpivirine, PIs	INSTIs, other NNRTIs	Use with caution in patients on anti-androgen therapy or with other risk factors for QT prolongation (electrolyte abnormalities, other QT interval prolonging drugs)
Renal effects	Risk of nephrotoxicity with TDF	TAF or other NRTIs	TAF can be used if Clcr>30 mL/minute; consider using affirmed gender in creatinine clearance calculator
Transaminitis	G/P, SOF/VEL/VOX	SOF/VEL, SOF/LDV, ELB/GZR	Measure ALT, AST during DAA therapy, particularly during first 4 weeks

of GAHT in trans adults [86], but the GAHT regimens were standardized according to a study protocol, and generalizability to other settings is unknown.

Long-term bone health outcomes related to ART in trans persons are unknown. TDF is associated with decreased bone mineral density in cis adults taking either suppressive ART or TDF-based pre-exposure prophylaxis [87,88]. TAF may be preferred for individuals taking GAHT with risk factors for osteoporosis (including older age, low body mass index, and smoking). The Endocrine Society recommends monitoring bone mineral density in trans adults with osteoporosis risk factors using sex assigned at birth on a case-by-case basis [2]. Additionally, we encourage adherence to U.S. DHHS recommendations for monitoring TDF- or TAF-based ART [11]. The International Society for Clinical Densitometry recommends using a female reference when calculating T-scores for both trans men and women [89].

6.2.2. Cardiovascular disease

Among trans women taking GAHT, venous thromboembolism and stroke incidence are elevated compared with cis women and men [90,91]. Getahun *et al*. reported higher venous thromboembolism (VTE) incidence in trans women who initiated GAHT (n = 853) compared with cis men (aHR: 3.2; 95% CI: 1.5, 6.5) and cis women (aHR: 2.5; 95% CI: 1.2, 5.0) [90]. Similarly, Nota *et al*. reported higher VTE incidence in trans women taking GAHT compared with cis men and women [91]. Neither analysis adjusted for different GAHT regimens (duration, preparations). One single-center retrospective study in the U.S. investigated VTE incidence among trans women taking oral 17β-estradiol [92]. Over 600 U.S. trans women were included, and only one participant had a VTE (incidence rate: 7.8/10,000 person-years) [92]. All patients took oral 17β-estradiol, and most took spironolactone (>90%); less than 10% took at least one of each of the following: conjugated equine estrogen, oral progesterone, and/or DMPA. These findings suggest that the thrombogenicity of modern GAHT (excluding oral ethinyl estradiol and conjugated equine estrogens) may be low. Among trans men initiating testosterone (n = 585), VTE incidence was modestly higher compared with cis men (aHR: 2.7; 95% CI: 0.6, 12.1) and cis women (aHR: 1.5; 95% CI: 0.4, 5.6) [89]. Nota *et al*. observed higher myocardial infarction incidence in trans men taking testosterone compared with cis women only (standardized incidence ratio: 3.69; 95% CI: 1.94, 6.42), although this study was limited by lack of adjustment for smoking or psychosocial stressors [91].

Abacavir and protease inhibitors (pharmacokinetically-enhanced darunavir and lopinavir/ritonavir) are associated with myocardial infarction in cis adults [87,93]. Clinicians should calculate a cardiovascular disease risk score in all trans patients living with HIV, and consider alternative ART options, as appropriate. Clinicians may consider using a patient's affirmed gender rather than sex assigned at birth to calculate the cardiovascular disease risk scores, accounting for factors such as duration of GAHT use, hormone doses, and history of gonadectomy [94–97]. Among trans patients with an elevated cardiovascular disease risk score, unboosted INSTI-based regimens are preferred, due to the lipid-neutral effect of this ARV class (see section 6.2.4 *Dyslipidemia*). NNRTI-based ART, including doravirine- or rilpivirine-based regimens, may be an alternative.

Clinicians should consider the potential cumulative effect of GAHT- and ART-associated weight gain on cardiovascular disease risk in trans patients. A meta-analysis reported that total body weight was increased among trans women taking GAHT (up to 3.7 kg, pooled total body weight change estimate: +1.8 kg [95% CI: 0.2, 3.4]); investigators observed similar outcomes in trans men taking GAHT (total body weight increase up to 3.5 kg, pooled estimate effect: +1.7 kg [95% CI: 0.7, 2.7]) [98]. Many ARV classes are associated with weight gain: INSTIs, second-generation protease inhibitors (darunavir, lopinavir/ritonavir), and NNRTIs [99]. Data are limited to cis adults living with HIV, but mean weight gain is higher following bictegravir- (4.24 kg, 95% CI: 3.71, 4.78) or dolutegravir-based ART (4.07 kg, 95% CI: 3.51, 4.62) compared with elvitegravir/cobicistat-based ART (2.72 kg, 95%: 2.45, 3.00) [100]. For NRTIs, mean weight gain is higher during TAF- (4.25 kg, 95% CI: 3.94, 4.56) compared with TDF-containing ART (2.07 kg, 95% CI: 1.84, 2.30) [100]. Cis adults who switched to TAF- from TDF-containing ART experienced increased body mass index (mean increase: 0.45 kg/m^2, 95% CI: 0.14, 0.76) and increased ASCVD risk scores (mean increase: 13%, 95% CI: 4%, 23%) [101].

Clinicians should monitor body mass index within the first 12 months of ART initiation, as short-term weight gain is associated with increased diabetes or cardiovascular disease risk [102]. Waist circumference, a measure of visceral obesity, is recommended by the European AIDS Clinical Society in adults living with HIV and initiating ART [103], and may also be considered in trans adults [104]. Patients should be counselled on lifestyle modifications for weight management, including smoking cessation, dietary changes and increased physical activity [100].

6.2.3. Cholelithiasis

No studies are available describing cholelithiasis in trans women taking GAHT, although at least one case study has described cholelithiasis in a trans woman taking estrogen (dose, formulation not reported) [105]. Estrogen therapy is linked with gallstone formation in cis adults [106,107], likely from decreased gallbladder motility [28]. Atazanavir precipitates in the bile [108], and long-term (>2 years) exposure is associated with cholelithiasis [109]. Additive cholelithiasis risk when taking feminizing GAHT and atazanavir are unknown. During GAHT, the role of laboratory monitoring for gallstone-induced complications is unclear. Among cis adults (n = 14, 86% cis men), serum total bilirubin is elevated during confirmed atazanavir-associated cholelithiasis (median, range: 34.5, 7–180 umol/L) [108]. However, laboratory abnormalities (including grade 3 or 4 total bilirubin elevations) may occur during atazanavir-based ART [110], particularly because it competitively inhibits UGT1A1 and increases the unconjugated bilirubin fraction. In accordance with U.S. DHHS guidance [11], clinicians may monitor liver function tests in trans women taking GAHT plus atazanavir-based ART. Clinicians should also monitor patient-reported symptoms like right upper quadrant abdominal pain, and refer patients

to a gastroenterologist as needed for appropriate follow-up care.

6.2.4. Dyslipidemia

No studies have systematically evaluated dyslipidemia in trans adults taking GAHT plus ART. Among HIV-negative trans women taking GAHT for 24 months, a systematic review and meta-analysis observed increased triglyceride levels compared with baseline (0.36 mmol/L, 95% CI: 0.04, 0.68) [111]. Triglyceride concentrations were increased among participants taking oral compared with transdermal estrogen (P= 0.04). In the same study, trans men had altered lipids through at least 24 months of GAHT compared with baseline: increased serum triglycerides (0.24 mmol/L; 95% CI: 0.00, 0.48) and low-density lipoprotein cholesterol (LDL-C) (0.46 mmol/L; 95% CI: 0.09, 0.83); decreased high-density lipoprotein cholesterol (HDL-C) (−0.22 mmol/L; 95% CI: −0.34, −0.10) [111].

While no data are available in trans adults, several ARVs (pharmacokinetically enhanced protease inhibitors, efavirenz) are associated with increased triglycerides, LDL-C, and altered HDL-C concentrations in cis adults [11,112]. Unboosted INSTIs have a lipid-neutral profile [87], and switching to INSTIs from PI-based regimens may decrease triglycerides, total cholesterol, and non-HDL cholesterol [113]. NRTIs have varied influences on lipid profiles. TDF significantly improves lipid concentrations in patients with dyslipidemia [114], whereas TAF, zidovudine, and abacavir are associated with dyslipidemia [11]. The cumulative effect of ART-associated dyslipidemia in trans adults taking GAHT is unclear. However, given the link between dyslipidemia and increased risk of cardiovascular disease, unboosted INSTI-based regimens are preferred when possible, and clinicians can monitor patients according to U.S. DHHS Antiretroviral Guidelines [11].

6.2.5. Psychiatric effects

Depression, anxiety, and substance use are more prevalent among trans individuals compared with the general population [115], but psychological outcomes improve during GAHT [116,117]. NNRTIs and INSTIs have well-characterized neuropsychiatric adverse effects in cis adults. Efavirenz and rilpivirine are linked with anxiety, depression, and increased suicidality [118–120]. Doravirine, a novel NNRTI, has lower neuropsychiatric adverse event rates than efavirenz ($P\leq$ 0.033) [121]. Among INSTIs, bictegravir and dolutegravir have similar neuropsychiatric adverse event rates, which are elevated compared with other INSTIs [87]. The risk of cross-reactivity between dolutegravir and bictegravir is unknown.

Routine monitoring is recommended for trans patients with a history of mental health diagnoses who are taking GAHT plus ART, particularly among individuals taking dolutegravir, bictegravir, or efavirenz. Given the apparent concentration-response relationship between daily 600 mg efavirenz-based ART and neuropsychiatric adverse events, [122] low-dose efavirenz (400 mg)-based ART may be an alternative, although this dosage is not widely available as a single-tablet regimen. Other NNRTIs (doravirine) or INSTIs may be considered if depression develops or worsens after ART initiation.

6.2.6. QT Interval prolongation

Electrocardiographic (ECG) abnormalities are poorly characterized among trans individuals taking GAHT. Among cis men, androgen deprivation therapy is used as first-line therapy for disseminated prostate cancer [123]. Similar to GAHT in trans women, the goal of androgen depletion therapy in advanced prostate cancer is to suppress total testosterone serum concentrations (<3.47 nmol/L) either surgically or with medication therapy. Randomized clinical studies among cis men receiving advanced prostate cancer treatment report consistent associations between androgen depletion therapy and QT interval prolongation (up to 20 ms) [123]. While extension of these findings to trans patients is unknown, clinicians should carefully evaluate ART regimens that may potentiate QT interval prolongation during GAHT. In modern ART, NNRTIs and protease inhibitors are associated with QT interval prolongation. Efavirenz-based ART is associated with an increased corrected QT interval (QTc) through 48 weeks of therapy [124], and there is a concentration-response relationship between efavirenz plasma exposure and QTc prolongation [125]. Rilpivirine is also associated with QT interval prolongation in HIV-negative adults, however the QTc gradually stabilizes after 48 weeks following standard daily dosing (25 mg) [126,127]. Similarly, protease inhibitor-based ART is associated with QTc prolongation [128].

Given the link between androgen suppression and QT interval prolongation, efavirenz-, rilpivirine-, or protease inhibitor-based ART may have an additive impact on overall QT prolongation risk in trans women receiving feminizing GAHT and should be used with caution in trans individuals taking GAHT. In patients with other risk factors for torsades de pointes, alternative ART classes should be considered.

6.2.7. Renal effects

No data are available to characterize the impact of GAHT on renal function. Recent retrospective studies of clinical laboratory data from trans adults have observed altered serum creatinine concentrations before and during GAHT, with significant increases at 12 months in trans men on masculinizing hormones, and significant decreases at 12 months in trans women taking femininizing hormones. In 28–40% of individuals, the changes in creatinine resulted in shifting of eGFR category compared to baseline, when using birth sex in the Modification of Diet in Renal Disease (MDRD) equation [97]. ARVs, including certain INSTIs (bictegravir, dolutegravir), rilpivirine, and pharmacokinetic-enhancers (cobicistat), inhibit creatinine secretion and may elevate serum creatinine concentrations. These changes occur soon after ART initiation and remain stable throughout therapy, and are not associated with altered renal function [129]. Nephrotoxicity may occur among HIV-infected patients taking TDF-containing regimens, and regular renal function monitoring is recommended [11].

The combined influence of GAHT and ART on serum creatinine concentrations and glomerular filtration rate estimates in trans adults is unknown. When monitoring renal function during HIV and/or HCV treatment in trans patients taking GAHT, clinicians may consider estimating renal function

based on a patient's affirmed gender rather than sex assigned at birth, taking into account factors such as time on GAHT, changes in weight/muscle mass, etc [94,130]. Further, alternative renal function biomarkers like cystatin-C may be considered among trans patients with marginal renal function [11].

6.2.8. Transaminitis

Certain DAAs are associated with elevated ALT concentrations in cis adults, although clinical data specific to trans patients taking GAHT with DAAs are not yet available. In cis adults, coadministration of glecaprevir/pibrentasvir with ethinyl estradiol-containing oral contraceptive medications resulted in grade 1–3 ALT and AST elevations, with no substantial changes noted in the exposures of glecaprevir, pibrentasvir, or components of the oral contraceptives which could explain these observations. No ALT/AST elevations were seen when glecaprevir/pibrentasvir was administered with the progesterone only contraceptive norethindrone [131]. As such, the coadministration of glecaprevir/pibrentasvir with medications containing ethinyl estradiol is not recommended. The product monograph recommends that EE-containing products including combined oral contraceptives, vaginal ring or patch should be discontinued prior to starting glecaprevir/pibrentasvir and may be restarted two weeks after completion of glecaprevir/pibrentasvir therapy [62]. It is unclear whether these precautions with ethinyl estradiol can be extended to 17β-estradiol, since the mechanism of ALT/AST elevations is unknown. In phase 2/3 trials, 18 subjects were taking estradiol as hormone replacement therapy. ALT/AST elevations in these subjects were similar to that observed in the overall study population [131].

Similarly, the Canadian and European product monographs for sofosbuvir/velpatasvir/voxilaprevir state that coadministration with ethinyl estradiol-containing products may increase the risk of ALT elevation, despite lack of any significant pharmacokinetic interaction noted [59,132]. The Canadian monograph recommends that ALT monitoring may be required, while the European Summary of Product Characteristics contraindicate concomitant use of sofosbuvir/velpatasvir/voxilaprevir with ethinyl estradiol-containing products including oral contraceptives and vaginal rings. In contrast, the US package insert states that there is no clinically significant interaction with ethinyl estradiol/norgestimate and does not include any mention of ALT elevations with coadministration. Again, it is unclear whether these precautions apply to 17β-estradiol use in GAHT. 17β-estradiol is a substrate of OATP1B1. DAAs which inhibit this transporter (glecaprevir, pibrentasvir, velpatasvir and voxilaprevir) could theoretically increase estradiol exposure, although this has not been studied and the clinical relevance is unclear.

A post-hoc analysis examined 1022 identified cis women with HCV genotypes 1 or 4 who received 12 weeks of elbasvir/grazoprevir therapy; participants were stratified according to whether they received oral contraceptives or hormone replacement therapy (HRT) during the study period. Of the 81 women taking contraceptives/HRT, 17 (21%) used estradiol for at least 7 days during DAA treatment. Efficacy and safety of elbasvir/grazoprevir were similar in those receiving contraceptives/HRT compared to those not on contraceptives/HRT [9,133]. These limited observations suggest that elbasvir/grazoprevir may be safely used with concomitant hormone therapy, including estradiol.

Given the importance of GAHT in the context of mental health and quality of life outcomes [20], GAHT should not be discontinued during HCV treatment if possible. Liver function test monitoring should be completed in trans women taking feminizing GAHT within 4 weeks of HCV treatment initiation with regimens that may influence ALT concentrations, including glecaprevir/pibrentasvir and sofosbuvir/velpatasvir/voxilaprevir. Clinicians should also monitor for patient-reported symptoms including fatigue, weakness, lack of appetite, nausea or vomiting, or jaundice, as these may indicate hepatic toxicity.

7. Conclusions

Antiretrovirals and DAAs may significantly interact with GAHT used in trans patients, with potential consequences including lack of GAHT efficacy or increased toxicity. Clinically significant pharmacokinetic interactions that may impact GAHT efficacy are most likely to occur via ARV-mediated induction or inhibition of CYP isoenzymes. Some DAAs may potentially increase estradiol concentrations via inhibition of OATP transporters, but the clinical significance is unclear. Pharmacodynamic interactions between GAHT and ART or HCV treatment may occur in trans patients with certain comorbidities, and clinicians should monitor these patients regularly for additive toxicities or adverse events influenced by ART or HCV therapies and consider alternative ARVs or DAAs if possible.

8. Expert opinion

Given the improved health and quality of life outcomes associated with GAHT [20], the high rate of HIV infection among trans women, and the risk of HIV-HCV co-infection in this population, it is critical for clinicians to be aware of unique medical needs of transgender individuals in order to provide affirming medical care to this underserved population. This includes understanding and managing potential drug-drug interactions between GAHT and ART and/or HCV therapies, since concerns regarding the impact of drug-drug interactions on GAHT efficacy and safety may serve as a barrier to optimal care for transgender adults [17].

While it is tempting to use data from clinical drug-drug interaction studies between ARVs or DAAs and hormonal contraceptives to estimate the direction of potential pharmacokinetic interactions with feminizing GAHT, the extent of these interactions likely cannot be predicted based on these data alone. This limitation is largely due to differences in the metabolic pathways of synthetic hormones used for contraception compared with those used for feminization. For example, EE and 17β-estradiol are both metabolized by CYP3A4, yet the extent of CYP3A4 hydroxylation, and the influence of oral versus non-oral estradiol administration, has not been systematically compared between these estrogens. Similarly, differential activity of secondary CYP or UGT isoenzymes has not been characterized, and the role of these isoenzymes in mediating clinically relevant drug-drug interactions involving EE compared with 17β-estradiol remains unclear. An important distinction between EE and estradiol metabolism is that estradiol is

a substrate of OATP1B1 and OAPT1B3, and thus is susceptible to interactions via inhibition of these transporters by ARVs and DAAs. Such interactions would not be identified by simply extrapolating drug-drug interaction data from studies with EE. Thus, it is important for clinicians to use caution when predicting clinically relevant GAHT drug-drug interactions based on synthetic hormone data.

The NNRTIs efavirenz, nevirapine, and etravirine may decrease estradiol via CYP3A4-mediated induction; monitoring for estradiol efficacy is recommended, with measurement of estradiol concentrations and dose adjustment as needed. Limited case report experience suggests that transdermal estradiol may mitigate this effect, but this strategy has not been evaluated in clinical studies and has not been consistently observed to avoid drug-drug interactions with other hormones that are given via non-oral routes of administration. In contrast, cobicistat-boosted regimens may be more likely to increase estradiol concentrations. The net effect of ritonavir on estradiol is unclear. Thus, monitoring for estradiol toxicity and efficacy is recommended when administering with boosted ARV regimens. Generally, no significant interactions are anticipated between unboosted INSTIs, or the NNRTIs doravirine and rilpivirine with GAHT. When possible, these agents may be preferable for trans individuals receiving GAHT to avoid drug-drug interactions.

GAHT drugs are not generally considered to cause drug-drug interactions, although emerging pharmacokinetic data suggest that NRTI concentrations, specifically tenofovir (administered as TDF) and emtricitabine, may be altered by feminizing GAHT in HIV-negative trans women. One pharmacokinetic study observed intracellular concentrations of active NRTI phosphorylated moieties that were higher in trans women compared with ranges reported in the literature among cis adults [73]. The magnitude of these findings are modest, and further studies are needed to understand the influence of GAHT on NRTI efficacy. No data are available with GAHT and tenofovir administered as TAF. No dose adjustments are currently recommended among trans adults taking NRTIs as either PrEP or as a backbone regimen in ART.

While DAAs including glecaprevir/pibrentasvir and sofobuvir/velpatasvir/voxilaprevir are contraindicated or to be used with caution with ethinyl estradiol due to risk of ALT elevation, it is unclear whether use of estradiol poses the same risk, given differences in pharmacology. In phase 2/3 trials, limited use of estradiol in combination with either glecaprevir/pibrentasvir or elbasvir/grazoprevir was well tolerated. Nevertheless, there is potential for glecaprevir/pibrentasvir, sofosbuvir/velpatasvir and voxilaprevir to increase estradiol exposures via inhibition of OATP1B1/3. As such, regular monitoring for adverse effects, including elevated transaminases, is recommended during coadministration.

The antiandrogens cyproterone, dutasteride, finasteride, the progestogens medroxyprogesterone and progesterone, and testosterone may be subject to CYP3A4-mediated interactions with ritonavir, cobicistat, and NNRTIs that induce CYP isoenzymes (efavirenz, etravirine, nevirapine). Some DAAs have weak CYP3A4-inhibiting effects, but these are not expected to have clinically relevant interactions with these GAHT agents. Monitoring for desired GAHT clinical effects and regular measurement of serum sex hormone concentrations is recommended. In trans women taking GAHT, spironolactone may have a more favorable safety profile compared with cyproterone, in addition to having a lower potential for clinically significant drug-drug interactions. Oral spironolactone may be preferred among trans women at risk for thromboembolic events.

Pharmacodynamic drug-drug interactions between GAHT and ART or DAA regimens are poorly characterized. Certain ARVs and DAAs have side effect profiles that may exacerbate co-occurring morbidities in trans persons, such as depression, cardiovascular disease, or hyperlipidemia, or have side effects such as renal toxicity or transaminitis with GAHT that require monitoring. Clinicians should be aware of these factors when initiating or modifying GAHT, ART, or HCV treatment. In patients living with HIV, unboosted INSTI-based regimens are recommended as first-line ART by U.S. DHHS based on their efficacy and favorable safety profiles compared with other ARVs. Certain INSTIs, including bictegravir and dolutegravir, may be associated with elevated rates of neuropsychiatric adverse events and ART-associated weight gain in trans individuals. Mental health status and total body weight should be monitored among trans adults who are initiating ART, regardless of GAHT use. Among patients taking tenofovir-containing ART, TAF may be preferred over TDF due to improved renal and bone safety. When calculating risk scores, it may be appropriate to use calculations and reference ranges that are based on a patient's affirmed gender rather than sex assigned at birth, taking into consideration factors such as age at GAHT initiation, duration of use, consistency/adherence, and dose(s) of GAHT, as well as history of gonadectomy [94,95,97]. Clinical studies are urgently needed to identify and characterize significant pharmacokinetic and pharmacodynamic interactions that may occur between GAHT, ARVs and DAAs. We highly recommend collaboration and communication between providers of gender-affirming care and experienced HIV/HCV clinicians to manage potential pharmacodynamic drug-drug interactions in trans patients.

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Weddle Declaration
Exhibit I

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SHORT REPORTS

Transgender Women Living with HIV Frequently Take Antiretroviral Therapy and/or Feminizing Hormone Therapy Differently Than Prescribed Due to Drug–Drug Interaction Concerns

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Abstract

Purpose: Both hormone therapy (HT) and antiretroviral therapy (ART) can be lifesaving for transgender women (TW) living with HIV, but each has side effects and potential drug–drug interactions (DDI). We assessed how concerns about HT–ART interactions affect treatment adherence.
Methods: This study used a cross-sectional survey of TW ($n = 87$) in Los Angeles, CA.
Results: Fifty-four percent were living with HIV; 64% used HT. Only 49% of TW living with HIV discussed ART–HT DDI with their provider; 40% reported not taking ART (12%), HT (12%), or both (16%) as directed due to DDI concerns.
Conclusion: Imperfect HT/ART use and limited provider communication suggests a need for improved HT–ART integration.

Keywords: antiretroviral therapy, health disparities, HIV, medication adherence, transgender

Introduction

Feminizing hormone therapy (HT) is used to harmonize gender identity and secondary sex characteristics for transgender women (TW), and antiretroviral therapy (ART) is essential for individuals living with HIV; both therapies can be lifesaving.[1–3] Despite a 34-fold higher likelihood of having HIV among TW in the United States compared with the general population,[4] transgender people (approximately 0.4%–0.6% of the U.S. population[5,6]) have comparatively low healthcare utilization rates[7] and may seek gender-affirming therapies (including HT and body modification services) outside of traditional, supervised medical settings.[8,9] Both HT and ART have potential side effects, and drug–drug interactions (DDI) may exist between some ART medications (such as nonnucleoside reverse transcriptase inhibitors [NNRTI] and protease inhibitors [PIs]) and HT (particularly ethinyl estradiol),[10] making unsupervised or uncoordinated HT and ART use potentially risky for TW taking feminizing HT.

Limited data exist that address knowledge and consequences of ART and/or HT side effects and ART–HT DDIs among TW. Qualitative studies have identified fear among TW that ART limits the effect of hormones.[11] However, few studies have explored levels of adherence to either regimen resulting from these fears about interaction. Using survey data from a cross-sectional, community-based study, we assessed knowledge of and concern about HT and ART side effects and DDIs, including effects on treatment adherence, among TW living with HIV and TW not living with HIV in Los Angeles, California.

Methods

Participants

From March to July 2016, self-identified TW were recruited from APAIT, a community-based AIDS service organization

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serving diverse communities in Los Angeles, CA, for a cross-sectional, pilot project to determine differences in biomarkers of inflammation and cardiovascular risk among TW living with HIV, TW not living with HIV, and age- and race-matched control cisgender men living with HIV and not living with HIV. For this trial, eligibility criteria included being assigned male sex at birth and age ≥18 years (or 17 years with parental consent). The study sought to enroll at least 40 participants per arm (total $n = 160$, including a minimum of 80 TW). In our current analysis, we further restricted the sample to participants self-identifying as a TW.

Procedures

At the time of questionnaire administration, blood was collected for the parent study's assessment of cardiovascular risk, for which TW living with HIV were required to be on ART and have HIV-1 RNA <50 copies/mL. Eligible participants self-reported sociodemographics, medical history, healthcare access, and knowledge of ART and HT side effects and ART–HT DDIs. Participants living with HIV were asked if concern about ART–HT DDIs had prevented them from taking either/both therapies as prescribed.

Consent/permissions

The study was approved by the Institutional Review Board of the University of California, Los Angeles. Written informed consent was obtained from all study participants before performance of study procedures.

Data analysis

The main outcome for this analysis was self-reported history of HT or ART use different than prescribed due to concerns about ART–HT DDI (TW living with HIV only), which we constructed as a dichotomous variable. We calculated descriptive summaries of participant characteristics as well as self-reported beliefs and healthcare experiences. Significance was defined as $P < 0.05$. All analyses were exploratory using chi-square and *t*-test, without adjusting for multiple testing. Prevalence ratios were calculated using generalized linear models to estimate the associations of participant clinical or sociodemographic characteristics with our main outcome of imperfect use of HT and/or ART. All analyses were performed using Stata 14.0 (StataCorp LLC, College Station, TX).

Results

Eighty-seven TW were enrolled, 47 (54%) of whom were living with HIV and on ART. Participants were predominantly Hispanic (62%), black (17%), or multiracial (13%), with a mean age of 45 (Table 1). In our sample, TW living with HIV were older than TW not living with HIV (48 vs. 43 years, $P = 0.03$) and more likely to report substance use during the last 90 days (47% vs. 25%, $P = 0.04$). Median $CD4^+$ T lymphocyte count among TW living with HIV was 555 cells/μL. ART regimens included nucleoside reverse transcriptase inhibitors (98%, including 79% with tenofovir and 23% with abacavir), integrase inhibitors (40%), PIs (32%), and NNRTIs (28%).

Most TW (77%) had a regular healthcare provider, and 64% were currently using feminizing HT. Eighty-six percent of insured TW reported that their insurance covers HT fully or in part. Twenty-five percent of HT users (not living with HIV 13%, living with HIV 34%, $P = 0.07$) were accessing HT outside of the medical system and obtaining nonprescription HT from: the street (9%), a friend (4%), a pharmacy without a prescription (4%), multiple (7%), or other (2%) sources.* TW took HT in the form of pill only (40%), injection only (28%), patch only (2%), or multiple delivery routes (30%), and took estrogen (67%), progesterone (2%), antiandrogen (4%) or combination (26%) HT.† While most (78%) took their hormones regularly, those who did not commonly reported fears of side effects (31%), financial difficulties (23%), limited access to a prescribing clinician (8%), multiple (31%), or other challenges (8%)‡ as barriers to taking HT as directed.

Only 68% of TW (78% not living with HIV, 61% living with HIV, $P = 0.12$) discussed potential HT side effects with their provider, including the risks of blood clots (71%), heart attacks (69%), stroke (55%), or other side effects (24%). Fifty-seven percent of TW living with HIV reported concern for ART–HT interactions, and 40% cited this concern as a reason for not taking ART (12%), HT (12%), or both (16%) as directed, although only 49% reported discussing these concerns with their provider. Of note, taking ART differently than prescribed was not associated with significantly lower $CD4^+$ T lymphocyte counts (not as directed: 493 cells/μL vs. as directed: 563 cells/μL, $P = 0.45$) among this group with an undetectable plasma HIV-1 RNA.

In bivariate models, no clinical or sociodemographic factors were significantly associated with our main outcome of taking HT or ART differently than prescribed, although our outcome frequency was small ($n = 17$). We observed suggested associations between this outcome and recent (last 90 days) substance use (crude prevalence ratio [cPR] 1.92, 95% confidence interval [CI] 0.87–4.25, $P = 0.10$) or alcohol use (cPR 1.92, 95% CI 0.87–4.25, $P = 0.10$). We also observed a trend that current HT users were more likely to take HT and/or ART as directed (cPR 1.81, 95% CI 0.90–3.64, $P = 0.10$).

Discussion

In this cohort of 87 TW in Los Angeles, we noted high rates of concern about ART–HT DDIs and side effects, but insufficient communication on this topic with healthcare providers. We also found high rates of taking HT, ART, or both differently than prescribed because of these concerns. These results support previous research demonstrating TW's concern that adverse ART–HT DDIs delay the desired effects of hormones.[11] Our findings are concerning for numerous reasons: suboptimal ART adherence increases the risk of developing ART resistance and virologic failure.[12,13] Suboptimal adherence also increases HIV transmission risk to sexual partners during periods of uncontrolled viremia,[14–16] and possibly increases risk of transmission of drug-resistant virus.[17,18] While incompletely studied, decreased HT adherence or intermittent use may cause suboptimal feminization and/or increased risk of side effects or adverse outcomes of HT.[19]

*Percentages do not total 25 due to rounding.
†One participant (2%) did not recall the feminizing HT. Percentages do not total 100 due to rounding.
‡Percentages do not total 100 due to rounding.

TABLE 1. DEMOGRAPHICS AND SELF-REPORTED TREATMENT REGIMENS OF TRANSGENDER WOMEN ($N=87$); LOS ANGELES, CA, 2016

		HIV serostatus	
	All (n=*87*)	*Not living with HIV* (n=*40*)	*Living with HIV* (n=*47*)
Age (years)*	45.3 (SD 10.8)	42.6 (SD 11.6)	47.5 (SD 9.7)
Living with HIV	47 (54%)	N/A	N/A
Race/ethnicity			
Hispanic	54 (62%)	26 (65%)	28 (60%)
Black/African American	15 (17%)	5 (13%)	10 (21%)
Multiracial	11 (13%)	3 (8%)	8 (17%)
Asian, Alaskan Native/American Indian, White, other	7 (8%)	6 (15%)	1 (2%)
Health insurance coverage			
Medi-Cal (California's Medicaid Program)	39 (45%)	14 (35%)	25 (53%)
Medicare	5 (6%)	4 (10%)	1 (2%)
Dual Medi-Cal–Medicare coverage or private plan	20 (23%)	9 (23%)	11 (23%)
No healthcare insurance	23 (26%)	13 (33%)	10 (21%)
Feminizing HT use			
Current use	56 (64%)	25 (63%)	31 (66%)
HT acquisition outside of medical system ($n=55$; $n=23$ HIV− and $n=32$ HIV+)	14 (25%)	3 (13%)	11 (34%)
Planning future use	17 (20%)	10 (25%)	7 (15%)
No current or planned use	14 (16%)	5 (13%)	9 (19%)
Substance use (last 90 days)*	32 (37%)	10 (25%)	22 (47%)
Alcohol use (last 90 days)	43 (49%)	19 (48%)	24 (51%)
Current tobacco use	31 (36%)	12 (30%)	19 (40%)
Past tobacco use	14 (16%)	9 (23%)	5 (11%)
Unsupervised injections for body modification ($n=81$; $n=38$ HIV− and $n=43$ HIV+)	11 (14%)	5 (13%)	6 (14%)
Antiretroviral therapy			
NRTI	—	1 (2.5%) [PrEP]	46 (98%)
Tenofovir[a]	—	1 (2.5%)	37 (79%)
Abacavir[a]	—	—	11 (23%)
NNRTI	—	—	13 (28%)
PI	—	—	15 (32%)
INSTI	—	—	19 (40%)
Current $CD4^+$ T lymphocyte count (cells/μL, median [IQR], $n=44$)	—	—	555 (320–763)
HT and/or ART taken differently than prescribed due to DDI concern ($n=43$)	—	—	17 (40%)
ART (only) taken differently than prescribed due to DDI concern	—	—	5 (12%)
HT (only) taken differently than prescribed due to DDI concern	—	—	5 (12%)
Both HT and ART taken differently than prescribed due to DDI concern			7 (16%)

Mean (standard deviation) or number (percent), unless specified. Percentages may not total 100 due to rounding.
*$P<0.05$ for transgender women living with HIV compared with transgender women not living with HIV.
[a]Participants were able to report therapy with both tenofovir and abacavir.
ART, antiretroviral therapy; DDI, drug–drug interactions; HT, hormone therapy; INSTI, integrase inhibitor; N/A, not applicable; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; PrEP, preexposure prophylaxis.

These data affirm the importance of generating evidence-based data on ART–HT DDIs, as well as educating patients and providers on perceived versus actual risks. These findings also extend to ART for preexposure prophylaxis (PrEP) to prevent HIV acquisition, as TW may have concerns about possible DDIs between PrEP and feminizing HT.[20]

In looking at the evidence for DDIs, published studies predominantly address HT–ART DDI between ART (typically NNRTI/PI-based regimens) and ethinyl estradiol, a synthetic estrogen used in contraception but not currently recommended for feminizing HT due to increased thrombotic risk.[21] A recent systematic review found that the most noteworthy interactions occurred for cisgender women using NNRTIs, and particularly efavirenz, although these outcomes were predominantly pharmacokinetic in nature and assessed interactions at doses used for contraception rather than feminizing HT.[22] No studies have specifically addressed interactions between ART and the estrogen regimens/doses used for feminizing HT. Thus, there are insufficient data to fully understand the risk of DDIs between ART and HT for TW.[23] However, even relatively minor or rare interactions warrant attention, as both HT and ART may be long-term or lifelong medications. In addition, TW living with

HIV, like nontransgender patients, have a baseline cardiovascular disease risk influenced by both traditional risk factors (smoking, obesity, etc.)[24,25] and HIV-specific risk factors (independent of ART),[26,27] so the additive risk of ART–HT DDIs is worth defining. Evidence-based guidance for feminizing HT for TW living with HIV or taking PrEP is needed.

Considering the recent findings that (1) TW may have suboptimal ART adherence,[28,29] and (2) higher HT adherence and access to other transgender-specific healthcare factors is associated with higher ART adherence,[30] opportunities exist to utilize this synergy to ensure greater participation in HIV care by TW. Given our results that current HT users may report higher rates of HT or ART adherence, our findings support previous data,[29,30] suggesting that gender-affirming healthcare, including clinical integration of HT and ART services, may improve engagement in HIV care for TW.

Care for TW can also be improved through active engagement by healthcare providers and both professional and community-based organizations. While more data are needed before providing specific clinical recommendations to providers on preferred HT and ART regimens/doses for TW living with HIV, professional organizations (such as the World Professional Association for Transgender Health) could help by issuing HIV-specific expert consensus statements. Clinicians serving transgender patients should be attentive to possible HT–ART DDI and address them similarly to other DDIs, if such concerns arise.

Several limitations to our pilot study exist. First, our small sample size, although common among studies of TW, limits generalizability to larger populations of TW. Replication of this study with participants of more varied ethnicities and ages may be necessary as our sample was predominantly Hispanic with a mean age of 45, possibly limiting generalizability to other groups. In addition, the study site was a community center that did not provide medical care. Therefore, we were unable to capture whether the participant's hormone therapy (when prescribed and not acquired from an illicit source) was provided within an informed consent framework, a model of HT provision that addresses the medical and social benefits and risks of HT, including potential side effects. The parent study, a community-based assessment, was not focused exclusively on TW living with HIV, and therefore did not address other topics that may influence ART adherence, such as stigma or discrimination. Finally, TW living with HIV were required to have undetectable plasma HIV-1 RNA, which limits our ability to examine adherence. However, our racially diverse sample of TW and the limited number of studies addressing transgender-specific issues in HIV care make these data an important contribution to the field.

Conclusion

Our data show significant concerns about ART–HT DDIs among TW, which impact adherence to both therapies and suggest a need for comprehensive care programs for TW living with HIV. Future research will address ART–HT DDIs and side effect profiles for TW, including cardiovascular disease risk, and investigate approaches to mitigate risk. An improved understanding of these interactions will likely improve engagement and retention in healthcare for TW and may increase clinician comfort discussing TW's concerns regarding ART–HT side effects and DDIs.

Acknowledgments

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Author Disclosure Statement

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Weddle Declaration
Exhibit J

DEPARTMENT OF HEALTH & HUMAN SERVICES

Health Resources and Services Administration

Rockville, MD 20857
HIV/AIDS Bureau

Disclaimer: Per a court order, HHS is required to restore this website as of 11:59 PM February 14, 2025. Any information on this page promoting gender ideology is extremely inaccurate and disconnected from the immutable biological reality that there are two sexes, male and female. The Trump Administration rejects gender ideology and condemns the harms it causes to children, by promoting their chemical and surgical mutilation, and to women, by depriving them of their dignity, safety, well-being, and opportunities. This page does not reflect biological reality and therefore the Administration and this Department rejects it.

December 16, 2021

Dear Ryan White HIV/AIDS Program Colleagues,

Ensuring that transgender people with HIV have access to care, treatment and support services that improve their health and decrease risk of morbidity and mortality related to HIV is a priority for the Health Resources Services Administration's (HRSA) HIV/AIDS Bureau (HAB). Of the more than half a million people served by the Ryan White HIV/AIDS Program (RWHAP) 2.1 percent, approximately 11,600, are transgender.[1] Providing gender-affirming care is an important strategy to effectively address the health and medical needs of transgender people with HIV. HRSA HAB strongly encourages RWHAP service providers to harness and mobilize the existing RWHAP infrastructure and services to support gender-affirming services within allowable RWHAP parameters.

Gender-affirming care and treatment services are described in the *HHS Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV* (Guidelines).[2] According to the Guidelines, gender affirmation describes processes whereby a person receives social recognition, value, and support for their gender identity and expression. Gender affirmation is often described across several dimensions, including: social (e.g., social support and acceptance, use of pronouns, names, or clothing that align with their gender identity); medical (e.g., use of hormones or surgery); legal (e.g., legal name change or changing gender markers on identity documents); and psychological (e.g., the degree of self-acceptance and comfort with their gender identity).

RWHAP funds may be used to support gender affirming care across various HRSA RWHAP core medical and support service categories as outlined in *Policy Clarification Notice #16-02 Ryan White HIV/AIDS Program Services: Eligible Individuals & Allowable Uses of Funds.*[3]

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[1] Health Resources and Services Administration. Ryan White HIV/AIDS Program Annual Client-Level Data Report 2020. www.hab.hrsa.gov/data/data-reports Published December 2021.
[2] Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. Department of Health and Human Services. Available at: https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/AdultandAdolescentGL.pdf, pp. J61-J70.
[3] Policy Clarification Notice 16-02: Eligible Individuals & Allowable Uses of Funds Clarification Notice. Available at: https://hab.hrsa.gov/sites/default/files/hab/program-grants-management/ServiceCategoryPCN_16-02Final.pdf.

Many RWHAP AIDS Drug Assistance Programs (ADAPs) provide access to gender-affirming hormone therapy.[4] RWHAP ADAP funds, along with RWHAP funds allocated under the service category *Health Insurance Premium and Cost Sharing Assistance for Low-Income Individuals*, can be used to purchase and maintain private health insurance, Medicaid, and Medicare coverage, which can support a broader range of health needs for transgender people with HIV. In addition, RWHAP recipients and subrecipients may provide behavioral and mental health services to clients experiencing gender dysphoria and social and emotional stress related to transgender discrimination, stigma, and rejection. RWHAP funds may be used to provide housing, case management, and substance use disorder treatment services, which are fundamental in reducing health disparities and improving HIV-related outcomes among transgender people. RWHAP AIDS Education and Training Centers provide training and education to clinicians and healthcare staff on cultural humility, cultural sensitivity, and inclusive care for diverse populations. HRSA HAB funds activities that support patient-centered, trauma-informed, and inclusive environments of care for RWHAP recipients through training, technical assistance, and other initiatives[5] to reduce barriers to antiretroviral therapy adherence and maximize the likelihood of achieving viral suppression.

As an outpatient ambulatory healthcare program, surgeries and inpatient care are not allowable uses of RWHAP or Ending the HIV Epidemic in the U.S. (EHE) initiative funds. This general prohibition applies to surgeries conducted in inpatient and outpatient settings, even when performed "same-day" as an ambulatory procedure under general anesthesia.

Among transgender clients receiving RWHAP HIV medical care in 2020, 84.5 percent were virally suppressed, which is lower than the national RWHAP average (89.4 percent).[6] While viral suppression rates among transgender clients in our programs are higher than the national non-RHWAP average, we recognize that more efforts are needed to help achieve our goal of ending the HIV epidemic and those set forth in the National HIV/AIDS Strategy (2022-2025).[7] This is true especially of Black and Hispanic/Latino/a transgender women who are disproportionally impacted by HIV and other intersecting social and health challenges.

HRSA HAB will continue to monitor HIV clinical outcomes and ensure evidence informed, evidence based, and emerging interventions are shared to support recipients with providing gender-affirming services for transgender people with HIV. We appreciate your efforts to provide affirming, whole person care to transgender people with HIV.

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[4] National ADAP Formulary Database: Other medication categories. Available at: https://www.nastad.org/adapformulary.

[5] SPNS Transgender Women of Color Initiative Intervention Manuals. Available at: https://targethiv.org/library/spns-transgender-women-color-initiative-manual

[6] Health Resources and Services Administration. Ryan White HIV/AIDS Program Annual Client-Level Data Report 2020. www.hab.hrsa.gov/data/data-reports Published December 2021.

[7] *National HIV/AIDS Strategy (2022-2025)*. Available at: https://hivgov-prod-v3.s3.amazonaws.com/s3fs-public/NHAS-2022-2025.pdf

Sincerely,

/Laura W. Cheever/
Laura Cheever, MD, ScM (she/her)
Associate Administrator

Weddle Declaration
Exhibit K

HRSA
Health Resources & Services Administration
HIV/AIDS Bureau
5600 Fishers Lane
Rockville, MD 20857

December 20, 2024

Dear Ryan White HIV/AIDS Program Colleagues,

As many of you know, earlier this year the Health Resources and Services Administration's (HRSAs) HIV/AIDS Bureau (HAB) introduced **Ryan White Program 2030 (RWP 2030),** a renewed vision for the Ryan White HIV/AIDS Program (RWHAP). Building on 35 years of success and innovation, RWP 2030 integrates lessons learned from the RWHAP and the Ending the HIV Epidemic in the U.S. (EHE) initiative. This framework is designed to sustain high-quality care and treatment for people currently receiving services through the RWHAP **while expanding efforts to identify and engage individuals with HIV who are undiagnosed or out-of-care[1].**

Achieving this goal will require a comprehensive, collaborative approach that builds upon existing successes and resources while fostering innovation[2]. At its core, RWP 2030 reflects our shared commitment to improving health outcomes for people with HIV. This vision calls on the HIV community to establish and strengthen partnerships, prioritize community engagement, and utilize focused interventions to end the HIV epidemic.

Since 2010, viral suppression among people receiving HIV medical care through the RWHAP has increased significantly, from 69.5% to 90.6% in 2023. Thanks to advancements in treatment, HIV is now a manageable chronic condition for individuals who remain engaged in care, allowing them to live long, healthy lives while preventing transmission to others. Despite this progress, we recognize that approximately 40% of people with HIV in the U.S. are either undiagnosed or not receiving regular care, contributing to most new HIV infections. Addressing these gaps is essential to achieving our goal of ending the epidemic.

Through EHE, we have seen the power of targeted investments and innovative strategies. In 2022, EHE-funded providers served over 22,000 individuals who were new to care and re-engaged more than 19,000 individuals who were out of care. Remarkably, 79.2% of individuals new to care achieved viral suppression, underscoring the effectiveness of our collective efforts. These successes highlight the importance of combining strategic investments with community-driven planning to achieve high-impact outcomes.

Ryan White Program 2030 emphasizes the importance of sustaining care for those already engaged in the RWHAP, while expanding our reach to ensure timely diagnosis and sustained treatment for underserved communities. This will require collaboration across sectors, innovation in care delivery, and a commitment to addressing barriers to care. We must also engage individuals with lived experience and non-traditional partners to inform program planning[3] and care models that are responsive to the needs of diverse communities.

[1] Legal authority: §§ 2602(b)(4), 2617(b), 2664(a), and 2671(c) of the Public Health Service (PHS) Act.
[2] Legal authority: §§ 2603(b)(2)(B), 2620, 2654(c), and 2691 of the PHS Act.
[3] Legal authority: § 2681 of the PHS Act.

Ryan White HIV/AIDS Program recipients play a critical role in advancing the goals of RWP 2030 and are responsible for employing sound planning and decision-making processes to determine which HIV related services are prioritized and how much to fund them. As part of these responsibilities, RWHAP recipients must continue to base service priorities and resource allocation decisions on the size, demographics, and needs of people with or affected by HIV. RWP 2030 specifically entails a renewed focus on reaching those who are undiagnosed or out of care. This may necessitate a re-evaluation of existing resource allocations to ensure outreach, engagement, and support efforts are effectively scaled to meet the needs of these especially high-need populations while still addressing the needs of individuals who are currently receiving care through the RWHAP.

We encourage you to begin engaging your partners in discussions about this vision and its implications for your work. Over the next several months, HRSA HAB will work to develop additional guidance and tools to support your efforts in implementing RWP 2030. The RWHAP Best Practices Compilation contains effective innovative interventions and best practices on outreach, linkage to and engagement in care. TargetHIV also contains a number of trainings, resources, and reference guides to support recipients and subrecipients in providing care to people with HIV. HAB is also planning a series of listening sessions in 2025 to ensure that RWP 2030 is informed by diverse perspectives and to better understand the challenges and barriers to implementing this vision.

We are confident that, with your continued partnership, we can realize the goals of RWP 2030 and bring us closer to ending the HIV epidemic. If you have questions, please contact your HRSA HAB Project Officer.

Thank you for your unwavering dedication to improving the lives of people with HIV.

Sincerely,

/Laura W. Cheever/

Laura Cheever, MD, ScM
Associate Administrator, HIV/AIDS Bureau
Health Resources and Services Administration

Weddle Declaration
Exhibit L

Ryan White Program 2030: Engaging People with HIV in Care to End the HIV Epidemic

Updated: January 21, 2026

In 2024, the Health Resources and Services Administration's (HRSA's) HIV/AIDS Bureau (HAB) introduced **Ryan White Program 2030 (RWP 2030)**, a renewed vision for the Ryan White HIV/AIDS Program (RWHAP). RWP 2030 builds on the foundation of the RWHAP and innovative, low-barrier strategies employed in the Ending the HIV Epidemic in the U.S. (EHE) initiative. This framework is designed to sustain high-quality care and treatment for people currently receiving services through the RWHAP **while expanding efforts to identify and engage individuals with HIV who are undiagnosed or out-of-care**[i]**.**

Achieving this goal requires a comprehensive, collaborative approach that builds upon existing successes and resources while fostering innovation[ii]. At its core, RWP 2030 reflects the RWHAP's shared commitment to improving health outcomes for people with HIV. This vision calls on the HIV community to establish and strengthen partnerships, prioritize community engagement, and utilize focused interventions to end the HIV epidemic. This requires collaboration across sectors, innovation in care delivery, and a commitment to addressing barriers to care. The RWHAP must also engage individuals with lived experience and non-traditional partners to inform program planning[iii] and care models that are responsive to the needs of these communities.

Since 2010, viral suppression among people receiving HIV medical care through the RWHAP has increased significantly, from 69.5% to 91.4% in 2024. Thanks to advancements in treatment, HIV is now a manageable chronic condition for individuals who remain engaged in care, allowing them to live long, healthy lives while preventing HIV transmission to others. Preventing new HIV infections not only reduces the spread of the virus but also reduces long-term healthcare costs. Despite this progress, approximately 87% of new HIV transmissions are estimated to result from persons who do not know of their HIV status or are not engaged care[iv]. Addressing these gaps is essential to achieving the goal of ending the HIV epidemic.

The EHE initiative has demonstrated the power of targeted investments and innovative strategies. In 2023, EHE-funded providers served over 26,800 individuals who were new to care and re-engaged more than 17,300 individuals who were out of care. Remarkably, 81.4% of patients who were new to care and receiving HIV treatment reached viral suppression, underscoring the effectiveness of the RWHAP's collective efforts. These successes highlight the importance of combining strategic investments with community-driven planning to achieve high-impact outcomes.

Ryan White HIV/AIDS Program recipients play a critical role in advancing the goals of RWP 2030 and are responsible for employing sound planning and decision-making processes to determine which HIV-related services are prioritized, and how much to fund them. As part

of these responsibilities, RWHAP recipients must continue to base service priorities and resource allocation decisions on the size, demographics, and needs of people with or affected by HIV. RWP 2030 specifically entails a renewed focus on reaching those who are undiagnosed or out of care. This may necessitate a re-evaluation of existing resource allocations to ensure outreach, engagement, and support efforts are effectively scaled to meet the needs of people and communities disproportionately impacted by HIV while still addressing the needs of individuals who are currently receiving care through the RWHAP.

HRSA HAB encourages RWHAP recipients and HIV community members to engage subrecipients and partners in discussions about this vision and its implications for your work. HRSA HAB is working to develop additional guidance and tools to support your efforts in implementing RWP 2030.

Moving forward, the HIV community can leverage the infrastructure and expertise of the RWHAP, and the innovations and high impact activities learned from the EHE initiative, to accelerate reaching people with HIV who are out of care, ensuring that no one is left behind in our efforts to end the HIV epidemic.

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[i] Legal authority: §§ 2602(b)(4), 2617(b), 2664(a), and 2671(c) of the Public Health Service (PHS) Act.
[ii] Legal authority: §§ 2603(b)(2)(B), 2620, 2654(c), and 2691 of the PHS Act.
[iii] Legal authority: § 2681 of the PHS Act.
[iv] Baxter A, et al. Updates to HIV Transmission Rate Estimates Along the HIV Care Continuum in the United States, 2019. *JAIDS*. 2025. 99(1):47-54.

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE; HIV MEDICINE ASSOCIATION, a division of the INFECTIOUS DISEASES SOCIETY OF AMERICA; INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE; JENNIFER K. BRODY, MD; and CHRISTOPHER B. FOX, NP, *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION; THOMAS J. ENGELS, in his official capacity as the Administrator of the Health Resources and Services Administration; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., in his official capacity as Secretary of the U.S. Department of Health and Human Services, *Defendants*.	Case No.

DECLARATION OF JOSÉ M. ZUNIGA, PRESIDENT AND CHIEF EXECUTIVE OFFICER OF THE INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE

I, José M. Zuniga, hereby state as follows:

1. I am over 18 years of age, of sound mind, and in all respects competent to testify.

2. I have personal knowledge of the facts set forth in this declaration and would testify competently to those facts if called to do so.

3. I am the President and Chief Executive Officer of the International Association of Providers of AIDS Care ("IAPAC"), which is an organizational plaintiff in this case bringing claims on behalf of its members and the transgender patients of its members.

4. I joined IAPAC in 1997 as Vice President and have served as its President and CEO since 2000. In 2020, I also became the President and CEO of the Fast-Track Cities Institute, a global network of urban providers and the world's largest urban health initiative, which unites more than 600 cities and municipalities worldwide to accelerate progress towards achieving health-related goals in relation to HIV. As IAPAC's President and CEO, I oversee the association's medical education and technical assistance initiatives. As part of this role, I lecture at various academic institutions, publish research, and write and edit books related to HIV/AIDS care. I also serve as an Editor Emeritus for the *Journal of the International Association of Providers of AIDS Care*, and I am a trustee of IAPAC. I formerly served as a member of the Joint United Nations Programme on HIV/AIDS Scientific and Technical Advisory Committee.

5. I submit this declaration in support of Plaintiffs' Motion for Preliminary Relief under 5 U.S.C. § 705 and for a Preliminary Injunction, which seeks to prevent Defendants from giving effect to certain conditions relating to transgender people and gender-affirming medical care set forth in Ryan White HIV/AIDS Program ("Ryan White Program") Notices of Funding Opportunity issued or forecasted to be issued in 2026 and the 2026 Updated HRSA General Terms and Conditions, issued on March 11, 2026.

6. In this declaration, I explain that transgender people are more likely than others to acquire HIV for many reasons, including social, economic, and legal exclusion, and that the Ryan White Program is a lifeline that ensures comprehensive primary care for people living with HIV. Using survey results, I show that providers are experiencing unwanted operational changes that

impact the most vulnerable populations, including transgender people, and that losing the ability to provide gender-affirming medical care will cause patients to discontinue HIV care. I conclude by explaining that the Challenged Conditions will cause long-term harm to clinic providers and their patients, such as loss of revenue and closure of clinics, poor health outcomes for transgender patients, and the further destabilization of the American HIV response.

I. Background on IAPAC

7. IAPAC is a 501(c)(3) nonprofit membership organization and the largest world-wide association of clinicians and allied health professionals working to end AIDS as a public health threat by 2030 with programming in over 150 countries.

8. IAPAC's mission is to expand access to and improve the quality of prevention, care, treatment, and support services provided to people affected by and living with HIV and its co-occurring conditions.

9. IAPAC's history spans decades. The Physicians Association for AIDS Care ("PAAC") was established in 1985 as the first organization to support physicians as they struggled to care for people who, given limited treatment options, were dying of AIDS-related complications.

10. PAAC was the precursor to IAPAC. In 1995, coinciding with the advent of antiretroviral therapy ("ART"), PAAC expanded its U.S.-centric geographic focus to one inclusive of all regions of the world. That same year, the association was renamed the International Association of Physicians in AIDS Care. The association was again re-named in 2012 to the International Association of Providers of AIDS Care to reflect the variety of clinicians and lay-providers engaged in the global battle against HIV/AIDS.

11. IAPAC has over 30,000 clinical provider and community health worker members worldwide, with more than 8,500 members in the United States. IAPAC performs traditional functions of professional medical associations, develops HIV care guidelines, and advances global initiatives to end the HIV epidemic. IAPAC also manages the Fast-Track Cities network.

12. IAPAC members represent a broad cross-section of clinicians across the country. Those members accept a mix of Medicaid, Ryan White funding, private insurance, and other sources to fund their HIV care. Survey research conducted by the Emergency HIV Clinical Response Task Force, of which IAPAC is a member, indicates that 67% of HIV medical providers rely on the Ryan White Program to provide comprehensive HIV care. A copy of the Emergency HIV Clinic Response Task Force's report, titled *HIV Response in U.S. Experiencing Renewed Strain*, published in April 2026 is attached hereto as **Exhibit A**.

13. Indeed, over 60% of IAPAC's members provide medical care to their patients with HIV with funding from the Ryan White Program, including through funding under all its parts as well as any supplementary funding. For their transgender patients, this often includes hormone therapy as treatment for their gender dysphoria (also known as "gender-affirming hormone therapy" or "gender-affirming medical care").

14. One of IAPAC's functions is providing clinicians and allied health professionals with education on scientific advancements and best practices in HIV medicine. IAPAC hosts conferences and workshops, publishes the *Journal of the International Association of Providers of AIDS Care*, and coordinates multidisciplinary online educational activities specific to key challenges in reaching hard-to-reach populations of people who are vulnerable to HIV.

15. Given the disproportionate impact of the HIV epidemic on LGBTI+ people, IAPAC has published several resources specific to the health of these populations in relation to HIV care.

For example, in 2021, IAPAC conducted a study that included assessments of fifty cities and municipalities from four geographic regions, as well as 275 key informant interviews with people involved in LGBTI+ health issues at the community level. The study's results are featured in "LGBTI+ Health Equity: A Global Report of 50 Fast-Track Cities," which reflects outcomes across multiple public health and social determinants of health indicators that affect the lives of LGBTI+ people across the Fast-Track Cities network. A copy of the report is attached hereto as **Exhibit B.** IAPAC also published a fact sheet on transgender people that is available on its website and was last reviewed in June 2025. A copy of IAPAC's transgender people fact sheet is attached hereto as **Exhibit C.**

II. HIV and Transgender People

16. The link between LGBTI+ health equity and our work at IAPAC is perhaps obvious given the longstanding and staggering disparities that LGBTI+ individuals[1] face with respect to HIV. And given my work in this field as well as my role at IAPAC, I am familiar with and must keep informed of the relation between LGBTI+ people and HIV.

17. The first cases of what came to be known as AIDS were detected in gay men in 1981. At the beginning, AIDS was perceived not as a national health problem but as a problem for "homosexuals" and people who inject drugs. As a 2011 report by the Institute of Medicine documents: "Because of the marginal status of these groups, societal response to the epidemic was slow. It was not until there was widespread awareness that AIDS was affecting the 'mainstream'

[1] In health research, including some of IAPAC's publications, we refer to sexual and gender minorities in lieu of using "LGBT" or "LGBTI+" people. Sexual minorities are individuals whose sexual attraction, behavior, and/or identity is something other than exclusively heterosexual. Gender minorities include individuals whose gender identity is something other than cisgender and may also include individuals whose gender expression rather than identity does not conform with established social norms. In this declaration, I use the terms "sexual and gender minorities" to be synonymous and encompassing of "LGBT" people. The acronym LGBTI+ is used as an umbrella term to describe sexual and gender minorities as well as intersex individuals.

population that the disease garnered significant attention. Indeed, it was Ryan White, an Indiana adolescent who acquired AIDS through treatment for hemophilia, who became the sympathetic face of AIDS to the nation."[2]

18. The response of the federal government to the epidemic was likewise slow. Throughout most of the 1980s, AIDS was seldom acknowledged by the federal government, and research and prevention efforts were hampered by the stigma associated with being gay. Moreover, virtually no attention was paid to infection rates in the transgender community until the mid-1990s, because transgender people were not understood to be separate from the category of gay men in federal research efforts. As a result, AIDS claimed the lives of a significant portion of the generations of LGBT people who came of age during and after the World War II era and dramatically altered the LGBT community in numerous ways.

19. While the cultural climate in the United States affecting people with HIV has positively improved since the early days of the AIDS epidemic, stigmatization continues to affect all LGBT people, including those living with HIV. Indeed, HIV continues to be a major public health concern among sexual and gender minority populations.

20. As our LGBTI+ Health Equity report documents, the risk of acquiring HIV among transgender and other gender minority individuals is thirteen times that of the cisgender population. While HIV prevalence data among the transgender community remains scarce, we know that transgender people are disproportionately affected by the HIV epidemic. According to the Centers for Disease Control and Prevention ("CDC"), transgender people make up 2% of new

[2] Inst. of Med., The Health of Lesbian, Gay, Bisexual, and Transgender People: Building a Foundation for Better Understanding 68 (2011).

HIV diagnoses in recent year-to-year data[3] despite comprising only about 1% of the United States population aged 13 and older.[4]

21. The existing data specific to transgender people demonstrate a heavy burden of HIV among transgender women, specifically transgender women who have sex with cisgender men. Transgender women are one of the groups most affected by HIV and are forty-nine times more likely to have HIV than the general population.

22. Disparities exist even within this population on intersectional aspects of their identity. For example, racial and ethnic disparities are stark among transgender women in the United States: 62% of Black/African-American transgender women and 35% of Latina/Hispanic transgender women have HIV, while only 17% of White transgender women have HIV. In other words, and as the LGBTI+ Health Equity report states, in the United States, Black transgender individuals are five times more likely to be living with HIV than transgender and nonbinary people in general.

23. CDC data also show that in the United States, HIV diagnoses among transgender people vary by region, with the highest number of new HIV diagnoses among transgender people occurring in the South.

24. There are many factors that put transgender people at heightened risk of HIV, including social, economic, and legal exclusion. As documented in our fact sheet, transgender people face stigma and discrimination, which contributes to higher levels of unemployment,

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[3] Ctrs. for Disease Control and Prevention, *Fast Facts: HIV and Transgender People* (Mar. 28, 2024) https://tinyurl.com/4a38tazk [https://web.archive.org/web/20250103203335/https://www.cdc.gov/hiv/data-research/facts-stats/transgender-people.html]. A copy of the CDC Fact Sheet is attached hereto as **Exhibit D**.

[4] Williams Inst., Ucla Sch. Of L., *How Many Adults and Youth Identify as Transgender in The United States?* (Aug. 2025), https://tinyurl.com/3haevkt5 [https://perma.cc/M2BZ-9QXK].

poverty, homelessness, sex work, depression and other mental health issues, substance use, incarceration, and violence, all of which are linked to higher rates of HIV. Most transgender people have experienced some form of abuse or harassment because of their gender identity or presentation. This may negatively impact access to HIV testing, care, and/or treatment for HIV. Many patients of IAPAC members report co-occurring social conditions that exacerbate the risk of HIV, such as homelessness, sexual violence, and poverty.

25. In addition, many transgender people have had negative experiences with healthcare providers, which discourages them from seeking care. Finding providers who are knowledgeable about and sensitive toward transgender people can be challenging, but is critically important. Transgender people may not have access to HIV prevention information or adequate treatment when providers are not affirming of their identities. In fact, transgender people may delay seeking treatment due to transphobia and insensitivity among healthcare professionals.

26. Delays in treatment initiation lead to increased morbidity and mortality, and deny transgender patients the therapeutic and preventive benefits of achieving an undetectable viral load. The WHO has reported that a person living with HIV who achieves an undetectable viral load cannot sexually transmit HIV to a sexual partner.[5]

27. As the World Health Organization's *Consolidated Guidelines on HIV, Viral Hepatitis and STI Prevention, Diagnosis, Treatment and Care for Key Populations*, published in 2022, and which IAPAC's transgender people fact sheet references, states: "The high vulnerability and specific health needs of trans and gender diverse people necessitates a distinct and independent

[5] Ministry Of Pub. Health Of Thail., World Health Org. & Joint United Nations Programme On Hiv/Aids, People Living With Hiv With An Undetectable Viral Load Cannot Transmit Hiv Sexually (Feb. 21, 2020), https://tinyurl.com/2mr3ejfy [https://perma.cc/AY6V-S5V8].

status in the global HIV response."[6] This means that "[g]ender affirmation is often a priority intervention for the trans and gender diverse community."[7]

III. HIV Healthcare Disruptions Since 2025

28. Despite decades of progress in HIV prevention and treatment, the HIV response in the United States is experiencing renewed strain. Funding uncertainty, workforce attrition, policy shifts, and rising social and economic precarity are reshaping the delivery of HIV services at the clinic and community levels. In June 2025, in response to reports of HIV clinical and supportive service disruptions, five U.S.-based professional medical and nursing associations—the American Academy of HIV Medicine, Association of Nurses in AIDS Care, Gay and Lesbian Medical Association, HIV Medicine Association, and IAPAC—launched the Emergency HIV Clinical Response Task Force. We launched the task force because we were hearing reports of HIV clinical and supportive service disruptions in the United States caused by the Trump administration, despite decades of progress in HIV prevention and treatment. The Task Force administered two nationwide Emergency HIV Clinical Response Surveys in the summer and winter of 2025 to quantify the scope, nature, and equity dimensions of these disruptions as experienced by frontline HIV service providers across the United States. In April 2026, the Task Force published the results of the winter survey, titled *HIV Response in U.S. Experiencing Renewed Strain* (Exhibit A). Just under 400 clinical providers completed the survey across forty-seven states and Puerto Rico. Respondents included physicians, nurses, pharmacists, case managers, social workers, and community-based providers working across academic medical centers, Federally Qualified Health Centers, hospitals,

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[6] World Health Org., Consolidated Guidelines on HIV, Viral Hepatitis & STI Prevention, Diagnosis, Treatment and Care for Key Populations 54 (2022), https://tinyurl.com/4jr928hy [https://perma.cc/9GNL-6CGG].

[7] *Id.*

private medical practices, and outreach settings. Moving forward, the Task Force will continue to field this survey quarterly until the need dissipates.

29. 68% of HIV care providers who responded to the surveys reported unwanted operational changes in their clinical settings from July to October 2025 due to changes in federal or state policies or funding cuts. Respondents reported medical service disruptions to patients caused by the closure of programs, reduction in ability to provide services, and adjustment of staffing, including staff layoffs. 61% of respondents reported at least one HIV service disruption in their clinic setting. These disruptions in medical service spanned the HIV care continuum, with the highest amount of disruption impacting gender-affirming medical care. These disruptions were largely caused by federal policy directives under the current administration.

30. These disruptions impacted the most vulnerable populations, with respondents identifying transgender people (40%) and immigrants (38%) as key populations most affected by population-level disruptions in HIV care. HIV care disruptions are particularly harmful for vulnerable patients who are less likely to receive adequate healthcare due to barriers to care, including housing instability, food insecurity, loss of health insurance, fear of immigration enforcement, loss of employment, and mistrust in healthcare systems.

31. Most respondents experiencing care disruption identified the predominant cause as insurance lapses or loss and reported that the most urgent resource needed to safeguard continuity of HIV services was funding, with specific emphasis on the Ryan White program. Several respondents gave detailed responses beyond the pre-written survey options, specifically noting "continued access to gender-affirming care" and "protection for gender-affirming care" as the most urgent resources or assistance needed to safeguard the continuity of HIV-related services. Additionally, multiple providers described losing transgender patients living with HIV because the

providers could no longer provide gender-affirming medical care due to institutional or state policies. One provider explained that "continued profiling of immigrants and transgender individuals is causing severe mental health issues and distress," leading to current and anticipated service disruptions. Another provider explained that a loss of Ryan White funding would be devastating, and that transgender patients who "perceive changes" have already stopped following up with care, even when those changes have not occurred." Yet another provider wrote, "had to take gender-affirming care off my provider info page on our website because HRSA told us we had to." These prohibitive policies are impacting transgender patients' funding for care, access to care, and mental health due to discrimination.

IV. Harms to IAPAC Members and their Transgender Patients

32. Given my experience in this field as well as my role in IAPAC, I am aware of the impacts that the restrictions on how HIV care providers may treat their transgender patients with HIV, including the use of Ryan White funding for gender-affirming medical care, may have on HIV care providers like IAPAC's members and their transgender patients.

33. Addressing disruptions in HIV care is imperative to safeguarding lives and decades of progress in the United States's HIV response. The Ryan White Program is vital to prevent these disruptions, as other sources of funding are not sufficient to cover patient needs.

34. Gender-affirming medical care is a vital pathway for transgender patients to receive HIV treatment. Consistent with the Ryan White Program's emphasis on ensuring comprehensive primary care and addressing people living with HIV's co-occurring conditions, we believe that ending the HIV epidemic requires that we meet people's whole health needs in the context of HIV prevention and treatment.

35. As noted, transgender people, and transgender women in particular, are vulnerable to HIV due to socioeconomic marginalization and discrimination in healthcare settings, and we know that transgender people are less likely to maintain regular contact with the healthcare system due to high costs and historic discrimination from providers. Research, like that presented at IAPAC's Continuum Conference and with which we are familiar, consistently shows that when transgender people feel supported and affirmed in their gender identity by health care providers, they are more likely to access HIV testing, engage with pre-exposure prophylaxis, adhere to ART, and achieve viral suppression.[8] Ryan White-funded clinics open the door for treatment for transgender patients who often do not access routine healthcare because clinicians can address patients' comprehensive health needs, including gender-affirming medical care, when administering HIV care.

36. It is my understanding that the current administration indicated that it is conditioning Ryan White funding on the non-promotion of gender ideology, which I understand the administration defined as acknowledging and respecting transgender patients' identities, and prohibiting the use of Ryan White funding for the provision of gender-affirming medical care, notwithstanding that this is an outpatient service for a co-occurring condition that many IAPAC members provide to their transgender patients with HIV.

37. IAPAC members are worried that they will lose their ability to provide gender-affirming medical care in the face of a restriction on gender-affirming medical care for the Ryan White Program. They report that hospital systems will likely end gender-affirming medical care programs rather than risk their funding. Members also fear legal exposure amid confusion about

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[8] Martha O. de la Paz & Harry Barbee, Beyond Prevention: How Gender-Affirming Care Can Transform HIV Outcomes for Transgender and Gender-Diverse Populations, 115 AM. J. PUB. HEALTH 1613–14 (2025). A copy is attached as **Exhibit E**.

how they may address their transgender patients and what care they are permitted to provide to these patients. As such, this restriction would suddenly change the way providers engage in patient health literacy as well as create a barrier for HIV care and other critical services for transgender Ryan White patients.

38. Our members are concerned that transgender Ryan White patients are likely to discontinue HIV care if this restriction goes into effect. Many transgender patients distrust medical systems because of historic discrimination. Accordingly, trust between medical professionals and transgender patients is crucial for good health outcomes because it reduces healthcare avoidance—but the sudden inability to provide gender-affirming medical care will shatter that hard-earned trust in a way that cannot be repaired. As a result, patients will be less likely to continue any care, including HIV care, with their doctor. These patients will experience worse health outcomes without consistent HIV care, including an increase in viral load, immune system damage, and health complications. Moreover, an increase in viral load will allow for HIV transmission to others. Members worry that the nationwide gains made over the last few decades in decreasing HIV incidence will be reversed due to a key population largely losing access to care, which protects patient health and the broader health of the public.

39. Transgender patients who receive services with Ryan White Program funding would also experience immediate harm if their doctors are unable to provide their gender-affirming medical care with Ryan White funds or are prohibited from acknowledging or respecting their identities. Members worry that many transgender patients would lose access to gender-affirming medical care altogether because they simply could not afford it, or even—if alternative avenues of funding were available——would not come for visits for care unrelated to gender-affirming medical because their Ryan White-funded HIV care provider is prohibited from addressing them with the

right pronouns or in a manner that respects their identity. Most transgender patients in the Ryan White program who have healthcare coverage do so through Medicaid, which does not universally cover gender-affirming medical care.

40. The restriction would also undermine our members' ability to treat their patients by erasing data on transgender people living with or at risk of HIV. The Ryan White program generates significant amounts of data about its patients, which is helpful for our members' understanding of the HIV epidemic and patient needs. Without data on transgender patients, epidemiological data would become inaccurate, noncomprehensive, and create unnecessary HIV risks for both transgender and non-transgender populations. Providers and the communities they serve will be left in the dark about the scope of HIV outbreaks.

41. The restriction would also cause a drop in patients for providers, and as a result cause a loss of revenue for clinics. Members are anxious about the potential closure of clinics specializing in gender-affirming medical care, whether it be from funding loss, loss of revenue, or political pressure.

42. The downstream impacts of these restrictions will harm the ability of the United States to control the HIV epidemic. When any population is omitted from HIV care, it destabilizes the structures in place intended to prevent further cluster events and HIV outbreaks because health professionals lose key information needed to determine causes and solutions. Transgender patients, already vulnerable to HIV, will see worse health outcomes, while providers will have less capacity to address these issues.

V. Conclusion

43. In the United States and around the world, transgender people are disproportionately affected by HIV. With early testing and treatment, transgender people with HIV

can live longer, healthier lives and prevent the sexual transmission of HIV among those who achieve an undetectable viral load.

44. Based on IAPAC and our members' experience and research, providing HIV care and comprehensive care, including gender-affirming medical care, that affirms transgender patients and addresses their health needs holistically, is an essential component of HIV treatment for transgender patients.

45. Omitting this piece from comprehensive medical care is contrary to best practice, accepted standards of care, and the experiences of IAPAC's members. It will only cause irreparable harm to HIV care providers and the health of their transgender patients. If the restrictions challenged in this case are allowed to go into effect and be incorporated into the Ryan Program, IAPAC members are at imminent risk of losing critical funding that they need to fulfill their obligation as medical providers and meet the health needs of their patients, and the health and wellbeing of transgender people with HIV will be endangered.

46. As IAPAC's LGBTI+ Health Equity report notes, the bottom line is that we cannot adequately address HIV and other health conditions without including LGBT populations, and we cannot adequately serve this population unless we understand its diversity and complexity. To end the HIV epidemic, those of us working in the field of HIV care and in any other area relevant to LGBT health equity must work holistically to end the disparities key populations face, including the transgender community.

I declare under penalty of perjury that the foregoing is true and correct. Dated: June 8, 2026



José M. Zuniga
President and CEO, IAPAC

EXHIBIT A

AMERICAN ACADEMY OF HIV MEDICINE

ANAC Association of Nurses in AIDS Care

GLMA Health Professionals Advancing LGBTQ+ Equality

hivma hiv medicine association

IAPAC INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE

HIV Response in U.S. EXPERIENCING RENEWED STRAIN

Emergency HIV Clinical Response Task Force
April 2026

KEY TAKEWAYS

- HIV service disruptions are occurring, especially for vulnerable populations. These disruptions affect clinical care, prevention and supportive services, and workforce capacity.
- Structural and social determinants of health – particularly unemployment, housing instability, food insecurity, and insurance loss – are emerging as drivers of disruption.
- Clinics are making operational adjustments to their services and staffing that may further limit access to HIV prevention, treatment, and care services.
- Vulnerable populations are falling out of care, notably transgender people, migrants and undocumented individuals, and people experiencing homelessness.
- Continuing to monitor service disruptions will be important as state AIDS Drug Assistance Programs (ADAPs) contract and the Medicaid expansion cuts take effect.

BACKGROUND

Despite decades of progress in HIV prevention and treatment, the HIV response in the United States is experiencing renewed strain. Funding uncertainty, workforce attrition, policy shifts, and rising social and economic precarity are reshaping the delivery of HIV services at the clinic and community levels. In response to reports of HIV clinical and supportive service disruptions, five U.S.-based professional medical and nursing associations – the American Academy of HIV Medicine, Association of Nurses in AIDS Care, Gay and Lesbian Medical Association, HIV Medicine Association, and International Association of Providers of AIDS Care – launched the Emergency HIV Clinical Response Task Force (Task Force) in June 2025.

The Task Force fielded an online Emergency HIV Clinical Response Survey in July 2025 to quantify the scope, nature, and equity dimensions of these disruptions as experienced by frontline HIV service providers across the U.S. A follow-up survey was fielded in November through December 2025 to map additional dimensions related to HIV service disruptions, including structural and social determinants of health, as well as operational austerity measures in the face of federal funding cuts.

METHODOLOGY

Between November 6, 2025, and December 11, 2025, a follow-up online Emergency HIV Clinical Response Survey was distributed to HIV service providers nationwide through the five members of the Emergency HIV Clinical Response Task Force. Analyses are based on 383 clinical provider respondents who completed the survey across 47 states and Puerto Rico. Respondents included physicians, nurses, pharmacists, case managers, social workers, and community-based providers working across academic medical centers, Federally Qualified Health Centers (FQHCs), hospitals, private practices, and outreach settings. Questions were intended to capture the breadth of disruptions and impacts experienced from July to October 2025.

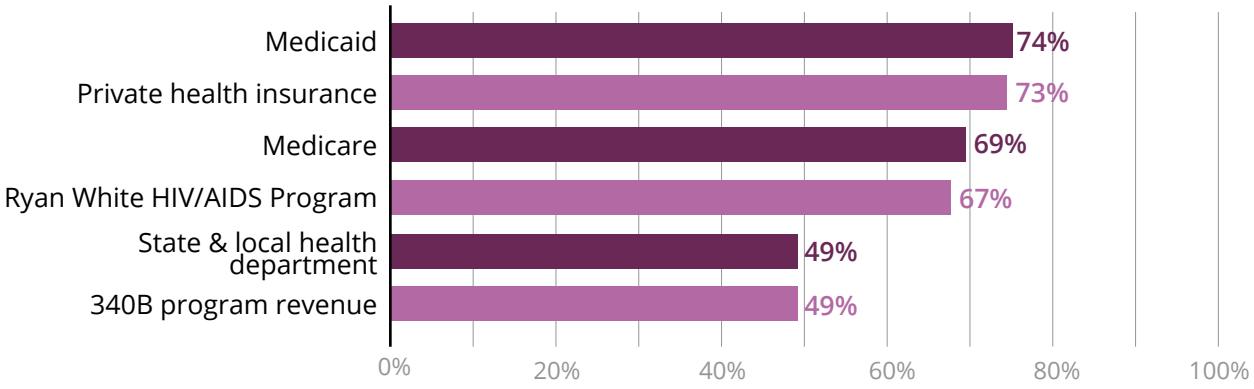
RESPONDENT AND SITE PROFILES

The perspectives captured reflect a cross-section of the HIV workforce and a diversity of clinical settings that deliver HIV care:

- Clinical roles dominated the sample, with physicians (30%), nurse practitioners (23%), and registered nurses (14%) comprising two-thirds of respondents.
- Over 65% of responses came from hospital-based clinics (33%) and community health centers and FQHCs (32%), underscoring impacts within core HIV care infrastructure.
- The South accounted for more than one-third of responses (36%), with responses from three other regions: Northeast (24%), West (23%), and Midwest (18%).

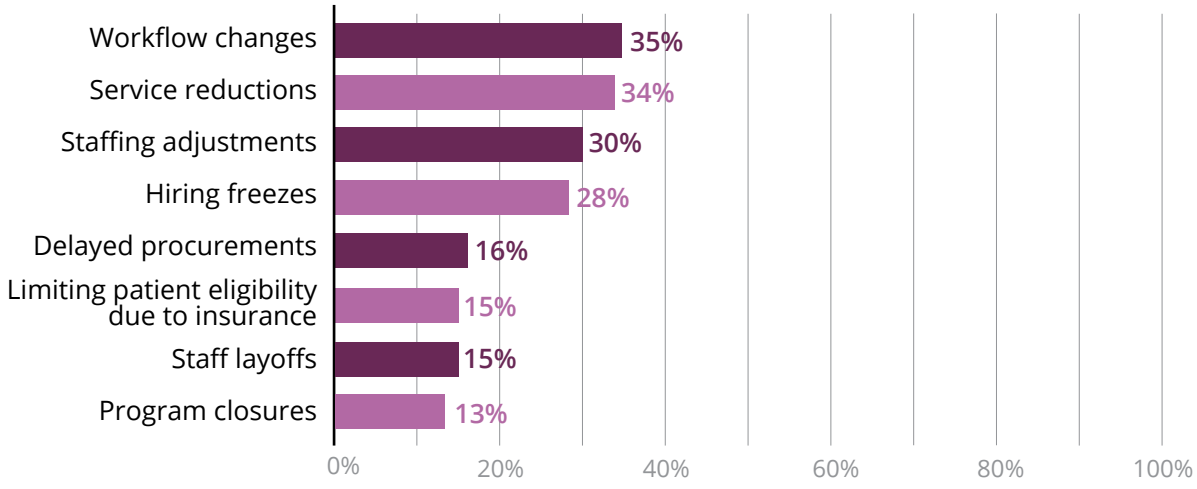
SOURCES OF FUNDING

Respondents reported a combination of funding sources for their clinical settings, including:



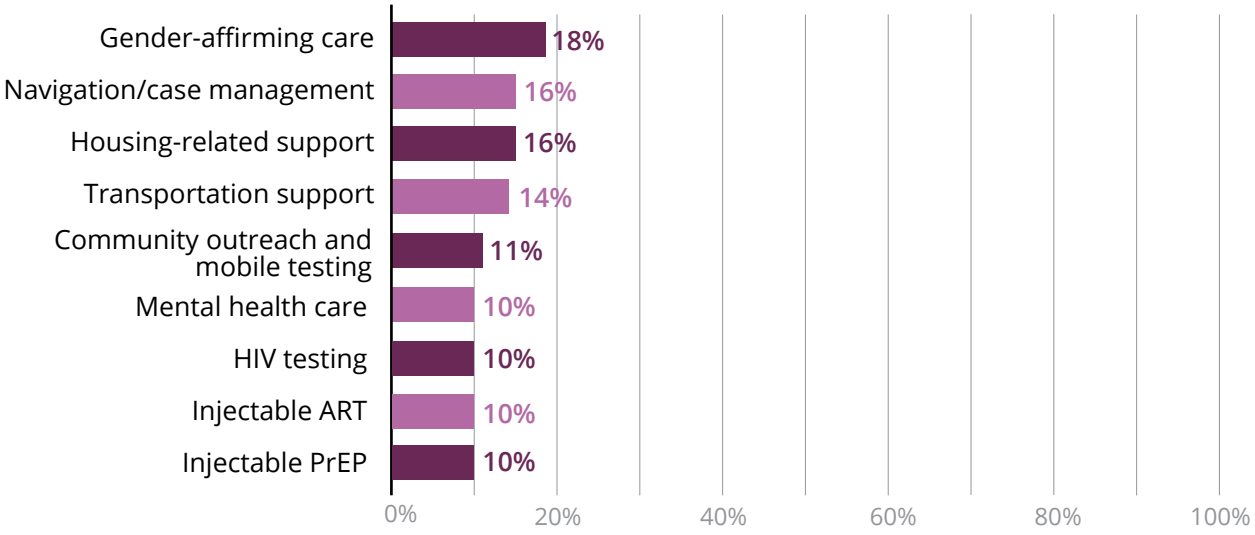
OPERATIONAL DISRUPTIONS

Sixty-eight percent of respondents reported one or more operational changes in their clinical settings due to changes in federal or state policies or funding cuts, including:



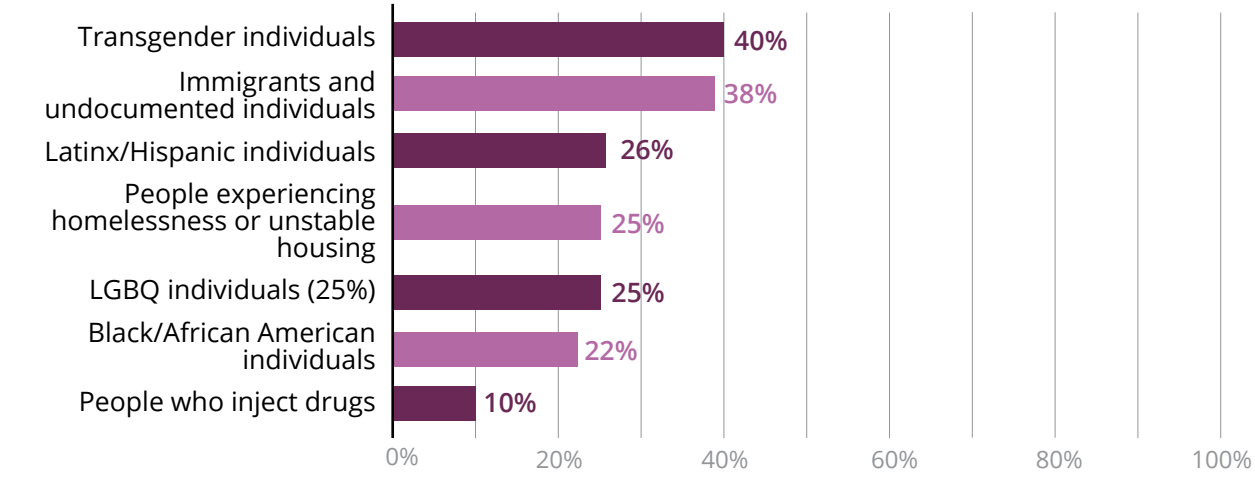
HIV AND OTHER HEALTH SERVICE DISRUPTIONS

Sixty-one percent of respondents reported at least one HIV service disruption in their clinical setting. Reported service disruptions spanned the HIV care continuum and beyond:



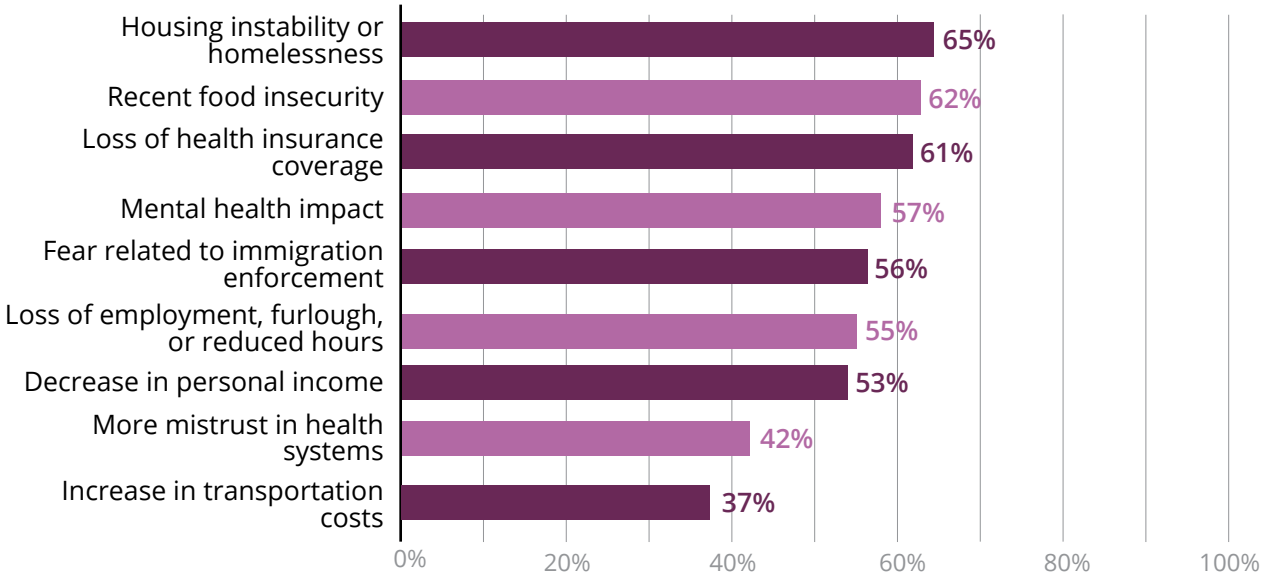
EQUITY IMPACTS: POPULATIONS MOST AFFECTED

Of the 69% of respondents who reported at least one population-level service disruption, the following key populations were cited as most affected:



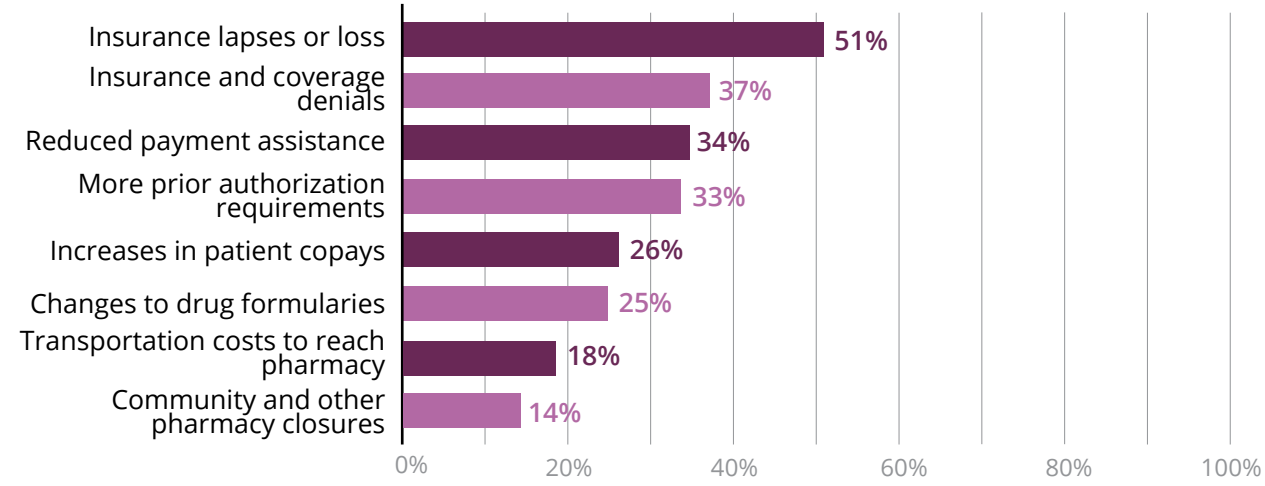
PATIENT-REPORTED BARRIERS TO ENGAGEMENT IN CARE

Among the 92% of respondents who reported hearing from patients about specific barriers to remaining engaged in care, the following were the most cited:

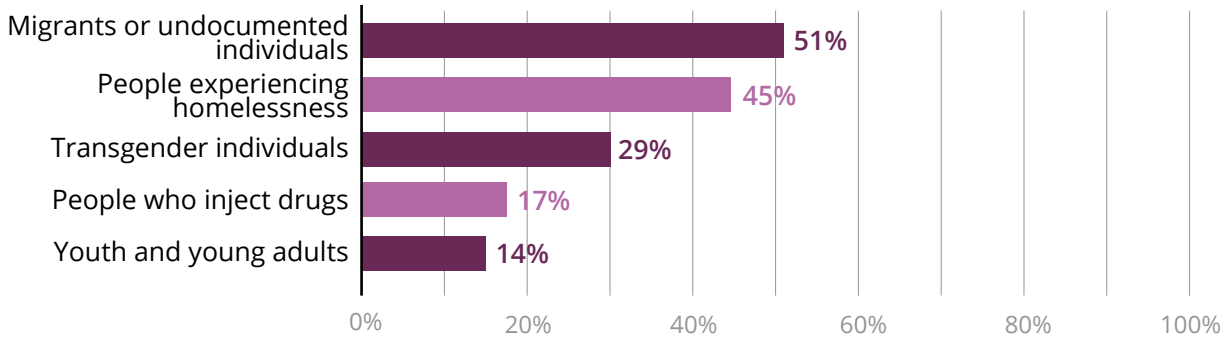


MEDICATION ACCESS AND LOSS TO FOLLOW-UP

Of the 69% of respondents who reported their patients spoke with them about medication access, the following factors were most associated with medication access barriers:



Although 14% of respondents reported no significant population-specific effects on retention in HIV care, of the 86% of respondents who did report effects the following key populations were cited as the most affected:



INSIGHTS FROM OPEN-ENDED QUESTIONS

Forty-six percent of respondents provided additional insights through an open-ended survey question about the most urgent resources needed to safeguard continuity of HIV services:

- Funding concerns dominate the landscape, mentioned by 37% of respondents, with specific emphasis on Ryan White HIV/AIDS Program (20%) and 340B Drug Pricing Program (4%) sustainability.
- Health insurance coverage was reported as critical, with 27% of respondents citing Affordable Care Act/insurance concerns and 13% specifically mentioning Medicaid enrollment challenges.
- Social determinants of health, including housing (17%), transportation (13%), and food security (7%), were recognized as essential to maintaining HIV care continuity.

Forty-two percent of respondents answered a second open-ended question seeking insights into declines in clinic attendance by undocumented or migrant individuals observed in the respondents' clinical settings, with 83% of this subset of respondents citing fear of immigration enforcement and deportation as the primary contributing factor.

One survey response detailed a patient death directly attributed to this fear:

"Due to a fear of being detained by ICE, a patient with relapsed Hodgkin's lymphoma delayed care and then it became an emergency which resulted in his death."

CONCLUSION

The outcomes of the second Emergency HIV Clinical Response Survey document a clear warning signal that the Trump administration-led policy and funding actions taken over the last year are destabilizing the delivery of HIV services in the U.S.

Continued monitoring is critical in addition to locally-driven, novel, and nimble interventions to prevent disruptions in HIV testing, prevention, care, and treatment with a focus on key populations most affected by federal policy and budget shocks.

Addressing these disruptions is imperative to safeguarding lives and decades of progress in the U.S. HIV response.

EXHIBIT B

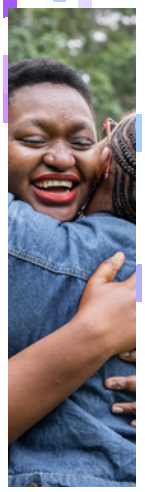
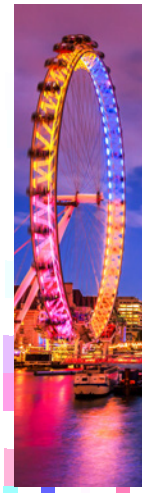
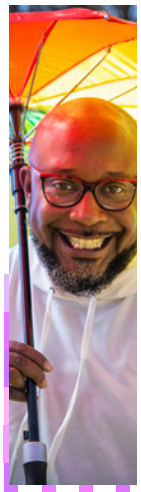
LGBTI+ HEALTH EQUITY

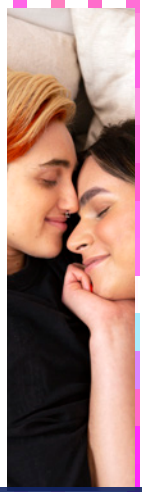
A GLOBAL REPORT OF **50 FAST-TRACK CITIES**

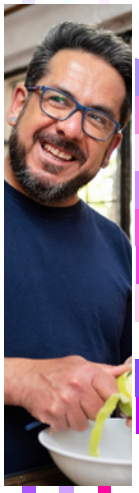
FAST-TRACK CITIES

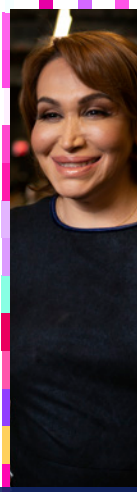
IAPAC
INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE









This report is made possible through a grant from ViiV Healthcare.

About IAPAC

The International Association of Providers of AIDS Care (IAPAC) was founded in 1985 with a mission to improve access to and the quality of prevention, care, treatment, and support services delivered to people living with and affected by HIV and comorbid diseases, including tuberculosis and viral hepatitis (HBV and HCV). With more than 30,000 members globally and programming in over 150 countries, IAPAC is the largest association of clinicians and allied health professionals working to end the epidemics of HIV, TB, and viral hepatitis by 2030.

About Fast-Track Cities

The Fast-Track Cities initiative leverages data-driven, equity-based public health policy and implementation science to mobilize and support cities and municipalities worldwide in their efforts to achieve Sustainable Development Goal (SDG) 3.3 — ending the epidemics of HIV, tuberculosis (TB), and viral hepatitis (HBV and HCV) by 2030 — and SDG 11 — making cities and municipalities inclusive, safe, resilient, and sustainable. The initiative is a global partnership between cities and municipalities around the world and four core partners: the International Association of Providers of AIDS Care (IAPAC), the Joint United Nations Programme on HIV/AIDS (UNAIDS), the United Nations Human Settlements Programme (UN-Habitat), and the City of Paris. Launched on World AIDS Day 2014, the network has grown to include more than 350 cities and municipalities.

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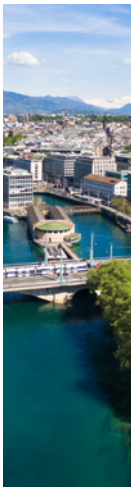
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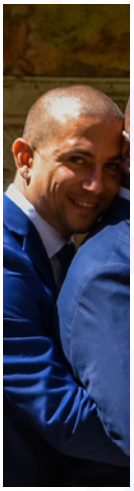
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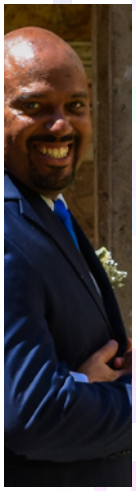
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DR. JOSÉ M. ZUNIGA

PRESIDENT/CEO

International Association of Providers of AIDS Care (IAPAC)

Fast-Track Cities Institute (FTCI)

Introductory Letter

Last year — in the midst of COVID-19 (a global pandemic unlike anything we have seen in the last century) — the International Association of Providers of AIDS Care (IAPAC) began an ambitious plan to launch a global report on LGBTI+ health equity during Copenhagen 2021, a WorldPride celebration and human rights forum. The report, which we are launching today, is unique for its focus on cities, where half of the world's 7 billion citizens live, and because it allows us to compare LGBTI+ health equity issues globally. We selected 50 cities that are or soon will be part of the Fast-Track Cities network to serve as examples in a report aimed at informing current and future Fast-Track Cities as well as all of those working to end LGBTI+ health inequities.

The link between LGBTI+ health equity and our work at IAPAC is perhaps obvious given the longstanding and staggering disparities that LGBTI+ individuals face with respect to HIV. While HIV continues to be a critical issue in LGBTI+ health, we cannot allow that to be the only LGBTI+ health topic that is studied, discussed, funded, and actioned. Fundamentally, LGBTI+ health equity is about stigma, discrimination, and injustice, but also about resilience. The history of conditions facing LGBTI+ communities has led to myriad health inequities — including physical, mental, and behavioral — that are all interwoven.

Globally, 275 key informants from four geographic regions scored their local LGBTI+ quality of life an average score of 3.2 on a 1 to 5 scale — about halfway between "poor" and "excellent." No region came close to perfect on markers of LGBTI+ health equity, including access to care, quality of life, and nondiscrimination. Even cities with relatively good scores had room for improvement. And while cities that had better policies and more community visibility tended to score better among key informants, there were some surprises. For example, Tokyo scored slightly lower on LGBTI+ quality of life than did Kampala, where an anti-LGBTI+ political agenda has made headlines for years.

These results reveal two important insights. First, no one factor is determinative in LGBTI+ well-being, and many aspects of health equity (e.g., social determinants of health, quality care, nondiscrimination) must all be addressed to achieve better outcomes. Inclusive policies on paper will do little to change LGBTI+ health inequities if they are not correctly implemented and if cultural change does not occur concurrently. Moreover, the colliding COVID-19 and HIV pandemics have taught us that medical and scientific advancements can increase health inequities if entire populations are denied access to their benefits.

Second, LGBTI+ community leaders likely judge their city based on local factors, such as how LGBTI+ people are faring relative to non-LGBTI+ people locally and compared to other LGBTI+ people regionally — not in terms of global conditions. This helps explain how key informants in cities with vast differences in wealth, for example, often scored LGBTI+ socioeconomic problems as being roughly equal. The results should encourage those working in areas considered to be LGBTI+ inclusive that there is still much work to be done; the report should also bring pride to LGBTI+ advocates working in difficult conditions, knowing that their communities are more resilient than many people might think.

The bottom line is that we cannot adequately address HIV and other health conditions without including LGBTI+ populations, and we cannot adequately serve LGBTI+ populations unless we understand the diversity and complexity of these communities and their needs. Those of us working in the field of health and in any other topic area relevant to LGBTI+ health equity must recommit ourselves to working holistically to end the disparities these communities face. No one law, policy, or program will fix these challenges; rather, we must address the pervasive issues of stigma and inequality that comprise their core. Doing so begins with understanding what we know about disparities, and what we still need to learn, and in that respect, I hope this report will contribute to ending LGBTI+ health inequities.

In solidarity with LGBTI+ communities,



18 August 2021
Washington, DC

Executive Summary

BACKGROUND

Sexual and gender minority groups experience health disparities because of myriad overlapping social-ecological, cultural, and political factors. Lesbian, gay, bisexual, transgender, intersex, and other sexual and gender minority (LGBTI+) populations have higher incidence and prevalence of life-threatening physical conditions, mental health problems, chronic and infectious disease risk, violence and victimization, and discrimination; experience significant barriers to accessing health care, treatment, and retention in care; and face substantial threats to quality of life. Understanding and improving the health of LGBTI+ communities is critical to the goals of the Fast-Track Cities initiative because of the disproportionate burden of HIV among this population but also because of the interconnectedness between HIV and other health and social conditions facing them. The main objective of this project is to advance health equity among LGBTI+ individuals across current and prospective Fast-Track Cities by studying and comparing LGBTI+ health inequities. Fast-Track Cities are signatories of the *Paris Declaration on Fast-Track Cities* and thus members of the Fast-Track Cities network, and they have committed to ending AIDS as a public health threat by 2030.

METHODS

This study examined 50 current and prospective Fast-Track Cities, including 10 from Africa, 20 from the Americas, five from the Asia-Pacific region, and 15 from Europe. The study included two components. First, a key informant survey was conducted among individuals who study, work, or volunteer in LGBTI+ health equity related fields and who have knowledge of their local LGBTI+ community. Participants were recruited through virtual outreach and snowball sampling. The second component of the study were comprehensive assessments of publicly available data and policies. Four domains were developed for assessing health equity among LGBTI+ populations: health outcomes, socioeconomic factors, community trauma, and community resiliency. These domains were designed to assess health equity in broad terms that includes social determinants of health and underlying socioeconomic, political, and legal conditions that affect health equity.

RESULTS

Overall, 275 key informants rated quality of life for LGBTI+ people at 3.2 out of 5, about in the middle between a “poor” rating of one and an “excellent” rating of five. Only 15 key informants worldwide said that LGBTI+ quality of life in their city was “excellent.” The regional averages ranged from a low of 2.7 in the African cities to a high of 3.6 in the Asia-Pacific region cities, with the Americas and Europe falling in the middle with scores of 3.2 and 3.3, respectively. However, within each region there was wide variability; for example, in the Asia-Pacific region, Quezon City scored a 4.0 while Tokyo scored only 2.2.

Data assessments revealed many health disparities among LGBTI+ people, including with respect to HIV, sexually transmitted infections (STIs), mental health, substance use, and noncommunicable diseases. However, many cities lacked data beyond HIV among sexual minority men and transgender women, and some other conditions with respect to sexual minority men only. These results indicate a dire need for disaggregated data on LGBTI+ health, particularly at the local level, where interventions are implemented.

How Concerning are Issues Relating to Social Determinants of Health, on a 1-4 Scale?*

Housing access	3.2
Gender identity discrimination	3
Intersectional discrimination	3
Employment access	2.9
Sex worker treatment	2.9
Criminal justice for people of color	2.8
Sexual orientation discrimination	2.7
Police mistreatment	2.6
HIV status discrimination	2.4
Food access	2.4
Police targeting	2.3

* Scores on a scale of 1 (“not a problem”) to 4 (“serious problem”).

HIV-related services received by far the best rating when looking at access to care for LGBTI+ individuals, scoring a 3.8 on a 1 to 5 scale. Primary care was next, with a score of 3.1, followed by mental health care at 2.8, and gender-affirming care at 2.7. These trends were relatively consistent across the study's four regions and reaffirm the status of HIV care providers as leaders in LGBTI+ health equity, but also highlight the need for more focus on mental health and services for transgender individuals.

The vast majority of key informants found issues relating to social determinants of health — including socioeconomic opportunity, discrimination, and criminal justice involvement — to be at least somewhat problematic for their communities. Globally, housing access was rated as the most pressing challenge, with a score of a 3.2 on a 1 to 4 scale, in which a 1 indicated the issue was "not a problem," 2 indicated a "minor problem," 3 indicated a "moderate problem," and 4 indicated a "serious problem." Housing was followed by gender identity-based discrimination (3), discrimination against LGBTI+ people with multiple marginalized identities (3), employment access (2.9), and issues relating to sex work (2.9). In most cities, sexual orientation-based discrimination (2.7) and HIV discrimination (2.4) were found to be less problematic than gender identity discrimination (3), although there was some variation by city. Among socioeconomic issues, food access (2.4) was rated well below employment opportunities (2.9) and housing access (3.2), and among criminal justice issues, problems such as mistreatment by police (2.6) and the impact on LGBTI+ people of color (2.8) were rated higher than whether LGBTI+ people are being targeted or arrested by police due to anti-LGBTI+ bias (2.3).

While the severity of these social challenges varied between regions and individual cities, many of the trends were consistent. Most key informants found socioeconomic challenges to be problems for their community regardless of the overall wealth or poverty in their city. For example, the three cities in which the problem of housing access was most highly rated were San Francisco (where every key informant said it was a "serious problem"), Denver, and Dublin; these cities may be wealthy on a global scale, but the survey results demonstrate that inequities facing LGBTI+ people persist. Key informants rated the response by local institutions to these socioeconomic challenges to be at or below the midway point on a 1 to 5 scale; for example, the local response to LGBTI+ housing problems was rated just a 2.6.

Similarly, while LGBTI+ nondiscrimination laws varied widely, key informants considered discrimination against LGBTI+ people to be a problem in every city. Many key informants noted nondiscrimination policies as being a positive factor for those cities that had enacted them, and a prospectively positive factor for those who desired them, but concerns relating to underlying stigma and discrimination were universally reported. This helps explain how only 6% of key informants globally said that gender identity-based discrimination was "not a problem" in their city, despite the fact that more than 6% of them hailed from cities where nondiscrimination policies are in place.

In terms of sources of resilience, community-based organizations (CBOs) and informal social networks were the two most common sources named by key informants. When asked which type of entity best engaged with local LGBTI+ communities, CBOs scored highest at 3.9 globally compared to 3.1 healthcare providers, 3.0 for local government, and a 2.9 for the private sector. Suggestions for improving resilience included more and equitable access to funding for local CBOs; visible support from local political, community, and religious leaders; policies that recognize LGBTI+ identities and address discrimination; consistent, institutionalized, and authentic engagement with LGBTI+ communities; a stronger focus on subpopulations within the LGBTI+ population that face particularly strong challenges, such as transgender people and racial and ethnic minorities; and education of the public and those in the healthcare field to reduce LGBTI+ stigma, including within the context of improving health services.

RECOMMENDATIONS

To address both the health inequities documented in this research and the gaps in data that it revealed, action is needed at all levels of government and from external partners. While the focus of this report is on cities, urban and municipal leaders are most effective when they have the support — rather than opposition — of national and international actors. More detailed recommendations are included at the end of the report, but following is a summary of the overarching recommendations:

1. **PRIORITIZE** the elimination of inequities within LGBTI+ communities. These include those affecting racial and ethnic minorities, immigrants, low-income individuals, and people with disabilities, as well as needs specific to transgender and nonbinary people.
2. **ADDRESS** underlying socioeconomic factors. Issues such as access to housing, employment, and food were identified as LGBTI+ community challenges by the majority of key informants, even in resource-rich settings.
3. **IMPROVE** inclusive data collection. There is a dearth of disaggregated data to offer insights into LGBTI+ health, particularly outside of HIV and notably relevant to key populations beyond sexual minority men.
4. **ADDRESS** criminal justice disparities. Even in places where LGBTI+ identities are not formally criminalized, issues relating to police mistreatment, sex work laws, and criminalization of HIV exposure were identified as barriers to LGBTI+ health equity.
5. **ENSURE** LGBTI+ nondiscrimination. Many cities lacked even basic LGBTI+ legal protections, including nondiscrimination ordinances or laws, and even where these legal protections exist, many key informants reported the need for better education and awareness to address LGBTI+ stigma.
6. **ENGAGE** LGBTI+ communities. While most cities had some formal means in place of engaging with LGBTI+ communities, key informants indicated that more engagement was needed, and rated CBOs as better than other local actors in their efforts to sustain engagement.
7. **RECOGNIZE** gender minorities and their health needs. Healthcare services for transgender people were rated well below general LGBTI+ inclusive care, and key informants noted that discrimination based on gender identity was a major concern.
8. **IMPROVE** health systems. Key informants revealed a dire need for training and inclusion measures to improve the LGBTI+ experience in accessing and utilizing LGBTI+ inclusive health services.
9. **FOSTER** multisectoral collaboration. While this report is focused on cities, the LGBTI+ health challenges identified herein require collaboration between local, national, and international entities, including multisectoral representation. The Fast-Track Cities initiative itself offers evidence that such an approach is possible and effective.
10. **SUPPORT** HIV service providers as LGBTI+ care leaders. These providers scored better than others in health systems and can help lead the way in policy and practice.

CONCLUSION

THE LGBTI+ HEALTH INEQUITIES IDENTIFIED IN THIS REPORT ARE WIDE-RANGING AND PERVASIVE.

While many differences exist between local contexts, the underlying stigma, discrimination, and lack of visibility that causes these inequities are largely the same, as are the sources and effects of the LGBTI+ communities' resilience and the policies that could foster change. Ending health inequities must include addressing social determinants of health (e.g., housing, employment, public safety) that are intertwined with health conditions. Lasting and widespread progress must be achieved through a multisectoral and multilateral approach in which diverse actors — including city governments and local communities — are helping lead the way.

Background

LGBTI+ COMMUNITIES AND THEIR HEALTH

SUSTAINABLE DEVELOPMENT GOALS AND FAST-TRACK CITIES

To address LGBTI+ health equity in Fast-Track Cities, the issue must be framed within the context of the Sustainable Development Goals (SDGs) and the Fast-Track Cities initiative. The SDGs were launched in 2015 as part of the *2030 Agenda for Sustainable Development*.[1] In relation to LGBTI+ communities, SGD 3 calls for United Nations (UN) member-states to "[e]nsure healthy lives and promote well-being for all at all ages," and it includes subgoals that relate directly to areas where LGBTI+ populations experience disparities. These include with respect to efforts to end the HIV epidemic, ensure access to sexual and reproductive health services, and realize the right to universal healthcare. While SDG 3 is the goal within which health is explicitly addressed, all of the SDGs are relevant to health in that they address social determinants of health, or "the non-medical factors that influence health outcomes" and "the conditions in which people are born, grow, work, live, and age."[2] The SDGs that address inequality, resilience, and sustainability all relate to health in important ways. Moreover, SDGs 10 and 11 relate quite explicitly to LGBTI+ health in particular, calling for UN member-states to achieve gender equality and promote inclusive societies.

LGBTI+ HEALTH EQUITY DEFINITIONS AND CONCEPTS

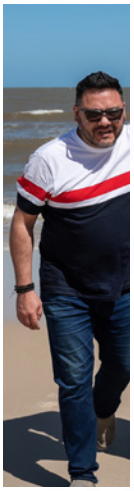
The populations that make up LGBTI+ communities are diverse even within a single city or neighborhood. On a global scale, these communities are even more challenging to define and discuss in uniform terminology. In broad strokes, however, LGBTI+ communities can be described as those comprised of sexual and gender minorities, as well as intersex individuals and those with related identities.

Sexual minorities are individuals whose sexual attraction, behavior, and/or identity is something other than exclusively heterosexual. Some individuals who have sexual relationships that would be described as non-heterosexual — for example, a man who has sexual relations with men and women — may still identity as heterosexual, especially given the different cultural contexts in which sexual orientation is interpreted. While such an individual would not identify as being part of an LGBTI+ community, many of the health risks, stigma, and potential discrimination that they would encounter would be similar. Gay, lesbian, and bisexual are among the most common sexual minority identities, but there are many others, especially outside of the English language and the perspective of the global North.

Gender minorities include individuals whose gender identity is something other than cisgender and may also include individuals whose gender expression rather than identity does not conform with established social norms. Cisgender individuals are those whose sex assigned at birth is the sex or gender with which they identify. For example, someone who was identified as female at birth and who currently identifies as female is likely to identify as cisgender, even if that term is still largely unknown among people outside of the LGBTI+ community. Therefore, gender minorities are typically those whose gender is something other than the sex they are assigned at birth. For example, a person who was assigned female at birth but who actually identifies as male would be a transgender man, and a gender minority. This population also includes a growing number of people who identify as not being either male or female (e.g., genderqueer individuals, nonbinary individuals), those whose gender identity shifts over time (i.e., gender fluid individuals), and those who identify as having no gender at all (i.e., agender individuals). To understand the concept of gender minorities, it is important to understand the difference between sex, which is assigned at birth and is generally related to biological characteristics, and gender — a social construct built around societal and individual norms and individual senses of self.

Intersex individuals are those whose sex characteristics do not fall exclusively into those associated with males or females. These can include differences in chromosomes, primary sex characteristics (i.e., genitalia), secondary sex characteristics, and/or other factors. Most individuals who are intersex are nonetheless assigned male or female at birth, and many are exposed to treatment (criticized by advocates) that attempts to put them in conformity with the sex selected by their healthcare provider or parents, often without the knowledge or consent of the individual. Because intersex identities relate to sex rather than sexual orientation or gender, intersex individuals do not necessarily consider themselves part of sexual or gender minorities, respectively, unless they also happen to have a sexual orientation or gender identity that places them within those categories.

In this report, the acronym LGBTI+ is used as an umbrella term to describe this broad population. Some of the health inequities and needs facing members of this population are similar, yet many are different. Nonetheless, the underlying influences of stigma and discrimination that facilitate the health inequities facing this community are largely interrelated, as are many of the solutions, such as antidiscrimination laws, clinical and service provider trainings, and community outreach. Additionally, members of this population have often banded together to increase their political power and influence, an important practical step given the marginalization they have faced. Therefore, while more research that focuses with exactitude on subpopulations within this broader community is needed, it is also useful to explore the strengths and challenges of LGBTI+ communities as a whole — largely the approach taken by this report. This approach is also necessary in large-scale research (such as what is presented in this report) given the varying approaches taken in data collection — for example, defining sexual minorities by sexual behaviors versus attractions versus identities — which can produce subtle or major differences in the results that require a nuanced rather than direct comparison.





Finally, this report mostly discusses “equity” rather than “equality.” Equality means that two or more things are equal, whereas equity accounts for differing needs as well as concepts relating to justice. For example, providing the same sexual health outreach and services to all individuals might be equal, but it might not be equitable if certain populations have different risks or needs. Similarly, it is important to acknowledge that the differences in health outcomes between LGBTI+ people and others are not only unequal, but are also inequitable, in that they are the result of stigma, discrimination, and other unjust social conditions.

EXPLORING LGBTI+ HEALTH INEQUITIES

There are myriad LGBTI+ health inequities and issues that manifest in different ways across the life course. These are mostly explained, often nonexclusively, by two factors: inherent differences between LGBTI+ people and others, and social conditions that impact LGBTI+ health. For example, transgender individuals need certain forms of care (i.e., gender-affirming hormone therapy) that cisgender people generally do not; they also face difficulties accessing that care for socially constructed reasons (e.g., discrimination, lack of competent providers, underlying financial insecurity due to limited opportunity). Therefore, the unique needs and challenges regarding gender-affirming care reflects both different necessities and also issues related to social justice. The former are important to know, understand, and respond to, but cannot be changed; the latter can be changed through advancing positive policies and changing social conceptions. Higher rates of tobacco use, on the other hand, are an example of a problem affecting the LGBTI+ community not because of an inherent difference in health needs, but rather because of changeable factors in society, such as the targeting of the community by tobacco company advertising and marketing, as well as the minority stress that may cause LGBTI+ people to feel the need to smoke. This concept is critical in that it explains that LGBTI+ health disparities exist not because LGBTI+ people are inherently risky, unsafe, or unhealthy, but because they have different needs from the general population that are frequently not met, and because they face persistent, underlying LGBTI+ related stigma and discrimination.

Physical and Sexual Health

As has been noted, sexual health disparities among LGBTI+ populations — particularly disparities relating to HIV — are among the most widely documented. The Joint United Nations Programme on HIV/AIDS (UNAIDS) reports that the risk of acquiring HIV among transgender and other gender minority individuals is 13 times that of the cisgender population.[3] They also found sexual minority men to be at 26 times higher risk for acquiring HIV than other men, with this population comprising 23% of new HIV infections worldwide — a highly disproportionate number compared to their share of the population.[4] Risk behaviors for HIV acquisition are similar to those of other sexually transmitted infections (STIs) and HIV and certain STIs can also have synergistic relationships in which contracting one makes an individual more susceptible to contract another and/or experience negative health outcomes as a result.[5] This helps explain why LGBTI+ individuals also have a disproportionate burden of other syndemic conditions such as syphilis or comorbid conditions such as hepatitis C virus (HCV) infection.[6,7]

Beyond sexual health, there are various physical health conditions for which LGBTI+ populations may be at greater risk. Major noncommunicable disease factors include tobacco and alcohol use as well as insufficient exercise and poor diet.[8] These risk factors are likely more prevalent among LGBTI+ populations for the reasons described below regarding mental and behavioral health, as well as social determinants of health, and a lack of access to culturally competent care that would allow physical conditions to be quickly diagnosed and effectively treated.

Mental and Behavioral Health

The significant inequities that LGBTI+ people face with respect to mental and behavioral health can be understood through a minority stress framework, in which individual and structural discrimination, stigma, and bias are seen to cause negative mental health outcomes for the population.[9] At least some level of anti-LGBTI+ bias is found in nearly every society, with much of it being state-sponsored or at least not fully banned. For example, in a global survey of laws relating to sexual minorities, not a single country met every indicator of protections and social recognition for LGBTI+ people.[10] Thus, through the minority stress framework mental health inequities for the LGBTI+ population can be reasonably projected globally, even where research does not exist.

Additionally, there is a large body of literature to provide specific examples of minority stress and/or negative mental health outcomes in a variety of settings. A global review found that LGBTI+ people experienced higher levels of emotional distress, victimization, and other negative health factors, and also faced barriers to getting related care.[11] Another international systemic review found specifically that self-stigmatization among gender minorities (a factor of minority stress) was an important factor related to increased incidence of depression, anxiety, and suicidality among this population.[12] Stress within LGBTI+ circles was another factor associated with anxiety and less connectedness to the community among sexual minority women.[13]

Substance use, minority stress, and other mental health conditions are all interconnected among LGBTI+ populations, causing these issues to compound one another.[14] For example, one study found that sexual minority women were more likely to consume alcohol on days when they experienced instances of minority stress or discrimination.[15] In the United States, sexual minority adults were about 50% more likely to have past year tobacco use than were their heterosexual peers,[16] a disparity that arises out of LGBTI+ individuals using tobacco to cope with stress, as well as tobacco companies leveraging LGBTI+ social vulnerabilities to aggressively market their products to this population.[17]

Youth and Aging

Health issues can evolve in LGBTI+ people throughout their life cycle, with LGBTI+ youth and older adults facing particular challenges and needs. For example, among youth, bullying in schools is a major problem that denies educational opportunities and creates mental health and other challenges.[18] The UN Independent Expert on sexual orientation- and gender identity-based violence has called for a global ban on efforts to "convert" LGBTI+ people to cisgender and/or heterosexual identities,[19] a practice that disproportionately affects youth and that is legal in most jurisdictions.[20] One issue affecting transgender and nonbinary youth in particular is the need to access to gender-affirming care, which they are too often denied despite their vital importance in the lives of this population, according to experts.[21]

With respect to aging, LGBTI+ older adults face many challenges due to their lower levels of social support, including decreased likelihood of being partnered and having children, as well as lower levels of financial support, given a lifetime of compounded limits to their socioeconomic opportunities.[22] In places where LGBTI+ rights and social acceptance have been expanding rapidly in recent years, LGBTI+ older adults have not been able to benefit — in terms of their health, socioeconomic standing, internalized acceptance, and acceptance from their peers — to the degree that have younger individuals. This is further complicated by the increased needs faced by older adults with respect to health, housing, and social support.



Intersectionality

Intersectionality is the concept that people of color who are also members of another marginalized identity face unique forms of discrimination. For example, women of color do not just face racism and sexism, but rather encounter intersectional discrimination as women of color that is unique to their population and must be independently understood and addressed.[23] Kimberlé Crenshaw, who originated the concept of intersectionality, has since applied the concept to LGBTI+ people of color.[24] Thus, it is important to understand intersectionality not as just interconnected forms of identity, which are part of everyone's identities, but rather intersecting forms of oppression, a condition that applies only to people who confront multiple forms of marginalization. While this concept will look different across societies, the idea of intersectionality as a framework remains consistently useful and important. For example, issues of race and ethnicity are very different in Amsterdam, Kigali, and Mexico City (three of the Fast-Track Cities featured in this report), each of these societies has both internal dynamics and global contexts (i.e., colonialism) that make the concept of intersectionality important to understanding local LGBTI+ equity. In the United States, for instance, Black transgender and nonbinary individuals are five times more likely to be living with HIV than transgender and nonbinary people in general, and are also more likely to have attempted suicide, been sexually assaulted, or faced violence while incarcerated.[25]

Social Determinants of Health

In assessing the status of LGBTI+ health equity — and LGBTI+ equity in general — it is critical to consider the underlying social determinants of health that effect LGBTI+ communities. These social determinants are interrelated with LGBTI+ health issues. For example, lack of access to a safe and inclusive education early in the life could cause an LGBTI+ person to have reduced employment opportunities in the future, thus limiting access to adequate housing, nutritious food, and quality healthcare. Most countries do not have full legal protections against LGBTI+ discrimination in areas such as employment and housing,[26] and even in jurisdictions that do ban or protect against such discrimination, it still occurs.[27] Furthermore, equal access to one aspect of socioeconomic opportunity does not ensure equitable access; for example, a discrimination-free housing market that does not have supports for those who have been denied educational or employment opportunities may be equal, but not equitable.

Criminal Justice Systems

Criminal justice is another issue that has an impact on the health of LGBTI+ individuals, and it is closely intertwined with many social determinants of health. In addition to countries that actually criminalize LGBTI+ identities or behaviors, other criminal laws — such as those criminalizing the transmission of HIV or sex work — can have a disproportionate effect on LGBTI+ people. Moreover, LGBTI+ people are both disproportionately represented in criminal justice systems and can face violence and abuse once in such systems.[28] Involvement in the criminal justice system has significant health implications for LGBTI+ people, not only because it impacts other social determinants (by depriving individuals of employment, education, and stable housing, for example) but also because of the connection between criminal justice involvement and mental health[29] and conditions such as HIV, HCV, and TB.[30]

Healthcare Access

Many LGBTI+ health disparities can be caused or compounded by a lack of access to affordable, quality, and culturally competent or responsive care. In countries where LGBTI+ identities or behaviors are criminalized, "coming out" to one's healthcare provider can have deleterious effects, and in countries where the "promotion" of LGBTI+ identities or behaviors is illegal, providing care to these individuals can represent a criminal act. Furthermore, harmful medical practices such as conversion therapy are harmful in and of themselves, but also serve to discourage future healthcare use; these harmful practices are not banned in the vast majority of jurisdictions.[31] Another challenge for LGBTI+ healthcare access is a lack of culturally competent healthcare providers who are both able to respectfully interact with LGBTI+ individuals and who understand and respond to their unique health needs.

Urban Health

Finally, while much of this report applies to LGBTI+ health equity broadly, its specific focus is on 50 urban settings. Cities can provide both advantages and disadvantages to LGBTI+ health equity. For example, LGBTI+ resources of all types tend to be concentrated in urban areas, and also may be more accessible due to the presence of public transportation. There are also more healthcare and service providers from which to choose, increasing the chance that LGBTI+ people can confidentially find competent care. On the other hand, the social determinants of health that are particular to or exacerbated in urban areas — which are context-dependent but can include poverty, violence, poor environmental health, and other factors — impact LGBTI+ populations as they do all others. Additionally, because of the underlying socioeconomic vulnerability of LGBTI+ individuals, issues such as poor environmental health due to pollution, unsafe building conditions, and overcrowding might have a more significant impact on LGBTI+ people than non-LGBTI+ people. Therefore, while every city (and its contrasting non-urban surrounding environment) is different, urban health concerns such as these should be considered in assessing LGBTI+ health equity in cities.



Methods

Designing a Global LGBTI+ Health Report

Fifty cities were selected for inclusion in this study, representing four regions: Africa (10), the Americas (20), Asia-Pacific (5), and Europe (15). All but one of the selected cities (Tokyo) are signatories of the *Paris Declaration on Fast-Track Cities* and thus members of the network of more than 350 Fast-Track Cities that have committed to ending the epidemics of HIV, TB, and viral hepatitis by 2030.

Cities Included in the Study

REGION	CITIES
AFRICA	Bamako, Durban (eThekwini), Kampala, Kigali, Lagos, Lusaka, Maputo, Nairobi County, Yaoundé, Windhoek
AMERICAS	Atlanta, Baton Rouge, Buenos Aires, Charleston, Chicago, Columbia, Dallas, Denver, District of Columbia, Kingston, Mexico City, Miami-Dade County, Montréal, New Orleans, New York City, Oakland, Phoenix, Rio de Janeiro, São Paulo, San Francisco
ASIA-PACIFIC	Bangkok, Melbourne, Quezon City, Taipei, Tokyo
EUROPE	Amsterdam, Athens, Berlin, Brussels, Copenhagen, Dublin, Glasgow, Kyiv, Lisbon, London, Madrid, Milan, Paris, Prague, Vienna

Four domains were developed for assessing health equity among LGBTI+ populations, based on a review of existing research on this topic: health outcomes (e.g., prevalence of HIV, mental health conditions, noncommunicable diseases), socioeconomic factors (e.g., employment, housing), community trauma (e.g., discrimination, criminal justice), and community resilience (e.g., civic engagement, resources). These domains were designed to assess health equity in broad terms that includes social determinants of health and underlying socioeconomic, political, and legal conditions that affect health equity. These domains formed the foundation of a two-pronged study whose protocol was granted an institutional review board waiver by Pearl IRB.

This study used two means of gathering data. The first method was an assessment conducted by study personnel regarding health equity across the four domains in each city. Data were collected for regional and global

analyses based on a series of indicators selected to cover a range of topics within each domain. Researchers sought city-specific, population-wide data with sexual orientation and gender identity disaggregated for each indicator. When such data were not available, researchers gathered alternative data, such as national data, data from smaller studies, or data that only included a subpopulation of the LGBTI+ community. Some indicators were based on factors beyond public health data. For example, several indicators relate to the criminalization of acts or identities related to LGBTI+ health.

The second method of research was a key informant survey designed to gather the expert opinions of individuals who study, work, or volunteer in fields related to LGBTI+ health equity across the study's four regions. The survey was shared with local contacts in the cities selected for the study, who were asked to participate in the survey themselves if they qualified and/or to share the survey with colleagues, to allow for virtual snowball sampling. The survey was made available in English, French, Portuguese, and Spanish, and included both numerical and open response questions, including several questions across each of the four domains plus a question on overall quality of life for local LGBTI+ people. Some questions utilized a 1 to 5 scale, in which 1 was "poor" and 5 was "excellent," with regard to the availability of services or the performance of different local institutions. Other questions asked key informants to rate potential challenges (i.e., housing access) as being "not a problem," a "minor problem," a "moderate problem," or a "serious problem." City, regional, and global averages were created for the numerical responses and thematic analyses were conducted for open responses.

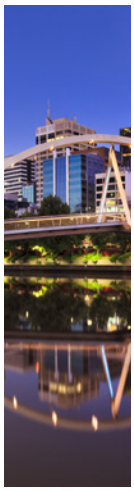
The following limitations exist with respect to the study:

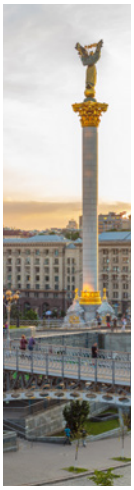
- There are many gaps in data around LGBTI+ populations and differing cultural understandings and methods of assessing LGBTI+ identities. This makes comparability of data a challenge and thus requires a more nuanced analysis of the data.

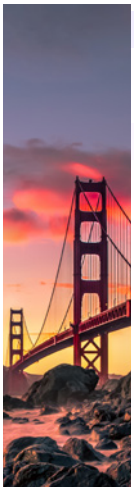
- While the key informant survey was open to the public, IAPAC and Fast-Track Cities initiative contacts were encouraged to share the survey with others, thus participation was biased towards those who are connected to IAPAC and/or the Fast-Track Cities network. It is possible that the survey participants were more likely to work in HIV or related fields and were more likely to engage in collaboration with major institutions than the average LGBTI+ health activist or professional. This survey bias towards those who are better connected with major institutions and international collaboration may have been furthered by the limited number of languages in which the survey was available.

- Finally, the cities selected for this study, because they form a part of the Fast-Track Cities network, are perhaps more favorable towards LGBTI+ populations than the global average of cities, not to mention smaller municipalities and rural areas. Therefore, while this study presents findings that might be widely useful outside of the 50 selected cities and the Fast-Track Cities network in general, the results may understate the extent of LGBTI+ inequities in other urban, peri-urban, and nonurban areas.

Notwithstanding these limitations, this study was designed to help identify and fill gaps in the global LGBTI+ health literature — including the lack of consistent and comparable data across cities and regions — and to act as a catalyst for future research and action.





Results

Global, Regional, and City Analyses

This report is novel for its focus on LGBTI+ life in diverse cities but is also in the minority of LGBTI+ research due to its global focus. While the health and well-being of LGBTI+ communities look very different across contexts, this report found a great deal of similarity in the issues and the relative severity of health, policy, socioeconomic, and other challenges LGBTI+ people face.

This section of the report begins with a global overview of research findings and proceeds into regional analyses. Three cities from each region were also selected for individual analyses to provide more in-depth examples of the research findings.

GLOBAL OVERVIEW

In total, there were 275 survey respondents (or key informants) globally who were deemed eligible for inclusion, of whom the majority (51%) are associated with non-profit organizations, 21% with clinics or hospitals, 12% with government, 9% with academia, and the remainder with other settings.

Quality of Life and Care

The overall quality of life for LGBTI+ people was rated at 3.2 out of 5 (mode: 3; SD: 0.95), about in the middle between a "poor" rating of 1 and an "excellent" rating of 5. Only 15 of 275 key informants worldwide said that LGBTI+ quality of life in their city was "excellent," demonstrating significant room for improvement. While there was some correlation between the quality of life score and factors such as local LGBTI+ laws and socioeconomic conditions, there was still a surprising diversity in which cities scored poorly or well. For example, Tokyo and Kampala scored about evenly (2.2 and 2.3, respectively) at the bottom of a sample of cities, despite LGBTI+ people in Tokyo having a better legal landscape and an overall

Quality of Life on a 1-5 Scale in a Sample of 20 Cities *

Tokyo	2.2
Kampala	2.3
Athens	2.8
Kingston	2.8
Dublin	3
Maputo	3
Mexico City	3.2
Charleston	3.2
Miami	3.3
New Orleans	3.3
Bangkok	3.4
Chicago	3.4
London	3.4
Copenhagen	3.5
Denver	3.6
Phoenix	3.6
San Francisco	3.6
Melbourne	3.8
New York City	4
Quezon City	4

* Scores on a scale of 1 ("poor") to 5 ("excellent").

stronger economy and health system. Similarly, New York City and Quezon City both achieved a relatively high score of a 4 out of 5, despite residents of Quezon City experiencing fewer legal protections and having a less established LGBTI+ community. These results likely reflect the fact that quality of life for LGBTI+ people is largely conceptualized on a local rather than a global basis. Key informants may think about their local LGBTI+ community's quality of life in terms of the overall quality of life among people in their city, and perhaps how their experiences of LGBTI+ life in their city compare to perceptions of LGBTI+ life elsewhere in their country. More than anything, the survey findings suggest that conventional wisdom about where LGBTI+ communities enjoy better or worse conditions stands to be questioned, and that this topic merits more research.

"Health, legal, and educational professionals are not trained in matters related to the LGBTI+ community... [There is a] lack of knowledge on the primary needs facing the community."

Key Informant, Maputo

With respect to healthcare access, the knowledge and cultural competency of clinical health providers was ranked slightly better (3.1 out of 5; mode: 3; SD: 1.01) than was that of mental health service providers (2.8 out of 5; mode: 2; SD: 1.08), although both rankings were concerning given the critical need for all health providers to address existing inequities. The availability and affordability of gender-affirming care for gender minorities was also rated poorly, with an average score of 2.7 out of 5 (mode: 3; SD: 1.16), suggesting that the healthcare needs of transgender and gender-nonconforming individuals should be a priority in addressing LGBTI+ health equity. According to the assessments, most cities in which access to gender-affirming care was guaranteed, and where other policies that facilitate access were in place (e.g., access to documents reflecting one's name and gender, access to gender-based facilities of one's choice) were in the Americas.[32] However, it bears noting that these policies reflect fairly new trends and, in the United States in particular, have been met with a backlash that has also spurred anti-transgender policies and legislation.[33]

The availability of low-cost, low-barrier HIV services for LGBTI+ people fared better than other areas of healthcare access, with an average score of 3.8 out of 5 (mode: 4; SD: 1.07). This relative strength is promising given that all cities included in the study are part of the Fast-Track Cities initiative and have thus committed to ending AIDS as a public health threat by 2030. This result is also important given the persistent HIV-related disparities facing LGBTI+ people in these 50 cities, as described below. Regarding HIV prevention services in particular, 29 key informants discussed access to pre-exposure prophylaxis (PrEP) in their qualitative responses, including 10 who raised concerns, including about availability and cost, lack of knowledgeable providers to prescribe PrEP, stigma within the healthcare system against those who use PrEP, and lack of awareness within the LGBTI+ community on the use of PrEP. Nine key informants, on the other hand, said that PrEP access has been improving and noted this as being a positive for their community. The remainder discussed their involvement with PrEP without making a negative or positive commentary regarding its availability. Beyond PrEP, there were various key informant comments regarding how LGBTI+ stigma and discrimination, as well as a lack of comprehensive sexual health education, were hindering HIV prevention measures, including the use of condoms and other safer sex methods.

Health Outcomes

Globally, HIV continues to be a major public health concern among LGBTI+ populations. There have been continued improvements in HIV prevention and treatment, yet sexual minority men — often referred to as men who have sex with men (MSM) in the HIV literature — remain one of the populations most affected by HIV across the globe. Data on HIV prevalence in assessments of the selected cities were relatively complete for sexual minority men, with city-specific estimates varying in great degree based on specific subgroups of sexual minority men and sampling methods. There was a general lack of HIV prevalence data available among the transgender community; however, these data were more readily available among transgender women comparted to transgender men who report having cisgender male sexual partners. Among the cities with HIV prevalence data reported for both MSM and transgender women (two groups that are sometimes wrongly conflated), transgender women universally experienced the greatest disparity. For example, in Rio de Janeiro, 54.0% of transgender women were living with HIV compared to 13.9% of MSM. Although effective testing and treatment of chlamydia, gonorrhea, and syphilis have been available for decades, eradication of these diseases remains an elusive objective for LGBTI+ populations globally. A similar pattern with respect to lifetime prevalence of bacterial STI emerged, with CT (up to 26.0%), GC (up to 18.3%), and syphilis (up to 37.9%) data available in the majority of cities among sexual minority men, but mostly absent for all other LGBTI+ populations.[34]

The prevalence of mental health problems among LGBTI+ populations is higher when compared to non-LGBTI+ populations, according to the assessments, although not to the level of serious pathology. Specifically, mental health problems such as depression, anxiety, and post-traumatic stress disorder (PTSD) were high across cities for this assessment. Although the majority of the cities had data on the prevalence of depression among sexual minority men, this was not the case for both anxiety and PTSD, and certainly not the case for other LGBTI+ populations. Furthermore, in general, availability of suicide data is scant among LGBTI+ populations, particularly outside of the Americas.

Data revealed alarmingly high rates of substance use among LGBTI+ populations when compared to demographically matched peers. Notably, in multiple cities, sexual minority men report higher rates of substance use (e.g., drug and alcohol use, smoking) compared with the general population, with extensive use of stimulants and other party drugs, including 3,4-methylenedioxymethamphetamine (commonly known as MDMA or ecstasy), γ-hydroxybutyric acid (commonly known as GHB), and ketamine. Alcohol use is also more common among sexual minority men in the 50 cities than among the general population. Similarly, across cities, lesbian and transgender women had higher rates of substance use compared with the general population. According to available literature, a major underlying reason for these disparities stems from the internalization of societal stigma as a result of growing up in non-affirming environments, leading to sexual and gender minority stress and suboptimal health outcomes in reaction to these adverse experiences.

How Big a Problem is Housing Access on a 1 to 4 Scale?*

Quezon City	1.8
Melbourne	2.4
Copenhagen	2.5
Tokyo	2.5
Bangkok	2.6
Kingston	2.8
Chicago	3
Miami	3
Kampala	3.1
London	3.2
Athens	3.2
Maputo	3.2
Lisbon	3.3
Mexico City	3.3
New Orleans	3.3
New York	3.4
Charleston	3.6
Phoenix	3.6
Dublin	3.8
Denver	3.9
San Francisco	4

* Scores on a scale of 1 ("not a problem") to 4 ("serious problem").

One issue contributing to mental health disparities among the population is the practice of conversion therapy, which is a term for harmful, non-evidence-based, and discredited practices that seek to "change" LGBTI+ people to have heterosexual and/or cisgender identities. Too often, LGBTI+ people receive such treatment in lieu of the evidence-based, affirming mental health support that they actually need. Most of the cities where this practice was banned were in the Americas.

"An over-emphasis on the success story of affluent white gay men distorts perceptions of LGBTI+ reality."

Key Informant, London

Data on other health indicators among LGBTI+ populations — including diabetes, obesity, and mortality rate — are even more scarce, with only a handful of cities having disaggregated results based on sexual orientation or gender identity. LGBTI+ populations did show a higher prevalence of disability than their non-LGBTI+ counterparts. On average, across cities, data show the prevalence of disability to be about 36% among lesbians, 36% among bisexual women, 26% among gay men, and 40% among bisexual men. None of the cities had disaggregated data on the prevalence of disability by gender identity.

Socioeconomic Factors

"Many are still expelled from their home or repress their sexuality or gender identity for fear of being expelled, which leads to several problems, especially in mental health."

Key Informant, São Paulo

In terms of socioeconomic factors, finding and maintaining housing was a major factor for LGBTI+ communities, with eight in 10 key informants (80%) saying that it was a serious or moderate challenge. A slightly smaller percentage (71%) said the same about finding and maintaining adequate employment. However, this trend was driven by results in the Americas and, to a lesser extent, Europe; in both of these regions, housing outranked employment as a concern, whereas in Africa and Asia-Pacific, that trend was reversed. A smaller percentage (50%) globally felt that access to sufficient and nutritious food was a serious or moderate challenge for LGBTI+ people. The ability of local governments, nonprofit organizations, the private sector, and other actors to respond to these challenges was rated highest with respect to food access (3.0 out of 5; mode: 3; SD: 1.16) and lowest with respect to housing (2.6 out of 5; mode: 2; SD: 1.05). This finding is concerning in that it indicates that the areas in which support is most badly needed, housing first and employment second, are also the areas in which the local response remains weakest.

With respect to the data assessments, there were no city-specific, population-based data on the indicators used herein — unemployment rate, homelessness rate, poverty rate, or food insecurity — that were disaggregated by sexual orientation and/or gender identity. However, national (or, in the United States, state-specific) rates on these topics for the selected cities were high, particularly with respect to poverty, where rates ranged from 9.1% (Colorado, USA)[35] to 55.5% (South Africa).[36] These high overall poverty rates, in and of themselves, are a public health concern, since a significant relationship between income inequality and HIV prevalence has been documented across many countries throughout the world.[37] Countries with greater inequality have higher HIV prevalence, particularly in sub-Saharan Africa but also to a lesser extent across Asia-Pacific, Europe, and the Americas.

Discrimination

Key informants identified discrimination against LGBTI+ people to be a major problem for their communities, and research supports that discrimination is a contributing factor to the health inequities LGBTI+ people face. Cities were mixed with respect to nondiscrimination laws pertaining to sexual orientation, gender identity, gender expression, and HIV status, as well as laws recognizing LGBTI+ related hate crimes. The majority of cities with LGBTI+ protections are in the Americas, Europe, and Asia-Pacific, whereas cities without protections were mostly among those selected from the Africa region, excluding Durban (eThekwini), South Africa. The African cities and, to a lesser extent, cities in Asia-Pacific were also less likely than those in the Americas and Europe to legally recognize same-sex relationships, an important if not primary legal step in combatting discrimination.

According to key informants, discrimination against LGBTI+ people with other marginalized identities (e.g., racial, ethnic minorities) was the most problematic form of discrimination facing their community. Thirty-five percent of key informants said discrimination was a "serious" problem, 39% said it was a "moderate" problem, 19% said it was a "minor" problem, and >7% said it was "not a problem" at all. "I think the main issue in Denver around this would be the intersections of LGBTI+ identity and race and gender," said one key informant who works in public health. "For white, cisgender LGBTI+ individuals, Denver is [a] 'safe' place to live and one without much discrimination compared to other parts of our country. I think for individuals of color, this is not the case. And I do know that non-white LGBTI+ [people] consistently express their own experiences of racism within the larger LGBTI+ communities."

"Migrants are particularly demonized under the current UK government," said a key informant in London. "There is a serious risk here around refugees and asylum seeker and their access to adequate health and care, including support to manage sexual health and chronic conditions."

Regarding the types of discrimination facing the LGBTI+ community, key informants cited gender identity-based discrimination as being more of a problem than discrimination based upon sexual orientation or HIV status. Only 6% of key informants said that gender identity-based discrimination was "not a problem" in their community, while one in three said it was a "serious" problem. Particularly in jurisdictions that have banned sexual orientation-based discrimination but not gender identity-based discrimination, this presents an urgent need for legal reform and other interventions. Sexual orientation-based discrimination was also found to be a concern among 90% of key informants, including 19% who found it to be a "serious" challenge. HIV-related discrimination was a concern for 91%, including 24% who said it was a "serious" concern in their local LGBTI+ community.

In open-ended responses, many key informants wrote that open discrimination against LGBTI+ people in healthcare settings or lack of inclusive care (e.g., intake forms not being sensitive to gender minorities, competent care not being available) had an impact on health. Other key informants discussed how stigma and minority stress take a toll on mental health, with one in Columbia, SC, USA, writing that LGBTI+ people are "not treated like humans, but almost as if they're contaminated by something. Consequently, this encourages them to skip out on needed routine medical [and] preventive care, which drives STI and infectious disease rates." Still other key informants described how discrimination has an impact on social determinants of health, especially housing and homelessness, which leads to ripple effects across various aspects of overall well-being.

How Big a Problem is Intersectional Discrimination on a 1 to 4 Scale?*

Quezon City	1.6
New York	2.2
San Francisco	2.4
Charleston	2.6
Bangkok	2.6
Copenhagen	2.7
Tokyo	2.7
Phoenix	2.8
Chicago	3
Denver	3.1
Melbourne	3.2
Miami	3.3
Mexico City	3.3
London	3.4
Lisbon	3.4
Athens	3.4
Maputo	3.4
Dublin	3.4
Kampala	3.6
Kingston	3.7
New Orleans	4

* Scores on a scale of 1 ("not a problem") to 4 ("serious problem").

Criminal Justice

Key informants rated criminal justice issues slightly less in terms of their significance than were housing and employment issues. Eighty-five percent of key informants said that mistreatment or abuse of LGBTI+ people by law enforcement was a problem in their city, including 24% who said it was a "serious" problem, 31% a "moderate problem," and 30% a "minor" problem. A slightly smaller percentage (71%) said that targeting of LGBTI+ people in their city was a "serious," "moderate," or "minor" challenge, while slightly more than that percentage (77%) reported the same about criminalization of HIV exposure and/or nondisclosure of HIV status. Most cities for which this issue was raised are in countries with laws that criminalize transmission and non-disclosure of HIV status to sexual partners, and criminalization of HIV can still occur in places that do not have laws that specifically mention HIV; instead, laws against endangerment, physical or sexual assault, and even attempted homicide are often employed. In fact, more than half of the current cases worldwide criminalized HIV exposure and non-disclosure of HIV status to sexual partners using general criminal laws.[38,39]

"There is no gender recognition law in Thailand. Transgender people are not allowed to change their gender marker on their ID. They often face stigma and discrimination going to the hospital as their appearance will usually not match with their gender marker. They often get questioned with unnecessary and irrelevant questions. This creates massive discomfort for transgender people and it drives [them away from] health services."

Key Informant, Bangkok

Criminalization of sex work and/or mistreatment of sex workers was ranked as more of a concern than treatment of the LGBTI+ community itself, with 90% of key informants saying it was a problem, including 34% who said it was a "serious" problem. Although sex work is reportedly widespread in every city included in this report, more than 40 of 50 cities have laws governing sex work as illegal. This statistic is particularly concerning given that the legal environment, including policy, law enforcement, and the judicial system, is a significant structural determinant of HIV acquisition and transmission risk in the context of transactional sex and should remain at the center of the HIV prevention agenda. Moreover, LGBTI+ people are disproportionately represented in the field of sex work due, in part, to limited economic opportunities elsewhere, and can be the targets of arrest and mistreatment when sex work criminalization laws are enforced.

Critically, the majority of key informants (90%) said that there was a disparate impact among racial and ethnic minorities with respect to these criminal justice issues, including 30% who said it was a "serious" problem and 32% who said it was a "moderate" problem. Therefore, while not all criminal justice issues were rated as being as problematic as socioeconomic and discrimination issues, nine in 10 key informants felt that they were problematic with respect to impact on racial and ethnic minorities in particular. This problem was ranked highest in the Americas, followed by Africa, Europe, and Asia-Pacific. This ranking may relate to recent attention in the Americas, and especially the United States, regarding the disproportionate impact of criminal justice systems on people of color in general, which would apply in this case to LGBTI+ people of color. The relatively weak ranking of this issue in Europe is slightly surprising given many key informants noted problems facing LGBTI+ people from racial and ethnic minorities in their cities, especially migrants, though it could reflect relatively liberal criminal justice systems compared to those found in, for example, the United States.

Community Resilience

Community-based organizations, nonprofits, and informal social networks of other LGBTI+ people were most frequently named as major sources of community resilience in open responses from key informants. In terms of which sector did best at engaging in productive and respectful dialogue with the local LGBTI+ population, nonprofits scored best, with an average of 3.9 out of 5 (mode: 4; SD: .92). Healthcare providers, local government, and the private sector all scored lower and roughly equally, with averages of 3 (mode: 3; SD: 1.08), 3 (mean: 4; SD: 1.23), and 2.9 out of 5 (mode: 3; SD: 1.10), respectively. While nonprofits scored well, some key informants called on them to take more of a leadership role in influencing other actors and society at large. Nonprofit organizations "could influence change if they invest in evidence-based advocacy," said the executive director of an organization serving transgender women in Kampala. "Capacity building of healthcare providers about transgender women and the need to support them to access services would also influence change."

Many key informants also called for more funding for community-based organizations, health services, and social spaces, noting that good work was being done but that more support was needed. "Give us funding to work," stated the director of an organization providing health services to sex workers in Lagos. Strategies proposed by the key informants included lowering barriers to accessing grants, reducing bureaucracy, and diversifying which organizations receive grants.

Other common themes regarding how institutions can improve LGBTI+ resilience included engaging in meaningful and formal dialogue; supporting socioeconomic opportunity for LGBTI+ individuals; increasing LGBTI+ inclusive data collection to better identify needs and demonstrate inclusivity; visible displays of LGBTI+ support, such as LGBTI+ flags in public spaces and the participation of political leaders in LGBTI+ community celebrations; and supporting changes to laws to eliminate criminalization of LGBTI+ identities and eliminate LGBTI+ discrimination.

In terms of the assessments, evidence varied from city to city, pointing to a major need that local, national, and international actors could support. Although most heavily concentrated in cities in the Americas and Europe, many of the 50 cities globally had one or more LGBTI+ community spaces, as well as public funding for LGBTI+ community resources (e.g., tourism association, pride events). Similarly, many cities had spaces identified — either via known areas that are open to the public or hidden but known via word of mouth — where LGBTI+ populations could socialize. Furthermore, many cities had a local LGBTI+ office, liaison, public report, or public plan on advancing LGBTI+ equity, although little evidence was found of such supports in the African cities, with the notable exception of Durban (eThekwini).

How Concerning are Issues Relating to Social Determinants of Health on a 1-4 Scale? *

Housing access	3.2
Gender identity discrimination	3
Intersectional discrimination	3
Employment access	2.9
Sex worker treatment	2.9
Criminal justice for people of color	2.8
Sexual orientation discrimination	2.7
Police mistreatment	2.6
HIV status discrimination	2.4
Food access	2.4
Police targeting	2.3

* Scores on a scale of 1 ("not a problem") to 4 ("serious problem").

How Well Do Actors Engage with the Local Community, on a 1-5 Scale?*

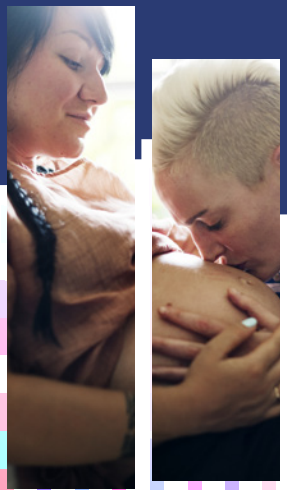
Nonprofits	3.9
Providers	3.0
Government	3.0
Private Sector	2.9

* Scores on a 1 ("poor") to 5 ("excellent") scale.

Conclusion

The global analysis of the LGBTI+ health equity survey and assessment reveal that LGBTI+ communities face wide-ranging and widespread health inequity and that access to health and other critical services is particularly poor for gender minorities. Discrimination was a concern among an overwhelming number of key informants, but laws addressing discrimination remained absent or incomplete in a majority of jurisdictions. Communities facing multiple forms of marginalization, including communities of racial and ethnic LGBTI+ people, were found to face higher levels of discrimination and criminal justice involvement. And, despite greater public attention to civil and political issues such as same-sex marriage and discrimination laws, key informants noted that socioeconomic issues — which are key social determinants of health — were among their chief concerns. The opinions of these key informants, each one a local LGBTI+ stakeholder, helped to fill in the many gaps in data that the assessments revealed, including limited information on health disparities beyond HIV and STIs, and almost no large-scale data on socioeconomic conditions among LGBTI+ populations. Much of the data that did exist were focused on sexual minority men, including relating to HIV, STIs, and rates of depression, and occasionally data relating to HIV among transgender women.

Despite the many alarming results it presented, the research outcomes also highlighted the remarkable resilience of LGBTI+ communities. Even where formal programming or spaces for LGBTI+ people were limited, key informants noted the presence of informal spaces and social networks as a source of strength. HIV services stood out as a clear leader in health services for LGBTI+ people and nonprofit organizations led the way as being a source of collaboration and respectful dialogue with the community. The study also demonstrated that LGBTI+ advocates, communities, resources, and spaces exist throughout diverse cities, and that even in places with harsh anti-LGBTI+ laws and limited public resources to support LGBTI+ communities, these communities have found ways to support each other and survive.





Africa

2.7
QUALITY OF LIFE SCORE
REGIONAL

This study included 10 Fast-Track Cities in Africa: Bamako, Durban (eThekwini), Kampala, Kigali, Lagos, Lusaka, Maputo, Nairobi County, Yaoundé, and Windhoek. Three cities were selected from these to serve as examples with more detailed analyses, which follow this regional description; they are Durban (eThekwini), Kampala, and Maputo.

Among the lingering injustices of the colonial era in Africa are still-standing socioeconomic inequalities and anti-LGBTI+ legislation (particularly laws regarding same-sex male relations), both of which complicate progress for LGBTI+ communities. The continent also faces major inequities with respect to HIV that — while more widespread than elsewhere in the world — still disproportionately affect LGBTI+ people. Key informants in the 10 African cities also reported different priorities than those in the Americas and Europe, which often drive (financially, politically, and culturally) LGBTI+ movements elsewhere — a cautionary finding for those wishing to best support LGBTI+ health equity in Africa.

Quality of Life and Care

On average, key informants in Africa rated their local LGBTI+ quality of life at 2.7 (mode: 3; SD: .97), well below the global average of 3.2. Key informants also rated all health services worse than the global averages, with LGBTI+ affirming mental healthcare being rated worse of all, at only a 2.3 on a 1 to 5 scale (mode: 2; SD: 1.05) compared to a 3.2 score worldwide. Disturbingly, given the continent's disproportionate burden of the disease, HIV services were among those rated worse than the global average, at 3.3 out of 5 (mode: 3, SD: .98), compared to 3.8 across all cities.

"People (including healthcare providers) lack information about LGBTI+ [health]."

Key Informant, Kigali

Stigma was the most common barrier to health service access and utilization that was cited by the key informants, especially for transgender individuals. "The biggest challenge is the negative judgment," said an HIV project manager in Bamako, "however you translate it: stigmatization, rejection, discrimination."

Only one of the 10 African cities, Durban (eThekwini), had laws banning the practice of conversion therapy, or the nonscientific practice of attempting to change one's sexual orientation or gender identity. The persistence of such practices may contribute to the negative scores given to various types of care, and also contributes to mistrust of healthcare systems.[40]



69%

of key informants in Africa said access to **employment** was a "serious" problem for LGBTI+ people, compared to just 27% of key informants globally

Health Outcomes

Data regarding HIV prevalence was relatively complete among the African cities and demonstrated a clear need for HIV to remain a priority among LGBTI+ populations, as well as for LGBTI+ populations to remain a key group for city stakeholders coordinating HIV responses. With the exception of Yaoundé, the nine other African cities had some city-specific data available on population-wide HIV prevalence and all but Nairobi County, Lusaka, Windhoek, and Yaoundé had some city-specific data specifically on prevalence among sexual minority men. Bamako had the largest disparity between MSM and the general population, with 13.7% of sexual minority men living with HIV compared to 1.1% of the overall population, a 12.5 times higher prevalence.[41] Inequities in HIV burden were also found in Lagos (17.4%[42] versus 1.4%[43]), Durban (eThekwini) (48.2%[44] versus 27%[45] in Durban's province of KwaZulu-Natal), Kampala (12.2%[46] versus 6.9%[47]), Maputo (41.4% versus 10.4%)[48], and Kigali (10%[49] versus 4.3%[50]), when comparing sexual minority men to the overall population.

Regarding other aspects of sexual health, disaggregated data for sexual minority men exist in Kampala and Kigali with respect to chlamydia, gonorrhea, and syphilis, and with respect to chlamydia and gonorrhea in Lagos and Maputo. While prevalence of these conditions was generally lower than HIV, many of the rates were concerningly high. Kampala had relatively low rates of chlamydia and gonorrhea among sexual minority men than did the other cities, but a relatively high rate of syphilis at 10.3%.[51] The highest rates of chlamydia and gonorrhea among sexual minority men and transgender women were found in Lagos (18.3% and 25.8%, respectively)[52] and Kigali (9.1% and 8.8%, respectively).[53]

Data on mental health were relatively limited among the African cities. No city had population-based, SOGI-disaggregated data on anxiety, PTSD, or suicide, nor was any national SOGI-disaggregated data identified. Data existed in one city, Bamako, regarding depression among MSM, with a reported rate of 8%.[54] Additionally, there were national data applicable to Durban (eThekwini) (44% of MSM in South Africa).[55] These numbers suggest that depression and other mental health problems among sexual and gender minorities throughout cities in the African region could be quite high but requires additional epidemiological research to document the prevalence of mental health disorders and determine an appropriate response that is informed by both the data and the science.

Data on other indicators included in the study — obesity, smoking, drug use, and mortality — were even more limited, with only a few cities or national population-based data available that disaggregated results based on sexual orientation or gender identity. In Lagos, 15.4% of sexual minority men were reported to be current smokers. In terms of alcohol consumption, 34.1% of MSM in Lagos were current drinkers, and half of the current drinkers were described to have a drinking problem using the CAGE assessment for alcohol dependence.[56] In terms of alcohol consumption, 43.7% of MSM in Maputo were classified as problem drinkers using the AUDIT-C scale. Cannabis use in the 12 months preceding the survey was reported by 12% of MSM in Maputo; less than 3% of MSM used other drugs.[57]



Socioeconomic Factors

In terms of socioeconomic factors, perhaps not surprising given the longstanding socioeconomic injustices affecting African nations, key informants identified employment, housing, and food access for LGBTI+ individuals to be "serious" problems. For example, while globally, 27% of key informants said that LGBTI+ employment access was a "serious" concern, that number skyrocketed to 69% in Africa, where less than 3% said it was "not a problem."

With respect to the assessments, no city population-level had relevant data on the indicators used herein — unemployment rate, homelessness rate, poverty rate, or food insecurity — that were disaggregated by sexual orientation and/or gender identity. However, national rates for the selected cities on these topics were high, particularly for poverty, where rates ranged from 17.4% for Windhoek (Namibian national data) to 55.5% for Durban (eThekwini) (South African national data).[58] These high overall poverty rates, combined with the survey data on socioeconomic inequities facing LGBTI+ populations, support that the conclusion that this is a major issue in addressing LGBTI+ health equity in African cities, despite the lack of relevant LGBTI+ specific data.

Discrimination

Regarding discrimination, African key informants rated discrimination on the basis of gender identity, HIV status, and intersectional factors roughly the same as their global counterparts. However, key informants rated sexual orientation-based discrimination about 25% higher as a problem than did the average key informant worldwide. A majority (60%) said that sexual orientation-based discrimination was a "serious" problem, while less than 9% said it was "not a problem." Many key informants said that discrimination facing LGBTI+ people prevented access to services, hindered HIV responses, and caused significant mental health problems in their local communities.

Only one out of the 10 African cities selected — Durban (eThekwini) — has nondiscrimination laws pertaining to sexual orientation, gender identity, gender expression, and HIV status.[59] A similar pattern emerged with respect to the legality of same-sex relationships, with LGBTI+ rights in African cities ranging from having the same legal protections as non-LGBTI+ people (again, Durban (eThekwini)) to punishments that start with fines to life imprisonment (i.e., Lagos).[60] There are many reasons for this, but homophobic colonial laws, religious morality, and the idea that homosexuality is imported by the West are among the most influential. Among the African cities that were selected, only Durban (eThekwini) had regulations and policies that protect transgender individuals; the Alteration of Sex Description and Sex Status Act allows people to apply to have their sex status changed in the population archive, and consequently to receive identity documents and passports indicating their gender identity. The law necessitates the person to have undergone medical or surgical treatment, such as hormone replacement therapy, but gender affirmation surgery is not required.[61]

Criminal Justice

African key informants found the problems of police mistreatment, police targeting, and criminal treatment of sex workers to be more severe than the average across all 50 cities. About half rated all three of these issues as being "serious," with only a handful of key informants saying they were "not a problem." This corresponds with the findings of the assessments, which demonstrated that African LGBTI+ communities faced more penalizing laws and fewer protective laws than did communities in other regions. Criminalization of HIV issues and the disproportionate impact on people with multiple marginalized identities both ranked closer in line with global averages.

Most African cities have laws that criminalize transmission and non-disclosure of HIV status to sexual partners. Even when laws do not explicitly mention HIV in this context, some African cities, such as Durban (eThekwini), have used existing laws to charge individuals in cases such as this

"Discrimination by health care workers acts as a barrier to accessing health services."

Key Informant, Nairobi County

"Stigma and discrimination [make] people living with HIV default from accessing antiretroviral therapy services at health facilities."

Key Informant, Nairobi County

with attempted homicide;[62] in fact, more than half of the current cases worldwide criminalized transmission and non-disclosure of HIV status to sexual partners using general criminal laws.[63] Although sex work is widespread in African cities, each have laws governing sex work as illegal.

Community Resilience

Three trends emerged when key informants were asked about sources of resilience for their local communities: support from within the LGBTI+ community itself, including stemming from the resilience of individuals themselves; services from local organizations, including through support groups; and international donors, who funded many of these efforts (although organizational reliance on these sources caused some concerns about sustainability). When asked how local institutions can best support their community to grow its resilience, the most common requests were more collaboration with LGBTI+ individuals and organizations, public education about LGBTI+ identities, and advocacy to change negative laws and policies impacting the community.

"The main sources of resilience of this group are civil society organizations that have done their work in defense of human rights and have been the only institutions to work with these groups."

Key Informant, Maputo

"Even us at the frontline are feeling threatened and disempowered," said the director of a nonprofit in Durban (eThekwini). "Visible partnerships towards advancing lives and promoting rights" would provide a boost to the community, they said, as would "more meaningful dialogues or community activities than these last-minute tick boxes we have been having."

Key informants in Africa gave a lower score to how their local governments interact with LGBTI+ communities compared to the global averages, with an average score of 2.4 (mode: 2; SD: 1.19) compared to 3.0 worldwide. They ranked providers (3; mode: 3; SD: 1.15) and nonprofits (4; mode: 5; SD: 1.01) about equally to their global peers, and the private sector (2.7; mode: 2; SD: 1.19) just slightly behind the global average (2.9).

In terms of assessment factors used to gauge LGBTI+ community resilience, almost no evidence was found. This points to a major need that local, national, and international actors could support. In Durban (eThekwini), at least one LGBTI+ community space was identified, as was public funding for LGBTI+ community resources such as a tourism association and pride events.[64] Durban (eThekwini) also had other LGBTI+ spaces, and while all cities lacked any permanent social spaces (i.e., LGBTI+ bars), there have been places identified where gay men can socialize. Such spaces, community resources, and funding were not found in any of the other African cities included in the study. Furthermore, no cities had a local LGBTI+ office or liaison, or a public report or plan on advancing LGBTI+ equity.

Conclusion

The study's findings indicate a wide variety of challenges affecting LGBTI+ communities in African cities. Key informants in Africa scored their services and relationships with institutions as worse, and their challenges greater, than the global averages around most issues on which they were surveyed. The challenges facing these communities were reinforced by the findings of the assessments, which indicated fewer legal and political supports (as well as less visibility and data) than was available elsewhere in the world. Nevertheless, internal community strengths and support from nonprofits stood out as bright spots in reflections on community resilience, with nonprofits scoring slightly better in Africa than the global average, as a plurality gave nonprofit organizations a 5 out of 5 score on relationships with LGBTI+ people. Additionally, a comparison with other cities around the world demonstrates that while the challenges facing LGBTI+ people in Africa may be greater than those in some other parts of the world, the underlying issues — and solutions — also bear many similarities.



4.0
QUALITY OF LIFE SCORE
CITY

Select Cities

Durban (eThekwini)

Situated in South Africa, the city of Durban (eThekwini) faces national contexts that includes one of the highest poverty rates among the cities included in this study as well as a high overall rate of HIV. At the same time, because of national and local LGBTI+ inclusive measures, Durban (eThekwini) stood out among the 10 African cities as a clear leader on LGBTI+ health equity.

In Durban (eThekwini) alone, same-sex marriage was legal, conversion therapy was banned, and transgender people were able to change their gender markers on their identification documents — a key means by which to access health services and avoid LGBTI+ violence and stigma.

Durban (eThekwini) also stood out for its community supports, including having a community space for LGBTI+ people and some public funding of LGBTI+ events. Nevertheless, key informants said these resources were limited and urged institutions to increase their support, especially given the violence that LGBTI+ individuals must still confront. “Organizing Durban Pride in Durban is a nightmare,” said the director of a local LGBTI+ organization, who says support for the event has dwindled. Pride is meant “to create an awareness, build bridges, showcase talent, and promote Durban and eThekwini as a Safer City.”

Another key informant who works as a psychotherapist in the community encouraged local actors to “create safe spaces, more support groups, and encourage more family building amongst their respective communities in order to spread awareness... Just allow [LGBTI+ individuals] to live as normal people. If they don’t want to change to suit anyone, they shouldn’t be killed for it.”



2.3

QUALITY OF LIFE SCORE

CITY

Kampala

Kampala is one of the fastest growing cities in Africa and is situated in a country known throughout the world for its efforts to pass extreme anti-LGBTI+ legislation, the worst of which has so far been stymied. Sadly, but not surprisingly, key informants in Kampala gave their city one of the lowest quality of life scores (2.3; mean: 2; SD: .71) of the 50 cities included in the study.

Unlike the global trend, in Kampala, key informants rated sexual orientation-based discrimination as a greater problem than discrimination on the basis of gender identity, with all but one informant saying that sexual orientation-based discrimination was a "serious" problem. Still, many noted in their comments that the situation for transgender women in Kampala was particularly dire, indicating that perhaps homophobic attitudes driven by the higher visibility of that issue are also affecting transgender people, regardless of their sexual orientation.

"The existing laws and policies inhibit open provision of service [and] successful HIV treatment."

Key Informant, Kampala

Moreover, in Kampala, the mistreatment and targeting of LGBTI+ people by law enforcement were considered greater concerns than they were internationally. "Transgender people face the hardest hardships and queer sex workers, too, where they have been beaten up and jailed," said a local activist working with LGBTI+ women. Additionally, the director of a local HIV organization said, "In my city, it's still illegal to say you're an LGBTI+ member. This makes it hard to even advertise the organizations that provide [services]."

The biggest request from key informants was for more funding and support from local and international actors. The director of a local organization for people living with HIV said key to their success has been the "availability of caring non-state actors," specifically naming the US President's Emergency Plan for AIDS Relief (PEPFAR), the Global Fund to Fight AIDS, Tuberculosis and Malaria, and diplomatic missions from countries such as the United States and Sweden.

Most key informants also noted the need for legal reform and some placed this above all other concerns. "First," advised one key informant, "address the harsh policy."



3.0
QUALITY OF LIFE SCORE
CITY

Maputo

Key informants in Maputo rated their socioeconomic, criminal justice, and discrimination issues as being more problematic than the global averages. The most significant concern raised by key informants was lack of access to employment, followed by mistreatment by the police and discrimination facing people with multiple marginalized identities. These issues are likely caused in part and exacerbated by the city's lack of legal protections for LGBTI+ people as well as laws recognizing and affirming their identities.

"Poor access to employment and employability" were among the top concerns of one key informant, along with "poor access to education due to stigma and discrimination" facing the LGBTI+ community. Other key informants concurred that stigma was a "serious" concern. One key informant noted that psychological violence may seem like less of a concern than physical violence, "but if we go deeper, we can see that this violence affects most people and has been the reason that people in this community even hang themselves or have mental disorders."

Healthcare services were rated more closely to the global average, with HIV services faring particularly well, with an average score of 4 on a 1 to 5 scale. Additionally, key informants gave better ratings to how local government, providers, and the private sector interact with their local LGBTI+ community than did the average key informant worldwide. While these scores (all averaging 3.6 on a 1 to 5 scale) still left significant room for improvement, they represented a potentially relevant strength for the LGBTI+ community in Maputo compared to others.

One local LGBTI+ activist who gave above-average scores to how local institutions interact with the community called for more support: "Not monetary, but visibility: having the right to walk without being discriminated against or stoned just for carrying the LGBT flag... Many of us need that support."



"Generally, effeminate gay men and the transgender community face additional challenges by the way these groups freely express their sexuality and gender, which is contrary to heterosexual expressions."

Key Informant, Maputo



3.2
QUALITY OF LIFE SCORE
REGIONAL

The Americas

In the Americas, 20 cities participated in the study: Atlanta, Baton Rouge, Buenos Aires, Charleston, Chicago, Columbia, Dallas, Denver, District of Columbia, Kingston, Mexico City, Miami-Dade County, Montréal, New Orleans, New York City, Oakland, Phoenix, Rio de Janeiro, San Francisco, and São Paulo. Three of these cities — Kingston, New Orleans, and Mexico City — were selected to serve as examples with more detailed analyses, which appear after this regional description.

Together, these Fast-Track Cities span the entire Western hemisphere and represent a variety of cultures and political climates for LGBTI+ individuals. While the region has been making significant progress in recent years in recognizing same-sex marriages and banning certain forms of discrimination — and while many of these cities are known for their vibrant LGBTI+ communities — the results of this study show that there remain significant challenges.

Quality of Life and Care

Overall, key informants in the Americas gave their cities an average quality of life score that matched the global average: 3.2 on a 1-to-5 scale (mode: 3; SD: 0.95). Less than 6% gave their city a 5 out of 5, indicating that few believed that their city had no room for improvement.

Key informants from the Americas also rated access to LGBTI+ inclusive care roughly the same as did their global counterparts. As with the global trend, gender-affirming care (2.8 on a 1 to 5 scale; mode: 3; SD: 1.10) and mental health care (2.8; mode: 2; SD: 1.03) were rated lower than primary care (3.2; mode: 3; SD: 1.12) and HIV care (3.8; mode: 4; SD: 1.06), which was rated the best.

Even in cities known to be LGBTI+ friendly, many gave mediocre scores to the availability of inclusive and quality care. “In San Francisco, we are on the cutting edge of LGBTQ+ services, although there is always room for improvement,” said one local community advocate who specifically noted care for older adults as an area in which more attention was needed.



Many key informants pointed to nonprofit organizations and LGBTI+ leaders as driving LGBTI+ inclusive care. “Most of that work is being taken up by LGBTQI+ health providers, nonprofits, and advocates to push government and private sectors to be more inclusive and address LGBTQI+ disparities,” said a key informant in Chicago.

Health Outcomes

Compared to the other regions, data regarding HIV prevalence with respect to sexual and gender minority populations were the most complete among the cities in the Americas included in the study. Data were the most comprehensive among sexual minority men, with the highest HIV prevalence reported in Baton Rouge (44.7%),[65] followed by Miami-Dade County (42.8%) and New Orleans (36.9%).[66] Universally, across all cities in the Americans, extremely concerning racial and ethnic disparities exist for HIV prevalence data. In the United States, Black sexual minority men having the highest prevalence out of any racial group, followed closely by Latinx sexual minority men.[67] Similarly, across cities, transgender women represent a population that is most severely affected by HIV with an average estimated HIV prevalence of 42.2% across the cities in the Americas. Cities with the highest HIV prevalence among transgender women included Atlanta (58.4%), New York City (52.2%), New Orleans (44.6%), and San Francisco (41.2%). Among transgender women, similarities among racial and ethnic disparities exist for HIV prevalence data, with Black transgender women having the highest HIV prevalence out of any racial group.[68] The constant and unrelenting exposure to sexual and gender minority stigma compounded by the psychosocial challenges associated with social disadvantage and economic marginalization exacerbates disparities in HIV prevalence among these populations. Among sexual minority men and transgender women, this invalidates their sexual and gender identity and can lead to behaviors (e.g., substance use, sex work, healthcare avoidance) that potentiate HIV acquisition and transmission risk.

Disaggregated data for sexual minority men exist in nearly all of the selected cities with respect to chlamydia, gonorrhea, and syphilis. Overall, STI prevalence and incidence among sexual minority men — including primary and secondary syphilis and antimicrobial-resistant gonorrhea — is greater than that reported in sexual minority women and both heterosexual women (who have sex with men only) and men (who have sex with women only). There was a general lack of city-specific, population-level STI data available for transgender individuals. While the prevalence of these diseases is generally lower than HIV among sexual and gender minorities, many of the rates were still concerningly high. Furthermore, both chlamydia and gonorrhea differed in prevalence by anatomical site (e.g., urethral, rectal, pharyngeal) among sexual minority men. With respect to urethral chlamydia among sexual minority men, Miami-Dade County (5%) had the lowest prevalence and the highest was seen in San Francisco (5.9%); rectal chlamydia rates were much higher, ranging from 14.3% in Miami-Dade County to 18.4% in San Francisco.[69] As far as urethral gonorrhea rates among sexual minority men, Miami-Dade County (5.4%) had the lowest prevalence and the highest was seen in New York City (8.9%); rectal gonorrhea rates were much higher, ranging from 12.2% in Miami-Dade County to 14.8% in San Francisco. The prevalence of syphilis among sexual minority men ranged from 8.3% in Denver to 21.9% in San Francisco.[70]

Population-level data on the prevalence of specific mental health disorders among sexual and gender minorities was robust for the cities in the Americas, but there remains plenty of room for strengthening these data. Rates of depression and anxiety among all sexual and gender minority groups are consistently higher than those among the general adult population. Among MSM, rates of depression range from 47.3% (San Francisco) to 47.8% (New York City) across cities as compared to 5-12% among the general adult population.[71,72,73] For alcohol and drug use across cities in the Americas, on average 26.2% of sexual minority men reported drinking alcohol at least three days per week, and 10.6% were heavy drinkers (i.e., they consumed at least four drinks per day or consumed an amount equal to six drinks per occasion).[74] Furthermore, among sexual minority men, marijuana was the drug most likely to be used (average for New York City,

Chicago, San Francisco, and Denver, with negligible variation: 46.3%), followed by poppers (amyl nitrates) (36.6%); hallucinogens, including ecstasy (24%); cocaine (19.3%); amphetamines (12.9%); and injection drug use (10%).[75] Among the cities (New York City, San Francisco, Chicago) with population level data specific to transgender women, the average prevalence (differences by city are insignificant) of specific disorders was as follows: lifetime and current major depressive episode, 35.4% and 14.7%, respectively; suicidality, 20.2%; generalized anxiety disorder, 7.9%; and posttraumatic stress disorder, 9.8%. Among transgender women, the average prevalence (differences by city are insignificant) of alcohol dependence is 11.2% and substance use dependence is 15.2%.[76]

Socioeconomic Factors

On socioeconomic issues, key informants from the Americas reported more significant problems regarding LGBTI+ access to adequate housing and food than the global average. In the Americas, 55% said that housing access was a "serious" concern, compared to 42% who said the same globally. Regarding food access, 92% of key informants in the Americas felt that this was at least somewhat of a problem, compared to 76% globally who felt the same. Most of the key informants from the Americas came from the United States, a country with ample resources to address these concerns, and yet the response by institutional actors to address socioeconomic concerns facing the LGBTI+ community were ranked worse in the Americas than globally. Latin America is also known to face rising socioeconomic disparities generally. These factors — combined with limited antidiscrimination laws (described below) — likely explain why the Americas fared poorly on these key social determinants of health.

With respect to the assessments, there was scant city-specific, population-level data on unemployment rates, homelessness rates, poverty rates, or food insecurity that were disaggregated by sexual orientation and/or gender identity. In the United States, there were limited state-specific and country-level population data; on average LGBTI+ people collectively have a poverty rate of 21.6%, which is much higher than the rate for cisgender heterosexual people of 15.7%. It is important to note that among LGBTI+ people, transgender people have an especially high rate of poverty (29.4%).[77] A major contributor to the high rate of poverty among transgender individuals is their high (15%) unemployment rate — three times higher than the unemployment rate in the U.S. population at the time of the survey (5%). On average, lesbian (17.9%) and heterosexual (17.8%) cisgender women have higher poverty rates than gay (12.1%) and heterosexual (13.4%) cisgender men. But cisgender lesbian women do not have significantly different poverty rates than cisgender heterosexual women. Finally, bisexual cisgender women (29.4%) and men (19.5%) had higher poverty rates than heterosexual straight women and men, respectively.[78] As far as population-level data on recent homelessness in the US, 8% of transgender and 3% of cisgender sexual minorities experienced this versus 1% of cisgender heterosexuals.[79]

Discrimination

Key informants from the Americas rated discrimination relating to sexual orientation and HIV status about equally with respect to the global ratings. However, they rated the problems of discrimination on the basis of gender identity and intersectional discrimination facing LGBTI+ racial and ethnic minorities as more significant problems than the overall average of key informants surveyed.

In the United States, same-sex relations have been legal nationwide since 2003[80] and same-sex marriage has been legal in every state since 2015.[81] In the Brazilian cities of Rio de Janeiro and São Paulo, LGBTI+ rights are among the most advanced in Latin America, including the right for same-sex couples to marry since 2013.[82] Montréal, Mexico City, and Buenos Aires have also legalized same-sex relations and same-sex marriage since 2004,[83] 2009,[84] and 2010,[85] respectively.

Across all selected cities in the Americas, hate crime is recognized and punishable by law. In all selected United States cities, hate crimes based on sexual orientation or gender identity are punishable by federal law.[86] Universally, across the Americas, transgender people are allowed to access appropriate gender-based facilities and are able to change their gender marker on legal documents, although the requirements and therefore ease of doing so varies.[87,88,89]

Criminal Justice

The Americas saw sharp disparities compared to their global neighbors with respect to criminal justice issues. For example, key informants in the Americas scored the problem of LGBTI+ people being targeted for arrests about 13% higher than the global average and scored about 16% higher than the global average the disproportionate impact of the criminal justice system on LGBTI+ racial and ethnic. Indeed, 41% of key informants in the Americas said that the disproportionate impact on LGBTI+ people of color was a "serious" problem, compared to 30% who said so globally.

As noted, LGBTI+ identities and relationships were not criminalized in any of the cities from the Americas included in the study. With respect to the legality of transactional sex in the Americas, all selected cities have laws making the practice of exchanging sex for money illegal, except for Buenos Aires, Mexico City, Rio de Janeiro, and São Paulo; however, it is illegal to operate a brothel in these cities, and vagrancy laws are routinely used against sex workers soliciting clients on the street. In Montréal, offering sexual services is not illegal; however, purchasing and using sexual services is illegal.[90] With respect to the exposure and non-disclosure of HIV status to sexual partners, only Montréal,[91] Phoenix, District of Columbia, and Dallas have no criminalization laws, while Atlanta, Baton Rouge, Charleston, Chicago, Columbia, Miami-Dade County and New Orleans criminalize or control behaviors through HIV-specific statutes and regulations.[92]



Community Resilience

Key informants in the Americas rated LGBTI+ community engagement by local government and healthcare providers about the same as did their peers globally, but rated nonprofits and businesses more poorly than did key informants worldwide. Still, as in other parts of the world, nonprofit organizations were the clear leaders, scoring an average of 3.8 on a 1-to-5 scale compared to a 3.0 score for local government and providers, and a 2.8 score for businesses.

According to the assessments, factors thought to support LGBTI+ community resilience across the selected cities in the Americas were robust. All cities in the Americas are appointed with LGBTI+ community spaces and community resources (e.g., tourism association, pride event) and have allocated funding for LGBTI+ specific service organizations. Similarly, in existence for all selected cities in this region, are publications on LGBTI+ scientific research, or reports or plans on advancing LGBTI+ health equity.[93-109]

Conclusion

Overall, there were no areas in which key informants from the Americas provided average ratings that were better than the global average, and in several areas (e.g., housing, criminal justice, racial impact) they rated their local conditions worse. Therefore, despite the progress that has been made on LGBTI+ issues in the Americas in recent decades, the participants from these cities reported worse overall conditions than did their colleagues around the globe. Many of these challenges seem related to factors connecting LGBTI+ identities to other social justice issues, namely poverty and racism.



2.7
QUALITY OF LIFE SCORE
CITY

Select Cities

Kingston

"I would say nonprofit organizations in Jamaica are leading the way in providing services to LGBT+ people, such as free HIV/STI testing, HIV care/treatment, offering PrEP (especially [to those in] serodiscordant relationships), and psychosocial support for those that need it."

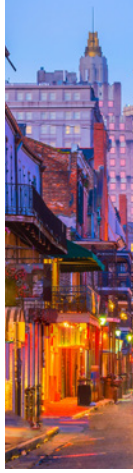
Key Informant, Kingston

Key informants in Kingston rated the quality of life for their LGBTI+ population at 2.7 on a 1 to 5 scale, well below the 3.2 global average. They also rated access to various types of care below global averages, although the difference was particularly stark with respect to mental health care (2.3 locally versus 2.8 globally) and gender-affirming care (2.3 locally versus 2.7 globally).

Every key informant noted that nonprofit organizations were doing the most to address inequities, while others needed to do more. LGBTI+ health "is mostly being addressed by nonprofit organizations and some clinical and service providers," said one key informant, "so these services [are] not adequate in relation to access and the quality of service." While the local government scored low on its interactions with the LGBTI+ community (1.5 on a 1 to 5 scale), the data assessment promisingly found numerous formal engagement mechanisms on LGBTI+ issues (such as an advisory group and inclusion in public reports), indicating that the basic infrastructure was in place for the government to work on these relationships.

Sexual orientation and gender identity-based discrimination were both rated equally in Kingston, with all but one key informant saying these were both "serious" problems. Notably, key informants pointed to widespread stigma and discrimination in different facets of life as impacting mental health, socioeconomic opportunity, and the willingness of LGBTI+ people to seek care.

One key informant called for more education "for the general population [and] especially healthcare workers for them to understand [the] LGBTI+ community, their gender identity/sexual orientation, etc. The community needs support — whether psychosocial or financial — to be sustainable in society."



3.3
QUALITY OF LIFE SCORE
CITY

New Orleans

Overall, key informants in New Orleans gave their city a quality of life score for LGBTI+ people (3.3) roughly equal to the global average (3.2). However, with respect to healthcare access, key informants rated the city considerable worse on access to HIV services (3.3 compared to 3.8 globally) and gender-affirming care (2.3 versus 2.7).

Across the board, key informants scored socioeconomic challenges in New Orleans as being more severe than the global average, although the difference was particularly striking with respect to access to sufficient and nutritious food. While only 13% of global key informants said food access for LGBTI+ people is a "serious" problem, 58% of key informants in New Orleans reported this challenge as being "serious," a stark reality for a city in one of the world's wealthiest nations.

Similarly, key informants rated their LGBTI+ community as having much more significant criminal justice issues than the global average. Eighty-three percent of key informants said that criminal justice disparities among LGBTI+ people of color is a "serious" challenge, compared to just 30% of key informants globally.

"There are areas of our city that are very accepting and LGBTI+ friendly and some LGBTI+ persons in New Orleans have robust support systems of family and friends," said one key informant, "but this is not universal."

Many key informants noted the importance of community organizations as a source of resiliency but said that more was needed. "Local governments, healthcare providers, nonprofit organizations, and the private sector should seek out the advocates that are making efforts and trying to get something done," said one key informant. Another recommended, in what was a common theme, "actually providing funding and resources to the organizations that can do this well" and "avoiding concentrating too much funding or resources in any particular organization."

"Housing discrimination and employment discrimination are pretty rampant... We have a lot of hard-working people that can never get their head fully above water."

Key Informant, New Orleans



3.2

QUALITY OF LIFE SCORE

CITY

Mexico City

"Mexico City defines itself as being LGBTI+ friendly, but in fact, it is far from being so."

Key Informant, Mexico City

"Those with low education background face a lot of challenges to get easy access to health facilities due to the complexity of bureaucratic processes... There are few options for the transgender community."

Key Informant, Mexico City

Overall, key informants in Mexico City gave LGBTI+ conditions in their community lower marks than did key informants globally. On access to care, they gave their city worse scores on the availability of primary LGBTI+ inclusive care (2.8 versus 3.1 globally, on a 1 to 5 scale), mental health care (2.7 versus 2.8 globally), and HIV care (3.3 versus 3.8 globally). However, they rated access to gender-affirming care as marginally better (2.8 versus 2.7 globally). The differences in scores were mostly minor deviations from the global averages, with the exception of HIV care, which is concerning given the high burden of HIV among LGBTI+ people.

On socioeconomic issues, key informants rated both employment and housing access as bigger problems than did their peers worldwide. The exception was on food access, for which one-third said it was "not a problem" compared to one-quarter of key informants globally, while no key informants in Mexico City said it was a "serious" problem compared to 13% who did so globally.

Discrimination on the basis of sexual orientation was rated as slightly more problematic in Mexico City than globally, and intersectional discrimination was rated equally. However, discrimination on the basis of gender identity and regarding HIV status was rated as more of a problem. Most criminal justice issues were also rated as more problematic in Mexico City than globally, with the exception of issues relating to sex work, which (while still deemed a problem by most key informants) were rated as less of a problem than they were worldwide.

One key informant reported "arbitrary cases of detention of people who get found 'cruising,'" or looking for other LGBTI+ people publicly. Another noted "greater police violence" facing the LGBTI+ community, including those who engage in sex work, compared to the general population.

When asked about resilience in the local community, key informants noted nonprofit organizations, bars, and informal social spaces as key areas of support, but they said more support was needed from the government. One key informant, who named bars and other venues as the current center of LGBTI+ community, called for "implementation of permanent campaigns [and] creation of community centers and kitchens that give priority attention to LGBTI+ people."



Asia-Pacific

3.6
QUALITY OF LIFE SCORE
REGIONAL

Five cities from the Asia-Pacific region were included in this study: Bangkok; Melbourne; Quezon City; Taipei; and Tokyo. Three of these — Bangkok, Melbourne, and Quezon City — were selected as examples for individual analyses, which follow this regional description.

While the number of cities in this region was smaller than that for the other regions, it is reflective of the fact that the Fast-Track Cities network in the region is relatively small, although expanding (i.e., Tokyo is a prospective Fast-Track City). The expansion of the Fast-Track Cities network in the region is important because Asia has experienced a surge in HIV rates, particularly among sexual minority men and transgender individuals, over the past several years.

Quality of Life and Care

Key informants in Asia-Pacific rated the quality of life for LGBTI+ individuals at a considerably higher rate than the global average, giving their cities a score of 3.6 on a 1 to 5 scale (mode: 4; SD: 0.91) compared to the worldwide average of 3.2. Tokyo received the lowest score of the cities included in the study, with an average rating of 2.2, while Quezon City received the highest score, with a rating of 4.0.



Access to all types of care were similarly rated better in Asia-Pacific than they were globally, though they followed the same trends as were observed worldwide, in which access to HIV-related care was rated best (4.2 on a 1 to 5 scale; mode: 5; SD: 0.99), followed by culturally competent primary care (3.6; mode: 4; SD: 0.91). Lowest-scoring types of care were gender-affirming care (3.1; mode: 3; SD: 1.30) and mental health care (3.3; mode: 4; SD: 1.20).

"LGBTI+ health disparities are addressed mainly by non-profit organizations working for LGBTI+ people," said a key informant in Tokyo who rated healthcare access there to be fairly poor. "Women, transgender people, racial and ethnic minorities, and people with disabilities" all face additional barriers to accessing care.

Health Outcomes

Data on HIV prevalence with respect to sexual and gender minority populations is the most detailed among the selected cities in Asia. Disaggregated data were complete among sexual minority men with the highest HIV prevalence reported in Bangkok (19.5%)[110] followed by Quezon City (8.8%),[111] Melbourne (4.9%),[112] Taipei (4.3%),[113] and Tokyo (3%).[114] Similarly, transgender women in Asia also are at considerable risk for HIV, with the highest estimated HIV prevalence seen in Bangkok (12%-13.5%).[115,116] In Melbourne, the limited data show an approximate HIV prevalence among transgender women of 4.5% and 2.5% among transgender men.[117] These groups experience higher rates of HIV in their communities due to varying social, demographic, and economic factors, including victimization, stigma, discrimination, and harassment, all of which leads to further socioeconomic marginalization and exacerbates disparities in HIV among these populations. The HIV rates experienced by LGBTI+ people, particularly sexual minority men and gender minority individuals, are concerning as HIV rates in the region have trended upward over the past decade.[118]

Despite effective treatments, lack of access to culturally competent and stigma-free health care for sexual and gender minorities in the cities in the Asia-Pacific region leads to higher STI rates. In addition, the high prevalence of STIs is facilitated by a sex industry fueled by tourism and

local consumption. Among the selected cities that had disaggregated data on the prevalence of chlamydia and gonorrhea among sexual minority men, the lowest rate was seen in Quezon City (0.7% and 3.5%, respectively)[119] and the highest in Bangkok, with chlamydia prevalence at 16% and urethral, rectal, and oropharyngeal gonorrhea, 34.7%, 29%, and 27.9%, respectively.[120] Syphilis infection among sexual minority men in the selected cities in Asia was also relatively elevated with the highest prevalence seen in Bangkok (24.4%)[121] and the lowest in Taipei (2.2%)[122] followed by Quezon City (2.1%).[123] Across selected cities in the Asia-Pacific region, there is a general lack of city-specific, population-level STI data for both transgender women and men. However, data from Bangkok show that a high prevalence of syphilis (3.2%), chlamydia (22.9%), and gonorrhea (14.3%) among transgender women.[124]

"It is difficult to be open as LGBTI+ and... live a normal, socially-acceptable life if sexual orientation is not disclosed."

Key Informant, Tokyo

Across the globe, substantial evidence has shown that sexual and gender minorities experience overall poorer mental health outcomes compared to their heterosexual counterparts or the general adult population. Although the governments within the selected cities in Asia have increased legislation and provided more accessible mental health services recently, there remains a general taboo and stigma around mental health, particularly within families and the community in which people live. Hence, people often do not seek treatment for fear of being ostracized; instead, they turn to either traditional family care alternatives or religious alternatives that maintain a sense of pride within one's immediate family. Overall, there was a lack of disaggregated data at the population level across cities. Rates of depression and anxiety among sexual and gender minority groups remain significantly higher due to a combination of discrimination, victimization, and internationalization of stigma, among other factors. Concerningly, transgender women in Bangkok have an estimated 58.2% prevalence of depression,[125] and in Melbourne, depression rates range from 21.3% among intersex individuals[126] to 57.2% among transgender women and men.[127] In terms of suicidality, among gay and bisexual men in Taipei, 31% reported experiencing suicide ideation or attempting suicide, including 14.6% who reported having attempted suicide at some point in their lifetime.[128] In Melbourne, 30.3% of LGBTI+ individuals reported a suicide attempt at some point in their lives, including 5.2% who reported this within the past year.[129]

Comparisons on drug and alcohol use were challenging because not every city had disaggregated data among sexual and gender minority groups at the population level and the way data were measured and reported varied in terms of quantity, frequency, and severity of use versus substance use disorder. Data that were available at the population level showed that 79.1% of transgender women and 75.1% of transgender men in Bangkok reported alcohol use in the past 12 months.[130] In terms of meeting diagnostic criteria for alcohol use disorder, the highest was seen in Quezon City with a prevalence of 24.7% among sexual minority men.[131] Data on alcohol consumption in Melbourne grouped sexual minorities, including lesbian, gay and bisexual individuals, indicating that 22% reported drinking that exceeds lifetime risk guidelines and 38% reported drinking that exceeds single-occasion risk guidelines.[132] Regarding other substance use, among transgender individuals in Bangkok, marijuana prevalence was the highest (12% compared to 5.5% among cisgender counterparts), followed by kratom (9%), amphetamine pills (3.0%), and crystal methamphetamine (2%).[133] Moreover, the prevalence of any substance use in Melbourne among lesbian, gay and bisexual individuals is 40%.[134]

Tobacco use is also highly prevalent among gender minorities in Bangkok, with 67% of transgender women and 56.9% of transgender men having smoked tobacco in the past 12 months;[135] in Melbourne, 16% of sexual minority individuals reported daily smoking.[136] Sexual minority women in Quezon City have a 24.3% prevalence of smoking, whereas among sexual minority men, there is a 71.3% prevalence of smoking.[137] Finally, in Melbourne, research shows that 39% of LGBTI+ individuals identify as having some form of a disability or chronic health condition.[138]

Socioeconomic Factors

Key informants in these cities rated socioeconomic concerns of employment, housing, and food access below the global averages. Access to employment was the biggest socioeconomic concern, of which only 8% said it was not a concern at all, but only 14% said it was a "serious" concern, with a majority of the latter being from Bangkok. The remaining 78% of key informants rated employment as a minor or moderate concern. Access to food was the lowest of these concerns, with 61% saying that was "not at all a problem" for their local LGBTI+ population; again, Bangkok was the city in which this which concern levels for this issue were highest. Overall, key informants in the Asia-Pacific region gave better ratings to the local response to these socioeconomic challenges than did key informants globally.

With respect to the assessments, there was a general lack of disaggregated population-level data among sexual and gender minorities with respect to the prevalence of unemployment, homelessness, poverty, and food insecurity. There exists little city-specific, but some country-level, population data on the prevalence of poverty among LGBTI+ individuals collectively, ranging from 9.9% in Bangkok to 12.6% in Melbourne and 16.6% in the Philippines. Regarding disaggregated population-level data on food insecurity, among LGBTI+ individuals, the prevalence of undernourishment ranged from 9.3% in Bangkok to 14.5% in the Philippines.[139]

"Many LGBTI+ people don't come out to others. Some LGBTI+ people are not accepted by their family. LGBTI+ teenagers don't get enough support in schools. Some LGBTI+ people are [unable] to find jobs."

Key Informant, Taipei

Discrimination

Overall, key informants in the Asia-Pacific region gave better scores on the problem of various types of discrimination than did the average key informant globally. However, unlike the global trend, HIV-based discrimination outranked intersectional discrimination as a concern in Asia-Pacific and roughly tied gender identity-based discrimination as a problem. Sixty-four percent of key informants said HIV-related discrimination was a "moderate" or "serious" problem, compared to 61% who said the same about gender identity-based discrimination, with fewer feeling the same about sexual orientation-based or intersectional discrimination. The relative strength of HIV discrimination as a concern should draw note as HIV advocates seek to address stigma as part of the global strategy to end the HIV pandemic.

In terms of the legal landscape explored in the assessments, neither same-sex marriage nor any other recognition of same-sex relationships are available in Bangkok, Quezon City, or Tokyo, while same-sex marriage is legal in Taipei and Melbourne.[140] Same-sex marriage has been legal in Taipei since 2019,[141] and Taipei enacts legal protection against discrimination based on sexual orientation and gender identity in education,[142] as well as protections against discrimination based on sexual orientation at work.[143,144] Bangkok enacted broad anti-discrimination laws covering sexual orientation and gender identity and as of 2019; a civil partnership is being discussed by the Thai government which, if passed, would grant same-sex couples several rights of marriage, including property and inheritance rights.[145] Additionally, Melbourne has enacted legal protections to support the LGBTI+ community from discrimination.[146] In 2003, Quezon City approved an ordinance banning discrimination against sexual minorities[147] and the Tokyo Metropolitan Government has passed legislation banning discrimination based on sexual orientation and gender identity in workspaces.[148] Universally, across the selected cities of the Asia-Pacific region, transgender people are allowed to access appropriate gender-based organizations and are able to change their gender marker on legal documents; however, some key informants made comments to the contrary, indicating ongoing challenges facing transgender people in navigating legal systems.

Criminal Justice

As with problems related to socioeconomics and discrimination, key informants in the Asia-Pacific cities rated as less serious issues relating to criminal justice, when compared to global averages. As was the case globally, the legality of sex work and treatment of sex workers is the criminal justice issue rated most severely. Fifty percent of key informants said that this issue represented a "serious" or "moderate" problem for the LGBTI+ community in their city, while 31% said it was

a “minor” problem and 19% said it was “not a problem.” The next highest-rated problem was the treatment of racial and ethnic LGBTI+ minorities by the criminal justice system, followed by mistreatment of LGBTI+ people by police, the criminalization of HIV, and finally, the targeting of LGBTI+ people by law enforcement, which most said was “not a problem.”

The assessments found that same-sex relations and identities were legal throughout the cities selected for the study in Asia-Pacific. Bangkok, Melbourne, Quezon City, and Tokyo all criminalize and attempt to modulate behaviors through HIV specific statutes and regulations which penalize people who choose to not to disclose their HIV status and hold others liable for transmitting HIV to their sexual partners.[149] Regarding the legality of transactional sex in the selected cities, all have laws prohibiting the practice of exchanging sex for money.[150] However, in Bangkok and Quezon City, sex work is somewhat tolerated among the society with minimal law enforcement and legal action against sex workers.[151] Furthermore, in Tokyo, the definition of “prostitution” is “intercourse with an unspecified person in exchange for payment,” and therefore fails to account for the sale of other sexual services which have become widespread and are considered legal.[152]

Community Resilience

In written comments, key informants presented as common sources of resilience the work being done by nonprofit organizations and the social networks of LGBTI+ people themselves, including families of choice. Other key informants mentioned LGBTI+ community events, greater visibility in recent years in the media, and support from friendly business and government leaders as sources of resilience.

In terms of supporting community resilience, all four sectors included in the survey — local government, providers, nonprofits and the private sector — fared better across the six Asia-Pacific cities than they did globally. However, while nonprofits still received the best marks, local government and the private sector more significantly outperformed the global averages. Nonprofits received a 4.1 score on a 1 to 5 scale (mode: 4; SD: 1.00) compared to a 3.9 globally; the private sector received a 3.5 (mode: 3; SD: 1.08) compared to 2.9 globally; and local government received a 3.4 (mode: 4; SD: 1.25) compared to 3 globally. In a change from the global trend, providers — who came in second worldwide in terms of how well they engage with the local LGBTI+ communities — came in last in the Asia-Pacific region, with a 3.3 score (mode: 4; SD: 1.16), although they were only modestly behind local government and the private sector.

Factors thought to support LGBTI+ resilience were found in all the selected cities in the Asia-Pacific region, including community spaces and resources (e.g., tourism association, pride events). Additionally, in all cities, public funding has been allocated for LGBTI+ specific service organizations. Similarly, LGBTI+ scientific research was available for all selected cities in this region, including reports or plans on advancing health equity in the local and wider community.

Conclusion

The cities in the Asia-Pacific region that were included in this study demonstrated a variety of strengths relative to the average city globally, including higher ratings for healthcare services and public engagement, and lower levels of concern around socioeconomic, discrimination, and criminal justice-related problems. Concerns regarding HIV-related discrimination rated relatively highly as community concerns, and providers scored relatively poorly in terms of their relationships with LGBTI+ communities. In addition, of all the problems included in the survey, only two — food access and targeting of LGBTI+ individuals by police — were rated as “not a problem” by a majority of key informants, indicating that a wide variety of challenges still exist for these communities.

Additionally, data assessments showed HIV disparities facing LGBTI+ individuals in the Asia-Pacific region that were of increasing concern, as well as other health inequities where data were available, such as with respect to substance use and mental health. Legal protections and policies recognizing LGBTI+ identities and relationships were also limited.



3.4
QUALITY OF LIFE SCORE
CITY

Select Cities

Bangkok

Overall, key informants in Bangkok gave their city a higher quality of life score than the global average, 3.4 on a 1 to 5 scale compared to 3.2 globally. However, on three out of four types of care, they rated their city well below the global averages; this was especially true regarding mental health care, in which a majority of key informants gave the lowest available score of 1, and the average was just 1.7, compared to a 2.8 worldwide.

However, with respect to gender-affirming care, key informants gave Bangkok a better score than the global average: 3.1 versus 2.7 globally. "Gender-affirming surgery is readily available in Bangkok," a physician and researcher said. "In fact, more transgender women undergo surgery in Bangkok than in any other city in the world. However, the procedure is not covered by insurance [and] gender-affirming hormone treatment is less available."

"Transgender health services are not included in any national health plan or coverage," said another key informant, who gave a low score to gender-affirming care access. "This left transgender people a massive barrier to access to proper healthcare."

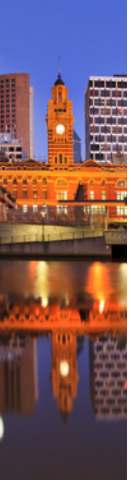
While key informants in Bangkok scored housing and food access as much less of problems than they were rated for LGBTI+ people globally, they rated employment access as a more serious problem than their global peers, with all key informants saying this was either a "serious" or "moderate" problem. "Transgender people still face massive stigma and discrimination on employment, which leaves them with very limited employment options," said one key informant. "For these reasons, many of them are forced to engage in sex work." Indeed, both discrimination on the basis of gender identity and the treatment of sex workers were rated as much more problematic in Bangkok than they were worldwide.

Given the wide variety of challenges facing Bangkok's LGBTI+ community, but its nonetheless above average quality of life score, community resilience is likely key. Even more so than with the global trends, nonprofits were rated quite well in how they support local LGBTI+ individuals compared to other actors, and most key informants named community organizations and the community itself as sources of strength.

"There are few LGBTI+ specific services available in Thailand. Due to stigmatization and the fear of discrimination, most LGBTI+ people do not reveal their sexual orientation or behavior when accessing health services and therefore do not receive appropriate care or counselling when accessing HIV/STI screening and prevention services."

Key Informant, Bangkok





3.8

QUALITY OF LIFE SCORE

CITY

Melbourne

Key informants in Melbourne rated their city above average in terms of quality of life for LGBTI+ people, with a 3.8 on a 1 to 5 scale, compared to 3.2 worldwide. Similarly, they rated access to LGBTI+ inclusive primary care, mental health care, and HIV services better than the global averages. With respect to gender-affirming care, the city was rated slightly below the global average, with a 2.6 average and no informant scoring said care above a three.

Across the board on socioeconomic and criminal justice issues, key informants in Melbourne rated these as being lesser problems than did key informants worldwide. The one exception was on the problem of a disproportionate impact of the criminal justice system on LGBTI+ people of color, where Melbourne key informants scored their city the same as the global average.

Melbourne also scored better in relation to discrimination on the basis of sexual orientation and HIV status, as well as intersectional discrimination, although the city received the same "moderate" problem average score as did the rest of the world on the issue of gender identity-based discrimination.

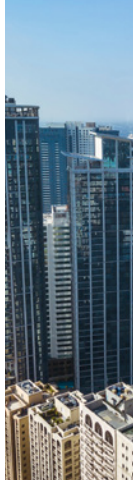
Key informants in Melbourne gave strong marks to how local actors engage with LGBTI+ individuals, and the local government in particular scored much better than the global average, receiving a 4.2 on a 1 to 5 scale, compared to 3.0 globally. Additionally, unlike global responses, Melbourne's key informants singled out LGBTI+ community events (e.g., pride events, fundraisers, festivals) as a major source of resilience, while calling for increased institutional participation in such activities.

The situation for LGBTI+ people "has improved enormously over the last 20 years with consistent state government support, increasing policy initiatives," said a clinician and researcher. "We are the envy of all other states in Australia."

"There seems to be a strong and committed focus on LGBTI+ health and wellbeing in our state government that is reflected in high levels of consultation with LGBTI+ communities and the distribution of some funding to address critical issues. The nonprofits seem to be addressing the impacts of intersectionality within our LGBTI+ communities and are starting to focus on the issues impacting a broader cross section of the community beyond the traditional gay white male focus."

Key Informant, Melbourne





4.0
QUALITY OF LIFE SCORE
CITY

Quezon City

Overall, key informants in Quezon City rated LGBTI+ quality of life in their city at 4 on a 1 to 5 scale, better than the global 3.2 average. They also rated access to care above the global averages, and followed the same trend as did ratings worldwide, in which HIV care was rated best, followed by primary care, with gender-affirming care and mental health care lagging.

While services were better rated in Quezon City than elsewhere, and many of the challenges facing LGBTI+ people were rated as less problematic, most key informants noted the persistent stigma and discrimination facing the community. "Although it has lessened, discrimination and lack of information regarding LGBTI+ and everything about it still serve as the major problem in the city," said one key informant.

Some key informants noted that the challenges facing the LGBTI+ community are particularly pronounced in the poorest sections of the city, where opportunity in general is lower, access to services is more limited, and knowledge about LGBTI+ individuals is low.

In terms of building resilience, some key informants praised the work being done by nonprofit organizations and the city government, while others suggested initiatives be more grassroots-oriented and participatory. "In order for a policy to be effective, it should be participatory," said one key informant. "In other words, let the LGBTI+ people create the policy they need and make sure that it is implemented down to the smallest community."

"The LGBTI+ community has been working hard... to prove to others that they are also capable of doing the same things as everyone else, or even more."

Key Informant, Quezon City



3.3
QUALITY OF LIFE SCORE
REGIONAL

Europe

This study included 15 cities from across Europe: Amsterdam, Athens, Berlin, Brussels, Copenhagen, Dublin, Glasgow, Kyiv, Lisbon, London, Madrid, Milan, Paris, Prague, and Vienna. Three of these cities — Athens, Kyiv, and London — were selected to serve as examples with individual analyses following this regional description.

Even among the majority of these cities that are part of the European Union, the cities face a variety of legal and policy landscapes that underpin LGBTI+ issues, as well as diverse LGBTI+ community histories and cultural backdrops that inform LGBTI+ health equity in each.

Quality of Life and Care

Overall, key informants in Europe gave their cities an average quality of life score of 3.3 (mode: 4; SD: 0.85) on a 1 to 5 scale, just slightly above the global average of 3.2. A plurality of key informants (40%) gave their city a score of 4.

Regarding quality of care, key informants scored each facet of care roughly the same as their global counterparts. As was the trend globally, HIV care scored best, with a 3.8 on a 1 to 5 scale (mode: 4; SD: 1.04) followed by general care with a score of a 3 (mode: 3; SD: 1.03), mental health care with a score of 2.8 (mode: 2; SD: 1.01), and finally gender-affirming care with a score of 2.6 (mode: 2; SD: 1.13).

Many key informants noted the work of nonprofits as being key to addressing health inequities, and many noted the need for additional resources to build on what services do exist. “LGBTI+ health concerns are largely addressed through symbolic gestures (speeches, pamphlet launches), and rarely through commitment of substantial resources,” said an anthropologist and sexuality expert in Dublin. “Specialist clinics have been at capacity for years.”



Health Outcomes

Data on HIV prevalence with respect to sexual and gender minority populations is the most detailed assessment area among the selected cities in Europe. Disaggregated data were complete among sexual minority men, with the highest HIV prevalence in Amsterdam (19.9%), followed by Berlin (19.7%), Lisbon (17.6%), Copenhagen (17.1%), Paris (16.3%), Kyiv (15.3%), London (14.6%), Brussels (14.5%), Athens (14.2%), Madrid (14%), Milan (12.3%), Prague (10.9%), Vienna (10.1%), Dublin (8.4%), and Glasgow (4.4%).[153] Although much of Europe has access to cutting-edge HIV treatment options and preventative strategies, sexual and gender minorities experience higher rates of HIV despite comprising a small percentage of Europe's population. As noted in HIV prevention literature in European cities, discrimination on the basis of sexual orientation or gender identity including for employment, public accommodations, housing, or healthcare can lead to mental health problems, such as anxiety and depression, which can then contribute to behaviors that place individuals at risk for HIV acquisition. The potential real-life consequences of bias, victimization, and discrimination with respect to social, cultural, demographic, and economic factors modulate the spread of HIV and exacerbate disparities in HIV prevalence and treatment among these populations. Furthermore, social determinants related to discrimination and oppression, including institutional discrimination in healthcare access and treatment, as well as a shortage of healthcare providers who are culturally competent and knowledgeable in LGBTI+ health modulates higher rates of STDs among sexual and gender minority populations in the majority of the selected cities in Europe.

Chlamydia infection among sexual minority men is relatively high compared to heterosexual counterparts or the general adult population with the highest prevalence rate reported in London (29.6%), followed by Athens (26%), Paris (11.7%), Amsterdam (10%), Glasgow (7.1%), Copenhagen (6.4%), Berlin (3.8%), Madrid (3.7%), Vienna (3.5%), Lisbon (2.9%), Kyiv (1.9%), Milan (1.5%), and Prague (1.2%). Disaggregated data among the selected cities in Europe reveal the highest Gonorrhea prevalence in London (44.3%), followed by Athens (18.3%), Amsterdam (11.8%), Paris (10.8%), Glasgow (8.0%), Lisbon (7.8%), Brussels (6.8%), Copenhagen (6.9%), Madrid (6.1%), Berlin (4.3%), Vienna (4%), Prague (2.4%), Milan (2.3%), and Kyiv (1.9%). The highest syphilis prevalence was reported in Athens (37.9%), followed by Paris (13%), Milan (9.1%), London (8.54%), Berlin (8.1%), Prague (5.6%), Madrid (5.4%), Lisbon (5.3%), Brussels (7.3%), Copenhagen (3.1%), Glasgow (3.1%), Vienna (3%), Kyiv (2.4%), and Amsterdam (2.3%).[154]

Across the cities in Europe, evidence revealed that sexual and gender minorities experience higher rates of mental health issues when compared to the general population. Disaggregated data regarding anxiety are the most complete among sexual minority men, with the highest anxiety prevalence Dublin (41.7%), Kyiv (12.1%), London (10.7%), Athens (9.1%), Prague (9%), Copenhagen (7%), Lisbon (6.9%), Paris and Brussels (6.5%), Madrid (5.9%), Berlin and Amsterdam (5.1%), and Vienna (3.6%).[155] Strikingly, the prevalence of anxiety is 60% among lesbian, gay and bisexual individuals in Glasgow and 72% and 47% among transgender women and men in Glasgow and Milan, respectively.[156,157] Data regarding depression rates that were available at the population level reveal, on average, 46.8% of sexual and gender minorities in Dublin reported some level of depression.[158] Additionally, the prevalence of depression is 49% among sexual minority individuals and 72% among transgender people in Glasgow,[159] 52% among LGBTI+ individuals in London,[160] and 63.1% among transgender individuals in Milan.[161] With respect to suicide prevalence, 21.4% of all LGBTI+ participants in Dublin had ever seriously attempted suicide,[162] whereas 46% of transgender individuals and 31% of sexual minority individuals in London attempted suicide.[163] Finally, the highest prevalence of attempted suicide (51.7%) was seen among transgender individuals in Milan.[164]

There is an overall general lack of disaggregated population-level data among sexual and gender minorities with respect to diabetes and obesity. Glasgow registered on the high end of diabetes prevalence, which was at 2% among sexual minority individuals there,[165] while London had the highest prevalence of being overweight or obese, which was true of 44% of sexual minority men.[166]

"Despite efforts to combat discrimination and stigma, there are still a number of obstacles in accessing certain services (i.e., housing). In this sense, the Lisbon City Council created a plan that seeks to provide specific responses to the LGBTI+ community and to fight transphobia and homophobia, integrating vulnerable populations such as migrants, refugees, [and] people who use drugs."

Key Informant, Lisbon

"These disparities are largely overlooked. No data are being collected on citizen's sexual orientation or gender identity [and] community surveys are largely missing in this area. The city has so far not addressed these disparities because they have so far not developed an interest and a sense of care for citizens who are not heterosexuals."

Key Informant, Prague

Comparisons regarding alcohol and drug use across the selected cities in Europe were challenging because not every city has disaggregated data among sexual and gender minorities and the data that was measured and reported varies in terms of quantity, frequency, and severity of use versus a diagnosis of substance use disorder. Data that were available at the population level reveal that 35.4% of sexual minority men in Dublin report current smoking[167] and in Copenhagen, one in five LGBTI+ individuals smoke daily and one in four bisexual women smoke cannabis.[168] In Glasgow and London, 15% of LGBTI+ individuals report smoking every day,[169,170] whereas 43.1% of sexual minority men in Paris report using cigarettes or e-cigarettes daily.[171] Furthermore, 54.5% and 35% of sexual minority men in Paris[172] and Dublin,[173] respectively, have a prevalence of any current illicit substance use. Importantly, in terms of active use, 11% and 13% of LGBTI+ individuals aged 18 to 24 in Glasgow[174] and London,[175] respectively, report using drugs at least once a month. In terms of meeting diagnostic criteria for potential alcohol dependency, the highest was seen in Kyiv with a prevalence of 30.6% among sexual minority men, followed by Berlin (22.1%), Vienna (21.8%), Lisbon (14.8%), Madrid (14.9%), Prague (14.4%), Amsterdam (13.5%), Milan (10.8%), and Athens (10.1%).[176] In Copenhagen, 16.0% of gay men exceed the high-risk limit (21 units of alcohol per week) and 17% of transgender individuals drink more than 17.5 units per week.[177] Among LGBTI+ individuals in London[178] and Glasgow,[179] 16% and 14% reported daily drinking, respectively. Among sexual minority men in Dublin, 58% reported binge-drinking in the last twelve months,[180] whereas 46.7% of sexual minority men in Paris reported alcohol use (five or more drinks in one sitting).[181]

Finally, no population level data on the prevalence of disability was available with disaggregation by sexual or gender minority status.

Socioeconomic Factors

On two socioeconomic questions — access to employment and housing — European key informants were almost exactly in line with key informants globally. Four percent said that employment access was "not a problem" (compared to 5% worldwide), 28% said it was a "minor" problem (25% worldwide), 43% said it was a "moderate" problem (43% worldwide), and 26% said it was a "major" problem (27% worldwide). A similar trend held for access to housing, which was considered more of a challenge, with 38% finding it to be a serious problem (compared to 42% worldwide).

However, the European cities did perform better than the global average when it came to access to sufficient and nutritious food for LGBTI+ individuals. Here, a third of key informants (33%) said it was "not a problem" (compared to 24% globally) while only 4% said it was a "serious" problem (compared to 13% globally), with the rest rating it a "moderate" or "minor" problem.

With respect to the data assessments, there is a lack of disaggregated population-level data among sexual and gender minorities relating to the prevalence of homelessness and food insecurity. There exists some city-specific and country-level, population data on the prevalence of unemployment with the highest rates in Greece (15.9%)[182] followed by Italy (10.7%),[183] Madrid (10.3%),[184] Portugal (6.9%),[185] London (6.5%),[186] Ireland (5.8%),[187] Belgium (5.6%),[188] Copenhagen (5.3%),[189] Scotland (4.3%),[190] Germany and Netherlands (3.8%),[191] and Czech Republic (3.4%).[192] As far as disaggregated country-level population-level data on poverty rates, the highest rates exist in Greece (31.8%)[193] followed by Spain (20.7%), Italy (20.1%), Portugal (17.2%), Switzerland (16%), Belgium and Germany (15.8%), France (13.6%), Austria (13.3%), Ireland (13.1%), Denmark (12.5%), and Czech Republic (10.1%).[194]

Discrimination

Key informants for the European cities scored sexual orientation and gender identity-based discrimination as being slightly less of a problem in their communities than the global average. HIV-related discrimination scored equally problematic, while discrimination against people with multiple forms of marginalization (i.e., LGBTI+ racial and ethnic minorities) scored as a bigger problem than it did worldwide.

On sexual orientation-based discrimination, while 87% of key informants said that it was a problem, only 12% said that it was a "serious" problem, compared to 19% globally who said the same. Regarding gender identity-based discrimination, a larger 92% share felt that it was a problem, and a more significant 29% said it was a "serious" problem — but, again, this was better than the 33% who said it was a "serious" problem globally.

Intersectional discrimination was noted as a serious problem by 36% of key informants in Europe, almost identical to the 35% who said so globally. This is in keeping with the fact that 66% of key informants specifically named migrants, refugees, and/or asylees as individuals facing particular hardships when asked if any groups within the LGBTI+ population face inequities.

The assessments found that discrimination on the basis of sexual orientation and, to a lesser extent, gender identity was banned in most of the selected cities in Europe. For example, only Milan does not have a regional or national ban on gender identity-based discrimination in employment settings. Across all selected cities in Europe, same-sex relations are legal and, in most cities, recognized. However, same-sex marriage is still not available in four of the cities included from Europe: Athens, Kyiv, Milan, and Prague.[195] Across all selected cities in Europe, hate crimes are recognized and punishable by law. Universally, across the European Union, transgender people are allowed to access appropriate gender-based facilities and are able to change their gender marker on legal documents.

Criminal Justice

Key informants in Europe scored criminal justice issues as being less of a problem for LGBTI+ individuals than did the average key informant worldwide, specifically in the areas of mistreatment or targeting by police, criminalization of sex work and treatment of sex workers, and a disproportionate impact on racial and ethnic minorities. However, the European cities did not score better than the global average on criminal justice issues relating to HIV status and disclosure, instead rating that problem equally with their global peers.

While key informants rated criminal justice issues as slightly less problematic in Europe than elsewhere in the world, most still believed they were at least a "minor" a problem for their community. Seventy-five percent said that mistreatment by the police was a "minor," "moderate," or "serious" problem; 56% said that targeting of LGBTI+ people for arrests was a problem; 94% said criminalization of sex work and/or treatment of sex workers was a problem; 78% said that criminalization of HIV exposure and/or nondisclosure of status was a problem; and 81% said a disproportionate impact on LGBTI+ racial and ethnic minorities was a problem. This was consistent with the global trend in which issues relating to sex workers were deemed the most problematic.

66%

of key informants in Europe volunteered **"migrants," "asylees," or "refugees"** when asked if any LGBTI+ subgroups face particular hardship

AND

96%

said that **intersectional discrimination** was a problem in their city

Regarding the assessments, LGBTI+ identities and relationships are not criminalized in any of the European cities included in the report. With respect to the transmission and non-disclosure of HIV status to sexual partners, all European countries criminalize or control behaviors through HIV-specific statutes and regulations; however, in Amsterdam, only intentional HIV exposure or transmission are criminalized, making it one of the most advanced cities in the world when it comes to laws seeking to criminalize transmission and non-disclosure of HIV status to sexual partners. With respect to the legality of transactional sex in Europe, nine of the selected cities have laws making the practice of exchanging sex for money illegal, while Amsterdam, Athens, Berlin, Copenhagen, Brussels, and Vienna do not. However, in most of the latter group of cities, there are regulations in place surrounding activities such as operating brothels, receiving money from or facilitating exchanges of sex and money between other parties, and soliciting money in exchange for sex. In Dublin and Paris, it is illegal to pay for sex, but not to be a sex worker (the client commits a crime, but not the sex worker).

"Copenhagen isn't a paradise for LGBT+ people just because we offer LGBT+ people extensive rights; the culture needs to change."

Key Informant, Copenhagen

Community Resilience

As with other parts of the world, key informants in Europe were most likely to name community organizations and the community's internal strength as the two main source of resilience. Key informants in Europe were, however, more likely than those elsewhere to name local LGBTI+ bars, cafes, and social establishments as a source of community strength.

European key informants gave their cities slightly better scores than the global averages in terms of how local governments, nonprofit organizations, and the private sector engage with their community, while giving the same score to providers as did key informants worldwide. Still, the scores showed much room for improvement. As with the global trend, nonprofit organizations received the best score for their community engagement, with a 4.1 on a 1 to 5 scale (mode: 4; SD: 0.78). Local governments scored a 3.1 (mode: 4; SD: 1.19), as did providers (mode: 4; SD: 1.05), while the private sector was only slightly behind with a 3 (mode: 3; SD: 1.01).

In all of the selected cities of Europe, assessment factors thought to enhance and support LGBTI+ resilience are available, including community spaces and resources (e.g., tourism association, pride events) and allocated funding for LGBTI+ specific service organizations. In an effort to overcome intersecting dynamics of discrimination, societal harassment, and stigma, community-building models of social work practice help alleviate feelings of alienation and oppression by creating a family-like community based on empathy and relatability which promotes perseverance and adaptability in the face of adversities. Among the selected cities of Europe, Kyiv is the only city that does not have an LGBTI+ office or liaison and does not offer or promote publications on sexual and gender minority scientific research, which includes reports or plans on advancing health equity in the local and wider LGBTI+ community.[196-204]

Conclusion

Overall, Europe performed better than the global average in many areas of the assessment (e.g., having positive policies in place, having available community resources), as well as in the key informant surveys (e.g., discrimination, criminal justice, food access, relationships with local institutions). However, the key informants in European cities gave their local LGBTI+ quality of life only a slightly better score than the global average, with a 3.3 on a 1 to 5 scale compared to a 3.2 globally. Additionally, LGBTI+ inclusive health services were not rated much better than the global average. These results suggest that while LGBTI+ people in European Fast-Track Cities enjoy better policies, more visibility, and greater inclusion than the average LGBTI+ person worldwide, there is still much room for improvement, particularly with respect to health services. Additionally, the assessment results reveal missing data on LGBTI+ issues in Europe, despite the communities' relatively high visibility and political support.



2.8
QUALITY OF LIFE SCORE
CITY

Select Cities

Athens

Key informants from Athens reported a quality-of-life score of 2.8 on a 1-to-5 scale — well below the global average of 3.2. Access to quality, inclusive types of care were also ranked more poorly than international averages, with access to gender-affirming care rated just 2.2 out of 5.

In a reverse of the global trend, key informants in Athens rated access to employment as an even bigger challenge than access to housing. Ninety-one percent of key informants said access to employment was a serious or moderate challenge, compared to 81% who said the same of housing.

Key informants in Athens were far more likely than their global counterparts to name all types of discrimination (based on sexual orientation, gender identity, HIV status, and intersectional factors) as being a "serious" problem for their community. While LGBTI+ Athenians enjoy strong nondiscrimination protections, a lack of other legal recognitions — such as same-sex marriage and adoption, as well as easier policies to change gender identity documents — may prevent the underlying stigma facing LGBTI+ people to be addressed.

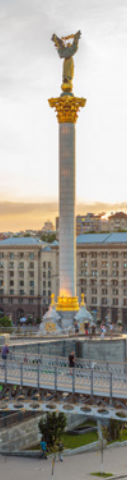
"There is not gender-affirming care in my city and also no planning in doing so in the future. There is no education about healthy sex practices not only for the LGBTI+ people but also for cisgender/ heterosexual people. Most of the progress that has been made is due to the work of non-profit organizations but there is still a long way ahead."

Key Informant, Athens



"Same-sex marriage is not legalized (apart from civil unions). Adoption by same sex couples is still a taboo issue. Homophobia and transphobia are rampant in Greek society and often enforced by the Orthodox Church and right-wing politicians."

Key Informant, Athens



2.7

QUALITY OF LIFE SCORE

CITY

Kyiv

"In general, the basic human rights remain a non-achieved dream for LGBTI+ [people]: equality in marriage and child adoption; be yourself in public openly; to take your partner's hand, kiss, hug without fear of attack."

Key Informant, Kyiv

Kyiv was in the minority of European cities with respect to several legal and policy factors, including in that it does not yet have legal recognition of same-sex couples. There was also no evidence found when completing the city's assessment of a formal LGBTI+ advisory group or a public LGBTI+ equity report.

A small sample of key informants in Kyiv reported that progress had been made but was incomplete. "The situation has been changing for the better in recent years," said one key informant working in public health. "LGBTI+ representatives hold public events, the local authorities allow and protect them. Doctors and society as a whole have become tolerant of LGBTI+ people, although it should be noted that there are problems... I would like more participation of local governments in support of the LGBTI+ movement." Intolerance, violence, and stigma, especially from certain political and cultural groups, were also identified as challenges by key informants.

Additionally, HIV remains a major issue for LGBTI+ people in Kyiv, with 15.3% of sexual minority men self-reporting that they are living with HIV; the same survey also found that 12.6% of sexual minority men in the city had recently experienced severe anxiety or depression.[205,206] However, Kyiv has made progress on HIV issues since joining the Fast-Track Cities initiative: between 2015 and 2019, the number of people living with HIV who were on ART jumped from less than 50% to over 80%, and the percentage of those individuals who were virally suppressed reached 96% in 2018.[207,208]



3.4
QUALITY OF LIFE SCORE
CITY

London

London's key informants gave their city a higher LGBTI+ equality of life score than the global average, with a 3.4 on a 1 to 5 scale, compared to 3.2 worldwide. They also gave above-average marks on primary, mental health, and HIV related care; for example, every key informant gave their city a four or five score on the availability of affordable, quality HIV services. On the other hand, key informants rated their city's availability of gender-affirming care at slightly below the global average, with a majority of key informants giving such care a score of a two.

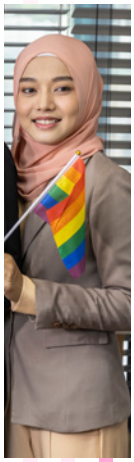
Key informants in London identified problems facing LGBTI+ racial and ethnic minorities. Disparate impact on this particular population by the criminal justice system was considered the most problematic of criminal justice issues on which they were surveyed, and intersectional discrimination was rated the most problematic form of discrimination, with all key informants saying it was a "moderate" or "serious" challenge. In contrast, just one key informant said that discrimination facing sexual minorities in general was a "moderate" or "serious" problem in the city.

Local government, providers, and nonprofits all scored above the global average for their work on engaging the community, while the private sector scored slightly worse than the global average. The assessment conducted for London also found a wide array of public supports thought to build community resilience, and the city has a favorable policy landscape, including nondiscrimination protections and same-sex marriage.

Still, several key informants called for engagement with a wider and more diverse segment of the LGBTI+ population. "Representation is not enough," said one key informant. "It needs to be supported by an evidenced, long-term commitment to challenging issues of poverty that have the biggest impact on all aspects of health and wellbeing."

"Regrettably, LGBTQIA+ health is overly pathologized — looking for things to 'fix' rather than taking a more holistic approach to overall health and wellbeing. However, considering the austere environment to funding and resource allocation, this is not surprising."

Key Informant, London



"Disruptions in education, employment, and housing are common issues, particularly for transgender people and migrants."

Key Informant, London

Recommendations

Overcoming LGBTI+ Health Equity Barriers

Based on the findings of this report, the following recommendations are being issued to advance LGBTI+ health equity in Fast-Track Cities and beyond. The overarching and cross-cutting recommendations include principles that are broadly applicable to a variety of actors who impact LGBTI+ health equity. These are followed by specific recommendations for local governments, providers and health systems, community-based organizations, national governments, and international actors.

OVERARCHING & CROSS-CUTTING

1. **PRIORITIZE THE ELIMINATION OF INEQUITIES WITHIN LGBTI+ COMMUNITIES.** The results of this report demonstrate that, while each local context is different, inequities are present *within* LGBTI+ communities around the world. These inequities affect racial and ethnic minorities, gender minorities, women, and other groups. LGBTI+ health equity cannot be addressed without identifying, engaging with, and prioritizing these disparately impacted subpopulations.

2. **ADDRESS UNDERLYING SOCIOECONOMIC FACTORS.** While data on social determinants of health rarely included disaggregated data on LGBTI+ populations, key informants shared many concerns with respect to access to employment, housing, and food. These issues are all key to achieving health equity and can be addressed through nondiscrimination laws, which were lacking or incomplete in most cities, as well as socioeconomic development policies and programs designed for LGBTI+ populations, such as enhancing inclusive labor policies and educational environments and providing LGBTI+ specific employment opportunities and academic scholarships.

3. **IMPROVE INCLUSIVE DATA COLLECTION.** Even in cities that were relatively highly resourced and LGBTI+ inclusive, data regarding LGBTI+ health equity were lacking, especially outside of the topic of HIV (such as with respect to noncommunicable diseases). Additionally, data on social determinants of health were lacking in most places. Surveillance systems and research must include sexual orientation and gender identity questions to fully define and understand the needs of these populations. For surveillance systems to effectively do so, LGBTI+ individuals must feel safe and comfortable in self-identifying as LGBTI+.

4. **ADDRESS CRIMINAL JUSTICE DISPARITIES.** While only a few cities were in countries that outright discriminate against LGBTI+ people through laws criminalizing same-sex relationships, many criminalized sex work and/or HIV exposure, which likely have a disparate impact on LGBTI+ populations. Additionally, key informants indicated an overall discriminatory impact of criminal justice systems, especially for LGBTI+ racial and ethnic minorities. Both criminal law and the practices of the criminal justice system must be reformed to protect and strengthen LGBTI+ civil rights and to ensure that LGBTI+ people can safely live their lives, enjoy socioeconomic opportunities, and access health services.

5. **ENSURE NONDISCRIMINATION.** Data assessments revealed that few jurisdictions had comprehensive nondiscrimination protections in place that guaranteed equitable access

to health services and insurance benefits, especially for transgender individuals, as well as to socioeconomic opportunities such as employment and housing. Furthermore, key informants indicated that access to these services and opportunities was limited and that discrimination was common. Nondiscrimination laws with proper enforcement are the first step on the path to full social inclusion.

6. **ENGAGE COMMUNITIES AT ALL LEVELS.** Key informants indicated that while nonprofits did relatively well at engaging with local LGBTI+ communities, far more work was needed with respect to healthcare providers, government entities, and the private sector. Assessments revealed that many local governments in Europe and the Americas had local LGBTI+ advisory groups and some funding for LGBTI+ organizations or events, but fewer cities had formal LGBTI+ liaisons, offices, or public reports on advancing equity. LGBTI+ communities in Africa and, to a lesser extent, Asia-Pacific were particularly in need of such formal support and engagement. While local responses to housing, food, and employment issues all left much room for improvement according to key informants, responses to the issue of housing were particularly rated as low, suggesting this could be an important area to increase engagement.

7. **RECOGNIZE GENDER MINORITIES AND THEIR HEALTH NEEDS.** Gender minorities in many cities lacked even a basic recognition of their gender identity, with many not having access to identity documents that reflect their name and gender or being able to access gender-based facilities that correspond with their identities. Transgender people also did not have equal access under the law to gender-affirming care in many jurisdictions, and actual access in practice was a need indicated across regions by key informants. This basic legal recognition and access to gender-affirming care is essential for meeting all other health equity goals among gender minority populations.

8. **IMPROVE HEALTH SYSTEMS.** Access to culturally competent care was noted as a significant need among key informants, with mental health and gender-affirming care options said to be particularly lacking. Cultural competency education should be encouraged or mandated to improve health systems' basic ability to respond to LGBTI+ health needs. Without such improvements, health systems themselves will be a barrier to rather than a partner in ending LGBTI+ health inequities.

9. **FOSTER MULTILATERAL COLLABORATION.** Advancing LGBTI+ health equity in cities around the world will require innovative collaboration between local, national, and international actors, including governments, nonprofits, and the private sector. The Fast-Track Cities network is an example of city multilateralism, in which cities augment traditional health diplomacy and engage with other cities as well as national and international actors to advance shared goals. This dynamic is especially important given the shared dependence between national governments (which set relevant laws, issue funding, and collect data) and local governments (which are more closely connected to communities and lead public health responses).

10. **SUPPORT HIV SERVICE PROVIDERS AS LGBTI+ CARE LEADERS.** Globally, access to low-cost, low-barrier HIV services was rated higher than other types of healthcare services. Those working in the field of HIV can help foster connections to other types of care, build trusted networks, and train other providers on engaging with LGBTI+ communities.

CITY AND MUNICIPAL GOVERNMENTS

Cities and municipal governments around the world have been leaders in advancing LGBTI+ equity and must continue to lead the way. In addition to offering the overarching recommendations above, this report is making the following recommendations specifically to city and municipal governments:

1. **ENACT LOCAL NONDISCRIMINATION ORDINANCES OR POLICIES.** While national nondiscrimination laws or constitutional provisions often offer the strongest protection for LGBTI+ individuals, local ordinances or policies could fill in many of the gaps identified in this report. Such actions, even if relatively limited, can also send a symbolic message of inclusion, make local LGBTI+ communities feel seen, and open a larger dialogue.

2. **ESTABLISH FORMAL COLLABORATIONS WITH LOCAL STAKEHOLDERS.** Many cities in Europe and the Americas, and a few cities in Asia-Pacific and Africa, have established formal collaborations with local stakeholders, such as LGBTI+ advisory groups, liaisons, or public plans, as well as funding for LGBTI+ organizations and events. This type of collaboration is an of what cities can often do better than countries, given their proximity and close ties to local populations. This is also an area in which local governments can generally act unilaterally, without the need for national policy changes or support.

3. **SUPPORT AND IMPLEMENT LGBTI+ SPECIFIC RESEARCH.** This report revealed a dearth of data that can be disaggregated based on sexual orientation and gender identity. While much of the relevant data is collected primarily at the regional or national levels, local governments gather data or support research that could be invaluable in informing local LGBTI+ health needs; this includes advancing comprehension of current health inequities and learning how to better implement policy and funding solutions. While this type of research can be challenging — especially when data collection follows national guidance or templates — increasing data whenever possible is a worthwhile step in the right direction. Local governments should avoid seeing the relative newness and scarcity of sexual orientation and gender identity questions as a reason for inaction.

4. **PROMOTE COMPREHENSIVE LGBTI+ CULTURAL COMPETENCY TRAINING.** Local governments can provide LGBTI+ cultural competency trainings to their staffs, as well as offer (and in some cases require) such training of local contractors and grantees. Regardless of how advanced LGBTI+ rights are in a given jurisdiction, training is important because it helps bring about the cultural change that is equally as important as legal change. Training of public-facing staff and contractors helps ensure that interactions with LGBTI+ individuals are respectful and inclusive, while training of staff such as administrators and managers can ensure that LGBTI+ populations are properly considered when policy and funding decisions are made.

5. **ADVOCATE FOR NATIONAL AND GLOBAL CHANGE.** The Fast-Track Cities initiative has proven that city governments can successfully engage in multilateralism and advance health goals through advocacy with national governments as well as through engaging with other cities and international actors. While cities may not always have the direct authority to act on all of the overarching recommendations noted above, they can be powerful forces in advancing change at home and abroad. This can be accomplished through direct advocacy as well as by serving as an incubator for change and providing an example of positive policies and strategies that can be more broadly applied.

PROVIDERS AND HEALTH SYSTEMS

Providers and health systems have an important role to play in addressing LGBTI+ health equity, both through the services that they provide to patients and the role they can play in advocating for systemic change. Following are recommendations for providers and health systems to take to strengthen local LGBTI+ health equity:

1. **IMPLEMENT NONDISCRIMINATION POLICIES.** Even in settings that do not have local or national nondiscrimination laws applying to LGBTI+ individuals, providers and actors within health systems can often add these to their practices. This type of policy — as well as other actions, such as LGBTI+ inclusive messaging and imagery in medical offices — sends the message that it is a safe and welcoming place for LGBTI+ populations. Where outward support of LGBTI+ patients is not legally permissible, general nondiscrimination and inclusion policies could be effective.

2. **CONDUCT LGBTI+ HEALTH EQUITY TRAINING.** Key informants indicated a dearth of LGBTI+ competent healthcare providers, particularly in the areas of mental health and gender-affirming care. Healthcare providers have an ethical responsibility to educate themselves about the needs of vulnerable populations. While systemic changes, such as the inclusion of LGBTI+ issues in health education curricula and licensing requirements, are needed, systems and providers can also take individual action, including through free or low-cost resources available online.

3. **COLLECT SOGI DATA.** The data assessments for this report demonstrated major gaps in knowledge on LGBTI+ health issues, particularly at the local level. Healthcare settings collect a wide range of data that could be invaluable to better understand and address LGBTI+ health equity, were it possible to disaggregate such data based on sexual orientation and gender identity. Collecting such data (when the local context is one in which it is safe to do so) also sends a welcoming and inclusive message to LGBTI+ patients and can serve as a catalyst for healthcare staff to learn more about LGBTI+ communities and their needs.

4. **CREATE A LOCAL REFERRAL NETWORK.** Social determinants of health for LGBTI+ people are equally important to healthcare access in addressing inequities. Providers and health systems can play a crucial role in helping to connect LGBTI+ patients to culturally competent legal, housing, employment, food, and other services. These referral networks also ensure the reverse — that LGBTI+ individuals seeking services from community resources are connected to LGBTI+ inclusive care. Participation in community events and developing medical-legal partnerships are other methods of developing connections to LGBTI+ serving organizations.

5. **ADVOCATE FOR CHANGE.** Policymakers should and often do take seriously the expert opinion of local healthcare entities and professionals. Individual providers can take action at the local level by advocating with decision-making bodies (i.e., submitting oral or written testimony at relevant proceedings), communicating with the public (i.e., writing an opinion piece on relevant policies), or advocating for change within their own clinic or hospital. Healthcare organizations can play a similar role, especially as many already engage regularly with local decision-makers. The healthcare sector can help bring a science-driven, evidence-based perspective to LGBTI+ issues that are often clouded by stigma and are over politicized.

COMMUNITY-BASED ORGANIZATIONS

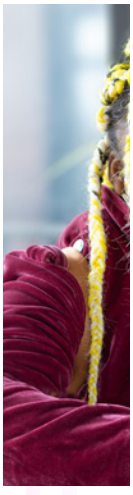
Community-based organizations are key to the resilience of local LGBTI+ populations and must continue to expand their work on behalf of these communities in the pursuit of health equity. Following are recommendations for an enhanced role for community-based organizations to promote LGBTI+ health equity:

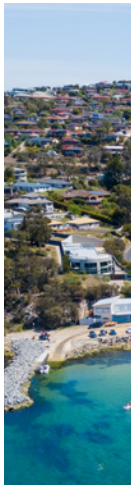
1. **LEAD THE WAY ON LGBTI+ ENGAGEMENT.** Key informants indicated that community-based organizations outperformed local government, providers, and the private sector in respectfully engaging local LGBTI+ communities. Community-based organizations should continue to play this vital role and use their strong connections to LGBTI+ individuals to lift up their voices and concerns among other stakeholders.

2. **PRIORITIZE LGBTI+ PEOPLE WITH MULTIPLE FORMS OF MARGINALIZATION.** This report indicates higher levels of unmet needs among subpopulations such as gender minorities and LGBTI+ racial and ethnic minorities. Given the critical role that community-based organizations play in supporting LGBTI+ communities, it is critical that they prioritize these disparately impacted groups, who historically have been left behind by many mainstream LGBTI+ serving organizations. Building connections with organizations that serve these populations could be a successful and mutually beneficial strategy.

3. **BUILD MULTISECTORAL PARTNERSHIPS.** As trusted gatekeepers among LGBTI+ populations, community-based organizations can serve a powerful role in connecting LGBTI+ people to other services. This report demonstrates that LGBTI+ health equity requires increased attention to issues such as housing, employment, criminal justice, and more, in addition to traditional health services. Local organizations can build LGBTI+ inclusive referral networks to help LGBTI+ people connect with the wide scope of services they may need in order to advance their wellbeing.

4. **EMPOWER COMMUNITIES TO ACT.** Community-based organizations can play a vital role in helping local LGBTI+ people advance justice, both within the LGBTI+ population (i.e., working to address racism or transphobia within the LGBTI+ community itself) and externally in their city, country, and beyond (i.e., providing community members with advocacy tools).



NATIONAL GOVERNMENTS

While this report focuses on LGBTI+ health equity in Fast-Track Cities, national governments play a critical and at times determinative role in addressing LGBTI+ health equity issues. Following are recommendations for the role that national governments can play in supporting cities and municipalities to achieve LGBTI+ health equity:

1. **ADOPT NATIONAL NONDISCRIMINATION LAWS.** The strongest protections against LGBTI+ discrimination — be it in healthcare access, employment, housing, or other areas — are generally national. Cities often have limited power to ban LGBTI+ discrimination and ensure inclusion through local ordinances and policies, placing the responsibility on national governments to ensure these critical measures come into effect. National governments should, at a minimum, not prohibit local governments from enacting their own nondiscrimination measures.

2. **IMPLEMENT INCLUSIVE DATA COLLECTION STANDARDS.** Even when data are being collected at subnational levels, said collection is often done in connection with national rules, standards, and guidelines. National governments should ensure that their own data collection is inclusive of sexual orientation and gender identity measures, and should also promote standardized, inclusive data collection by local governments, nongovernmental entities, and other relevant stakeholders.

3. **FUND LOCAL LGBTI+ SERVICES.** A great deal of funding for local health and other essential services is derived from national governments. Funding should be prioritized for organizations that explicitly serve local LGBTI+ populations and especially priority subpopulations (e.g., gender minorities, LGBTI+ racial and ethnic minorities). National governments can also require grantees to adhere to LGBTI+ nondiscrimination and inclusion policies.

4. **ENGAGE IN LGBTI+ HEALTH EQUITY DIPLOMACY.** National governments can use relationships with public and private entities to advance LGBTI+ health equity on the world stage. This engagement should be conducted in partnership with cities, which are often leaders in LGBTI+ issues, by supporting city multinationalism on issues relating to LGBTI+ health.



INTERNATIONAL ACTORS

International actors — including intergovernmental organizations, donors, and private entities — can all play a supportive role in advancing LGBTI+ health equity. Following are recommendations for the ways in which international actors can collaborate with cities to advance LGBTI+ health equity:

1. **SUPPORT RESEARCH AND PROGRAMMING RELATING TO LGBTI+ EQUITY.** Particularly when governmental entities fail to support LGBTI+ equity, either due to opposition to LGBTI+ rights or because of resource constraints, international actors have a responsibility to consider LGBTI+ populations in their work. International actors can help cities to better understand their local LGBTI+ communities and can support services for these individuals. Similar to the role of national governments, international entities can fund city-specific work to advance LGBTI+ equity and encourage or require nondiscrimination and inclusion among local partners and grantees.

2. **ADDRESS LGBTI+ HEALTH HOLISTICALLY.** International actors should avoid contributing to siloed responses that narrowly address LGBTI+ health issues. This report makes clear that social determinants of health, including socioeconomic opportunity, are critical to addressing LGBTI+ health and other inequities. Significant social change is needed to reject aspects of the status quo that have imbedded stigma and inequality into health and other systems.

3. **BUILD COLLABORATIVE NETWORKS.** The Fast-Track Cities initiative is an example of international nonprofits and intergovernmental organizations uniting with local partners to engage in innovative collaboration with respect to HIV. A similar model can be used to build novel partnerships to address LGBTI+ issues. Local actors could use such networks to access global support and solidarity, which is especially useful when local or national political climates hamper efforts to advance LGBTI+ health equity.

4. **LISTEN LOCALLY.** LGBTI+ communities are diverse, and as this report demonstrates, so are their strengths and needs. The issues facing one community or region should not be interpreted as representing the priorities of all LGBTI+ communities. All institutions working to effect change globally would benefit from letting people on the ground take the lead on LGBTI+ issues, including those related to health.



Conclusion

An Urgent Call to Action

This study demonstrates a dire need to improve the health and wellbeing of LGBTI+ people around the world — from cities in which LGBTI+ communities are visible and enjoy strong political support, to cities in which LGBTI+ identities are ignored or even punished. Data assessments of the 50 cities that were selected for this study reveal both significant disparities where data does exist, as well as many areas in which population-wide data are severely lacking. A survey of 275 key informants across the 50 cities further demonstrated that access to health and socioeconomic resources is limited, even in affluent cities, and that stigma and discrimination is relentlessly pervasive. Furthermore, both the assessments and the key informant surveys showed that meaningful engagement with LGBTI+ communities was limited, especially outside of community-based organizations.

There was a high degree of variability on the severity of challenges and the quality of services and institutional relationships relevant to LGBTI+ health, both across and within regions. The cities in the Asia-Pacific region scored best overall; the cities selected from Africa scored worst, on average; and the cities from the Americas and Europe fell in between. Within each region, cities with better policies on LGBTI+ issues tended to score better. Nonetheless, there was overall a great deal of consistency in how different challenges were ranked. For example, gender identity-related discrimination was rated as a more significant problem than sexual orientation-related discrimination nearly universally, and gender-affirming care was similarly rated as less available than general LGBTI+ inclusive care. Additionally, while the severity of the problems varied, most key informants said that access to housing and employment was a challenge for their local LGBTI+ population regardless of the overall socioeconomic strength of their city. In sum, the results of the study showed that LGBTI+ issues do indeed vary locally, but also that LGBTI+ populations around the world — even in “LGBTI+ friendly” cities with vast resources — face myriad challenges with respect to equity.

The recommendations made in this report call for broad changes to local and national laws and policies, improved data collection, increased LGBTI+ health training, and more robust community engagement. However, underlying these recommendations is a need for social transformation that holistically addresses topics such as equity and stigma, and that sees topics such as socioeconomic opportunity and criminal justice as being integral to improved health and well-being. Moreover, these recommendations cannot be meaningfully accomplished and, in fact, could serve to exacerbate inequities — if the most marginalized subpopulations within LGBTI+ communities are not prioritized. These populations include transgender and other gender minority individuals, racial and ethnic minorities, and people who face multiple forms of marginalization and social isolation.

Most of all, if health equity is to be achieved, stakeholders must leverage the profound resilience that LGBTI+ communities from around the world have consistently demonstrated. Despite the health inequities they face on a day-to-day basis, LGBTI+ people are not victims. They are community activists, essential workers, healthcare providers, artists, scientists, family members, neighbors, and much more. Undoubtedly, LGBTI+ people are the most powerful resource in undoing the inequalities that they themselves face. But that aspiration can be realized much sooner, and many lives can be saved, if more of the myriad actors with the power to change systems join in the march towards equity.

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FAST-TRACK
CITIES


IAPAC
INTERNATIONAL ASSOCIATION
OF PROVIDERS OF AIDS CARE

EXHIBIT C

Transgender People

WHAT DOES ASSIGNED FEMALE AT BIRTH MEAN?

Assigned female at birth (AFAB) is a term that is used for people who have external sex traits that are identified at birth as female. It is used as a way to refer to the sex on one's birth certificate or to discuss medical issues that primarily face AFAB people without making assumptions about current sex, body, or gender identity. AFAB people are typically raised with the assumption that they will identify as women, however AFAB people can be any gender and can have any gender presentation. The term AFAB is an umbrella term to describe the following people:

- Cisgender women (AFAB and identify as women)
- Transgender men (AFAB and identify as men)
- Non-binary and genderqueer people (AFAB and identify as something other than women)

Growing research on transgender men (transmen) and non-binary/genderqueer AFAB people shows increased HIV risk and burden, although not much is known about these transgender populations. Read more about HIV among cisgender women and girls.

WHAT DOES ASSIGNED MALE AT BIRTH MEAN?

Assigned male at birth (AMAB) is a term that is used for people who have external sex traits that are identified at birth as male. It is used as a way to refer to the sex on one's birth certificate or to discuss medical issues that primarily face AMAB people without making assumptions about current sex, body, or gender identity. AMAB people are typically raised with the assumption that they will identify as men, however AMAB people can be any gender and can have any gender presentation. The term AMAB is an umbrella term to describe the following people:

- Cisgender men (AMAB and identify as men)
- Transgender women (AMAB and identify as women)
- Non-binary and genderqueer people (AMAB and identify as something other than men)

Most of the information below refers to transgender women because there is a glaring lack of research and knowledge about vulnerability to HIV among all other transgender people. Read more about HIV among cisgender men who have sex with men (MSM).

ADDITIONAL TERMINOLOGY

Transgender: A person whose gender identity is different from their sex assigned at birth.

Cisgender: A person whose sex assigned at birth is the same as their gender identity.

Gender expression: A person's outward presentation of their gender (for example, how they act or dress).

Gender identity: A person's internal understanding of their own gender.

HOW SERIOUS IS HIV FOR TRANSGENDER PEOPLE?

There are an estimated 25 million transgender people living around the world. The existing data specific to transgender people demonstrate a heavy burden of HIV among transgender women, specifically transgender women who have sex with cisgender men. Transgender women are one of the groups most affected by HIV and are 49 times more likely to have HIV than the general population. Globally, it is estimated that around 19% of transgender women have HIV. HIV among transgender women sex workers is estimated to be 27%, compared with 15% among transgender women who did not engage in sex work.

In the U.S., nearly 1 million people identify as transgender. According to the Centers for Disease Control and Prevention (CDC), transgender people made up 2% of new HIV diagnoses in 2018 and 2,351 transgender people were diagnosed with HIV from 2009-2014. Of these, 84% were transgender women, 15% were transgender men, and 1% had another gender identity. Black/African American transgender women and young transgender women had the highest rates. About 42% of transgender women in the U.S. have HIV. Racial and ethnic disparities are quite stark among transgender women in the U.S.:

- 62% of Black/African American transgender women have HIV
- 35% of Latina/Hispanic transgender women have HIV
- 17% of White transgender women have HIV

WHY ARE TRANSGENDER PEOPLE PARTICULARLY AT RISK FOR HIV?

There are many factors that put transgender people at heightened risk of HIV. The following factors contribute to the global burden of HIV among transgender people:

Social, economic, and legal exclusion: Across the world transgender and gender-nonconforming people face stigma and discrimination, which contributes to higher levels of unemployment, poverty, homelessness, sex work, depression and other mental health issues, substance use, incarceration, and violence, all of which are linked to higher rates of HIV. Most transgender people have experienced some form of abuse or harassment because of their gender identity or presentation. This may negatively impact accessing HIV testing, care, and/or getting treatment for HIV.

Overlapping social, cultural, legal, and economic factors contribute to pushing transgender people to society's margins. Transgender people are more likely to drop out of school, be rejected from family and friends, and face workplace discrimination, limiting educational and economic opportunities. They can encounter problems accessing basic goods and services and even public spaces. These challenges are exacerbated by a lack of legal recognition of their gender and the absence of anti-discrimination laws that explicitly include them.

Data from the recently released *Trans Legal Mapping Report* showed the following about transgender people around the world:

- 13 countries have explicit laws specifically criminalizing transgender people, mostly using cross-dressing laws, punishing them with prison, corporal punishment and, where anti-gay laws are also used against trans people, even death

- 37 countries have de facto laws laws criminalizing transgender people (de facto refers to something that exists in practice but is not necessarily ordered by law or officially established)
- 47 countries prohibit transgender people from changing their gender legally

Racism and discrimination increase HIV risk-related behaviors and lead to health disparities in HIV, particularly among transgender women of color. Intersections of race, gender, and age contribute to disparities in HIV testing, prevention, treatment, and viral suppression. Issues associated with racism and discrimination—including limited access to health care, employment, and housing—can increase the risk for HIV and affect the health and well-being of transgender people.

In addition, many transgender people have had negative experiences with healthcare providers, which discourages them from seeking care. Finding providers who are knowledgeable about and sensitive toward transgender and gender-nonconforming people can be challenging. Transgender people may not have access to HIV prevention information that uses appropriate language to describe their body parts and how they have sex, and few HIV services are tailored to this population.

Sex work: Social exclusion, economic vulnerability, and lack of employment opportunities means that sex work is often the only form of income available to transgender people. The proportion of transgender people who engage in survival sex work is estimated to be up to 90% in India, 84% in Malaysia, 81% in Indonesia, 47% in El Salvador, and 36% in Cambodia.

Data suggests that HIV prevalence is up to 9 times higher for transgender sex workers compared to cisgender sex workers. Knowledge and reported use of condoms is generally low among transgender sex workers. In Asia and the Pacific, only 50% of transgender sex workers are aware of HIV and HIV testing, and only 50% report using condoms consistently with clients and casual partners. Sex workers may get paid more for unprotected sex and often feel pressured to not use condoms, which makes them highly vulnerable to HIV. Read more about HIV among sex workers.

High-risk sex: There are high rates of unprotected anal sex among transgender women. Receptive anal intercourse carries the highest risk because the lining of the rectum is very thin and can be damaged very easily during sexual activity. This makes it easier for HIV to enter the body. Stigma and discrimination, leading to low self-esteem and disempowerment, can make it harder for transgender women to insist on condom use. In many settings, condom use is often controlled by the insertive sexual partner, so many transgender women who have sex with cisgender men may feel unable to negotiate condom use. Gender affirming hormonal therapy (GAHT), which many transgender women use, can lead to erectile dysfunction, increasing the likelihood of taking the receptive role during sex.

There are other factors that make transgender people more likely to engage in high-risk sex. Some transgender people who want to affirm their gender identity through sex, or who fear rejection from sexual partners, can be more likely to agree to unprotected sex. The stress of social isolation may also lead to a much higher rate of drug and alcohol use among transgender people that can affect their judgement and make them less likely to use condoms.

For the above reasons, many transgender people do not use condoms or take medicines to prevent or treat HIV consistently. These medicines include pre-exposure prophylaxis (PrEP) to prevent HIV transmission and antiretroviral therapy (ART) to treat HIV infection.

Injecting hormones. Many transgender people self-administer injectable hormones as part of GAHT. Without counseling on safe injecting practices, people going through this process may be very vulnerable to HIV transmission because of the risk of sharing needles with others.

Source: https://www.avert.org/professionals/hiv-social-issues/key-affected-populations/transgender

WHAT DO WE KNOW ABOUT HIV AMONG TRANSGENDER MEN?

The transgender community is diverse and not enough research has been conducted with transgender people in general. In particular, very little is known about transgender men and their vulnerability to HIV. This is partly because transgender men are assumed to have sex primarily with other AFAB people and therefore be at low risk for HIV.

To date, research related to HIV among transgender people has almost exclusively focused on transgender women. However, there is evidence that there is a significant subgroup of transgender men that engage in unprotected sex with AMAB people, including some transgender men who engage in sex work. If cisgender men and transgender women are a priority for HIV prevention and sexual health care, transgender men should be as well.

Generally, HIV prevalence among transgender women is higher than transgender men. Few studies have been done on HIV prevalence among transgender men and gender non-conforming AFAB people, but there is reason to believe that these communities are more vulnerable to HIV than the general population.

Several studies show that a majority of transgender men report not using condoms consistently during receptive anal and/or frontal (vaginal) sex with AMAB partners, low rates of HIV testing, and low perception of risk.

HIV testing is the gateway to care for people who have HIV and to prevention services for people who don't have HIV. In the U.S., 96% of transgender women have ever been tested for HIV compared with 82% of transgender men.

Few HIV prevention interventions have been developed that address the unique needs of transgender men and specific eligibility criteria for PrEP have not been devised. Nonetheless, a review of U.S. data by the CDC showed that 15% of the 2,351 transgender people diagnosed with HIV in a five-year period were transgender men. A 2017 survey of more than 800 transgender men who have sex with AMAB people found that a majority engaged in behavior that could put them at risk for HIV, and most had heard of PrEP but only 22% were using it.

Many researchers have concluded that studies looking at HIV among transgender people should investigate behavioral risk as well as gender identity and that transgender men need to be included in HIV prevention efforts.

PREVENTING HIV INFECTION AMONG TRANSGENDER PEOPLE

It is evident that prevention strategies are failing to reach this group due to high HIV prevalence in communities around the world. When transgender people are targeted by HIV prevention campaigns they can be extremely effective. It is important that a combination of prevention programs are available.

Encourage less risky sexual behaviors

Unprotected receptive anal/vaginal sex (bottoming) is the riskiest type of sex for getting HIV. Unprotected insertive anal sex (topping) is less risky for getting HIV but very risk for passing HIV to others. In general, there is little to no risk of getting or transmitting HIV from oral sex. Read more about safer sex guidelines.

Limit the number of sex partners. The more partners you have, the more likely you are to have a partner with poorly controlled HIV or to have a partner with an STI. Both factors can increase the risk of HIV transmission.

Use condoms correctly every time you have sex. Read more about how to use condoms correctly and consistently.

HIV counseling and testing

Effective ways to encourage HIV testing among transgender people are to provide home-based testing and community-based testing. Community-based testing is carried out at local pop-up clinics or mobile vans in areas where transgender people feel comfortable. This removes the need to test in clinics where they may experience discrimination and mistreatment. Home-based testing has the benefit of the person being able to avoid identification by healthcare workers. The privacy of conducting an HIV test alone at home makes this an appealing option for many transgender people.

HIV self-testing should be made more widely available to help increase testing and earlier diagnosis. Transgender people should be educated about the use of self-testing kits to heighten their confidence in using them as an alternative to testing at regular healthcare settings.

Whether you test HIV positive or HIV negative, you can take action to protect your health and prevent HIV transmission. The CDC recommends that everyone between the ages of 13-64 get tested for HIV at least once as part of routine health care. People with certain risk factors should get tested at least once a year or more frequently. Find an HIV testing site near you.

Pre-exposure prophylaxis (PrEP)

PrEP is the daily use of antiretroviral medications (ARVs) to reduce the risk of HIV infection among HIV-negative people. PrEP can be combined with other prevention methods, such as condoms, to reduce the risk of HIV even further.

The first approved medication for PrEP, Truvada, has been tested in a few hundred transgender women and shown to be highly effective at preventing HIV when used consistently. Some studies have found that the drugs in Truvada do not reach as high a level in the vagina as they do in the rectum, so transgender men and other AFAB people who have vaginal/frontal sex should be especially careful to take PrEP consistently.

A large study of Descovy, the second PrEP option approved for some people, did not include AFAB people, and the Food and Drug Administration (FDA) declined to approve it for people who have vaginal/frontal sex until more research is done.

Many transgender people are concerned that the medications used for PrEP may interact with GAHT. But in studies so far, the drugs in Truvada have not been found to interfere with hormones.

Post-exposure prophylaxis (PEP)

PEP is the use of ARVs to prevent HIV infection as soon as possible after potential exposure to HIV. It must be taken within 72 hours of possible exposure. It must also be coupled with counseling about the importance of finishing the treatment course. PEP is not the right choice for people who may be exposed to HIV frequently. If a person is at ongoing risk for HIV, such as through repeated exposures to HIV, they should talk to a healthcare provider about taking PrEP.

ANTIRETROVIRAL THERAPY (ART) AMONG TRANSGENDER PEOPLE

Generally, data on transgender people's access to HIV treatment is scarce. One study of people with HIV in the U.S. found that only 59% of transgender participants, compared to 82% of cisgender people, were accessing ART.

As with access to HIV prevention information, transgender people may delay seeking treatment due to transphobia and insensitivity among healthcare professionals. Depression and isolation are often associated with poor adherence to HIV treatment. A lack of supportive relationships can affect important aspects of living healthily with HIV, such as remembering to take medication. One study found that transgender people with HIV were less likely to report adherence to treatment of above 90% compared to cisgender people. The study found that many transgender people found it difficult to take regular medication alongside other treatments such as hormone therapy.

In the U.S., transgender women have about the same viral suppression rates and transgender men have higher viral suppression rates compared to all people with HIV.

	Received some care	Retained in care	Achieved viral suppression
Transgender Women with HIV	84%	66%	65%
Transgender Men with HIV	87%	61%	72%
All people with HIV	76%	58%	65%

Source: https://www.cdc.gov/hiv/group/gender/transgender/viral-suppression.html

Taking HIV medicine every day can make the viral load undetectable. People who get and keep an undetectable viral load (or remain virally suppressed) can stay healthy for many years and have effectively no risk of transmitting HIV to their sex partners.

WHO has produced comprehensive guidance on HIV services for transgender people and recommends that adherence can be increased significantly by addressing HIV stigma and discrimination.

THE BOTTOM LINE

In the U.S. and around the world, transgender people are disproportionately affected by HIV. With early testing and treatment, transgender people with HIV can live longer, healthier lives.

There is a critical lack of data and limited funding for, and research about, transgender people and what drives

their vulnerability to HIV. This is particularly true for transgender men and non-binary/genderqueer transgender people.

Transgender people at high risk for HIV should get tested for HIV at least once a year, and in some cases more frequently. This is especially true for transgender people who have multiple sex partners, who are engaged in sex work, who inject drugs, or who share needles for gender affirming hormonal injections. If they test positive for HIV, they can take steps to reduce the risk of infecting their partners and ensure their own health.

The best way to prevent infection is by using condoms, taking PrEP if HIV-negative, and taking strong ART if HIV-positive. Transgender people who use intravenous drugs or inject hormones should not share injection equipment and supplies.

The most commonly used HIV medications do not interfere with hormones and vice versa. However, it is important to tell your healthcare provider about all the medications you are taking, including hormone therapy.

MORE INFORMATION

CDC: HIV and Transgender People

Avert: Transgender People, HIV And AIDS

WHO: Transgender People

WHO Policy Brief: Transgender People and HIV

Reviewed June 2025

EXHIBIT D

HIV

Fast Facts: HIV and Transgender People

MARCH 28, 2024

For Everyone

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AT A GLANCE

Nearly 1 million people (.3%) identify as transgender in the United States (US), and transgender people made up 2% (671) of new HIV diagnoses in the US and dependent areas in 2019. Get the latest data on HIV among transgender people.



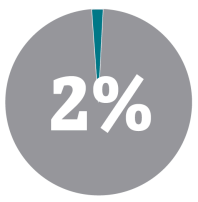
Fast facts

HIV affects some groups more than others. Social and structural issues—such as HIV stigma, homophobia, discrimination, poverty, and limited access to high-quality health care—influence health outcomes and continue to drive inequities.

HIV Diagnoses

HIV diagnoses refers to the number of people who received an HIV diagnosis during a given year.

HIV diagnoses among transgender people in the US and dependent areas, 2019



Of the **36,801 new HIV diagnoses** in the US and dependent areas in 2019, 2% (671) were among transgender people.

Ending the HIV Epidemic

Overall Goal: Decrease the number of new HIV diagnoses to 9,588 by 2025 and 3,000 by 2030.



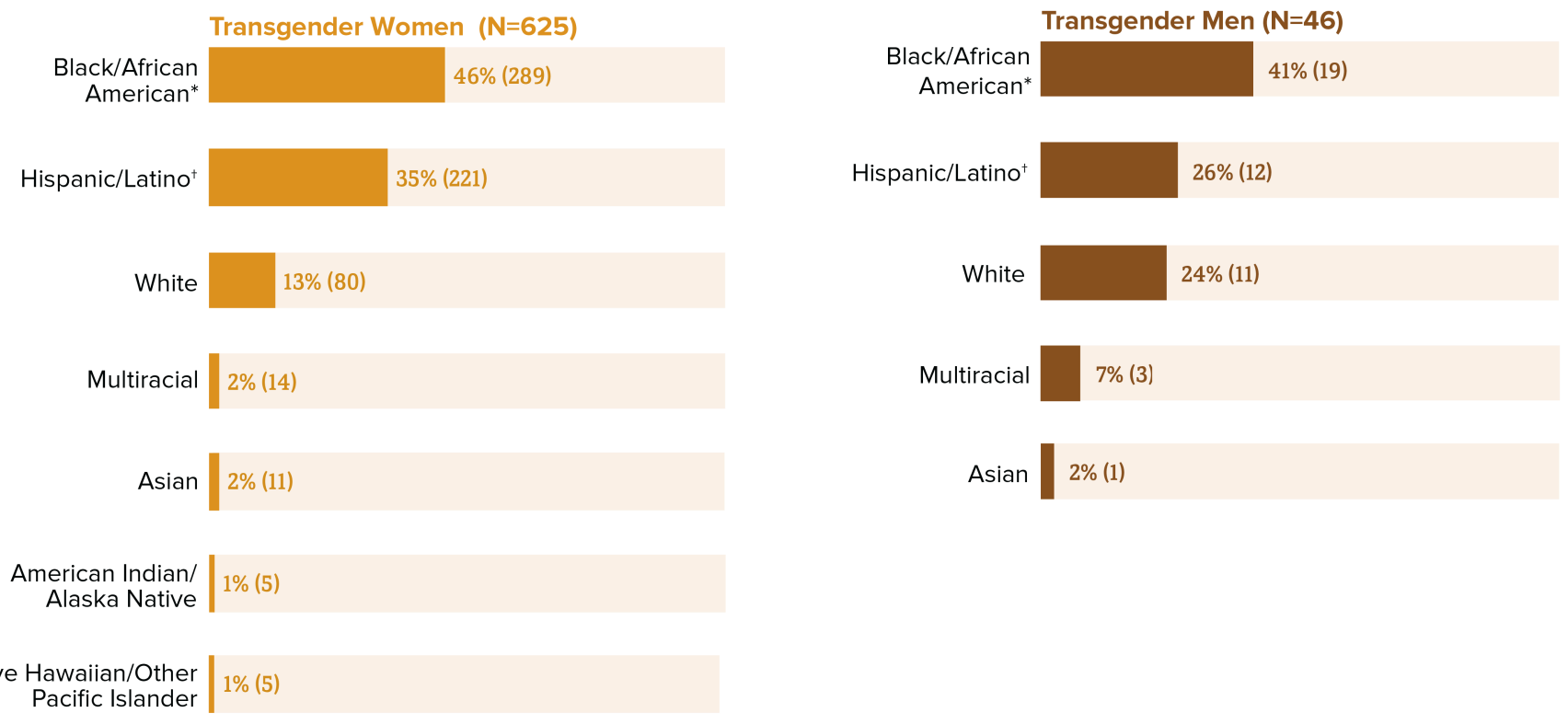
Learn more about HIV diagnoses among transgender people.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

HIV diagnoses among transgender people by race/ethnicity in the US and dependent areas, 2019

Most new HIV diagnoses among transgender people were among Black/African American people.





Learn more about HIV diagnoses among transgender people by race and ethnicity.

**Black* refers to people having origins in any of the Black racial groups of Africa. *African American* is a term often used for people of African descent with ancestry in North America.

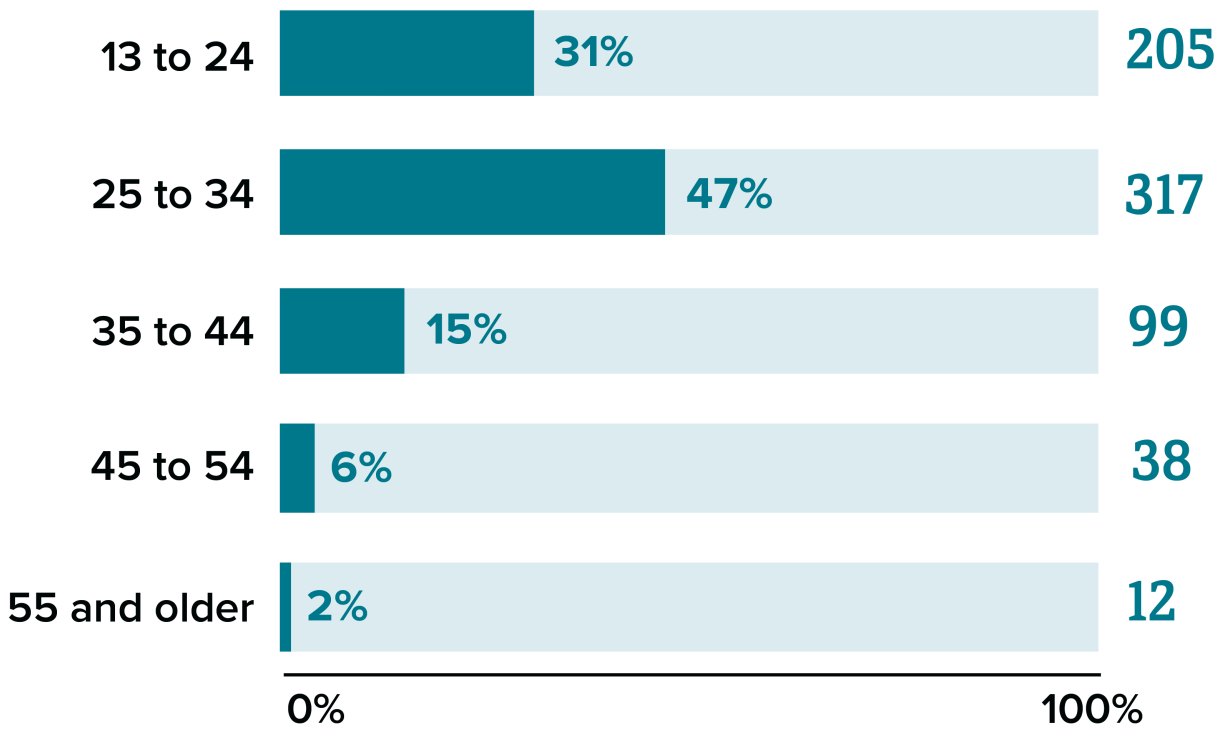
† Hispanic/Latino people can be of any race.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

HIV diagnoses among transgender people by age in the US and dependent areas, 2019

Among transgender people, most new HIV diagnoses were among people age 25 to 34.



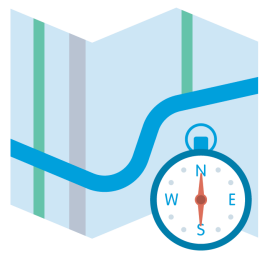


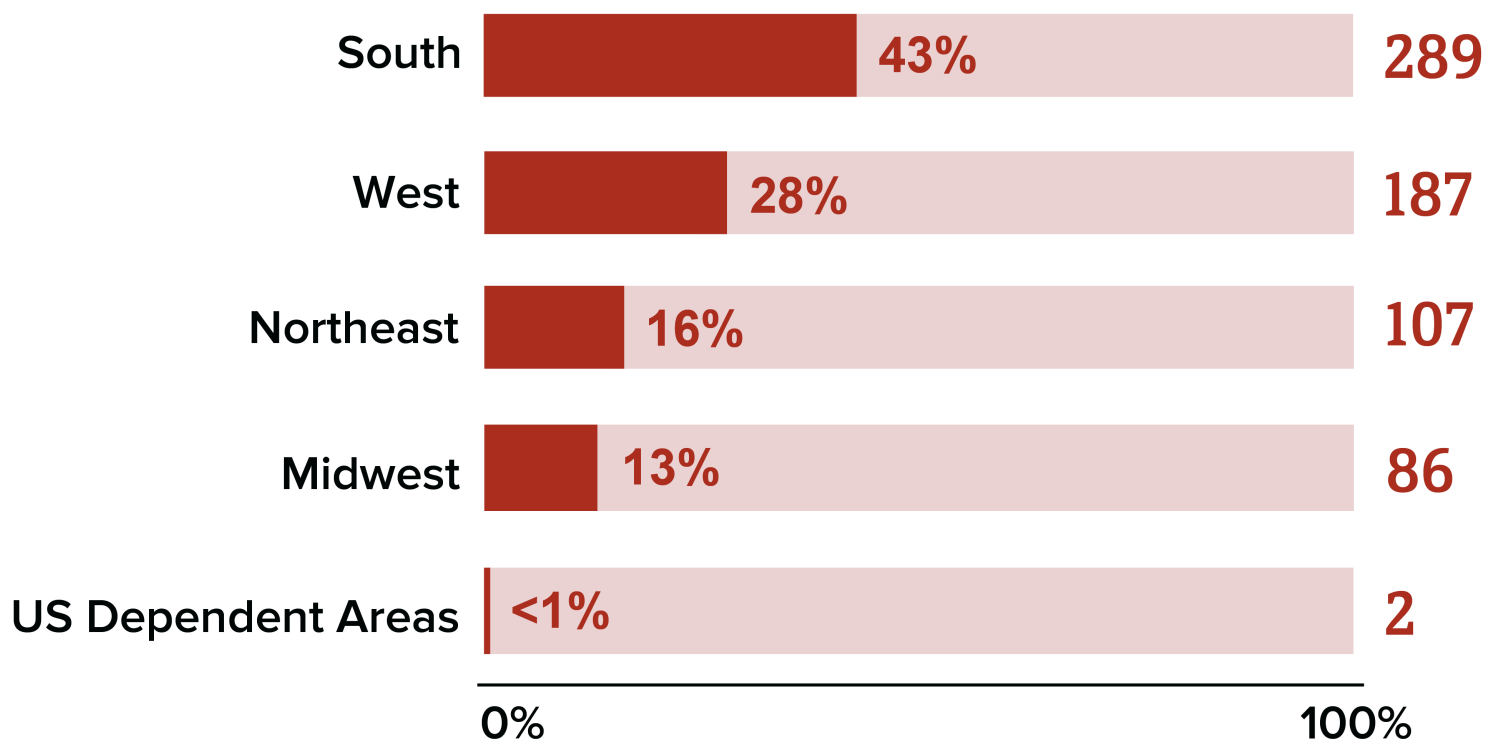
Learn more about HIV diagnoses among transgender people by age.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

HIV diagnoses among transgender people by region in the US and dependent areas, 2019*

The highest number of new HIV diagnoses among transgender people were in the South.





Learn more about HIV diagnoses among transgender people by region.

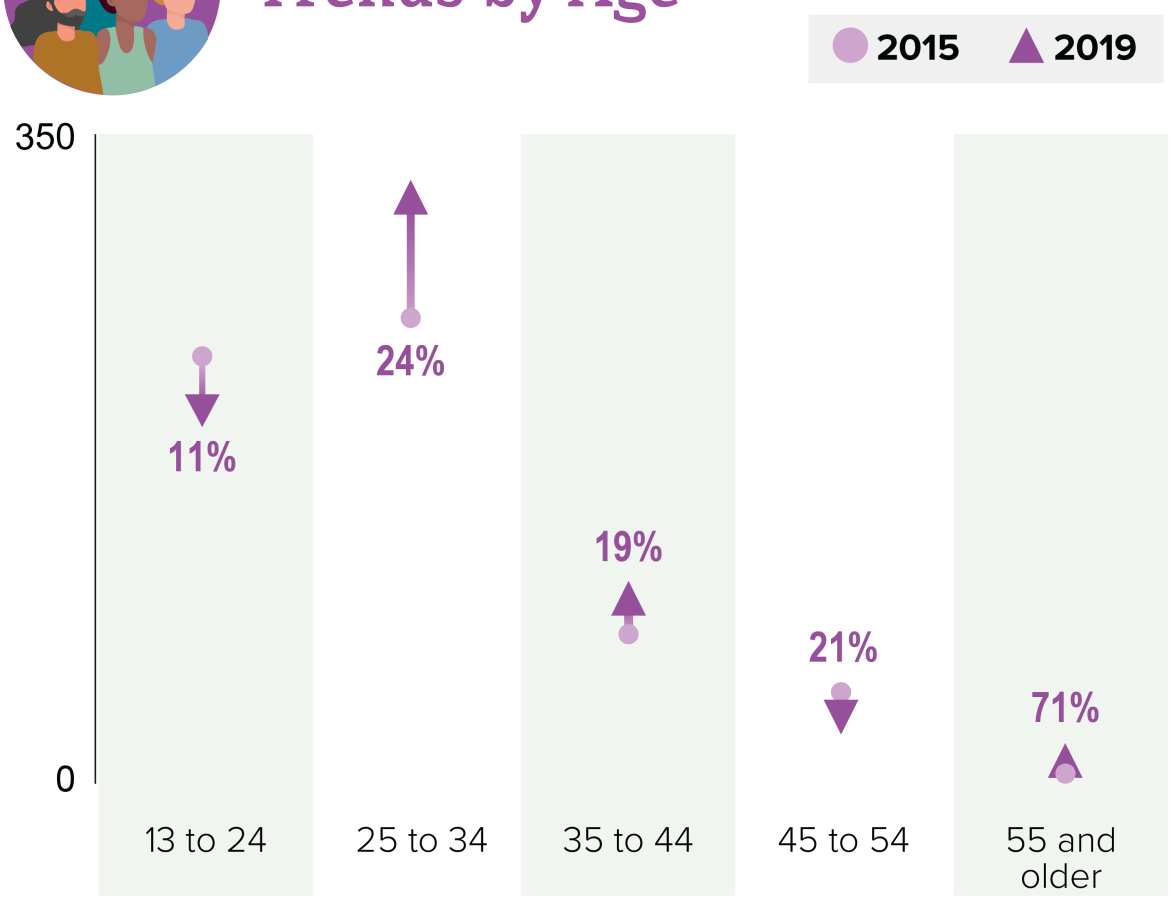
*Regions used in CDC's National HIV Surveillance System: Northeast: CT, ME, MA, NH, NJ, NY, PA, RI, VT Midwest: IL, IN, IA, KS, MI, MN, MO, NE, ND, OH, SD, WI South: AL, AR, DE, DC, FL, GA, KY, LA, MD, MS, NC, OK, SC, TN, TX, VA, WV West: AK, AZ, CA, CO, HI, ID, MT, NV, NM, OR, UT, WA, WY

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

HIV diagnoses among transgender people in the US and dependent areas, 2015-2019*



Trends by Age



Learn more about trends in HIV diagnoses among transgender people.

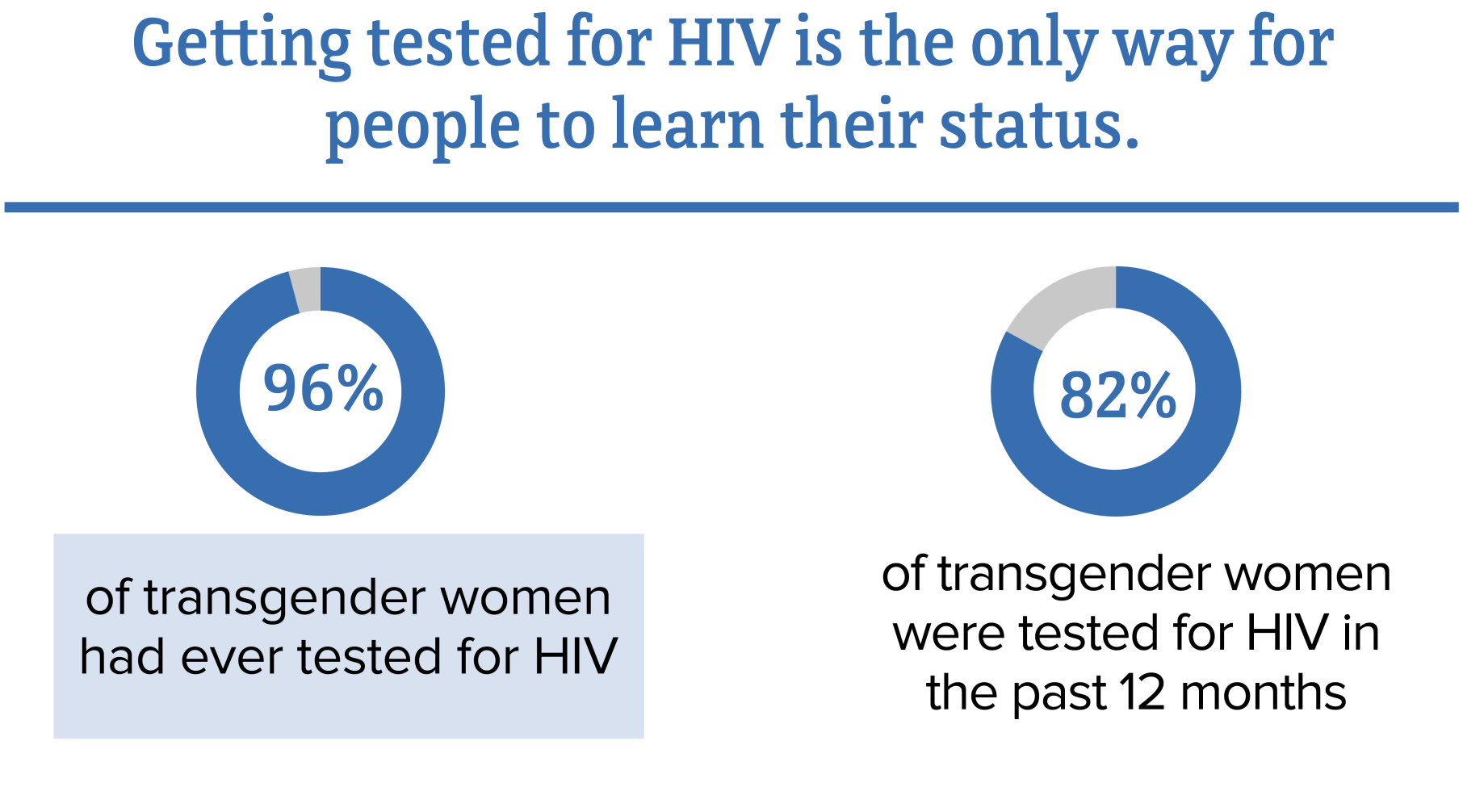
*Changes in subpopulations with fewer HIV diagnoses can lead to a large percentage increase or decrease.

Source: CDC. Diagnoses of HIV infection in the United States and dependent areas, 2019. *HIV Surveillance Report* 2021;32.

HIV testing

HIV testing is the gateway to care for people who have HIV and to prevention services for people who don't have HIV. CDC recommends that everyone between the ages of 13 and 64 get tested for HIV at least once as part of routine health care. People with certain risk factors should get tested at least once a year. A recent study found that transgender women have high rates of recent and lifetime HIV testing.

HIV testing among transgender women in 7 US cities, 2019–2020*



Learn more about HIV testing among transgender women.

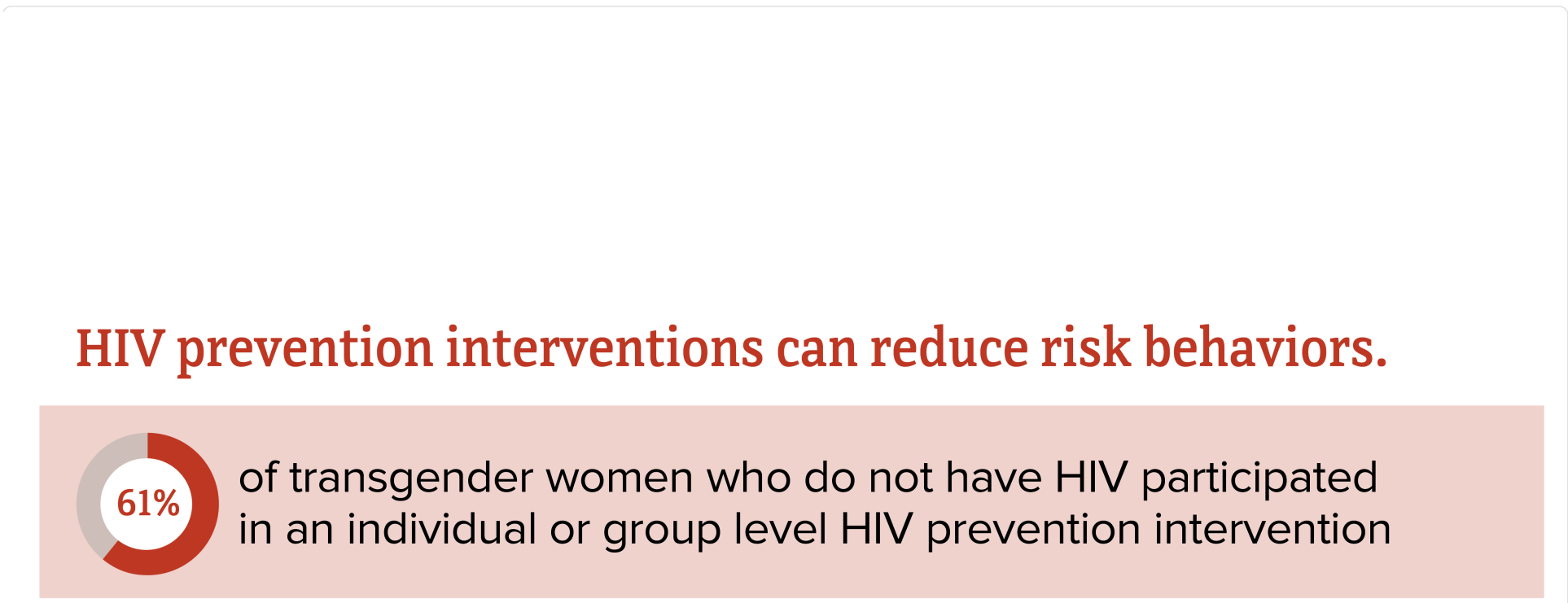
*Among people aged 18 and older.

Source: CDC. HIV infection, risk, prevention, and testing behaviors among transgender women–National HIV Behavioral Surveillance–7 U.S. Cities, 2019-2020. *HIV Surveillance Special Report* 2021.

HIV prevention

There are many HIV prevention strategies available, including condoms; pre-exposure prophylaxis (PrEP); post-exposure prophylaxis (PEP); as well as interventions focused on risk reduction; adherence to HIV medicine; linkage to, retention in, and re-engagement in care; structural approaches; and engagement in PrEP care. Additionally, for people with HIV, treatment provides substantial benefits for personal health and reduces HIV transmission to others. This is sometimes called HIV treatment as prevention.

HIV prevention interventions among transgender women in 7 US cities, 2019–2020*



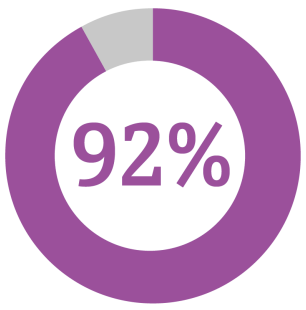
Learn more about HIV prevention interventions among transgender women.

*Among people aged 18 and older.

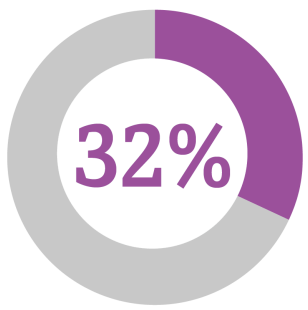
Source: CDC. HIV infection, risk, prevention, and testing behaviors among transgender women–National HIV Behavioral Surveillance–7 U.S. Cities, 2019-2020. *HIV Surveillance Special Report* 2021.

PrEP awareness and use among transgender women in 7 US cities, 2019–2020*

PrEP is highly effective for preventing HIV from sex or injection drug use.



of transgender women without HIV were aware of PrEP



of transgender women without HIV used PrEP

Learn more about PrEP awareness and use among transgender women.

*Among people aged 18 and older.

Source: CDC. HIV infection, risk, prevention, and testing behaviors among transgender women–National HIV Behavioral Surveillance–7 U.S. Cities, 2019-2020. *HIV Surveillance Special Report* 2021.

HIV prevalence

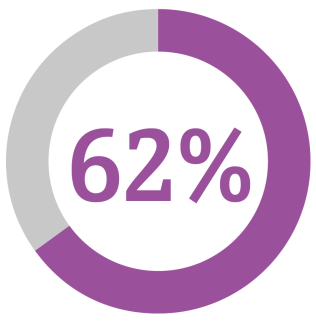
HIV prevalence is the number of people with HIV at a given time regardless of the time of infection.

HIV prevalence among transgender women in 7 US cities, 2019–2020*

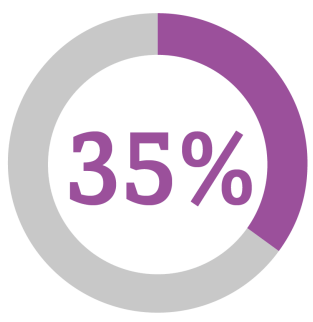
Racial and ethnic disparities exist among transgender women with HIV.



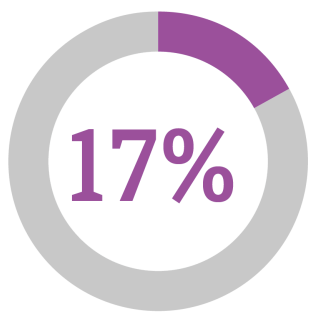
Among transgender women interviewed, 42% had HIV.



of Black/African American transgender women had HIV



of Hispanic/Latina transgender women had HIV



of White transgender women had HIV

Learn more about HIV prevalence among transgender women.

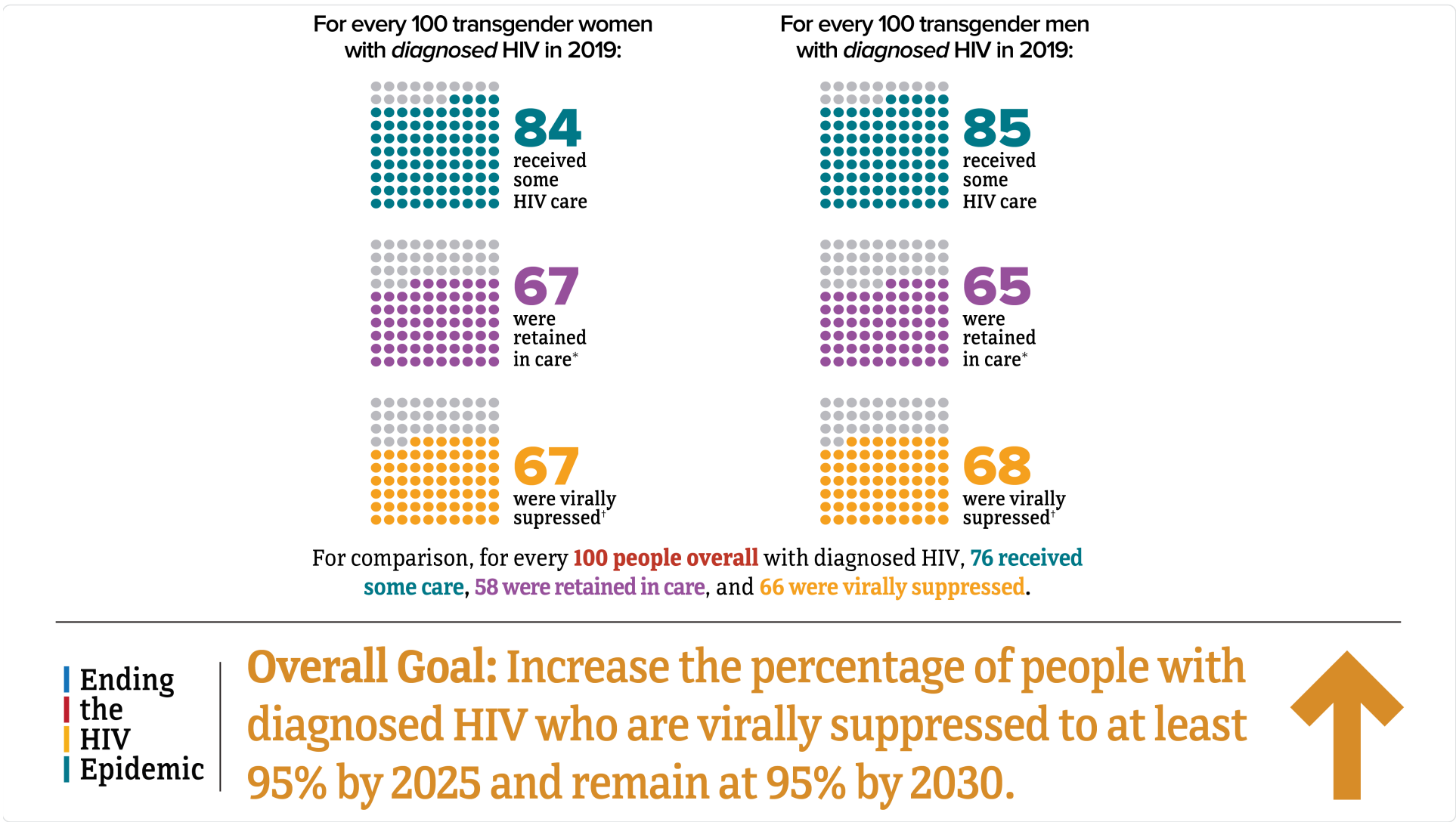
*Among people aged 18 and older.

Source: CDC. HIV infection, risk, prevention, and testing behaviors among transgender women–National HIV Behavioral Surveillance–7 U.S. Cities, 2019-2020. *HIV Surveillance Special Report* 2021.

Viral suppression and barriers to care

Viral suppression refers to the percentage of people with diagnosed HIV who have less than 200 copies of HIV per milliliter of blood.

Transgender people with diagnosed HIV in 44 states and the District of Columbia, 2019



Learn more about HIV care and viral suppression among transgender people with diagnosed HIV.

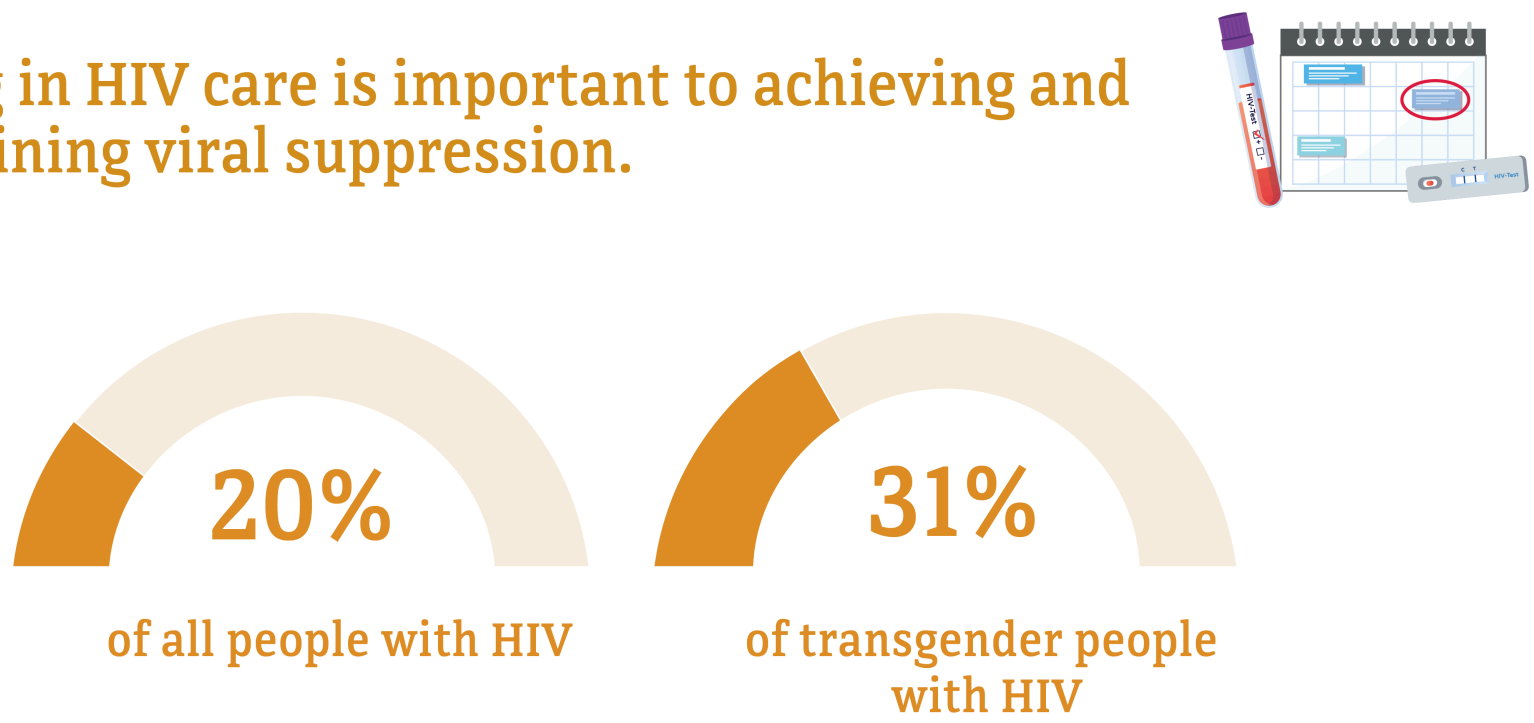
*Had 2 viral load or CD4 tests at least 3 months apart in a year.

† Had less than 200 copies of HIV per milliliter of blood on most recent viral load test.

Source: CDC. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 Dependent Areas, 2019. *HIV Surveillance Special Report* 2021; 26(2).

Many people with HIV experience challenges with achieving and maintaining viral suppression over time. Some of these challenges include missing HIV medical appointments, needing but not receiving other important health care services, or missing doses of HIV treatment.

Missed HIV medical care appointments among transgender people with diagnosed HIV in the US, 2020*

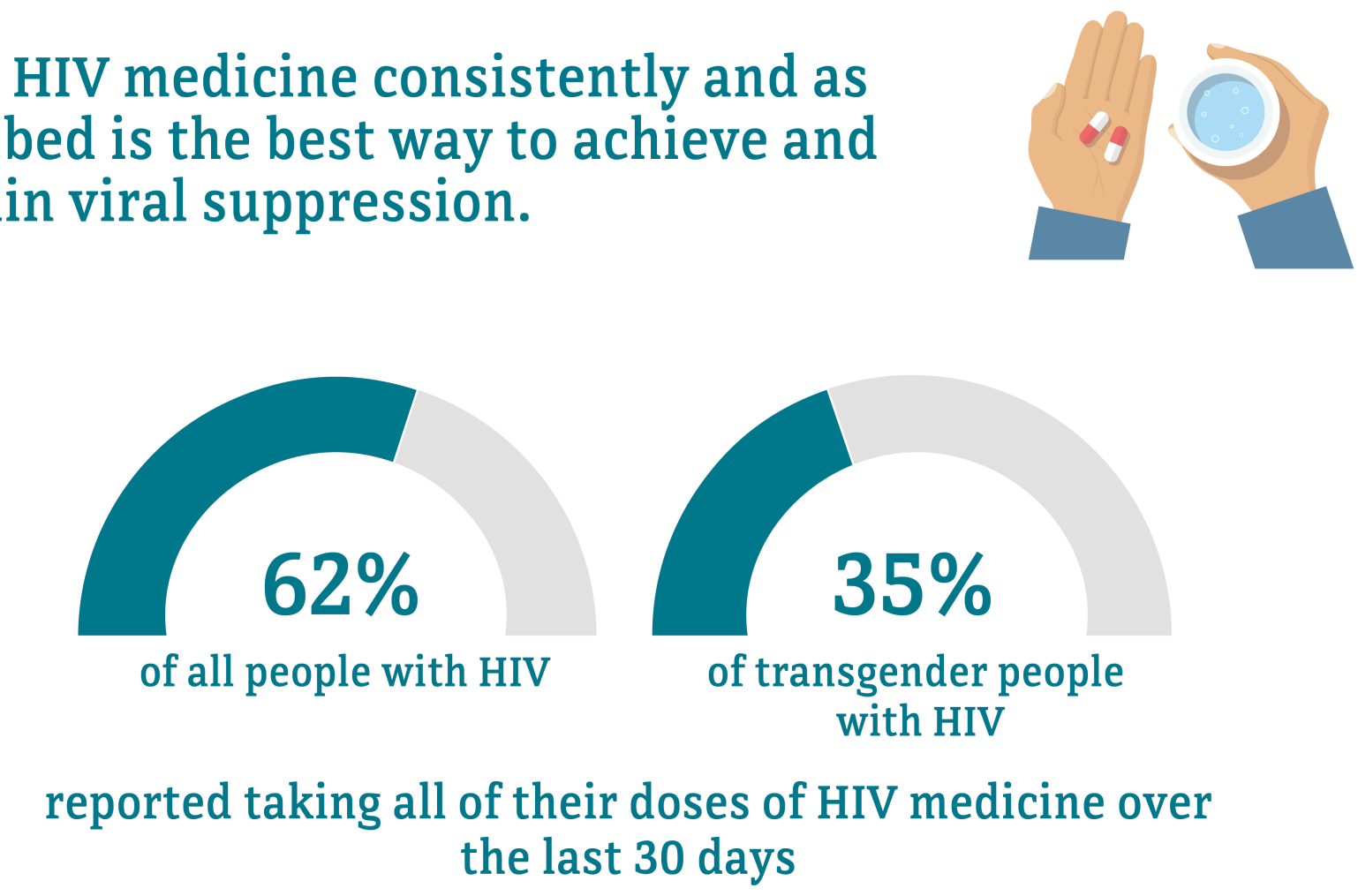


Learn more about missed HIV medical care appointments among transgender people with diagnosed HIV.

*Among people aged 18 and older.

Source: CDC. Medical Monitoring Project.

HIV treatment among transgender people with diagnosed HIV in the US, 2020*

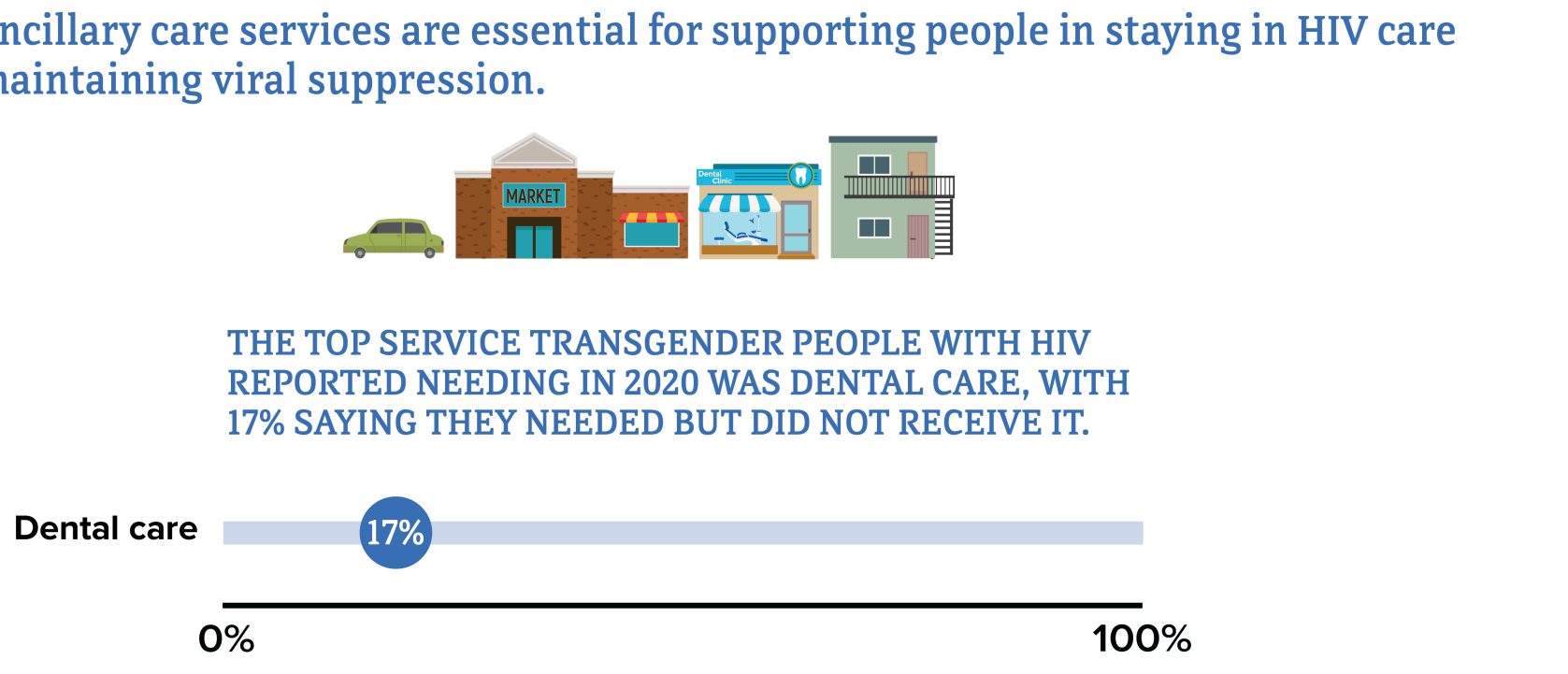


Learn more about HIV treatment among transgender people with diagnosed HIV.

*Among people aged 18 and older.

Source: CDC. Medical Monitoring Project.

Needed HIV ancillary services among transgender people with diagnosed HIV in the US, 2020*†



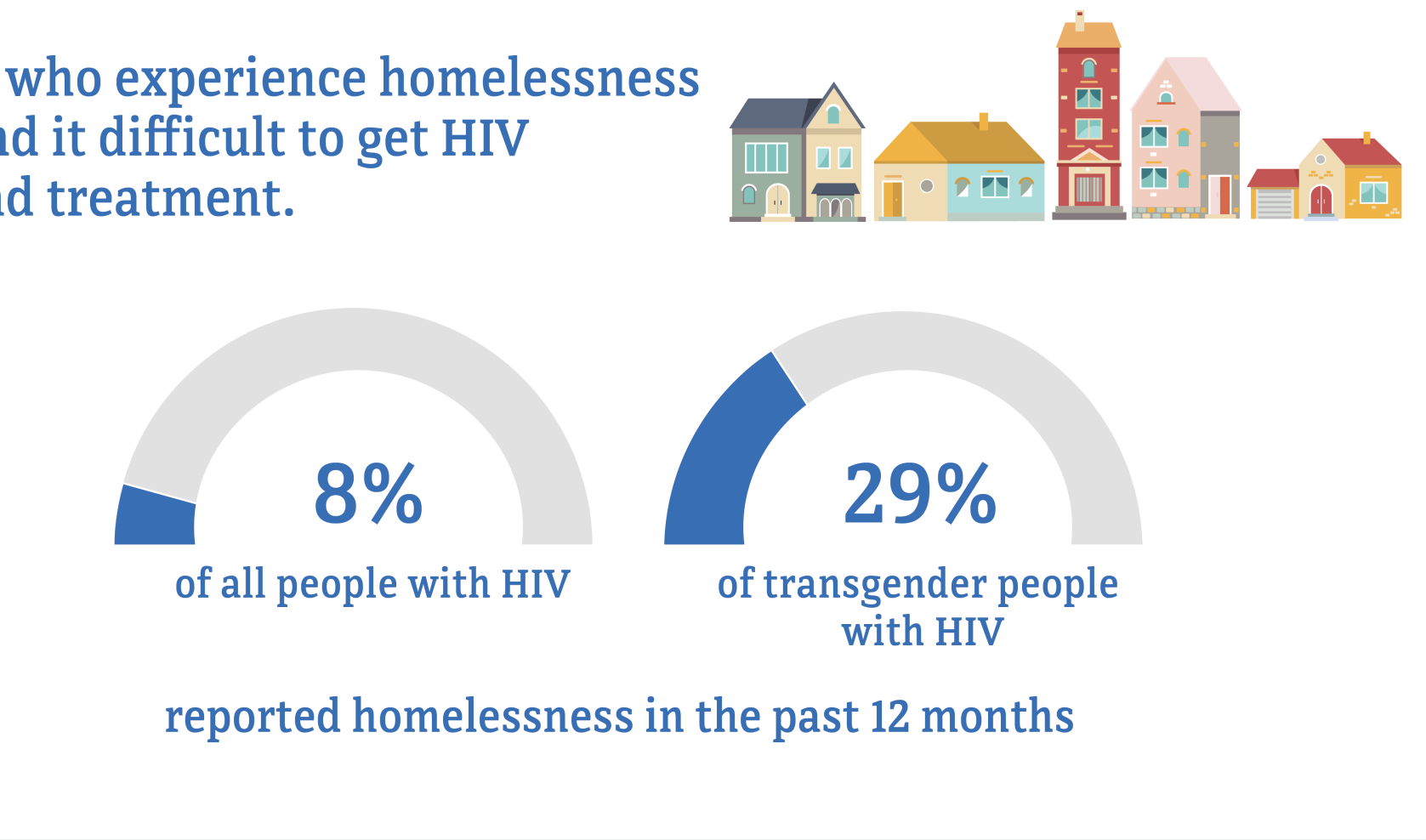
Learn more about needed HIV ancillary services among transgender people with diagnosed HIV.

*Among people aged 18 and older.

†HIV ancillary services, such as case management and mental health services, are services that support retention in HIV care and viral suppression.

Source: CDC. Medical Monitoring Project.

Homelessness among transgender people with diagnosed HIV in the US, 2020*

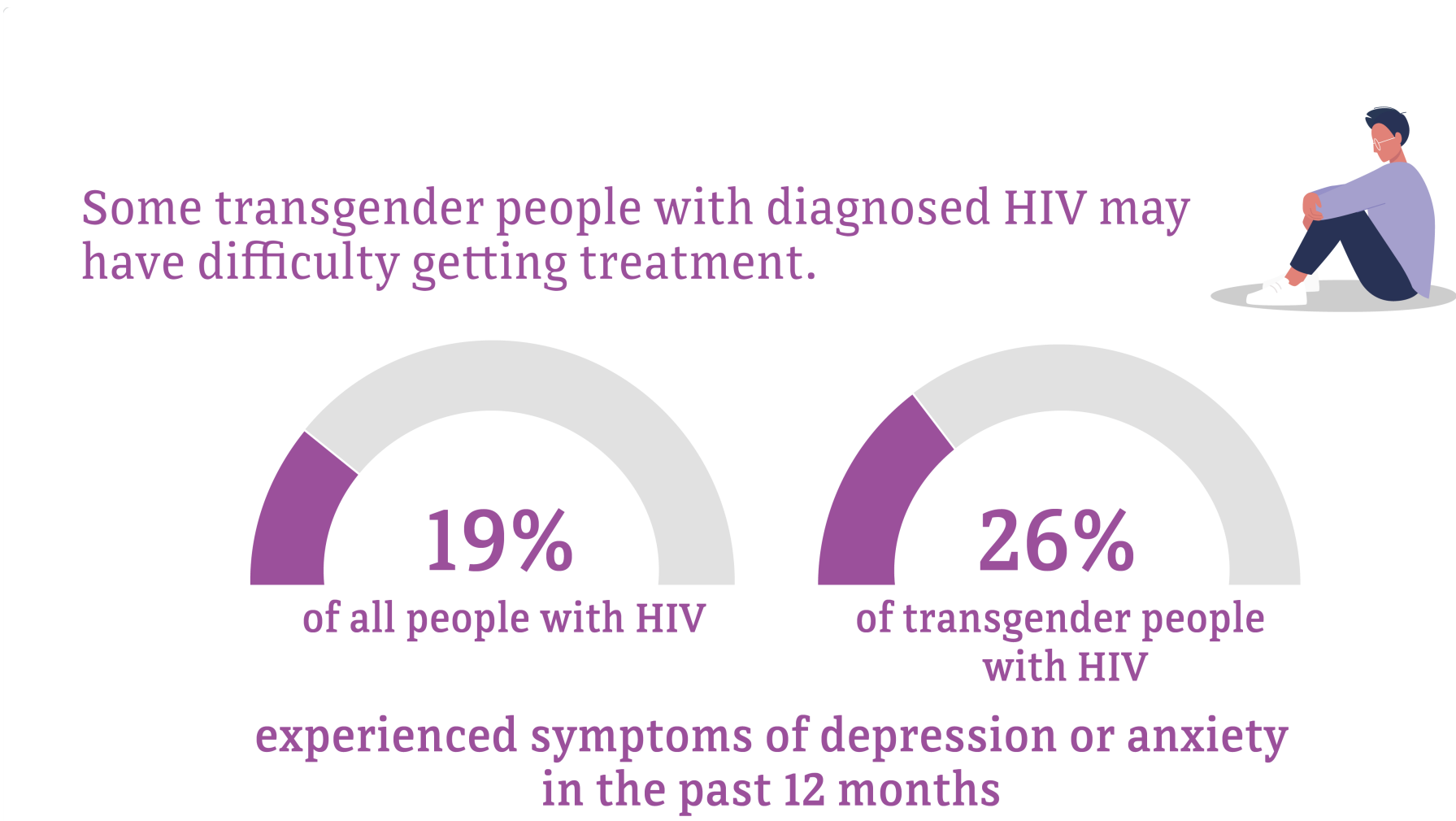


Learn more about homelessness among transgender people with diagnosed HIV.

*Among people aged 18 and older.

Source: CDC. Medical Monitoring Project.

Depression and anxiety among transgender people with diagnosed HIV in the US, 2020*

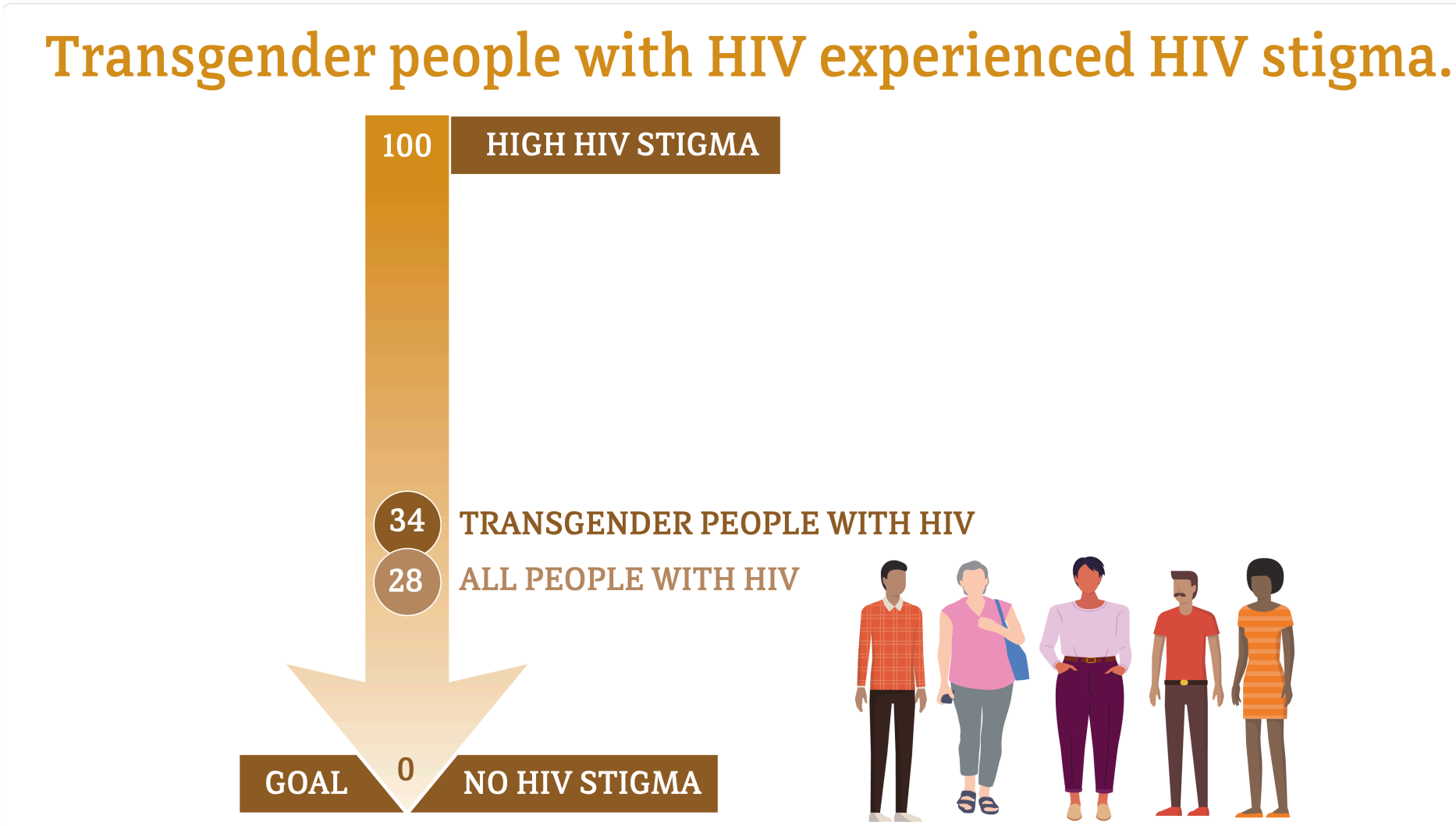


Learn more about depression and anxiety among transgender people with diagnosed HIV.

*Among people aged 18 and older.

Source: CDC. Medical Monitoring Project.

Median HIV stigma score among transgender people with diagnosed HIV in the US, 2020*



Learn more about HIV stigma experienced by transgender people with diagnosed HIV.

Median HIV stigma scores are presented based on a ten-item scale ranging from 0 (no stigma) to 100 (high stigma) that measures personalized stigma during the past 12 months, current disclosure concerns, current negative self-image, and current perceived public attitudes about people with HIV.

*Among people aged 18 and older.

Source: CDC. Medical Monitoring Project.

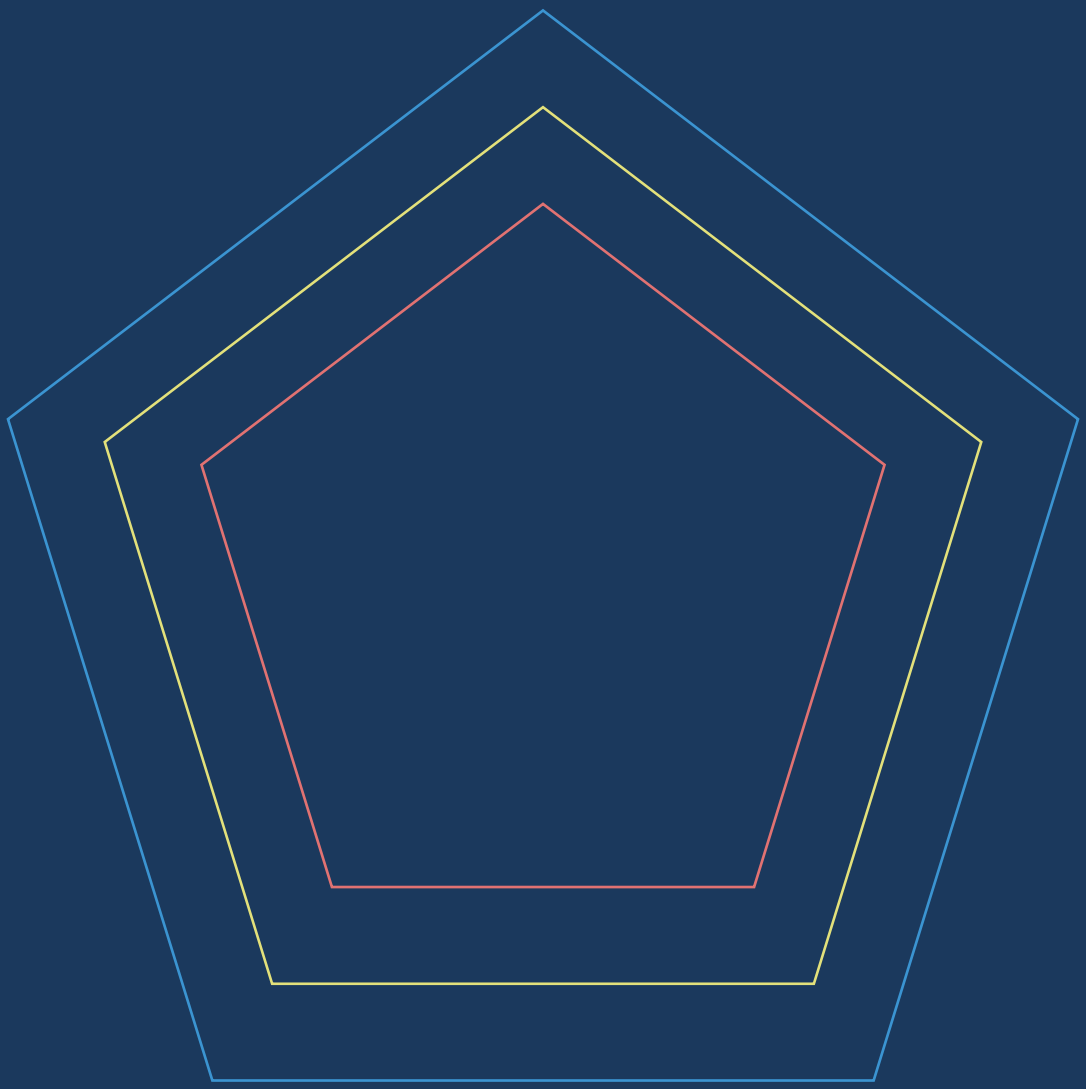
SOURCES

CONTENT SOURCE:

National Center for HIV, Viral Hepatitis, STD, and Tuberculosis Prevention; Division of HIV Prevention

EXHIBIT E

Consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment and care for key populations



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World Health Organization

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https://apps.who.int/iris/bitstream/handle/10665/360443/9789240053434-eng.pdf

Web Annex B. Values and preferences report
https://apps.who.int/iris/bitstream/handle/10665/360444/9789240053441-eng.pdf

Web Annex C. Systematic review findings and GRADE tables
https://apps.who.int/iris/bitstream/handle/10665/360445/9789240053458-eng.pdf

Web Annex D. Evidence to decision making tables
https://apps.who.int/iris/bitstream/handle/10665/360446/9789240053465-eng.pdf

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Acronyms and abbreviations

AIM	AIDS impact model
ALT	alanine aminotransferase
ANC	antenatal care
ART	antiretroviral therapy
ARV	antiretroviral drugs
CRC	United Nations Convention on the Rights of the Child
DAA	direct-acting antiviral
FGD	focus group discussions
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HBsAg	hepatitis B surface antigen
HBeAg	Hepatitis B e antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HPV	human papillomavirus
HRCT	human rights costing tool
HSV	herpes simplex virus
HTS	HIV testing services
ICER	incremental cost-effectiveness ratio
IUD	intrauterine device
LMIC	low- and middle-income countries
M&E	monitoring and evaluation
MEC	medical eligibility criteria for contraceptive use
MhGAP	mental health gap action programme
NAAT	nucleic acid amplification test
NSP	national strategic plan
NSPs	needle and syringe programmes
NSWP	Global Network of Sex Work Projects
OAMT	opioid agonist maintenance therapy
PEP	post-exposure prophylaxis
PICO	population, intervention, comparator, outcome
PPT	periodic presumptive treatment
PrEP	pre-exposure prophylaxis
py	person years
QALY	quality-adjusted life-year
RCT	randomized controlled trial
RDT	rapid diagnostic test
SDG	Sustainable Development Goal
SITE	syphilis interventions towards elimination
SSI	semi-structured interviews
STI	sexually transmitted infection
SVR	sustained virological response
TB	tuberculosis
UHC	universal health coverage
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNFPA	United Nations Population Fund
UNICEF	United Nations International Children's Emergency Fund
UNODC	United Nations Office on Drugs and Crime
WHO	World Health Organization

Glossary

Acute hepatitis C (HCV): a recently acquired HCV infection that meets certain clinical criteria (discrete onset of symptoms such as nausea or malaise plus either jaundice or elevated serum alanine aminotransferase (ALT) levels (tenfold increase).

Adolescents: individuals between the ages of 10 and 19 years old are generally considered adolescents. Adolescence is the developmental transition to adulthood accompanied by hormonal, physical and psychological developments in the period from puberty to adulthood. Adolescents are not a homogenous group; physical and emotional maturation comes with age, but its progress varies among individuals of the same age. Also, different social and cultural factors can affect their health, their ability to make important personal decisions and their ability to access services. This document primarily uses the term "adolescents". Adolescents may also belong to one or more key population groups. Other terms covering overlapping age groups include **youth** – this term refers to individuals between the ages of 15 and 24, and **young people** – this term refers to those between the ages of 10 and 24.

Antiretroviral therapy (ART): refers to using a combination of antiretroviral (ARV) drugs for treating HIV infection.

Antiretroviral (ARV) drugs: refer to the medicines used to treat HIV.

Chemsex: for the purpose of these guidelines, is defined as when individuals engage in sexual activity, while taking primarily stimulant drugs, typically involving multiple participants and over a prolonged time.

Children: according to Article 1 of the Convention on the Rights of the Child, "A child means every human being below the age of eighteen years unless, under the law applicable to the child, majority is attained earlier".

Chronic hepatitis B (HBV) infection: persistence of HBsAg for at least six months. The persistence of HBsAg in two specimens at least six months apart is frequently used in clinical practice to confirm chronic hepatitis B infection.

Chronic hepatitis C infection (HCV): defined by HCV antibody positivity and HCV RNA positivity with a duration of infection longer than six months.

Cirrhosis: an advanced stage of liver disease characterized by extensive hepatic fibrosis, nodularity of the liver, alteration of liver architecture and disrupted hepatic circulation.

Community-led organizations: groups and networks are those that are led by and for the constituencies they serve. They are self-determining and autonomous entities where the majority of governance, leadership, staff, spokespeople, membership and volunteers reflect and represent the experiences, perspectives and voices of their constituencies, and which have transparent mechanisms of accountability to their constituencies.

Community-led responses: can be understood as the actions and strategies undertaken by these groups to improve the health and human rights of their constituencies. These responses are informed and implemented by and for communities themselves and the organizations, groups and networks that represent them.

Community-led responses are determined by and respond to the needs and aspirations of their constituents, and include a range of activities, such as advocacy, campaigning and holding decision-makers to account; monitoring of policies, practices, and service delivery; participatory research; education and information-sharing; service delivery; capacity-building; and funding of community-led organizations, groups and networks.

Decentralization: the process of delegating or transferring significant authority and resources from the central ministry of health to other institutions or to field offices of the ministry at other levels of the health system (such as provincial, regional, district, subdistrict, primary health care post and community).

Differentiated service delivery: an approach that simplifies and adapts services to better serve the needs of people living with HIV, viral hepatitis or Sexually transmitted infections (STIs), and to optimize the available resources in health systems.

HCV self-testing (HCVST): a process in which an individual collects their own specimen (blood or oral fluid), performs a rapid diagnostic test for the presence of HCV antibodies, and then interprets the result, often in a private setting, either alone or with someone they trust.

HCV sustained virological response (SVR): undetectable HCV RNA in the blood at a defined time point after the end of treatment, usually at 12 or 24 weeks (SVR12 or SVR24).

Human immunodeficiency virus (HIV): There are two types of HIV: HIV-1 and HIV-2. The vast majority of HIV infections globally are HIV-1.

HIV self-testing: a process in which a person collects their own specimen (oral fluid or blood), performs a test and interprets the result, often in a private setting, either alone or with someone they trust.

Integrated service delivery: integrated health services are health services that are managed and delivered in a way that ensures that people receive a continuum of health promotion, disease prevention, diagnosis, treatment, disease management, rehabilitation and palliative care services at the different levels and sites of care within the health system and according to their needs throughout the life-course.

Key populations: defined groups who, due to specific higher-risk behaviours, are at increased risk of HIV, viral hepatitis or STIs irrespective of the epidemic type or local context. Also, they often have legal and social issues related to their behaviours that increase their vulnerability to HIV. These guidelines focus on five key populations: 1) men who have sex with men; 2) people who inject drugs; 3) people in prisons and other closed settings; 4) sex workers; and 5) trans and gender diverse people. People in prisons and other closed settings are also included in these guidelines because of the often high levels of incarceration of the other groups, and the increased risk behaviours and lack of HIV, viral hepatitis and STI services in these settings. The key populations are important to the dynamics of HIV, viral hepatitis and STI transmission. They also are essential partners in an effective response to the epidemic.

Lay provider: any person who performs functions related to health care delivery and has been trained to deliver specific services, but has not received a formal professional or paraprofessional certificate or tertiary degree.

Men who have sex with men: refers to all men who engage in sexual relations with other men. The words “men” and “sex” are interpreted differently in diverse cultures and societies and by the individuals involved. Therefore, the term encompasses the large variety of settings and contexts in which male-to-male sex takes place, regardless of multiple motivations for engaging in sex, self-determined sexual and gender identities, and various identifications with any particular community or social group.

Nucleic acid amplification test (NAAT): a molecular technology, for example, polymerase chain reaction (PCR) or nucleic acid sequence-based amplification (NASBA) that can detect very small quantities of viral nucleic acid (RNA or DNA), either qualitatively or quantitatively.

Ongoing risk exposure for HCV: includes engagement in activities that increase the risk of HCV transmission: e.g., exposure to HCV infectious blood or body fluids that contain blood, including injection drug use and male-to-male sexual contact.

Partner services: (sometimes referred to as disclosure, contact tracing, index testing or assisted partner notification): a voluntary process whereby a trained provider asks people diagnosed with HIV about their sexual partners and/or drug injecting partners, and then, if the HIV-positive client agrees, offers the partner voluntary HIV testing services (HTS). Partner services are provided using provider-assisted referral or patient referral approaches.

People-centred care: care that is focused and organized around the health needs and expectations of people and communities rather than diseases.

People in prisons and other closed settings: there are many different terms used to denote places of detention that hold people who are awaiting trial, those who have been convicted, or people who are subject to other conditions of security. Similarly, different terms are used for those who are detained. In this guidance document, the term "prisons and other closed settings" refers to all places of detention within a country, and the terms "prisoners" and "detainees" refer to all those detained in criminal justice and prison facilities, including adult and juvenile males, females, trans and gender diverse individuals, during the investigation of a crime, while awaiting trial, after conviction, before sentencing and after sentencing. This term does not formally include people detained for reasons relating to immigration or refugee status, those detained without charge, and those sentenced to compulsory treatment and to rehabilitation centres. Nonetheless, most of the considerations in these guidelines apply to these people as well.

People who inject drugs: refers to people who inject psychoactive substances for non-medical purposes. These drugs include, but are not limited to, opioids, amphetamine-type stimulants, cocaine and hypno-sedatives, including new psychoactive substances.[1] Injection may be through intravenous, intramuscular, subcutaneous or other injectable routes. People who self-inject medicines for medical purposes – referred to as "therapeutic injection" – are not included in this definition. While these guidelines focus on people who inject drugs because of their specific risk of HIV and HCV transmission due to the sharing of blood-contaminated injection equipment, much of this guidance is also relevant for people who use substances through other routes of administration such as snorting, smoking and ingestion.

People who use drugs: include people who use psychoactive substances through any route of administration, including injection, oral, inhalation, transmucosal (sublingual, rectal, intranasal) or transdermal. Often this definition does not include the use of widely used substances such as alcoholic and caffeine-containing beverages and foods.

Point-of-care testing: is conducted at the site at which clinical care is being provided, with the results being returned to the person being tested or caregiver on the same day as sample collection and testing, to enable clinical decisions to be made in a timely manner.

Pre-exposure prophylaxis (PrEP): is the use of ARV drugs by people who do not have HIV, to prevent the acquisition of HIV before exposure.

Post-exposure prophylaxis (PEP): is the use of ARV drugs by people who do not have HIV, to prevent the acquisition of HIV after exposure.

Recent hepatitis C infection: evidenced by:

- positive HCV RNA or antigen test in an individual that returned a negative antibody, RNA or antigen result within the preceding year (including instances where this represents re-infection);
- positive HCV RNA or antigen test AND a current negative HCV antibody test; and
- positive antibody, RNA or antigen test AND, within the preceding year, clinical symptoms of acute hepatitis.

[1] The United Nations Office on Drugs and Crime (UNODC) uses the term "new psychoactive substances" which are defined as "substances of abuse, either in a pure form or a preparation, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat". For more information visit the UNODC Early Warning Advisory on New Psychoactive Substances 2022 [Available from: https://www.unodc.org/LSS/Page/NPS].

Sex workers: include female, male, trans and gender diverse adults (18 years of age and above) who receive money or goods in exchange for sexual services, either regularly or occasionally. Sex work is consensual sex between adults, can take many forms, and varies between and within countries and communities. Sex work also varies in the degree to which it is more or less "formal" or organized. As defined in the Convention on the Rights of the Child (CRC), children and adolescents under the age of 18 who exchange sex for money, goods or favours are "sexually exploited" and not defined as sex workers.

Social network-based HIV testing: is an extension of partner services. A trained provider asks people with HIV, or those who are HIV-negative but at ongoing risk of HIV, to encourage and invite individuals in their sexual, drug-injecting or social networks to participate in voluntary HIV testing services. A social network refers to a group of individuals linked by a common set of relationships and includes sexual and drug-injecting partners, as well as social contacts.

Substantial risk (of HIV infection): HIV acquisition risk varies considerably within populations and geographical locations. Population-level HIV incidence is an important determinant of individual-level risk of HIV acquisition. However, when considering who could benefit from PrEP, it is important to consider the characteristics and behaviours of individuals and their partners that could lead to HIV exposure. Even in locations with a low overall HIV incidence, there may be individuals at substantial risk who could benefit from PrEP services. Individuals requesting PrEP should be given priority when offering PrEP since requesting PrEP indicates that there is likely to be a risk of acquiring HIV. When PrEP use is risk-informed (taken during periods of risk of HIV acquisition), PrEP can be cost-effective. Cost-effectiveness will vary across countries, populations, and PrEP products. However, cost–effectiveness should not be the only consideration when implementing PrEP programmes, since remaining HIV-negative and having control over HIV risk has intangible value to people and communities.

Task sharing: the rational redistribution of tasks between cadres of health care workers with longer training and other cadres with shorter training, such as lay providers.

Trans and gender diverse people: an umbrella term for those whose gender identity, roles and expression does not conform to the norms and expectations traditionally associated with the sex assigned to them at birth; it includes people who are transsexual, transgender, or otherwise gender nonconforming or gender incongruent. Trans and gender diverse people may self-identify as transgender, female, male, transwoman or transman, transsexual or one of many other gender nonconforming identities. They may express their genders in a variety of masculine, feminine and/or androgynous ways. The high vulnerability and specific health needs of trans and gender diverse people necessitate a distinct and independent status in the global HIV response.

Unprotected sex: refers to sex which does not involve evidence-based prevention interventions. These include condoms plus lubricants, which are protective against HIV, viral hepatitis and STIs and HIV pre-exposure prophylaxis. Successful ART with viral suppression prevents HIV transmission to sexual partners.

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Executive summary

Purpose

The *Consolidated guidelines on HIV, viral hepatitis and STI prevention, diagnosis, treatment and care for key populations* outlines a public health response to HIV, viral hepatitis and sexually transmitted infections (STIs) for five key populations (men who have sex with men, trans and gender diverse people, sex workers, people who inject drugs and people in prisons and other closed settings). The guidelines present and discuss new recommendations and consolidate a range of recommendations and guidance from current World Health Organization (WHO) guidelines.

These guidelines focus on the above five groups, originally defined as "key" in the HIV response across the three infectious disease areas. This is for the following reasons.

- The structural barriers which limit the five key populations' access to HIV services also limit their access to viral hepatitis and STI services.
- HIV risk behaviours such as condomless sex and unsafe injecting, which are in general more common in key populations, are also among those that increase the risk of acquiring viral hepatitis and STIs.
- Many of the interventions recommended for HIV prevention also have an impact on transmission of viral hepatitis and STIs.

Particularly for key populations, social, legal, structural and other contextual factors both increase vulnerability to HIV, viral hepatitis and STIs and obstruct access to health and other essential services. These guidelines highlight the critical importance of addressing structural barriers in all settings as a priority.

Guidelines principles

These guidelines are developed with the following principles:

- human rights;
- gender equality;
- equity and inclusion;
- medical ethics;
- universal health coverage;
- evidence-based public health;
- key population community-led response.

Guidelines development methodology

This publication is an update to the 2016 *Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations*. These guidelines include relevant existing recommendations, updated recommendations and new recommendations, good practice statements and other guidance.

For the development of new recommendations, WHO developed population, intervention, comparator, outcome (PICO) questions, and external researchers, supported by the WHO team, conducted the systematic reviews of the evidence to answer these questions.

WHO also commissioned four global networks of key populations (men who have sex with men, sex workers, trans and gender diverse people, and people who inject drugs) to undertake new qualitative research on values and preferences among their networks. The results formed part of the evidence synthesis.

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The evidence was synthesised and incorporated into an evidence-to-decision framework to help inform the discussions at a virtual Guideline Development Group meeting that occurred over six days between 30 August and 8 September 2021, chaired by two members of the Guideline Development Group, and all conflicts of interest were managed. The methodologist facilitated the Guideline Development Group's judgements, assisted by the chairs, on the potential benefits and harms of the intervention, stakeholder values and preferences, acceptability, feasibility, resource use and considerations of human rights and equity. Taken together and using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology, these judgements contributed to determining the strength and direction of the recommendation. All recommendations were made through consensus.

In these updated guidelines, guidance is provided to national programme managers, donors and advocates on how to prioritize different packages of health interventions to have the greatest impact on HIV, viral hepatitis and STIs, and to ensure universal coverage to address other health issues for key populations.

Each of the interventions listed, included in these guidelines based on initial scoping, was classified for each key population as follows.

1. **Essential for impact: enabling interventions**

   This includes all interventions recommended to address structural barriers to health services' access for key populations.

2. **Essential for impact: health interventions**

   This includes health sector interventions that have a demonstrated direct impact on HIV, viral hepatitis and STIs in key populations.

3. **Essential for broader health**

   This includes health sector interventions to which access for key populations should be ensured, but which do not have direct impact on HIV, viral hepatitis or STIs.

4. **Supportive**

   This includes other interventions which support the delivery of health sector interventions, such as creating demand, providing information and education.

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Summary of essential health and enabling recommendations

Essential for impact: enabling interventions

Removing punitive laws, policies and practices

Reducing stigma and discrimination

Community empowerment

Addressing violence

Essential for impact: health interventions

Prevention of HIV, viral hepatitis and STIs

Harm reduction (needle and syringe programmes (NSPs), opioid agonist maintenance therapy (OAMT) and naloxone for overdose management)

Condoms and lubricant

Pre-exposure prophylaxis (PrEP) for HIV

Post-exposure prophylaxis (PEP) for HIV and STIs

Prevention of vertical transmission of HIV, syphilis and HBV

Hepatitis B vaccination

Addressing chemsex

Diagnosis

HIV testing services

STI testing

Hepatitis B and C testing

Treatment

HIV treatment

Screening, diagnosis, treatment and prevention of HIV-associated tuberculosis (TB)

STI treatment

Hepatitis B and hepatitis C treatment

Essential for broader health: health interventions

Anal health

Conception and pregnancy care

Contraception

Gender-affirming care

Mental health

Prevention, assessment and treatment of cervical cancer

Safe abortion

Screening and treatment for hazardous and harmful alcohol and other substance use

TB screening and prevention

CHAPTER 1

Introduction



Key populations for HIV, viral hepatitis and STIs

The original (2014) and updated (2016) versions of the World Health Organization (WHO) *Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations (3)* focused on HIV prevention, diagnosis, treatment and care for five key populations: men who have sex with men, sex workers, people in prisons and other closed settings, people who inject drugs, and trans and gender diverse people. However, members of these populations are also disproportionally affected by viral hepatitis and sexually transmitted infections (STIs), and there is increasing acknowledgement of the importance of addressing all three infectious disease areas in an integrated, community-led, and person-centred manner. Further, the risk behaviours and vulnerabilities of key populations and their networks determine the dynamics of HIV, viral hepatitis and STI epidemics, creating syndemics (defined as two or more infections interacting synergistically, contributing to excess burden of disease in a population), and meaning that preventing, diagnosing and treating HIV, viral hepatitis and STIs in key populations is central to the elimination of these infectious diseases as public health threats.

While strategies for viral hepatitis and STIs include additional priority populations (such as health care workers for hepatitis B virus (HBV) and pregnant women for syphilis and HBV) *(4, 5)*, and other populations vulnerable to HIV, in these guidelines we will focus on the above five groups, originally defined as "key" in the HIV response across the three infectious disease areas. This is for the following reasons.

- The structural barriers which limit the five key populations' access to HIV services also limit their access to viral hepatitis and STI services.
- HIV risk behaviours, such as condomless sex and unsafe injecting, which in general are more common in key populations, are also among those at increased risk of acquiring viral hepatitis and STIs.
- Many of the interventions recommended for HIV prevention also have an impact on transmission of viral hepatitis and STIs.

It is important to note that people can be members of more than one key population group, have more than one risk behaviour, and some people may engage in risk behaviours without identifying as members of a particular group; for example, men who have sex with other men but do not identify as gay. People who inject drugs often stop using drugs, sex workers stop sex working and people move in and out of prison; therefore, it is important to recognize the complexities and changes in people's lives.

In most countries, inadequate coverage and poor quality of services for key populations continue to undermine responses to HIV, viral hepatitis and STIs. All countries should prioritize reaching these key populations and supporting key population communities to lead the response and provide equitable, accessible and acceptable services to these groups.

Structural barriers

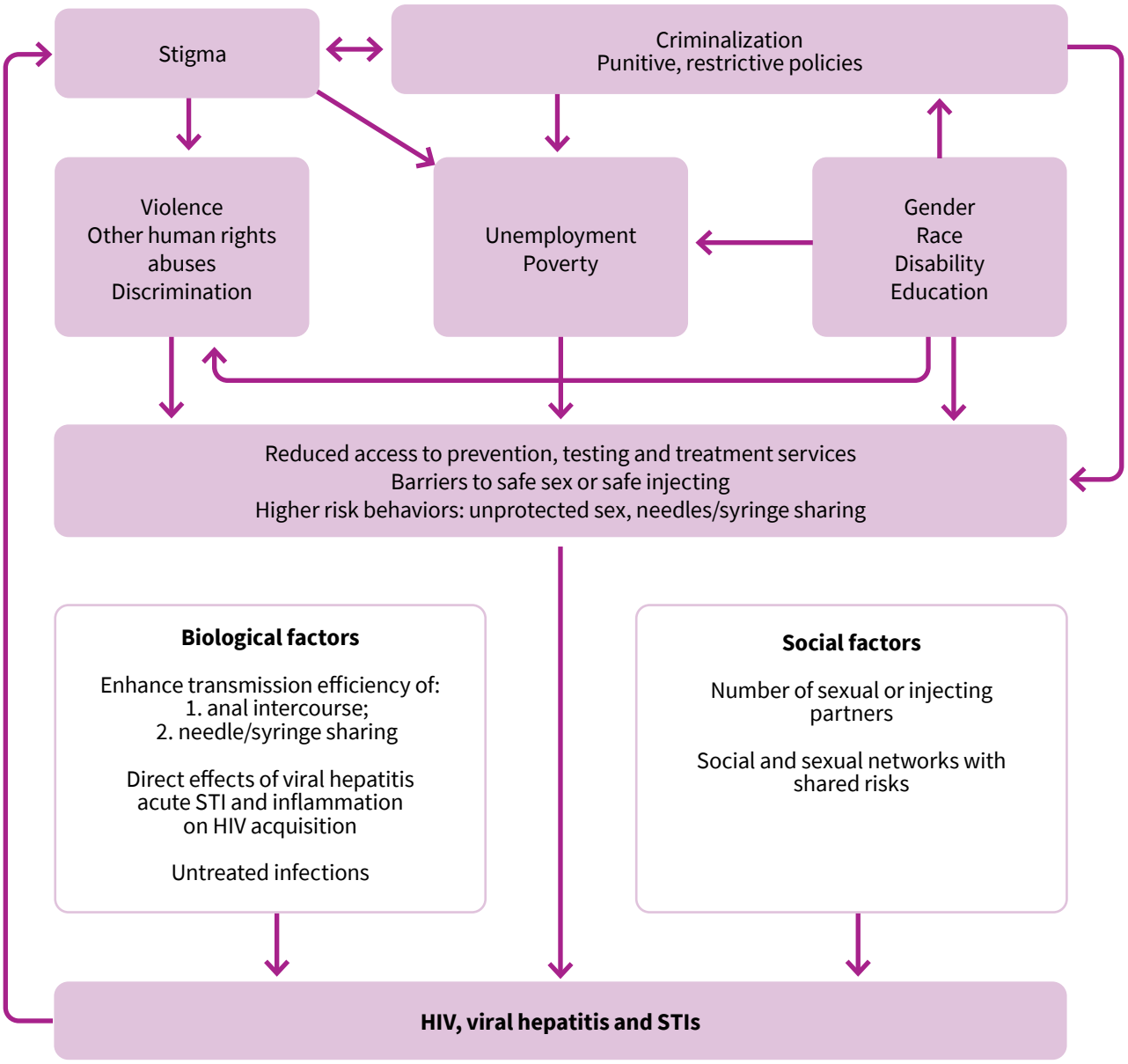
Particularly for key populations, social, legal, structural and other contextual factors both increase vulnerability to HIV, viral hepatitis and STIs, and obstruct access to health and other essential services. In many settings, one or more aspects of key population members' behaviour, work or gender expression are criminalized , and members are subject to punitive legislation and policing practices. Stigma and discrimination from/by the general population and health care workers and law enforcement officials are perpetuated by criminalization, which also means legal or policy change is more difficult to achieve. Stigma and discrimination in health care settings are common experiences among key populations and create significant barriers to achieving universal health coverage. Stigma and discrimination are related to unemployment as well as violence and human rights abuse. Violence and other human rights abuses are exacerbated by criminalization, making key population members less likely to report abuses and increasing vulnerability to such abuses.

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In combination, these reduce access to HIV, STI, viral hepatitis and other health services; can lead to poorer uptake and inconsistent use of prevention methods such as condoms, pre-exposure prophylaxis (PrEP) and post exposure prophylaxis (PEP) for HIV, and sterile needles/syringes; and to delayed diagnosis and poorer linkage and retention in treatment programmes (see Fig. 1).

Importantly, the complex intersections between the structural barriers which affect key populations and their gender, disability, education, race, religion and socioeconomic status cannot be ignored. For example, cisgender women and trans and gender diverse people experience extremely high rates of violence, racial minorities are over-represented in many prison settings, and all these factors increase stigma and discrimination.

Fig. 1. Factors contributing to HIV, STIs and viral hepatitis in key populations



HIV, viral hepatitis and STIs in key populations: dynamics and syndemics

There is a clear epidemiological rationale for HIV, viral hepatitis and STI programmes to focus on key population groups. This is related to each disease separately and also through biological and social interaction as syndemics.

As noted above, all five key populations are disproportionately affected by HIV, and in almost every setting have a higher prevalence and incidence than people outside of these groups. HIV epidemic models, which look beyond what are termed "static" modes of transmission (namely, looking at ongoing transmission over time, among networks of people rather than just incidence at one time point), show that preventing new infections and reducing viral load among key populations living with HIV has greater impact on ongoing transmission and population incidence and prevalence than focusing on lower-risk networks of people outside key population groups *(7–9)*. This means that all countries – those with high HIV burden across all populations as well as those with largely key population epidemics – must prioritize and address key population health needs for an effective, accelerated response.

HBV and hepatitis C virus (HCV) infections account for a significant global disease burden and high mortality from liver cancer and cirrhosis. HBV and HCV infections occur in all WHO regions; the HCV burden is particularly high in the Eastern Mediterranean and European regions, and the HBV burden in the African and Western Pacific regions. HCV burden has been documented as being high in people who inject drugs *(10)*, people in prisons *(11)* and men who have sex with men, particularly in men who have sex with men living with HIV *(12)*. Modelling shows that preventing, screening and treating HCV infection in key populations is needed to reach hepatitis C elimination goals *(13–16)*. Increased HBV prevalence and burden has been documented in all key populations *(17–20)*. Key populations also have higher rates of hepatitis D virus infection – which is a super-infection to HBV when compared to the larger population *(21)*. Outbreaks of hepatitis A are common among men who have sex with men *(22)*.

Sexually transmitted infections are spread predominantly by sexual contact (namely, vaginal, anal and oral sex), and have a profound impact on sexual and reproductive health worldwide. Some STIs are also responsible for severe adverse birth outcomes such as fetal and neonatal death and congenital anomalies. STIs are defined by multiple neglected pandemics that cause a significant global disease and economic burden. In 2020, more than 1 million curable STIs were estimated to be acquired every day worldwide, primarily caused by *Chlamydia trachomatis, Neisseria gonorrhoeae, Treponema pallidum* (syphilis) and *Trichomonas vaginalis*. Before the introduction of human papillomavirus (HPV) vaccines, over one in seven women were estimated to have prevalent HPV infection at any point in time *(23, 24)*. High-risk HPV types lead to cervical cancer cases and cervical cancer-related deaths and are important risk factors for anal cancer. In 2016, WHO also estimated that almost 500 million adults are currently living with herpes simplex virus (HSV) infection that causes genital herpes *(25)*.

Population groups that are at higher risk of STIs include sex workers and their clients, men who have sex with men, trans and gender diverse people in almost all settings *(26–31)*. There is increasing evidence of higher risk of STIs among people who inject drugs as well *(32)*. Adding to the burden of STI-related morbidity and mortality, emerging resistance to widely available antibiotics poses a risk of untreatable gonococcal infection. While this is not new, the rapid increase in resistance to some of the remaining effective therapies is leaving fewer options for treatment *(33)*.

Multiple epidemics and other adverse health outcomes may interact and mutually reinforce one another, increasing the risk and consequences of infection. These syndemic conditions generally develop in the context of social disadvantage and inequality, and are more commonly experienced by marginalized groups, such as key populations.

Coinfections of HIV and HBV and HCV can increase morbidity and mortality. For example, coinfection with HIV and viral hepatitis increases risk from accelerated liver disease and consequently cirrhosis, liver failure and hepatocellular carcinoma. In addition, coinfected individuals may have altered

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immunological responses and are at increased risk of antiretroviral therapy (ART)-related hepatotoxicity *(34, 35)*. Hepatitis C and HIV are highly prevalent among people who inject drugs, and disproportionately affect men who have sex with men and people in prisons and closed settings *(10–12, 36, 37)*.

HIV infection is more likely to occur if another STI is present and vice versa, creating synergies and syndemics which are often overlooked. For example, STIs increase infectiousness of people living with HIV who are not on treatment by increasing the viral concentration in the genital tract, and by increasing the potential for HIV transmission *(38, 39)*. Genital herpes *(40, 41)* and syphilis *(42)* almost triple the risk of HIV acquisition; while women living with HIV are at high-risk of infection with HPV and are approximately six times more likely to develop cervical cancer *(43, 44)*.

Responding to HIV, viral hepatitis and STIs in key populations

Sustainable Development Goal (SDG) 3 and related target 3.3 are: "By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases" *(45)*. Given disease dynamics and syndemics as described above, this can only be achieved by prioritizing the prevention, diagnosis and treatment of these infections in key populations. Figure 2 describes a theory of change for meeting these global targets by 2030 and is detailed in the text below.

To prevent, diagnose and treat infections, key populations need equitable access to services at an adequate scale to have impact. The Joint United Nations Programme on HIV/AIDS (UNAIDS) set HIV coverage targets for 2025 as part of its global strategy to end AIDS *(45)*, which applies to all populations: 95% use combination prevention; 95% of people living with HIV know their HIV status; 95% of people living with HIV who know their status initiate treatment; 95% of people on HIV treatment are virally suppressed and 95% of women access HIV and sexual and reproductive health services. Global targets for viral hepatitis include 90% of people living with HCV or HBV diagnosed and 80% treated (HBV) or cured (HCV) by 2030. For STIs targets are that by 2030 >90% of priority populations are screened for gonorrhoea or syphilis and >95% treated if positive. Few countries reach this proportion of key populations with services, contributing to ongoing epidemics.

Access to services for key populations to have an impact on HIV, viral hepatitis and STIs can only be improved if structural barriers are removed, such as stigma and discrimination, criminalization, restrictive policies and violence, and if other human rights abuses and enabling environments exist (please see Chapter 4 on enabling interventions for references). Women who belong to key populations, as well as women who are partners of key population members, experience alarmingly high risks of acquiring HIV and are less likely to access services. The UNAIDS Global Strategy to end AIDS *(45)* includes 2025 targets related to structural barriers: less than 10% of countries have punitive laws and policies that deny or limit access to services, less than 10% of people experience stigma and discrimination and less than 10% experience gender inequality and violence. Relatedly, community empowerment is needed to both increase access and coverage and to support necessary structural changes.

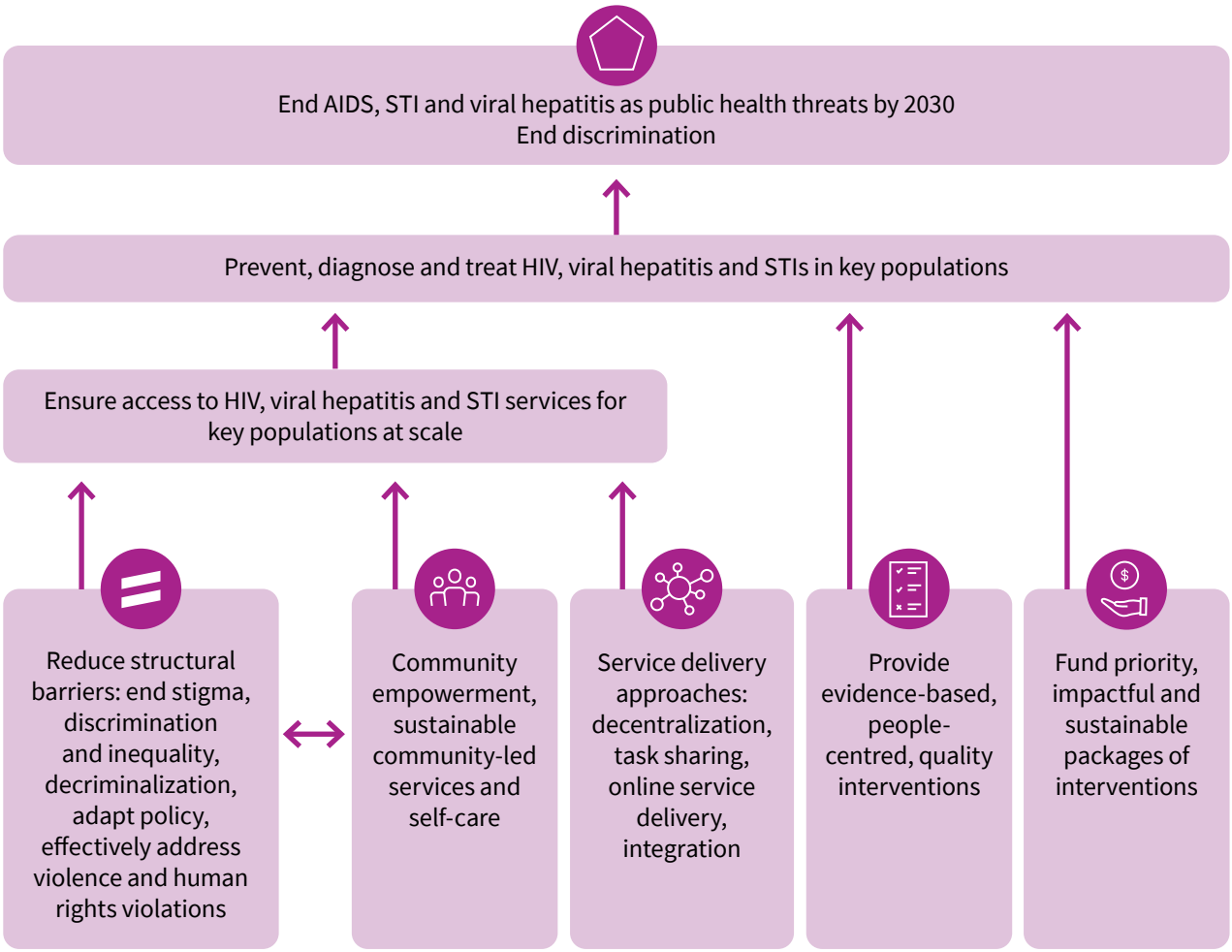
Putting key populations at the centre of health systems – by organizing services around people's needs rather than around diseases, and by promoting integrated patient-centred approaches and linkages with primary health care services – is key to ending these epidemics. Different service delivery approaches, including task shifting to key population peers as health workers, decentralizing provision of services to key population community-led programmes, providing services online and service integration are also needed to increase access to and availability of HIV, viral hepatitis and STI services for key populations *(46)*.

Prevention, diagnosis and treatment of STI, viral hepatitis and HIV can only be achieved if people are provided with correct and evidence-based interventions with consideration for their individual health needs through providing person-centred care. This requires understanding of what works to prevent, diagnose and treat these conditions.

Finally, several effective interventions which prevent and treat HIV, STI and viral hepatitis in key populations are cost effective and cost saving *(47–50)*, but without adequate funding their impact cannot be realized. Funding needs to be sustainable, predictable and focused on supporting communities.

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Fig. 2. Theory of change: addressing HIV, viral hepatitis and STIs in key populations



Scope of these guidelines

These guidelines outline a public health response to HIV, viral hepatitis and STIs for five key populations. They present and discuss new recommendations and consolidate a range of recommendations and guidance from current WHO guidelines.

They summarize the components of a package of interventions for each key population and consider implementation issues, challenges and opportunities. The guidelines also provide guidance to countries on how to prioritize packages of interventions to have greatest impact.

Goals and objectives

High incidence and prevalence of HIV; viral hepatitis and STIs in key populations; dynamics of the epidemics; and persistent discriminatory barriers, inequalities and human rights abuses compel national programmes and implementers to prioritize the provision of evidence-based health and enabling interventions to these populations to meet the Global Health Sector Goals for the three groups of infections.

The objectives of these updated key population guidelines are as follows:

1. To develop new recommendations through quality assessment of evidence;
2. To consolidate the most recent guidance and recommendations related to HIV, viral hepatitis and STI prevention, diagnosis, treatment and care applicable to key populations;
3. To promote a set of evidence-based enabling interventions relevant for all key populations; and
4. To outline priority HIV, STI and viral hepatitis health-service packages that are impactful, beneficial and acceptable for different key populations.

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Audience

These guidelines are addressed primarily to national HIV, viral hepatitis and STI programme managers and other decision-makers within ministries of health and those responsible for health policies, programmes and services in prisons. They also endorse the Global AIDS Strategy target that 80% of service delivery for HIV prevention programmes, 30% of testing and treatment services and 60% of programme support achievement of societal enablers for key populations and women are delivered by community key population-led and women-led organizations, and to expand this to include viral hepatitis and STIs. In addition, the guidelines will be relevant for managers and policy-makers at national and sub-national levels responsible for services for tuberculosis (TB), sexual and reproductive health, needle and syringe programmes (NSPs), opioid agonist maintenance therapy (OAMT), drug dependence, adolescent health, and mental health; community-led civil society organizations and implementing programmes; judiciary, law enforcement and senior prison management; advocates and development and funding agencies.

Guidelines' principles

These guidelines are developed with the following principles:

Human rights

The framework for the development of these guidelines is based on human rights principles reflected in a number of international agreements *(51, 52)*. Namely, the right to:

- the highest attainable standard of physical and mental health for all, without discrimination;
- accessible, acceptable, available and quality health facilities, goods and services, including medicines for the treatment of HIV, viral hepatitis and STIs on an equal basis without discrimination – including, but not limited to – on the basis of sex, gender, health status, disability, nationality, sexual orientation, gender identity, race, ethnicity, age and marital status;
- access to justice and the right to a fair trial;
- freedom from arbitrary arrest and detention;
- freedom from torture and cruel, inhuman and degrading treatment;
- privacy, bodily autonomy, security of the person and to be free from violence; and
- enjoy the same standards of health care in prisons and other closed settings that are available in the community.

The above are grounded in underlying core principles of human rights; namely, accountability, equality and non-discrimination and participation of all concerned stakeholders.

Gender equality

The promotion of gender equality is central to the achievement of HIV, viral hepatitis and STI prevention, diagnosis and treatment goals. This means recognizing and taking into account how unequal power in intimate relationships, harmful gender norms and lack of access to resources and control over them affects access to, and experiences with, health services.

Equity and inclusion

Recognizing and addressing the social determinants of health and promoting equity and inclusion is central to achieving health for all.

Medical ethics

Health care providers and institutions must serve people from key populations based on the principles of medical ethics regardless of personal philosophy, politics, religion, moral theory or opinion *(53)*. Particularly relevant are those related to the provider-patient/client relationships:

- patient or client autonomy;
- confidentiality;
- informed consent;
- voluntary involvement in health services.

Also relevant are codes of conduct and etiquette which require professionalism, quality, high standards and dedication to "providing competent medical service in full professional and moral independence, with compassion and respect for human dignity" *(53)*.

Universal health coverage

Universal health coverage (UHC) means that all individuals and communities receive the health services they need without suffering financial hardship. It includes the full spectrum of essential health services, from health promotion to prevention, treatment, ongoing recovery and palliative care across the life course.

Achieving UHC requires multiple approaches: primary health care and life course approaches are critical. A primary health care approach focuses on organizing and strengthening health systems so that people can access services for their health and wellbeing based on their needs and preferences, at the earliest and in their everyday environments. Applying a life course approach optimizes people's health by addressing their needs and maximizing opportunities across all phases of life.

Within the UHC framework, this guideline employs the principal of progressive universalism, where those who are most vulnerable are prioritized and reached first *(54)*.

Evidence-based public health

These guidelines only includes recommendations and good practice statements that are based on an impartial synthesis of evidence and guided by an independent group of experts, the Guideline Development Group.

Key population community-led response

This guideline upholds the principle of the greater involvement of people living with HIV (the GIPA principle) *(55)*, applies it to key populations, and commits to support the meaningful engagement of key populations in the response to HIV, viral hepatitis and STIs.

How to use these guidelines

This guideline consolidates WHO recommendations related to the prevention, diagnosis and treatment of HIV, viral hepatitis and STIs for key populations. The majority of these recommendations are described in full in other WHO guideline documents, including many which were first described in the 2014/2016 consolidated key populations guidelines *(3)*. For simplicity, in most cases the background, evidence and decision-making process related to each recommendation are not included in this guideline; rather the source document which includes this information is referenced. Certain recommendations were newly developed or updated in 2021/2022 as part of this guideline process; these are marked with a star and details of evidence and decision-making are provided in Chapter 9: Additional information on the development of new recommendations. All relevant recommendations are presented in Chapter 4: The recommended package of interventions. Chapter 5 presents prioritized packages by key population.

This guideline also includes chapters on service delivery, enabling interventions, considerations for young key populations and decision-making, planning and monitoring the response. Web Annexes A–D provide full details of the supporting evidence for the new and updated recommendations.

CHAPTER 2

Methods



Overview

The WHO Department of the Global HIV, Hepatitis and STIs Programmes led the development of these consolidated key populations guidelines, following the WHO procedures and reporting standards laid out in the *WHO handbook for guideline development*, second edition, 2014 *(56)*. The recommendations in the guidelines are based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach to reviewing evidence and formulating recommendations.

These guidelines are an update of the *Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations*, which were initially published in 2014 and updated in 2016 *(3)*. Importantly, these updated guidelines now combine existing WHO recommendations, new recommendations and guidance published by WHO related to viral hepatitis and STI prevention, in addition to HIV diagnosis, treatment and care for key populations.

Contributors to the guidelines

These guidelines were developed by technical staff of the WHO Department of the Global HIV, Hepatitis and STIs Programmes. The development process involved the formation of five main groups to guide and implement the process. Their specific roles are described in the next subsection. The members of all these groups and other contributors are listed in the Acknowledgements.

WHO Guideline Steering Group. The Testing, Prevention and Population Unit within the Global HIV, Hepatitis and STIs Programmes led this group and served as the WHO secretariat. Participants included WHO staff from other units within these programmes , as well as from the following WHO departments: Mental Health and Substance Use, and Sexual and Reproductive Health and Tuberculosis. This group also included WHO technical staff from two WHO Regional Offices (AFR and EUR).

Guideline Development Group. This group consisted of 25 members, with a balanced representation of geographic regions, gender and backgrounds, including academia and research, programme implementation and policy, and community organizations and networks. The global networks of people who use drugs, female, male and trans and gender diverse sex workers, gay men and other men who have sex with men and trans and gender diverse people were all represented on the Guideline Development Group. There is no global network of people in prisons and there were no prisoner representatives on the Guideline Development Group because participation was not feasible. The group members were selected in coordination with the Steering Group and WHO country and regional offices. This group was responsible for the formulation of the new and updated WHO recommendations. A full compilation and summary of the declarations of interest for Guideline Development Group members is available in Web Annex A.

External Review Group. This group was selected to ensure geographic and gender balance. It comprised 20 peer reviewers from academia, policy and research, programme implementation, UN agencies and community organizations and networks, including key population networks and civil society organizations and NGOs working in prisons.

External guideline contributors, guided by methodologist. Seven systematic reviews were conducted by three separate independent teams of experts, guided by one guideline methodologist, and with input from members of the WHO Steering Group and responsible technical officers. Qualitative research related to key populations' values and preferences was conducted by the global networks of people who inject drugs, sex workers, men who have sex with men and trans and gender diverse people. Additional evidence on feasibility, values and preferences and cost-effectiveness were also compiled and summarized by the systematic review teams. The Guideline Development Group, along with WHO technical officers, worked closely with the guideline methodologists to appraise the evidence using the GRADE methodology.

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External partners and observers. Representatives of the United States Agency for International Development (USAID), Centers of Disease Control and Prevention (CDC), Global Fund, Bill & Melinda Gates Foundation, Joint United Nations Programme on HIV/AIDS (UNAIDS), United Nations Development Programme (UNDP), United Nations International Children's Emergency Fund (UNICEF), United Nations Population Fund (UNFPA), United Nations Office on Drugs and Crime (UNODC), World Hepatitis Alliance (WHA), Clinton Health Access Initiative (CHAI) and World Professional Association of Transgender Health (WPATH) attended the Guideline Development Group meeting as observers. All representatives and organizations are potential donors and implementers of the proposed guideline, with a long history of collaboration with WHO's Global HIV, Hepatitis and STIs Programmes.

Competing interests

All external contributors to the development of guidelines, including members of the guideline development groups and the external review groups, completed a WHO declaration of interest form. Every effort is made to ensure that any potential influence of conflicts of interest is minimized. Individual participation was reviewed with regard to the interests declared. All declaration of interest forms are on electronic file at the WHO Department of Global HIV, Hepatitis and STIs Programmes, and will be maintained for 10 years.

To assess competing interests of the Guideline Development Group, the WHO responsible technical officers reviewed declarations of interest forms, curricula vitae and performed Google searches. The proposed membership list was posted for public review and comment 14 days prior to the guideline meeting before finalization. A management plan for each declared conflict was agreed on and recorded at the time of the meetings. One potential conflict related to receipt of funds that was considered significant in relation to one topic area was identified. The WHO team decided that this member would participate partially, excusing themselves from participating in decision-making discussions and formulation of a recommendation related to hepatitis C treatment (see Web Annex A).

Defining the scope of the guidelines

This publication is an update of the 2016 *Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations*. In line with principles of Universal Health Care (UHC), a person-centred care and the rationale for increased public health impact, we identified areas for improvements to the former guidelines:

1) including and consolidating relevant recommendations related to viral hepatitis and STIs for key populations;

2) providing guidance to countries on prioritized packages of health interventions for each key population group; and

3) highlighting the central importance of critical enablers in ensuring UHC for key populations.

For initial scoping for the updated guidelines, WHO technical officers reviewed all the health intervention recommendations included in the 2014/2016 guidelines with the following objectives: 1) identify ways in which the guideline could be clearer, and easier to read and implement; 2) identify recommendations that required updating; and 3) identify where new recommendations were needed. Technical officers from HHS/TPP rated all of the 146 recommendations from the 2014/2016 key populations guidelines using the following actions:

Remove: It has been superseded and is no longer relevant. Review of the evidence is not necessary, and the recommendation is deleted ("remove (not relevant)") OR it should be removed from recommendations box because it is a "consideration" and can be highlighted in the narrative or in a separate section on structural interventions ("remove (move to narrative or structural)").

Validate: The recommendation is clearly established, and it is unlikely anyone would disagree with the recommendation. A review of the evidence and decision-making process is not necessary; the recommendation should be retained unchanged.

Edit: There is no change in the evidence or in the intention of the recommendation, but the precise wording needs editing to improve clarity.

Update: New evidence synthesis is required, and the topic and new evidence synthesis need to be reviewed by the Guideline Development Group with a full evidence-to-decision procedure, **or** there has been an update of the recommendations since 2016 conducted by another team or department in WHO.

New: A new topic, subgroup or intervention needs to be covered. A new evidence synthesis is required and the Guideline Development Group needs to perform a full evidence-to-decision procedure.

Following this exercise, a community and expert consultation was organized. The objectives of the consultation were: 1) to give an update on the consolidated key populations guidelines process and future timelines; 2) to discuss changes to the guidelines format and structure; 3) to gain feedback on proposed recommendations to be updated and new areas for future recommendations; and 4) to improve community engagement and transparency. Participants in the consultation included members of the key population community, young people and adolescents, donors, technical partners, implementers, representatives of national programmes and UN partners. The consultation also included a post-meeting survey. Overall, participants agreed with the proposed structure of the guidelines, with separate packages per key population, inclusion of STIs and viral hepatitis and the inclusion of prioritized packages of health interventions.

Values and preferences of key population members

WHO commissioned a qualitative study of key populations' values and preferences related to the new and updated recommendations being considered by the Guideline Development Group, as well as their general health priorities, service delivery preferences and experience of structural barriers. Unfortunately, it was not possible to include people in prisons in this study, given a lack of networks of people in prisons and logistical issues.

Global Action for Trans Equality (GATE), International Network of People who Use Drugs (INPUD), Global Action for Gay Men's Health and Rights (MPACT) and Global Network of Sex Work Projects (NSWP), following ERC approval of the protocol, conducted a total of 61 individual semi-structured interviews (SSIs) and 32 multi-country focus group discussions (FGDs). The global key population networks selected participants through their regional and country-based networks to participate in SSIs and FGDs, with attention given to balancing representation by region, gender, age and HIV status. All SSIs and FGDs were conducted virtually over secure communication platforms. Interviews were conducted in English, French, Spanish or Russian, as appropriate. Three interviews were additionally conducted by NSWP consultants in Thai, Hindi and Nepali, using community interpreters.

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Data were collected by community experts engaged by the global key population networks as consultants. Participant responses were documented, electronically recorded and, where possible, participant responses were transcribed verbatim with respect to the safety and anonymity of personal data. Responses were then collated and coded using an inductive, thematic analysis approach based on an analytical framework developed by the key population networks. Data summaries from each of the key population studies were prepared by one principal investigator from each network, inputted into a joint draft, and analysed to create a consolidated key population report (see Web Annex B for the full report).

Developing prioritized packages

In this updated guideline, guidance is provided to national programme managers, donors and advocates on how to prioritize different packages of health interventions to have the greatest impact on HIV, viral hepatitis and STIs, and to ensure universal coverage to address other health issues for key populations.

Each of the interventions listed and included in this guideline, based on initial scoping, was classified for each key population as:

1. **Essential for impact: enabling interventions**

   This includes all interventions recommended to address structural barriers to health services access for key populations.

2. **Essential for impact: health interventions**

   This includes health sector interventions which have a demonstrated direct impact on HIV, viral hepatitis and STIs in key populations.

3. **Essential for broader health**

   This includes health sector interventions to which access for key populations should be ensured, but which do not have direct impact on HIV, viral hepatitis or STIs.

4. **Supportive**

   This includes other interventions which support the delivery of health sector interventions, such as creating demand, providing information and education.

Plans for dissemination and updating

These guidelines will be updated in full or in part, based on regular scoping exercises of available evidence and experience from country implementation that will guide and trigger the need for new guidance. As the evidence base or user needs change, consideration will be given to producing technical updates on specific subjects.

The guidelines will be disseminated electronically on the WHO Global HIV, hepatitis and STIs Programmes' website and made available as a print publication on demand. Dissemination will be supported by publication of selected systematic reviews and evidence in peer-reviewed journals, as well as policy briefs, web and mobile phone-based apps.

CHAPTER 3

Critical enablers



Introduction

HIV, viral hepatitis and STI epidemics, particularly among key populations, continue to be fuelled by laws and policies criminalizing sex work; drug use or possession; diverse forms of gender expression and sexuality; stigma and discrimination; gender discrimination; violence; lack of community empowerment and other violations of human rights. These sociostructural factors limit access to health services, constrain how these services are delivered and diminish their effectiveness.

"Critical enablers[2]", as used in this guideline, means strategies, activities and approaches that aim to improve the accessibility, acceptability, uptake, equitable coverage, effectiveness and efficiency of HIV, viral hepatitis and STI services. Enablers operate at many levels – individual, community, institutional, societal and national, regional and global. They are crucial to developing strategies and implementing comprehensive HIV, viral hepatitis and STI programmes and services for key populations in all epidemic contexts.

The health sector has an important role to play, but successful implementation of critical enablers requires collaboration across different sectors, such as health, justice, housing, education, welfare and labour. It also requires multiple partners from government, civil society, religious institutions and the private sector. Full and meaningful involvement of key population-led organizations is crucial.

Special considerations for adolescents and young people

The barriers and critical enablers outlined in this chapter apply to both adults and adolescents in key populations. For adolescents from key populations, these factors may be further exacerbated by their rapid physical and mental development and complex psychosocial, familial, and social, educational and economic vulnerabilities. Also, adolescents from key populations experience sociostructural barriers to services, notably policy and legal barriers related to age of consent. Children of key populations can experience stigma and discrimination, and hence face the same difficulties in access to services. Health care providers may be prosecuted for providing services to adolescents without parental/guardian consent, further reducing access to services.

Key populations' experience, values and preferences related to structural barriers and critical enablers

Qualitative research conducted by the global key population-led networks for the development of this guideline (for a detailed report, please see Web Annex B) found that all key populations reported criminalization, stigma and discrimination as persistent barriers to accessing health services and remaining in treatment, as well as being driving factors in perpetuating vulnerability, human rights abuses and poor health outcomes. Participants from the trans and gender diverse people's network additionally emphasized structural barriers to legal gender recognition.

The criminalization of drug use or possession, sex work, same-sex relations and gender expression deter members of key populations from accessing services due to fears of legal repercussions. It was also noted how criminalization perpetuates the exclusion of key population-led and rights-based health programming from funding mechanisms and state health responses. Participants in the qualitative study additionally noted that law enforcement using the possession of condoms and injecting equipment as so-called evidence of sex work and drug use or possession further hinders the use of evidence-based prevention services and commodities.

[2] These are referred to as societal enablers in the *Global AIDS Strategy 2021–2026 (45).*

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Stigma and discrimination, exacerbated by criminalization, also remain a salient barrier to accessing services and remaining in treatment for key populations. Participants across key population groups emphasized the pervasive problem of provider-based stigma and discrimination, including judgemental attitudes, breaches of confidentiality, denial of treatment, violence and abuse – even in contexts where legal protections exist.

To improve key populations' access to, and retention in, HIV, STI and viral hepatitis services, and to promote their health and human rights in general, participants stressed the need for legal and policy reform, community-led responses, community empowerment and capacity-building, and anti-violence initiatives.

Community empowerment was emphasized across all key population-led networks participating in the qualitative research project. Participants discussed the importance of key population-led responses, including peer outreach and other peer-based services, awareness-raising, advocacy, drop-in-centres, capacity-building and resource mobilization to ensure sustainable, community-led programming. These initiatives were seen both as a means to improve access to services, as well as an essential measure for addressing structural barriers undermining key populations' health and human rights.

In addition, participants noted the importance of sensitizing health care staff, law enforcement, NGO workers and the broader community. Key population-led sensitization training was perceived as an effective intervention to decrease stigma and discrimination and improve the acceptability of health services. Participants also recommended anti-violence interventions as enabling interventions.

Participants felt that because violence can be common (largely due to the effects of criminalization that require systemic solutions), violence prevention interventions need to be incorporated in an ongoing way into an overall wellness approach that views health as much more than "simply a set of interventions". In this context, they stressed the need for services to think more about what might bring people in and empower them to think about and address their health.

Lastly, all key population-led networks noted the critical role that funding plays in community-led initiatives, indicating an ongoing need to prioritize funding for key population-led programming, given the serious lack of funding for community and key population-led initiatives, and highlighting the importance of achieving the Global AIDS Strategy targets; namely, 80% service delivery for HIV prevention programmes for key populations, delivered by key populations; 30% testing and treatment services, delivered by community-led organizations; and 60% programme support achievement societal enablers, to be delivered by community-led organizations.

Essential interventions for impact: critical enablers

This chapter outlines a range of structural barriers that compromise access to health services for key populations, and then identifies critical enablers to overcome these barriers. This chapter includes a number of good-practice recommendations that are based on those made in the 2014/2016 WHO consolidated key population guidelines *(3)* with updated references, where available. While these barriers and enablers are interrelated, we attempt to discuss each individually.

Legal and policy barriers and enablers

Key population members are entitled to the full protection of their human rights, as specified in international human rights instruments. Human rights include, but are not limited to, the right to equal enjoyment of rights and non-discrimination; security of person and privacy; recognition and equality before the law; fair trial of law; the highest attainable standard of mental and physical health; education; employment and just and favourable conditions of employment; freedom of movement; peaceful assembly and association; freedom from arbitrary arrest and detention, and from cruel and inhumane treatment; and protection from violence. States have an obligation to ensure that the above rights are enjoyed without discrimination on the basis of race, nationality, sex, age, religion, sexuality, gender identity, health status, disability, marital status or other status *(57–60)*.

Most countries have laws, regulations or policies that are barriers to effective HIV, viral hepatitis, STI and other health services for key populations, including criminalization of sex work, drug use and possession, gender identity or expression, and sexual relations between people of the same sex. A number of countries criminalize gender identity in a de facto manner, by criminalizing cross-dressing or impersonation of the opposite sex. For trans and gender diverse people, the lack of legal gender recognition is a key barrier to access, and retention of, health services, in addition to the full enjoyment of other rights, such as freedom of mobility, housing, education and employment. This further isolates trans people and increases their vulnerabilities. In many settings, adolescents under 18 years of age are classified legally as minors and, therefore, must have consent from a legal responsible adult for medical care. Other barriers are related to restrictive or punitive policies and practices, such as criminalizing the possession of needles/syringes, which restricts the ability of programmes to operate NSPs, and using possession of condoms as evidence of sex work and as a basis for arrest *(61)*. Other harmful practices include forced anal examinations, which are used to investigate or punish alleged same-sex behaviour between consenting men or transgender women *(62)*.

These legal barriers have measurable, detrimental effects on the health of members of key populations, shown by modelling and other research *(63–74)*. For example, a systematic review found associations between exposure to arrest and HIV infection in people who inject drugs *(64)*; in countries in sub-Saharan Africa, the odds of living with HIV were found to be 7.2 times higher for sex workers in countries that criminalize sex work compared to countries that partially legalize sex work *(68)*; repressive policing of sex workers was associated with increased risk of HIV or other STIs (odds ratio of 1.87); and sex workers exposed to repressive policing were three times more likely to be physically or sexually assaulted *(75)*. The criminalization of the clients of sex workers has also been repeatedly shown to negatively affect sex workers' safety and health, including reducing condom access and use, and increasing the rates of violence *(68, 76)*. Studies show the negative effect of criminalization of same-sex practices on HIV prevalence and access to prevention, diagnosis and treatment services *(77, 78)*.

For trans and gender diverse people, the legal recognition of preferred gender and name may be important to reduce stigma, discrimination and ignorance about gender variance. Such recognition by health services can support better access, uptake and provision of HIV services *(79)*. Additionally, it is likely to improve trans and gender diverse people's health and wellbeing *(80)*. However, legal recognition must be accompanied by training, sensitization, education and enforcement.

Legal reforms, such as decriminalizing drug use or possession, sex work and same sex relationships; legal recognition of trans or gender diverse status; lowering the age of consent for accessing health services; and considering exceptions to a standard age of consent policy (such as mature minors) are critical enablers that can change a hostile environment for key populations to a supportive environment. Without protective policies and decriminalization of drug use or possession, and of diverse forms of gender identity and sexuality and sex work, barriers to essential health services will remain; many people from key populations may fear that seeking health care will expose them to adverse legal consequences. Specific consideration should be given to such legal reforms as part of any revision of policies or programmes for key populations.

Laws and policies that criminalize and punish key populations also constrain people from obtaining justice and legal services. Policies and procedures are needed to ensure that individuals from key populations can report rights violations such as discrimination, gender-based violence and other crimes, issues with policing, violations of informed consent, violations of medical confidentiality and denial of health care services. Reporting options, beyond going to the police, will encourage reporting of human rights violations. For example, persons from key populations can be trained as paralegals, and key population-led organizations and other organizations that work with key populations can serve as a third-party reporter of complaints *(61, 81)*.

Law enforcement has a statutory duty and obligation to ensure key populations enjoy equal protection under the law, and that the human rights of key populations are not violated. Law enforcement agents should receive continual training in ways to support – or at least not to impede – key populations' access to essential health services, including not surveilling or arresting people accessing OAMT, NSPs and drug dependence treatment clinics; avoiding confiscation of drug treatment medication, and not using possession of sterile needles or condoms to justify arrest. Systems to promote good policing practices and to provide safe avenues for reporting human rights violations will help ensure that police are protecting both the public health and the human rights of all persons *(61)*.

Overarching recommendations related to enabling interventions to address legal and policy barriers are listed below. Please see the recommended interventions chapter for full details.

Overarching good practice and guidance statements: removing punitive laws, policies and practices	
Existing good practice statement (adapted)[3]	Countries should work toward decriminalization of drug use/injecting, drug possession, sex work, same-sex activity and nonconforming gender identities, and toward elimination of the unjust application of civil law and regulations against people who use/inject drugs, sex workers, men who have sex with men and trans and gender diverse people *(3, 45, 79, 82–85)*.
Existing guidance statement	Laws, legal policies and practices should be reviewed and, where necessary, revised by policy-makers and government leaders, with meaningful engagement of stakeholders from key population groups, to allow and support increased access to services for key populations *(3, 79, 83, 84)*.

Stigma and discrimination

Stigma is a difference that is pejoratively labelled, stereotyped or named. Stigma can lead to discrimination; namely, unfair and unjust action towards an individual or group on the basis of real or perceived status or attributes, a medical condition, socioeconomic status, employment, drug use, gender, race, sexual identity, age or other perceived differences or characteristics, with the purpose or effect of impairing or nullifying the recognition, enjoyment or exercise – on an equal basis with others – of all human rights and fundamental freedoms *(61)*.

People from key populations are often particularly subjected to stigma, discrimination and negative attitudes related to their behaviour, sexual orientation, gender identity or engagement in sex work – and doubly so if also living with HIV, viral hepatitis or STIs. Many key populations also face intersecting forms of discrimination on the basis of their age, sex, race or ethnicity, physical or mental health status, disability, nationality, asylum or migration status, or criminal record. This is the basis for discrimination, which is common in many health facilities and law enforcement services. It may seem to be tacitly endorsed by the lack of national laws and policies that protect key populations against discrimination, and by the implementation of punitive and restrictive policies.

Within the health sector, stigma and discrimination can take many forms at the individual and systems levels. The lack of training and educational programmes to inform health workers of the needs, health issues and rights-based strategies and interventions for key populations contributes to marginalization. It leaves providers ill-equipped to address health needs and perpetuates stigmatizing and discriminating practices, even to the point of refusing services. Health care

[3] In the 2014 *Consolidated Guidelines for HIV prevention, diagnosis, treatment and care*, the wording of this good practice statement was: Countries should work toward decriminalization of behaviours such as drug use/injecting, sex work, same-sex activity and nonconforming gender identities, and toward elimination of the unjust application of civil law and regulations against people who use/inject drugs, sex workers, men who have sex with men and trans and gender diverse people.

workers may be biased against certain people, but may also experience discrimination themselves when working with key populations *(86)*.

The effects of stigma and discrimination against key populations can manifest in delayed testing and missed diagnoses, poor retention in treatment programmes and poor treatment outcomes, concealment of health status and, in general, poor uptake of health services *(61, 87–102)*.

There are many interventions designed to reduce stigma and discrimination in health care settings, with some randomized controlled trials and observational studies showing positive effects *(92, 103–114)*. However, given the heterogenous nature of the interventions and outcomes measured, meta-analyses are often not possible, and systematic reviews do not clearly indicate which are the most effective interventions when it comes to reducing stigma and discrimination in health care settings *(86, 115–117)*. Instead, it is useful to consider a range of interventions that can address different aspects of stigma and discrimination as listed below *(61, 115)*.

Intervention approach	Description
Information based	Providing information about health and health-related stigma
Skills building	Conducting sensitization or other skills-building activities for health care workers, law enforcement officers and others
Counselling and support	Supportive services for members of key population groups
Contact with key populations	Facilitating interactions between key population members and health care workers, law enforcement officers and others
Structural	Institute anti-stigma and anti-discrimination policies and codes of conduct with monitoring, oversight and opportunities for key population members to report discrimination, including redress and accountability mechanisms
Biomedical	Ensuring UHC and professional, non-discriminatory provision of care, including HIV, viral hepatitis and STI services for key populations

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Enabling interventions to address barriers related to stigma and discrimination are listed below:

Overarching good practice and guidance statements: stigma and discrimination	
Existing good practice statement	Countries should work towards implementing and enforcing anti-discrimination and protective laws, derived from human rights standards, to eliminate stigma, discrimination and violence against people from key populations *(3)*.
Existing good practice statement	Policy-makers, parliamentarians and other public health leaders should work together with civil society organizations in their efforts to monitor stigma, confront discrimination against key populations and change punitive legal and social norms *(3, 79, 81, 83–85, 118, 119)*.
Existing guidance statement	Health services should be made available, accessible and acceptable to people from key populations, based on the principles of medical ethics, avoidance of stigma, non-discrimination and the right to health *(3, 79, 81, 83–85, 118–120)*.

Community empowerment

Key populations often have little or no control over HIV, STI and viral hepatitis risk factors driven by the legal, political and social and programmatic environment, and the context of their lives. These constraints can hinder people's control over their health and wellbeing, as well as increasing their risk of HIV, viral hepatitis and STIs. This lack of control is exacerbated if people are unaware of available health services, of their legal and human rights, specifically their right to health, and what to do if these rights are violated. Few young people from key populations receive adequate information and education centred on their sexual lives. Instead, they receive negative, critical, conflicting or confusing messages about gender, drug use, unintended pregnancy and STIs, including HIV *(121)*.

Empowerment is the process by which people with little power work together to increase control over events that determine their lives and health. Community empowerment means increasing key population communities' control over their health by addressing the structural constraints to health, human rights and wellbeing; making social, economic and behavioural changes; and improving access to health services. Community empowerment can take many forms, such as fostering key population-led groups and key population-led programmes and service delivery; meaningful participation of people from key populations in designing and operating services; peer education or navigation; task shifting to key population peers; self-care; implementation of legal literacy and service programmes; and ensuring civil space in which key populations can function without fear of reprisals.

Evidence, mainly among sex workers, shows that community empowerment has a measurable impact on key populations' health *(122–134)*, including reductions in STI incidence *(127)*, HIV incidence *(128, 134)*, high-risk sex *(131)* and increased uptake of family planning *(132)*.

Figure 3 shows a framework for fostering key population services included in key population networks' developed implementation tools *(135–138)*.

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Fig. 3. Framework for community empowerment



It is important to foster and support services, facilities and research led by organizations of people from key populations. Key population-led organizations, collectives and networks can play key roles in training staff of health services, law enforcement and social service agencies; facilitating interaction with the communities of key populations; and developing, implementing, monitoring and managing services. Key population communities can build understanding of, and alliances with, other neglected, at-risk groups, such as youth networks, persons with disabilities, adolescent girls and young women. They have special strengths in providing and leading community-based and outreach services.

Meaningful participation can mean not only having a voice in decision-making, but also contributing to service delivery and monitoring and evaluation (M&E). Community-led monitoring, an accountability mechanism led by key populations and other affected communities, which involves trained peer monitors and structured reporting mechanisms, is particularly important *(139)*.

WHO has several relevant recommendations related to roles for key population peers in service delivery, which can be found in the service delivery chapter.

The meaningful participation of key populations in programming is critical to ensure the appropriateness and acceptability of services to the intended clientele. It is also important for building trusting relationships between the community and service providers, who may be accustomed to establishing the parameters by which services are provided, and prescribing how relationships or partnerships are to be conducted, a norm that needs to be shifted to allow for community empowerment and service access.

Meaningful participation means that key populations: 1) choose whether to participate; 2) choose how they are represented, and by whom; 3) choose how they are engaged in the process; and 4) have an equal voice in how partnerships are managed.

Enabling interventions to improve community empowerment are listed below.

Overarching good practice and guidance statements: community empowerment[4]	
Existing guidance statement	Key population-led groups and organizations should be made essential partners and leaders in designing, planning, implementing and evaluating health services *(3)*.
Existing good practice statement	Programmes should implement a package of interventions to enhance community empowerment among key populations *(3, 79, 84, 85)*.

Violence

Violence against people from key populations is a common occurrence and can take various forms – physical, sexual or psychological, and can be perpetrated by different people, including intimate partners, clients, family members, strangers, service providers, law enforcement officers and others in positions of power *(140–147)*. Violence can be fuelled by the imbalance in the power dynamics of gender – by prejudice and discrimination against persons perceived to depart from conventional gender and sexuality norms and identities. Other characteristics such as age, disability or race can increase vulnerability to violence. Also, multiple structural factors influence vulnerability to violence, including discriminatory or harsh laws, and policing practices and cultural and social norms that legitimize stigma and discrimination.

Experience of violence has been shown to negatively impact on key populations' health, including increasing drug-related harms *(142, 148–152)*, reduced uptake of sexual and reproductive health services *(141)*, inconsistent condom use *(141, 147, 149, 153)*, depression and other mental health issues *(143, 154)*, and increased HCV infection risk *(155, 156)*, as well as having a direct impact on HIV and STI acquisition *(157)*. A modelling study estimated that reduced sexual violence against sex workers could reduce new HIV infections by 25% among sex workers and their clients *(158)*. Women, especially young women from key populations, including women who use drugs, female sex workers, people in prisons and transgender women, experience particularly high rates of physical, sexual and psychological abuse *(159)*.

The health sector has an important role to play in addressing violence by providing comprehensive health services, including: for sexual and reproductive health; providing referrals to other support services; gathering evidence through data and research; fostering prevention policies in other sectors; and advocating for violence to be recognized as a public health problem and for resource allocation *(160)*.

Those who experience sexual violence need timely access to post-rape care, including emergency contraception, safe abortion, post-exposure prophylaxis for HIV and other STIs, hepatitis B immunization and psychosocial care and support, as well as referrals to legal services *(161)*. HIV, viral hepatitis and STI prevention, diagnosis and treatment for key populations should include either on site or through strong referral and linkage, clinical and psychosocial care and support

[4] Please note, in the WHO guideline: *Prevention and treatment of HIV and other sexually transmitted infections for sex workers in low and middle-income countries: recommendations for a public health approach*, WHO recommended a package of interventions to enhance community empowerment among sex workers. This was a strong recommendation with very low quality of evidence. In 2014, all WHO recommendations related to key populations were consolidated and a new good practice statement developed to expand this recommendation to all key population groups, as included in the table above.

for survivors of violence, in line with WHO guidelines for responding to sexual violence *(161-162)*. Survivors may need treatment for physical injuries and longer-term mental health care. Health services also can document medico-legal evidence, which can assist survivors' access to justice. Supportive services also include hotlines, staffed by trained peer and other counsellors, to offer psychosocial support, as well as crisis response interventions, with multidisciplinary teams that link survivors to various services and safe spaces, without restrictions based on ongoing drug use *(84)*.

Efforts to address violence against people from key populations must involve other sectors along with the health sector. Together, they must create an enabling environment to promote physical, sexual and emotional wellbeing and safety. Critical enablers include mechanisms for documenting and monitoring violence, training people from key populations and other stakeholders to understand human rights, and for fostering the accountability of law enforcement officials to prevent and respond to violence and infringements of human rights *(162, 164)*. Evidence shows the effectiveness of participatory programmes that engage multiple stakeholders as well as community mobilization interventions *(165)*. Law enforcement practices can increase the risk of violence faced by key populations. Indeed, law enforcement officers themselves can be perpetrators. Work with law officers can involve training on the human rights of key populations, as well as promoting accountability for rights-based law enforcement *(162)*. Efforts to prevent violence can be promoted by advocacy for law and policy reforms that protect the rights and safety of key populations; increasing awareness of reporting mechanisms and disciplinary action; conducting sensitization workshops for people with pivotal roles (for example, government officials, law enforcement officers, prison staff, media, health care workers and religious leaders); the creation of safe spaces; and by creating early warning and rapid response mechanisms with the involvement of key population community members, health workers and law enforcement officials. Integrating community representatives into these efforts also helps to create channels of communication among key populations, civic officials and law enforcement officers *(162)*.

It also is important to monitor and document incidents of violence, both as evidence for advocacy and to inform programme design. Documenting the levels of violence faced by key populations is often the first step in creating awareness.

Enabling interventions to address violence against key populations are listed below.

Overarching good practice statements: violence	
Existing good practice statement	Violence against people from key populations should be prevented and addressed in partnership with key population-led organizations. All violence against people from key population groups should be monitored and reported, and redress mechanisms should be established to provide justice *(3, 79, 84, 85, 162)*.

CHAPTER 4

The recommended package of interventions



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Introduction

This guideline consolidates WHO recommendations related to the prevention, diagnosis and treatment of HIV, viral hepatitis and STIs for key populations. The majority of these recommendations are described in full in other WHO guideline documents, including many that were first described in the 2014/2016 consolidated key populations guidelines *(3)*. For simplicity, in most cases the background, evidence and decision-making process related to each recommendation are not included in this guideline; rather the source document, which includes this information, is referenced. Certain recommendations were newly developed or updated in 2021/2022 as part of this guideline process; these are marked with a star, and details of evidence and decision-making are provided in the additional information chapter.

The interventions listed here have been categorized as follows:

1. **Essential for impact: enabling interventions**

   This includes all interventions recommended to reduce structural barriers to health services access for key populations.

2. **Essential for impact: health interventions**

   This includes health sector interventions that have a demonstrated direct impact on HIV, viral hepatitis and STIs in key populations.

3. **Essential for broader health**

   This includes health sector interventions to which access for key populations should be ensured, but do not have direct impact on HIV, viral hepatitis or STIs.

4. **Supportive**

   This includes health sector interventions which support the delivery of other interventions, such as creating demand, and providing information and education.

The tables below include recommendations which have been made through the GRADE process (see methods for details), good practice statements and summaries and links to relevant documents. The GRADE recommendations include the strength of the recommendation and certainty of the evidence as agreed by relevant Guideline Development Groups.

Packages of recommended interventions are provided for each key population group in Chapter 5.

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Recommended package

Note that these interventions are not in order of priority.

Also please note that this package includes a mix of existing and new recommendations, good practice statements and guidance statements. These can be classified as follows:

★ **New GRADE recommendation** – a recommendation which was newly developed as part of this guideline's development process, using the GRADE methodology as described in the methods section;

Existing GRADE recommendation – a recommendation which was developed as part of an already published WHO guideline;

★ **New good practice statement** – a good practice statement newly developed by the guideline development group as part of this guideline's development process, as described in the methods section;

Existing good practice statement – a good practice statement which was developed as part of an already published WHO guideline;

Existing guidance statements – overarching statements which summarize groups of existing recommendations and approaches;

WHO position – from position papers of the WHO Strategic Advisory Group of Experts (SAGE) on immunization; and

Adapted – for some of the recommendations and good practice statements, small changes to the wording have been made without substantial change.

Essential for impact: enabling interventions

Overarching good practice statements: removing punitive laws, policies and practices

Existing guidance statement	Laws, legal policies and practices should be reviewed and, where necessary, revised by policy-makers and government leaders, with meaningful engagement of stakeholders from key population groups to allow and support increased access to services for key populations *(3, 79, 83, 84)*.
Existing good practice statement (adapted)[5]	Countries should work toward decriminalization of behaviours such as drug use/injecting, sex work, same-sex activity and nonconforming gender identities, and toward elimination of the unjust application of civil law and regulations against people who use/inject drugs, sex workers, men who have sex with men and trans and gender diverse people *(3, 79, 82–85)*.

[5] In the 2014 *Consolidated guidelines for HIV prevention, diagnosis, treatment and care for key populations*, the wording of this good practice statement was: Countries should work toward decriminalization of behaviours such as drug use/injecting, sex work, same-sex activity and nonconforming gender identities, and toward elimination of the unjust application of civil law and regulations against people who use/inject drugs, sex workers, men who have sex with men and trans and gender diverse people.

Essential for impact: enabling interventions

Other good practice statements: removing punitive laws, policies and practices	
Existing good practice statement (adapted)[6]	Where criminalization continues, countries should work toward developing non-custodial alternatives to incarceration of people who use drugs, trans and gender diverse people, sex workers and people who engage in same-sex activity *(3, 82, 85)*.
Existing good practice statement (adapted)[7]	Countries should ban compulsory treatment[8] for key populations *(3, 82, 83, 85, 166)*.
Existing good practice statement	Countries should work toward developing policies and laws that decriminalize the use of sterile needles and syringes (and that permit NSPs) and that legalize OAMT for people who are opioid dependent *(3)*.
Existing good practice statement	The police practice of using possession of condoms as evidence of sex work and grounds for arrest should be eliminated *(3, 84)*.
Existing good practice statement	Countries should work towards legal recognition for trans and gender diverse people *(3, 79)*.
Existing good practice statement	Countries are encouraged to examine their current consent policies and consider revising them to reduce age-related barriers to HIV, STI and viral hepatitis services, and to empower providers to act in the best interests of adolescents *(3, 120)*.
Overarching good practice and guidance statements: stigma and discrimination	
Existing good practice statement	Countries should work towards implementing and enforcing anti-discrimination and protective laws, derived from human rights standards, to eliminate stigma, discrimination and violence against people from key populations *(3)*.
Existing good practice statement	Policy-makers, parliamentarians and other public health leaders should work together with civil society organizations, including key population-led organizations, in their efforts to monitor stigma, confront discrimination against key populations and change punitive legal and social norms *(3, 79, 81, 83–85, 118, 119)*.
Existing guidance statement	Health services should be made available, accessible and acceptable to people from key populations, based on the principles of medical ethics, avoidance of stigma, non-discrimination and the right to health *(3, 79, 81, 83–85, 118–120)*.

[6] In the 2014 *Consolidated guidelines for HIV prevention, diagnosis, treatment and care for key populations*, the wording of this good practice statement was: Countries should work toward developing non-custodial alternatives to incarceration of drug users, sex workers and people who engage in same-sex activity.

[7] In the 2014 *Consolidated guidelines for HIV prevention, diagnosis, treatment and care for key populations*, the wording of this good practice statement was: Countries should ban compulsory treatment for people who use and/or inject drugs.

[8] Compulsory, or involuntary, treatment includes treatment for drug dependence, so-called conversion therapy or rehabilitation of sex workers, which is against human rights and medical ethics principals of consent, freedom from arbitrary arrest, access to quality health, freedom from torture and cruel, inhumane and degrading treatment.

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Essential for impact: enabling interventions

Other good practice statements: stigma and discrimination

Existing good practice statement	Health care workers should receive appropriate recurrent training and sensitization to ensure that they have the skills and understanding to provide services for adults and adolescents from key populations, based on all persons' right to health, confidentiality and non-discrimination *(3)*.
Existing good practice statement	Services should be safe spaces that increase protection from the effects of stigma and discrimination, where adolescents can freely express their concerns, and where providers demonstrate patience, understanding, acceptance, non-judgement and knowledge about the choices and services available to the adolescent *(120)*.

Overarching guidance statement: community empowerment

Existing guidance statement	Key population-led groups and organizations should be made essential partners and leaders in designing, planning, implementing and evaluating health services *(3)*.

Other good practice statements: community empowerment

Existing good practice statement	Programmes should implement a package of interventions to enhance community empowerment among key populations *(3, 79, 84, 85)*.
Existing good practice statement	Programmes should be put in place to provide legal literacy and legal services for and by key populations, so that they know their rights and applicable laws and can receive support from the justice system when aggrieved *(3, 79, 84, 85)*.

Overarching good practice statement: addressing violence

Existing good practice statement	Violence against people from key populations should be prevented and addressed in partnership with key population-led organizations. All violence against people from key population groups should be monitored and reported, and redress mechanisms should be established to provide justice *(3, 79, 84, 85, 162)*.

Other good practice statements: addressing violence

Existing good practice statement	Health and other support services should be provided to all persons from key populations who experience violence. In particular, persons experiencing sexual violence should have timely access to comprehensive post-rape care in accordance with WHO guidelines *(3, 162)*.
Existing good practice statement	Law enforcement officials and health and social care providers need to be trained to recognize and uphold the human rights of key populations, and to be held accountable if they violate these rights, including perpetration of violence *(3, 79, 84, 85, 162)*.

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Essential for impact: health interventions

Prevention of STIs, HIV and viral hepatitis

Harm reduction (NSPs, OAMT and naloxone for overdose management)

Existing GRADE recommendation	All individuals from key populations who inject drugs should have access to sterile injecting equipment through NSPs *(strong recommendation, low certainty of evidence) (3, 83, 167)*.
Existing GRADE recommendation	It is suggested that NSPs also provide low dead-space syringes (LDSSs), along with information about their preventive advantage over conventional syringes *(this recommendation is conditional on local acceptability and resource availability) (168)*.
Existing GRADE recommendation	All people from key populations who are dependent on opioids should be offered OAMT[9] in keeping with WHO guidance (*strong recommendation, low certainty of evidence) (3, 83, 169)*, including those in prison and other closed settings *(170)*. Important considerations related to OAMT, including recommended doses, use in pregnancy and drug interactions are included in: Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence Guidelines for the identification and management of substance use and substance use disorders in pregnancy
Existing GRADE recommendation	People likely to witness an opioid overdose should have access to naloxone and be instructed in its use for emergency management of suspected opioid overdose *(strong recommendation, very low certainty of evidence) (27)*.
	More details of community distribution of naloxone for overdose management can be found in the WHO guideline Community management of opioid overdose.

Condoms and lubricant

Existing GRADE recommendation	The correct and consistent use of insertive and receptive condoms with adequate supply of condom compatible lubricants is recommended to prevent sexual transmission of HIV, viral hepatitis and STIs through anal or vaginal sex[10] *(strong recommendation, moderate certainty of evidence) (3)*.

[9] Methadone or buprenorphine.

[10] Both HCV and HBV can be transmitted sexually, although sexual transmission of HCV is rare as it requires blood contact.

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Essential for impact: health interventions

Prevention of STIs, HIV and viral hepatitis (cont.)

Pre-exposure prophylaxis (PrEP) for HIV

Existing GRADE recommendation	Oral PrEP (containing tenofovir disproxyl fumarate) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches *(strong recommendation, high certainty of evidence) (171).*
Existing GRADE recommendation	The dapivirine vaginal ring may be offered as an additional prevention choice for cisgender women at substantial risk of HIV infection as part of combination prevention approaches *(conditional recommendation, moderate certainty of evidence) (171).*
★ **New GRADE recommendation**	Long-acting injectable cabotegravir may be offered as an additional prevention choice for people at substantial risk of HIV infection, as part of combination prevention approaches *(conditional recommendation, moderate certainty of evidence) (172) .*

For detailed guidance on PrEP please see Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach.

For implementation guidance, please see *Differentiated and simplified pre-exposure prophylaxis for HIV prevention: Update to WHO implementation guidance.*

Post-exposure prophylaxis (PEP) for HIV and STIs

Existing guidance statement	PEP should be available to all eligible people from key populations on a voluntary basis after possible exposure to HIV *(3).*
Existing guidance statement	For women who have been raped, a package of PEP, emergency contraception and presumptive treatment of STIs is recommended *(173).*

For detailed guidance on HIV PEP regimens, please see Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach.

For detailed guidance on PEP for adults who have been sexually abused, please see WHO guidelines Responding to intimate partner violence and sexual violence against women.

For detailed guidance on PEP for children and adolescents who have been sexually abused, please see WHO guidelines Responding to children and adolescents who have been sexually abused.

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Essential for impact: health interventions

Prevention of STIs, HIV and viral hepatitis (cont.)

Prevention of vertical transmission of HIV, syphilis and HBV

Existing GRADE recommendation (adapted)[11]	HIV, syphilis and hepatitis B surface antigen (HBsAg)* tests should be offered at least once and as early as possible in pregnancy, ideally at the first antenatal care (ANC) visit *(syphilis: strong recommendation, moderate quality of evidence; HBsAg*: strong recommendation, low certainty of evidence) (174, 175).* * Particularly in settings with a ≥2% HBsAg seroprevalence in the general population. Recommended time points for HIV retesting for pregnant and postpartum key populations: early in pregnancy (first ANC visit); late in pregnancy (third trimester ANC visit); one additional postpartum retest (14 weeks, six months or nine months postpartum) *(175)*. Please see also STI testing below; chlamydia and gonorrhoea screening is recommended for all key populations, including those who are pregnant.
Existing guidance statement	Dual HIV/syphilis rapid diagnostic tests (RDTs) can be the first test in HIV testing strategies and algorithms in ANC *(176)*. HBsAG testing should be considered in addition when dual testing is performed.
Existing good practice statement (adapted)[12]	ART should be initiated urgently among all pregnant and breast and chest feeding people living with HIV, even if they are identified late in pregnancy or postpartum, because the most effective way to prevent HIV vertical transmission is to reduce maternal viral load *(171)*.
Existing GRADE recommendation (adapted)[13]	For early syphilis in pregnancy, the WHO STI guideline suggests using benzathine penicillin G 2.4 million units once intramuscularly over procaine penicillin 1.2 million units intramuscularly once daily for 10 days *(conditional recommendation, very low certainty of evidence) (177)*.
Existing GRADE recommendation (adapted)[14]	WHO recommends that those who test positive for HBV infection (HBsAg positive) with an HBV DNA ≥ 5.3 log10 IU/mL (≥ 200,000 IU/mL) during pregnancy receive tenofovir prophylaxis from the 28th week of pregnancy until at least birth, to prevent vertical transmission of HBV. This is in addition to three-dose hepatitis B vaccination in all infants, including timely birth dose *(conditional recommendation, moderate certainty of evidence) (178)*.
Existing GRADE recommendation (adapted)[15]	WHO recommends that in settings in which antenatal HBV DNA testing is not available, hepatitis B e antigen (HBeAg) testing can be used as an alternative to HBV DNA testing to determine eligibility for tenofovir prophylaxis to prevent vertical transmission of HBV2 *(conditional recommendation, moderate certainty of evidence) (178).* Please see also: WHO technical brief: preventing HIV during pregnancy and breastfeeding in the context of PrEP.

[11] Recommendations related to prevention of vertical transmission of HIV, syphilis and HBV have been reworded to be more gender inclusive.
[12] Ibid.
[13] Ibid.
[14] Recommendations related to prevention of vertical transmission of HIV, syphilis and HBV have been reworded to be more gender inclusive.
[15] Ibid.

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Essential for impact: health interventions

Prevention of STIs, HIV and viral hepatitis (cont.)

Hepatitis B vaccination

Existing WHO position	WHO recommends hepatitis B vaccination of persons at high risk of HBV infection.[16] Please find further details in WHO position paper: Hepatitis B vaccines: – July 2017
Existing GRADE recommendation	It is suggested to offer people who inject drugs the rapid hepatitis B vaccination regimen[17] *(conditional recommendation, very low certainty of evidence) (168).*

Addressing chemsex

★ **New good practice statement**	Addressing chemsex*, especially for key populations and their sexual partners, requires a comprehensive, non-judgemental and person-centred approach. This can include integrated sexual and reproductive health, mental health, access to sterile needles and syringes and OAMT services, with linkages to other evidence-based prevention, diagnostic and treatment interventions. *Chemsex, for the purpose of these guidelines, is defined as when individuals engage in sexual activity, while taking primarily stimulant drugs, typically involving multiple participants and over a prolonged period. Further details on evidence, decision-making, implementations, considerations and research gaps related to this new recommendation can be found in Chapter 9.

Diagnosis

HIV testing services

Existing guidance statement	In high and low HIV-burden settings, HIV testing should be offered to all key populations and their partners in all services as an efficient and effective way to identify people with HIV *(175).*
Existing guidance statement	It is recommended to offer retesting at least annually to all people from key populations. Depending on individual risk behaviours, more frequent voluntary retesting can be offered *(175).* Mathematical modelling among key populations in Viet Nam shows that retesting for key populations is cost effective. Bi-annual testing for key populations may be considered in similar settings, and should prioritize those at higher risk *(179).*

[16] Including key populations, persons with chronic liver disease, including those with hepatitis C, persons with HIV infection, and sexual contacts of persons with chronic HBV infection, as well as health care workers and others who may be exposed to blood, blood products or other potentially infectious body fluids.

[17] While this recommendation includes only people who inject drugs, this approach may be appropriate for all key populations receiving HBV vaccination.

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Essential for impact: health interventions

Diagnosis (cont.)

HIV testing services (cont.)

Existing GRADE recommendation	Community-based HIV testing services for key populations linked to prevention, treatment and care services are recommended, in addition to routine, facility-based HIV testing services in all settings (*strong recommendation, low certainty of evidence*) *(175)*.
Existing GRADE recommendation	Lay providers who are trained can, using rapid diagnostic tests, independently conduct safe and effective HIV testing services *(strong recommendation, moderate certainty of evidence) (175)*.
Existing GRADE recommendation	HIV self-testing should be offered as an approach to HIV testing services (*strong recommendation, moderate certainty of evidence*) *(175)*. *Please note that self-testing means an individual performing a test on themselves in private or under observation of a professional if they so desire. It should be voluntary and cannot be forced or coerced by anyone. Importantly, people who have self-tested should not be forced to disclose the results of that test to anyone, and should only do so on a voluntary basis.*
Existing GRADE recommendation	Social network-based approaches can be offered as an approach to HIV testing key populations as part of a comprehensive package of care and prevention *(conditional recommendation, very low certainty of evidence) (175)*.
Existing GRADE recommendation	Provider-assisted referral should be offered for all people with HIV as part of a voluntary comprehensive package of testing and care (including key populations) *(strong recommendation, moderate certainty of evidence) (175).* *Please note that particularly for sex workers, the risks associated with disclosing an HIV diagnosis to either clients or regular partners must be carefully considered and should always be voluntary. People who are experiencing intimate partner or other violence need assessment, support, documentation, treatment of any injuries and referral to appropriate services (162).*
Existing guidance statement	Dual HIV/syphilis RDTs may be considered for use among key populations and can increase access to both HIV and syphilis testing services *(181)*. Further testing to confirm syphilis diagnosis or offer of treatment depends on local epidemiology, past treatment history, available resources and confirmatory testing capacity, and national protocols. Mathematical modelling among key populations in Viet Nam shows that using dual HIV/syphilis RDT is cost-saving compared to separate HIV and syphilis tests at current coverage *(179)*.
	For detailed guidance on HIV testing, please see Consolidated guidelines on HIV testing services.

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Essential for impact: health interventions

Diagnosis (cont.)

STI testing

Existing guidance statement	Screening and diagnosing STIs for key populations is a crucial part of a comprehensive response to HIV and STIs *(3)*.
Existing GRADE recommendation	Offering periodic testing for asymptomatic urethral and rectal *N. gonorrhoeae* and *C. trachomatis* infections using nucleic acid amplification tests (NAAT) is suggested over not offering such testing for men who have sex with men and trans and gender diverse people *(conditional recommendation, low certainty of evidence) (79)*.
Existing GRADE recommendation	Offering periodic serological testing for asymptomatic syphilis infection to men who have sex with men and trans and gender diverse people is strongly recommended over not offering such screening *(strong recommendation, moderate certainty of evidence) (79)*.
Existing GRADE recommendation	WHO suggests offering periodic screening for asymptomatic sexually transmitted infections* to sex workers *(conditional recommendation, low certainty of evidence) (84)*. *Chlamydia, gonorrhoea and syphilis
Existing GRADE recommendation	Self-collection of samples for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* should be made available as an additional approach to deliver STI testing services *(strong recommendation, moderate certainty of evidence) (182)*.
Existing GRADE recommendation	For people with symptoms of: 1) urethral discharge from the penis or 2) anorectal discharge and report receptive anal sex, management is recommended to be based on the results of quality-assured molecular assays. However, in settings with limited or no molecular tests or laboratory capacity, WHO recommends syndromic treatment to ensure treatment on the same day of the visit *(strong recommendation, moderate certainty of evidence) (183)*.
Existing GRADE recommendation	For people who present with genital ulcers (including anorectal ulcers), WHO recommends treatment based on quality-assured molecular assays of the ulcer. However, in settings with limited or no molecular tests or laboratory capacity, WHO recommends syndromic treatment to ensure treatment on the same day of the visit *(strong recommendation, moderate certainty of evidence) (183)*.
	For detailed guidance screening and diagnosis of different STIs please see: Guidelines for the management of symptomatic sexually transmitted infections WHO guidelines for the treatment of *Neisseria gonorrhoeae* WHO guidelines for the treatment of *Treponema pallidum* (syphilis) WHO guideline on syphilis screening and treatment for pregnant women WHO guidelines for the treatment of *Chlamydia trachomatis* WHO guidelines for the treatment of genital herpes simplex virus

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Essential for impact: health interventions

Diagnosis (cont.)

Hepatitis C testing

Existing GRADE recommendation	In all settings (and regardless of whether delivered through facility- or community-based or self-testing testing), it is recommended that serological testing for HCV antibody (anti-HCV) be offered, with linkage to prevention, confirmatory diagnosis, care and treatment services, to the following individuals *(184)*: • adults and adolescents from populations most affected by HCV infection (i.e., who are either part of a population with high HCV seroprevalence or who have a history of exposure and/or high-risk behaviours for HCV infection)[18]; and • adults, adolescents and children with a clinical suspicion of chronic viral hepatitis C (i.e., symptoms, signs, laboratory markers). *(strong recommendation, low certainty of evidence).* For detailed guidance on HCV testing: how to test, how to confirm viraemic HCV infection and which assays to use, please see Guidelines on hepatitis B and C testing.
★ **New GRADE recommendation**	People at ongoing risk and a history of treatment-induced or spontaneous clearance of HCV infection may be offered 3–6-monthly testing for presence of HCV viremia (*conditional recommendation, very low certainty of evidence*). Remarks: • Testing should be voluntary and not be used to further stigmatize any populations at ongoing risk. • Testing should be offered alongside primary prevention services that are evidence-based and reduce transmission risks, and in combination with appropriate treatment access and linkage. • To detect presence of viremic infection, the use of quantitative or qualitative nucleic acid testing (NAT) for detection of HCV RNA, or alternatively an assay to detect HCV core antigen, can be performed. Further details on evidence, decision-making, implementation considerations and research gaps related to this new recommendation can be found in Chapter 9.
Existing GRADE recommendation	HCV self-testing should be offered as an additional approach to HCV testing services (*strong recommendation, moderate certainty of evidence) (185)*.

[18] Includes those who are either part of a population with higher seroprevalence (e.g., some mobile/migrant populations from high/intermediate endemic countries, and certain indigenous populations), or who have a history of exposure or high-risk behaviours for HCV infection (e.g., people who inject drugs, people in prisons and other closed settings, men who have sex with men and sex workers, and HIV-infected persons, children of mothers with chronic HCV infection, especially if HIV-coinfected).

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Essential for impact: health interventions

Diagnosis (cont.)

Hepatitis B testing

Existing GRADE recommendation

In all settings (and regardless of whether delivered through facility- or community-based testing), it is recommended that HBsAg serological testing and linkage to prevention, care and treatment services be offered to the following individuals *(184)*:

- adults and adolescents from populations most affected by HBV infection (i.e., who are either part of a population with high HBV seroprevalence or who have a history of exposure and/or high-risk behaviours for HBV infection);
- adults, adolescents and children with a clinical suspicion of chronic viral hepatitis (i.e., symptoms, signs, laboratory markers);
- all pregnant women (at least once and as early as possible, ideally at the first ANC visit); and
- sexual partners, children and other family members, and close household contacts of those with HBV infection.

(strong recommendation, low certainty of evidence)

For detailed guidance on HBV testing and diagnosis, please see Guidelines on hepatitis B and C testing.

Treatment

HIV treatment

Existing GRADE recommendation

ART should be initiated in all adults living with HIV, regardless of WHO clinical stage and at any CD4 cell count (*strong recommendation, moderate certainty of evidence*) *(171)*.

For detailed guidance on HIV treatment, please see Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach.

Please also see the service delivery chapter for details of differentiated service delivery for ART.

★

New guidance statement

Successful ART with viral suppression prevents HIV transmission to sexual partners: there is no transmission when viral load is undetectable or suppressed (less than or equal to 1000 copies/ML) *(186–188)*.

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Essential for impact: health interventions

Treatment (cont.)

HIV-associated TB

Existing GRADE recommendation	People living with HIV should be systematically screened for TB disease at each visit to a health facility *(strong recommendation, very low certainty of evidence) (189)*.
Existing GRADE recommendation	ART should be started as soon as possible within two weeks of initiating TB treatment, regardless of CD4 cell count, among people living with HIV* *(strong recommendation, low-moderate certainty of evidence for adults and adolescents, very low certainty of evidence for children).* *Except when signs and symptoms of meningitis are present
Existing GRADE recommendation	WHO recommends ART for all people with HIV and drug-resistant TB, requiring second-line anti-TB drugs irrespective of CD4 cell count, as early as possible (within the first eight weeks) following initiation of anti-TB treatment *(strong recommendation, very low certainty of evidence) (190, 191)*.
Existing GRADE recommendation	Adults and adolescents living with HIV who are unlikely to have active TB should receive TB preventive treatment as part of a comprehensive package of HIV care. Treatment should also be given to those receiving ART, to pregnant women and to those who have previously been treated for TB, irrespective of the degree of immunosuppression, and even if TB infection testing is unavailable *(strong recommendation, high certainty evidence) (192)*.
Existing GRADE recommendation	Routine co-trimoxazole prophylaxis should be given to all people living with HIV with active TB disease regardless of CD4 cell count *(strong recommendation, high certainty of evidence) (190)*.
	For detailed guidance on TB/HIV, please see Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach. WHO guidelines on TB can be accessed here.

STI treatment

	STIs disproportionately affect key populations and should be diagnosed and treated in a timely manner following WHO guidelines. For detailed guidance on treating different STIs please see: Guidelines for the management of symptomatic sexually transmitted infections WHO guidelines for the treatment of *Neisseria gonorrhoeae* WHO guidelines for the treatment of *Treponema pallidum* (syphilis) WHO guideline on syphilis screening and treatment for pregnant women WHO guidelines for the treatment of *Chlamydia trachomatis* WHO guidelines for the treatment of genital herpes simplex virus

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Essential for impact: health interventions

Treatment (cont.)

HCV treatment	
Existing GRADE recommendation	WHO recommends offering treatment to all individuals diagnosed with HCV infection who are 12 years of age or older, irrespective of disease stage *(strong recommendation, moderate certainty of evidence) (193).*
Existing GRADE recommendation	WHO recommends the use of pan-genotypic direct-acting antiviral (DAA) regimens for treatment of all adults, adolescents and children aged 3 years and above with chronic hepatitis C virus infection, regardless of stage of disease. Adults (18 years and above): *(strong recommendation, moderate certainty of evidence).* Adolescents (12–17 years): *(strong recommendation; moderate-low certainty of evidence).* For detailed guidance on HCV treatment, please see: Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection and, Updated recommendations on treatment of adolescents and children with chronic HCV infection and HCV simplified service delivery and HCV diagnostics
★ **New GRADE recommendation**	Pan-genotypic DAA-HCV treatment should be offered without delay to people with recently acquired HCV infection and ongoing risk *(strong recommendation, very low certainty of evidence).* Remarks: • Individuals with recently acquired infection must have the option to make an informed choice about starting treatment immediately or delaying treatment initiation. • Treatment for recently acquired infection should be offered alongside additional, evidence-based interventions to reduce HCV risk and primary prevention services. Further details on evidence, decision-making, implementation considerations and research gaps related to this new recommendation can be found in the Chapter 9.

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Essential for impact: health interventions

Treatment (cont.)

HBV treatment

Existing GRADE recommendation	As a priority, all adults, adolescents and children with chronic hepatitis B and clinical evidence of compensated or decompensated cirrhosis (or cirrhosis based on APRI score >2 in adults) should be treated, regardless of ALT levels, HBeAg status or HBV DNA levels *(194)* *(strong recommendation, moderate certainty of evidence).*
Existing GRADE recommendation	Treatment is recommended for adults with chronic hepatitis B who do not have clinical evidence of cirrhosis (or based on APRI score ≤2 in adults), but are aged more than 30 years (in particular), and have persistently abnormal ALT levels and evidence of high-level HBV replication (HBV DNA >20 000 IU/mL), regardless of HBeAg status *(194)* *(strong recommendation, moderate certainty of evidence).*
Existing GRADE recommendation	Where HBV DNA is not available: Treatment may be considered based on persistently abnormal ALT levels alone, regardless of HBeAg status *(194) (conditional recommendation, low certainty of evidence).* For detailed guidance on HBV treatment, please see Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection.

Essential for broader health: health interventions

Anal health

★ **New guidance statement**	WHO does not have specific recommendations about anal health or anal cancer, but people infected with HIV are at least 20 times more likely to be diagnosed with anal cancer than uninfected people *(195)*. Like cancer of the cervix, anal cancer is associated with human papillomavirus (HPV) and HPV is vaccine-preventable for all people.[19] Cytological screening can be performed for anal cancer and its precursors, known as anal high-grade squamous intraepithelial lesions, particularly for men who have sex with men, trans and gender diverse people and other people who are more likely to engage in anal sex.

Conception and pregnancy care

Existing guidance statement (adapted)[20]	It is important that all members of key population groups have the same support and access to services related to conception and pregnancy care as pregnant people who are not members of key population groups, as indicated by WHO guidelines *(3)*.
	WHO has various guidelines on conception and pregnancy. Please see the WHO maternal health webpage. For specific recommendations related to pregnancy and HIV, please see Consolidated guideline on sexual and reproductive health and rights of women living with HIV.

[19] Achieving high HPV vaccination coverage in girls (>80%) reduces the risk of HPV infection for boys. Vaccination of secondary target populations, e.g., females aged ≥15 years or males, is recommended only if this is feasible, affordable, cost-effective, and does not divert resources from vaccination of the primary target population or from effective cervical cancer screening programmes *(196)*.

[20] This guidance statement has been reworded to be more gender inclusive.

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Essential for broader health: health interventions

Contraception

	WHO does not have an overarching recommendation related to contraception for key populations, but publishes medical eligibility criteria for contraceptive use (MEC), which provides guidance on the safety of various contraceptive methods for use in the context of specific health conditions and characteristics *(197)*.
Existing guidance statement	All hormonal contraceptive methods and intrauterine devices (IUDs) now fall into Category 1 of the MEC for women at high risk of HIV. Thus, women at high risk of HIV can use all methods of contraception without restriction.
	For detailed guidance on contraception, please see: Medical eligibility criteria for contraceptive use Selected practice recommendations for contraceptive use Contraceptive eligibility for women at high risk of HIV Please see also the service delivery chapter for details of integrating HIV, family planning and STI services.

Gender-affirming care[21]

Existing guidance statement	Trans and gender diverse individuals who self-administer gender-affirming hormones require access to evidence-based information, quality products and sterile injection equipment *(182)*. The principles of gender equality and human rights in the delivery of quality gender-affirming hormones are critical to expanding access to this important intervention and reducing discrimination based on gender identity *(182)*.

Mental health

Existing guidance statement	Routine screening and management for mental health issues (particularly depression and psychosocial stress) should be provided for people from key populations in keeping with the principles of consent, confidentiality and evidence-based quality *(3)*.
	WHO does not have overarching recommendations related to preventing or treating mental health issues for key populations. Instead, specific mental health issues and recommendations and a practical guide on addressing mental health issues in non-specialized health settings is provided by the mental health gap action programme (MhGAP): MhGAP Evidence Resource Centre MhGAP intervention guide

[21] WHO guidelines on health services for trans and gender diverse people are under development at the time of writing. They should be available in 2023.

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Essential for broader health: health interventions

Prevention, assessment and treatment of cervical cancer

Existing WHO position	WHO recommends that all countries proceed with nationwide introduction of HPV vaccination. For the prevention of cervical cancer, the WHO-recommended primary target population for HPV vaccination is girls aged 9–14 years, prior to becoming sexually active. Vaccination strategies should initially prioritize high coverage in this priority population *(196)*.
Existing GRADE recommendation	HPV self-sampling should be made available as an additional approach to sampling in cervical cancer screening services for individuals aged 30–60 years *(strong recommendation, moderate certainty of evidence) (182)*.
Existing guidance statement	All people with a female reproductive system are at risk for cervical cancer. Recommendations for cervical cancer prevention, screening and treatment can be found in the WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, which includes 16 new and updated recommendations and good practice statements for women living with HIV *(198, 199)*. For detailed guidance on cervical cancer prevention, screening and treatment, please see: WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention New WHO recommendations on screening and treatment to prevent cervical cancer among women living with HIV

Safe abortion

Existing guidance statement	Abortion laws and services should protect the health and human rights of all women, including those from key populations *(3)*.
Existing GRADE recommendation	WHO recommends the full decriminalization of abortion; recommends against laws and other regulations that restrict abortion by grounds; recommends that abortion be available on the request of the woman, girl or other pregnant person; and recommends against laws and other regulations that prohibit abortion based on gestational age limits (*strong recommendations*) *(200)*. For detailed guidance on safe abortion, please see Abortion care guideline.

Screening and treatment for hazardous and harmful alcohol and other substance use

Existing GRADE recommendation (adapted)[22]	All key populations with hazardous and harmful alcohol or other substance use should have access to evidence-based interventions, including brief psychosocial interventions involving assessment, specific feedback and advice *(conditional recommendation, very low certainty of evidence) (3, 201, 202)*.
	For details on recommended, evidence-based interventions for the screening and treatment of hazardous and harmful drug and alcohol use please see: MhGAP Evidence Resource Centre MhGAP intervention guide The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) International standards for the treatment of drug use disorders

[22] The original wording of the recommendation was: All key populations with harmful alcohol or other substance use should have access to evidence-based interventions, including brief psychosocial interventions involving assessment, specific feedback and advice.

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Essential for broader health: health interventions

TB prevention, screening, diagnosis and treatment

Existing GRADE recommendation	Systematic screening for TB disease should be conducted in prisons and penitentiary institutions *(strong recommendation, very low certainty of evidence) (189)*.
Existing GRADE recommendation	Systematic screening for TB disease may be conducted among subpopulations with structural risk factors for TB. These include urban poor communities, homeless communities, communities in remote or isolated areas, indigenous populations, migrants, refugees, internally displaced persons and other vulnerable or marginalized groups with limited access to health care *(conditional recommendation, very low certainty of evidence) (189).*
Existing GRADE recommendation	Systematic TB infection testing and treatment may be considered for people in prisons, health workers, immigrants from countries with a high TB burden, homeless people and people who use drugs *(conditional recommendation, low to very low certainty in the estimates of effect) (192).*

TB prevention, screening, diagnosis and treatment

Existing GRADE recommendation	In settings where the TB prevalence in the general population is 100/100 000 population or higher, systematic screening for TB disease may be conducted among people with a risk factor for TB* who are either seeking health care or who are already in care (*conditional recommendation, very low certainty of evidence*) *(189).* *Substance use disorders and alcohol use disorders are considered risk factors. Additional guidance on TB prevention, screening, diagnosis and treatment is available: Consolidated guidelines on tuberculosis Module 1: Prevention: Tuberculosis preventive treatment Consolidated guidelines on tuberculosis Module 2: Screening – Systematic screening for tuberculosis disease Consolidated guidelines on tuberculosis Module 3: Diagnosis – Rapid diagnostics for tuberculosis detection Consolidated guidelines on tuberculosis Module 4: Treatment – Drug-resistant tuberculosis treatment

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Supportive interventions

Behavioural interventions, counselling, demand creation, information and education can all support the interventions listed above. In the development of this guideline, we did not find evidence for the effectiveness of counselling behavioural interventions that aim to change risk behaviours (see below).

While we did not review evidence related to other types of behavioural or supportive interventions, and there is limited WHO guidance on these interventions, they may be helpful depending on the context and population. These include:

- information and education which support key populations to understand their health, health risks, available services and legal rights;
- interventions which aim to increase demand (demand creation) for evidence-based HIV, viral hepatitis and STI services;
- supportive counselling which does not aim to change behaviours; and
- counselling for mental health issues.

In general, the structural barriers which are described in the previous chapter make changing behaviours and improving uptake and retention in services for key populations difficult, and these should be addressed as a priority.

Behavioural interventions

★

New good practice statement

When planning and implementing a response for HIV, viral hepatitis and STIs, policy-makers and providers should be aware that counselling behavioural interventions that aim to change behaviours to reduce risks associated with these infections for key populations have not been shown to have an effect on HIV, viral hepatitis and STI incidence nor on risk behaviour such as condom use and needle sharing. Counselling and information-sharing, not aimed at changing behaviours, can be a key component of engagement with key populations, and when provided it should be in a non-judgmental manner, alongside other prevention interventions and with involvement of peers.

Remarks:

- Addressing structural and social barriers is critical to create environments which permit supportive and impactful counselling.
- Counselling interventions which promote abstinence from drug use, rehabilitation or cessation of sex work or drug use, or a so-called cure for homosexuality or gender incongruence (for example, so-called conversion therapy)* are not recommended, and create barriers to key population service access.

* Compulsory, or involuntary, treatment for drug dependence, so-called conversion therapy or rehabilitation of sex workers is against human rights and medical ethics principals of consent, freedom from arbitrary arrest, access to quality health, freedom from torture and cruel, inhuman and degrading treatment.

Further details on evidence, decision-making, implementation considerations and research gaps related to this new practice statement can be found in Chapter 9.

CHAPTER 5

Packages by key population



Introduction

This chapter presents the above-recommended interventions as packages per key population. It should be noted that there is much cross over between key populations; for example, sex workers who inject drugs and men who have sex with men who sell sex, and for those people, additional interventions to the ones presented below may be needed. Person-centred care means assessing each person's health needs and providing evidence-based interventions in an integrated and accessible way. The tables of packages below are provided as guidance only.

Sex workers

Background

Sex workers include female, male, trans and gender diverse adults (18 years of age and above) who receive money or goods in exchange for sexual services, either regularly or occasionally. Sex work is consensual sex between adults, can take many forms, and varies between and within countries and communities. Sex work also varies in the degree to which it is more or less "formal", or organized *(3, 84)*. Increasingly, sex workers are meeting and staying in contact with their clients online.

As defined in the Convention on the Rights of the Child (CRC), children and adolescents under the age of 18 who exchange sex for money, goods or favours are "sexually exploited" and not defined as sex workers *(203, 204)*. (Please see Chapter 7 on young key populations.)

Sex workers in many places are highly vulnerable to HIV and STIs due to multiple factors, including large numbers of sex partners, unsafe working conditions, barriers to the negotiation of consistent condom use, and intersecting social determinants of poor health. These include lack of social protection and housing, food insecurity, reduced education opportunities and disability. Moreover, sex workers often have reduced control over these factors due to structural barriers that increase their risk of unprotected sex and reduce access to health services (please see the chapter on critical enablers). In particular, sex workers may be harassed by law enforcement officers, including the practice of officers confiscating and using condoms and mobile phones as evidence of sex work; be subjected to violence from law enforcement officers, clients and intimate partners; and experience stigma and discrimination in health and other settings. As a result, sex workers are disproportionately affected by HIV and STIs. For the most recent data related to HIV, syphilis and sex workers, please access UNAIDS Key Populations Atlas.

The recommended package of interventions for sex workers includes enabling interventions that should be implemented as a priority, including the decriminalization of sex work (namely, removing all offences that criminalize sex workers, clients and third parties). Addressing these barriers would not only ensure sex workers' human rights, but also have an impact on HIV, STIs and viral hepatitis in all settings where sex work is criminalized and sex workers experience stigma, discrimination and violence *(68, 75)*. Other essential interventions are health interventions related to HIV and STI prevention, testing and treatment.

The majority of participants in the key populations values and preferences qualitative research (for the detailed report, please see Web Annex B) were opposed to the periodic presumptive treatment (PPT) of STIs, citing both health and ethical concerns. Participants noted an array of potential health risks associated with prolonged antibiotic use, including antibiotic resistance, kidney damage, depression and impacts on vaginal health. Additionally, participants expressed concerns surrounding the ethical implications of PPT and its role in perpetuating stigma and vulnerability. Others attested to the role of PPT in reinforcing stereotypes of sex workers as vectors of disease. Rather than offering sex workers PPT for STIs, participants stressed the need for increased access to STI testing and evidence-based prevention methods. For these reasons, the recommendation to provide PPT for STIs for sex workers is not included in these guidelines. If sex workers wish to prevent STI acquisition through PPT, this should always be voluntary, in full understanding of the potential complications, only in settings where aetiological diagnosis is not possible, and in consultation with health care providers.

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WHO recommends expanding access to aetiological diagnosis of STIs for sex workers as a priority, as well as suggesting offering periodic screening for asymptomatic STIs to sex workers. Offering voluntary periodic screening for HIV and the other main curable STIs, such as syphilis, gonorrhoea and clamydia, is particularly relevant for sex workers, due to the severe consequences of STIs, including infertility. In cases of pregnancy, untreated STIs can also lead to severe adverse pregnancy outcomes, such as prematurity, neonatal death, low-birth weight and congenital anomalies. WHO has specific recommendations for the treatment of the main STIs, suppressive therapy for genital herpes, and for the management of syndromes when the aetiology cannot be investigated for the most appropriate treatment *(183)*.

While evidence of increased prevalence of HCV and HBV in men who have sex with men is clear *(12)*, concerns about viral hepatitis in female and trans and gender diverse sex workers are new and emerging, and there is little data available to understand global prevalence of HBV and HCV among these populations. For female and trans and gender diverse sex workers who are living with HIV, there may be an increased risk of HCV and HBV *(205)*, although evidence is scarce, and additional small studies have shown increased risk for mono-infections *(18)*. However, HCV prevalence is high in people who inject drugs *(206)* and in people in prisons *(207)*, and there is considerable intersection between female and trans and gender diverse sex workers and these other key populations, indicating a need to ensure access to viral hepatitis prevention, testing and treatment for these groups. For this reason, viral hepatitis prevention, testing and treatment are included in the package of essential health interventions for all sex workers.

Other health issues are of particular concern to sex workers, including: those related to sexual and reproductive health (safe abortion, contraception, conception and antenatal care); those related to cervical and anal cancer prevention; and those related to screening and treatment for mental health issues, and for hazardous or harmful alcohol and substance use. In particular, the results of qualitative research undertaken by four global networks of key populations showed that addressing mental health was a priority for key populations. While global data on TB among sex workers is not available, sex workers who live and work in cramped conditions may be at increased risk of TB. These are essential interventions to address broader health beyond HIV, STIs and viral hepatitis, and access for key populations should be ensured.

The package of essential interventions for sex workers does not include those that are specifically related to HIV and viral hepatitis prevention for people who inject drugs (namely, NSPs, OAMT and naloxone for overdose management), or to gender-affirming care for trans and gender diverse people. However, for sex workers who inject drugs or who are trans and gender diverse, these are relevant interventions that should be made available, as outlined in the specific packages for these key populations.

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Recommended package for sex workers

These interventions are not in order of priority.

Essential for impact: enabling interventions
Removing punitive laws, policies and practices
Reducing stigma and discrimination
Community empowerment
Addressing violence
Essential for impact: health interventions
Prevention of HIV, viral hepatitis and STIs
Condoms and lubricant
Pre-exposure prophylaxis for HIV
Post-exposure prophylaxis for HIV and STIs
Prevention of vertical transmission of HIV, syphilis and HBV
Hepatitis B vaccination
Addressing chemsex
Diagnosis
HIV testing
STI testing
Hepatitis B and C testing
Treatment
HIV treatment
Screening, diagnosis, treatment and prevention of HIV associated TB
STI treatment
HBV and HCV treatment
Essential for broader health: health interventions
Anal health
Conception and pregnancy care
Contraception
Mental health
Prevention, assessment and treatment of cervical cancer
Safe abortion
Screening and treatment for hazardous and harmful alcohol and other substance use

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People who inject drugs

Background

People who inject drugs refers to people who inject psychoactive substances for non-medical purposes. These drugs include, but are not limited to, opioids, amphetamine-type stimulants, cocaine and hypno-sedatives including new psychoactive substances.[23] Injection may be through intravenous, intramuscular, subcutaneous or other injectable routes. People who self-inject medicines for medical purposes – referred to as "therapeutic injection" – are not included in this definition. While these guidelines focus on people who inject drugs because of their specific risk of HIV and HCV transmission, due to the sharing of blood-contaminated injection equipment, much of this guidance is also relevant for people who use substances through other routes of administration, such as snorting, smoking and ingestion *(3)*.

In many countries drug use or possession is criminalized, and in almost every country it is considered immoral and significant stigma and discrimination is experienced by people who use drugs (please see the critical enablers chapter). At the time of writing there is extremely low coverage of the evidence-based package of NSPs and OAMT *(208)*. As a direct result, people who inject drugs are disproportionately affected by HIV and viral hepatitis. For most recent data related to HIV, viral hepatitis and people who inject drugs, please access UNAIDS Key Populations Atlas, the World Drug Report and the Global state of harm reduction.

For impact on HIV and viral hepatitis, structural barriers for people who inject drugs need to be addressed, including decriminalizing drug use and possession for personal use, ending forced detention in compulsory drug treatment centres, addressing violence, stigma and discrimination, and empowering communities of people who use drugs. People who use drugs in particular face additional barriers to accessing health services where cessation of drug use is a condition for eligibility. Women who inject drugs may be more stigmatized than their male counterparts, and many sell sex to pay for both their and their partner's drugs. Fear of losing custody of their children may make mothers who inject drugs less likely to access reproductive and other health services (*209*). They may experience more police harassment and violence than men who inject drugs. The impact of these barriers on HIV and viral hepatitis acquisition is clear *(64, 73, 210)*, and for this reason the enabling interventions listed in the table below are considered essential for impact for people who inject drugs.

Harm reduction is one of the key elements of a public health promotion framework (or response) that has been proven highly effective in reducing and mitigating the harms of injecting drug use for individuals and communities. WHO defines harm reduction as a comprehensive package of evidence-based interventions, based on public health and human rights, including NSPs, OAMT and naloxone for overdose management. Harm reduction also refers to policies and strategies that aim to prevent major public and individual health harms, including HIV, viral hepatitis and overdose, without necessarily stopping drug use.

High prevalence and incidence of HIV and viral hepatitis B and C in people who inject drugs call for countries to prioritize the provision of HIV and viral hepatitis prevention (particularly NSPs, OAMT and naloxone for overdose management), testing and treatment interventions.

Pre-exposure prophylaxis (PrEP) is an evidence-based HIV prevention intervention. Although there is strong evidence that PrEP is highly protective for sexual HIV transmission, evidence is more limited for the prevention of parenteral HIV transmission. PrEP services for people who inject drugs and their sexual partners can provide benefits both in the prevention of sexual transmission, and likely in the prevention of HIV, acquired through unsafe injection practices. PrEP services should

[23] UNODC uses the term "new psychoactive substances" which are defined as "substances of abuse, either in a pure form or a preparation, that are not controlled by the 1961 Single Convention on Narcotic Drugs or the 1971 Convention on Psychotropic Substances, but which may pose a public health threat" *(2)*.

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not replace NSPs. NSPs have the greatest impact in preventing the transmission of HIV and other bloodborne infections, including HCV associated with injecting drug use.

More research is needed on the values and preferences of people who inject drugs on PrEP as part of comprehensive HIV prevention approaches, and on how to best deliver PrEP services for this population to improve uptake and effective use (including through comprehensive and integrated community-based delivery models).

While global estimates of STIs among people who inject drugs are not known, people who inject and use drugs may be at increased risk of STIs, particularly those engaging in chemsex or those using stimulants. Values and preferences research showed a strong preference for STI services among women who inject drugs. For this reason, people who inject drugs should have access to STI testing, diagnosis and treatment.

People who inject drugs are at increased risk of TB, irrespective of their HIV status, and TB is a leading cause of HIV-related mortality among people who inject drugs *(211, 212)*. For this reason, TB prevention, screening, diagnosis and treatment are included in the package of interventions essential for broader health of people who inject drugs. Other common health issues related to unsafely injecting drugs include nerve and vein damage, abscesses and skin infections.



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Recommended package for people who inject drugs

These interventions are not in order of priority.

Essential for impact: enabling interventions
Removing punitive laws, policies and practices
Reducing stigma and discrimination
Community empowerment
Addressing violence
Essential for impact: health interventions
Prevention of HIV, viral hepatitis and STIs
Harm reduction (NSPs, OAMT and naloxone for overdose management)
Condoms and lubricant
Pre-exposure prophylaxis for HIV[24]
Post-exposure prophylaxis for HIV and STIs
Prevention of vertical transmission of HIV, syphilis and HBV
Hepatitis B vaccination
Addressing chemsex
Diagnosis
HIV testing
STI testing
Hepatitis B and C testing
Treatment
HIV treatment
Screening, diagnosis, treatment and prevention of HIV associated TB
STI treatment
HBV and HCV treatment
Essential for broader health: health interventions
Conception and pregnancy care
Contraception
Mental health
Prevention, assessment and treatment of cervical cancer
Safe abortion
Screening and treatment for hazardous and harmful alcohol and other substance use
TB prevention, screening, diagnosis and treatment

[24] Please note, results of qualitative research found that people who inject drugs prioritize access to harm reduction (NSPs, OAMT and naloxone for overdose management) over PrEP.

Men who have sex with men

Background

Men who have sex with men refers to all men who engage in sexual relations with other men. The words **men** and **sex** can be interpreted differently in diverse cultures and societies and by the individuals involved. Therefore, the term encompasses the large variety of settings and contexts in which male-to-male sex takes place, regardless of multiple motivations for engaging in sex, self-determined sexual and gender identities, and various identifications with any particular community or social group.

Men who have sex with men are disproportionately affected by HIV, hepatitis C *(12)*, hepatitis B *(213)* and STIs *(28, 31, 214)*. Hepatitis A outbreaks among men who have sex with men are common *(215–219)* and could be prevented with vaccination. This heightened risk is in part due to greater efficiency of transmission of the three disease groups through unprotected anal sex and syndemic features, such as increased risk of HIV acquisition in those with STIs *(221)*, or increased risk of HCV acquisition in men who have sex with men who live with HIV *(12)*.

Some men who have sex with men may also engage in chemsex – defined as when individuals engage in sexual activity while taking primarily stimulant drugs, typically involving multiple participants and over a prolonged time, which increases risk to all three infectious disease groups when there is no access to, and use of, prevention, diagnosis and treatment services.

Persistent structural barriers, such as criminalization of male-to-male consensual sex, stigma, discrimination and violence against men who have sex with men, reduces access to prevention, testing and treatment services, contributing to increased risk of infection (please see the critical enablers chapter).

The essential package of interventions for men who have sex with men includes enabling interventions to address structural barriers as a priority, including the decriminalization of same-sex intimacy. Essential health interventions for impact on HIV, STIs and viral hepatitis include prevention, such as PrEP, diagnosis and treatment for the three disease groups. Men who have sex with men who inject drugs also need access to harm reduction interventions (NSPs, OAMT and naloxone for overdose management).

Those interventions essential for broader health, and to which access for men who have sex with men should be ensured, include screening and treating mental health, and hazardous or harmful alcohol and drug use. Additionally, given the disproportionate rates of anal cancers among men who have sex with men, screening and treatment for anal cancer should be considered for men who have sex with men.

For most recent data related to HIV, syphilis and men who have sex with men, please access UNAIDS Key Populations Atlas.

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Recommended package for men who have sex with men

These interventions are not in order of priority.

Essential for impact: enabling interventions
Removing punitive laws, policies and practices
Reducing stigma and discrimination
Community empowerment
Addressing violence
Essential for impact: health interventions
Prevention of HIV, viral hepatitis and STIs
Condoms and lubricant
Pre-exposure prophylaxis for HIV
Post-exposure prophylaxis for HIV and STIs
Prevention of vertical transmission of HIV, syphilis and HBV
Hepatitis B vaccination
Addressing chemsex
Diagnosis
HIV testing
STI testing
Hepatitis B and C testing
Treatment
HIV treatment
Screening, diagnosis, treatment and prevention of HIV associated TB
STI treatment
HBV and HCV treatment
Essential for broader health: health interventions
Anal health
Mental health
Screening and treatment for hazardous and harmful alcohol and other substance use

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Trans and gender diverse people

Background

Trans and gender diverse people is an umbrella term for those whose gender identity, roles and expression does not conform to the norms and expectations traditionally associated with the sex assigned to them at birth; it includes people who are transsexual, transgender or otherwise gender nonconforming or gender incongruent. Trans and gender diverse people may self-identify as transgender, female, male, transwoman or transman, trans-sexual or one of many other gender nonconforming identities. They may express their genders in a variety of masculine, feminine and/or androgynous ways. The high vulnerability and specific health needs of trans and gender diverse people necessitates a distinct and independent status in the global HIV response *(3, 222)*.

Trans and gender diverse people experience structural barriers such as criminalization, stigma and discrimination, as do all key populations, but experience very high rates of sexual and physical violence *(223–226)*. High levels of stigma and discrimination against trans and gender diverse people in health care settings have been widely reported *(100)*. Violence and stigma and discrimination increase vulnerability to substance use disorders, eating disorders, depression, suicide attempts, HIV and other sexually transmitted infections, among others, and compromise trans and gender diverse people's access and utilization of health services *(101, 102, 222)*. Depression, for example, has been reported to affect more than half of the trans and gender diverse population in certain settings *(222)*, and their quality of life has been shown to be significantly poorer than that of the general population prior to receiving hormonal treatment, when desired *(227)*. Additionally, there are specific barriers caused by the lack of legal recognition of other gender identities and expressions, which hinder access to health and other services, and limit entry into both public and private health insurance schemes. In particular, gender-sensitive care for trans and gender diverse people is often not available, with health care providers untrained regarding the specific needs of trans and gender diverse people *(228)*.

Trans and gender diverse people are disproportionately affected by HIV and STIs *(30, 229)*. While data are limited, studies have also shown high prevalence of viral hepatitis B and C in trans and gender diverse people *(20)*. For the most recent data related to HIV, syphilis and trans and gender diverse people, please access UNAIDS Key Populations Atlas.

Gender-affirming care can include any of the following: hormone therapy; upper (for example, face, chest, breast) surgery; and/or lower (for example, vaginoplasty, phalloplasty, metoidioplasty, etc.) surgery. Gender affirmation is often a priority intervention for the trans and gender diverse community, but access is often hindered by poor availability, high cost and exclusion of gender-affirming interventions from national health service packages. Administration of industrial-grade silicone or other illicit subcutaneous injections, as well as non-medical-grade fillers, are reported to be common, especially in low- and middle-income countries (LMICs) *(231, 232)*. These interventions can cause body disfigurement, skin damage, allergic reactions, thrombosis, pulmonary silicone embolism and severe autoimmune and connective tissue disorders, among others *(233)*. Likewise, the use of unsafe and unregulated hormones was reported to be very common among trans and gender diverse people *(234)*.

It is important that hormones administered for gender affirmation remain within appropriate physiological levels to avoid negative health consequences, and trans and gender diverse people who self-administer hormones need access to evidence-based information, products and sterile injection equipment *(182, 235)*. Moreover, other non-medical body modification strategies are often used by both youth and adult trans and gender diverse people, including genital tucking and chest binding; little research has described either the prevalence or health risks and benefits of these methods of gender affirmation *(235)*.

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The recommended package of interventions for trans and gender diverse people includes enabling interventions that should be implemented as a priority to address barriers, in particular, recognizing gender diversity in laws, policies and practices.

The health intervention package reflects the complex and varied needs of trans and gender diverse people. Trans and gender diverse people need access to the entire range of HIV, viral hepatitis and STI prevention, testing and treatment interventions for greatest impact. These interventions include access to prevention of vertical transmission of HIV, HBV and syphilis for pregnant trans and gender diverse people; and include harm reduction (NSPs, OAMT and naloxone for overdose management) for trans and gender diverse people injecting drugs, including the injection of hormones and other products, such as silicon gel, for gender affirmation. Interventions for broader health include sexual and reproductive health interventions; screening for and treating hazardous or harmful drug and alcohol use and mental health issues; and preventing, assessing and treating cervical and anal cancers. Access to safe and evidence-based gender-affirming care should be seen as central to trans and gender diverse people's broader health, as well as an important entry point for HIV, STI and viral hepatitis health services, and other health services in general.

The international classification of diseases (ICD–11) has redefined gender identity-related health as gender incongruence, and has reclassified gender incongruence as a condition related to sexual health rather than a mental and behavioural disorder *(236)*. This reflects evidence that trans and gender diverse identities are not conditions of mental ill health and classifying them as such can cause enormous stigma. Inclusion of gender incongruence in the ICD should ensure trans and gender diverse people's access to gender-affirming health care, as well as adequate health insurance coverage for such services.

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Recommended package for trans and gender diverse people

These interventions are not in order of priority.

Essential for impact: enabling interventions
Removing punitive laws, policies and practices
Reducing stigma and discrimination
Community empowerment
Addressing violence
Essential for impact: health interventions
Prevention of HIV, viral hepatitis and STIs
Condoms and lubricant
Pre-exposure prophylaxis for HIV
Post-exposure prophylaxis for HIV and STIs
Prevention of vertical transmission of HIV, syphilis and HBV
Hepatitis B vaccination
Addressing chemsex
Diagnosis
HIV testing
STI testing
Hepatitis B and C testing
Treatment
HIV treatment
Screening, diagnosis, treatment and prevention of HIV associated TB
STI treatment
HBV and HCV treatment
Essential for broader health: health interventions
Anal health
Conception and pregnancy care
Contraception
Gender-affirming care
Mental health
Prevention, assessment and treatment of cervical cancer
Safe abortion
Screening and treatment for hazardous and harmful alcohol and other substance use

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People in prisons and other closed settings

Background

There are many different terms used to denote places of detention, which hold people who are awaiting trial, who have been convicted or who are subject to other conditions of security. Similarly, different terms are used for those who are detained. In this guidance document, the term "prisons and other closed settings" refers to all places of detention within a country, and the terms "prisoners" and "detainees" refer to all those detained in criminal justice and prison facilities; included are adult and juvenile males, and females and trans and gender diverse people, who are detained during the investigation of a crime, while awaiting trial, after conviction, before sentencing and after sentencing. This term does not formally include people detained for reasons relating to immigration or refugee status, those detained without charge, and those sentenced to compulsory treatment and to rehabilitation centres, including people who use drugs and sex workers. Nonetheless, most of the considerations in these guidelines may apply to these populations as well *(3)*. Prison staff are also affected by HIV, viral hepatitis, STIs and other health issues, and may lack access to health services, particularly if they live in prison compounds without health services *(237)*.

People in prison are disproportionately affected by HIV *(212)*, hepatitis B and C *(207, 238)* and TB *(11, 212)*. This is, in part, due to the crossover between other key populations, particularly considering the criminalization of behaviours such as drug use, drug possession and sex work, and their overrepresentation in prison populations. Besides this, there is the transmission of HIV and viral hepatitis within prison through unprotected sex, sexual violence, sharing injection equipment, tattooing or parent-to-child transmission. HIV and hepatitis prevention interventions are often unavailable in prisons, although the risks persist *(239)*. There is a frequent intersection with people in prisons and those who are poor, have little education, and come from socioeconomically deprived sectors of the population, and in many prisons there is an overrepresentation of racial minorities. In particular, the prevalence of substance use and dependence in prison populations is much higher than in the community, particularly for women *(240–242)*.

People in prisons also have high exposure to TB, including multi-drug resistant TB, because of factors including overcrowding, poor ventilation and poor infection control practices. Assuring equitable access to TB services for all people in prisons, regardless of HIV status, is critical for reducing increased burden of HIV-associated TB among people in prisons. Contributing to poor health of people in prisons are: limited access to health care, with delays in diagnosis (due to insufficient laboratory capacity and diagnostic tools); inadequate treatment; frequent transfer of people in prisons between prisons, without continuity of treatment; and poor nutrition. Additionally, after release from prison there is often little support for ongoing health and social care.

For most recent data related to HIV and people in prisons and other closed settings, please access UNAIDS Key Populations Atlas.

The right to equivalent health services for people in prisons (namely, equivalent to that available outside of prisons) is enshrined in several internationally recognized documents *(243)*, and respect for these should be reflected in prison policies and practices. Violence in prisons is common and often clandestine because of the fear of reprisal when it is reported, therefore it is easily overlooked or underestimated *(244)*. Structural barriers within prisons, in particular regarding violence, where it is also important to develop measures for safe reporting and protection of victims, need to be urgently addressed, and are essential and priority interventions for impact.

People in prisons are adolescents, adults, male, female, trans and gender diverse and have urgent, varied and complex health needs. For impact on HIV, viral hepatitis and STIs, the package of interventions which prevent, diagnose and treat these diseases is essential, and should be provided within prisons and other closed settings, with continuity during inter- and intra-prison transfers and after release. This package should include condoms and lubricant and harm reduction

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interventions (NSPs, OAMT and naloxone for overdose management), given that drug use is prevalent in prisons.

People in prisons have broader health needs, and the package of interventions includes mental health and hazardous or harmful drug and alcohol use screening and treatment; sexual and reproductive health interventions; and prevention, screening and treatment of cervical and anal cancers. Importantly, TB prevention, screening and treatment should be implemented in all prisons and closed settings.

UNODC recommends a package of 15 interventions for HIV prevention, diagnosis and treatment for people in prisons *(245)*. These guidelines address multiple disease areas and present a different package, although almost all the 15 UNODC recommended interventions are included here.[25]

[25] Interventions included in the UNODC package which are not included here are: Prevention of transmission through medical and dental services and Protecting staff from occupational hazards.

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Recommended package for people in prisons and other closed settings

These interventions are not in order of priority.

Essential for impact: enabling interventions
Removing punitive laws, policies and practices
Reducing stigma and discrimination
Community empowerment
Addressing violence
Essential for impact: health interventions
Prevention of HIV, viral hepatitis and STIs
Harm reduction (NSPs, OAMT and naloxone for overdose management)
Condoms and lubricant
Pre-exposure prophylaxis for HIV
Post-exposure prophylaxis for HIV and STIs
Prevention of vertical transmission of HIV, syphilis and HBV
Hepatitis B vaccination
Addressing chemsex
Diagnosis
HIV testing
STI testing
Hepatitis B and C testing
Treatment
HIV treatment
Screening, diagnosis, treatment and prevention of HIV associated TB
STI treatment
HBV and HCV treatment
Essential for broader health: health interventions
Anal health
Conception and pregnancy care
Contraception
Mental health
Prevention, assessment and treatment of cervical cancer
Safe abortion
Screening and treatment for hazardous and harmful alcohol and other substance use
TB prevention, screening, diagnosis and treatment

CHAPTER 6

Service delivery



Background

Based on the principal of the human right to health, health services for key populations (as for all populations) should be:

Available – There needs to be sufficient number of functioning health care facilities, goods and services that can, in coordination, provide a package of interventions as described in these guidelines for all key populations.

Accessible – Health facilities, goods and services must be accessible to all key populations. This means they should be physically accessible, affordable and non-discriminatory.

Acceptable – Health services must respect medical ethics, be culturally and developmentally appropriate, sensitive to gender, and non-judgemental. Acceptability requires that health facilities, goods, services and programmes are people-centred, and cater for the specific needs of key population groups, and do so in accordance with international standards of medical ethics of confidentiality and informed consent.

Quality – Quality health services are: evidence-based, safe, effective, people-centred, timely, equitable, integrated and efficient.

The coronavirus disease (COVID-19) pandemic highlighted deficiencies in health systems, with most countries unprepared and experiencing considerable disruptions to health services, including HIV, viral hepatitis and STI services for key populations. This is due in part to divergence of funds from essential health services and barriers to health service access, such as restricted movement, reduced ability to pay and fear of infection. The inequities experienced by key populations increased their vulnerability to COVID-19 as well as HIV, viral hepatitis and STIs. At the same time, there are positive examples of resilience from key population communities to help their peers to continued access to life-saving services, such as ART and harm reduction.

To strengthen health systems to respond to the current and potential future pandemics, WHO recommends: investment in essential public health functions; building a strong primary health care foundation; increased domestic and global investment in health system foundations; involving communities (including key population communities) and societies; and addressing pre-existing inequities and the disproportionate impact of COVID-19 on marginalized and vulnerable populations, including key populations *(1)*.

The service delivery and enabling interventions recommended in these guidelines will not only increase accessibility, availability and acceptability of HIV, viral hepatitis and STI services for key populations, but will strengthen systems to provide universal health coverage and mitigate the impact of health emergencies.

The majority of health interventions included in these guidelines are relevant for all populations, but key populations experience particular structural barriers to access health services, as described in the chapter on enabling interventions. In combination with the recommended enabling interventions, service delivery strategies described in this chapter, particularly community and key population-led delivery of services, can address these barriers, as well as contribute to person-centred care and UHC, ensuring key populations' right to health.

While different in every country, key populations access health interventions through a range of services. Traditional, facility-based services, which may not be targeted towards key populations, offer a range of health interventions, including for HIV, STI and viral hepatitis prevention, testing and treatment, which should be able to be accessed by key populations. However, stigma, discrimination and restrictive policies often deter key populations from accessing these services.

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Other services include community-based services, which may or not be key population led. Youth-friendly services can be accessed by young key populations. Often these services also conduct regular outreach and can provide mobile prevention, testing and/or treatment services as well. Some of these community-based services provide integrated HIV, STI and viral hepatitis interventions, as well as other health and social interventions, such as family planning, additional reproductive health and cancer screening, and sometimes legal services; these are often referred to as "one-stop-shops". Methadone and buprenorphine are often provided by specialized services, which may or may not integrate HIV, viral hepatitis, TB and/or STI services as well.

This chapter describes a range of service delivery strategies: integration; decentralization; online services; self-care; involvement of peers and task sharing.

Community-led services, task-sharing and involvement of key population peers

Key populations have a central role to play in leading programmes and services: reaching groups; providing prevention, testing and treatment services; as well as helping their peers navigate and remain in treatment services. Qualitative research conducted by four key population networks (for detailed report, please see Web Annex B) found that community-led services were unanimously endorsed and preferred by participants. Key populations described community-led services as being critical to promoting the health and human rights of marginalized groups, especially as a counterbalance to stigma experienced by some in traditional health care environments. Accordingly, participants across all population networks advocated for the scale-up of community-led interventions, as well as resources to support community-led services.

UNAIDS defines community-led organizations, groups and networks as those that are led by and for the constituencies they serve. They are self-determining and autonomous entities: for which the majority of governance, leadership, staff, spokespeople, membership and volunteers reflect and represent the experiences, perspectives and voices of their constituencies, and who have transparent mechanisms of accountability to their constituencies *(246)*.

UNAIDS further defines community-led responses as the actions and strategies undertaken by these groups to improve the health and human rights of their constituencies. These responses are informed and implemented by and for communities themselves and the organizations, groups and networks that represent them. Community-led responses are determined by and respond to the needs and aspirations of their constituents, and include a range of activities, such as advocacy, campaigning and holding decision-makers to account; monitoring of policies, practices, and service delivery; participatory research; education and information-sharing; capacity-building; and funding of community-led organizations, groups and networks. Community-led organizations and responses must be understood as distinct from those that are community-based. "Community-based" refers to where a response happens, regardless of who is implementing it, while "community-led" refers to who leads and implements the response *(246)*.

Community-led services with peers as providers have a positive impact on HIV, STI and viral hepatitis, with increased access, availability and acceptability of services *(247–252)*. Peers have an important role in reaching other key populations through outreach *(253)*, giving information, providing commodities (such as condoms, lubricants, needles/syringes, PrEP, PEP and naloxone) and providing services, including testing and treatment.

As well as key population peers, other non-specialist health care providers and lay people can provide health interventions, including nurses and outreach workers, which can reduce the workload of doctors and increase access and equity.

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This guideline includes a new GRADE recommendation specific to key population peers.

Peer navigation

NEW RECOMMENDATION

Peer navigators are recommended to support people from key populations to start HIV, viral hepatitis or STI treatment, and to remain in care *(conditional recommendation, moderate certainty of evidence).*

Remarks:

- A peer navigator's role is to assist key population members to access health services, navigate these services and stay in care.
- Peer navigators require adequate remuneration, recognition, training and other support to fulfil their role.
- Peer navigators are often highly valued by their peers.

Further details on evidence, decision-making, implementation considerations and research gaps related to this new recommendation can be found in Chapter 9.

Relevant WHO guidelines include those related to task sharing and peer navigation for:

- HIV treatment. See Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach;
- HIV testing. See Consolidated guidelines on HIV testing services;
- Hepatitis testing. See Guidelines on hepatitis B and C testing;
- For general recommendations related to task sharing, please see Task shifting: global recommendations and guidelines;
- For guidance for task sharing in family planning services, please see Task sharing to improve access to family planning/contraception;
- Updated recommendation on treatment of adolescents and children with chronic HCV infection and HCV simplified service delivery and HCV diagnostics



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Integration

Integration is the management and delivery of health services so that people receive a continuum of prevention, testing and treatment services, according to their needs, over time and across different levels of the health system. This is particularly relevant for people, such as some key population members, who have complex health needs and who are affected by health issues. Health systems organized around the needs of people and communities perform more effectively, cost less, improve health literacy, increase patient engagement, and are better prepared to respond to health crises *(254)*. Health service integration includes the development of referral systems and networks, and empowering patients and communities to participate in their own care, as well as the provision of multiple interventions at one site.

Table 1 provides one way of classifying health service integration, and how these can be applied to the recommendations and implementation of prioritized packages as outlined in these guidelines *(255)*.

Table 1. Types of health service integration

Type of health service integration	Definition	Application to these guidelines
Organizational	Organizations and departments within organizations plan and budget together	National programmes for HIV, STIs and viral hepatitis and other relevant health programmes review these guidelines, and use them to inform the development of integrated strategies, plans, budgets, guidelines and protocols for key populations.
Service	Different clinical services integrated at organizational level, through coordinated referral or linkage	Clinical service managers at different levels and for different clinical services review these guidelines, and work together to ensure key population members' access to the comprehensive package of health interventions across health services, through referral or linkage.
Site level	Provision of multiple interventions at one site	Site level managers of primary health care, community-based or other clinics, which serve key populations, are supported to provide multiple, appropriate, evidence-based interventions, as included in the WHO recommended package.

WHO recommends the integration of HIV, viral hepatitis and STI services, and also the integration of these with a range of other relevant clinical services, such as those for TB, maternal and child health, mental health, sexual and reproductive health services, and drug dependence treatment.

The following WHO guidelines related to integration are particularly relevant to key populations. However, this is not an exhaustive list of integration strategies, and programmes should endeavour to integrate services based on the needs of their clients.

- For guidance on HIV and TB integration, sexual reproductive health and HIV integration, ART and OAMT integration, please see Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach.

- For guidance on integrating hepatitis C services, please see Updated recommendation on treatment of adolescents and children with chronic HCV infection and HCV simplified service delivery and HCV diagnostics
- Integration of HIV testing and linkage in family planning and contraception services: implementation brief

Decentralization

Decentralization is the transfer of formal responsibility and power to make decisions regarding the management, provision and/or financing of health services to geographically or organizationally separate actors. In effect, this moves services out of tertiary health care facilities, physically and managerially, and means that health interventions can be provided and managed at different lower- level sites, including community-based services. Key populations may feel less comfortable and may experience stigma and discrimination in tertiary hospitals, and so the provision of health services outside of hospital settings in community-based and key population-targeted services can increase acceptability and accessibility. Decentralizing health services can also reduce barriers such as transport costs and long waiting times in central hospitals. However, decentralization of services for key populations may not always be appropriate or acceptable, and people may prefer to receive services in tertiary facilities where there is greater anonymity.

- For guidance on decentralized HIV testing, please see Consolidated guidelines on HIV testing services
- For guidance on decentralized HIV treatment, please see Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach.
- For guidance on decentralized HCV testing and treatment, please see Updated recommendation on treatment of adolescents and children with chronic HCV infection and HCV simplified service delivery and HCV diagnostics

Differentiated service delivery

Differentiated service delivery can be defined as a client-centred approach that simplifies and adapts services, in ways that both serve the needs of affected people better and reduce unnecessary burdens on the health system *(256)*. Differentiated service delivery for key populations considers where, when and by whom relevant interventions are provided, with the goal of increasing access to health services, increasing equity and increasing efficiencies in health systems. For example, to achieve these goals, service planners may decide to reduce the frequency at which people need to collect methadone doses for OAMT and support community-based distribution.

WHO has several recommendations related to differentiated service delivery for ART, including rapid ART initiation, reduced frequency clinical visits and ART pick-up and adherence support, as well as recommendations for differentiated HIV testing services.

- Please see Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach for more details.

Virtual interventions

Increasingly, services designed for key populations are using virtual platforms, conducting outreach to reach people at risk; providing information about available services; providing self-test information and tests; booking appointments for testing; and linking people diagnosed with HIV, viral hepatitis or STIs with treatment service providers *(257–259)*. This approach to service delivery may be of particular relevance and importance to complement and enhance existing health

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infrastructure and service delivery for the younger key population community, always under the condition that potential concerns about sensitive content and data privacy can be addressed *(257)*.

Different interventions are implemented online. Common categories include the following.

1. **Online outreach** to potential key populations service users through online platforms. This involves reaching out to those who had not been reached before, by using systems and structures like websites and social media apps, where key populations can communicate, access information and socialize.
2. **Online case management** for key populations diagnosed with HIV, HCV or STIs who need to engage in services to assess risk and adhere to necessary treatment. Providing case management through online systems can potentially reduce loss to follow-up, provide helpful prompts (such as reminders to book an appointment or take a medication) and support for key populations.
3. **Targeted health information** uses internet sites and social networking apps to allow for communication to be targeted, based on user demographics and characteristics. For example, social media advertisements can target users of certain ages, political profiles, geographic locations, etc. Population segmentation may allow for more specific targeting of key population audiences to provided tailored information or linkage to health services.

The potential advantages of online services include reaching a broader audience, reaching people who are geographically isolated, targeting information to specific people, improved efficiencies and convenience for clients.

Online services should be complementary to face-to-face services and not replace them. Online services may not reach all key populations, and some key population members may prefer face-to-face services, or have concerns about privacy when accessing online. Some key population members, often the most vulnerable, have additional barriers, such as the cost associated with network data, illiteracy, language barriers and limited access to phones, tablets or computers.

Online platforms can provide a safe space for key populations to access information and services; however, efforts to protect the safety of users and eliminate online mistreatment need to also be implemented and monitored closely. The engagement and involvement of key populations, in all their diversity and ages, in the development of apps or online tools and services will increase the likelihood of apps being culturally and age-appropriate and friendly, and ensure the information is age-appropriate *(257, 260)*. Lastly, it is important to ensure trustworthy platforms, with staffing by trained operators, counsellors, and key populations themselves, to provide developmentally appropriate health and welfare information to young key populations, as well as the opportunity for referrals to relevant services *(257)*.

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Online interventions

NEW RECOMMENDATION

Online delivery of HIV, viral hepatitis, and STI services to key populations may be offered as an additional option, while ensuring that data security and confidentiality are protected *(conditional recommendation, low certainty of evidence).*

Remarks:

- Choice is important, and online services should form a part of a menu of interventions, not stand-alone interventions, and should not be a replacement for face-to-face services.
- Efforts should be made to increase equitable access to the internet, improve literacy and provide appropriate training for key population members where needed.
- Consideration should be given to the preferences of different key population groups, given the current lack of published evidence from sex workers and people who inject drugs.

Further details on evidence, decision-making, implementation considerations and research gaps related to this new recommendation can be found in Chapter 9.

Self-care

WHO uses the following working definition of self-care: Self-care is the ability of individuals, families and communities to promote health, prevent disease, maintain health, and cope with illness and disability with or without the support of a health worker *(182)*. The scope of self-care as described in this definition includes health promotion; disease prevention and control; self-medication; self-testing; providing care to dependent persons; seeking hospital/specialist/primary care if necessary; and rehabilitation, including palliative care. It includes a range of self-care modes and approaches. While this is a broad definition that includes many activities, it is important for health policy to recognize the importance of self-care, especially where it intersects with health systems and health professionals.

For key populations, who may feel a lack of control of their health in the face of persistent structural barriers, engagement in self-care can be empowering, as well as increasing accessibility and availability of health interventions.

Relevant, recommended approaches that can be self-administered or managed include:

- emergency contraception;
- abortion and post-abortion contraception;
- HPV, chlamydia, and gonorrhoea self-sampling;
- self-care after sexual assault and violence;
- pregnancy testing; and
- HIV and HCV self-testing.

For more details on self-care, please see WHO guideline on self-care interventions for health and well-being.

For more details on HIV self testing, see WHO Consolidated guidelines on HIV prevention, testing, treatment, service delivery and monitoring: recommendations for a public health approach.

For more details on HCV self-testing, see Recommendations and guidance on hepatitis C virus self-testing.

CHAPTER 7

Programme and service considerations for young key population groups



"The barriers that impede our access to high-quality health services also affect us uniquely. We know the solutions to these barriers, but we need spaces to engage in mitigating them."

Fahe Kerubo, Y+ Global

This chapter summarizes and updates information from four WHO HIV technical briefs for young key population groups published in 2015[26] *(261–264)*. WHO did not publish a technical brief on HIV and young people in juvenile detention and prison, but many considerations for young people who sell sex, young men who have sex with men, young trans and gender diverse people, and young people who inject drugs will also apply to this population. This chapter aims to catalyse and inform discussions about how best to provide health services, programmes and support for young key populations. While the focus is on health for young key populations, the considerations will be relevant to other programmes: welfare, justice, protection, education and social protection *(261–264)*.

Background

Attention is growing globally on the importance of addressing the specific health needs of young people (those aged from 10 to 24 years). Adolescence and young adulthood are periods with significant physiological changes, and a time where young people establish identities and sexual preferences and explore new life experiences *(265)*. Structural factors and the vulnerabilities of youth (power imbalances in relationships; evolving identity and capacity; restricted access to sexual and reproductive health; effective prevention interventions; and, sometimes, alienation from the school system, family and friends) reduce young people's access to prevention, harm reduction, and reproductive health services, and put them at higher risk of infection from HIV, STIs and viral hepatitis *(261–264, 266–268)*.

Epidemiological data on the global status of HIV, STIs and viral hepatitis among young people remain limited, with significant gaps for young key populations *(265, 269, 270)*. Available data show that young key populations are disproportionally vulnerable to, and affected by, HIV *(270)* and STIs compared to their peers and older key populations *(183, 271–276)*. For HCV infection, data show that rates are high and rising among young people who inject drugs and young men who have sex with men *(277–280).* Transmission of HBV mainly occurs in early childhood, from mother to child, and many countries have high HBV immunization programme coverage. Despite this, young people born before the initiation of the infant immunization programme, or not vaccinated, will remain susceptible to HBV infection *(19, 281)*. Young people remain at higher risk for STIs, and may be biologically more susceptible to STIs, particular younger women *(183, 282)*.

The global response to HIV, STIs and viral hepatitis has not reached adequate numbers of young key populations *(269)*. Young key populations' lower access to prevention, diagnosis and treatment is due to a range of factors *(282–290)*:

- misconceptions about risks;
- lack of knowledge and accurate age-appropriate information;
- lack of comprehensive sexuality education (CSE);
- low awareness of available, friendly health services; and
- barriers to access and uptake of services (including legal and policy barriers around consent requirements).

In addition, social determinants, such as wealth, race and gender inequality, and access to education greatly impact health behaviour and outcomes for this population *(269, 291)*.

[26] Young trans and gender diverse people, young men who have sex with men, young people who sell sex and young people who inject drugs.

Services and providers are often poorly equipped to provide services for young key populations, and staff frequently lack training, skills and knowledge to deliver acceptable and appropriate services for young key populations *(292–294).* Furthermore, inadequate investments and availability, or use of age- and sex-disaggregated data in primary research, monitoring and evaluation is a barrier to programming for young key populations *(295–298)*.

States have a legal obligation to respect, protect and fulfil children's right to life, health and development. Societies share an ethical duty to ensure this right for all young people. Addressing underlying structural barriers for young key populations is critical.

One of the added structural barriers specifically young key populations face that is distinct from their adult counterparts' barriers is the requirement for parental, caregiver or guardian consent *(261–264)* to access services, including harm reduction services. For young people who do not wish to disclose an issue to their caregivers, this can be directly inhibitive to accessing care, resulting in missed opportunities for prevention and treatment. Countries are encouraged to examine their age of consent policies, and to consider revising them to reduce age-related barriers to access and uptake of services and interventions that are critical to the health and wellbeing of this population.

Changes to the legal and policy environments

The United Nations Convention on the Rights of the Child (CRC) obliges the state to protect the rights of all young people under 18 years of age. The treaty includes protection from sexual exploitation and sexual abuse; it emphasizes four guiding principles: non-discrimination; the best interests of the child; the right to life, survival and development; and respect for the young person's views *(299)*. Commitment to the CRC includes lowering the risk of infectious diseases and strengthening protective systems to reduce vulnerabilities for young people. The rights of children are contravened when those young people under 18 years of age are excluded from effective HIV, STI and viral hepatitis prevention and life-saving prevention, testing, treatment, care and support services *(261–264)*.

Elements of successful programming for young key populations

WHO recommended interventions and service delivery strategies for all key population groups also apply to young key populations (See Chapters 4–7).

Fig. 4. Summary of key characteristics of effective young key population services



Informed by WHO and UN partner publications, the elements of successful programming for young key populations update the 2015 WHO policy briefs *(261–264)*. Services must be designed and delivered to consider the differing needs and rights of young people according to their age, gender identity, sexual orientation, specific behaviours, the complexities of their social and legal environment and the epidemic setting, while simultaneously respecting the CRC.

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Meaningful involvement of young people

The WHO global consensus statement on meaningful adolescent and youth engagement states that meaningful adolescent and youth engagement requires a mutually-respectful partnership between adolescents, youth and adults. Power is thereby shared; respective contributions are valued; and young people's ideas, perspectives, skills and strengths are integrated into the design and delivery of programmes, strategies, policies, funding mechanisms and organizations that affect their lives and their communities, countries and world *(300)*. Meaningfully and ethically involving young key populations in the planning, design, implementation, monitoring and evaluation of services requires acknowledging and building upon the strengths, competencies and evolving capacities of young key populations, especially their ability to express their views and articulate what services they need *(301)*.

- Global consensus statement: meaningful adolescent and youth engagement. Geneva: WHO; 2020.

Work with trusted partners and existing infrastructure to design and deliver services

It is important to partner with community-led youth and key population organizations, build upon their experience and credibility, and use appropriate, effective and efficient approaches to design and provide services for young people.

- UNAIDS. Young people's participation in community-based responses to HIV — from passive beneficiaries to active agents of change. Geneva: WHO; 2019.

Provide quality, comprehensive and adolescent-friendly services

It is crucial to ensure that health (including immunization), welfare, justice, protection, education and social protection services are integrated, linked and multidisciplinary in nature, with a strong system for referral along the continuum of care. Provision of a comprehensive range of services with online delivery options (see the service delivery chapter) can help to address the overlapping vulnerabilities and intersecting behaviours of different young key populations. The WHO adolescent-friendly health services principles guide adolescent-friendly health services *(302)*. WHO and UNAIDS have also published global standards that define the quality in delivering of health services for adolescents *(303)*.

- Adolescent-friendly health services for adolescents living with HIV: from theory to practice. Geneva: World Health Organization; 2019.
- United Nations Children's Fund (UNICEF). Improving HIV service delivery for infants, children and adolescents: a framework for country programming. Geneva: WHO; 2020.
- UNAIDS, WHO. Global standards for quality health-care services for adolescents: a guide to implement a standards-driven approach to improve the quality of health care services for adolescents. Geneva: WHO; 2015.
- Youth-centred digital health interventions: a framework for planning, developing and Implementing solutions with and for young people. Geneva: WHO; 2021.

Improve access to and retention in services

It is essential to ensure that young key populations have access to the necessary health services and information regardless of their marital status and caregiver consent. Medical treatment without caregiver consent is possible and should be considered when in the individual's best interests. Making services accessible includes ensuring that service locations are easy, affordable, confidential and safe for young key populations to access, and are provided at times that are convenient to young people. Providers have discretion to provide services to young people and should not be prosecuted for doing so. Adolescents, irrespective of age, should be permitted access to counselling and advice without the consent of a parent or guardian *(303)*. Young people should be made aware of their rights to confidentiality, and any limits of confidentiality made clear by those with mandatory reporting responsibilities *(304)*.

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Provide developmentally appropriate information and education

Services for young key populations must provide developmentally appropriate, accurate and inclusive information and education. Prevention of HIV, STI and viral hepatitis prevention, in addition to comprehensive sexuality education for young key populations and their partners (including for adolescents and young people out of school) should focus on skills-based risk reduction. Information can be shared using various media platforms, such as online, mobile phone technology and participatory approaches *(261–264, 305–307)*.

Build capacity in the health sector and beyond

Sufficient capacity amongst professionals, particularly in the health, social welfare, justice and education sectors, to work with young key populations and apply rights-based approaches and evidence-informed practice is critical. Capacity-building involves expanding knowledge on the health needs and rights of different young key populations, and relevant overlapping vulnerabilities (namely, injecting drugs, sexual exploitation or selling of sex) *(308, 309)*. Training is needed on providing respectful, non-judgemental services that consider sexual and gender diversity, gender and power relations, gender-affirming care, and further development of communication and negotiation skills – as they relate to key populations *(310)*.

- Assessing and supporting adolescents' capacity for autonomous decision-making in health care settings. Geneva: WHO; 2021.
- Core competencies in adolescent health and development for primary care providers. Geneva: WHO; 2015.
- How to plan and conduct telehealth consultations with children and adolescents and their families. Geneva: WHO; 2021.
- Guidelines to strengthen social service workforce for child protection. UNICEF; 2019.

Implement peer-driven models

Adolescent and youth peer-driven models and support are key implementation strategies towards the global standard of adolescent participation *(311, 312)*. Young people highly value peer support programmes. Peer navigators are crucial in bridging online information and offline action, such as accessing testing and treatment services *(313)*. Appropriate training, support and mentoring are essential to help young key populations advocate within their communities to support them in accessing services *(204, 261, 263, 264)*. The WHO technical brief *Adolescent-friendly health services for adolescents living with HIV (302)* provides implementation considerations for adapting and scaling-up peer-based, adolescent-friendly models.

- Adolescent friendly health services for adolescents living with HIV: from theory to practice. Geneva: WHO; 2019.

Strengthen protection and welfare for families

Helping parents and families to fulfil their responsibilities to protect, care for and support young key populations effectively is critical. For adolescents aged between 10 and 17 years old, it is important to try to reintegrate them with their families when appropriate, if in their individual best interests, or to provide other appropriate living arrangements and care options in line with the 2010 *UN Guidelines for Alternative Care (314)*.

Update national policies

To ensure harmonized implementation across programmes, evidence-informed services for young key populations must be clearly stated in national policies; that is, the National Strategic Plans (NSPs). (See Chapter 9.)

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- WHO, UNAIDS, UN WOMEN, UNFPA, WORLD BANK GROUP, UNICEF. Accelerated Action for the Health of Adolescents (AA-HA!) A manual to facilitate the process of developing national adolescent health strategies and plans. WHO; 2019.
- Online toolkit for adolescents and young key populations. UNICEF; 2021.
- This toolkit is a collection of online resources to help plan and scale-up HIV prevention programmes with adolescents and young key populations (ayKP) – people aged 10–24 years.

Monitoring and evaluation

Programming for young people needs to consider the population size, demographics and epidemiology; data disaggregation should be done by sex or gender and age group *(298)*. Collect and collate baseline measurements, monitoring and evaluation systems into programmes to strengthen quality and effectiveness and develop a culture of learning and evidence-based practice to better inform future policies and programmes. (See Chapter 9.)

- Strengthening the adolescent component of national HIV programmes through country assessments. UNICEF; 2016.
- Collecting and reporting of sex- and age-disaggregated data on adolescents at the sub-national level. UNICEF; 2016.

Addressing the additional needs and rights of young key populations

Ensuring that the needs of young key populations are met will improve health outcomes and overall wellness for these populations. The following particular needs should be considered when designing and implementing programmes and services *(261–264)*.

- Protection is needed from all forms of physical, emotional and sexual violence and exploitation, whether by law enforcement officials or other perpetrators *(315–320)*.
- Access to information on the harm that early marriage and early pregnancy can cause is needed.
- Young people who become pregnant need access to health services sensitive to their rights and needs. This includes providing access to sexual and reproductive health services, including family planning, contraception and information and access to youth friendly safe abortion services, adequate and comprehensive obstetric care, and counselling *(321–323)*.
- Psychosocial support services are called for; namely, therapy, counselling, peer support groups and networks to address the impact of self-stigma, discrimination, social exclusion, coming out, gender-affirming care, and to address mental health issues *(312, 324)*.
- Support is critical to remain in or to access education or vocational training, and opportunities to return to school need to be offered, and access to preventative strategies for bullying, stigma and discrimination *(307, 315, 317, 325, 326)*.
- Independent living and group housing shelter are necessities as immediate or long-term accommodation arrangements *(327, 328)*.
- Food security, including nutritional assessments, is all-important *(329, 330)*.
- Livelihood development, economic strengthening, and support to access social services and state benefits are needed *(331)*.
- Access to free or affordable legal information and services is critical, including information about their rights, reporting mechanisms and access to legal redress.
- Counselling for families when requested to facilitate access to services is essential, especially where parental/guardian consent is required.

CHAPTER 8

Developing the response: the decision-making, planning and monitoring process



Introduction

Action on the guidance in these guidelines requires a strategy appropriate to the local context. Planning, decision-making and monitoring are parts of an ongoing process. Once a plan is developed and implemented, it must be monitored and evaluated. The resulting findings then inform revision of the strategy and its implementation.

Situational analysis

> Data and a strong evidence base should guide the response, but lack of this information is not a reason to stop or not initiate a response to improve the health of key populations and work towards the elimination of HIV, viral hepatitis and STIs as public health threats.

Particularly when programmes and services are first being developed, it is important to undertake a situational analysis. For a local response to be appropriate, acceptable and most effective, risks and needs must be examined locally, and local key population members must be consulted and actively involved in this situational analysis. Local people from key populations should ideally be drawn from networks, where they exist, or people acknowledged as community leaders who can represent community opinions.

It is critical to understand the dynamics of local epidemics; the characteristics of the populations affected; the physical, social and political environments that influence risk and vulnerability; the specific needs of people from key populations, and any factors that might enable or hinder efforts to address these needs; and the health systems and community infrastructure. With this information in hand, an evidence-informed plan can be developed and implemented.

As already described, people from key populations face elevated HIV, viral hepatitis and STI risk and burden, and have specific and sometimes complex health-related needs. While many of these risks and needs may be common across key populations in different settings, some factors will differ among key populations, and some will be specific to a particular context.

It is also important to recognize the diversity and varying levels of risk within each key population. In many settings, those most at risk are likely to be people who could be considered members of more than one key population; for example, some men who have sex with men may also inject drugs or engage in sex work. People from key populations may also have other characteristics that could increase their risk or vulnerability, or create additional health or welfare needs. For example, people from key populations may be homeless, impoverished, educationally disadvantaged, disabled, experience mental health conditions, or have other acute or chronic health concerns.

Key population size and location (that is, where people live or congregate) can vary from place to place, with some constants, such as the overall proportion of adult men who have sex with other men *(332)*. To determine the required scale of the response, the appropriate balance and cost effectiveness among different interventions and where interventions should be targeted, it is important to appreciate the size and concentration of key populations, among other factors. (See Box 2 and Section 3.) It is important to note the difficulty in conducting key population size estimates and the lack of reliable data about key population size *(333)*. Efforts should be made to validate key population size estimates and limitations recognized.

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Box 1. Stakeholders to include in the planning process

- Key population-led community organizations and key population community representatives, including young key population members;
- Managers and health care workers from the following fields in both the public and private sectors: HIV programmes and clinics, hepatology service providers, sexual and reproductive health programmes and clinics, including family planning and STIs, maternal and child health, mental health, TB services, drug dependence, NSPs, OAMT services and prison health programmes;
- Civil society, including people living with HIV and viral hepatitis, women's and youth groups, religious leaders and people with disabilities;
- Technical specialists in specific areas, such as laboratory services, pharmacology, drug resistance, toxicity management, supply chains and community health;
- Government partners, including representatives of relevant ministries, such as health, justice and law enforcement, internal affairs, finance, planning and regional (such as provincial) authorities;
- Non-governmental organizations, including international agencies, faith-based organizations, other local nongovernmental and community-based organizations, and private-sector service organizations;
- Finance and budget experts, such as programme budget officers and health economists;
- Academic institutions, including experts in operational research, implementation science, ethics, training and supervision;
- International donors and implementers;
- Human rights institutions; and
- Professional associations of various cadres of health workers (such as physicians, nurses and community health workers).

The makeup, characteristics and needs of key populations change over time, as do various contextual and environmental factors. Updating a situational analysis through ongoing monitoring and evaluation will identify changing parameters, and make it possible to refine or refocus the response.

A situational analysis will almost certainly identify gaps in knowledge. An agenda for further research can address these gaps.

It is also important, whenever analysing and interpreting data, to evaluate the quality of the data and the presence of any sources of bias.

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Box 2. Key information required for decision-making and planning

Information required	Source of information
Key population size	Population size estimation
Prevalence of HIV, viral hepatitis B and C and priority STIs among key populations	Sero-surveillance
Key population location/geographic distribution; identification and mapping of key populations accessible online	Mapping exercises (including online mapping)
Key population characteristics, risk behaviours and health concerns	• Demographic surveys • Behavioural surveys • General health surveys
Important structural factors, barriers to implementing a response to HIV, viral hepatitis and STIs, and the needs of key populations	• Audit of current legislation, policy and practice • Consultation with community members, community-led organizations and other stakeholders • Behavioural surveys
Accessibility, coverage, quality, outcome and impact of interventions	• Programmatic data • Disease notification registries • Integrated bio-behavioural surveys (See Box 3 for further description of national programme monitoring and evaluation framework)

In settings where services for key populations are not well established, and where much of the information listed above has not been previously compiled, undertaking a rapid assessment may be appropriate. Rapid assessment and response guides are available to help guide initial and ongoing assessments, using multiple methods to gather data and to conduct analyses at multiple levels. These guides focus largely on HIV, and were developed earlier in the HIV epidemic, but the principles and methods described remain relevant to gathering information on HIV, as well as viral hepatitis and STIs:

- Rapid assessment and response adaptation guide on HIV and men who have sex with men. Geneva: WHO; 2002
- The rapid assessment and response guide on injecting drug use (IDU-RAR). Geneva: WHO; 1998
- The rapid assessment and response guide on psychoactive substance use and sexual risk behaviour (SEX-RAR). Geneva: WHO; 2002
- Rapid assessment and response adaptation guide for work with especially vulnerable young people. Geneva: WHO; 2004
- HIV in prisons: Situation and needs assessment toolkit. Vienna: UNODC; 2010

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Planning and implementing the response

The effectiveness of the interventions included in the essential health interventions package is well established. Experience in multiple countries has demonstrated the generalizability of these interventions in diverse settings. While national strategies should be guided by the health intervention packages recommended in these guidelines, local factors do have a bearing on intervention effectiveness and impact, and have a bearing on how an intervention is implemented to optimize access and effectiveness. With the information gathered on the local setting, as described above, planning processes should be taken forward with participation of stakeholders, particularly key populations, and decisions can be made on how interventions should be implemented.

The following are some of the decisions that need to be taken while developing and implementing a national response to HIV, viral hepatitis and STIs among key populations. Guidance on planning and implementing the response is listed in Box 3.

Targeting the response

- Which key populations and which subgroups within key populations are most at risk?
- Which strategies, legislation, policies and guidelines need to be developed or revised?

Implementation

- Are key populations' members effectively leading the response?
- Which interventions need to be implemented and where, and how should implementation be prioritized?
- How can services addressing HIV, viral hepatitis, STIs and broader health be integrated at the organizational, service and site levels (see the service delivery chapter) to optimize accessibility and impact for key populations?
- Where and at what scale do interventions need to be provided?
- What targets and timelines should be set for the implementation and scale-up of interventions?
- How and to what extent should services be decentralized and integrated to provide the best service coverage for key populations?
- Which modes of service delivery are most appropriate?
- What are the roles and responsibilities of the various stakeholders in implementing the response and achieving the agreed targets?

Resources required

- What financial, human and other resources and infrastructure are required to implement the response? What resources are currently available, what additional inputs will be required and how might these be obtained? What types of health care and other workers (including key population peers) are required, and how will they be recruited and trained? How can task shifting and sharing optimize the use of available human resources and expand service delivery?
- How will economies of scale and synergies among interventions save on costs and improve service provision?
- What resources are available from donor organizations and what resources will need to be mobilized from national sources? Greater funding for HIV may be available through The Global Fund and PEPFAR, but funds for STIs and viral hepatitis may need to be integrated in national plans.

Monitoring and evaluation

- How will implementation of the response be monitored and evaluated?
- How do strategic information systems for M&E need to be strengthened?

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Risks, outcomes and impacts

- What are potential risks and vulnerabilities of the planned response, and what strategies would mitigate their impact? Risks might include domestic factors such as budget cuts, theft of consumables, attrition of health care workers, and emergence of drug resistance. External factors could include loss of external financial support, political instability and natural disasters.

Box 3. Guidance on planning and implementing the response to HIV, viral hepatitis and STIs for key populations

- Considerations in planning and budgeting for a key population trusted access platform. Global HIV Prevention Coalition; 2020
- Establishing community-led monitoring of HIV services — Principles and process. UNAIDS; 2021

Monitoring and evaluating the responses

Monitoring and evaluation is an essential part of the HIV, viral hepatitis and STI response for key populations

A monitoring and evaluation system is needed to assess both structural and health sector components of the response to HIV, viral hepatitis and STIs in key populations. It is critical that these systems are practical, not overly complicated, and that they collect information that is current, useful and readily used while adhering to human rights principals as described previously.

WHO and UN partner agencies have developed frameworks for monitoring the response to HIV in the general population and key populations. The following documents described these frameworks:

- Tool to set and monitor targets for HIV prevention, diagnosis, treatment and care for key populations. Geneva: WHO; 2015;
- Consolidated strategic information guidelines for viral hepatitis: planning and tracking progress towards elimination. Geneva: WHO; 2019;
- Consolidated guidelines on person-centred HIV patient monitoring and case surveillance. Geneva: WHO; 2017;
- Consolidated HIV strategic information guidelines: driving impact through programme monitoring and management. Geneva: WHO; 2020;
- Strategies and laboratory methods for strengthening surveillance of sexually transmitted infection. Geneva: WHO; 2012.

These frameworks recommend sets of national-level indicators. These indicators assess key factors related to the enabling environment; measure the availability, coverage and quality of specific interventions; and examine their outcome and impact (Box 4). The indicators can also be used when preparing proposals or reporting progress to donor organizations.

The M&E process requires data from a variety of sources, including behavioural and sero-surveillance surveys, programmatic and administrative data, community-led monitoring as well as information gathered through reviewing policy documents and legislation, and consultation with experts and stakeholders (Box 5). The quality and limitations of these data should be assessed and considered when undertaking analysis and interpretation.

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Ongoing planning and development of the response

Setting clear, achievable but ambitious targets is crucial when planning to scale-up interventions to have an impact on HIV, viral hepatitis and STIs. Targets concretely define what a successful national programme or project should achieve within a specified timeframe. Targets can be set for both intervention-specific indicators and cross-cutting outcome and impact indicators (Box 4).

Intervention and enabling environment indicators reflect the availability, coverage and quality of an intervention or service, or assess changes in environmental factors, such as revision of legislation, within a specified timeframe. Targets are set with the aims of achieving reductions in HIV, viral hepatitis and STI risk, sufficiently to reduce transmission and ensure the adequate provision of appropriate treatment and care for those living with HIV, viral hepatitis or with an STI.

Outcome and impact indicators seek to gauge the impact that interventions have had on outcomes that affect exposure to risk, such as changes in risk behaviours (for example, the percentage of people who use condoms consistently) or on impacts on the course of HIV, viral hepatitis or STI epidemics; for example, reductions in incidence of HIV, viral hepatitis or STIs (Box 4).

Like planning overall, the target-setting process should be collaborative, involving a range of stakeholders. Those setting the targets should consider whether they are realistic and whether data can be practically collected. Targets, in keeping with programme strategies, should be tailored to the local epidemic and what the strategy can realistically achieve with obtainable funding and resources. Modelling can help to identify how different target levels would affect epidemics.

Baseline assessment – initial assessment should measure the scale of the current response, assessing the availability, coverage and quality of current interventions, and appraise current environmental enablers and barriers using agreed indicators. This information serves as a baseline for tracking progress. Also, currently available resources and technical capacity must be determined to estimate what more is needed, and how to scale the intervention appropriately. From this information, realistic, achievable targets can be set and the timeframe specified.

Estimating cost associated with implementation is a key step in planning the roll-out. Several costing tools and resources are available.

Spectrum, for example, is a suite of models and analytical tools to support decision-making for HIV and STI programming. It comprises several software apps, including AIM (AIDS Impact Model) and Goals (Cost and Impact of HIV Interventions). Most countries already have AIM files prepared as part of their national epidemiological estimates, and so both modules can be rapidly applied. Spectrum can be accessed online at: https://www.unaids.org/sites/default/files/media_asset/QuickStartGuide_Spectrum_en.pdf.

OneHealth is a software tool designed to strengthen health system analysis and costing, and to develop financing scenarios at the country level. It is specifically designed for LMICs. It provides planners with a single framework for planning, costing, impact analysis, budgeting and financing of strategies for all major diseases and health system components. OneHealth can be downloaded free of charge (Avenir Health, 2021) at: https://www.avenirhealth.org/software-onehealth.php.

UNAIDS has developed The Human Rights Costing Tool (HRCT), a flexible tool for costing investments in critical enablers (such as integrated treatment and rights literacy programmes, legal services, stigma and discrimination reduction programmes, and training for health care workers and law enforcement). This, too, can be downloaded free of charge along with a user guide at: http://www.unaids.org/en/media/unaids/contentassets/documents/data-and-analysis/tools/The_Human_Rights_Costing_Tool_v_1_5_May- 2012.xlsm and http://www.unaids.org/en/media/unaids/contentassets/documents/document/2012/The_HRCT_User_Guide_FINAL_2012-07-09.pdf.

WHO commissioned Avenir Health to develop the Syphilis Interventions Towards Elimination (SITE) tool which is a dynamic transmission model to evaluate and project the impact, cost and cost-effectiveness of syphilis interventions (screening, treatment and prevention) to support national control programmes: https://avenirhealth.org/software-site.php.

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Box 4. Indicators for monitoring and evaluating the response

To understand how well the response is functioning and its effects, its various key requirements need to be monitored for each key population. For each of these requirements there are a number of useful indicators.

These indicators are described in detail in WHO key population guidance:

- Tool to set and monitor targets for HIV prevention, diagnosis, treatment and care for key populations. Geneva: WHO; 2015
- Consolidated strategic information guidelines for viral hepatitis: planning and tracking progress towards elimination. Geneva: WHO; 2019

Specific impact indicators related to validating elimination of viral hepatitis in people who inject drugs can be found in:

- Interim guidance for country validation of viral hepatitis elimination. Geneva: WHO; 2021

Successful implementation and impact requires supportive policy, legislation and other structural factors.

Measured by ***structural*** (or enabling environment) indicators:

- audit of current legislation and policy;
- number of key population-led organizations;
- achievement of meaningful involvement of people from key populations in policy and strategy formulation;
- legal support services for key populations have been established;
- support services for people from key populations who experience violence are functioning;
- sensitization training on key populations is regularly conducted for law enforcement officers; and
- sensitization training on key populations is regularly conducted for health care and social services providers.

Interventions need to be accessible to people from key populations.

Measured by ***availability*** indicators:

- the number of sites where each intervention is available, including availability of online interventions;
- the number and percentage of key population-focused programme sites where the intervention is provided;
- the number and percentage of mainstream programme sites where the intervention is provided and that meet key population sensitization standards;
- the percentage of all sites where the intervention is currently provided that are either mainstream programmes meeting key population sensitization standards, or are key population-focused programmes;
- the percentage of the key population sample reporting that the intervention is readily accessible; and
- geographic mapping of key populations in relation to where interventions are provided.

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Box 4. Indicators for monitoring and evaluating the response (cont.)

Interventions must reach those who need them.

Measured by ***coverage*** indicators:

- number and percentage of key population provided with the intervention during a specified reporting period;
- number of consumable items (such as needles and syringes or condoms) distributed per member of key population during a specified reporting period; and
- percentage of the key population sample reporting that they received the intervention during a specified reporting period.

Interventions need to be properly implemented to be effective.

Measured by ***quality*** indicators:

- review of programme policy and practice using programme quality assessment checklist;
- percentage of staff that has received key population sensitization training;
- percentage of key population reporting intervention was received, and also a specific important activity or service was delivered (such as the provision of compatible lubricant with condoms); and
- percentage of occasions when intervention was provided, along with specific important activity of service (see previous).

Intended aims should be achieved.

Measured by ***outcome*** and ***impact*** indicators:

- prevalence of risk behaviour in key population;
- incidence of HIV, viral hepatitis and STI infections in key populations;
- prevalence of infection in key population;
- incidence of HIV-related mortality in key population;
- prevalence in key population of experiencing stigma or discrimination; and
- incidence of violence against people from key population.

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Box 5. Data sources

Behavioural and sero-surveillance surveys. These surveys of key populations can provide prevalence data and information on the experiences, risks and service utilization of people from these groups. Many countries already undertake bio-behavioural surveys of key populations periodically as part of the ongoing monitoring of the HIV and viral hepatitis epidemics. The generalizability of survey findings depends on how representative the sample is of the entire key population; it is important to consider selection bias in how participants were recruited. Behavioural surveys are susceptible to bias toward socially desirable responses and to recall bias.

Programmatic or administrative data. Most programmes routinely record at least some basic information when providing a service. This might include the number of people who received a service, basic information about the client, and numbers of supplies used or distributed. To assess services provided to people from key populations requires programme data to be disaggregated by key population, where information on key population status and behaviours can be collected safely and securely and where feasible. Key population-focused programmes may be able to provide data specific to the populations they serve, but this information is not commonly available from programmes that provide services to many different groups or to the general population.

Desk review and expert consultation. Reviewing various policy documents and legislation can identify the presence or absence of various laws or policies that may affect people from key populations.

Population size estimation. Deriving reliable population size estimates for key populations can be challenging. Various methods can be employed; each has its own advantages and limitations. Common methods include census and enumeration, general population surveys, and capture-recapture, multiplier and network scale-up methods. Deriving multiple estimates through different methodologies and triangulating the results is helpful. Definitions of key populations should be clear.

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CHAPTER 9

Additional information on the development of new recommendations

Introduction

As highlighted in previous chapters, this updated guidelines contains seven new recommendations or new practice statements that are included in the overall framework of health interventions and service delivery.

Methodology

WHO developed seven PICO questions. In an online survey, the Guideline Development Group members ranked the importance of each outcome to those affected by the intervention using the GRADE rating scale of 1–9 (0–3: not important; 4–6: important; 7–9: critical). Once the PICO question and priority outcomes were agreed, external researchers, supported by the WHO team, conducted a systematic review of the evidence.

The systematic review teams developed protocols and conducted a systematic review of the relevant scientific evidence. The appointed independent methodologist assessed and reviewed the protocols, as did the Steering Group, key population networks and WHO technical officers. The methodologist advised the review team on analytical decisions and synthesis and the grading of evidence . Studies providing information on feasibility, values and preferences, and cost-effectiveness were also included and summarized. The scientific evidence supporting the recommendations was evaluated using the GRADE approach, and the effectiveness and overall certainty of evidence for each intervention was determined.

The risk of bias for studies included in systematic reviews were assessed using the Cochrane Collaboration's risk of bias tool for randomized controlled trials (RCTs) *(334)* and the ROBINS-I tool for non-randomized studies *(335)*.

WHO also commissioned four global networks of key populations (men who have sex with men, sex workers, trans and gender diverse people, and people who inject drugs) to undertake new qualitative research on values and preferences among their networks. The results formed part of the evidence synthesis. Further details are provided in the next section.

Table 2. Domains considered when assessing the strength of recommendations

Domain	Rationale
Benefits and harm	When a new recommendation is developed, desirable effects (benefits) need to be weighed against undesirable effects (risks or harm), considering any previous recommendation or an alternative. The larger the gap or gradient in favour of the benefits over the risks, the more likely that a strong recommendation will be made.
Certainty of evidence	High certainty of evidence is likely to lead to a strong recommendation.
Values and preferences	If the recommendation is likely to be widely accepted or highly valued, it is likely that a strong recommendation will be made. If there is a great deal of variability or strong reasons why the recommended course of action is unlikely to be accepted, it is more likely that a conditional recommendation will be made.
Cost and financial implications	Lower costs (monetary, infrastructure, equipment or human resources) or greater cost-effectiveness contribute to a strong recommendation.
Feasibility	If an intervention is achievable in a setting where the greatest impact is expected, a strong recommendation is appropriate.
Equity and human rights	If the recommendation is likely to increase access to an intervention for those most in need, a strong recommendation is likely.
Acceptability	The greater the acceptability to all or most stakeholders, the greater the likelihood of a strong recommendation.

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The GRADE approach specifies four levels of certainty of evidence (Table 3.) The certainty of evidence is a key determinant of the strength of a recommendation, which can be either strong or conditional.

Table 3. Interpretation of the four GRADE levels of evidence

Certainty of evidence	Rationale
High	We are very confident that the true effect lies close to the estimate of effect.
Moderate	We are moderately confident in the estimate of effect. The true effect is likely to be close to the estimate of effect, but it could be substantially different.
Low	Our confidence in the estimate of effect is limited. The true effect may be substantially different from the estimate of effect.
Very low	We have very little confidence in the estimate of effect. Any estimate of effect is very uncertain.

Good practice statements are sometimes appropriate for use when the supporting evidence is indirect and therefore difficult to collect and summarize, but the certainty or confidence surrounding an intervention's impact is high, and when the desirable consequences of an intervention clearly outweigh the undesirable ones. Often data is not disaggregated by key population group and there is a lack of supporting evidence related to key populations, meaning that good practice statements were appropriate in the development of these guidelines. Good practice statements are, by nature, strong recommendations *(56)*.

Following the WHO guideline development process *(56)*, the Guideline Development Group formulated recommendations according to the GRADE approach to appraise evidence. The Guideline Development Group also made good practice statements. The evidence was synthesized and incorporated into an evidence-to-decision framework to help inform the discussions at the Guideline Development Group meeting. WHO convened a virtual Guideline Development Group meeting that occurred over six days between 30 August and 8 September 2021, chaired by two members of the Guideline Development Group. All conflicts of interest were managed. The methodologist assisted by the chairs facilitated the Guideline Development Group's judgements on the potential benefits and harms of the intervention, stakeholder values and preferences, acceptability, feasibility, resource use and considerations of human rights and equity. Taken together, these judgements contributed to determining the strength and direction of the recommendation *(334)*. All the recommendations were arrived at through consensus. Voting was not required, but the group agreed a priori that two thirds of the votes would be required for a decision. The draft guidelines were circulated for review to members of the Guideline Development Group and the External Review Group in November 2021.

Evidence and decision-making for new recommendations

Behavioural interventions

Background and rationale

Behavioural interventions are widely used in programmes which aim to reduce transmission of HIV, STI and viral hepatitis. There are a range of different behavioural interventions, including those that focus on providing information and education and those that take a counselling approach, but all aim to increase health-seeking behaviours and/or reduce behaviours that increase risk of HIV, STIs and viral hepatitis, including needle and syringe sharing and unprotected sex. Counselling behavioural interventions can be provided by health care workers or by peers, can be a single session or multiple sessions, can be brief or long, can be provided in groups or individually, and can be online or face-to-face.

The 2014 and 2016 WHO *Consolidated key population guidelines (3)* included recommendations related to behavioural interventions that were based on low certainty of evidence and lack of standard comparators. During the scoping exercise to review which recommendations required updating and the community and expert consultation in 2019–2020 (see methods), these recommendations were identified as in need of an update. To inform the decision-making process, the evidence review focused on behavioural interventions with a counselling component, in particular whether provision of counselling behavioural interventions impacts HIV, STIs and viral hepatitis acquisition and transmission for key populations.

Evidence review

A systematic review was commissioned by WHO to update existing recommendations, to answer the PICO question of whether counselling behavioural interventions reduces risk behaviours associated with transmission or acquisition of HIV, STIs and viral hepatitis. The primary outcomes were HBV, HCV, HIV or STI incidence and the secondary outcomes were unprotected sex (for example, condomless sex, sex without lubricant, sex without PrEP), needle and syringe sharing and mortality.

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A systematic review of published articles from 1 January 2010 to 1 March 2021 identified nine eligible randomized control trials (see Web Annex C). Five studies were among adult key populations and two studies were among young men who have sex with men (16–25 years old) *(336)* and young females (13–17 years old) released from juvenile detention *(337)*. Together these indicated that counselling behavioural interventions probably make little to no difference on HIV *(336, 338–343)*, viral hepatitis *(341)* or STI *(337–340, 342–344)* incidence in key populations. This was also true for unprotected sex *(336–342)* and needle and syringe sharing *(340, 341)*. There was moderate certainty in the lack of effect across outcomes.

Moderate certainty evidence from six randomized controlled trials (RCTs) among men who have sex with men, transgender women, people who inject drugs and sex workers in China, Kazakhstan, Kenya and the USA showed counselling behavioural interventions had probably no effect on *HIV incidence* in meta-analysis (combined risk ratio (RR): 0.700, 95% CI: 0.409–1.197), with no important benefit or harm *(336, 338–342)*. Low certainty evidence from one RCT among sex workers who inject drugs in Mexico showed no impact on HIV/STI incidence when findings were meta-analysed across study sites (RR: 0.663; 95% CI: 0.224 to 1.960) *(343)*.

Moderate evidence from six RCTs among people in prisons, men who have sex with men, transgender women, people who inject drugs and sex workers in China, Kazakhstan, Kenya and the USA showed probably little to no difference in *STI incidence* in meta-analysis (RR: 0.985; 95% CI: 0.741–1.308), with no statistically significant heterogeneity (Q=2.120, p=0.832, I-squared=0.000).

Moderate certainty evidence from one RCT among people who inject drugs in Kazakhstan showed probably little to no difference in *HCV incidence* when calculated as an unadjusted RR directly (RR: 0.447; 95% CI: 0.158–1.267), but there was a reduction in HCV incidence when calculated by the study authors as a rate ratio adjusting for a baseline measure of unsafe injection in the past 90 days (rate ratio: 0.31, 95% CI: 0.10–0.90).

There was very low certainty evidence from seven RCTs among people in prisons, men who have sex with men, people who inject drugs and sex workers in China, Kazakhstan, Kenya and the USA on the impact of counselling behavioural interventions on *unprotected sex* (using various measures of condomless sex; RR: 0.821, 95% CI: 0.663–1.018). This meta-analysis showed statistically significant heterogeneity (Q=22.015, p=0.001, I-squared=72.746), which was not clearly explainable by subgroup analyses or other reasons, and it is uncertain whether counselling behavioural interventions reduce unprotected sex.

Low certainty evidence from two RCTs among people who inject drugs in the USA and Kazakhstan showed that there may be no impact on *needle and syringe sharing* in meta-analysis (RR: 0.719; 95% CI: 0.317–1.628), with no statistically significant heterogeneity (Q=1.135, p=0.287, I-squared=11.909).

Feasibility, cost and cost effectiveness

A systematic review identified two studies with cost data on counselling behavioural interventions for key populations, both from the USA. Costs ranged from US$ 682 to US$ 782 for a single session and from US$ 1823 to US$ 3890 annually *(345, 346)*.

One cost-effectiveness analysis of an intervention among sex workers along the Mexican and USA border that included multiple components was identified *(346)*. For a hypothetical 1000 sex workers, receiving a once-only intervention, they calculated an incremental cost of US$ 78 200, 33 HIV cases prevented and 5.7 months of quality-adjusted life-years (QALYs) gained, compared to no intervention. Additional cost per QALY gained was US$ 183. For sex workers receiving the intervention annually, they calculated an incremental cost of US$ 389 000, 29 additional HIV cases prevented and 4.5 additional months of QALY compared to the once-only intervention. The additional cost per QALY was US$ 1075.

There is little evidence of cost or cost effectiveness of counselling behavioural interventions in different settings or for different modalities.

Values and preferences

Two studies from the USA, one with men who have sex with men and one with transgender women, both focused on HIV, found that participants generally viewed specific counselling behavioural interventions favourably *(347, 348)*.

Qualitative research conducted by four global networks of key populations found that key population members (see Web Annex B for full report) value peer-led education information, counselling and outreach as it is more likely to be non-judgemental and is provided by people who understand key populations' needs. They indicated a preference for multiple, consistent interventions, rather than one-off interventions and interventions delivered through a variety of mechanisms.

People who inject drugs appreciate access to information and education, but adequate access to evidence-based harm reduction approaches, such as NSPs, OAMT, and overdose management, remains a priority, in order to put health education into practice.

The focus of comments from all four key population networks in relation to other factors impacting access to behavioural interventions (including education and counselling) overwhelmingly related to structural issues, including: negative community and service-provider attitudes; problematic approaches and messaging; stigma and discrimination; and the need for law reform and education to change the way that key populations are perceived and treated.

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Equity and acceptability

Provision of counselling behavioural interventions may increase access if a wide range of different interventions are available with tailored content that focuses on increasing access to health services and empowering key populations. However, the key population networks research identified a lack of formal education and literacy as barriers to HIV, STI and HCV prevention education. It noted the need for more specific, ongoing, peer-based and community-led HIV, STI and HCV education. When delivered through a variety of mechanisms and formats to account for different levels of access, knowledge and literacy, and when combined with counselling and other psychosocial supports, it leads to maximum effectiveness.

Key populations reported that behavioural interventions that promoted abstinence from drug use, or rehabilitation or cessation of sex work would reduce equity by creating barriers to service usage and should be avoided. Methods claiming to so-called cure homosexuality, such as conversion therapy, or other alleged methods to change gender identity or sexual orientation are harmful, are human rights violations and should never be conducted *(349)*. Potential individual harm may occur when counsellors or counselling behavioural interventions promote abstinence from drug use, rehabilitation, cessation of sex work or advocate so-called cures for homosexuality, which can discourage key population members from accessing services. Moreover, diversion of funds to these forms of interventions can limit the availability of evidence-based interventions.

Evidence assessment and decision-making

Following the WHO guideline development process, the Guideline Development Group considered the evidence and concluded that it was not possible to recommend counselling behavioural interventions to reduce HIV, viral hepatitis and STI incidence, given that there was no evidence of impact of the intervention on the outcome. However, the Guideline Development Group felt strongly that counselling and information sharing can enable informed consent and decision-making to initiate and continue certain interventions such as PrEP, ART, OAMT and NSPs. Counselling can enhance relationships between providers and clients and may encourage service access. The group determined to develop a good practice statement to make policy-makers and providers aware that while counselling interventions have other potential positive effects, there is moderate certainty of evidence that they probably do not reduce HIV, viral hepatitis or STI incidence.

Implementation considerations

Given that a systematic review did not find any effect of counselling behavioural interventions on the incidence of HIV, viral hepatitis or STI, the choice to include counselling behavioural interventions in standard and minimum packages of interventions for key populations should be made with an understanding of the potential limitations on incidence outcomes.

If behavioural interventions are implemented, ongoing training for peers and health care workers is needed, and stigmatizing attitudes within the health system and structural barriers to care should be addressed urgently.

If implemented, behavioural interventions should be developed and implemented in collaboration with key population groups. These interventions should be tailored to specific key population groups and individuals, recognizing that people are in different stages of life and have different priorities and needs. Some people may be currently unable to change their risk behaviours, or may not want to make changes, and this should be accepted without judgement. Interventions which focus on cessation of drug use, rehabilitation, ending employment as a sex worker and purported cures for homosexuality create barriers to service usage, are not recommended and should be avoided.

Research gaps

While further research to measure the impact of counselling behavioural interventions on HIV, STIs and viral hepatitis is not required, future research may allow us to better understand the effect of different aspects of counselling interventions on building client and provider relationships, psychosocial improvements and mental health. Research is required across a range of settings and for each of the key population groups. For young people, peer-based counselling has been shown to be a strategy that improves ART adherence, but more research is required on its impact on PrEP adherence for HIV prevention *(350)*.

For the detailed evidence profile, please see Web Annex C.

Chemsex

Background and rationale

Chemsex is a growing phenomenon where individuals engage in sexual activity while taking stimulant drugs such as methamphetamine, mephedrone or gamma-hydroxybutyrate (GHB). Chemsex typically involves multiple participants, the use of multiple drugs (including injecting drug use), and occurs over a prolonged time, for example, in group sex or orgy parties *(351–353)*. Chemsex is also known by other names, such as slam sex (associated with injecting drug use), party and play, or sexualized drug use. There have been increasing reports of chemsex in some communities of men who have sex with men *(352)*, most often in high income settings in Europe and North America, though a recent qualitative scoping review of sexualized drug use and chemsex among men who have sex with men and transgender women found it to be increasingly common in Asia *(354, 355)*. The associate editor of The New England Journal of Medicine *Journal Watch Infectious Diseases* commented in 2018 that the "markedly high rate" of HIV infections among men who have sex with men participating in chemsex in a London study *(356)* "identifies a high-priority (but often challenging) population for

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prevention efforts (including pre- and postexposure prophylaxis, mental health, chemical health, health promotion, and harm minimalization interventions)" *(357)*.

Chemsex may be associated with unprotected sex and unsafe injecting, as well as hazardous drug use, overdose, drug dependence and adverse mental health outcomes *(358)*, with one systematic review finding inconsistent evidence of increased HIV and HCV prevalence in those engaging in slam sex (injecting drugs before or during planned sexual activity) *(351)*.

During the scoping exercise for the development of these guidelines, there was a request from key stakeholders for WHO to investigate further whether behavioural interventions can help increase uptake of services among people engaging in chemsex, reduce harms, and have an impact on HIV, viral hepatitis and STIs.

A systematic review did not identify any articles meeting the inclusion criteria for effectiveness or cost-effectiveness. Five articles assessing values and preferences were identified in the review *(359–363)* and qualitative values and preferences research on the topic (see Web Annex C) was undertaken by four key population networks. Overall, the values and preferences research revealed a preference for:

- specialist chemsex services (for example, specialized counselling with a single professional about both drug and sex-related issues);
- tailored, non-judgemental, peer-led services focusing on the principles of harm reduction rather than cessation of drug use;
- integrated sexual health and HIV, STI and viral hepatitis services; and
- more chemsex specific information and education to be available through various modalities that include explanations of potential risks.

Qualitative values and preferences research (see Web Annex B) showed that perceptions surrounding chemsex and its relevance varied both across and within the four key population networks. Although chemsex is most widely recognized and practiced among gay, bisexual and other cis men who have sex with men, participants beyond these communities also noted that they engage in drug use to enhance or prolong sexual experiences or both. Some participants described this activity without using the term chemsex. Some sex workers reported engaging in chemsex due to pressure from clients and from financial necessity.

The key population groups highlighted the need to promote awareness and education surrounding chemsex, as well as to address stigma and discrimination towards those who engage in chemsex. People who inject drugs stressed the importance of expanding the understanding and changing the framing of chemsex to the concept of "sexualized drug use" to help reduce judgement and rather encourage and support people to engage in "cultures of care", including ideas such as "hosting packs" or "safety kits" that are harm-reduction focused and encourage people to "plan to be safe".

WHO recommends various HIV, STI and viral hepatitis prevention options, which are relevant for those engaging in chemsex, including recommendations for condoms and lubricant for the prevention of sexual transmission of HIV and STIs, pre-exposure prophylaxis and post-exposure prophylaxis for HIV prevention, and provision of sterile needles and syringes for the prevention of HIV and viral hepatitis *(3)*. Despite this guidance, communities and clinicians are increasingly concerned about the low uptake of these prevention interventions before, during and after engaging in chemsex, and about the ongoing risk. Interventions which aim to increase the uptake of these evidence-based prevention interventions, as well as the linkage to testing and treatment services and the integration of services, could have an impact on transmission among people engaging in chemsex. Referral to other relevant services for those reporting instances of non-consensual sex or drug use is essential.

Based on the available preferences of the key population community, the experience gained from implementation and from the evidence-based interventions already recommended by WHO, the Guideline Development Group made a good practice statement. The group recognized the importance of highlighting this phenomenon to HIV, STI and hepatitis programmes to ensure people engaging in chemsex are linked to the appropriate services in a non-judgemental manner.

Online interventions

Background and rationale

Increasingly, services designed for key populations are going online, conducting outreach to identify people at risk, providing information about available services, providing self-test information and tests, booking appointments for testing, and linking people diagnosed with HIV, viral hepatitis or STIs with service providers. The potential advantages of online services include: reaching a broader audience, reaching people who are geographically isolated, targeting information to specific people, improved efficiencies and convenience for clients.

Different forms of interventions are implemented online, the most common of which are:

1) **Online outreach** to potential key populations service users through online platforms involves reaching out to those who previously hadn't been engaged, by using systems and structures like websites and social media apps, where key populations communicate and learn information and socialize.
2) **Online case management** for key populations who have tested positive and need to engage in services. Providing case management through online systems could potentially reduce loss to follow-up and provide helpful nudges (such as reminders to book an appointment or take a medication) and support for key populations.

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3) **Targeted health information** uses internet sites and social networking apps to allow for messages to be targeted at user demographics and characteristics. For example, Facebook advertisements can target users of certain ages, political profiles, geographic locations, etc. Population segmentation may allow for more specific targeting of key population audiences to provide tailored information or linkage to health services.

Evidence review

A systematic review was commissioned by WHO to answer the question of whether providing services online improves uptake of HIV, viral hepatitis, STI prevention, testing, linkage to treatment and treatment retention for key populations, compared to standard care .

Given the range of online interventions, the evidence review was split to consider the following separately: online outreach, online case management and targeted health information. The outcomes tested were for the following:

- online outreach – number or proportion of previously unreached people reached, use of prevention services, PrEP adherence, PEP uptake, PEP adherence, counselling, condoms, uptake of testing services for HIV, viral hepatitis and STIs, and treatment initiation for HIV, viral hepatitis and STIs;
- online case management – use of prevention services, uptake of testing services for HIV, viral hepatitis and STIs, treatment initiation for HIV, viral hepatitis and STIs, treatment retention or completion for HIV, viral hepatitis and STIs, viral load (for example, HIV and HCV), cure (for curable STIs, for instance HCV, syphilis and gonorrhoea) and mortality; and
- targeted online health information – use of prevention services, uptake of testing services for HIV, viral hepatitis and STIs, treatment initiation for HIV, viral hepatitis and STIs, treatment retention/completion for HIV, viral hepatitis and STIs, viral load (for example, HIV and HCV), cure and mortality.

Two RCTs *(364, 365)* and one serial cross-sectional study *(366)*, all among men who have sex with men, were included in a review of online outreach; four RCTs *(367–370)* among men who have sex with men, transgender women and people in prisons, and three observational studies *(371–373)* among men who have sex with men, transgender women and people in prisons were included in the review of online case management; and two RCTs *(374, 375)* and one observational study *(376)*, all among men who have sex with men, were included in the review of targeted online health information.

Online outreach

A stepped-wedge cluster RCT among men who have sex with men (aged 16 years and older) in China found comparable (little or no difference) in self-reported condom use between clusters who received the online HIV testing intervention compared to conventional HIV testing programmes, routinely provided by local centres of disease control and community-based organizations (RR: 1.00, 95% CI: 0.86–1.17). There was high certainty that the estimated lack of effect is close to the true effect *(364)*. Another RCT of men who have sex with men in China found that online outreach may make little or no difference to self-reported condom use, regardless of partner type, with low certainty evidence (RR: 0.90, 95% CI: 0.39–2.06) *(377)*.

Moderate certainty evidence from a meta-analysis of the same two RCTs showed a probable increase in HIV testing (RR: 1.39, 95% CI: 1.21–1.60) *(364, 377)*. Moderate certainty evidence from one of these RCTs showed probably no difference in syphilis testing (RR: 0.92, 95% CI: 0.70–1.21) *(364)*.

Moderate certainty evidence from one serial cross-sectional study among men who have sex with men in the USA showed probably more previously unreached people getting reached *(366)*. When only traditional outreach methods were used (October 2011 to March 2012) the local public health department had contact with 60 men who have sex with men. After implementing outreach via Grindr (from October 2013 to March 2014), the department made contact with 816 men who had had sex with men. There was no denominator to calculate rates, only number of contacts (which may include duplicates), and possible confounding from other factors, creating the potential risk of bias.

Online case management

In terms of PrEP adherence, low certainty evidence from one RCT among young men who have sex with men and transgender women (from 15 to 19 years old) in Thailand showed that there may be no difference in use of PrEP services when comparing those who used an online case-management application (provided alongside standard youth-friendly services) to no application, but with the same youth-friendly services (RR: 1.12, 95% CI: 0.78–1.59) *(370)*.

One RCT among men who have sex with men in the USA showed no difference in uptake of repeat HIV testing (RR: 1.24, 95% CI: 0.78–1.95) *(367)*, but due to the very low certainty there is limited confidence in this estimate.

A cohort study among people in prisons living with HIV in the USA found that there may be no difference in linkage to care after release from prison, when comparing those who used an online tailored or personalized website with those who only have access to an online provider directory webpage (RR: 1.09, 95% CI: 0.92–1.29) (low certainty) *(373)*. Another cohort study among men who have sex with men and transgender women in the USA found that there may be a modest increase in the proportion who received primary HIV care in the last six months, when comparing those who completed a six-month digital HIV care navigation intervention with those who did not (RR: 1.20, 95% CI: 1.01–1.42) (low certainty) *(372)*.

One RCT with moderate certainty among 90 stimulant-using men who have sex with men living with HIV in the USA found probably higher overall ART adherence in the intervention than the control arm at 4 months: 89.0% (95% CI: 83.4–94.6)

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intervention versus 77.2% (95% CI: 66.7–87.7) control, giving a difference in ART adherence of 11.8% (95% CI: 0.34–23.2; p= 0.04). However, two months after the intervention the improvements in adherence had probably dissipated: 85.3% (95% CI: 80.0–90.6) intervention versus 89.0% (95% CI: 83.2–94.9) control, giving a difference of -3.7% (95% CI: -11.4–4.0; p =0.34) *(368)*.

One RCT with low certainty among 110 soon-to-be or recently released people in prisons living with HIV in the USA found that online outreach may make little or no difference in engagement in HIV care, measured by having seen an HIV care provider in the community at least once in the past 24 weeks (RR: 0.98, 95% CI: 0.85–1.12) *(369)*. A cohort study with low certainty among 120 men who have sex with men and transgender women living with HIV in the USA found online case management may make little to no difference in the proportion of people in each group self-reporting currently taking ART (RR: 1.19, 95% CI: 0.97–1.45) *(372)*.

The RCT with low certainty among people in prisons living with HIV in the USA found that being in an intervention group that received a computerized motivational interview and individual risk reduction plan pre-release, plus text messaging about care navigation post-release, made little or no difference to viral suppression (lab-assessed viral load < 200 copies/ml) (RR: 0.97, 95% CI: 0.69-1.36) *(369)*. A cohort study among men who have sex with men and transgender women living with HIV in the USA also found that using online case management makes little or no difference to viral suppression (self-reported viral load < 200 copies/ml) (RR: 1.05, 95% CI: 0.79–1.40) *(372)*. However, another cohort study with moderate certainty among 1201 people in prisons in the USA found probable improvement in the proportion of participants who had lab-assessed virologic suppression at any of their first six care visits (RR: 1.53, 95% CI: 1.43–1.64) *(371)*.

No studies measured our other outcomes of cure (for example, HCV, syphilis or gonorrhoea) or mortality.

Targeted health information

One RCT with low certainty among men who have sex with men in the USA found that targeted health information may make little or no difference in testing for HIV (measured by following up for HIV test result after requesting a HIV self-test kit and returning the kit) (RR: 2.19, 95% CI: 1.20–4.01), though more participants in the intervention arm requested the kit than in the control arm *(375)*. A serial cross-sectional study among men who have sex with men in Canada with low certainty determined with GRADE methodology also found little or no difference in the number of people who ordered a syphilis test before, during or after a syphilis testing advertisement campaign (RR: 1.00, 95% CI: 0.94–1.07) *(376)*. Another RCT was conducted among young men who have sex with men (aged from 15 to 24 years old) in the USA . Based on these results, it is uncertain whether virtual targeted health information improves testing rate for HIV or STIs (RR: 1.46, 95% CI: 0.72–2.94) because the sample size was very small *(374)*.

Based on evidence from one RCT among men who have sex with men in the USA, it is uncertain whether targeted health information improves uptake of prevention services (STI vaccination) because the certainty of evidence is very low *(374)*. No studies measured other outcomes of interest: treatment for HIV, viral hepatitis and STIs, treatment retention or completion for HIV, viral hepatitis and STIs, viral load (for example, HIV and HCV), cure (for STIs, for example, syphilis and gonorrhoea) or mortality.

Feasibility, cost and cost effectiveness

Access to the internet and social media apps has grown exponentially in recent years, even in low-income settings. Many government and community-based programmes are already using online services for key populations, suggesting it is a feasible intervention in many settings *(378)*.

Only one study was included in the cost review *(379)*. This study among men who have sex with men in Canada found that syphilis testing campaign advertisements released over one month over four platforms had the lowest cost-per-click ratio on the hook-up platforms Grindr and Squirt, compared to more traditional social media platforms like Facebook and the Gay Ad Network. No studies measured cost effectiveness.

Indirect evidence from FHI360 *Going online budgeting guide (380)* shows a wide range of costs for programmes, depending on scope of work, including, but not limited to: country or regional costs, connectivity level, programme intensity or scale, vendors, in-person trips or training needs and equipment needs.

Values and preferences

Related to online outreach, in Spain, men who have sex with men thought it acceptable to receive unsolicited messages about rapid HIV, syphilis or HCV testing on social media or hook-up apps *(381)*. In Kenya, Rwanda, South Sudan, Tanzania and Uganda, almost half of respondents who self-identified as a sexual or gender minority were “very likely” to engage in a sexual health programme if outreach was conducted online using either text messages or emails *(382)*. In China, men who have sex with men stated high interest and willingness to use a “men who have sex with men-friendly physician finder function” within gay mobile on-line applications *(383)*.

Related to online case management, men who have sex with men in China expressed interest in features or functions related to sexual health that could be embedded in existing smartphone apps or developed as standalone apps *(384)*. Men who have sex with men in the USA were strongly in favour of a smartphone app developed for online case management *(385)*. Positive features of such apps were their ease of use (easy to navigate, fast and convenient), the ability to set reminders or alarms to take medication at a certain time each day, trackers for adherence and communication with providers, which helped users feel supported in their care process. Several studies mentioned concerns regarding ensuring confidentiality in the online environment *(368, 385, 386)*.

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When asked about targeted online health information specifically, men who have sex with men expressed a diverse range of acceptability; however, most were comfortable interacting with health services online *(376)*.

Qualitative research conducted by four key population networks (see Web Annex B) showed that, overall, participants across key population groups and regions supported the use of online services and platforms to augment in-person services. At the same time, many participants described challenges associated with varying levels of internet access, digital competencies, as well as the broader implications of poverty.

It was stressed across all key population groups that online services and platforms cannot replace in-person health services. Participants emphasized the importance of maintaining in-person, face-to-face services as a gateway to broader health and support services, as well as a means to foster personal connections and trust. Participants raised security concerns associated with leaving a digital footprint.

Equity and acceptability

In a qualitative, questionnaire-based study among frontline outreach workers, managers or public health volunteers who worked with men who have sex with men in Canada *(387, 388)*, it was noted that online technologies have reshaped the "gay or queer community", changed norms for social and sexual interactions, and that these online technologies can help reach out to hard-to-reach people. They found that, generally, online outreach allowed for more non-intrusive and anonymous communication (beneficial for clients), yet quick feedback helped them be responsive to user needs. They also outlined some barriers to online outreach, such as quality of service, collaboration between outreach service agencies and companies that own apps and websites, budgetary and staff or volunteer capacity constraints, and data security and safety. From their own experiences, service providers mentioned four ethical dilemmas as outreach moved to online platforms: 1) managing personal and professional boundaries with clients; 2) disclosing personal and identifiable information to clients; 3) maintaining client confidentiality and anonymity; and 4) security and data storage measures of online information.

While noting that online platforms can be particularly impactful amongst harder-to-reach sub-populations, such as migrant sex workers or young men who have sex with men, participants in the key population networks' values and preferences research also highlighted the role that digital inequality plays in mediating access to, and uptake of, online services. Concerns, including reduced access to technology or electricity, high data costs and differing levels of digital competencies, were all cited as factors affecting the use and impact of online tools and platforms. Those with limited or controlled access to mobile devices, particularly women and adolescents, were particularly vulnerable to digital inequality *(378)*. These issues can be exacerbated by criminalization and law enforcement actions.

Evidence assessment and decision-making

Overall, the evidence indicates that online service delivery is at least as effective as face-to-face services in terms of reaching new people, use of HIV and STI prevention services, linkage to and retention in HIV care. While the evidence of effect was modest or small for some outcomes, and for other outcomes there was no effect found, the evidence did not show worse outcomes when employing any online service delivery method. These interventions are feasible, acceptable and may increase equity. The resource requirements will vary depending on setting and intervention, and cost effectiveness is uncertain.

For some people who are unable to attend face-to-face services, online services may offer the only means of receiving information, support, referral and case management. But while the use of online services is increasing, there are still limitations related to reach. Furthermore, key populations said they value online services, but felt strongly that these services should complement and not replace face-to-face services. Potential harms related to data security and confidentiality was of particular concern for key populations who may engage in criminalized and stigmatized activities and experience discrimination, arrest or harassment if confidentiality is breached. For these reasons a conditional recommendation was made in favour of online services.

Implementation considerations

Online services complement but do not replace face-to-face interactions and should be part of larger HIV, STI and viral hepatitis programmes for key populations. Systematic planning of the ways in which online services can complement other services and target audiences should be conducted with key populations playing a central role in their design, implementation and monitoring. Content development should be informed by appropriate and accurate health content and information aligned with recommendation practices (for example, from health programme guidelines or evidence-based normative practices) *(389)*. Demand creation plans, service delivery packages and approaches need to be customized, based on country contexts and priorities. Online services can effectively be managed and implemented by key population peers.

Efforts should be made to make access to the internet equitable, improve literacy and provide appropriate training where needed. Where barriers to key populations accessing online services remain, this needs to be taken into consideration when planning and implementing online programmes.

Safety and security in online services need to be maintained by the following means: monitoring for harm, explicitly stating and using de-identified information as much as possible; maintaining data protection and storage, and training all staff in data security measures; thinking about the setting and using broad branding that does not lead to identifying certain groups of key populations; training staff in client confidentiality; verifying health worker licenses and credentials

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where applicable; using secured internet, devices and apps; and providing services only with informed consent from clients *(390)*.

WHO has further guidance and recommendations on general population digital health, as well as a framework for planning, developing and implementing solutions with and for young people *(180, 389)*.

Research gaps

Available published research about online services for key populations is mainly among men who have sex with men in high income countries and related to HIV. Further research is needed on the accessibility, safety and effectiveness of online services for other key populations, the various experiences and preferences of different key populations in low- and middle-income settings, and their effect on outcomes related to STIs and viral hepatitis. Continuing monitoring and evaluation and publishing the implementation results will also support and help to refine future guidance.

More research is needed on the cost effectiveness of different types of online services by key population groups.

Peer navigators

Background

Peer navigation is rooted in the concept of *patient navigation*, where vulnerable patients are directly assisted to help find their way through complex health care systems to obtain timely diagnoses and treatment. Instead of formal health workers, lay staff members who are peers of the participants and therefore could promote trust among the population fill this role *(391)*. While lay providers, including key populations, are recommended to provide HIV testing and ART distribution *(190)*, the role of a peer navigator is different. Key population peer navigators are often employed at community-based services, primary health care settings and testing and treatment facilities that are designed to serve people from key population groups. Their role is to support key populations, after screening positive, to access confirmatory diagnosis and treatment services; to support the early stage of treatment with regular peer support, as well as to accompany key populations to appointments; and support navigation to other related health services. This is important as key population members are often under-represented in treatment programmes, and can be reticent to access treatment due to their fear of discriminatory attitudes among health care providers and other staff in health care settings, and due to their lack of experience with traditional, facility-based programmes.

Evidence review

WHO commissioned a systematic review to answer the question of whether peer navigators improve initiation and retention in HIV, viral hepatitis and STI treatment programmes for people from key populations. The outcomes tested were: time to diagnosis or linkage to care , treatment initiation, treatment retention and completion, viral load, cure and mortality.

Four studies (two RCTs and two observational studies) were included in the systematic review designed to find the effect of peer navigators on time to diagnosis, linkage to care, treatment retention or completion, and viral load or disease cure. All these studies measured HIV outcomes, and none measured STI or viral hepatitis outcomes.

One RCT in the USA, with high certainty evidence, found no difference in probability of HIV care visits after release from jail for people in prisons with involvement of peer navigators (RR 0.95, 95% CI: 0.81–1.12) *(391)*, one RCT among sex workers in Tanzania found there may be improvements in linkage to care (RR 1.44, 95% CI: 1.15–1.80), but there was low certainty of this effect *(128)*, and one observational study among transgender women in the USA found improvements in linkage to care when people were assisted by peer navigators (regression coefficient 0.38; 95% CI: 0.09–0.67) with moderate certainty that the true effect was close to this estimate *(392)*.

The employment of peer navigators was found to result in modest improvements in current ART use in one RCT in Tanzania (RR 1.28, 95% CI: 1.05–1.55) *(128)* and one observational study in the Dominican Republic (RR 1.11, 95% CI: 1.03–1.19*) (393)*, both with low certainty of evidence. The RCT among people in prisons found no difference in ART use with peer navigation (RR 0.97, 95% CI: 0.87–1.08) and there was moderate certainty that the true effect was close to this estimate *(391)*.

One RCT showed improvements in undetectable viral load with peer navigation (RR 1.38, 95% CI: 1.03–1.85) with high certainty indicating that this estimate is very close to the true effect *(391)*, but the other studies found no difference *(128, 392, 393)*, all with moderate certainty. No studies measured the outcomes of treatment initiation, cure or mortality.

Feasibility, cost and cost effectiveness

Peer navigators have been employed at community and facility-based services in several different settings, and it is feasible to introduce this role to new or existing programmes.

A systematic review did not identify any research on the cost or cost effectiveness of key population peer navigators in HIV, STI or viral hepatitis programmes. Guideline Development Group members judged that as peer navigators work to support existing programmes, the cost associated with their employment may be considered to be moderate and related to salary, training, transport and tools such as mobile phones.

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Values and preferences

Key population network-led qualitative research was undertaken to assess values and preferences associated with peer navigation in all key population groups, except for people in prisons (for detailed report, please see Web Annex B). Although the term "peer navigators" was not universally recognized by all participants, the practice of peers assisting with health service access, information, education and referral was greatly valued by participants across all four key population groups. Participants both supported the concept of peer navigators, as well as their capacity to "act as a bridge between two different worlds". In some settings, peer navigators were described as one of the only available tools for reaching communities. Peer navigators were considered as facilitators throughout the testing and treatment cascade – including treatment linkage, continuity and re-engagement.

Equity and acceptability

Key population peer navigators improve linkage to care and retention in treatment programmes for populations who may otherwise be excluded due to structural barriers, including stigma, poor literacy and poverty. In this respect, peer navigators have an important role in improving equity by assisting those with inequitable access to health care to enter testing and treatment programmes.

A systematic review identified two studies of acceptability related to key population peers, which found overloaded health workers welcomed assistance from peer navigators and suggested appropriate tasks for them. However, concerns were expressed about clients becoming too dependent on peer navigators (that they are not able to self-manage), and there were some negative and discriminatory community reactions to support groups for men who have sex with men *(394)*. In Mexico, staff at a community-based organization felt peer navigators could address stigma and social support. However, they discussed concerns about police interference with peer navigators, and whether it put peers and their clients at risk of harassment and arrest *(395)*.

Assessment of evidence and decision-making

The benefits of using peer navigators include, as described above, the prospect of them improving linkage to care and retention in treatment. Key population members highly value services provided by their peers, and community empowerment is an evidence-based intervention *(122, 127)*. It was noted that support from peer navigators is not always desired by all key population members, particularly when people do not wish to disclose their disease status to a peer.

Peer navigators increase equity, and peer navigation is a feasible intervention. The costs vary greatly depending on setting, and cost effectiveness is unknown.

The evidence included in the systematic review was only relevant to HIV programmes, although STI and viral hepatitis programmes also employ peer navigators. It was decided that there was adequate indirect evidence to make a recommendation that applies to the three disease areas. Based on the moderate certainty of evidence supporting peer navigators, the value placed on peer navigators by key populations, and the likely beneficial effect on equity, the Guideline Development Group made a conditional recommendation in favour of peer navigation.

Implementation considerations

Key population peer navigators are increasingly employed at health services, along with key population peers who undertake different roles (including planning, mapping, management, education, adherence support, outreach, testing, distribution of medicines, overdose management, condoms and needles/syringes, etc). All peers who work within HIV, STI and viral hepatitis services need to be recognized as part of the health workforce, be fairly remunerated and receive ongoing training and development to fulfil their roles. Peer navigators can be subject to additional risks, such as arrest and violence, because they can be identified by police or others as members of the key populations; therefore, efforts should be made to protect peer navigators, in particular young key population peers, from any additional risks.

According to participants in the key populations' values and preferences research, the key traits of successful peer navigators include: passion for the community and the health issue, communication, compassion, supportive listening skills, first-hand experience, trustworthiness, empathy and dedication. Participants also stressed the importance of having peer navigators with appropriate age, gender, cultural and linguistic backgrounds.

While valued by key populations in general, not all key population members need or want the support of a peer navigator. Concerns about confidentiality may mean that some people prefer not to disclose their infectious disease status to a peer; therefore, they will not be comfortable using the services of a peer navigator, which highlights the importance of informed choice when implementing this intervention.

Research gaps

While there is considerable research about the effectiveness of peers as treatment support staff and patient navigators, there is far less research that is specific to key populations. More studies are needed to understand the effectiveness of different approaches for various key population groups of all ages, as well as for STIs and viral hepatitis. Overall, better research on what works to improve treatment outcomes among key populations is needed.

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HCV recommendations: introduction

Effective and affordable diagnostics and treatment are available for HCV and recommended by WHO *(184, 185, 193, 396)*, but a rapid increase in the availability and accessibility of HCV testing and treatment for all populations, including those at increased risk and those with HCV reinfection, will be needed to reach the elimination targets.

HCV causes both acute and chronic infection. Acute HCV infections are usually asymptomatic, and most do not lead to a life-threatening disease. Following recently acquired HCV infection, approximately 30% (15–45%) of infected persons spontaneously clear the virus within 6 months of infection without treatment *(15)*, with a median time to clearance of 16.5 weeks. Spontaneous clearance is more likely to occur in women, genotype 1 infection, and people with clinical evidence of acute hepatitis, but less likely to occur in people with HIV *(397)*. The remaining 70% (55–85%) will develop chronic HCV infection. Of those with chronic HCV infection, the risk of cirrhosis ranges from 15% to 30% within 20 years *(193)*. Importantly, individuals that clear HCV infection spontaneously or after treatment are not immune to the virus, and those with ongoing risk and exposure can become reinfected.

"Treatment-as-prevention" is becoming a key part of a multifaceted public health approach to HCV elimination. Early identification of primary and recurrent HCV infections, as well as timely treatment, is vital for a treatment-as-prevention approach, in order to reduce transmission and liver disease-related morbidity and mortality *(398)* – especially in countries where many of the new HCV infections are among key populations.

HCV retesting after resolved HCV infection

Background and rationale

After HCV infection and DAA treatment or spontaneous clearance of HCV, ongoing risk behaviours, poor access to prevention interventions, and persistent structural barriers for groups such as people who inject drugs and men who have sex with men may lead to HCV reinfection, which often goes undiagnosed. The potential for HCV reinfection remains a major obstacle to achieving the HCV elimination goals. From a patient perspective, concern for HCV reinfection remains a major driver for provider and health system-level barriers to HCV treatment of persons perceived to be at high risk for reinfection after cure *(399)*. From a population perspective, elimination is dependent on diagnosing and treating enough infected individuals, so as to reduce overall population prevalence, and thereby reduce the pool of individuals who can sustain the epidemic by transmitting infections to others. If people with high risk of transmission do not receive HCV diagnosis and treatment in a timely manner, this may present an ongoing challenge to community-wide and global HCV elimination *(220)*.

To address missed diagnoses of HCV reinfection among priority groups, to offer continued care and to increase access to treatment, several national and international guidelines, including WHO's, suggest serial testing for hepatitis C reinfection in priority groups, but do not state a specific testing frequency *(184, 400)*. Determining this optimum frequency will assist in a treatment-as-prevention approach to reduce HCV incidence and prevalence, notably among most-affected populations.

Evidence review

A systematic review was commissioned by WHO to answer the question of how often people with ongoing risk of HCV infection should be retested for evidence of viremia (using NAAT) for HCV RNA or HCV core antigen after treatment-induced or spontaneous HCV clearance. The primary outcome tested was the detection rate of HCV reinfection and the secondary outcomes were testing uptake for viremia (RNA or HCV core antigen) testing; linkage to clinical assessment or treatment initiation following reinfection or both; risk behaviour and adverse events or social harm.

No RCTs or comparative studies were identified. Thirty-five other studies were included in the review; 33 were single-armed observational studies and two were modelling studies. The 33 observational studies comprising 10 857 participants (key population groups included in the literature were people who inject drugs, people in prison or closed settings and men who have sex with men) at risk of HCV reinfection reported HCV reinfection incidence per 100 person-years (py), hence were included in a meta-analysis. The included studies did not report results for any of the secondary outcomes.

The studies had varying testing intervals; in order to answer the research question, the most meaningful comparison was between studies testing at 3–6-monthly intervals versus studies testing at greater than 6-monthly intervals.

The overall pooled HCV reinfection incidence estimate was 4.73 per 100 py (95% CI: 3.68, 5.78). The pooled incidence estimate among people who inject drugs was 3.94 per 100 py (95% CI: 2.83, 5.05), among men who have sex with men 7.11 per 100 py (95% CI: 4.16, 10.06) and among people in custodial settings 6.00 per 100 py (95% CI: 0.00, 12.31). Very low certainty evidence showed that among studies that reported a testing interval of 3–6 months, the pooled incidence estimate of 5.88 per 100 py (95% CI: 4.14, 7.61) was higher than studies reporting testing less frequently than every 6 months (up to every 12 months) at 3.08 per 100 py (95% CI: 1.81, 4.35). Additionally, among the people who inject drugs population, very low certainty evidence showed that pooled reinfection incidence was higher in those tested every 3–6 months at 5.39 per 100 py (95% CI: 3.47, 7.31) compared to those tested less frequently than every 6 months (up to every 12 months) at 1.84 per 100 py (95% CI: 0.64, 3.05). Given the very low certainty, confidence in these results is limited. Differences in incidence were not reported in other population groups from the studies included.

Two modelling studies were also identified that directly compared more and less frequent HCV testing regimes. A modelling study in India used a closed Markov model of reinfection among people who inject drugs in India. They

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assumed 6.2 million chronic HCV patients, 10% infections diagnosed/year, a reinfection rate 1.0/100 py, baseline DAA efficacy off 90%, the cost of DAAs US$ 900 for a 3-month course, and standard Indian costs for hepatitis C treatment. In a sensitivity analysis post successful treatment, the authors compared a one-off testing strategy at 1 year post-SVR compared to a regular annual testing strategy. They found that ongoing annual testing was more effective (0.4 QALY/person treated), cost-saving (US$ 993 per person), and very cost effective, with a negative incremental cost-effectiveness ratio *(401)*.

A modelling study in France used a deterministic dynamic compartment model among HIV-positive men who have sex with men in France, assuming a baseline HCV prevalence of 3.6%. Their baseline scenario involved DAA treatment of all patients and 12 monthly population testing, and projected that HCV incidence would fall from 0.98 to 0.24/100py. The authors found that more frequent testing (3, 3–6 or 6-monthly) was associated with further reductions over baseline in overall HCV incidence by 2030. The reinfection incidence in these scenarios was also modelled, and demonstrated that 3, 3–6 and 6-monthly testing reduced HCV reinfection incidence by 2030 significantly more than baseline (12 monthly) testing, though there was little difference between reductions from 6-monthly (18.5%), 3–6-monthly (21.5%), and 3-monthly testing (23%) *(402)*.

Overall, there is very low certainty evidence that more frequent testing may identify more infections, and therefore be beneficial in contributing to preventing onward transmission if individuals are linked to treatment and care. Some of the differences between testing intervals may have been found because researchers and clinicians were more likely to frequently test patients at higher risk of reinfection.

Values and preferences

Preferences regarding frequency of HCV testing varied greatly across the three key population groups who were asked this question in the key population-led values and preferences qualitative study (people who inject drugs, men who have sex with men, and sex workers) (see Web Annex B). Men who have sex with men pointed out a lack of protocols and the need for evidence to guide frequency of HCV testing recommendations. Meanwhile, sex workers had a wide range of preferred HCV testing frequencies – from once a week to once a year – with many participants considering 3–6 months as optimal. People who inject drugs suggested that individuals be tested every 3-months for the first year following viral clearance, and then subsequently every 6 or 12 months, depending on risk profile.

Sex workers and people who inject drugs preferred that regular HCV RNA testing and retesting following cure be made available, and promoted similarly to HIV "Test and Treat" approaches, whereby regular monitoring is publicly and positively promoted, widespread testing is facilitated, and immediate treatment for those diagnosed is encouraged. All groups highlighted concerns associated with criminalization, stigma, and discrimination, noting that testing should always be voluntary.

Overwhelmingly, key populations preferred HCV services to be community-led and available within community settings, in order to address concerns related to safety, confidentiality, stigma and discrimination, as well as criminalization. Increased training and resources to support community organizations in this work will be required. People who inject drugs emphasized the importance of embedding HCV testing within a broader harm reduction approach that did not focus on abstinence, including offering pan-genotypic DAA treatment and HCV prevention for people in prisons.

No additional studies on related values and preferences were identified through the systematic review.

Resource-use: cost and cost effectiveness

The costs, both for tests confirming the presence of HCV viremia and for treatment for those identified HCV positive, vary considerably, depending on settings and countries. In particular, NAAT and HCV core antigen are relatively expensive in many lower- and middle-income settings.

More frequent testing could involve increased short-term costs of tests, costs of outpatient visits, including personnel and, if more reinfections are identified, the short-term costs of increased treatment. The approach may also entail opportunity costs for time and attention spent by medical personnel and administrators. Testing people more often after they have been successfully treated may also divert resources away from other testing programmes, such as those aiming to reach a larger population of people who have not had access to testing or treatment.

In the long-term, there may be cost savings by averting costs of advanced hepatitis disease and liver failure. There is some support from modelling evidence *(401, 403)*, with one modelling study suggesting that more frequent annual testing for reinfection of people who inject drugs post-treatment was overall cost-saving, compared to a one-time only retest *(220)*.

Equity

More frequent HCV testing could potentially increase early diagnosis and treatment of HCV reinfection in priority groups, thus reducing HCV infection and improving health equity. However, increased testing frequency could also potentially increase the burden of medical interventions for patients who may have multiple comorbidities and a high treatment and investigation burden. Testing should be voluntary, and streamlining medical visits and investigations should always be considered.

Feasibility and acceptability

NAAT and HCV core antigen testing accessibility and cost vary widely across settings. Thus, feasibility is dependent on the context, availability of resources and health system capacities. In settings with existing point-of-care solutions or

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well-developed linkage services, frequent retesting may be a feasible approach. For some people though, offers of more frequent testing based on risk may be stigmatizing and create barriers to accessing services. Also, it may be difficult to correctly assess ongoing risk, particularly in settings where key populations are criminalized and stigmatized, as people may choose not to disclose risk behaviours, and equally it will not always be possible to know about individuals' history of treatment or clearance. Moreover, increased frequency of testing, especially in the 3–6-monthly range, may be a significant time and resource burden, which may influence acceptability among providers and policy-makers.

Assessment of evidence and decision-making

The review found very low certainty evidence, from one-armed observational studies and limited modelling studies, in favour of more frequent retesting in people at ongoing high risk for HCV reinfection, particularly in people who inject drugs. Overall, the Guideline Development Group determined the certainty of evidence to be very low. While evidence of effect was small across the principal outcome, the Guideline Development Group highlighted that testing for presence of viremia in people with ongoing risk and previously cleared infection may be beneficial at both the individual and population level.

The main physical harms of more frequent blood testing for HCV are relatively minor, such as short-lived discomfort and bruising. The very rare risk of false positives should also be considered.

Considering the evidence of benefits for 3–6-monthly testing for reinfection; the relatively strong support from community values and preferences; the potential for expanding patient choices; the feasibility to implement; as well as potential for cost-effectiveness and improved equity, the Guideline Development Group deemed that the overall benefits outweigh the potential harms and risks. More frequent testing of people at ongoing risk can identify more people with viraemic HCV; the potential benefits of this include population-level ones, such as reduced HCV incidence and prevalence over time, due to more infections being treated and accordingly less potential for community transmission, and better individual patient outcomes related to early diagnosis. Patients may also benefit from better engagement in the health care system for other interventions, such as OAMT.

The Guideline Development Group recognized that testing frequency for reinfection should be contextualized and adapted to the reinfection incidence of a population. Furthermore, short-term costs and accessibility of diagnostics for presence of viremia (NAAT and HCV core antigen testing) may be a limitation to scaling-up the recommendation in some settings. Given the range consideration, the Guideline Development Group agreed to make a conditional recommendation.

Implementation considerations

In general, a successful response to HCV requires available, accessible, affordable and coordinated prevention, testing and treatment services, with well designed integrated service delivery and referral pathways**.** It is important to highlight that the frequency of retesting needs to be contextualized, and that the recommendation is meant to orientate programmes towards a potential testing frequency. Planning country-level testing frequency needs to factor in resource needs and evolving epidemiological patterns in certain populations and settings. Additionally, HCV management should include screening for HIV, STIs and voluntary partner notification for HCV testing where appropriate. Importantly, testing approaches and policies need to be developed with support from, and in exchange with, affected communities.

One of the major objectives of extending testing, referral and linkage to treatment to people with ongoing risk is the potential of population level benefits and a reduction of HCV transmission. Frequent testing for viremia should be offered alongside additional, evidence-based interventions to reduce HCV risk, and primary prevention services, such as harm reduction (NSPs and OAMT), which remain a priority and should be offered alongside testing for reinfection and not be de-prioritized. This new recommendation is particularly relevant for countries and settings where the reduction of HCV incidence is a major aim of the programme, and includes approaches such as micro-elimination in certain population groups.

Given that NAAT for occurrence of HCV RNA and HCV core antigen testing accessibility varies widely across settings and is often centralized, with the majority of tests requiring processing at central laboratories, decentralized models of care – with increased availability of point of care testing – are needed to make more frequent retesting feasible. It is important that frequent retesting is implemented in a way that does not reduce the number of people assessed for longstanding chronic HCV infection.

It is important to differentiate between HCV reinfection and treatment relapse in people with past DAA treatment. Evidence of HCV clearance and cure is evaluated 12 weeks after end of treatment (sustained virological response at 12 weeks post-treatment (SVR12)). SVR12 is widely considered to be equivalent to virologic cure. In the oral DAA era, rates of virologic relapse after the achievement of SVR12 are very low *(399)* and, when it occurs, it is usually within the first four weeks after end of treatment. Thus, a diagnosis of HCV reinfection can be made when HCV viremia is detected in persons who achieved SVR12 following completion of treatment with an effective oral DAA combination regimen, notably in persons who also have probable or definite risk factors for reinfection. In people with viremia between treatment completion and SVR12 assessment, or people for whom SVR12 is unknown, a further differentiation between relapse and reinfection may be useful and needed to orientate treatment decisions.

Monitoring and reporting systems are critical for all approaches to viral hepatitis testing and treatment, and it is essential for programmes to utilize or adapt existing systems to monitor and report on adverse events, in order to address harm if and when it occurs.

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Research gaps

Current research about HCV testing and detection of viraemic infections in people with ongoing risk comes largely from high-income countries.

Therefore, more research, ideally through comparative longitudinal studies comparing 12 monthly testing with more frequent testing or modelling, is needed to answer the question of whether more frequent testing after reinfection, followed by immediate treatment (namely, test and treat), would support a treatment-as-prevention strategy and micro-elimination of HCV with population-level benefits. There is a need for more research from LMICs. Real-world studies in different settings are needed to further establish cost-effectiveness and assess resource needs, feasibility and acceptability.

HCV treatment for recently acquired infection

Background and rationale

WHO currently recommends HCV therapy with pan-genotypic DAAs for all persons with chronic infection over the age of 18 years and irrespective of disease's stage. DAAs can cure most persons with chronic HCV infection, and treatment duration is short (usually from 12 to 24 weeks), depending on the absence or presence of cirrhosis *(193)*. However, DAA treatment is not currently approved by certain regulators for the treatment of recently acquired hepatitis C *(404)*. The rationale for this policy is to avoid unnecessary treatment and costs, since around 30% of people will clear the virus without treatment. This argument may become less important in contexts in which the costs of treatment is reducing. More recently, clinical guidelines from umbrella organizations in Europe and the USA recommend the treatment of recently acquired infection, recognizing the benefits, such as reductions in loss to follow-up, avoiding chronic infection and reducing ongoing transmission *(405, 406)*.

Evidence review

A systematic review was commissioned by WHO to determine the benefits and harm of immediate treatment of recently acquired hepatitis C in people at ongoing risk, and to update the current body of evidence informing the timing of HCV treatment. The outcome measures were hepatitis C incidence, treatment initiation, engagement in care (adherence), overtreatment, adverse events, treatment completion and SVR12.

A post-hoc review of the search results was conducted to identify modelling studies evaluating the effectiveness of treating recently acquired HCV infection, and any studies that reported on values and preferences of stakeholders.

No randomized controlled trials nor comparative studies were identified in the systematic review. Twelve noncomparative studies were included in the review: three single-group prospective cohort studies *(407–409)* five retrospective cohort studies *(410–414)*, three cohorts embedded in open label trials *(415–417)* and one case series study *(412)*. Across all these studies, all outcomes were rated as providing very low certainty evidence using the GRADE approach. In general, this was due to the noncomparative nature of these study designs and the indirectness and inconsistency of the data.

Two retrospective cohort studies and one prospective cohort (embedded within an open label trial) reported HCV incidence among men who have sex with men living with HIV, and allowed a comparison of incidence before and after the implementation of an HCV treatment policy for recently acquired infection *(411, 412, 416)*. Two of these studies reported a decrease in HCV incidence at the end of the study period; a study set in a Swiss cohort which reported a decrease in incidence from 0.53/100 py in 2014 to 0.12/100 py in 2019 *(416)*, and a study set in the United Kingdom, which reported a decrease from 11.28/1000 py in 2016 to 4.63/1000 py in 2018 *(412)*. One study found an increase in incidence over the study duration, from 0.73/100 py in 2015 to 1.25/100 py in 2018 *(412)*. These studies were in large cohorts of men who have sex with men, where most of the patients were being treated in the chronic phase of infection rather than recently acquired infections. As treating chronic hepatitis C can reduce incidence on population level as well *(418)*, it was not possible to identify the distinct effect of treating acute infection on incidence in these cohorts. Given the very low certainty, there is limited confidence in these results.

Seven studies (three retrospective and two prospective cohorts, one open label trial and one case series), including a total of 567 participants with recently acquired hepatitis C, reported SVR12 in men who have sex with men, people living with HIV and people who inject drugs *(407, 409, 410, 413, 414, 417, 419)*. The studies showed with a very low certainty evidence that people with ongoing risk treated for recently acquired HCV infection with DAA achieved consistently high rates of cure, consistent with the rates of cure seen for those treated with antivirals for chronic HCV in key risk groups. Pooled SVR12 across all risk groups was 95.9% (95% CI: 92.6–99.3%; I2 = 61.3%). With men who have sex with men, the pooled SVR12 was 96.9% (95% CI: 93.1–100%); with people living with HIV, pooled SVR12 was 97.0% (95% CI: 90.7–100%); and with people who inject drugs, pooled SVR12 was 80.4% (95% CI: 66.1–90.6%). Overall, confidence in these results is limited due to the very low certainty.

The one case series and one open label trial reported 100% HCV treatment completion rates in 25 men who have sex with men living with HIV *(419)* and among 27 people living with HIV *(415)*. Two open label trials *(415, 417)* reported on adherence: one found adherence of 81% amongst people living with HIV *(415, 417)* and another found adherence ranging from 79% to 85% among people who inject drugs, men who have sex with men and people living with HIV *(417)*.

Adverse events were reported in four studies *(409, 415, 417, 419)*; one serious adverse event, an episode of rhabdomyolysis (rash and raised creatinine kinase) requiring hospitalization was described *(417)*, while all other adverse events were considered minor. Adverse event rates ranged from 22% (21/95) to 36% (9/25). However, confidence in these results and those for adherence is limited due to the very low certainty.

No studies included a comparator group, so it was not possible to assess overtreatment.

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Values and preferences

Qualitative research carried out by key global population networks (see Web Annex B) found that awareness of and access to HCV treatment with pan-genotypic DAAs varied greatly across key populations. Of those participants who were aware of, and felt able to comment on, HCV and HCV treatment, most reported ongoing barriers to the access and utilization of HCV services, including cost, treatment delays, stigma and discrimination, and lack of research and political will. Some sex workers had not heard of pan-genotypic DAA treatments for HCV. People who inject drugs in particular noted that in certain contexts, cessation or abstinence from drug use (and sometimes OAMT) continues to be used as a criterion for HCV treatment access. This major barrier continues to occur, despite WHO recommendations to provide HCV treatment regardless of ongoing drug use.

People who inject drugs conveyed the most knowledge of pan-genotypic DAA treatment and recommended the expansion of HCV DAA treatment options and settings to maximize access and uptake, including at NSPs, OAMT clinics, drop-in centres and general health care settings. Given the high cure rates, good tolerability, low pill burden, fewer drug–drug interactions and significantly fewer side effects than the previous therapies, people who inject drugs expressed strong preferences for reducing barriers to treatment and making HCV DAA treatment as accessible as possible for people who inject drugs, including people who may have already been successfully treated and subsequently contracted a new HCV infection, as well as people with recently acquired HCV infection.

People who inject drugs did not express concern about the potential for overtreatment associated with offering treatment without delay for recently acquired infection, either among people who are treatment naïve or for retreatment. Rather, they expressed the concern that it is dangerous to deny access to treatment purely on the basis that some people will spontaneously clear (without treatment) – not only for the health of the individual concerned (and potential loss to follow-up), but also due to the potential for further transmission. People who inject drugs were more concerned about the ongoing lack of access to the highly effective HCV DAA treatments in certain countries and regions than about any hypothetical risk of overtreatment. Finally, people who inject drugs also emphasized the importance of offering HCV DAA treatment (and HCV prevention, including NSPs and OAMT, as well as management overdose) for people in prisons. This is particularly important in the context of an overwhelming lack of access to sterile injecting equipment and other harm-reduction measures in most prisons globally, coupled with high levels of incarceration associated with drug-related offences.

Most participants from other key population groups expressed limited knowledge about treatment with pan-genotypic DAAs, and the implications of treating recently acquired infection without delay or not. Nonetheless, most participants were open to this treatment, provided that they receive adequate information on its efficacy and side effects, as well as sufficient education and research to guide treatment implementation.

No additional studies on related values and preferences were identified through the systematic review.

Resource-use: cost and cost effectiveness

None of the studies identified from the systematic review and meta-analysis directly addressed resource requirements or cost-effectiveness.

A post-hoc modelling search to identify additional cost-effectiveness models in both high- and low-income settings *(420–423)* supported the value of treatment without delay of recently acquired HCV infection and potential population-level benefits. For example, in a Dutch model, earlier treatment of recent infection will cost €68.3 million over 40 years, compared to €75.1 and €98.4 million to delay treatment – either waiting for spontaneous clearance or delaying treatment until F2 stage[27], respectively. This study model also reported treatment of recent infection will prevent 7070 new infections and gain 3419 QALYs compared to F2 treatment, with resulting cost saving incremental cost effectiveness ratio (ICER) *(423)*. Other modelling studies from China *(421)* and the USA *(420)* also showed that treating acute HCV is cost effective and cost saving compared to deferring treatment to the chronic stage; however, there were increased costs associated with HCV treatment for recent infection in patients who were not at risk of transmitting HCV *(420)*.

One modelling study demonstrated a potential reduction in HCV incidence as a result of immediate treatment *(423)*. This study modelled treatment scenarios in a Dutch cohort of HIV-positive men who have sex with men, and found that treatment of recently acquired HCV infection lowered incidence from 1.2/100 py to 0.2/100 py, an 88% reduction in incidence compared to treatment at liver fibrosis stage F2.

The Guideline Development Group was of the view that overall costs in the short term for treatment and testing could be increased if people are treated for recently acquired infection with significant uncertainty due to variation in costs of testing and treatment between settings, including low-, middle- and high-income countries, changes in DAA and other medication costs over time, and the variable opportunity cost of diverting staff and attention.

Equity

No studies assessing equity were identified in the systematic review.

It can be argued that providing DAA treatment to people with recently acquired hepatitis C expands choice (namely, by providing a second option to deferral of treatment until chronic infection) for key populations, and may reduce loss to follow-up, thereby increasing the number of people accessing treatment. It is important that there are no restrictions

[27] METAVIR liver biopsy scoring system which ranges from 0 to 4.

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related to treatment of chronic or acute HCV infection and concurrent ongoing drug use, or drug dependence treatment or ongoing sexual risk.

In settings where access to DAAs is limited, implementing treatment for people with recently acquired infection without increasing overall DAA supply may have a negative health equity impact if DAAs are re-allocated from people with chronic hepatitis C, who are beyond the point of spontaneous clearance, and require treatment to prevent future morbidity and mortality. People with recently acquired hepatitis, on the other hand, may not necessarily require treatment, due to the remaining possibility of spontaneous clearance. Increased availability of affordable HCV treatment is needed to achieve elimination goals and ensure equity.

Feasibility and acceptability

None of the identified studies from the systematic review and meta-analysis directly addressed feasibility or acceptability.

Overall, it could be argued that feasibility will depend greatly on context and health systems' capacities. Offering treatment without delay to people independent of chronicity may simplify HCV treatment and care algorithms and increase patient choice, and thus be a feasible option in many different settings and countries. In settings with existing decentralized services for HCV testing and treatment, or well-developed linkages, treatment without delay may be particularly feasible. Furthermore, improving awareness of HCV and DAA among key population members will be required.

It is possible that the risk of adverse events from HCV treatment – however mild – may be unacceptable to people with recently acquired hepatitis C if the possibility of achieving spontaneous clearance has not yet been exhausted. Allowing individuals to make an informed choice between immediate and deferred treatment is therefore important. Similarly, it is unclear whether routinely prescribing a treatment to individuals with recently acquired hepatitis C without a period of observation for spontaneous clearance is acceptable to clinicians.

The Guideline Development Group judged that the intervention would probably be acceptable to most key stakeholders. There was some uncertainty around whether routinely prescribing a treatment to individuals with recently acquired hepatitis C without a period of observation for spontaneous clearance would be acceptable to clinicians.

Assessment of evidence and decision-making

The Guideline Development Group agreed that the issue of treating recently acquired HCV infection in persons with continuous risk exposure was a priority for public health and HCV elimination, and that the benefits clearly outweighed the harm. Benefits overall were judged to be large or moderate, and the related harm was trivial or small. Overall, the Guideline Development Group determined the certainty of evidence to be very low.

While evidence of effect was small across all outcomes, the Guideline Development Group highlighted that HCV treatment without delay for recently acquired HCV infection for those with ongoing risk can be beneficial, at both the individual and population level. Improved identification and treatment of recently acquired HCV may bring the benefit to the individual of being cured as soon as possible after diagnosis, rather than having to wait to access treatment and the associated risk of loss-to-follow-up, and thus would increase patient choices. The Guideline Development Group acknowledged the potential broader population-level benefit from curing an individual as soon as possible; namely, reducing the period of time during which they are infectious, and thereby reducing HCV incidence in certain population networks.

The group acknowledged that, following infection with hepatitis C, approximately one third of individuals will spontaneously clear the virus (that is, cure without any medical intervention). Therefore, treating all people with recently acquired hepatitis C immediately means that people who would have otherwise cleared their infection spontaneously are unnecessarily exposed to treatment. However, adverse events are very rare, and there was a clear preference for having treatment as an option.

Considering the evidence regarding good treatment outcomes of recently acquired infection in people with ongoing risk, the potential for reduction of HCV transmission in certain communities and populations, the strong support from community values and preferences, the potential for expanding patient choices and its feasibility to implement, as well as potential for cost-effectiveness and improved equity, the Guideline Development Group deemed that the overall benefits largely outweigh the potential harm and risk. The recommendation was thought to provide a potential for reduced stigma and simpler clinical care. Given all these elements, the group made a strong recommendation that applies to all populations with ongoing risk in all settings.

Implementation considerations

Extending HCV treatment to people with ongoing risk and recently acquired infection, requires several areas to be considered in order to facilitate implementation in countries. The latest WHO HCV treatment and care guidelines should be consulted for further details on the clinical management of HCV *(424)*.

Firstly, treatment without delay, independent of chronicity, is an additional indication for HCV treatment, and national treatment guidelines need to be amended. Furthermore, insurance policies for the treatment for recently acquired infection would ideally be streamlined with those for chronic HCV infection; this needs policy change and dialogue with funders and health insurance schemes in order to achieve this policy harmonization. Amendments to treatment guidelines or treatment policies need to provide a case definition for recently acquired infections, describe how a distinction can be made for treatment failure among people with a history of past HCV treatment, and how respective

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treatment strategies may differ. Moreover, it is important to identify and define certain subpopulations in which a treatment delay should be strongly considered, such as pregnant women. Furthermore, people at ongoing risk need to be offered adequate and frequent testing in order to be able to describe and discover recent HCV infection.

Secondly, patients need to be informed about the benefit and harm associated with both immediate and deferred treatment. Individuals with recently acquired infection must have the option to make an informed choice about starting treatment immediately or delaying treatment initiation. Key populations expressed preference for decentralization, with an expansion of treatment settings and simplified test and treat approaches.

Finally, one of the major objectives of extending treatment to people with recent infection and ongoing risk is the potential of population-level benefits and a reduction of HCV transmission. For the greatest impact, treatment for recently acquired infection should be offered alongside additional, evidence-based interventions to reduce HCV risk and primary prevention services, as outlined in these guidelines.

The Guideline Development Group discussed the importance and relevance of, in the future, expanding this new recommendation to promote treatment without delay in all populations, and not only for those people at ongoing risk.

Research gaps

Current research about HCV treatment without delay for key populations is mainly among men who have sex with men in high income countries. Further research is needed to describe the impact and added value of extending treatment without delay to recent HCV infection on individual and population level in different settings and populations.

Real world cost-effectiveness and feasibility studies would be valuable to further strengthen the case for treatment of recently acquired HCV infection. Implementation science that evaluates feasibility and acceptability of this approach in different key populations would be beneficial.

The potential for truncated courses of DAAs administered during recently acquired HCV may prove to be a benefit to early treatment of HCV and warrants further research.

Pooling samples from different anatomical sites for the diagnosis of *Neisseria gonorrhoeae* and *Chlamydia trachomatis*

Recommendation

Where biologic samples are collected from multiple anatomical sites in the same individual, they may be pooled for molecular testing of *Neisseria gonorrhoeae* and *Chlamydia trachomatis* infections *(conditional recommendation, moderate certainty of evidence for men who have sex with men, and low certainty of evidence for other key populations).*

Remarks:

- Collection of biological samples from all anatomical sites should always be voluntary.
- WHO recommends NAAT for the detection of *N. gonorrhoeae* and *C. trachomatis*.
- WHO recommends self-collection of samples for NAAT for the detection of *N. gonorrhoeae* and *C. trachomatis*.
- Community values and preferences did not include cisgender women, transgender men and non-binary people assigned female at birth, to inform this recommendation.

Background

Key populations are disproportionately affected by STIs. Several STIs are highly transmissible and often asymptomatic. Syndromic management of STIs misses asymptomatic cases and results in overtreatment. Furthermore, overtreatment contributes to antimicrobial resistance *(425)*. For example, inappropriate management of *N. gonorrhoeae* may accelerate the emergence of multidrug-resistant *N. gonorrhoeae* and increase onward transmission *(426)*. This underscores the need for aetiological diagnosis to optimise STI case management, particularly among key populations who practice oral and anal sex.

N. gonorrhoeae and *C. trachomatis* can infect different anatomical sites. Thus, aetiological screening of all appropriate anatomical sites (oropharynx, urethra, endocervix and anorectum) is needed when an individual engages in anal or oral sex or both. Considering the high proportion of asymptomatic infections caused by these pathogens, a significant proportion of cases would be missed if only genital screening was undertaken *(427)*. Studies have demonstrated that up to one third of gonorrhoea cases would be missed if only urethral or urine samples were tested in men who have sex with men *(428, 429)*.

Whilst separate testing from different anatomical sites is preferable, there is an additional cost associated with testing samples from each site. This is especially relevant in LMICs where the cost of NAAT recommended for the diagnosis of these infections is a major barrier *(430)*.

Evidence review

A systematic review was commissioned by WHO to answer the question of whether pooling of samples from different anatomical sites should be used for STI laboratory screening of gonorrhoea and chlamydial infection, compared to individual samples from three anatomical sites (urethra, anorectum and oropharynx). The outcome of interest was diagnostic accuracy.

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For chlamydial infection, a meta-analysis of sensitivity and specificity included 15 estimates from 14 studies of 5891 patients *(431)*. For multisite pooled testing for chlamydia infection, the review found the combined sensitivity[28] was probably 93.1% (95% CI: 90.5–95.0, I(2)=43.3), and combined specificity[29] was probably 99.4% (95% CI:99.0–99.6, I(2)=52.9) (moderate certainty evidence). This means, if 1000 people are tested with a background prevalence of 10% for chlamydial infection (100 cases), switching from single-site testing to pooled testing will probably result in seven missed cases (out of 100 true cases), and five people being overtreated.

For gonorrhoea, 14 estimates from 13 studies were used for the meta-analysis with data from 6565 patients. For multisite pooled testing for gonorrhoea, the review found the combined sensitivity using NAAT was probably 94.1% (95% CI: 90.9–96.3, I(2)=68.4) (low certainty evidence), and pooled specificity may be 99.6% (99.1–99.8, I(2)=83.6) (moderate certainty evidence). This means, if 1000 people are tested with a background prevalence of 10% for gonorrhoea, switching from single-site testing to pooled testing will probably result in six missed cases (out of 100 true cases), and four people being overtreated.

Meta-regression analyses did not show any significant impact on the accuracy of multisite pooled testing according to study population (men who have sex with men compared to men who have sex with women), study population size (<100 versus >100), country-income level, sample collection (self-collected versus clinician-collected) or publication year (before 2020 versus 2020 or after).

Four studies among men who have sex with men provided information specifically on the sensitivity of detecting oropharyngeal infections using pooled testing versus the standard of care (namely, testing individual samples from the three anatomic sites for chlamydia and gonorrhoea) *(432-435)*. All oropharyngeal infections with *C. trachomatis* were detected using pooled testing in three out of four studies *(10–12)*. In the remaining study, pooling samples resulted in one case missed out of six with oropharyngeal infection *(433)*. On the other hand, overall, the sensitivities of oropharyngeal gonorrhoea testing using individual samples were found to be lower for identifying infection across all studies *(432–435)*. The authors hypothesised that the reduced sensitivities were attributed to the lower bacterial load in the pharynx compared to other anatomic sites. Furthermore, two studies highlighted that most *N. gonorrhoeae* infections occurred in the pharynx, several of which would have been missed if this anatomical site was not sampled *(9)*.

It is also important to note that the studies included in the systematic review were predominantly conducted in high-income countries (82.6%, 14/17) and men who have sex with men were the most frequently studied population (70.6%, 12/17).

In summary, although different methods of pooling were used across the studies (related to flow and timing, different order of pooling sample, different volumes of urine used), the consistently high accuracy of multisite pooled testing, despite diverse methodologies of pooling, suggest that accuracy was not significantly impacted by the method of pooling. Overall, the certainty of evidence was downgraded to moderate, mainly because of potential risk of bias in most studies due to patient selection bias, with moderate heterogeneity observed for studies contributing to gonorrhoea sensitivity results.

Feasibility, cost and cost-effectiveness

No study included in the systematic review reported the feasibility to combine samples for multisite pooled testing. However, the Guideline Development Group noted that while pooling samples was generally feasible, this could vary depending on setting due to different laboratory structures, flow and technical capacities, among other things.

The systematic review identified three studies that estimated the cost savings of pooling samples from different anatomical sites for chlamydia or gonorrhoea testing. One study of 1064 men who have sex with men attending sexual health clinics and hospital sites between October 2012 and August 2013 in the United Kingdom suggested that pooled testing offers cost savings of up to two thirds of the costs of the assays alone, as well as savings in consumables, processing time and clinical pathway efficacy *(433)*. A prospective study between February 2018 and July 2019 of 501 female sex workers in Belgium demonstrated a 35% decrease in reagent costs and lab technician time when using pooled testing (calculated using the obtained prevalence of 6.5% and 3.5% for chlamydia and gonorrhoea, respectively) *(436)*. Finally, one study assessed the efficacy of pooled testing among 497 men who have sex with men in four West African countries, and demonstrated a 56% decrease in costs, in which unpooling of triple-site pooling was only undertaken when the pooled sample result was invalid *(437)*.

One cost-effectiveness study was identified. For men who have sex with men attending sexual health clinics in the United Kingdom, researchers reported that using a willingness to pay threshold of £60 per person tested, pooled testing had a 100% probability of being cost-effective. Compared with individually analysed samples, pooled testing saved £13.37 to £18.22 per individual tested, depending on the symptom status or population group (namely, men who have sex with men and women from the general population) *(438)*.

Values and preferences

Qualitative research by key population networks of gay and other men who have sex with men and sex workers of all genders on values and preferences associated with pooled sampling for STI testing was conducted with men who have sex with men, cisgender males and transgender women sex workers, but not among people who inject drugs, cisgender

[28] Sensitivity is a measure of how well a test can identify true positives.

[29] Specificity is a measure of how well a test can identify true negatives.

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women who work as sex workers or others assigned female at birth. Most participants in the research indicated that they were not familiar with this method for chlamydia and gonorrhoea screening. Nonetheless, most participants stated that they were willing to have samples taken from three anatomical sites and pooled, particularly if this method would yield the most accurate results. There was uncertainty across all regions among men who have sex with men about how accurate these tests using pooled samples are. This would indicate that more education must be done at the clinical and community level about the efficacy of these testing choices.

Men who have sex with men noted that due to the stigma surrounding anal sampling, the practice of simultaneously collecting and pooling samples from anorectum, oropharyngeal and urethral swabs could offer a less stigmatizing way to test for STIs. Pooling samples would also reduce the need for health care providers to ask clients what kind of sex they engage in, thus decreasing judgement and potential risky disclosure on sexual practices. Caution should be taken in extending the practice of not asking clients what kind of sex they engage in to other key populations, as the other populations were not consulted. For a detailed report, please see Web Annex B.

Additionally, two studies identified through the systematic review indicated that individuals (men who have sex with men and cisgender women) found self-sampling for chlamydia or gonorrhoea testing to be acceptable and easy to perform *(433, 439)*.

Equity and acceptability

Seven studies discussed the health equity impact pooling could bring by increasing testing coverage *(434–437, 440–442)*, especially for asymptomatic individuals who would not otherwise have been tested in LMICs *(437)*. A study also suggested that pooled testing should be incorporated in HIV PrEP programmes in resource-limited countries *(17)*. In addition, cost savings via pooled testing would allow more people with infection to be detected and treated, or for those at higher risk of infection to be tested more frequently with a similar budget.

A web-based survey of clinic heads in the United Kingdom from 2018 reported that 84% (41/49) of sexual health clinicians in England considered the most significant benefit of pooling was cost savings, but were concerned about barriers such as lack of national guidance, loss of infection site information and a perceived reduction in sensitivity or specificity *(441)*. In addition, most (77%, 40/52) clinicians requested more validation studies on diagnostic accuracy, 75% (39/52) wanted clinical guidelines of pooling and 48% (25/52) of clinicians requested further cost analysis *(441)*.

Assessment of evidence and decision-making

The Guideline Development Group discussed the benefits of pooling samples from three anatomical sites for gonorrhoea and chlamydia testing, based on the evidence review and the values and preferences of the communities.

Considering the high sensitivity and specificity of pooling samples for molecular testing for both chlamydia and gonorrhoea, the benefits of pooling samples include:

1) increased detection of extra-genital infections by using the same test for multiple anatomical sites, and an increase of test coverage, especially testing more asymptomatic individuals at higher risk of STIs, due to potentially significant cost savings;
2) potential decrease in the risk of HIV acquisition if more extra-genital infections and individuals are correctly diagnosed and treated; and
3) decreased workload for laboratories and other health services, especially when implementing testing at or near the point of care.

Furthermore, self-sampling, which is highly acceptable, does not affect the accuracy of multisite pooled sampling.

The values and preferences research among the key population communities (see Web Annex B) was limited to men who have sex with men, cisgender male sex workers and transgender women sex workers, and did not include cisgender women who work as sex workers, transgender men and other people assigned female at birth. For this reason, the Guideline Development Group felt that there was a possibly important uncertainty and variability in the assessment of key populations' values and preferences for pooled-site sampling. The Guideline Development Group member from NSWP in particular expressed their concern about the omission of cisgender women and transgender men in the values and preferences survey and requested that this research be undertaken as a matter of priority.

Potential harms discussed by the Guideline Development Group were that, compared to a gold standard, single-site test, there would be small numbers of missed cases (five for chlamydia, six for gonorrhoea) and overtreated cases (five for chlamydia, four for gonorrhoea) if pooling samples from multiple anatomical sites in a population of 1000 people with a 10% background prevalence. Furthermore, there is uncertainty about the sensitivity of pooled-site sampling to detect oropharyngeal gonorrhoea, and without retesting, it is not possible to know exactly which sites are infected. However, this small loss in sensitivity was balanced by the opportunity to test the multiple anatomical sites when using pooled testing in settings where oropharyngeal sampling is not routinely performed because of cost.

The potential benefits of pooling samples from multiple anatomical sites to diagnose these two pathogens outweighed the harms of slightly lower accuracy. Thus, the Guideline Development Group decided to make a recommendation in favour of the intervention. There was overall moderate certainty evidence of sensitivity and specificity of pooled samples for both chlamydia and gonorrhoea. However, the limited data from LMICs and from other key populations, besides

men who have sex with men, led the Guideline Development Group to downgrade the certainty for other populations to low. Based on the above considerations the Guideline Development Group made a conditional recommendation with moderate certainty of evidence for men who have sex with men and low certainty of evidence for other key populations.

Implementation considerations

Multisite pooled-sample testing is highly sensitive and specific with potential associated cost-saving benefits and creates an opportunity to increase the detection of extra-genital infection and screening coverage, particularly in LMICs using NAAT.

Countries should consider conducting national lab validation methods for the use of pooled samples to diagnose chlamydial and gonococcal infections, and to include pooled sampling into national quality assurance and control protocols. The question of who would pool the samples has to be considered; for example, would the task be completed by self-sampling, health providers or lab technicians. Each approach will require adapting national protocols, training providers when point-of-care or near point-of-care tests are used and, when applicable, lab procedures and logistics, including the reorganization of sample flow, testing platform, and adjusting necessary supplies for sample collection.

Pooling samples from multiple anatomical sites can also have an impact on countries with national guidelines recommending different dosages and treatment schedules, depending on the anatomical site. In this case, there may be a need to retest samples from the different sites separately to prescribe the recommended treatment. If new samples need to be collected from positive individuals, it must be balanced against the risk of treatment delays and lost-to-follow-up patients. These concerns will not apply to countries following current WHO recommendations for the treatment of genital or anorectal chlamydial infection, for which doxycycline can be used in the same dosage in both cases as first line, or for gonorrhoea using dual therapy as the first line, when either no or insufficient data are available from local gonococcal antimicrobial resistance *(443, 444)*. However, due to growing gonococcal antimicrobial resistance to ceftriaxone and azithromycin, WHO is updating the treatment guidelines for *N. gonorrhoea* infections, which may have implications for the treatment of infection at different anatomical sites.

Research gaps

Based on the review of the evidence, a critical knowledge gap to be addressed is the accuracy of testing for *N. gonorrhoeae* – comparing oropharyngeal samples alone versus pooled with samples from other anatomical sites. Regarding the performance of pooled-sample testing, further studies are needed to define the optimal dilution of pooled samples for best accuracy, including optimal urine volume (when urine samples are used instead of swabs), and to understand the potential effects of the order of samples for pooling.

Additionally, there is a need to study the cost-effectiveness of pooling samples against different background prevalence of infections, and to model the optimal cut-off point for the utility of single-site pooled testing to maximise cost-effectiveness in different settings.

It is also critical to better understand the values and preferences of key population members who are cisgender women, transgender men and non-binary people assigned female at birth, as they were not included in the values and preferences research conducted for the development of these guidelines. Implementation research is important to support the adoption of multisite testing, including exploring the perception of those men who have sex with men interviewed as part of the values and preferences study, regarding the possibility of having biological samples collected from the three anatomical sites as a standard of care; namely, not requiring the disclosure of sexual practices to providers, has the potential to reduce perceived stigma and discrimination, and to increase access to care by men who have sex with men.

Finally, for countries using different treatment regimens for gonococcal and chlamydial infections or both based on anatomical site, it would be relevant to better understand the benefits versus harms of opening sample pools (retesting samples) after a positive result, considering potential treatment delays and lost-to-follow-up in different settings. Conducting an economic evaluation of retesting multiple sites in different contexts should also be considered.

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World Health Organization

UNAIDS

UNDP

UNFPA

UNODC
United Nations Office on Drugs and Crime

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE; HIV MEDICINE ASSOCIATION, a division of the INFECTIOUS DISEASES SOCIETY OF AMERICA; INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE; JENNIFER K. BRODY, MD; and CHRISTOPHER B. FOX, NP, *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION; THOMAS J. ENGELS, in his official capacity as the Administrator of the Health Resources and Services Administration; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., in his official capacity as Secretary of the U.S. Department of Health and Human Services, *Defendants*.	Case No.

DECLARATION OF JENNIFER K. BRODY, MD

I, Jennifer K. Brody, MD, hereby declare and state as follows:

1. I am over 18 years of age, of sound mind, and in all respects competent to testify.

2. I have personal knowledge of the facts set forth in this declaration and would testify competently to those facts if called to do so.

3. I am a plaintiff in the above-captioned case, bringing claims on behalf of myself and on behalf of my transgender patients.

4. I submit this declaration in support of Plaintiffs' Motion for Preliminary Relief under 5 U.S.C. § 705 and for a Preliminary Injunction, which seeks to prevent Defendants from giving effect to certain conditions relating to transgender people and gender-affirming medical care set forth in Ryan White HIV/AIDS Program ("Ryan White Program") Notices of Funding Opportunity issued or forecasted to be issued in 2026 and the 2026 Updated HRSA General Terms and Conditions, issued on March 11, 2026 (collectively, "the Challenged Conditions").

5. I oversee a Ryan White-funded HIV program serving people experiencing homelessness and other significant barriers to care through an integrated model that combines HIV treatment, behavioral health services, case management, housing support, and gender-affirming medical care. Many of our patients rely on Ryan White-funded services as their consistent source of healthcare. Ryan White funding supports not only HIV treatment itself, but the integrated and wraparound services necessary to keep patients engaged in care and virally suppressed. For our transgender patients living with HIV, gender-affirming medical care and affirming treatment environments are crucial components of effective HIV care. Without that care, patients are more likely to disengage from treatment, lose trust in providers, and experience interruptions in care that jeopardize their health and increase the risk of HIV transmission. The Challenged Conditions would dismantle this integrated model of HIV care we have relied upon for years, force providers to withhold medical treatment from transgender patients, undermine patient trust, worsen health outcomes, and threaten the continued operation and staffing of essential Ryan White-funded programs.

I. Background and Professional Role

6. I am a physician and hold both an M.D. and Master of Public Health. I serve as the Director of HIV Services at Boston Health Care for the Homeless Program ("BHCHP"), where I

lead clinical programs focused on the treatment and care of people living with HIV who are experiencing homelessness and housing instability.

7. I am a resident of Boston.

8. I am a member of the American Academy of HIV Medicine, the HIV Medicine Association, and the International Association of Providers of AIDS Care.

9. I have been an attending physician providing HIV care since 2009 and have seventeen years of experience in this field. I am board-certified in Internal Medicine and Addiction Medicine and am an American Academy of HIV Medicine-certified HIV Specialist. My clinical and academic work has focused on HIV care, health equity, and improving outcomes for structurally marginalized populations, particularly individuals experiencing homelessness.

10. In my role, I oversee and provide comprehensive HIV primary care to approximately 350–400 patients living with HIV, many of whom are experiencing homelessness or unstable housing. My work includes delivering care in nontraditional settings such as shelters, street outreach programs, and specialized clinics designed to meet patients where they are, in addition to more traditional clinical environments.

11. My patient population is predominantly composed of individuals from marginalized communities who face overlapping structural barriers to care. Approximately three-quarters of my patients are Black or Latinx, and approximately 7% are transgender, which is significantly higher than the proportion of transgender individuals in the general population, reflecting the disproportionate impact of HIV and related barriers to care on transgender communities. Many of my patients also experience co-occurring conditions, including substance use disorders, mental health conditions, and chronic medical comorbidities, all of which complicate engagement in consistent HIV care.

12. The services I oversee and provide include comprehensive HIV treatment and primary care, addiction medicine, behavioral health services, specialized nursing care, case management, and support groups. Since 2011, I have also provided hormone therapy to my transgender patients who need it as treatment for their gender dysphoria (also known as "gender-affirming medical care" or "gender-affirming hormone therapy") as part of my clinical practice.

13. The health services I provide are delivered through an integrated, multidisciplinary model that addresses both medical needs and the social determinants of health, such as housing instability, stigma, and access to basic resources, that are critical to achieving and maintaining HIV viral suppression.

III. BHCHP's Use of Ryan White Funding

14. The Ryan White Program is designed to provide comprehensive holistic clinical and support services to low-income people living with HIV.

15. In my experience, the Ryan White Program enables a model of care that is both clinically effective and humanizing. It recognizes patients as whole people and affirms their identities while addressing their medical and social needs.

16. As part of my practice through BHCHP, I rely on Ryan White funding under Parts A, B, and C.

17. BHCHP uses Part B funding provided through the Massachusetts Department of Public Health to fund a special outreach program for patients who struggle to stay engaged in care and take their HIV medications. This includes transgender patients with HIV who often feel stigmatized by healthcare providers or are less likely to adhere to their HIV care when their gender-affirming medical care needs are left unaddressed. BHCHP also used part B funds indirectly by

referring patients to our state AIDS Drug Assistant Program which supports access to medication coverage when needed.

18. BHCHP uses Part C funding to support critical staffing to the clinic, primarily nurses who provide intensive case management, counseling, and care navigation. It also supports portions of my administrative role, including quality improvement initiatives. Part C is used in case management, as well as medication education and adherence support with regards to our gender-affirming medical care services.

19. BHCHP uses Part A to fund medical case management, including for transgender patients, housing advocacy, rental assistance, and medical transportation.

20. Ryan White funding is deeply integrated into all aspects of care we provide. It supports both clinical services, including gender-affirming health services, and the wraparound services that enable patients to engage in and remain in care. Ryan White Funding is a majority of our grant-supported budget for the HIV program.

IV. Importance of Gender-Affirming Medical Care for my Transgender Patients with HIV

21. Gender-affirming care is an integral component of primary care for many of my transgender patients with HIV and is essential to effective HIV treatment.

22. Many of my transgender patients have experienced significant stigma and harm within the healthcare system. Providing gender-affirming medical care to these patients is often necessary to establish and maintain a therapeutic doctor/patient relationship. For many transgender people living with HIV, their primary health concern is access to the gender-affirming medical care that enables to them to live as themselves. Indeed, often, the only reason many of our transgender patients started coming to us for care is because they were seeking gender-affirming medical services.

23. Providing gender-affirming medical care also keeps people connected to HIV care and increases trust with the community. In my clinical experience, patients experiencing homelessness are particularly vulnerable to discontinuity in medication adherence. Without stable housing, safely storing medications and maintaining a daily regimen is already challenging. Removing gender-affirming medical care from the clinical setting would exacerbate these challenges by reducing patients' motivation to remain engaged in care, leading to missed medications, treatment interruptions, and increased risk of viral rebound.

24. Patients experiencing homelessness face significant structural barriers to maintaining consistent HIV care, including lack of stable transportation, limited access to communication (such as phones or internet), and competing priorities like securing food and shelter. These challenges make continuity of care difficult even under ideal circumstances. Gender-affirming medical care, when integrated into HIV services, helps stabilize engagement by addressing a core aspect of patients' identity and well-being, making it more likely that they will return for care and remain connected to treatment.

25. Every single one of our patients experiencing homelessness relies on Ryan White funded programs not only for HIV treatment, but also for wraparound services such as case management, mental health care, and referrals to housing and social services. These integrated services are critical to addressing the social determinants of health that directly impact HIV outcomes.

26. There are few, if any, alternative providers in Boston who can meet the complex needs of patients experiencing homelessness, particularly those who are transgender and living with HIV. As a result, if I am unable to provide my transgender patients with gender-affirming medical care within my practice, many of these transgender patients would have no realistic

pathway to obtain that care elsewhere. Although I could technically continue to provide HIV treatment alone, that is not how care functions in practice for this population. My patients often seek care from me precisely because I provide affirming, integrated services in a setting they trust. If I am unable to acknowledge and respect my transgender patients' identities within my practice, even if unconnected to the gender-affirming medical care, many of these transgender patients would feel discriminated against and be unlikely to remain in our care. Many of my transgender patients have experienced stigma or discrimination in traditional medical environments and are unwilling to engage with providers who lack the cultural competency to treat them holistically.

27. If I am unable to acknowledge and respect my transgender patients' identities and to provide them with gender-affirming medical care when they need it, my patients may lose trust in me and in the healthcare system more broadly, and they may disengage from care altogether.

V. Gender-Affirming Medical Care and the Ryan White Program

28. Because Ryan White funding has long supported comprehensive, patient-centered HIV care, including services necessary to meet the needs of HIV patients' co-occurring conditions, including for transgender patients, and realizing the clinical importance of gender-affirming medical care for this population, I obtained specialized clinical training in gender-affirming medical care, including the provision and management of hormone therapy, and incorporated these services into my practice in 2011.

29. In reliance on the Ryan White Program's longstanding directives and funding structure prioritizing medically underserved populations and populations disproportionately affected by HIV, we have intentionally developed and structured our model of care to meet the needs of transgender and gender-diverse people living with HIV. Consistent with Ryan White Program requirements, guidance, local planning priorities, and identified community needs, we

integrated gender-affirming healthcare and related supportive services into our HIV care delivery model.

30. In our practice, Ryan White funding enhances our ability to deliver integrated care by supporting the services and infrastructure necessary to provide gender-affirming medical care for those transgender patients with HIV who need it through Parts A, B, and C.

31. The Ryan White Program funds most of the clinical and support systems that make HIV care possible for our clinic, including case management, behavioral health services, and care coordination. All of the patients who receive gender-affirming medical care in our program do so as part of concomitant, fully integrated, Ryan White-funded services.

32. In many cases, gender-affirming medical care serves as an entry point into HIV care. Patients may initially seek care for gender-affirming medical services, and through that relationship, engage in HIV treatment. If gender-affirming medical care is restricted within these programs, it would disrupt this comprehensive model of care and further marginalize patients who already have limited alternatives.

VI. Impact of the Challenged Conditions on HIV Care

33. The Challenged Conditions, including prohibitions on acknowledging and respecting transgender people's identities and on the provision of gender-affirming medical care in connection with Ryan White-funded services, would have severe consequences for my patients.

34. Many of my HIV patients, particularly those experiencing homelessness, prioritize their most immediate and pressing needs. If gender-affirming medical care is their primary need and if I cannot provide it, they are unlikely to return for HIV care.

35. Similarly, transgender patients with HIV seek and need access to care, even if unrelated to gender-affirming medical care, that is affirming and respectful of their identities. If

am prohibited from acknowledging and respecting my transgender patients' identities, such as by using pronouns consistent with their identities, they are likewise unlikely to return for HIV care.

36. The Challenged Conditions would thus lead to disengagement from care; loss of viral suppression; increased risk of HIV transmission; and significant deterioration in mental health, including increased depression and suicidality.

37. In my experience, patients who lose access to routine HIV care and instead rely on emergency services experience worse health outcomes, causing increased strain on the healthcare system and other social impacts. This dynamic is particularly pronounced among patients experiencing homelessness, who already face significant barriers to accessing consistent outpatient care. Without stable access to HIV services, these patients are more likely to show up at emergency rooms with advanced or preventable conditions, including complications related to untreated HIV or interruptions in antiretroviral therapy, which are significantly more difficult to treat once they have progressed to that stage.

38. Emergency care settings are not equipped to provide the continuity, trust, or comprehensive services required for effective HIV management or gender-affirming medical care, resulting in fragmented treatment and poorer health outcomes. This shift not only undermines individual patient health but also increases overall healthcare costs and places additional burden on already strained emergency systems. Intermittent access to HIV medications through acute and emergency care settings also can contribute to viral resistance to medications which can make HIV more difficult to treat over time both at the individual and community level. Viral resistance can be transmitted to others, making treatment more complex and challenging at the time of diagnosis (often requiring more medications with more side effects and drug interactions) which can impact chances of viral suppression over the life course.

VII. Impact of the Challenged Conditions on My Ability to Provide Care

39. A prohibition on using Ryan White funding for gender-affirming medical care would force me to deny medically necessary care to my transgender patients, thereby denying the comprehensive care that Ryan White seeks to provide, and override my clinical judgment in ways that conflict with accepted standards of care. For my patients experiencing homelessness, this conflict is especially acute because they often have no alternative source of care; my clinic may be the only place where they can access both HIV treatment and gender-affirming health services in a coordinated, low-barrier setting. Denying this care would mean not only withholding necessary treatment but also removing a critical point of engagement that allows these patients to remain connected to the healthcare system at all.

40. This would cause significant moral and ethical distress to me. As a physician, I understand gender-affirming medical care to be medically necessary for many patients, and being unable to provide it would cause moral and ethical injury. This distress is compounded in the context of homelessness, where I routinely care for patients with profound unmet needs and limited options. Being forced to withhold care from patients who already face extreme marginalization and barriers to access would directly conflict with my professional obligation to provide equitable, evidence-based, patient-centered care.

41. Such a prohibition, along with any prohibition on my acknowledging and respecting the identities of my transgender patients, would also harm my ability to provide effective HIV care by damaging the trust and therapeutic relationships I have built with my patients. Among patients experiencing homelessness, trust is often fragile and must be built over time through consistent, respectful, and affirming care. Being able to access care that is affirming and inclusive of gender-affirming medical care is frequently a cornerstone of that trust. If patients

perceive that I am unable or unwilling to meet their basic healthcare needs, they may disengage entirely, leading to missed appointments, interruptions in antiretroviral therapy, and increased risk of viral rebound and forward transmission.

42. Even uncertainty or perceived restrictions on the ability to affirm patients and to provide them with gender-affirming medical care would be harmful. Providers avoid assessing, documenting, or addressing gender-related needs, which could compromise patient safety and continuity of care. For patients experiencing homelessness, who often receive care across multiple settings, including shelters, street outreach, emergency departments and acute care hospitals, accurate and complete assessments and documentation of any conditions is essential to maintaining continuity. Any reluctance to provide care that is needed, or to document conditions experienced and the need for such care, would exacerbate fragmentation, increase the risk of medical errors, and further destabilize already tenuous care relationships.

43. Operationally, such a policy would create confusion and disruption. Compliance with the Challenged Conditions would be difficult to implement without fundamentally altering core aspects of patient care, including standard assessments and treatment planning. In programs serving patients experiencing homelessness, where care is often delivered in flexible, non-traditional settings and must be responsive to complex, co-occurring needs, such restrictions would be particularly unworkable. They would interfere with integrated care models, strain limited clinical resources, and undermine the ability of providers to deliver comprehensive, coordinated services that are essential for both HIV treatment and overall patient stability.

VIII. Financial and Programmatic Impact of the Challenged Conditions

44. Ryan White funding is essential to the operation of my program. If we were found non-compliant with funding conditions, we could lose critical funding, particularly under Parts A, B and C. The majority of the grant funding for my clinic comes from Ryan White.

45. The Ryan White Program is a "payer of last resort," designed specifically to fill gaps for patients who have no other source of coverage or whose insurance is insufficient to meet their medical needs. Many of my patients have inconsistent access to health insurance and rely on the Ryan White Program to access core HIV treatment, medications, and support services that are not otherwise available to them through Medicaid, Medicare, or private insurance.

46. There is no comparable funding source that could replace these services if our Ryan White funding was lost. My transgender patients would have no other source of coverage outside of Ryan White to receive affirming HIV care and gender-affirming medical care. Even where patients have some form of insurance, Ryan White funding remains necessary to cover gaps such as cost-sharing, coverage limitations, and essential support services that enable patients to remain in care and achieve viral suppression. Without Ryan White-supported services, many patients would face reduced or interrupted access to care, as other parts of the healthcare system are not structured to absorb or replace this safety-net function.

47. Loss of such funding would jeopardize staffing, including nursing and case management positions, and could cause the program to collapse or be absorbed into less comprehensive primary care services.

48. This would significantly reduce access to specialized HIV care and support services for an already extremely vulnerable population.

IX. Public Health Impact of the Challenged Conditions

49. Prohibiting HIV care providers from acknowledging, affirming, and respecting their transgender patients and limiting access to gender-affirming medical care for transgender patients with HIV would undermine efforts to achieve viral suppression and control the HIV epidemic. In my clinical experience serving patients experiencing homelessness, affirming transgender patients' identities and gender-affirming medical care are often critical components of engagement in HIV treatment. When patients feel respected and affirmed, they are more likely to attend appointments, adhere to antiretroviral therapy, and remain in care - each of which is essential to achieving and sustaining viral suppression.

50. Limiting access to such care would harm not only transgender individuals. This impact would be especially severe for transgender patients experiencing homelessness, who already face intersecting barriers related to stigma, poverty, housing instability, and limited access to healthcare. These patients often rely on a small number of safety-net providers, such as BHCHP, for comprehensive and affirming care. Restricting gender-affirming medical care in these settings would further isolate an already underserved population.

51. The resulting disengagement from care would likely lead to increased HIV transmission, as well as worsening outcomes for other communicable and chronic conditions. Especially among patients experiencing homelessness, even short disruptions in care can result in loss of follow-up, treatment interruptions, and rapid clinical decline. In addition to HIV, many of my patients have co-occurring conditions - including hepatitis C, substance use disorders and treated or untreated mental illness - that require consistent management. Disengagement from care would therefore have cascading effects across multiple health conditions, increasing both individual and public health risks.

52. Broader impacts would include increased emergency room utilization, declining mental health, loss of employment, housing instability, and overall community harm. For patients experiencing homelessness, the healthcare system often serves as a primary point of stability and support. When access to comprehensive, affirming care is disrupted, patients are more likely to cycle through emergency departments and inpatient settings, rather than receiving preventive and ongoing care. This not only increases healthcare costs but also exacerbates mental health crises, undermines efforts to secure and maintain housing, and destabilizes already vulnerable communities.

X. Additional Harms Caused by the Challenged Conditions

53. The harms caused by the Challenged Conditions would be difficult or impossible to reverse. In my experience caring for patients experiencing homelessness, disruptions in care often have lasting consequences because re-engagement is extremely challenging once patients are lost to follow-up. When patients disengage due to a loss of affirming and comprehensive care, there is often no reliable way to reconnect them to services, particularly given the instability of their living situations and the limited availability of outreach resources.

54. Trust between patients and providers is hard-won and easily lost. Once patients disengage from care, they may not return. This is especially true for patients experiencing homelessness, many of whom have had repeated negative or stigmatizing encounters within the healthcare system. Establishing trust requires consistent, respectful, and affirming interactions over time. If that trust is broken, particularly by prohibiting acknowledgement and affirmation of a transgender patient's identity or by denying medically necessary gender-affirming medical care, patients may avoid not only my care but healthcare systems more broadly, making future engagement significantly more difficult.

55. Interruptions in HIV treatment can result in lasting health consequences, including disease progression and increased transmission risk. For patients experiencing homelessness, maintaining consistent access to antiretroviral therapy is already challenging due to factors such as unstable housing, lack of medication storage, and competing survival needs. Any disruption in care increases the risk of viral rebound, development of drug resistance, and progression of HIV-related illness.

56. In practical terms, when a patient stops or misses their HIV medications, the virus can quickly begin to multiply again, increasing the amount of the virus in their body. As the virus replicates, it can mutate and become resistant to the medications that were previously effective, making the disease harder to control and limiting future treatment options. At the same time, a rising viral load weakens the immune system, leaving the patient more vulnerable to serious infections and chronic complications that are more difficult to treat once they occur. These interruptions also undermine public health efforts to reduce transmission, as patients who are not virally suppressed are more likely to transmit HIV.

57. Patients may also experience severe psychological harm, including trauma, depression, and suicidality. Among patients experiencing homelessness, particularly those who are transgender, the burden of mental health conditions is already high due to chronic stress, stigma, and exposure to violence and discrimination. Access to care that is respectful and affirming and gender-affirming medical care are critical components of psychological stability and well-being for these patients. Removing access to this care would exacerbate existing mental health conditions, increase feelings of isolation and hopelessness, and heighten the risk of self-harm and suicidality, with consequences that may be immediate and enduring.

XI. Conclusion

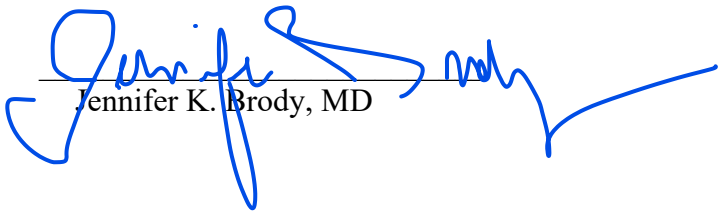
58. Based on my experience, providing care that is affirming and respectful of the identities of transgender patients with HIV as well as gender-affirming medical care are essential components of effective HIV treatment for my transgender patients with HIV. Conditioning Ryan White funds on not doing so would have immediate and harmful consequences for my patients.

59. Many of my transgender patients rely on integrated care, where HIV treatment and gender-affirming services are provided together in a trusted and affirming clinical setting. If that care is disrupted, I expect that some patients will disengage from treatment altogether. This not only harms the individual patient but also increases the risk of HIV transmission in the community. In my opinion, these disruptions will lead to preventable complications, and in some cases, could result in patient deaths.

60. Prohibiting Ryan White funding recipients from affirming and respecting the identities of transgender patients with HIV or the use of Ryan White funds for gender-affirming medical care would harm my transgender patients, undermine public health, and prevent me from fulfilling my obligations as a physician.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: June 8, 2026



Jennifer K. Brody, MD

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE; HIV MEDICINE ASSOCIATION, a division of the INFECTIOUS DISEASES SOCIETY OF AMERICA; INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE; JENNIFER K. BRODY, MD; and CHRISTOPHER B. FOX, NP, *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION; THOMAS J. ENGELS, in his official capacity as the Administrator of the Health Resources and Services Administration; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., in his official capacity as Secretary of the U.S. Department of Health and Human Services, *Defendants*.	Case No.

DECLARATION OF CHRISTOPHER B. FOX, NP

I, Christopher B. Fox, NP, hereby declare and state as follows:

1. I am over 18 years of age, of sound mind, and in all respects competent to testify.

2. I have personal knowledge of the facts set forth in this declaration and would testify competently to those facts if called to do so.

3. I am a plaintiff in this case, and I bring claims on behalf of myself and my transgender patients.

4. I submit this declaration in support of Plaintiffs' Motion for Preliminary Relief under 5 U.S.C. § 705 and for a Preliminary Injunction, which seeks to prevent Defendants from

giving effect to certain conditions relating to transgender people and gender-affirming medical care set forth in Ryan White HIV/AIDS Program ("Ryan White Program") Notices of Funding Opportunity issued or forecasted to be issued in 2026 and the 2026 Updated HRSA General Terms and Conditions, issued on March 11, 2026 (collectively, "the Challenged Conditions").

5. In this declaration, I explain that integrated primary healthcare is an essential component of HIV care. I emphasize the significance of providing gender-affirming medical care to my patients with HIV, drawing on two specific patient examples. I then describe how my clinic and patients utilize Ryan White Program funding. I also highlight the impossibility of segregating gender-affirming medical care in a clinic that relies on these funds and discuss the potential consequences for myself, my clinic and colleagues, and my transgender patients if there were restrictions on the ability to acknowledge our transgender patients and the provision of gender-affirming medical care under the Ryan White Program.

I. Background and Professional Role

6. I am a Nurse Practitioner and an Assistant Professor of Medicine in the Division of Internal Medicine and Geriatrics at Oregon Health and Science University ("OHSU"), where I provide patient care, teach, and conduct research. I am also a faculty member of the Oregon AIDS Education and Training Center/Oregon Primary Care Association.

7. Before joining OSHU in 2016, I was a Nurse Practitioner at the University of California San Francisco Medical Center and an Assistant Clinical Professor at the University of California San Francisco School of Nursing. I also worked as a volunteer clinician and clinical staff nurse for the San Francisco AIDS Foundation and as a Community Health Specialist for the San Francisco Department of Public Health.

8. I received my Master of Science in Nursing as an Adult Nurse Practitioner specializing in HIV/AIDS at the University of California San Francisco.

9. I am credentialed as an HIV Specialist by, and am a member of, the American Academy of HIV Medicine.

10. I serve as a clinician in the HIV clinic at OHSU. At the clinic, I provide primary care to patients with HIV. Although the majority of my patients live in Portland, I also use telemedicine to reach my HIV patients who live in rural Oregon to increase accessibility and reduce the frequency of trips they have to make to Portland for in-person clinical visits with me. For many of my rural patients, I provide the closest competent and accessible HIV care. I provide HIV primary care for approximately 300 patients, HIV treatment consultations for approximately 75 patients, and HIV prevention consultations for approximately 50 patients.

11. As part of my practice, I have several transgender patients to whom I provide not only HIV care but also hormone therapy as treatment for their gender dysphoria (also known as "gender-affirming medical care" or "gender-affirming hormone therapy").

12. In my faculty role with the Oregon AIDS Education and Training Center, my focus is on educating the HIV workforce. I provide regular educational presentations and individual mentoring on HIV prevention and treatment to healthcare providers statewide. And I founded and lead a monthly Community of Practice for Nurses who serve patients with HIV.

13. Likewise, my scholarship focuses on HIV prevention and treatment. My current research focuses on the implementation of long-acting antiretroviral therapy. I also wrote textbook chapters in Collins-Bride & Saxe's *Clinical Guidelines for Advanced Practice Nursing*, namely, the chapters titled *HIV Infection in Adolescents and Adults* and *Primary Care of HIV-Infected*

Adults. The Collins-Bride & Saxe's *Clinical Guidelines* also include chapters specific to the care of transgender patients with HIV.

14. From 2013 to 2016, I received a Human Resources & Services Administration grant called HIV/AIDS Primary Care Capacity in Nursing for curriculum development.

II. Integrated Primary Healthcare for HIV Patients

15. Fundamentally, HIV is a virus that attacks a person's immune system. Antiretroviral therapy, what people typically think of as HIV medication, reduces the amount of HIV in the blood, known as the viral load. When a patient with HIV has an undetectable viral load, they will not sexually transmit HIV to others.

16. Because HIV attacks the immune system, people with HIV are susceptible to many different infections and diseases throughout their lives. And because of the stigma and other social factors associated with people who have HIV, they are also likely to require healthcare associated with mental health challenges, substance use disorders, and other diseases prevalent in populations associated with HIV. Some who do not work within the field of HIV care believe that HIV care is focused solely on HIV medication management, but that could not be farther from the truth.

17. The field of HIV care has trended towards integrating HIV care with all primary care because this model has proven very effective for HIV patients. However, with many HIV patients, our visits focus on care for comorbidities—in particular, their chronic health conditions or mental health issues. A lot of our work is helping people navigate those other health conditions, such as management of diabetes, hypertension, cardiovascular disease, and other bread-and-butter issues of primary health care. This is important because it motivates our patients to show up and stay engaged with their HIV medication management.

18. If an HIV specialist takes care of the primary health needs of an HIV patient, the patient will have better outcomes. For instance, within HIV medicine, cardiovascular risks are an important part of patient care. People with HIV have heightened cardiovascular risks because of chronic inflammation, exposure to prior drug therapies with harmful cardiovascular effects, and lifestyle factors like smoking or substance use. Integrated care enables HIV providers to proactively monitor and treat these risks within the context of HIV treatment, leading to improved long-term health outcomes and reduced mortality. Therefore, HIV specialists typically focus on the cardiovascular aspects of their patients' primary health care.

19. Another benefit of integrated primary care is the providers' ability to monitor polypharmacy issues. People with HIV often take multiple medications for HIV and co-occurring conditions, increasing the risk of adverse drug interactions and side effects. The literature is clear that co-locating HIV care with primary care, including gender-affirming medical care, is beneficial for our patients. It allows a single clinical team to coordinate prescribing decisions, monitor for drug interactions, and adjust treatment in real time.

20. Restricting integrated primary care would undermine these clinical safeguards by fragmenting treatment, increasing the risk of harmful drug interactions, and undermining patients' engagement in their care. Further, this would disrupt the coordinated, patient-centered care that is essential to achieving optimal health outcomes for people living with HIV.

III. Importance of Gender-Affirming Medical Care for Transgender Patients with HIV

21. The clinic operates under a care model that ensures we provide competent HIV care to underserved populations, as is mandated under the Ryan White Program.

22. Several of my patients are transgender. For most of my transgender patients, I am their primary care provider. At OHSU, we have strong values guiding how we take care of our

transgender patients. Our electronic records reflect those values, and we make sure to respectfully record and use a patient's name, gender identity, and pronouns.

23. Gender dysphoria is a serious medical condition characterized by the clinically significant distress that a transgender person may experience because of the incongruence between their gender identity and their birth-assigned sex. It is codified as a diagnosis in the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, 5th edition, Text Revision.*

24. Well-established, evidence-based clinical guidelines, such as those published by the World Professional Association for Transgender Health and the Endocrine Society, provide for the multidisciplinary care of transgender individuals and describes criteria for medical interventions to treat gender dysphoria, including gender-affirming hormone therapy. The goal of medical treatment for gender dysphoria is to eliminate clinically significant distress by helping a transgender person live in accordance with their gender identity. The provision of gender-affirming medical care is widely accepted within the medical community, including by the vast majority of major medical organizations in the United States.

25. If left untreated, gender dysphoria can result in debilitating anxiety, severe depression, self-harm, and even suicidality.

26. At our clinic, beyond hormone therapy and surgical referrals, our gender-affirming care provides support to the whole person. Their experience with gender and holistic support is an integral part of their experience as a patient.

27. For example, I care for a transgender woman in her 30s living with HIV who suffered a life-threatening portal vein blood clot—a clot in the vein carrying blood from the intestines to the liver. Her hematologist concluded the clot was likely related to estradiol and

advised that she should never use hormone therapy again. From a traditional medical standpoint, that recommendation was understandable: avoid estrogen permanently to reduce the risk of another potentially fatal clot. But that recommendation failed to account for another serious risk—the harm caused by abruptly ending gender-affirming medical care that was addressing the patient's gender dysphoria. For this patient, estradiol was not an optional treatment. It was medically necessary treatment to address the distress associated with her diagnosed gender dysphoria and central to the affirmation of her identity, emotional stability, and overall well-being. Removing it entirely carried its own profound mental and physical health consequences, which would have negatively affected her HIV care. Instead of treating the issue as a simple contraindication, the patient and I approached it through shared decision-making. We openly discussed both risks: recurrence of a dangerous clot versus the consequences of terminating gender-affirming medical treatment. Ultimately, we chose a safer compromise by switching her from oral estradiol to a low-dose transdermal patch, which is associated with a lower clotting risk. The patient was deeply grateful to work with a provider who understood all of her medical needs and who respected her priorities.

28. This example demonstrates that gender-affirming medical care is not ancillary medicine. HIV care and gender-affirming medical care are medically necessary care that must be provided considering the whole person and their needs and priorities. Providers who understand this can help patients safely navigate complex risks, while providers who do not may unintentionally cause serious harm by ignoring what is at stake. In this case, the patient was at risk of losing trust in the medical system if she were required to end her gender-affirming care. Because I took care of my transgender patient's medical needs, she trusts me and has continued to show up for her HIV care.

29. I also care for a transgender woman in her 20s living with HIV, whom I first met shortly after she was diagnosed with HIV. Soon after we met, she disengaged from care. She missed follow-up visits and became unreachable for nearly a year. During that time, clinic staff funded through the Ryan White Program, including our nurse and medical case manager, continued persistent outreach rather than allowing her to fall through the cracks. When we finally reconnected, the underlying reasons became clear: the patient had been struggling with depression and methamphetamine use, both related to stigma from her HIV diagnosis. She had recently stopped using meth and wanted to re-engage in care. I managed her gender-affirming hormone therapy as part of her HIV care, reducing barriers by consolidating healthcare treatment in one place. Our social worker helped her qualify for breast augmentation surgery. Importantly, our nurse was able to connect her gender-affirming goals with her medical care, explaining that HIV viral suppression would likely be necessary for surgery. That goal became a powerful motivator. Over the past eight months, the patient has re-engaged successfully. She started long-acting injectable HIV treatment, is consistently attending medical appointments, and has an undetectable viral load. She obtained her mental health support letter, remains adherent to hormone therapy, and has completed her surgery consultation with surgery anticipated in the coming months.

30. This example illustrates that gender-affirming medical care can be a critical pathway to engagement in life-saving HIV treatment. For some patients, access to care that is affirming and respectful of their identities and to transition-related care is not separate from HIV care—it is the reason they return, stay connected, and achieve stability. When providers understand that, being respectful and affirming of a transgender patient's identity and providing gender-affirming medical care become tools for improving adherence, viral suppression, mental health, and long-term outcomes.

IV. Role of the Ryan White Program in Supporting Gender-Affirming Care

31. Working at an HIV clinic means that funding from the Ryan White Program is embedded in the infrastructure of our clinic. At our clinic, we rely on Ryan White Part A to fund the salary of our HIV clinic nurse. Without this funding, I'm not sure how we could keep her. She is the hub of our clinic, and she is the person that our patients work with to receive care. She is credentialed through the Association of Nurses and AIDS Care, and she understands the complexities of the medical therapies our patients receive. Our nurse knows our patients personally, communicates with them through the patient portal for me, and her presence makes a concrete difference in whether they show up for their appointments and how they follow their medical regimens. Our patients, including our transgender patients, must interact with her to receive expert care at our clinic. Our HIV clinic nurse teaches them about their hormone therapy and helps with referrals for surgery. She also monitors for medication side effects, provides counseling on self-management strategies, teaches self-injection techniques, provides counseling to support treatment adherence, flags abnormal test results, discloses laboratory and other test results to patients and counsels on their meaning, schedules follow up appointments and provides reminders, follows up when patients miss appointments to get them rescheduled or trouble-shoot attendance barriers like lack of transportation, coordinates care across the complicated health system, including advocating for the patient to providers at OHSU and in the community, and builds patient trust in the healthcare system by approaching patient care with an expert understanding of the specific issues and challenges that transgender people with HIV experience on a daily basis. I would not be able to provide primary care, including gender-affirming care, to our transgender patients without the support of our clinic nurse.

32. At OSHU, we also receive Ryan White Parts A and B funds through Partnership Project, which is our medical case management program. This program helps people stay connected to care, provides insurance assistance, and helps manage referrals to mental health and substance use treatment, housing, and more. It specifically helps support people in accessing hormone therapy and becoming appropriate surgical candidates, such as ensuring that patients have access to housing while recovering from gender-affirming surgery. This medical case management program is required to keep transgender patients connected to their HIV and gender-affirming care treatments. And I rely on it to provide primary care, including gender-affirming care, to my patients.

33. Ryan White Part B also funds the state program "Care Assist." Some of our patients use Care Assist funding to cover what is not covered by other forms of health insurance.

34. Providers at our clinic, including myself, also benefit from the use of Ryan White Part F funds to support workforce development.

V. Impact of Prohibiting Gender-Affirming Care

35. Logistically, I do not know how it would work to lose our Ryan White program funding for gender-affirming medical care or how to operationalize a policy that prohibits us from acknowledging, affirming, or respecting the identities of my transgender patients. This would be the first time we would need to discriminate based on the person who is receiving care, which is something our institution would not do.

36. I do not know how I would advise my clinic nurse and medical case management program staff. For example, can our nurse still teach our transgender patients how to do injections for hormonal therapy? And if we somehow found funding for these functions, although I am not aware that any such funding exists, to fund a non-Ryan White nurse to take care of just our

transgender patients, our patients would be at risk of harm without the special HIV expertise of Ryan White nurses. It seems impossible to provide my patients with appropriate gender-affirming care and HIV care without Ryan White-funded personnel.

37. There is already an HIV workforce shortage. We need to increase the number of doctors, nurse practitioners, physician associates, nurses, social workers, case managers, pharmacists, and others who know how to care for people with HIV.

38. Traditionally, co-location of gender-affirming medical care and HIV care has been the standard of care because it improves HIV outcomes. Co-location of care requires providers who are trained in both HIV and gender-affirming medical care. If the gender-affirming medical care part is removed, a generation of providers may never get the experience of managing hormone therapy, counseling patients about surgical procedures, or offering transgender-specific health screenings. This will degrade the HIV specialty profession for all healthcare disciplines and lead to a profound loss of professional knowledge over time. A generation of new providers may lose the ability to provide what is now considered the standard of care.

39. I also do not know how my colleagues at our clinic and I can comply with the Challenged Conditions' prohibition while acknowledging, affirming, and respecting the identities of our transgender patients. If we cannot continue to respectfully record and use a patient's name, gender identity, and pronouns, it is likely that our transgender patients would stop coming and would drop off from all care, including HIV care. But if we do, we risk losing all Ryan White funding.

40. The restrictions created by the Challenged Conditions will erode trust in the healthcare system. Exclusion of gender-affirming medical care and forbidding affirmation of their identities will cause many transgender patients to lose trust in their healthcare providers and the

clinic in general, leading to a lack of engagement in healthcare and avoidance of dealing with acute or chronic illness, including the cessation of HIV treatment. When patients do show up for care, they may not feel like they can be open and honest with their healthcare providers about symptoms, behaviors, and healthcare needs. Lack of honest communication leads to misdiagnosis, missed diagnosis, not being offered preventative health services like screenings, and other adverse health outcomes.

41. These restrictions will cause increased emotional distress and decreased self-esteem. Although all transgender people have unique life experiences, most of my patients have experienced discrimination and prejudice related to their gender at some point. Many have experienced physical or emotional violence, and, commonly, they have experienced rejection by family and friends. The combined toll of these experiences, along with the stigma associated with an HIV diagnosis, contributes to frequent mental health struggles like depression, suicidality, feelings of low self-worth, and low self-efficacy. If I had to stop providing gender-affirming medical care, or even stop respecting my patients' dignity by using pronouns that cause them harm, that would only make it more likely for them to drop out of care.

42. Without access to our Ryan White nurse and case managers, my transgender patients who become disengaged in care may not return to care until they have experienced a life-threatening complication of their HIV infection. When a patient disengages from care, too often they show up in the hospital with an AIDS-related illness from which they may not recover or could lead to severe disability.

43. And if all HIV clinics that are funded by Ryan White funding stop providing gender-affirming care to their transgender patients, some or many of those patients will likely stop receiving HIV care. Besides the adverse effects on the health of those individual patients, it will

increase the viral load population-wide and increase transmission rates. It will affect our clinic and our ability to provide the same level of care to each of our patients because we do not close our doors; we respond to the need. It would mean that I would have to work more hours, our patients would have decreased access, there would be delays in care, and my colleagues and I would all feel the increased stress. And we would all face an increased potential for burnout. We already do not have enough HIV providers due to losses from retirement and COVID. And a malfunctioning HIV system would require more funding. A restriction on gender-affirming care would disrupt the whole HIV care system.

44. The restrictions created by the Challenged Conditions, including prohibiting the use of Ryan White funds for gender-affirming medical care for my HIV patients, would cause me to question my ability to do the work that I am doing. I spend the vast majority of my work hours providing primary care. And there is a huge emotional stress to not being able to provide proper care to my patients. It is distressing for us as providers. But if I burned out and left HIV care, I would feel stress and guilt for abandoning the people who need me most. I really dread the emotional challenges that this ban would bring to my daily life.

45. I believe it is my ethical responsibility to continue providing the same integrated care to my patients that takes into account all their health needs as I have done to that and to be affirming and respectful of my patients. The restrictions created by the Challenged Conditions are contrary to my ethical responsibilities and my oath as a healthcare professional.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: June __, 2026

_____
Christopher B. Fox, NP

I declare under penalty of perjury that the foregoing is true and correct.

Dated: June 8, 2026

Christopher B. Fox, NP

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE; HIV MEDICINE ASSOCIATION a division of the INFECTIOUS DISEASES SOCIETY OF AMERICA; INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE; JENNIFER K. BRODY, MD; and CHRISTOPHER B. FOX, NP, *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION; THOMAS J. ENGELS, in his official capacity as the Administrator of the Health Resources and Services Administration; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., in his official capacity as Secretary of the U.S. Department of Health and Human Services, *Defendants*.	Case No.

DECLARATION OF DANIELLE DOE, NP

I, Danielle Doe, NP, hereby declare and state as follows:

1. I am over 18 years of age, of sound mind, and in all respects competent to testify.

2. I have personal knowledge of the facts set forth in this declaration and would testify competently to those facts if called to do so.

3. I am offering this declaration as a member of the American Academy of HIV Medicine, which is bringing claims on behalf of their members, like me, and on behalf of the transgender patients of their members, like mine.

4. Danielle Doe is a pseudonym. I am submitting this declaration under a pseudonym to protect my privacy and to protect my family and me from harassment, violence, and retaliation.

5. I submit this declaration in support of Plaintiffs' Motion for Preliminary Relief under 5 U.S.C. § 705 and for a Preliminary Injunction, which seeks to prevent Defendants from giving effect to certain conditions relating to transgender people and gender-affirming medical care set forth in Ryan White HIV/AIDS Program ("Ryan White Program") Notices of Funding Opportunity issued or forecasted to be issued in 2026 and the 2026 Updated HRSA General Terms and Conditions, issued on March 11, 2026 (collectively, "the Challenged Conditions").

6. I also submit this declaration in support of Plaintiffs' Motion for Leave to Submit Pseudonymous Declarations and for a Protective Order.

7. In this declaration, I describe how my clinic and patients use Ryan White Program funding to provide comprehensive HIV care. I explain how gender-affirming medical care is integral for our transgender patients' primary care and essential for their HIV services, and that their lives and health are improved by the comprehensive care made possible by the Ryan White Program. Disruption to structured care coordination would cause disease progression, preventable mortality, and the loss of continuity of care. As a result, public health would be in danger.

I. Background and Professional Experience

8. I am a Nurse Practitioner with full practice authority to practice advanced nursing in Massachusetts.

9. I work at a clinic in central Massachusetts.

10. I have provided HIV care and gender-affirming medical care since 2022. I also completed a community-based HIV fellowship funded in part by the Ryan White Program.

11. I am an HIV specialist credentialed through and a member of the American Academy of HIV Medicine ("the Academy").

12. I provide HIV care and gender-affirming medical care funded in part by the Ryan White Program.

13. My clinic provides comprehensive HIV treatment and primary care to approximately 400 patients living with HIV, many of whom are experiencing economic instability. The clinic provides gender-affirming medical care to all of our transgender patients with HIV. These services are delivered through an integrated, multidisciplinary model that addresses both medical needs and social determinants of health, such as housing instability, stigma, and access to basic resources, which are critical to achieving and maintaining viral suppression.

II. Need for Pseudonymity

14. I am submitting this declaration under a pseudonym because I reasonably fear professional and personal retaliation if my identity is publicly disclosed, as well as subject me, my family, and my patients to a substantial risk of harm, harassment, and retaliation.

15. Although Massachusetts generally supports access to HIV care and gender-affirming medical care, people in Massachusetts are not immune from the current national climate surrounding these issues, which is highly contentious. For example, I am aware of people making death threats against healthcare providers who provide gender-affirming medical care in

Massachusetts.[1] Similarly, just a few months ago, a member of the Massachusetts Commission on the Status of Women was subjected to harassment and death threats because she was transgender.[2]

16. Indeed, providers who serve transgender patients, particularly those relying on federal funding streams like the Ryan White Program, have increasingly been subject to harassment, targeted complaints, and threats to their employment and licensure.

17. Accordingly, I am concerned that public identification would endanger my safety as well as the safety of my family, my colleagues, and my patients.

18. I am also concerned that public identification could expose me to scrutiny or adverse action by federal agencies, jeopardize my institution's funding, and subject me to harassment that would interfere with my ability to provide care. Based on media reports, I am aware that the current federal administration has targeted those who support transgender care or oppose their priorities.

19. For these reasons, I believe it is necessary to proceed anonymously while still providing truthful and accurate information to the Court.

20. I am willing to disclose my identity to the Court as directed under a protective order.

III. The Ryan White Program Funding

21. The Ryan White Program is designed to provide comprehensive clinical and support services to low-income people living with HIV.

22. The clinic receives Ryan White funding under Parts B, C, D, and F.

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[1] *See* Leo Sands, *Man charged with threatening doctor caring for trans patients, LGBTQ kids*, The Washington Post (Dec. 4, 2022), https://tinyurl.com/4a8h7x8u [https://perma.cc/HF5P-CKPN]; Jessica Bartlett, *Boston Children's faced months death threats and hate mail. Here's how staff members are coping*, The Boston Globe (Dec. 3, 2022), https://tinyurl.com/ycxj2pwu [https://perma.cc/U9ZB-ZV25].

[2] *See* Sharman Sacchetti, Gov. Healey, Mass. Commission on the Status of Women back member amid transphobic attacks, WCVB (Nov. 17, 2025), https://tinyurl.com/bddvu8v7 [https://perma.cc/4C25-WQS7].

23. The clinic benefits from Ryan White Part C, which largely funds the case management team of nurses and staff. Our clinic's Ryan White-funded nurses are the bedrock of our HIV practice; they are deeply knowledgeable in HIV, administer vital HIV care, and have meaningful long-term relationships with our HIV patients. They provide comprehensive case management, which often includes going the extra mile. For example, our nurses call patients repeatedly to confirm appointments and labs, escort patients to pick up their medication from the hospital system's pharmacy, and sit with patients before they receive surgery.

24. The case management nurses and staff are vital to patients scared of engaging with the medical system—especially transgender patients who have historically experienced discrimination in medical settings—because they provide a sense of safety, making healthcare feel accessible. Our case managers are the foundation of the care we provide, and they are crucial for the health of our patients and my job as a provider.

25. The clinic also benefits from Ryan White Part B, which funds the Massachusetts HIV Drug Assistance Program.

26. Ryan White Part D, a funding stream that serves women of childbearing age and young people up to age 26, funds MassCARE, a system that supports our patients.

27. And the clinic benefits from Ryan White Part F funds, which contribute to our hospital system's HIV care education. Specifically, Part F funds supported my fellowship's focus on HIV education, and through that work, particularly in learning about populations disproportionately affected by HIV, it became essential to further engage with colleagues and external resources to deepen my understanding of gender-affirming medical care.

28. Ryan White funding is deeply integrated into all aspects of the care I provide. It supports both clinical services and the wraparound services that enable patients to engage in and remain in care.

IV. Importance of Gender-affirming Medical Care for Transgender Patients with HIV

29. At the clinic, we co-locate our services to help our patients live physically, mentally, and socially healthy lives. We provide a holistic, all-encompassing approach to medical care that covers the full spectrum of a patient's needs. When we co-locate services, we improve access to care and support engagement in treatment, which helps reduce HIV transmission and meet expected standards of care.

30. Gender-affirming medical care is an integral part of primary care for transgender patients and supports optimal HIV-related health outcomes. Transgender patients benefit from receiving both primary care and HIV care from a single competent and affirming provider.

31. If a component of this comprehensive approach were removed, it would force fragmentation of care and disproportionally impact patients with limited financial resources. It is imperative that patients stay engaged in care for both their health and the community's health.

32. In my experience, access to gender-affirming medical care as part of comprehensive healthcare motivates transgender patients to become engaged with and remain in HIV care. Providing gender-affirming medical care is necessary to establish the provider-patient relationship and begin building trust because many of our transgender patients, who frequently experience discrimination in healthcare settings, prioritize gender-affirming medical care over other areas of healthcare and may avoid healthcare settings altogether if it is not tied to supporting this care. When transgender people come to me to establish gender-affirming medical care, it is much easier to simultaneously provide them with HIV care.

33. My transgender patients who routinely attend appointments for gender-affirming medical care maintain viral suppression, which keeps them healthy and prevents HIV transmission.

V. One of My Patients Exemplifies the Importance of Ryan White Funding for Gender-Affirming Medical Care

34. I am the primary care provider for a transgender woman in her early 40s whom I have followed for 2.5 years after she relocated to the area and re-engaged in HIV care following nearly eight years out of treatment. At the time of re-engagement, she had also been without gender-affirming hormone therapy, having lost access during relocation due to the scarcity of providers offering co-located HIV and gender-affirming care.

35. She re-presented with advanced HIV following hospitalization for Pneumocystis jirovecii pneumonia, an AIDS-defining opportunistic infection reflecting severe immunosuppression. She had already sustained significant end-organ damage, including bilateral avascular necrosis of the hips and retinal detachment resulting in partial blindness. Despite restarting antiretroviral therapy and improving adherence, she later developed additional HIV-associated complications, including Kaposi sarcoma and multicentric Castleman disease, reflecting the long-term consequences of advanced untreated HIV.

36. Her care is among the most complex I manage. She follows with oncology, palliative care, orthopedics, and ophthalmology, and coordination across these services would not be manageable without strong system-level support, particularly given her blindness, chronic pain, significant mobility limitations, and inability to drive.

37. Ryan White–funded case management is central to her care. Her case manager coordinates across specialties, helps manage insurance and medication issues, facilitates communication between providers, and arranges transportation through a community-based

transport system. Without this level of support, she would be at high risk of disengaging from care, as has happened previously.

38. Her engagement is not driven by antiretroviral therapy alone. It is built on trust, specifically the ability to receive HIV care, behavioral health services, social support, and gender-affirming hormone therapy within a single affirming clinical environment. After spending years outside the medical system due to a lack of safe and competent care, that integration has been key to her re-engagement and stability.

39. Policies that restrict the ability to provide care that is affirming to our transgender patients or to provide gender-affirming medical care within Ryan White–supported settings would disrupt this model. For patients like her, the impact would not just be loss of hormone therapy and HIV care that is respectful of her identity, but fragmentation of care into separate systems. That would mean additional providers, more administrative burden, possible insurance issues, and loss of established clinical trust. For someone with her level of medical complexity, each added barrier increases the risk of falling out of care.

40. The Ryan White Program infrastructure that supports her transportation, case management, adherence, and specialty coordination also enables this integrated care model. These supports are not separate from her medical care. For this patient, with advanced HIV and significant dependence on structured care coordination, disruption of this system risks more than inconvenience. It risks treatment interruption, disease progression, preventable mortality, and loss of continuity with a provider who knows her full story.

VI. Impacts of Prohibiting Gender-affirming Medical Care

41. If I lose the ability to provide affirming care that is respectful of my transgender patients who rely on the Ryan White Program and/or to provide gender-affirming medical care

through the Ryan White Program, the impact on my patients and the broader public health would be catastrophic.

42. Building trust is essential to keep a patient in care—especially for transgender patients and those living with HIV who experience higher rates of discrimination in healthcare settings. In fact, transgender patients' viral suppression is associated with supportive clinical relationships. In my experience, when a provider is hostile or disrespectful to a transgender person's identity, the patient is less likely to return for care. This means that they may not get the additional medical treatment they need, which can lead to worsening health outcomes, including symptomology and ultimately higher viral loads.

43. My clinic works very hard to maintain patient trust and signal to new patients that we respect transgender identity. For example, staff members wear pronoun pins, we display gender-inclusive flyers in our clinical space, and we ask for sexual orientation and gender identity data on medical intake forms. Our staff is also trained in transgender identity competency, and our case managers have developed long-term relationships with transgender patients.

44. If the Challenged Conditions' prohibitions on respecting transgender patients' identities and the provision of gender-affirming medical care go into effect, they will obliterate the trust my clinic works so hard to build with transgender patients. For example, we have one nurse case manager who has been doing HIV work for over 30 years. This longevity has earned deep trust with our patients. I anticipate that the sudden loss of a key part of their healthcare will lead transgender patients feeling betrayed by their providers and to disengage care with us altogether. As a result, they will experience a disruption of their HIV care.

45. Disruptions in HIV care can cause serious health consequences. When patients fall out of HIV care, our hospital system sees an increase in them not adhering to their prescribed HIV

medication, which can lead to opportunistic infections, higher rates of emergency department utilization, and hospitalization. It can also lead to higher rates of community HIV transmission**.**

VII. Impact on Massachusetts

46. Massachusetts has developed a comprehensive, data-driven HIV response that depends on the Ryan White Program to provide integrated care to people living with HIV, particularly those who are low-income, uninsured, or underinsured. In the Boston Eligible Metropolitan Area ("EMA"), which includes Bristol, Essex, Middlesex, Norfolk, Plymouth, Suffolk, and Worcester counties, Ryan White funding supports a coordinated system of care designed to meet the needs of the populations most affected by HIV through an Integrated Care Plan. A copy of Massachusetts and Boston's EMA integrated HIV/AIDS prevention and care plan is attached hereto as **Exhibit A**.

47. In Massachusetts, HIV care for transgender patients is not delivered in isolation. Rather, it is provided through integrated care models that combine HIV treatment with behavioral health services, case management, housing support, and, where appropriate, gender-affirming medical care. A copy of Boston's EMA Ryan White Part A prevention and care plan is attached hereto as **Exhibit B**.

48. A federal restriction prohibiting providers from respecting transgender patients' identities as well as the use of Ryan White funds for gender-affirming medical care would directly undermine this integrated system. The Integrated Plans are premised on coordination across funding streams and service categories to eliminate gaps in care. The restrictions would force providers to fragment care, exclude necessary services for a defined population, and create gaps that the Integrated Plans are specifically designed to prevent.

49. The disruption would be particularly acute where the clinic is located because the majority of people living with HIV in Massachusetts reside in or near this area and receive services through Ryan White–supported providers.

50. Moreover, because Ryan White is a payer of last resort, many patients in Massachusetts who rely on this program have no meaningful alternative source of care. The Integrated Plans assume the continued availability of Ryan White–funded services to fill gaps in coverage and ensure continuity of care across systems. Removing a critical component of care from that system would leave many patients without viable options.

VIII. Impact on Our Ability to Provide Care

51. This restriction puts our medical institution in the impossible position to decide which medical care to cut, but this decision is heartbreaking. Transgender patients' lives and health are no less important than non-transgender plaintiffs.

52. If these restrictions go into effect, our clinic will be forced to discontinue providing gender-affirming medical care for Ryan White patients in order to continue participating in the Ryan White Program.

53. Personally, it would be devastating if I could not provide gender-affirming medical care for the patients who need it. I believe that patients should receive the proper care—including gender-affirming medical care—to live healthy lives. It would be horrible to discontinue this care for no justified medical reason. I would feel that the medical system had completely failed our patients, and with a finality that would make me feel discouraged about my job too.

54. One of my colleagues shared that she will leave her job if this restriction goes into effect. She said that she staked her profession on providing gender-affirming medical care and could not practice ethically as a medical practitioner with this restriction in place because it would

be a betrayal of both her own conscience and patients. She does not know what she would do next, but she said that staying in her job is not an option because doing so would be an abandonment of her personal and professional values.

55. Moreover, the restriction prohibiting providers from respecting transgender patients' identities is so unclear that our clinic is unsure how to implement it. We do not know if our nurse case managers could even call transgender patients regarding their HIV care. We do not know the boundaries of this restriction and our hospital system is likely to take a conservative approach, which will ultimately push transgender people further out of care.

56. This restriction would also accelerate a chilling effect on talking about gender-affirming medical care in our medical system. Our clinic is already operating in an environment of heightened concern about potential scrutiny related to recognizing transgender patients for who they are. As a result, providers may be hesitant to speak openly about gender-affirming medical care due to possible political or legal implications. No other class of patients faces this level of caution or indirect pressure around discussion of basic medical care.

57. This chilling effect is not limited to my hospital system. For example, a colleague shared that at a conference panel focused on HIV care and related to the Ryan White Program, panelists refused to answer a question about drug interactions with gender-affirming hormone therapy due to fear of backlash. After informing the audience that the panel could not say anything, the panelists turned over the question and answer to the audience to crowd source an accurate medical answer to the important question. Questions of drug interactions are not political; they are vital for our understanding as medical providers to administer competent care.

IX. Harms Caused by the Challenged Conditions

58. The harm caused by the Challenged Conditions' restriction would be difficult or impossible to reverse. It would destroy patient trust carefully and diligently built by our team over the course of many years. In my experience, once trust is lost, it becomes significantly more challenging to re-engage patients in any kind of care.

59. As a result, patients would experience a disruption in their gender-affirming medical care and HIV care. Many would no longer be able to receive gender-affirming medical care from a non-Ryan White provider due to their economic instability and would cease HIV care entirely. The result would be a patient population who experiences worse health outcomes and a potential community-wide increase in HIV transmission.

60. As a medical provider, I have tried to make contingency plans if my ability to provide gender-affirming medical care suddenly stopped. But none of these plans could circumvent the immediate harm caused by the loss of trust from patients, or the heartbreaking reality that they can no longer receive gender-affirming medical care from me.

X. Conclusion

61. Based on my experience and clinical judgment, gender-affirming medical care is an essential component of effective HIV management for many patients.

62. Prohibiting Ryan White funding recipients from respecting their transgender patients' identities and from using Ryan White funds for gender-affirming medical care would harm my patients, undermine public health, and prevent me from fulfilling my obligations as a medical provider.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: June 9, 2026

Danielle Doe

Danielle Doe, NP

EXHIBIT A

MASSACHUSETTS AND BOSTON EMA INTEGRATED HIV/AIDS PREVENTION AND CARE PLAN

ENDING THE HIV EPIDEMIC IN THE COMMONWEALTH: 2022-2026

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH (MDPH); BUREAU OF INFECTIOUS DISEASE AND LABORATORY SCIENCES (BIDLS); OFFICE OF HIV/AIDS (OHA)

BOSTON PUBLIC HEALTH COMMISSION; INFECTIOUS DISEASE BUREAU; RYAN WHITE SERVICES DIVISION

STATEMENT OF MISSION, VISION, AND COMMITMENT TO INTEGRATED HIV PREVENTION AND CARE PLANNING OVERVIEW

The *Massachusetts and Boston EMA Integrated HIV/AIDS Prevention and Care Plan, Ending the HIV Epidemic in the Commonwealth: 2022-2026,* was developed based on the mission, vision, and commitments described below. Community stakeholders and public health planners worked together to identify new priorities focused on achieving racial health equity.

INTEGRATED HIV PREVENTION AND CARE PLAN MISSION

The Boston Public Health Commission (BPHC), Infectious Disease Bureau (IDB), Ryan White Services Division (RWSD), and The Massachusetts Department of Public Health (MDPH), Bureau of Infectious Disease and Laboratory Sciences (BIDLS), Office of HIV/AIDS (OHA) are committed to eliminating new HIV infections, improving health outcomes and prosperity of people with HIV, and eliminating persistent disparities in health among affected populations, notably residents who are African American/Black, Latinx, gay and bisexual men and other men who have sex with men (including transgender, nonbinary, and gender expansive people who have sex with men), persons who use drugs, persons who are non-US born, and people who are transgender, nonbinary, and gender expansive.

"End transmissions, end stigma, promote health."

VISION

All Massachusetts residents and those in the Boston Eligible Metropolitan Area (EMA) have health and prosperity, free of stigma and disease.

VALUES

Caring and Respect: Individuals are treated with caring and respect across all sectors of HIV planning and response.

Collaborations: Collaborations and partnerships are valued to inform priorities and to deliver on them.

Inclusive and Equitable Community Engagement: Stakeholder engagements with traditionally marginalized people and communities improve our understanding of affected population needs to inform tailored responses.

Racial Equity: We focus on racial equity with new vigilance by using the levers to make change and by creating new service models.

End Stigma: Pursue opportunities to address the drivers and manifestations of stigma that may lead to avoidance of health services, nondisclosure, and people experiencing treatment failure.

GUIDING PRINCIPLES

Collaborators that developed this plan are committed to working together to meet the needs of affected populations, identify and address social determinants of health, and learn from those with lived experience to advance integrated and trauma-informed service models.

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SECTION I: EXECUTIVE SUMMARY OF THE INTEGRATED PLAN AND SCSN

The Boston Public Health Commission (BPHC), Infectious Disease Bureau (IDB), Ryan White Services Division (RWSD), and The Massachusetts Department of Public Health (MDPH), Bureau of Infectious Disease and Laboratory Sciences (BIDLS), Office of HIV/AIDS (OHA) are committed to eliminating new HIV infections, improving health outcomes and prosperity of people with HIV, and ending persistent disparities in health among affected populations, notably residents who are African American/Black, Latinx, gay and bisexual men and other men who have sex with men (including transgender, nonbinary, and gender expansive people who have sex with men), persons who use drugs, persons who are non-US born, and people who are transgender, nonbinary, and gender expansive.

– MISSION OF THE INTEGRATED HIV PREVENTION AND CARE PLAN

OVERVIEW

This Integrated HIV Prevention and Care Plan builds upon the findings and engagement efforts of previous planning efforts including the 2016-2021 Integrated HIV Prevention and Care Plans produced and submitted separately by MDPH and BPHC, the 2020 Ending the HIV Epidemic (EHE) in Suffolk County Massachusetts Plan, and the Massachusetts Getting to Zero Coalition's Massachusetts Comprehensive Plan to Eliminate HIV Discrimination, AIDS Related Deaths, and New HIV Infections.

This document, the joint Massachusetts and Boston EMA Integrated HIV Prevention and Care Plan - Ending the HIV Epidemic in the Commonwealth: 2022-2026, achieves several "firsts."

One, it is the first time that the Commonwealth of Massachusetts and the Boston Eligible Metropolitan Area (EMA) submit an Integrated HIV Prevention and Care Plan, including the Statewide Coordinated Statement of Need, jointly, to Centers for Disease Control and Prevention (CDC) and the Health Resources and Services Administration (HRSA). This partnership builds upon the cooperation engendered in preparing the 2020 Ending the HIV Epidemic in Suffolk County Massachusetts that initiated the ongoing and current collaboration between the two entities.

Two, this is the first large scale HIV plan in Massachusetts to explicitly center racial equity throughout the plan. It does this by incorporating a health and racial equity framework and an anti-racism lens through essential public health services such as health assessments, policy development, and the assurance that resources and services are aligned with data throughout its duration.

Three, this plan is the result of the largest scope of stakeholder engagement that both MDPH and BPHC implemented. This includes significant participation over a period of one year of both the Massachusetts Integrated Prevention and Care Committee (MIPCC) and the Boston EMA Planning Council (PC). In addition, MDPH groups representing Black, Latinx, Transgender, Gay Men, and Women populations met repeatedly over several months. In addition, "all stakeholder" meetings were held that included representatives of behavioral health, people who use and/or inject drugs as well as the Statewide [HIV] Consumer Advisory Group. All these groups include a significant number of people at risk for and with

HIV. Information gleaned at group meetings generated suggestions for assessments, objectives, activities, and strategies that have been incorporated into this plan. All stakeholders understood that they were contributing to a "living document" that will continue to evolve and improve as it is implemented.

PLAN SUMMARY

The Massachusetts and Boston EMA Integrated HIV/AIDS Prevention and Care Plan - Ending the HIV Epidemic in the Commonwealth: 2022-2026 sets out a blueprint for public health action on HIV over the stated five-year period while meeting all the requirements set out in the joint CDC-HRSA Guidance.

This blueprint for public health action is based upon the Epidemiologic Snapshot, Continuum of Care, and Needs Assessment information outlined in Sections III. Throughout this section, data current as of December 31, 2020, are used consistently for both Massachusetts and the Boston EMA, including the EMA's three New Hampshire counties.

Based on information in Section III, men who have sex with men continues to be the largest percentage of incident cases (39%) followed by no identified risk (28%), people who inject drugs (14%), heterosexual sex (8%), and presumed heterosexual sex (7%). Only the category of people who inject drugs has increased in recent years.

From 2018-2020, with respect to race/ethnicity, white, non-Hispanic, people have the highest incidence (36%), followed by Black, non-Hispanic/non-Latinx (32%), Hispanic/Latinx (27%) and Asian/Pacific Islander (3%). However, when looked at by population rate, Black, non-Hispanic/non-Latinx, and Hispanic/Latinx individuals were diagnosed with HIV during 2018–2020 at rates eight and four times that of white, non-Hispanic/non-Latinx, individuals, respectively.

From 2018-2020, 38% (N=620) of all individuals diagnosed with HIV were born outside the US. An additional 12% of Hispanic/Latinx individuals diagnosed with HIV during this time were born in Puerto Rico. Recent, newly arriving immigrants crossing the U.S. southern border have included an increased number of women of color with HIV from Haiti, Uganda, and other countries.

Both the situational analysis and the goals/objectives section recognize that this Integrated Plan is and will be a living document. Thus, with ongoing input and engagement from the multiple stakeholder groups, this Integrated Plan will continue to evolve to achieve its goals regarding the local HIV epidemic with a lens toward strategies and activities that counter structural racism to improve overall effectiveness across the entire HIV continuum and reduce (and where possible eliminate) racial inequities.

Monitoring and implementation of the plan (Section VI) will both lead to improvements in the plan but will also inform the next procurements by BPHC and MDPH of the HIV system of prevention and care in Massachusetts. This substantial investment in the HIV system will present an opportunity to restructure how HIV prevention and care services will be designed and implemented in Massachusetts and the Boston EMA. The procurement will be developed using a racial equity lens and many of the goals/objectives indicate that change-related strategies and activities will feed into the procurement language.

APPROACH TO PREPARING THE PLAN

In Section II, the Integrated Plan documents how MDPH and BPHC used a combination of existing material and new material to develop this plan. This Integrated Plan builds previous plans including the 2016-2021 Integrated Plans produced and submitted separately by MDPH and BPHC, the 2020 Ending the HIV Epidemic in Suffolk County Massachusetts plan, and the Massachusetts Getting to Zero Coalition's Massachusetts Comprehensive Plan to Eliminate HIV Discrimination, AIDS Related Deaths, and New HIV Infections.

In addition, both the prior Epidemiological Profiles and Statewide Coordinated Statement of Need were reviewed to assist with the structure and contents of this Integrated Plan. For a full listing of where existing versus new material was used, see the Integrated Plan Checklist in Appendix 1. A full listing of the wide-ranging engagement of stakeholders is included in Appendix 4: People with HIV and Key Stakeholder Representation in Planning.

DOCUMENTS SUBMITTED TO MEET REQUIREMENTS

The Massachusetts and Boston EMA Integrated HIV/AIDS Prevention and Care Plan - Ending the HIV Epidemic in the Commonwealth: 2022-2026 meets all the requirements of the Integrated Plan Guidance issued by CDC and HRSA.

It meets the requirements for the Statewide Coordinated Statement of Need by including:

- Participation in the planning process by representatives of Ryan White HIV/AIDS Program (RWHAP) Parts A, B, C, D, and F located in Massachusetts.
- Inclusion and engagement in the planning process of people with lived experience including both people at risk for HIV and AIDS and people with HIV and AIDS.
- Inclusion of comprehensive needs assessment data including the most recent available information on HIV incidence, the HIV continuum of care, and results of assessments of access to services, including gaps and barriers. For each of these areas, overall findings are presented, as well as trend analysis and breakdowns by demographic factors including race/ethnicity, gender, age, exposure mode, and place of birth.

It meets the requirements for the Integrated Plan by including, in Section V, a minimum of three goals/objectives for each of the EHE strategies – Diagnose, Treat, Prevent, and Respond. In addition, this Integrated Plan includes a fifth strategy – Workforce. For each goal/objective there are related activities, partnerships, data indicators and sources, and which part of the HIV care continuum and which goal of the National HIV/AIDS Strategy each one will impact.

In addition to the documents mentioned in the Appendix 1 Checklist, this Integrated Plans has included the following documents as attachments:

- Appendix 2: Massachusetts and Boston EMA HIV Prevention, Care, and Treatment Resource Inventory
- Appendix 3: Massachusetts HIV Financial Inventory
- Appendix 4: People with HIV and Key Stakeholder Representation in Planning

Section II: Community Engagement and Planning Process

Engagements with community members, people with HIV/AIDS, and other key stakeholders are an essential component of the Commonwealth's response to the HIV epidemic. Massachusetts has a longstanding and highly effective state HIV/AIDS planning system. This network has historically contributed to prevention and care planning across state-, CDC- and HRSA-supported investments, and serves in an advisory capacity to the Office of HIV/AIDS (OHA) and Ryan White Services Division regarding the identification of population, local and regional service priorities, program development, and policy initiatives. Engagements to develop this plan were strategic, thoughtful, and bold for new efforts to end HIV. The ability to meet our HIV prevention and care goals relies on strategic application of health and racial equity approaches to all program investments, as described throughout this plan, but by also continuing to benefit from the knowledge, expertise, and experience of stakeholders, advisory bodies, and other partners within and outside of Massachusetts.[1]

Community and stakeholder engagement activities in Massachusetts embody the goals of the Integrated HIV Prevention and Care Plan, National HIV/AIDS Strategy (NHAS), and HIV Strategic Plan. Public health policies and programmatic responses are informed by consultative engagements with advisory groups, and frequent reports to those entities on the implementation status of their recommendations. Routine engagement with members of OHA-convened advisory groups, provider-led forums, and consumer-focused dialogues will serve to monitor progress, assess service needs, identify gaps and barriers, and implement responsive prevention and care initiatives. Engagements with the leadership and members of these groups ensure the prioritization of key initiatives and facilitates a sense of shared responsibility to achieve jurisdictional priorities.[2]

Initial planning efforts sought to effectively engage the coalitions that successfully created each of the existing plans, identify shared objectives and priorities, and synthesize complementary recommendations to accelerate our progress toward ending the HIV epidemic in Massachusetts and Boston EMA. An advisory response framework was developed to identify optimal practices based on the five core strategies (Diagnose, Prevent, Treat, Respond, and Workforce).

JURISDICTION PLANNING PROCESS

METHODS FOR CONDUCTING INTEGRATED PLANNING

An experienced public health planning partner was contracted to conduct advisory engagements and develop the joint Massachusetts and Boston EMA Integrated HIV Prevention and Care Plan - Ending the HIV Epidemic in the Commonwealth: 2022-2026. Weekly Zoom meetings were organized with members of the state and local public health staff to develop a schedule of advisory engagements, plan advisory meeting agendas, document proceedings, and discuss all phases of developing the plan. Meeting summaries of each advisory engagement were used to confirm priorities, goals, and objectives.

A year-long, rigorous schedule of distinct advisory group engagements concentrated on identifying population and service system priorities. To ensure the health and safety of advisory group members, planning partners, and public health staff, all advisory activities were conducted through Zoom virtual

[1] Massachusetts Department of Public Health, Office of HIV/AIDS, *Massachusetts Integrated HIV Prevention and Care Plan,* 2017, 43.
[2] Massachusetts Department of Public Health, Office of HIV/AIDS, *Massachusetts Integrated HIV Prevention and Care Plan,* 2017, 43.

platform to maximize the use of technology to conduct engagement remotely, to promote accessibility of these engagements, and to share important information.

ADVISORY GROUP FEEDBACK

MASSACHUSETTS INTEGRATED PREVENTION AND CARE COMMITTEE (MIPCC)

MIPCC is the integrated HIV prevention and care advisory group for the Commonwealth of Massachusetts is to design and provide guidance to implement the comprehensive HIV prevention, care, and treatment plan that promotes service integration.

MIPCC engages in activities required by both the Centers for Disease Control and Prevention (CDC) and the Health Resources and Services Administration (HRSA). MIPCC is an inclusive advisory body, with participation by individuals of diverse racial/ethnic backgrounds, gender diversity and expression, sexual orientation, HIV status, and ages. Members have a range of educational backgrounds, professions, lived experience, and perspectives reflecting Massachusetts's urban and rural areas and service settings. Additionally, expertise and representation from key governmental and non-governmental agencies ensures planning promotes inclusion of other partners.[3]

MIPCC identified the following concerns, priorities, strategies, and recommendations:

- Need to ensure inclusion of Black and Latinx communities affected by HIV in initial and ongoing priority setting, strategies to increase knowledge about local HIV prevention and care services, how to access services through print, digital, and online methods.
- Need to establish new dedicated infectious disease testing, linkage, and retention service initiatives, with increased funding and support, tailored to the needs of Black, Latinx, and gay, bisexual, and other men who have sex with men, including transgender, nonbinary, and gender expansive people in geographic hot spots.
- Require contractors to collaborate with partners, such as oral health settings, that may not regularly provide HIV services but could reach and engage people with or at risk for HIV who have not been effectively reached by existing services.
- Develop and fund integrated care models (where medical and behavioral health providers share treatment plans and coordinate services) to address the urgent need to screen, detect, and respond to behavioral health problems, particularly those among Black and Latinx communities and those who have experienced trauma and sexual and domestic violence.
- Increase flexibility and proportion of effort of infectious disease testing, linkage, and adherence services for programs that primarily focus on addressing complex needs of persons who inject and use substances (that deliver syringe services programs and overdose education and Naloxone distribution services).
- Need to eliminate barriers experienced by clients attempting to obtain substance use and behavioral health treatment services.
- Increase inclusion of paraprofessionals on prevention and care teams by advancing training, supervision, financing, and team-based care service delivery models.

[3] Massachusetts Department of Public Health, Office of HIV/AIDS, CDC PS19-1906: Strategic Partnerships and Planning to Support Ending the Epidemic in the United States, 2020, 5-6.

- Improve access to age- and developmentally-appropriate sexual health information about HIV, including information on the latest prevention options and the effectiveness of HIV treatments among youth and young adults, notably among Black, Latinx, gay and bisexual men and other men who have sex with men, including transgender, nonbinary, and gender expansive people, and sex workers.
- Provide resources, incentives, training, and technical assistance to expand workforce and system capacity to provide or link clients to culturally competent and linguistically appropriate HIV testing, prevention, and support services, notably in areas with shortages that are geographic (urban-rural), population, or facility based.
- Increase awareness of HIV among people, communities, and the health workforce in geographic areas disproportionately affected (urban-rural).
- Need to ensure community health workers and/or peers' roles are part of future integrated prevention and care service teams.
- Expand medical and non-medical case management services for people at risk for HIV infection and recently infected people with HIV, particularly for Black and Latinx communities.
- Establish a statewide expansion of rapid antiretroviral treatment.
- Enhance partnerships for people at-risk for HIV infection and people with HIV to obtain safe, affordable, and accessible housing.
- Improve coordination and communication between service providers when responding to disease outbreaks and provide guidance on "actions to take".
- Need for more open communication between members and funders on a regular basis as an opportunity to hear about priorities, system gaps, and emerging needs and trends.
- Need for flexible funding to support service innovations and community building activities, notably in non-clinical settings.
- Dedicate ongoing attention to the language used in planning and epidemiologic documents and other materials to avoid further stigmatizing and/or dehumanizing people, cultural and rural communities, and people with HIV.
- Engage the publicly-funded workforce in learning about the impact of white supremacy culture, racism, homophobia, transphobia, HIV-related stigma, and structural barriers to prevention, care, and treatments, and take action to create solutions.
- Support culturally tailored interventions and solutions to address digital inequities in communities heavily affected by HIV.
- Need to understand the social, behavioral, and economic effects of the COVID-19 pandemic and monkeypox outbreak on HIV risk and opportunities develop responsive, integrated public health messaging and service models.
- Improve diversity and representation in the workforce and governance, including hiring people with lived experience (lived experience of living with HIV, living Black, Latinx, Transgender, gay, immigrant in the US.
- Ensure hiring practices and job descriptions are screened for bias, prioritize lived experiences as much as learned.
- Prioritize and compensate staff at all levels in the program for language skills.
- Enhance engagement of people with lived experiences in agency-based advisory activities and groups, including direct participation in indecision-making.

- Require funded programs to become anti-racist, to dismantle white, hetero, cis supremacy through policy and practice changes – including support in shifting from retributive supervision/HR paradigms to more restorative and/or healing practices.
- Ensure funded programs are intentional with implementing justice, equity, diversity, and inclusion training.
- Promote hiring practices that actively encourages and prepares individuals who use funded services.
- Require funding to organizations in becoming anti-racist, working to dismantle white, hetero, cis supremacy through policy and practice revisions and to share lessons learned for replication.
- Give preference to funding organizations that shift from retributive supervision/HR paradigms to more restorative/healing practices.

Boston Part A EMA HIV/AIDS Services Planning Council

The Boston Part A EMA HIV/AIDS Services Planning Council (hereafter, the Planning Council) is a legislatively mandated planning body that works to organize, evaluate, prioritize, and allocate RWHAP Part A HIV funding in the Boston EMA. The Planning Council is appointed by the Mayor of Boston and works with staff of the BPHC Infectious Disease Bureau to administer the Part A grant. The Planning Council has thirty-eight members, representing HIV care providers, people with HIV, advocates, policy experts, and representatives from OHA, State Medicaid Office, and BPHC. The Planning Council meets monthly and assigns priority to service investments in particular service areas. Additionally, a variety of sub-committee meetings are convened throughout the year, including the Consumer Committee.[4]

The Boston Part A EMA Planning Council identified the following concerns, priorities, strategies, and recommendations:

- Ensure future service models include peer support programming, including capacity building and mentorship opportunities so that people with HIV can expand their participation in planning groups and consider direct service roles.
- Increase the capacity of the publicly funded care workforce to effectively identify, diagnose, and provide holistic care and treatments for people with HIV.
- Concern about workforce shortages and high turnover of staff are barriers to expanding and maintaining access to HIV care and treatment.
- Embrace, invest, and support new options, technologies, and approaches to receiving Ryan White Part A services.
- Expand and support social media anti-stigma efforts.
- Ensure required training for care providers to deliver medical case management services in a standardized, nondiscriminatory, confidential, and client-centered manner.
- Expand safe spaces where people with HIV feel supported to connect to and stay in HIV care, supports for adherence to treatment, and to get help with HIV disclosure skills.
- Support new and novel care strategies and support access to current and emerging therapeutics to better reach and retain the most vulnerable to non-adherence or dropping out of care.

[4] Massachusetts Department of Public Health, Office of HIV/AIDS, CDC PS19-1906: Strategic Partnerships and Planning to Support Ending the Epidemic in the United States, 2020, 7.

BOSTON EMA PLANNING COUNCIL – CONSUMER COMMITTEE

The Boston EMA Planning Council Consumer Committee identified stigma as a key priority of the Planning Council. Participants shared challenges and recommended innovative solutions, including the following:

- Offer rapid HIV testing when facing unique circumstances, e.g., people who inject drugs.
- Develop peer support groups across the state for various communities, e.g., sexual, and domestic sexual assault survivors, sex workers, parents in need of support, and remove barriers that limit acceptance into these programs.
- Support HIV and infectious disease education in schools, particularly in middle/high schools.
- Strategically using digital and social media to engage priority populations.
- Increase women's visibility and intentionally including them in planning, advisory, and review of service outcomes.
- Expand video and digital communications focusing on reducing HIV-related stigma.
- Ensure training opportunities and commensurate compensation for peers and community health workers.
- Incentivize and partner with clinical education initiatives on current biomedical prevention technologies for prevention and care (including the use of condoms).

STATEWIDE CONSUMER ADVISORY GROUP (SWCAG)

The SWCAG is a designated forum for engagements with people with HIV. The SWCAG meets quarterly to provide advisory regarding HIV prevention and care, treatment services, and policy strategies. Members of the SWCAG design and co-facilitate local forums for people with HIV in urban and rural areas to learn more about service delivery needs and make recommendations to improve HIV care continuum outcomes.[5]

The SWCAG identified the following concerns, priorities, strategies, and recommendations:

- Develop digital health technologies to address HIV-related stigma and other social determinants of health impacting linkage and retention in care.
- Provide new opportunities for people with HIV to engage with public health entities and others to ensure persons with lived experiences are centered in policy and program decision making.
- Develop, test, and implement telemedicine-based approaches and digital technologies for expanding the reach of HIV prevention and care for priority populations (urban-rural).
- Develop strategies for overcoming barriers to delivering prevention, care, and treatment for individuals with substance use disorders and HIV and other infectious illnesses.
- Support activities for the workforce on the effects of racial inequity, cultural differences, and social structures on health disparities in HIV care, and develop tools for ameliorating these disparities.
- Develop interventions to reduce the stigma that impedes access to health care for people with HIV, notably those with substance use disorders and co-occurring conditions (unstable housing, violence, etc.).
- Advance access to new treatment opportunities for Black and Latinx people with HIV.

[5] Massachusetts Department of Public Health, Office of HIV/AIDS, CDC PS19-1906: Strategic Partnerships and Planning to Support Ending the Epidemic in the United States, 2020, 6.

- Need for enhanced attention for those 50+ (and better) and receiving skilled nursing services to address their HIV and overall health service needs.
- Expand the publicly funded capacity to provide holistic care to older adults with HIV and long-term survivors.
- Concern about increasing numbers of people with HIV who are aging engaged in transitions in care, often leading to going without medication or are under-treated, especially if they are seeking non-HIV care.
- Concern that vulnerable older people with HIV are having transitions from independent living settings to assisted living or nursing facilities where they may experience stigma and where HIV care may not be optimal.
- Ensure condom promotion activities in funded organizations and that print and electronic materials include how to access, store, use and dispose of condoms.
- Support empowerment-based activities, including prevention and care bill of rights, to support clients in being active participants in prevention and care services.

Suffolk County Ending the HIV Epidemic (EHE) Steering Committee

The EHE Steering Committee is comprised of diverse representatives, including people with HIV or at-risk for HIV, Suffolk County local health departments and boards of health (Chelsea, Revere, and Winthrop); local healthcare facilities, behavioral health providers, family planning and women's health providers, correctional health providers, addiction treatment providers, including providers of medication-assisted treatment for opioid use disorder, professional associations, peer advocates, community-and faith-based organizations, and representatives from academic and research institutions. Members of the EHE SC were represented in MIPCC, the Boston EMA Part A Planning Council, SWCAG, and population health engagements to maximize coordination and map alignment of priorities.

COMMUNITY HEALTH IMPACT AND POPULATION HEALTH ADVISORY GROUPS

In its commitment to health and racial equity, and in response to recommendations from community members, the OHA created a new and expanded advisory system to improve service responses. In 2019, new advisory groups were formed, explicitly organized by sexuality, race, ethnicity, gender identity, and mode of exposure to provide specific input about ways to improve health outcomes, reduce new infections, and address health disparities among impacted populations – these groups include the Black Advisory Group, the Latinx Advisory Group, the Gay Men's Advisory Group, the Transgender, Nonbinary, and Gender Expansive Advisory Group, the Women of Color Advisory Group (2022), the Behavioral Health Advisory Group, and the Harm Reduction Workforce Advisory Group.

Members of each advisory group addressed factors that affect risks and resilience relative to HIV infection and health outcomes along the HIV care continuum. Members identified concerns, priorities that require further action, or expansion for their respective populations.

Black Advisory Group

The Black Advisory Group provides specific input about ways to improve health outcomes, reduce new HIV infections, and address health disparities among Black individuals. The advisory group examines data to identify assets and challenges experienced by Black residents, inclusive of African Americans and Black persons who are non-US born or with recent ancestry in a non-US born country. The group addresses factors that impact risks and resilience relative to HIV infection and health outcomes along the HIV care continuum.

This group identified the following concerns, priorities, strategies, and recommendations:

- Increase understanding of the Black community's experience with HIV and integrate into training and capacity building opportunities for prevention and care service providers.
- Fund flexible, culturally-adapted models and approaches that achieve core and optional service requirements in a way that is appropriate for the clients they serve.
- Initiate and sustain new and dedicated Black community HIV testing, linkage, and adherence initiatives that promote "whole community" engagement and response, centering efforts with non-medical and non-traditional partnerships.
- Develop and distribute a knowledge and experience assessment to the Black community to learn current attitudes, values, and beliefs about HIV, sex, and sexual health.
- Institute a system of low-threshold housing that does not involve strenuous qualification process and assigning separate housing case managers to individuals receiving these services.
- Ensure Black peers with HIV and community health workers are equitably compensated and offered professional development and advancement opportunities.
- Support program interventions that are tailored specifically to the Black community and place advertisements and other campaign messages in areas frequented by the Black community.
- Ease restrictions on emergency funds to allow them to be more culturally relevant financial assistance provided in a timely and low-threshold manner.
- Create new health promotion and disease prevention materials about accessing nPEP, PrEP, and current and future HIV treatments tailored for Black communities.
- Partner with schools and teaching hospitals and other institutions that offer education in the areas of public health, administration, and social work with a concentration of Black students for workforce recruitment.
- Allow direct engagement on social media applications (e.g., Grindr, TikTok, etc.) catering to disproportionately-impacted Black community members.

LATINX ADVISORY GROUP

The Latinx Advisory Group provides specific input about ways to improve health outcomes, reduce new HIV infections, and address health disparities among Latinx individuals. The advisory group examines data to identify assets and challenges experienced by Latinx people, and the ways those factors impact risks and resilience relative to HIV infection and health outcomes along the HIV care continuum.

This group identified the following concerns, priorities, strategies, and recommendations:

- Prioritize engagement of Latinx-serving health and social service provider organizations to address the lack of funded Latinx prevention and care service providers in all health service regions.
- Need for increased understanding of the unique Latinx communities impacted by HIV to tailor health communications, prevention, care, and treatment services.
- Initiate and sustain new dedicated Latinx community HIV testing, linkage, and adherence initiatives that promote "whole community" engagement and response, centering efforts with non-medical and non-traditional partnerships.
- Reduce language, service setting, and cultural barriers experienced by new Spanish speaking residents, notably improving access to nPEP, PrEP, and syringe service programs.

- Need to initiate MDPH-supported statewide program coordination activities among funded programs serving Latinx communities.
- Eliminate all barriers to using technology to educate, market, and link Latinx community members to prevention and care services.
- Allow direct engagement on social media applications (e.g., Grindr, TikTok, etc.) catering to disproportionately impacted Latinx community members.
- Continue to develop social marketing and print materials in Spanish.
- Concern about overall lack of culturally competent community-based and medical services providers.
- Recommendation to require outreach, engagement, and testing efforts in partnership with non-traditional partners, including Latinx businesses and nightclubs.
- Urgent need to increase awareness of and access to integrated HIV, STD, and HCV testing, linkage, and adherence services, nPEP, PrEP, and new methods of prevention and treatments to at-risk and newly diagnosed Latinx populations with HIV.
- Increase awareness and understanding of the U = U (undetectable = untransmittable) message in service settings and health promotion and disease prevention materials.
- Ensure workforce development opportunities are offered in Spanish to mirror service setting contexts.

Gay Men's Advisory Group

The Gay Men's Health Advisory group provides specific input to MDPH about ways to improve health outcomes, reduce new infections, and address health disparities among gay men and other men who have sex with men (MSM). The advisory group focuses on identifying assets and challenges experienced by gay men and the ways those factors impact risk and resilience relative to HIV infection and health outcomes along the HIV care continuum.

This group identified the following concerns, priorities, strategies, and recommendations:

- Recommendation to emphasize the importance of continuing to prioritize gay-identified men and other men who have sex with men since this is the most disproportionately impacted group relative to new HIV infections.
- Reduce barriers to retaining PrEP clients due to medication wait times, changes in employment status, and financial barriers implemented by clinical care organizations.
- Ensure each funded prevention and care provider has a dedicated and clearly understood pathway for same-day access to nPEP, PrEP, and HIV care, particularly during screening assessments and care appointments.
- Initiate and sustain new dedicated gay men's HIV testing, linkage and adherence initiatives that promote "whole community" engagement and response, centering efforts with non-medical and non-traditional partnerships, particularly among Black, and Latinx communities of gay and bisexual men and transgender and gender diverse individuals who have sex with men.
- Eliminate cultural biases by developing new strategies to address populations whose cultural norms prohibit the discussion of sexually related topics, types of relationships between men, and sexual behaviors.
- Ensure that language in procurements, guidances, and work plan tools don't further stigmatize gay men, men who have sex with men, including transgender, nonbinary, and gender expansive people.

- Require and monitor contractor diversity and representation with public health partners, particularly among gay-identified and non-traditional public health organizations.
- Encourage new and strengthen existing engagements with contacts of highly impacted sexual subcultures and entertainment figures as ambassadors to access underserved gay and bisexual men, including transgender, nonbinary, and gender expansive people (who have sex with men), particularly among those who are Black and Latinx.
- Recommendation to emphasized that HIV prevention health promotion messages be delivered in an affirming and sex positive manner, including increasing the utilization of U = U (undetectable = untransmittable) messages, improved access to nPEP and PrEP, expansion of the MDPH Care that Fits You campaign (https://carethatfitsyou.org/) in greater number of venues (subway and bus stations, service locations).
- Eliminate restrictions on the use of social media among funded programs to reach more diverse groups of gay men both with and at risk for HIV infection.
- Integrate infectious disease prevention, care, treatment, and adherence supports with current and emerging stimulant use treatment and recovery support services.

Transgender, Nonbinary, and Gender Expansive Advisory Group

The Transgender, Nonbinary, and Gender Expansive Health Advisory Group addresses challenges and identifies best practices and opportunities to improve prevention and care services for transgender, nonbinary, and gender expansive people. This group provides input to MDPH regarding transgender, nonbinary, and gender expansive health needs and informs plans that respond to policy and program priorities in accordance with those identified in service plans.

This group identified the following concerns, priorities, strategies, and recommendations:

- Need for system-wide competency training for health and social service providers to improve the service response for transgender, nonbinary, and gender expansive people with and at-risk for HIV infection.
- Need to ensure meaningful inclusion of transgender, nonbinary, and gender expansive people as members of direct service prevention and care teams.
- Need for continued input and advisory to MDPH to ensure tailored strategies that recognize the varying gender identities and sexual orientation of transgender, nonbinary, and gender expansive people and the ways in which those dynamics impact vulnerabilities for HIV infection or disease progression, and opportunities to optimize health.
- Need to align prevention, care, and treatment services alongside other gender affirming health care services remains an important service development need.
- Need for dedicated OHA-facilitated program development support for each program that identifies serving transgender, nonbinary, and gender expansive people.
- Need for ongoing clinical education focusing on the use of hormone drugs and their interactions with STD treatments, and biomedical interventions.
- Need to review epidemiologic and service utilization data to ensure accuracy in submission.
- Reduce challenges faced by transgender, nonbinary, and gender expansive youth in accessing sexual health and infectious disease testing, linkage, and retention services (e.g., services requiring approval by parents/guardians and disclosure to parents/guardians by insurance providers).
- Need to increase education among personnel in emergency departments and urgent care centers to ensure that the care provided by these facilities is culturally responsive for transgender, nonbinary, and gender expansive people.
- Need for dedicated attention to address challenges in hiring and retaining transgender, nonbinary, and gender expansive people in the HIV prevention and care workforce, specifically transgender, nonbinary, and gender expansive people from Black and Latinx communities.
- Need for dedicated advisory to engage transgender, nonbinary, and gender expansive people of color with HIV about their unique experiences receiving HIV prevention, care, and treatment services to inform quality improvement activities.

Women's Advisory Group

The Women's Advisory Group addresses challenges and identifies best practices and opportunities to improve prevention and care services for women-identifying individuals. This group provides input to MDPH regarding women's health needs and inform plans that respond to program priories in accordance with plans and initiatives. This group prioritizes the needs of women most affected, notably Black and Latinx women.

This group identified the following concerns, priorities, strategies, and recommendations:

- Need to develop peer support programs that extend beyond the traditional hours and days of operation.
- Insufficient attention to the needs of women at risk for HIV or with HIV, particularly Black and Latinx women, and recommended the development of a new training module for providers focusing on the needs of women.
- Need for increased statewide access to mental health services for women at risk and with HIV.
- Concern that there is typically disproportionate attention to other populations with greater number incident HIV infections resulting in too little focus on women.
- Urgent need to disseminate accurate and accessible information about HIV to women at risk in the areas of nPEP, PrEP, and HIV prevention and testing services as well as the benefits of early HIV treatments.
- Need to ensure that future advisory groups, including the newly formed Women's Advisory Group, include women from non-urban areas.
- There is an overall need to think more broadly in reaching women at risk and with HIV beyond the clinical setting – such as, nail and hair salons, addiction treatment programs, grocery stores, WIC, family planning, and reproductive health programs.
- Need for dedicated housing search and advocacy services, including housing case managers to help navigate housing options and application procedures.
- Need to ensure that childcare services are available for advisory activities and when obtaining services.

COLLABORATION WITH RWHAP PARTS – STATEWIDE COORDINATED STATEMENT OF NEED (SCSN) REQUIREMENT

- This plan is a joint submission between RWHAP Parts A (Boston EMA) and B (Massachusetts Department of Health) recipients
- Participation of RWHAP Part C directly-funded service providers, typically community health clinics, which includes the following:
    - Beth Israel Deaconess Hospital-Plymouth
    - Boston Healthcare for the Homeless, Inc.
    - Brockton Neighborhood Health Center
    - Cambridge Health Alliance
    - Dimock Community Health Center
    - East Boston Neighborhood Health Center
    - Family Health Center of Worcester, Inc.
    - Fenway Community Health Center
    - Greater Lawrence Family Health Center
    - Greater New Bedford Community Health Center
    - Harbor Health Services
    - Holyoke Health Center, Inc.
    - Lynn Community Health, Inc.
    - University of Massachusetts Medical School

- Participation of RWHAP Part D programs, which includes the following:
    - Boston Medical Center Corporation
    - Dimock Community Health Center
    - Greater New Bedford Community Health Center, Inc.
- Participation of RWHAP Part F programs which includes:
    - New England AIDS Education and Training Center
    - Boston University – Dental Program
    - Harvard University – Dental Program
    - Trustees of Boston University – Dental Program

ENGAGEMENT OF PEOPLE WITH LIVED HIV EXPERIENCE – SCSN REQUIREMENT

To ensure proper representation of all communities, people with HIV were regularly engaged in all stages of the Integrated Plan from priority setting and goals and objectives development to quality improvement activities. Both MIPCC and the Planning Council include, at a minimum, the required number of unaligned people with HIV who actively participated in the discussions of priorities. Each of OHA's population health advisory groups include people with HIV, and many of these group members represent individuals with intersectional identities and lived experience. The SWCAG is a critical stakeholder group that provides input to the OHA representing people with HIV across Massachusetts. Members of this group actively participated in other advisory group sessions.

Separate coordinated meetings were held with representatives of all Ryan White Parts to identify needs and syntheses priorities for the Statewide Coordinated Statement of Need (SCSN). The results were later reviewed and confirmed with all Ryan White part representatives.

Across all groups contributing to the SCSN, the following synthesized recommendations were identified:

- Ensure all service models prioritize racial equity, including assurance of access in locations and venues that are desirable and convenient to intended client populations.
- All services are to be tailored and delivered in a culturally and linguistically-competent manner and staffed by credible community members and peers.
- Flexibility in service models and eligibility requirements to optimize access to services in a timely manner.

SECTION III: CONTRIBUTING DATA SETS AND ASSESSMENTS

DATA SHARING AND USE

The data source for all Massachusetts HIV/AIDS epidemiological data is the MDPH BIDLS HIV/AIDS Surveillance Program. The data source for all HIV/AIDS epidemiological data for the three New Hampshire counties that are part of the Boston Eligible Metropolitan Area (EMA) is the New Hampshire Department of Health and Human Services (NHHS), Division of Public Health Services, Bureau of Infectious Disease Control HIV/STI/Viral Hepatitis Surveillance Program. BPHC receives epidemiological data from the two state health departments through data-sharing agreements that allow for aggregate-level data analysis. Both states also have representatives on the Boston EMA Planning Council. During the development of this Integrated Plan, epidemiologic data was presented to both MIPCC and the Boston EMA Planning Council in the interest of helping the two planning groups make data-driven decisions.

Data used to complete the HIV Prevention, Care and Treatment Resource Inventory primarily comes from the knowledge each recipient has about the various agencies and services funded directly in their jurisdiction, as well as their knowledge of service providers funded by other leveraged sources. This knowledge of other providers comes from long-standing relationship building via groups such as the Boston EMA Planning Council and MIPCC. Needs assessment data comes from focus groups and meetings conducted with MIPCC, the Boston EMA Planning Council, and population health advisory groups conducted specifically in preparation for this Integrated Plan.

Data-to-care approaches (i.e., using health information about newly diagnosed people with HIV and people with HIV in general to direct service development) are central to Massachusetts's efforts to reduce the impact of the HIV epidemic in ways that are responsive to the needs of at-risk populations, prevent new HIV infections, and improve health outcomes along the HIV care continuum. Examining recent trends in new diagnoses informs prevention approaches, while understanding the population of people with HIV in the Commonwealth guides the design, locations, and interventions delivered by the service system.

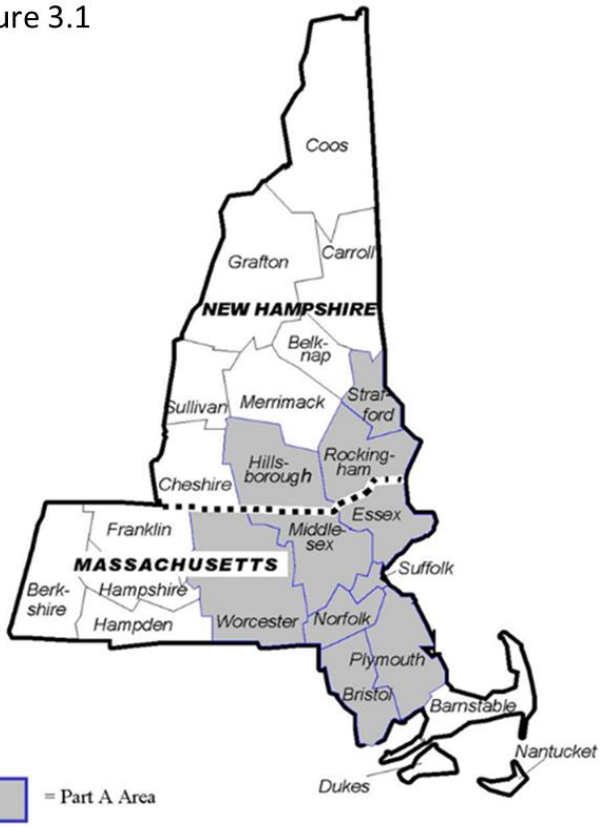
EPIDEMIOLOGIC SNAPSHOT

GEOGRAPHY AND GENERAL POPULATION

MASSACHUSETTS

Located in the Northeast region of the United States, the Commonwealth of Massachusetts is the most populous state in New England, the third most densely populated U.S. state, and the 15th most populous state in the U.S. As of July 1, 2021, the U.S. Census Bureau estimated that the Commonwealth is home to 6,984,723 individuals.[2] In terms of race and ethnicity, 70.1% of Massachusetts residents are white, 9.3% of residents are Black/African American, and 12.8% of the total population identifies as Hispanic/Latinx.[6]

Figure 3.1



BOSTON EMA

The Boston EMA includes ten counties, with seven in Massachusetts (Bristol, Essex, Middlesex, Norfolk, Plymouth, Suffolk, and Worcester) and three in New Hampshire (Hillsborough, Rockingham, and Strafford - Figure 3.1). These ten counties cover an area of 6,451 square miles and have a total population of 6,766,204,[7] as of July 1, 2021. In terms of race and ethnicity, 71.9% of Boston EMA residents are white, 8.9% are Black/African American, and 9.5% of the total population identifies as Hispanic/Latinx.

EPI SNAPSHOT - MASSACHUSETTS[8]

- The number of people with HIV (PWH) in Massachusetts increased by 16% from 20,094 in 2011 to 23,368 in 2020.
- After remaining relatively stable at approximately 700 diagnoses per year from 2011 to 2013 (three-year average = 695), then approximately 640 diagnoses per year from 2014 to 2018 (five-year average = 640), the number of new HIV diagnoses declined to a ten-year low of 539 in 2019. In 2020, the number of new HIV diagnoses declined to 437, although caution should be used in the interpretation of this decline due to the impact of COVID-19 on access to HIV testing and care services, and case surveillance activities.

[6] https://www.census.gov/quickfacts/MA
[7] https://www.census.gov/data/datasets/time-series/demo/popest/2020s-counties-total.html
[8] The following sections and graphics pulled from: Massachusetts Department of Public Health, Bureau of Infectious Disease and Laboratory Sciences. Massachusetts HIV/AIDS Epidemiologic Profile, Statewide Report – Data as of 1/1/2022 https://www.mass.gov/lists/hivaids-epidemiologic-profiles Published February 2022. Accessed October 19, 2022.

- The number of deaths due to any cause among PWH increased by 18% from 266 in 2011 to 314 in 2020.
- Although there have been reductions in new cases, vulnerable populations remain disproportionately impacted:
    - Men who have sex with men (MSM) continued to represent the largest proportion of new HIV infection diagnoses (39% overall and 54% among individuals assigned male at birth [AMAB] in 2018–2020, as of 1/1/2022).
    - During 2018–2020, the HIV diagnosis rates among Black (non-Hispanic) and Hispanic/Latino individuals were eight and four times that of white (non-Hispanic) individuals, respectively.
    - Individuals with IDU exposure mode accounted for 32% of deaths among individuals with HIV in 2020 but only 16% of all PWH in 2020.

TRENDS IN HIV DIAGNOSES OVER TIME - MASSACHUSETTS

- The number of individuals diagnosed with HIV has decreased over the past decade in Massachusetts, but disparities persist by exposure mode, race/ethnicity, place of birth, and age.
- Male-to-male sex (MSM) remained the predominant exposure mode from 2011 to 2020.[9]
- After declining by 48% from 2011 (N=60) to 2014 (N=31), the number of reported cases with injection drug use (IDU) as the primary exposure mode peaked at 116 in 2017 then decreased to 59 in 2019. The increase was primarily due to an outbreak among persons who inject drugs in the northeast part of the state between 2016 and 2018.[10] Following an intensive and targeted public health response, the number of HIV infection diagnoses attributed to IDU in the northeast has decreased. However, in early 2019, a new cluster of HIV infection was identified in Boston among PWID who were experiencing or had experienced recent homelessness, and the total statewide number of reported cases with IDU as the primary exposure increased to 76 in 2020. As of June 1, 2022, a total of 179 cases diagnosed since November 2018 have been investigated and identified as part of the Boston cluster. As it is an active cluster of concern, additional cases will continue to be investigated and added. Emerging trends among those newly diagnosed in the Boston cluster (N=66 cases diagnosed in 2020) include an increase in polysubstance and methamphetamine use.[11]
- The distributions of individuals diagnosed with HIV by sex assigned at birth, place of birth, and race/ethnicity remained relatively stable from 2011 to 2020.
- From 2011 to 2020, the proportion of individuals diagnosed with HIV at age 30–39 years increased from 25% to 35%, while the proportion of individuals diagnosed at age 40–49 years decreased from 29% to 14%.

[9] Please consider the impact of the COVID-19 pandemic on infectious disease screening, treatment, and surveillance in the interpretation of 2020 data.

[10] For more information, see: Charles Alpren et al. "Opioid Use Fueling HIV Transmission in an Urban Setting: An Outbreak of HIV Infection Among People Who Inject Drugs—Massachusetts, 2015–2018", *American Journal of Public Health* 110, no. 1 (January 1, 2020): pp. 37-44. https://doi.org/10.2105/AJPH.2019.305366

[11] For more information, see: Joint MDPH and BPHC Clinical Advisory: Increase in newly diagnosed HIV infections among persons who inject drugs in Boston, March 15, 2021, available at: https://www.mass.gov/doc/joint-mdph-and-bphc-clinical-advisory-hiv-transmission-through-injection-drug-use-in-boston-march-15-2021/download

RECENT HIV DIAGNOSES - MASSACHUSETTS

- Those with no identified risk (NIR), as defined by the CDC, comprised the second largest exposure mode group reported to the Massachusetts Department of Public Health (MDPH), accounting for 28% of recent HIV diagnoses and consisting predominantly of individuals AMAB (65%), individuals born outside the US (55%), and individuals of Black (non-Hispanic) (50%) race and Hispanic/Latino (24%) ethnicity. Beginning in 2019, all new diagnoses of HIV infection were assigned to field epidemiologists for partner services, education, and linkage to HIV care. Please note that although field epidemiologists offer additional support in the collection of risk information as part of this process, some of the information doesn't meet the CDC-defined exposure mode categories. For example, risks occurring outside the US, such as occupational exposure, are not assigned as a primary exposure mode because it is not possible to verify the information internationally. MDPH collects and maintains expanded risk information for local analyses and future use in case the CDC-defined exposure mode categories are updated.
- One in five (20%) individuals assigned female at birth (AFAB) and diagnosed with HIV from 2018 to 2020[12] reported IDU as their primary exposure mode, compared to one in eight (12%) individuals assigned male at birth (AMAB).
- Black (non-Hispanic) and Hispanic/Latino individuals were diagnosed with HIV during 2018–2020 at rates eight and four times that of white (non-Hispanic) individuals, respectively.
- During 2018 to 2020, 38% (N=620) of all individuals diagnosed with HIV were born outside the US. This proportion varied by race/ethnicity: 73% of Asian/Pacific Islander individuals diagnosed with HIV were born outside the US, compared to 55% of Black (non-Hispanic) and 46% of Hispanic/Latino individuals. An additional 12% of Hispanic/Latino individuals diagnosed with HIV during this time were born in Puerto Rico. Thirteen percent of white (non-Hispanic) individuals were born outside the US or in Puerto Rico.

[12] Please consider the impact of the COVID-19 pandemic on infectious disease screening, treatment, and surveillance in the interpretation of 2020 data.

FIGURE 3.2 Percentage of individuals diagnosed with HIV by current gender, age, race/ethnicity, and exposure mode, Massachusetts 2018-2020 (N=1,635)

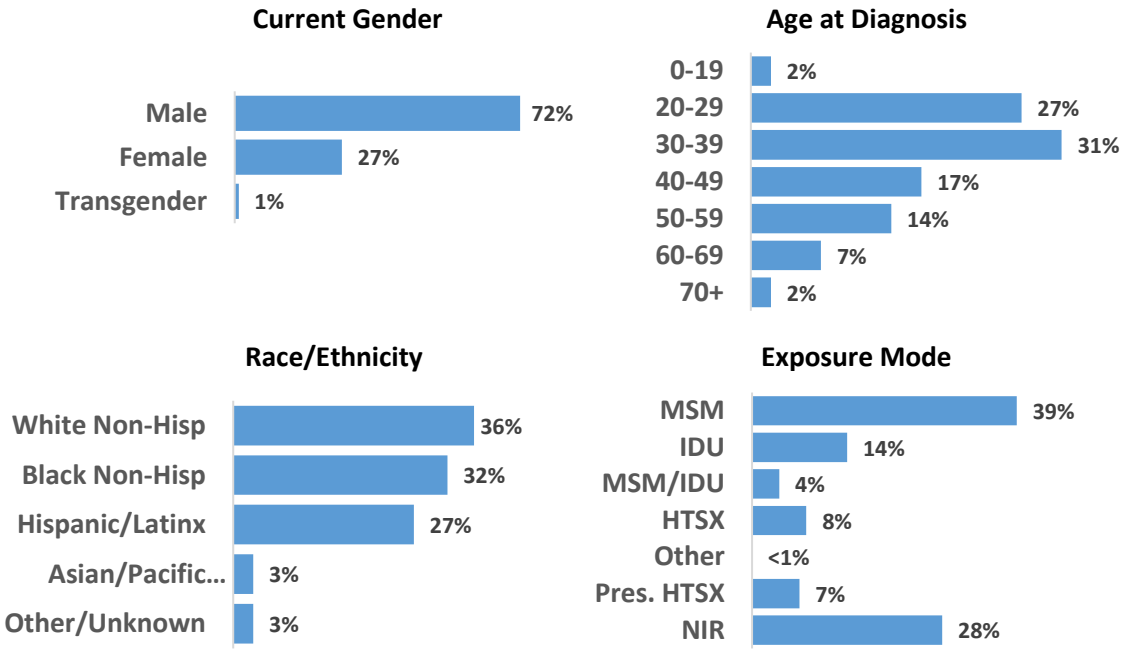


FIGURE 3.3 Percentage of individuals diagnosed with HIV by race/ethnicity and place of birth, Massachusetts 2018-2020

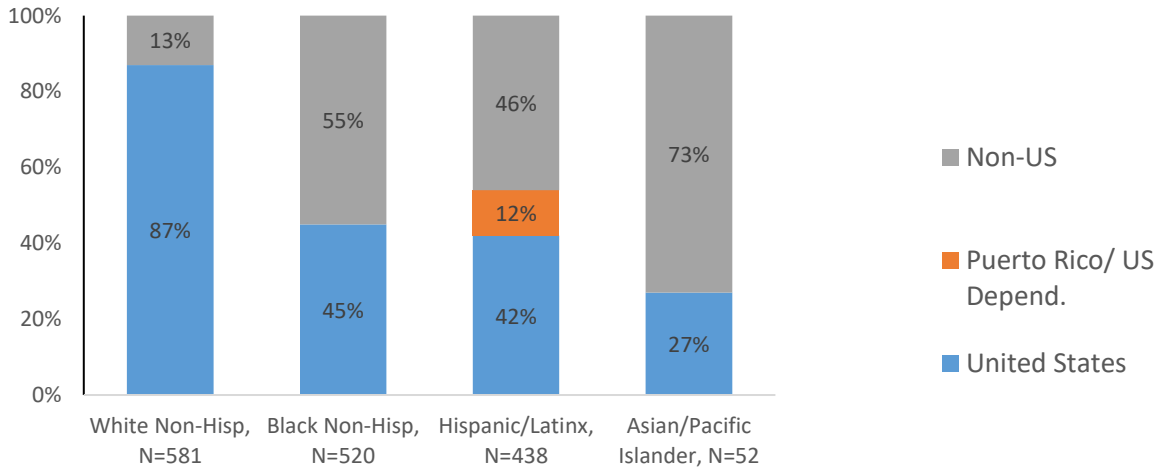


FIGURE 3.4 Percentage of individuals diagnosed with HIV by race/ethnicity, age, exposure mode, and place of birth by sex assigned at birth, Massachusetts 2018-2020

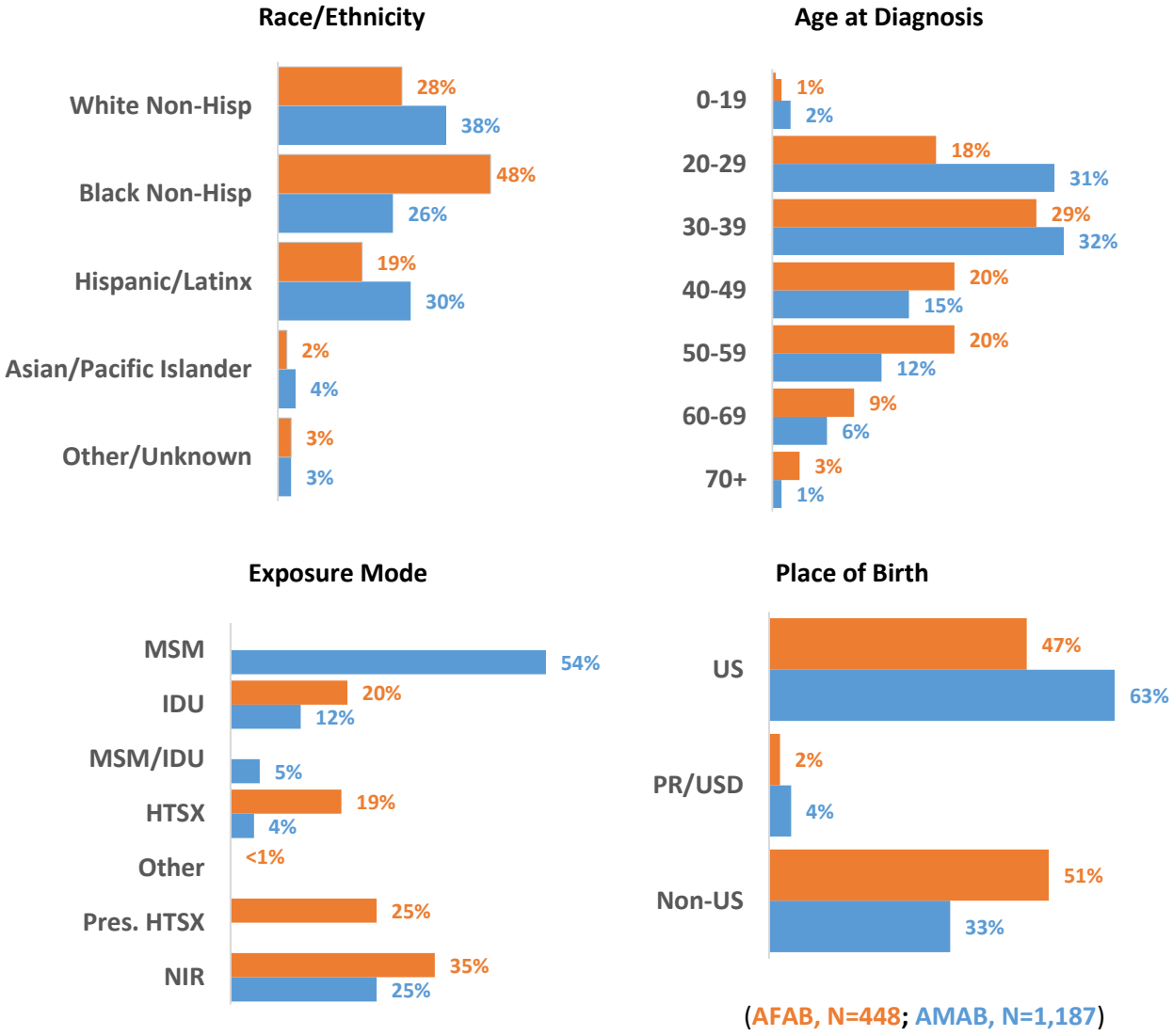


FIGURE 3.5 Percentage of individuals diagnosed with HIV by exposure mode and race/ethnicity, Massachusetts 2018-2020

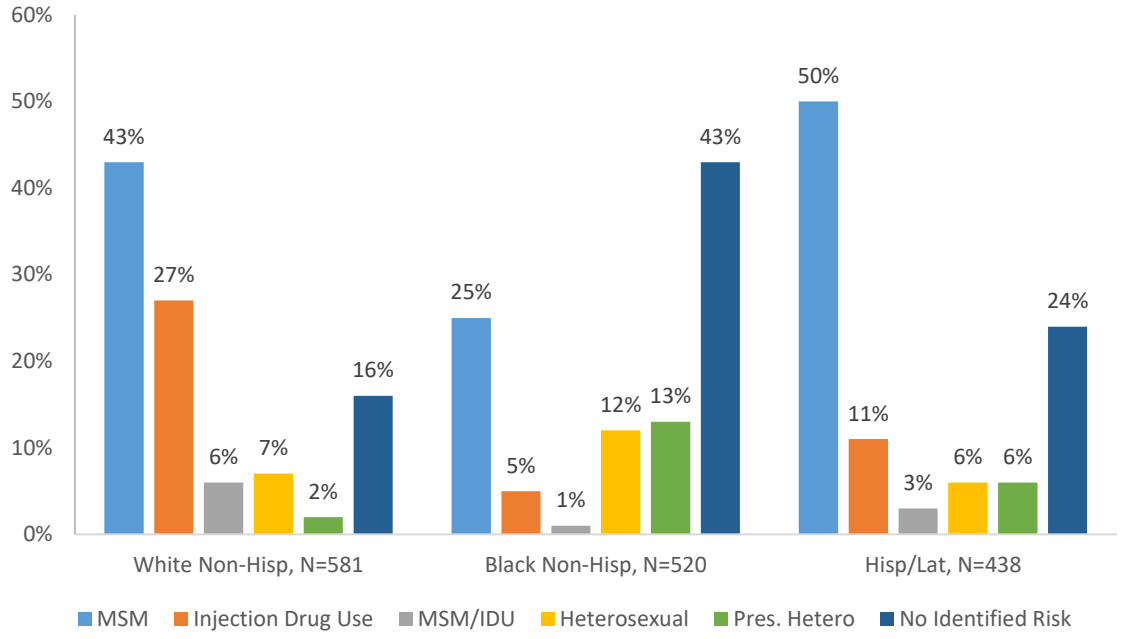
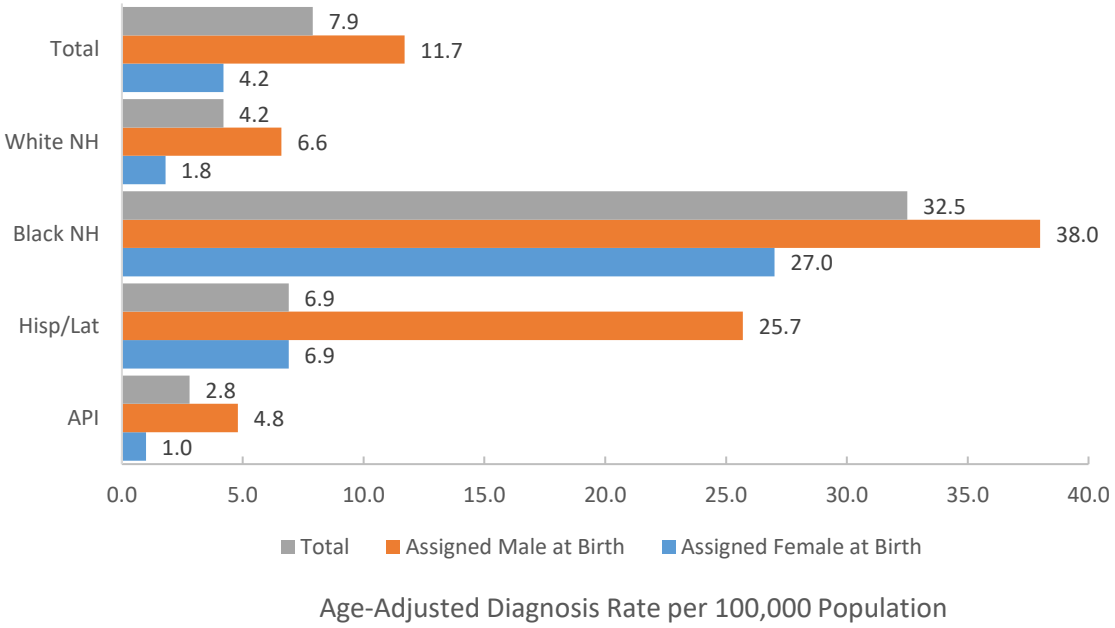


FIGURE 3.6 Average annual age-adjusted HIV diagnosis rates per 100,000 population by sex assigned at birth and race/ethnicity, Massachusetts 2018–2020 (N=1,635)



HIV PREVALENCE[13] - MASSACHUSETTS

- There were an estimated 24,600 (95% confidence interval: 23,500 - 25,600) persons living with HIV infection in Massachusetts in 2019. This estimate includes the 23,291 individuals diagnosed with HIV, reported to MDPH, and presumed to be living in Massachusetts, plus an estimated number of undiagnosed and unreported individuals.[14]
- Racial/ethnic disparities persist among PWH, and marked differences exist by current gender, age, and exposure mode. PWH in Massachusetts are predominantly male (70%), older (34% among 50–59-year-olds), and white non-Hispanic (40%). Male-to-male sex was the most frequently reported exposure mode, at 40%.
- A total of 77% of Asian/Pacific Islander PWH in Massachusetts in 2020[15] were born outside the US, compared to 51% of Black (non-Hispanic), 32% of Hispanic/Latino, and 8% of white (non-Hispanic) PWH.
- The distributions of PWH by race/ethnicity, exposure mode, and place of birth varied by sex assigned at birth: the largest proportion of PWH assigned male at birth (AMAB) was white (non-Hispanic) (46%), while the largest proportion of individuals assigned female at birth (AFAB) was Black (non-Hispanic) (47%). MSM (56%) was the predominant exposure mode among individuals AMAB compared to heterosexual sex (35%) and presumed heterosexual sex (31%) among individuals AFAB. A larger proportion of individuals AFAB (41%) than AMAB (25%) was born outside the US.
- The predominant exposure mode among white (non-Hispanic) PWH was MSM (60%). Among Black (non-Hispanic) PWH, the largest proportion was reported with no identified risk (26%), followed by heterosexual sex (21%), presumed heterosexual sex (19%), and MSM (19%). Among Hispanic/Latino PWH, the largest proportion was MSM (31%), followed by IDU (24%).
- In 2020, the age-adjusted HIV prevalence rate per 100,000 population of individuals assigned male at birth (AMAB) was three times that of individuals assigned female at birth (AFAB). There were large disparities in age-adjusted HIV prevalence rates by race/ethnicity: the rates among Black (non-Hispanic) individuals and Hispanic/Latino individuals were nine and six times that of white (non-Hispanic) individuals, respectively. The age-adjusted HIV prevalence rates among Black (non-Hispanic) and Hispanic/Latina individuals AFAB were 23 and 10 times greater than the rate among white (non-Hispanic) individuals AFAB, respectively. Among Black (non-Hispanic) and Hispanic/Latino individuals AMAB, the age-adjusted HIV prevalence rates were six and five times greater than the rate among white (non-Hispanic) individuals AMAB, respectively.

[13] Please note: 2019 HIV prevalence estimates are presented because CDC recommended against producing estimates of HIV prevalence for the year 2020. The CDC's CD4-based model did not produce reliable estimates due to the significant declines in HIV testing and diagnoses that occurred in the United States during the COVID-19 pandemic.

[14] Data source for HIV prevalence estimate: Massachusetts Department of Public Health (MDPH), Bureau of Infectious Disease and Laboratory Sciences (BIDLS), using CDC's methodology for estimating HIV prevalence. For more information, see: Centers for Disease Control and Prevention. Estimated HIV incidence and prevalence in the United States, 2015–2019. HIV Surveillance Supplemental Report 2021; 26(No. 1). http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html. Published May 2021

[15] Please consider the impact of the COVID-19 pandemic on infectious disease screening, treatment, and surveillance in the interpretation of 2020 data.

FIGURE 3.7 Percentage of PWH by current gender, age, race/ethnicity, and exposure mode, Massachusetts 2020 (N=23,368)

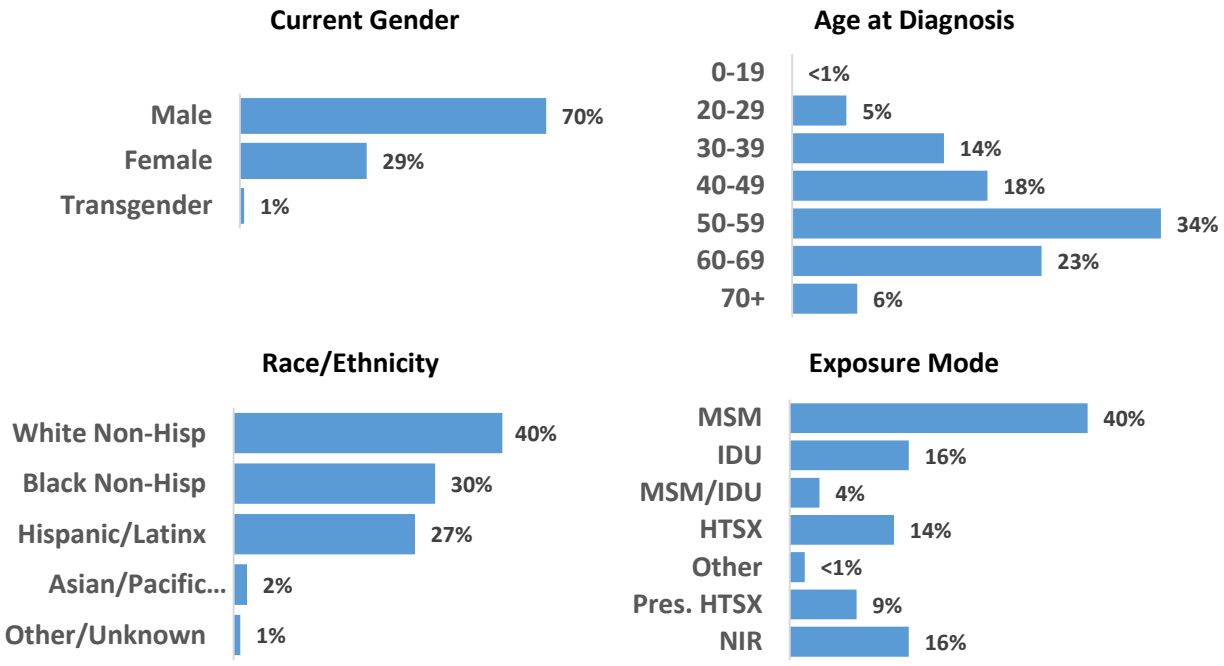


FIGURE 3.8 Percentage of PWH by race/ethnicity and place of birth, Massachusetts 2020

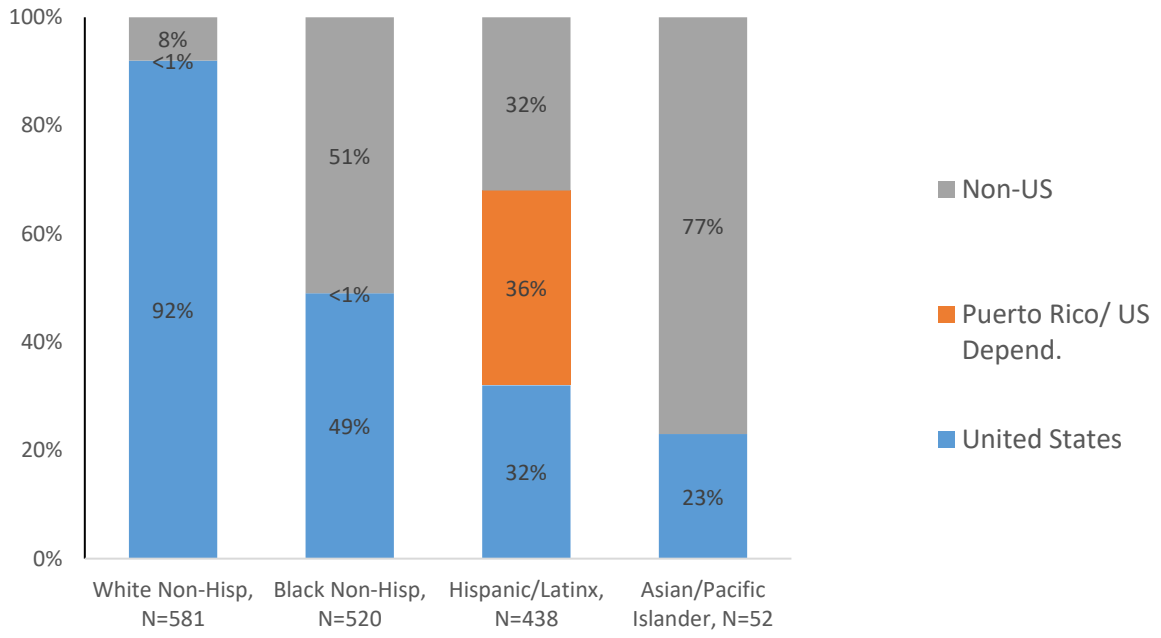


FIGURE 3.9 Percentage of PWH by race/ethnicity, age, exposure mode, and place of birth by sex assigned at birth. Massachusetts 2020

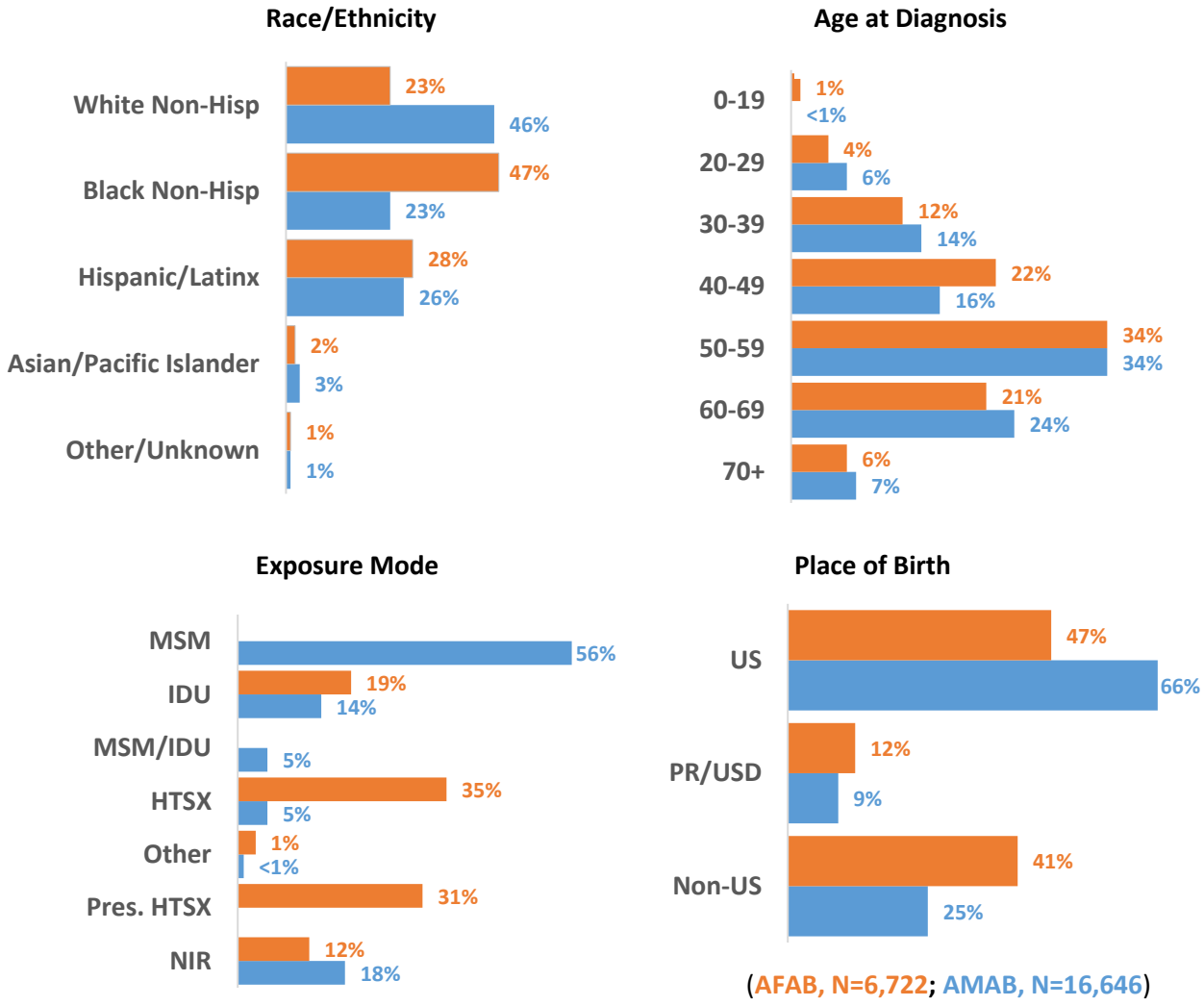


FIGURE 3.10 Percentage of PWH by exposure mode and race/ethnicity, Massachusetts 2020

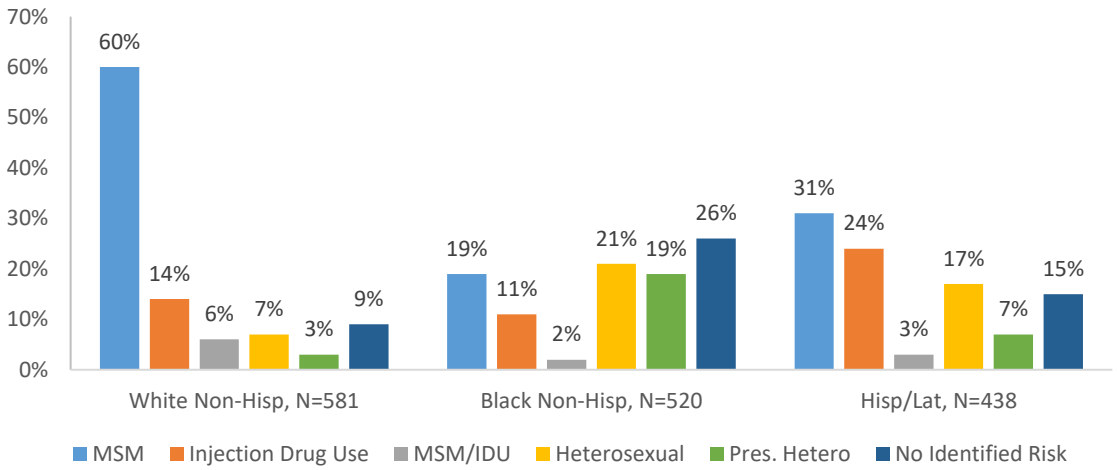
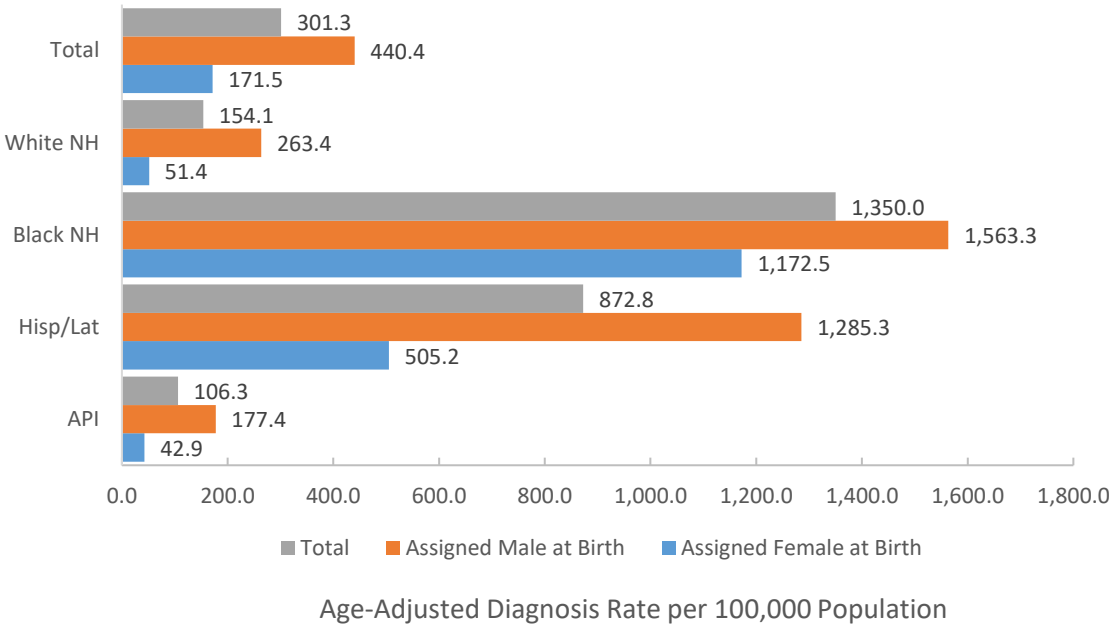


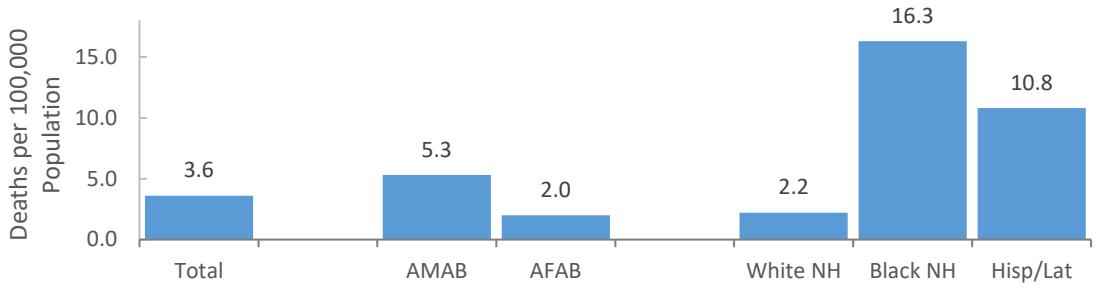
FIGURE 3.11 Age-adjusted HIV prevalence rates per 100,000 population by sex assigned at birth and race/ethnicity, Massachusetts 2020 (N=23,368)



MORTALITY AMONG INDIVIDUALS REPORTED WITH HIV/AIDS - MASSACHUSETTS

- Disparities in mortality among individuals reported with HIV paralleled those in diagnosis rates by sex assigned at birth, race/ethnicity, and place of birth, but not exposure mode. Individuals with IDU exposure mode were over-represented among PWH who died.
- The average age at death among PWH increased by 6.5 years, from 52.3 years in 2011 to 58.8 years in 2020. For comparison, the average age at death of the general Massachusetts population remained between 75.5 and 76.8 from 2011 to 2020.
- Survival of individuals diagnosed with AIDS has increased over time. In the earliest cohort of AIDS diagnoses (1986–1990), estimated survival at five years after AIDS diagnosis was 16%, compared to 87% in the most recent cohort (2016–2020).

FIGURE 3.12 Average annual age-adjusted death rates among individuals reported with HIV per 100,000 population by sex assigned at birth and race/ethnicity, Massachusetts 2018–2020 (Total number of deaths among individuals reported with HIV from 2018–2020=910)



TRENDS IN DEATHS AMONG INDIVIDUALS REPORTED WITH HIV/AIDS - MASSACHUSETTS

- The proportion of deaths among PWH attributed to HIV-related causes decreased from 34% (N=91/266) in 2011 to 16% (N=51/314) in 2020.

FIGURE 3.13 Trends in all-cause deaths among individuals reported with HIV, Massachusetts 2011–2020

All-Cause Deaths	2011	2020
Total	266	314
Sex Assigned at Birth		
Assigned Male at Birth	196	223
Assigned Female at Birth	70	91
Race/Ethnicity		
White NH	128	146
Black NH	71	91
Hispanic/Latino	65	69
API	0	1
Other/Unknown	2	7
Age Group (Years)		
0-12	0	0
13-19	1	0
20-29	4	8
30-39	21	19
40-49	82	29
50-59	105	107
60-69	37	98
70+	16	53

Exposure Mode		
MSM	54	82
IDU	115	102
MSM/IDU	19	17
HTSX	30	34
Other[16]	4	6
Pres. HTSX	9	16
NIR	35	57
Place of Birth		
US	195	231
PR/USD[17]	45	38
Non-US	26	45

GEOGRAPHIC DISTRIBUTION OF HIV - MASSACHUSETTS

- The cities and towns with the highest average annual rate of HIV diagnosis during 2018 to 2020 included Brockton (27.8 per 100,000), Everett (23.3), Lawrence (19.7), Lowell (18.9), and Chelsea (18.9). Boston had the highest number of new HIV diagnoses from 2018–2020 (N=364), followed by Worcester (N=93).
- Suffolk County was selected as one of 48 counties nationally that is prioritized for funding in the U.S. Health and Human Services' initiative "Ending the HIV Epidemic (EHE): A Plan for America". Suffolk County had the highest average age-adjusted rate of HIV diagnosis during 2018 to 2020 among all Massachusetts counties at 15.8 per 100,000.

EPI SNAPSHOT - BOSTON EMA[18]

- As of December 31, 2020, there were 20,539 people with HIV in the Boston EMA and 1,431 newly diagnosed HIV cases.
- 84% (n=19,580) of people with HIV in 2020 resided in the seven Massachusetts EMA counties, of which 32% (n=6,415 people with HIV) were living in Suffolk County.

RECENT HIV DIAGNOSES- BOSTON EMA

- **Race/Ethnicity:** HIV continues to disproportionately impact people of color in the Boston EMA. Although Black residents make up 7% and Hispanics make up 11% of the population, they accounted for 33% and 26%, respectively, of newly diagnosed HIV cases in 2020. By contrast, white residents, comprising 73% of the population, accounted for only 36% of all new cases in 2020.
- **Sex:** Individuals assigned male at birth (AMAB) continued to account for a majority of newly diagnosed HIV cases in the Boston EMA; 72% of newly diagnosed cases of HIV infection in 2020 were AMAB.
- **Age:** More than three-quarters (77%) of all new HIV cases in 2020 were persons 20-49 years of age. Additionally, 20% were between 50-69 years of age, 1% were ages 70 or older, and 2% were under 20 years of age.

[16] Other includes perinatal and clotting factor /transfusion/transplant-related exposures
[17] Ninety-nine percent of individuals reported with HIV/AIDS who died from 2011–2020 who were born in a US dependency (USD) were born in Puerto Rico (PR)
[18] Data consolidated from Massachusetts and New Hampshire HIV epidemiological data.

- **Transmission:** In 2020, 41% of new HIV cases in the Boston EMA had transmission risk category identified as MSM. Heterosexual contact, including presumed heterosexual, was the second most reported transmission risk category (16%). Presumed heterosexual transmission is defined as females who have sexual partners of unknown infection or risk status. IDU was the third most reported transmission risk category (15%). No Identified Risk (NIR) transmission risk category was 28% of cases.

HIV PREVALENCE - BOSTON EMA

- **Race/Ethnicity**: In the Boston EMA, evidence of HIV's disproportionate impact on people of color was observed within the prevalence data as well. Black and Hispanic people with HIV accounted for 32% and 24%, respectively, of people with HIV in 2020, at levels considerably higher than their 7% and 11% respective population proportions. By comparison, the proportion of white people with HIV (40%) was much lower than of white residents in the general population (73%).
- **Sex**: In 2020, individuals AMAB accounted for 71% of people with HIV in the EMA, consistent with national data.
- **Age:** Most (57%) people with HIV in 2020 were 50-69 years of age. Additionally, 37% were 20-49 years of age, 6% were 70 or older, and less than 1% were under age 20.
- **Transmission:** MSM and heterosexual contact were the two most common transmission risk categories, representing 40% and 23%, respectively, among all people with HIV in 2020, as well as in the two previous years, 2018 and 2019. IDU, including MSM/IDU, accounted for 18% of all cases. One percent were classified as pediatric transmission, and 17% were other/unknown.

HIV Care Continuum - Massachusetts[19]

The HIV care continuum is an important tool to measure and track the effectiveness of efforts to combat the HIV epidemic. Timely linkage to care after an HIV diagnosis and consistent engagement and retention in medical care are both critical to assure access to treatment and promote health for people with HIV. High rates of viral suppression are associated with improved health outcomes and substantially lower risk of HIV transmission. The HIV care continuum is a model used by federal, state, and local agencies to identify issues and opportunities related to improving the delivery of services to people with HIV across the entire continuum of care. The HIV care continuum is a way to show, in visual form, the proportion of people with HIV who are engaged at each stage of HIV care including linkage to care, retention and viral suppression.

- Among individuals newly diagnosed with HIV in 2019, 89% overall were virally suppressed,[20] with 92% of those linked to care,[21] and 94% of those retained in care[22] reaching viral suppression. Viral suppression was lowest among individuals with injection drug use exposure mode (77%, compared to 83% to 95% among other exposure modes).

[19] The following sections and graphics pulled from: Massachusetts Department of Public Health, Bureau of Infectious Disease and Laboratory Sciences. Massachusetts HIV/AIDS Epidemiologic Profile, Statewide Report – Data as of 1/1/2022 https://www.mass.gov/lists/hivaids-epidemiologic-profiles Published February 2022. Accessed October 19, 2022.

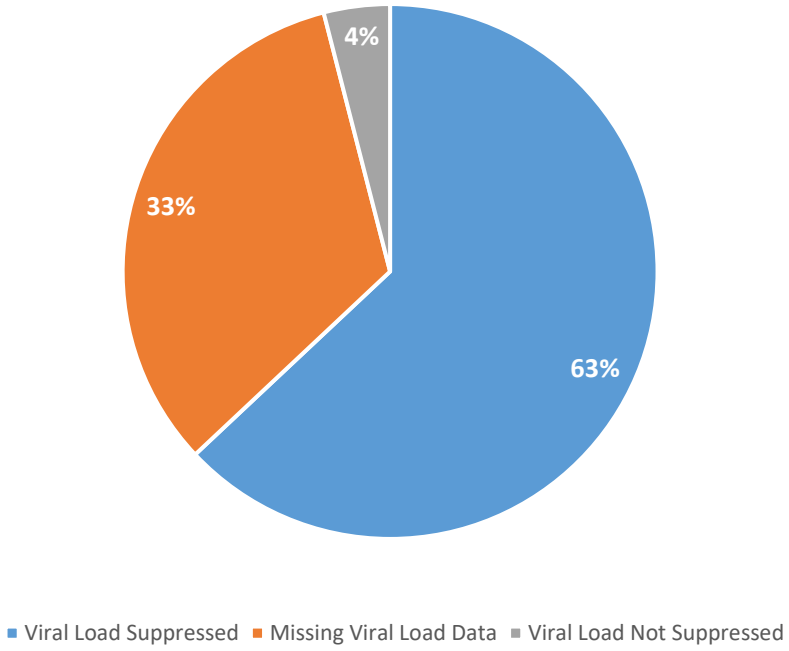
[20] Virally Suppressed" is defined as having a VL <200 copies/mL for the most recent VL test drawn during the 12-month period after diagnosis.

[21] "Linked to Care" is defined as having ≥1 viral load (VL) or CD4 test result within 3 months of diagnosis.

[22] "Retained in Care" is defined as having ≥2 VL or CD4 test results at least 3 months apart during the 12-month period after diagnosis.

- Among PWH in 2020, 63% overall were virally suppressed, with 91% of those engaged in care and 94% of those retained in care reaching viral suppression.
- Among 21,817 PWH in Massachusetts at the end of 2020 (and diagnosed through 2019), 63% were virally suppressed, 4% were not virally suppressed, and 33% did not have a viral load test in 2020. Rates of care engagement and retention were lower in 2020 (69% and 39%, respectively) than in 2019 (75% and 54% respectively), likely because of the COVID-19 pandemic. However, please note that the total number of PWH used to calculate these rates includes all individuals who have ever been diagnosed with HIV in Massachusetts with no evidence of death or having moved out of the state or country. Quality assurance efforts are currently being conducted to update the number of PWH used for this analysis.
- Among those PWH who were engaged in care (N=15,143) and retained in care (N=8,445), rates of viral suppression were higher at 91% and 94%, respectively.

FIGURE 3.15 Viral load status among people with HIV in Massachusetts, 2020 (N=21,817)



Note: Missing viral load includes individuals who have not had a lab reported in the past year.

FIGURE 3.14 Stages of HIV care among people with HIV in Massachusetts, 2020 (N=21,817)

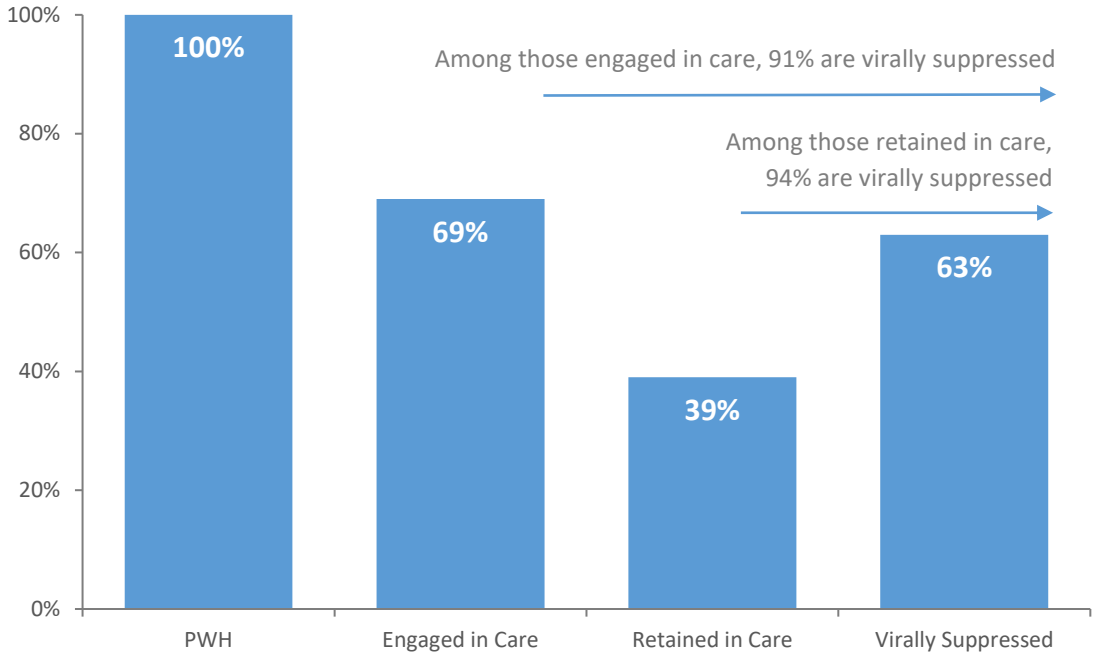


FIGURE 3.16 Engagement in care among people with HIV by sex assigned at birth, race/ethnicity, age, and exposure mode, Massachusetts 2020, (N=21,817)

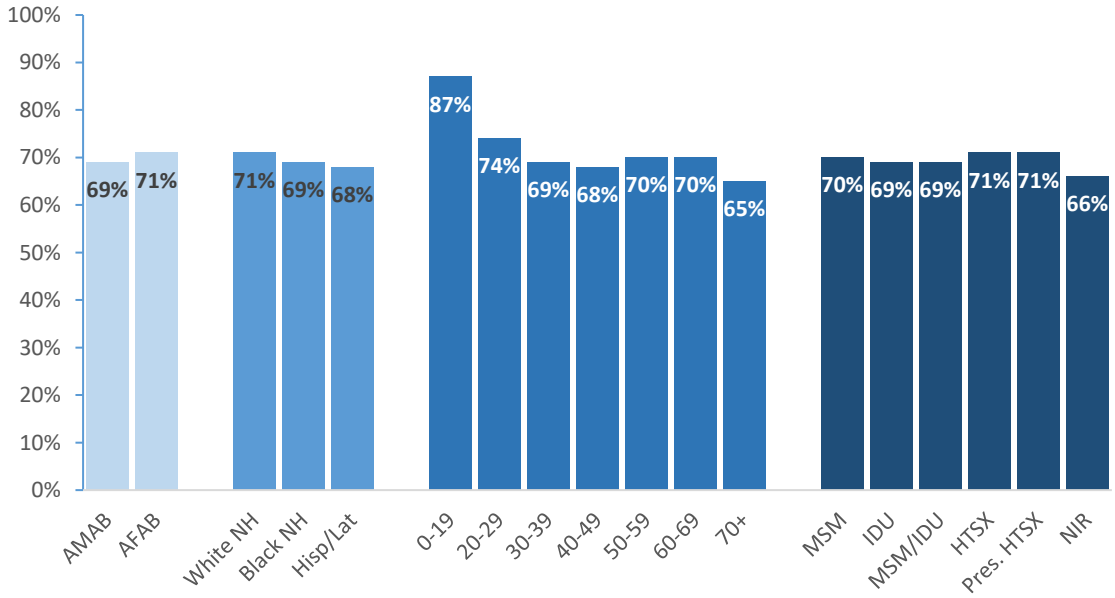


FIGURE 3.17 Viral suppression among people with HIV by sex assigned at birth, race/ethnicity, age, and exposure mode, Massachusetts 2020 (N=21,817)

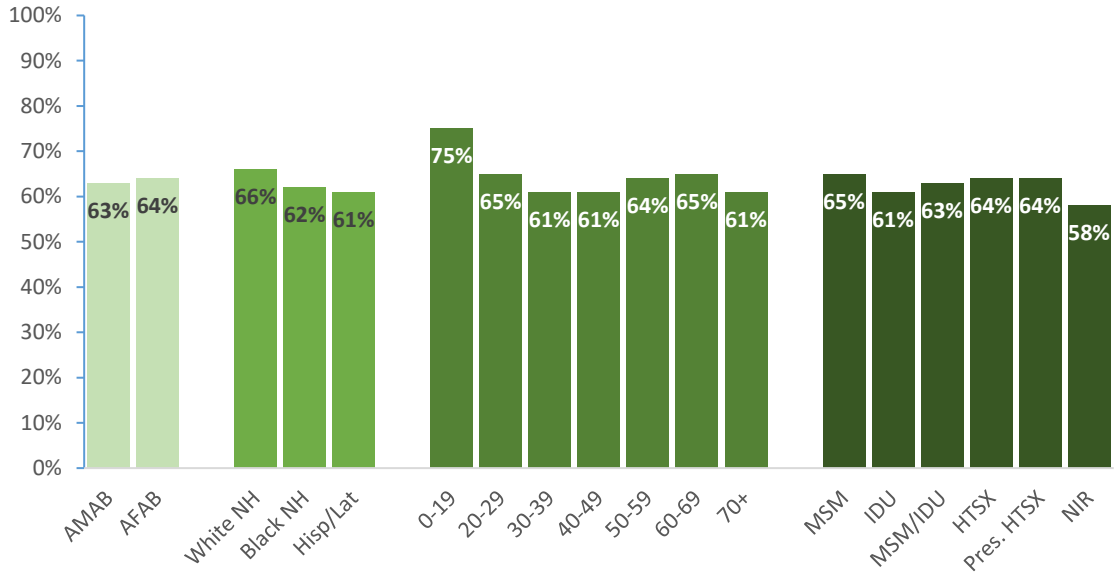
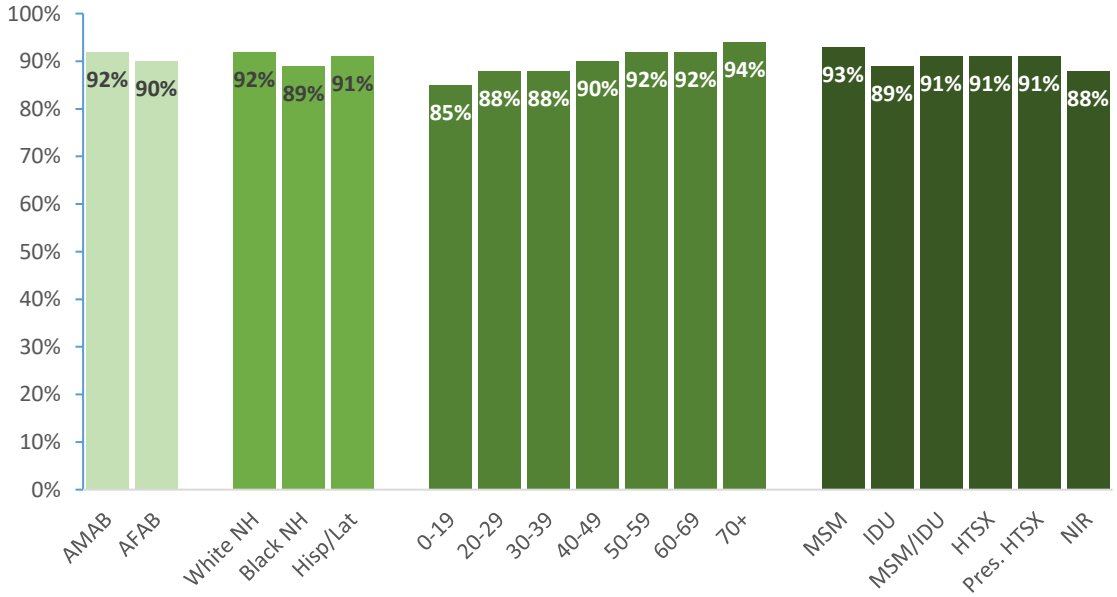


FIGURE 3.18 Viral suppression among people with HIV <u>engaged in care</u> by sex assigned at birth, race/ethnicity, age, and exposure mode, Massachusetts 2020 (N=15,143)



HIV PREVENTION, CARE AND TREATMENT RESOURCE INVENTORY

The Massachusetts and Boston HIV Prevention, Care and Treatment Resource Inventory is included as Appendix 2. The table includes the following information:

- Organizations and agencies providing HIV care and prevention services in the jurisdiction
- HRSA (including all RWHAP parts) and CDC funding sources
- Leveraged public and private funding sources, when the information was available, including HUD's HOPWA program and SAMHSA programs
- Services and activities provided by these organizations and which priority population(s) the agency serves

Massachusetts is fortunate to have a strong and stable resource base to provide highly effective services that reduce the impact of HIV, HCV, and STI infections and improve health outcomes.

Detailed information regarding funding sources in Massachusetts, including funding amounts and services provided, is outlined in Appendix 3: Massachusetts HIV Financial Inventory. Massachusetts relies on a combination of state and federal funds to accomplish a system that can ensure uninterrupted access to prevention, care, and treatment services; as well as partnerships with community-based organizations, and guidance from population health advisory groups, including the Massachusetts Integrated Prevention and Care Committee (MIPCC) and the Statewide Consumer Advisory Group (SWCAG).

STRENGTHS OF THE INVENTORY

Massachusetts is a national leader in the delivery of high quality and accessible healthcare. Massachusetts was the first state to accomplish state healthcare reform, enacting landmark legislation in 2006 that made affordable health insurance products available to all residents of the Commonwealth. Today, Massachusetts has the highest percentage of insured residents of any state in the U.S. at 97%[23]. Residents can access healthcare at leading medical facilities, private medical practices, academic teaching hospitals, or through a system of community health centers (CHC) located in communities disproportionately impacted by HIV throughout the Commonwealth.

In Massachusetts, the HIV/AIDS prevention and care infrastructure is woven into the fabric of this extensive healthcare system; prevention and care services are provided both in these medical care sites, as well as through a network of non-medical, community-based organizations (CBO). Massachusetts relies on a combination of meaningful community engagement and advisory, highly effective HIV prevention and care programs, and core public health activities and interventions. Massachusetts is committed to utilize the full range of tools available to reduce new HIV infections, support engagement and retention in care, and improve rates of viral suppression.

Boston EMA - BPHC communicates quarterly with HOPWA and Ryan White Parts B and D recipients to discuss jointly funded subrecipients, investment strategies, and the development, maintenance, and monitoring of service standards. These discussions help to inform where Part A funds are most needed to reduce service barriers for people with HIV along the HIV Care Continuum. BPHC continues to explore with its state partners the topics of surveillance data sharing and expansion of access to and coordination of syringe service programs. BPHC also collaborates heavily with various planning bodies to review community needs and investment strategies; specifically, to determine which Part A services require the greatest

23 https://www.kff.org/other/state-indicator/total-population/

support in future funding cycles. BPHC participates in MIPCC, the Boston EMA Planning Council, the New Hampshire HIV Planning Group and the EHE Steering Committee. In addition, BPHC regularly engages with agencies in other EMAs to inform its own activities. Examples of this engagement include conversations with other jurisdictions about the implementation of rapid start programs best practices for service provision and evaluation.

Public Health Investments

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

The mission of MDPH is to prevent illness, injury, and premature death; ensure access to high quality public health and health care services, and to promote wellness and health equity for all people in the Commonwealth. Health Department programming explicitly addresses health disparities through purposeful stakeholder and community engagements, improved collection and use of data, and rigorous monitoring to ensure equal access to health care services. Community based HIV/AIDS services in the Commonwealth are administered and supported by several bureaus, offices, and programs within MDPH and local public health departments.

BUREAU OF INFECTIOUS DISEASES AND LABORATORY SERVICES

A merger between the Bureau of Laboratory Sciences and Bureau of Infectious Diseases, completed in February 2016, created a new Bureau known as the Bureau of Infectious Disease and Laboratory Sciences (BIDLS). This new structure supports the shared work and priorities of the Office of HIV/AIDS (OHA) and the Massachusetts State Public Health Laboratory (MSPHL) and further enhances opportunities to improve communications and collaborations between these two important entities.

OFFICE OF HIV/AIDS (OHA)

The Office of HIV/AIDS (OHA) is the division within the BIDLS responsible to administer state and federal resources for HIV prevention, care, and treatment services. OHA works with medical and non-medical organizations, community-based programs, people with HIV, and other stakeholders to advance HIV prevention and care services. This includes needs assessment, community engagement and HIV service planning, awarding contracts for services, capacity building assistance, service monitoring, and evaluation.

OHA funds a range of services in medical, non-medical, and community-based settings across the state for persons living with or at risk for HIV infection. These services include prevention and risk reduction services, integrated testing for HIV, hepatitis C, and sexually transmitted infections, and linkage to care and treatment; as well as opioid overdose education and naloxone distribution (OEND) activities, syringe services programs (SSP), non-occupational post-exposure prophylaxis (nPEP) and pre-exposure prophylaxis (PrEP). OHA funds a range of direct care health promotion services for people with HIV with the aim of supporting engagement and retention in care and improving health outcomes. Medical case management programs assist in the coordination of medical care and support services, and either directly provide or coordinate access to, HIV treatment, adherence counseling, health systems navigation, peer support, nutrition, housing search and advocacy, rental/utility assistance, legal services, and benefits counseling services.

OHA staff work closely with programs throughout the Commonwealth serving a range of population groups, including gay and bisexual men and other men who have sex with men, including transgender, nonbinary, and gender expansive people, persons who inject drugs, LGBTQIA+ youth and young adults, racial/ethnic communities, non-US born immigrants and refugees, individuals who are homeless or unstably housed,

persons who are incarcerated or transitioning from a correctional facility, and other vulnerable population groups. OHA also collaborates with other MDPH programs that serve these individuals.

HEALTH PROMOTION AND DISEASE PREVENTION

The Health Promotion and Disease Prevention (HPDP) Unit is responsible for managing integrated prevention, medical case management, and health-related supportive services contracts to promote high quality service provision and to ensure compliance with federal, state, MDPH, and OHA requirements. Integration of prevention and care enables responsive community outreach and engagement services; access to risk reduction interventions relative to both sexual and drug injection behaviors; broad availability of integrated HIV, hepatitis C, and STI testing; rapid linkage to care and treatment for persons newly-diagnosed with HIV infection, including people with HIV reengaged in care through the prevention and screening system; linkage to treatment for individuals diagnosed with hepatitis C, Chlamydia, gonorrhea, and syphilis; and access to services that help individuals maintain treatment and ongoing access to healthcare.

BEHAVIORAL HEALTH AND INFECTIOUS DISEASE PREVENTION

The Behavioral Health and Infectious Disease Prevention Unit (BHID) integrates behavioral health, infectious disease frameworks, and population health data to inform service plans, models to better meet the needs of individuals disproportionately impacted by HIV and viral hepatitis. Public health interventions are planned and coordinated with stakeholders to effectively address complex health conditions to maximize outcomes in the OHA-contracted prevention and care service system. Coordination of community engagement, advisory, and planning activities are an integral component of this work.

FEDERAL GRANTS AND INFECTIOUS DISEASE DRUG ASSISTANCE PROGRAM

The Federal Grants and Infectious Disease Drug Assistance Program (FG & IDDAP) Unit is responsive for ensuring that the grant requirements for the HRSA RWHAP Part B and CDC HIV and EHE Funding awards are met, including applications for funding, annual narrative and data reports, fiscal and programmatic oversight of subrecipients, and the implementation of quality management activities. The Unit also oversees the Infectious Disease Drug Assistance Program contract, which includes the HIV Drug Assistance Program (HDAP), the TB Drug Assistance Program (TBDAP), and the PrEP Drug Assistance Program (PrEPDAP).

HIV DRUG ASSISTANCE PROGRAM

The Massachusetts HIV Drug Assistance Program (HDAP) ensures access to medication for the treatment of HIV and HIV-related conditions through three program components: full-pay medication coverage for individuals who are uninsured, under-insured, or serving sentences in a county correctional facility, assistance with premiums associated with health insurance coverage, and drug co-pay assistance for insured clients. State resources in the HDAP also enable coverage of non-occupational post-exposure prophylaxis (nPEP) and pre-exposure prophylaxis (PrEP) for individuals who experience HIV exposure or are at high risk for seroconversion. Finally, HDAP includes the Benefits Resources Infectious Disease Guidance & Engagement (BRIDGE) Team which provides education about HDAP and health insurance coverage opportunities available to individuals living with HIV/AIDS, as well as direct health insurance enrollment support.

MASSACHUSETTS STATE PUBLIC HEALTH LABORATORY

The mission of the Massachusetts State Public Health Laboratory (MSPHL) is to protect the health of the people of Massachusetts through excellence in public health laboratory science. The MSPHL is a critical

resource for the publicly funded HIV/AIDS prevention and care system. The MSPHL currently tests biologic samples for HIV and hepatitis C (though a co-testing platform), as well as gonorrhea, chlamydia, and syphilis. The MSPHL utilizes a 4th generation HIV testing algorithm, with the capacity to detect HIV infection during the acute phase.

DIVISION OF STD PREVENTION

The Division of STD Prevention (DSTDP) works to reduce the burden of chlamydia, gonorrhea, and syphilis in Massachusetts, reduce the risk of HIV acquisition and transmission, and reduce health disparities through strategies including accessible STD testing and treatment in accordance with CDC guidelines, delivery of partner services through deployment of Field Epidemiologists, training and technical assistance to STD care and treatment providers, and prompt linkage to care, treatment, and prevention services for persons newly diagnosed with an STD. The Division of STD Prevention oversees HIV and STD surveillance and monitors the quality and timeliness of the public health response to these infections.

MASSACHUSETTS HIV/AIDS SURVEILLANCE PROGRAM

The goal of the Massachusetts HIV/AIDS Surveillance Program (MHASP) is to provide a comprehensive picture of the HIV/AIDS epidemic through data collection, quality assurance, and analysis, to support prevention and health service activities delivered by the DPH and a statewide system of health care and social service organizations. Epidemiologists are responsible for the collection, analysis, and interpretation of adult and pediatric HIV/AIDS case data. HIV/AIDS Surveillance data are disseminated widely throughout the Commonwealth, to governmental agencies, public and private providers, advocacy groups and consumers. The program distributes specialized and routine data reports. The program also works collaboratively with planning and policy groups, health care providers and other Bureaus within the Department of Public Health, providing surveillance information and assisting with assessment of resource distribution and ongoing planning to ensure that the needs of people living with or at risk for infection are met.

VIRAL HEPATITIS PROGRAM

Hepatitis C (HCV) activities are integrated throughout the BIDLS, including within the OHA. Massachusetts conducts reflex testing of all HIV samples submitted to the MSPHL for HCV antibodies and promotes HCV prevention alongside HIV prevention in publicly funded programs that serve people who use drugs and other individuals at risk for HCV acquisition. HCV is reportable as an acute and chronic infection in Massachusetts, and OHA works with staff in the Division of Epidemiology and Immunization to ensure that the BIDLS programmatic response is driven by and evaluated with up-to-date surveillance data and understanding of HCV epidemiology. The Bureau holds an ad hoc Viral Hepatitis Advisory Committee that includes staff from multiple areas within the BIDLS, other areas within MDPH (including the Bureau of Substance Abuse Services), and community partners. This group guides BIDLS on issues ranging from interpretation of the HCV care cascade to perinatal HCV infection and other policy related issues.

BIDLS OFFICE OF RESEARCH AND EVALUATION

The Office of Research and Evaluation (OR&E) is tasked with advancing the science of BIDLS activities to improve the quality of life of all Massachusetts residents through the elimination of communicable diseases. OR&E aims to support ongoing activities to increase the scientific dissemination of BIDLS work in the form of reports, abstracts and peer-reviewed papers, support evaluation of BIDLS partner activities to improve quality of services, facilitate the application of evaluation data for policy decisions, and to lead and

facilitate new scientific studies to further the understanding of the communicable diseases and the impact of prevention interventions.

NATIONAL HIV BEHAVIORAL SURVEILLANCE: BRIEF HIV BIO-BEHAVIORAL ASSESSMENT (NHBS-BHBA)

The National HIV Behavioral Surveillance (NHBS) is a comprehensive system for bio-behavioral surveillance conducted since 2003 in populations with high burden of HIV. Traditional NHBS circulates through three populations – Men who have sex with Men, Persons who inject Drugs, and Heterosexually active persons at increased risk for HIV infection and collects data on behavioral risk factors for HIV (e.g., sexual behaviors, drug use), HIV testing behaviors, receipt of prevention services, and use of prevention strategies (e.g., condoms, PrEP). All NHBS participants are offered an HIV test. Massachusetts has participated in NHBS since the beginning (2002). This year, BIDLS received funding for a new approach to NHBS, utilizing Brief HIV Bio-Behavioral Assessments (BHBAs). This mixed methods approach to behavioral assessments will allow for flexibility in the area of the state and the populations assessed. It requires increased input from community stakeholders and allows for more rapid analysis of collected data and dissemination of results. The project team is committed to producing actionable data that integrates into the overall approach to ending HIV transmission in Massachusetts.

MASSACHUSETTS COMMUNITY AIDS RESOURCE ENHANCEMENT (MASSCARE)

MassCARE (Massachusetts Community AIDS Resource Enhancement) is a statewide program which provides access to coordinated, comprehensive, family-centered, culturally, and linguistically competent medical care, social service support and peer services for women, infants, children, and youth living with HIV and their affected family members. MassCARE promotes early identification and enhances available care in a community-based setting with an HIV medical home approach. It is funded under Ryan White Part D and is in federally qualified community health centers in three sites.

BUREAU OF SUBSTANCE ADDICTION SERVICES (BSAS)

Since the MPDH's early response to the HIV/AIDS epidemic in Massachusetts, BIDLS and the Bureau of Substance Addiction Services (BSAS) have had an ongoing, strategic, and successful partnership. This partnership addresses the continuum of prevention, care, treatment for persons living with and at risk for HIV and viral hepatitis due to substance use disorders and specifically, the sharing of injection equipment. This collaboration is essential to the implementation of the Integrated Plan, ensuring the needs of people who inject drugs are represented and reflected throughout our goals, objectives, and strategies.

OFFICE OF LOCAL AND REGIONAL HEALTH

The Office of Local and Regional Health (OLRH) provides a focus for state-local public health systems coordination. The OLRH supports improvements in local public health performance and quality, promotes a skilled public health workforce, connects local public health partners with MDPH programs, services, and resources, and advances public health planning at the local level.

Working with the Massachusetts Coalition for Local Public Health (CLPH) and other stakeholders, the OLRH collaboratively addresses the needs of local boards of health and establishes priorities from among identified challenges and needs. CLPH comprises the five statewide public health professional associations: Massachusetts Health Officers Association, Massachusetts Association of Health Boards, Massachusetts Association of Public Health Nurses, Massachusetts Environmental Health Association, and Massachusetts Public Health Association.

BOSTON PUBLIC HEALTH COMMISSION

The Boston Public Health Commission (BPHC), the local health department for the City of Boston, administers Ryan White Part A HIV funding to the Boston Eligible Metropolitan Area (EMA). The Boston EMA is home to 83.5% of persons living with HIV in Massachusetts, and the work of BPHC supports delivery of responsive, highly effective services to people with HIV in eastern Massachusetts. Awards from BPHC support the following services: medical case management, psychosocial support, medical transportation, housing search and advocacy, and nutritional programs. BPHC staff provides programmatic support to Ryan White-funded agencies in the Boston EMA. Support includes contract management, monitoring client demographics and service utilization data, working with agencies to maximize distributed funds, and providing technical assistance on grant management and reporting requirements. BPHC also awards City funding to support evidence-based interventions for HIV-negative individuals at high risk for HIV, HCV, and STI acquisition. OHA and BPHC annually collaborate on the annual Clinical Chart Review to assess the quality of medical care in Ryan White funded agencies, relative to established treatment and quality measures.

RYAN WHITE DENTAL PROGRAM

The Ryan White Dental Program is a comprehensive dental access program for people with HIV in Massachusetts, funded under Ryan White Part A and supported by funds from the Massachusetts Department of Public Health. The program is designed to remove or reduce barriers to oral health services for people with HIV. The program provides access to oral healthcare for eligible and enrolled clients through referrals to nearly 200 public and private dental providers. Oral health services in Massachusetts are also supported through resources directly awarded by HRSA to eligible dental care providers.

NEW ENGLAND AIDS EDUCATION AND TRAINING CENTER

Supported by Ryan White Part F funding, the New England AIDS Education and Training Center (NEAETC) provides training on HIV-related clinical issues to physicians, nurse practitioners, physician assistants, nurses, mental health professionals, dentists, and other health care providers throughout the six-state New England region. Recent efforts by the NEAETC include increased training to primary care providers to respond to acute HIV infection, managing HIV and hepatitis C co-infection, and maximizing HIV treatment options to improve viral suppression.

OPPORTUNITIES FOR IMPROVEMENT

HEALTH EQUITY

During community engagement sessions, community members identified significant gaps in organizations that historically and currently serve communities of color (Black, Latinx) had closed in recent years due to funding changes and other impacts. Members of the Black and Latinx Advisory Groups, MIPCC, and SWCAG expressed significant concerns about the cultural responsiveness of some provider agencies, including whether staff is reflective of people with and at risk for HIV.

GEOGRAPHIC DISPARITIES

Like many other jurisdictions, rural areas of both Massachusetts and the Boston EMA tend to have fewer HIV prevention and care services available than urban and suburban areas. Transportation, concerns about confidentiality, stigmas, lack of available or reliable digital infrastructure, technological devices, and digital literacy have a direct impact in engagement in prevention and access to care activities for people living in rural areas.

OCCURRENCES OF HIV CLUSTERS OR OUTBREAKS

The most notable recent HIV outbreaks in Massachusetts and the Boston EMA were among persons who inject drugs, a population that had seen declines in new infections for many years prior. To strengthen the outbreak and cluster response, providers recommend increased collaboration and coordination, particularly among substance use providers, homeless agencies, local businesses, and other partners that may not commonly be engaged with HIV work to reach the population more effectively.

UNDERUSE OF NEW HIV PREVENTION TOOLS

Advisory stakeholders noted a lag of nPEP and PrEP uptake among MSM of color, women, particularly Black and Latinx, and populations living in rural areas, due to a variety of factors including lack of promotion of these options and medical mistrust. At the time this Plan was in development, uptake of injectable PrEP remained low among all populations. Across all advisory groups, there was consistent call for increasing the utilization of technology and digital platforms to educate, promote services, and adherence supports.

OTHER ENVIRONMENTAL IMPACTS

The ongoing impact of COVID-19 across nearly every aspect of service provision cannot be overstated, even as conditions improve. Both MDPH and BPHC are closely monitoring and responding to the emerging needs of the Monkeypox pandemic and the potential impacts it may have on HIV prevention and care service delivery and how it will affect populations already disproportionately impacted by HIV.

APPROACHES AND PARTNERSHIPS

Data used to complete the HIV Prevention, Care and Treatment Resource Inventory primarily comes from the knowledge each jurisdiction of RWHAP and HIV Prevention and care recipient has about the various agencies and services funded directly in their jurisdiction, as well as their knowledge with service providers funded by other leveraged sources. This knowledge of other providers comes from long-standing relationship building with groups such as the Boston Ryan White Planning Council and MIPCC. Additional data on leveraged resources came from listings of recipients and grantees on federal websites (e.g., Ryan White Part C recipients, HOPWA).

NEEDS ASSESSMENT

BOSTON EMA NEEDS ASSESSMENT FY 2020

The Boston EMA Planning Council's most recent Assessment of Needs was released in FY 2020. The survey was informed by consumers of HIV services, community members affected by HIV, and providers who treat people with HIV. The assessment findings were like previous years. The populations most in need of HIV services are those who are minoritized people and groups; specifically, Black and Latinx MSM, Black and Latinx heterosexual women, persons who inject drugs, and immigrants. BPHC will provide support for the residual and disproportionate impact that COVID-19 has had on Black and Latinx people with HIV. For example, the Planning Council decided to increase MAI Other Professional Services, Legal, in comparison to the prior fiscal year due to expected housing insecurity resulting from COVID-19. This service will assist racial and ethnic cultural communities of people with HIV if housing evictions occur during or post pandemic.

MASSACHUSETTS ADVISORY GROUPS INPUT SESSIONS

Between January to November 2022, MDPH and BPHC worked with a third-party public health contractor to conduct community input sessions with various advisory groups including MIPCC, the Boston EMA

Planning Council, and population health advisory groups. This dynamic system of community engagement has generated considerable progress toward identifying ways to promote access and address gaps currently and for the future. These input sessions are described in further detail in Section II of this plan.

Summary of Needs Assessment Data

SERVICES FOR PEOPLE AT-RISK NEED TO STAY NEGATIVE

All groups identified the importance of accessible HIV testing. Massachusetts has a strong system in place to provide comprehensive and integrated HIV, STI, and Hepatitis testing through blood draws and utilizing 4th generation HIV testing technology. One area of concern brought up in all input sessions was the lack of MDPH funding for rapid HIV testing, in non-clinical settings working with people who inject drugs, and others.

PrEP and continued investment in condom availability was identified as important prevention tool by all advisory groups. There are noted disparities of PrEP uptake in the Black and Latinx MSM communities compared to the white MSM community, and in women compared to men. Advertising and promoting PrEP among at risk populations in culturally appropriate ways was raised as an essential component of this plan.

Input session members frequently mentioned the need for using community health workers and peers as important influencers to encourage at-risk populations to get tested and engage in other prevention activities such as PrEP. Though they were not named specifically, the proposed interventions were very similar in design to behavioral intervention such as Social Network Strategies and Popular Opinion Leader.

SERVICES NEWLY DIAGNOSED PEOPLE WITH HIV NEED TO RAPIDLY LINK TO HIV MEDICAL CARE AND TREATMENT

Rapid Start programs for people newly diagnosed with HIV exist in some parts of Massachusetts, but not in all areas. Rapid start programs work in different ways depending on the provider, but essentially every program allows for a newly diagnosed person to walk away from the testing appointment where they have received a diagnosis of HIV, with a starter prescription for ART. Further expansion and use of this model throughout the jurisdiction would lead to more equitable linkage to care.

SERVICES PEOPLE WITH HIV NEED TO STAY IN HIV CARE AND TREATMENT AND REACH VIRAL LOAD SUPPRESSION

One of the most common needs identified for people with HIV related to long-term engagement in care was the lack of support groups through many parts of the jurisdiction. Though some groups have continued to meet during the COVID pandemic, the groups can be challenging to attend virtually for people with HIV who do not have access to technology and/or the internet. Other support groups have stopped meeting over the years prior to COVID, but many people expressed their strong recommendation to bring back these groups.

Related to technology issues, many providers began offering telehealth options for HIV medical appointments. Though there has been a return to in-person appointments, many providers do still cover telehealth appointments as an option. Telehealth options can be helpful for people with HIV who have transportation issues, but there are people with HIV who do not have access to the required technology, available (particularly in rural communities) or reliable internet of have digital literacy.

BARRIERS TO ACCESSING EXISTING HIV TESTING, HIV PREVENTION SERVICES, AND HIV CARE AND TREATMENT SERVICES

One important need identified across all services during the needs assessment process was the need for culturally tailored, competent, and responsive services. This need was identified for race/ethnic-specific groups, as well as among the Gay Men's and the Transgender, Nonbinary, and Gender Diverse Population Advisory Groups.

The disparities in the number and variety of services potentially available to people with HIV compared to what is available to at-risk populations who test negative was also noted. Many of the same determinants of health impact both populations and not having access to stable and safe housing, community and partner violence, substance use and addiction, reliable transportation, healthcare, insurance, and other benefits continue to put many at-risk for HIV.

PRIORITIES

In addition to the priorities identified above, refer to Section II for priorities identified by the various advisory groups consulted.

FURTHER ADVISORY INITIATIVES: ADDRESSING RAPID HIV TESTING, HIV AND OVER 50 POPULATION, STIGMA, AND INTEGRATION OF BEHAVIORAL HEALTH SERVICES

During the development of this plan, four areas were identified requiring further advisory consultation. Results from these future advisory activities will be updated in this plan and be used to respond to client needs.

MDPH will convene a Rapid HIV Testing Consultation to further explore initial feedback and recommendations for the use of rapid HIV testing technology for select clients, notably among persons who inject drugs.

Members of all advisory groups, specifically the SWCAG, noted the importance of conducting additional planning to support the HIV prevention, care, and service needs of people with HIV over 50. Members of this group noted the importance of aligning planning with the local HIV and Over 50 conference activities with partners at NEAETC. Members also expressed concern about the lack of available testing and prevention tailored to 50+, notably senior (60+) populations. These seniors often feel more vulnerable, invisible, and isolated by retirement. Historical and ongoing discrimination have created significant and lifelong challenges for this demographic group: limited wealth and savings, low wages, few labor protections, changeable housing, food insecurity, stigma, immigration, HIV status, and high mortality from treatable conditions. These challenges and experiences contribute to a lack of well-being and lower quality of life.

Members of the Behavioral Health Advisory group noted the well-documented crisis in mental health in Massachusetts prior and after the acute phase of the COVID-19 pandemic. Members of this group recommended further advisory to identify opportunities to integrate behavioral health services and training of staff into HIV prevention and care programming. Members of this group noted that HIV prevention, care, and treatment programs are in a unique position to identify behavioral health problems and to provide effective ease of access to practical and clinical management of problems, including monitoring conditions and collaborating with allied community partners.

APPROACH

People with HIV and other key stakeholders were engaged in the planning process through a series of meetings and input sessions conducted over the last year. Groups engaged included MIPCC, the Boston EMA Planning Council, and various population health groups representing priority populations. Section II of this Plan describes how people with HIV and other key stakeholders were engaged in the needs assessment process in further detail. Appendix 4 includes a table showing the representation of people with HIV and other key stakeholders in the planning process, including the Needs Assessment process.

SECTION IV: SITUATIONAL ANALYSIS

This situational analysis includes a coordinated synthesis of priorities identified from extensive stakeholder engagement, analysis of local data, policy and program success in the HIV response, current HIV plans, and new opportunities to expand on best practices. For each pillar, planning included discussions on what is working, what is not, new, or expanded opportunities, additional partners to be engaged, resources and funding to be obtained or redirected, and data to be shared to optimize the response. A set of priority activities for each of the pillars, as well as corresponding workforce development objectives, were identified and serve as the basis to implement service responses.

INITIAL FRAMING FROM EXISTING PLANS

As demonstrated by the four existing plans from MDPH, BPHC, and The Getting to Zero Coalition, the needs of people at risk and with HIV in the Commonwealth are diverse, complex and will evolve as conditions and circumstances change. This plan builds upon the findings and engagement efforts of these previous plans. The existing plans and corresponding situational analyses may be access at the following links: (put links here to current Integrated Plans, EHE Plan, Boston EMA Plan, and Getting to Zero).

The overarching themes from these situational analyses emphasize that over the past 20 years, Massachusetts have seen declines in the overall number of new HIV infections, and these declines have been experienced across racial/ethnic populations and exposure mode groups. People with HIV are also living longer and healthier lives. Massachusetts has made strides over the decades to improve community engagement, HIV prevention and care services, including the following:

- Integrated HIV prevention and care services and planning systems.
- Expanded access to Medicaid for non-disabled persons with HIV who are low-income.
- Authorization of verbal consent to HIV testing.
- Operation and rapid expansion of locally approved syringe services programs (SSPs).
- Legalization of over-the-counter sterile syringes.
- Legislation that requires public and private insurers to cover prescribed HIV-related lipodystrophy treatments, the first of its kind in the country.
- Universal public health follow-up for all individuals new diagnosed with HIV infection.
- Integrated testing for HIV, hepatitis C, and sexually transmitted infections in all MDPH-supported testing and linkage programs.
- More funding available to provide food vouchers to address food insecurity among people with HIV, especially people who have lost jobs recently due to pandemic related reasons.
- Ability to deliver food to clients who are unable to leave their houses to do grocery shopping.
- Implementation of molecular HIV surveillance to optimize HIV cluster response and care services.
- Urgency to further integrate behavioral health and non-HIV infectious disease services to address gaps in care and respond to emerging diseases of public health importance for priority populations.
- Strong coordination among state and local public health and advisory partnerships.

State and EMA-level data revel major gaps in health outcomes by race, ethnicity, gender identity,

Sexual orientation, and other factors. To address these gaps, this plan prioritized several key populations

that are disproportionately impacted by HIV and other infections, such as STDs and viral hepatitis. These priority populations include men who have sex with men (MSM), Black individuals, Latinx individuals, non-US born immigrants and refugees, persons who inject drugs, and transgender, nonbinary, and gender expansive people. This plan aims to improve the health of all residents at situational or ongoing risk, and living with HIV, but this goal is not possible without first addressing the needs of historically minoritized and stigmatized communities and groups. The explicit focus on race/ethnicity will require paradigm shifts, such as utilizing a universal design framework, to promote access for all who can benefit from affirming service environments for optimal client experience. If we prioritize those individuals and groups who experience the most barriers to prevention and care and develop new strategies and interventions to reduce those barriers, we will be improving access for all.

Notably, there is overlap between several priority populations listed below (e.g., MSM who are Black and non-US born individuals). For this reason, advisory bodies emphasized an intersectional approach to health equity is critical. To address the concern around "low risk" populations, specifically cisgender women not receiving testing or counseling, there are several calls for universal testing and screening in the Goals section of this plan.

RACIAL EQUITY

Providers, advocates, consumers, and community leaders called for increasing tailored population-level responses and new investments with dedicated health department supports to optimize prevention and care services. Despite higher levels of engagement in care, retention in care, and viral suppression as compared to nationwide data, there continue to be unacceptable disparities in HIV incidence and health outcomes based on race, ethnicity, age, gender, mode of exposure and other factors.

The inequities that systemic racism produces in housing, education, access to quality food options/nutrition, employment, the built and social environments, and health care are felt across generations, across the urban-rural divide and intersect with inequities based on gender identity and sexual orientation. Stakeholders recommended this plan explicitly center on racial equity, within the continuum of prevention and care, while also addressing intersecting HIV-related disparities by gender identity and sexual orientation.

Planning partners affirmed our commitments to leading explicitly – though not exclusively – with race. Our analysis and strategy to address systemic racism will be applied as a framework to address the intersecting forms of oppression and discrimination that impact heath including homophobia, transphobia, sexism, ableism, classism, xenophobia, violence, and others. We will leverage and expand opportunities to achieve equitable prevention, care, and treatment by allocating resources based on data, exercise the influence of our institutions to advance system changes and improvements, and work in close partnership with stakeholders to understand health related social needs and factors influencing social determinants of heath. This plan recognizes addressing health care disparities is an important step to prioritize racial equity and we acknowledge that we are still learning how to best to do this effectively.

Advisory input identified future investments in integrated service models to function as equity-driven public health response models to intentionally meet the needs of Black and Latinx communities, gay men, persons who use drugs, transgender, nonbinary, and gender expansive people. Advisors further identified that future service models focus on leveraging a comprehensive care team that includes investment in community health workers, peers, and integrated behavioral health care that leverages strengths-based

approaches to build on the resilience of populations to identify and mitigating health risks, and actively address the impacts of racism to reduce service barriers.

The MDPH Office of Health Equity (OHE) has published both a Racial Equity Road Map Graphic and a Racial Equity Data Road Map to support departmental programs in assessing and addressing health inequities. The OHE provides information and linkage to Interpreter Services at Health Care Facilities across Massachusetts.

Both health departments jointly submitting this plan have increased fiscal resources for language access services, improvement in racial equity training series for all levels of public health leadership and employees, implementation of new data collection standards, increased racial equity practices for local public health, and integration of racial equity principles into competitive procurements.

BOSTON RYAN WHITE EMA

Racial equity in health is a necessity to address many health disparities across the United States and in Massachusetts and the Boston Ryan White EMA. Racial inequities in HIV diagnoses have grown worse over the course of the epidemic. Similarly, recent reports show that the racial gap in access to PrEP is increasing. Health departments recognize the importance of centering racial equity in their work on HIV/AIDS, as well as COVID-19, monkeypox, environmental health, and other health and public health concerns.

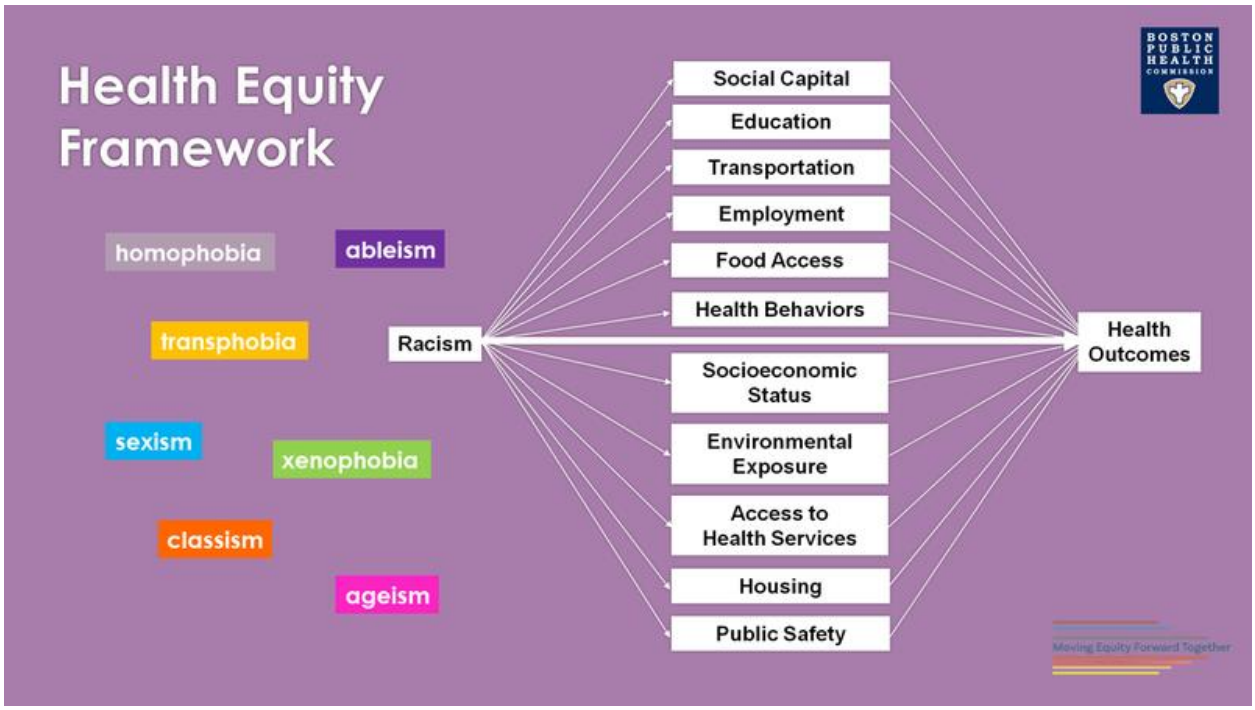
The Boston Public Health Commission has been centering racial justice and health equity since 2000.[24] The City of Boston, where the Part A recipient, the Boston Public Health Commission (BPHC) is based, is a city with majority of residents are people of color and Boston continues to be listed as one of the most racially segregated cities. There are persistent inequities in health outcomes for Black and Latinx Bostonians compared to white Bostonians. On June 12, 2020, the city officially declared racism to be a public health crisis.

The BPHC defines Racial Justice as "The creation and proactive reinforcement of policies, practices, attitudes, and actions that produce equitable power, access, opportunities, treatment and outcomes for all people, regardless of race."[25]

[24] Accessed online at https://www.boston.gov/government/cabinets/boston-public-health-commission/racial-justice-and-health-equity

[25] CityofBoston/BostonPublicHealthCommission/RacialJusticeandHealthEquity/Framework Accessed online at https://www.boston.gov/sites/default/files/file/2021/03/Racial%20Justice.pdf

The following graphic depicts the BPHC Health Equity Framework and how it views the impact of racism on health:



PRIORITY POPULATIONS

The populations most in need of HIV prevention and care services are those who are most often marginalized and for whom health inequities are the greatest. Based upon input from community engagement and population advisory groups, as well as the epidemiologic data regarding HIV incidence and prevalence, viral suppression, and the HIV care continuum, six main populations of emphasis are as follows:

- Black people including gay, bisexual, and other men who have sex with men, transgender, nonbinary, and gender expansive people, and both cisgender and transgender women
- Black women who have recently immigrated to the United States
- Gay, bisexual, and other men who have sex with men
- Injection drug users (IDU)
- Latinx people including gay, bisexual, and other men who have sex with men, transgender, nonbinary, and gender expansive people, and both cisgender and transgender women
- Transgender, Nonbinary, and Gender Diverse People

POPULATION HIGHLIGHTS

POPULATION GROUPS: BLACK PEOPLE INCLUDING GAY, BISEXUAL, AND OTHER MEN WHO HAVE SEX WITH MEN, TRANSGENDER, NONBINARY, AND GENDER EXPANSIVE PEOPLE, AND BLACK WOMEN WHO HAVE RECENTLY IMMIGRATED.

There are significant gaps in prevention and care for Black individuals in Massachusetts, both those who are living with HIV and those at risk for HIV infection. Black individuals represent just 8.4% of the state's

population, but 30% of people with HIV. Barriers to care identified during planning efforts include stigma, historic mistrust of the healthcare system, lack of public transportation in communities with a high proportion of Black residents, and insufficient investment of prevention and care resources in Black communities and neighborhoods among non-medical organizations. One of the ongoing challenges in serving Black MSM people is reaching those who do not traditionally seek care, particularly non-gay-identifying MSM.

INCIDENCE AND PREVALENCE OF HIV AMONG BLACK PEOPLE

As mentioned in the Epidemiological Profile, HIV continues to disproportionately impact people of color in the Boston EMA and Massachusetts. Although Black residents make up 7% of the population within the Boston EMA, they accounted for 32% of newly diagnosed HIV cases in 2020. By contrast, white residents, comprising 73% of the population, accounted for only 39% of all new cases in 2020. With respect to HIV prevalence in the Boston EMA, Black people with HIV accounted for 33% of people with HIV in 2020, at levels considerably higher than their 7% of the population. By comparison, the proportion of white people with HIV (39%) was much lower than of white residents in the general population (73%).

In terms of recent HIV diagnoses across Massachusetts, Black (non-Hispanic) individuals were diagnosed with HIV during 2018–2020 at a rate eight times that of white (non-Hispanic) individuals. Among people living with HIV in Massachusetts in 2020, 64% of Black (non-Hispanic) people were virally suppressed compared with 66% of white (non-Hispanic) people.

The concerns of the Black population were expressed through the Black Advisory Group as well as other community engagement groups and needs assessment activities. For Black people including gay, bisexual, and other men who have sex with men, transgender, nonbinary, and gender expansive people, and cisgender and transgender women several barriers and potential solutions were suggested that apply across strategies. Barriers include historic lack of responsiveness of the medical system and of providers to members of the Black community, the fragmentation of care that disrupts the ability to address people's needs holistically, and insufficient attention to the social determinants of health. Each of these barriers reduces the perceived urgency of HIV prevention compared with maintaining stable housing, putting food on the table, and maintaining wellness within a culture permeated with structural racism and violence. These barriers increase the difficulty of delivering services in a trauma-informed, nonjudgmental, and holistic way. The system of care for HIV prevention and treatment services needs to address these issues to engage Black men who are gay, bisexual, same-gender loving or non-identified men who have sex with men, Black transgender, nonbinary, and gender expansive people, and cisgender women at-risk for HIV to deliver, effectively, HIV prevention messages including information regarding access to PrEP.

One strategy to address these barriers is to bring information about HIV prevention and care services to locations within the Black community, for example salons, barber shops, and Black-owned businesses. Ideally service providers are from the Black community, will employ Black HIV prevention workers and/or use community health workers with lived experience in the Black community to provide education messages about the impact that HIV has on people's health to motivate people to avoid becoming infected, will provide information about where and how to find culturally competent and trauma-informed treatment services.

POPULATION GROUP: LATINX PEOPLE INCLUDING GAY, BISEXUAL, AND OTHER MEN WHO HAVE SEX WITH MEN, TRANSGENDER, NONBINARY, AND GENDER EXPANSIVE PEOPLE, AND CISGENDER WOMEN

Over one quarter (27%) of people with HIV in Massachusetts identify as Latinx, while only 11.2% of the total population in the Commonwealth identifies as Latinx. Planning participants highlighted homophobia, heterosexism, lack of Latinx serving organizations, and stigma around sexuality and HIV as contributing to disparities among individuals who identify as Latinx. Other access barriers include poor access to culturally and linguistically appropriate services at HIV prevention and care programs, and inconsistent access to PrEP and nPEP.

As mentioned in the Epidemiological Profile, HIV continues to disproportionately impact people of color in the Boston EMA and Massachusetts. Although Latinx residents make up 11% of the population within the Boston EMA, they accounted for 25% of newly diagnosed HIV cases in 2020. By contrast, white residents, comprising 73% of the population, accounted for only 39% of all new cases in 2020. With respect to HIV prevalence in the Boston EMA, Latinx people with HIV accounted for 25% of people with HIV in 2020, at levels considerably higher than their 11% of the population. By comparison, the proportion of white people with HIV (39%) was much lower than of white residents in the general population (73%).

In terms of recent HIV diagnoses across Massachusetts, Hispanic/Latinx individuals were diagnosed with HIV during 2018–2020 at a rate four times that of white (non-Hispanic) individuals. Among people living with HIV in Massachusetts in 2020, 62% of Hispanic/Latinx people were virally suppressed compared with 66% of white (non-Hispanic) people.

The feedback from the Latinx Advisory Group as well as from other community stakeholder group touched on several ways that linguistic and cultural barriers impacted the ability of Hispanic/Latinx people with HIV or at risk for HIV to access HIV prevention, care, and treatment services.

Concerns include lack of available Latinx serving provider organizations and lack of adequate availability of HIV materials in Spanish. There are online resources in Spanish available at the MA DPH Office of HIV AIDS website and at the Massachusetts Health Promotion Clearinghouse. However, it is unclear how recently the resources have been updated as well as ongoing distribution mechanisms for reaching people newly diagnosed with HIV or those at high risk for infection.

Second, up-to-date information on HIV service providers across the state and their ability to serve monolingual Spanish speakers needs to be updated annually and more easily accessible online and at gathering sites for Spanish speaking people at risk. The expanded use of community health workers and resources who are bilingual in English and Spanish can help monolingual Hispanic/Latinx people at risk for or with HIV navigate a care system where specific programs or service providers for this population are not readily available.

Third, due to funding cuts, there is no longer a statewide organization specifically advocating for the HIV prevention and treatment needs of Hispanic/Latinx people with or at risk for HIV. One of the important functions of statewide organizations is to provide capacity building including training and technical assistance that are delivered in Spanish.

Another of the ongoing challenges in serving Latinx MSM people is reaching those who do not traditionally seek care, particularly non-gay-identifying MSM.

POPULATION GROUP: BLACK WOMEN WHO HAVE RECENTLY IMMIGRATED TO THE UNITED STATES

Recently, many immigrant women of color have arrived in Massachusetts and a large number of them have been identified as having HIV. Fourth generation HIV tests and CD4 tests have identified that many of these women were not infected recently indicating that exposure likely occurred prior to their arrival in Massachusetts.

Stigma continues to be a significant barrier for prevention and treatment, especially among immigrant communities. People who are new to this country are often not aware that having HIV or being undocumented is not a barrier to accessing HIV prevention and treatment services, at least not in Massachusetts or the Boston EMA. Therefore, it is important that information about the availability of these services be disseminated widely and in networks and locations (supermarkets, schools) where newly arrived women immigrants of color spend their time.

In general, non-US born individuals account for 29% of persons living with HIV and 37% of persons recently diagnosed in the state of Massachusetts. For non-US born individuals, (especially those who have newly arrived) there are significant gaps in HIV prevent and care services. Among the barriers identified by community engagement groups were insufficient cultural and linguistic competencies of direct service providers, limited sources of financial support and housing, and the lack of mental health and psychosocial support capable of addressing issues such as experiences of violence and trauma. These barriers are further exacerbated for individuals who are undocumented and therefore increase the need for HIV prevention and care services that are not only culturally and linguistically competent but that are also trauma informed.

POPULATION GROUP: GAY, BISEXUAL MEN AND OTHER MEN WHO HAVE SEX WITH MEN (MSM)

In addition, the first three priority groups, another group of concern remains white gay, bisexual and other men who have sex with men who account for a significant percentage of people affected by HIV within Massachusetts and the Boston EMA. It is important to address co-occurring substance use that increases their risk for HIV. Many AIDS service organizations are still recovering from previous reductions in federal funding for resources directed towards MSM in Massachusetts and the Boston EMA. Community advocates continue to stress the importance of having dedicated funding streams that ensure that MSM communities continue to receive key prevention and linkage to care services. In addition, Native American and Asian-American and Pacific Islander (API) gay, bisexual and other MSM are also at high risk for HIV. API gay, bisexual and other MSM are a smaller but consistent group impacted by HIV in Massachusetts and the Boston EMA.

In Massachusetts, men who have sex with other men is the most reported exposure mode among newly diagnosed individuals. During planning efforts, participants identified lack of access to routine HIV testing, limited provider education, absence of diversity in prevention messaging designed to reach MSM, and limited access to behavioral health services (including substance use disorder treatment) as some of the barriers to adequate HIV prevention and care services for MSM populations.

POPULATION GROUP: TRANSGENDER PEOPLE

In Massachusetts, transgender individuals comprised 1% (n=17) of all new HIV diagnoses from 2018 to 2020 and 1% (N=136) of all persons living with HIV infection in Massachusetts as of December 31, 2020. Sex with men was the exposure mode for the majority (80%) of transgender women reported to be living with HIV infection. By comparison, male-to-male sex was the leading exposure mode for all persons living with HIV infection at 39%. Half of transgender women living with HIV infection were Hispanic/Latina compared to 28% of cisgender women and 27% of all persons living with HIV infection in MA. Most

transgender women living with HIV infection in Massachusetts were under 40 years old. A total of 57% of transgender women were ages 20–39 years old as of December 31, 2020,[6] compared to 16% of cisgender women and 19% of all persons living with HIV infection in Massachusetts. The distribution of place of birth among transgender women living with HIV infection on December 31, 2020, was more like that of all persons living with HIV infection (PLWH) in Massachusetts than cisgender women. Sixty-two percent of transgender women were born in the United States compared to 61% of all PLWH and 47% of cisgender women. Forty-seven percent of transgender women reported to be living with HIV infection in Massachusetts on December 31, 2020[7] were living in the Boston HSR, compared to 22% of cisgender women and 27% of all persons living with HIV infection. A total of 14% of transgender women were living in the Western HSR, 11% in both the Central and Northeast HSRs, and 9% in both the Metrowest and Southeast HSRs.

During the development of this Integrated Plan, the transgender, nonbinary, and gender expansive community continue to experience increased attacks and other forms of harassment and violence locally, including a bomb threat at a Boston-area hospital and nationally, at Club Q, an LGBTQ+ club in Colorado Springs (on the eve of Trans Day of Remembrance). The need for safe spaces to socialize, obtain peer support and life affirming care and services are underscored by the recommendations of the Transgender Health Advisory Group to the OHA to fund a bundle of prevention and care services (now and into the future) that include gender-affirming care, training on cultural competency, including the impact of violence (including gun violence) in the lives of these populations when seeking care, and hiring community members to deliver services whenever feasible.

POPULATION GROUP: PEOPLE WHO INJECT DRUGS

After more than a decade of decline, injection drug use has emerged as an increasing risk factor for HIV infection in the region. According to surveillance data provided by MDPH, the percentage of newly diagnosed HIV infection with IDU transmission risk (excluding MSM/IDU) increased from 4% in 2013 to 17% in 2020. In New Hampshire, while the numbers are small, there has been an increase in cases related to IDU transmission risk between the 6-year period 2010 to 2015 (4 cases) and the 4-year period 2016-2019 (13 cases). As mentioned previously, an investigated cluster of new HIV diagnoses in the Lowell/Lawrence region of the Boston EMA within the Commonwealth of Massachusetts (Middlesex and Essex Counties), identified 129 molecularly and/or epidemiologically linked cases of HIV infection, with additional linked cases also occurring throughout the Boston EMA (including in New Hampshire). In addition to the Lawrence/Lowell cluster, there was an increase in the number of HIV cases among persons who inject drugs in the Boston area starting in November 2018. There have been 164 cases diagnosed thorough the end of 2021.

Among people who inject drugs, the COVID-19 pandemic has been noted as a stressor that has resulted in an increase in deaths related to opioid overdoses in both urban and rural communities. This indicator of increase used of drugs by injection increases vulnerability to HIV infection. Reaching HIV+ injection drug users with Part A funding provides different challenges. While the opioid epidemic continues to be a focal point of concern in the Boston EMA, the substance use services (residential) category has stayed stable in its funding level given the significant resources available from SAMHSA and Massachusetts Behavioral Health Partnership. The BPHC has funded subrecipients to deliver Health Education/Risk Reduction Services to people who inject drugs. Many young, often homeless, people who inject drugs are difficult to reach, as well as difficult to link to and retaining care because of the often changeable and inconsistent conditions in

which they live. They are a mobile population moving throughout the Boston EMA and all of Massachusetts (and beyond).

One response to the ongoing challenge of HIV transmission through needle sharing and the sexual activity of people who inject drugs is the Massachusetts Prevention and Rapid Response to Outbreaks of HIV Transmission through Interventional Epidemiology and Linkage to Care and Treatment (Massachusetts PROTECT) The target population for the demonstration project is people who inject drugs newly diagnosed or at risk for HIV infection, and are identified in clusters/outbreaks of HIV attributed to injection drug use in one of the seven counties of Eastern MA, encompassing 75% of the state's resident population. In MA, small to medium size cities (although not exclusively) are most affected by the opioid epidemic, and there are unique qualities to outbreak response in urban areas (highly mobile population and accessible connections to injection networks in neighboring cities and other states.). BPHC will initially focus activities on Essex, Middlesex, and Suffolk counties, where recent diagnoses of HIV attributed to IDU have most occurred. BPHC will establish capacities and protocols that can be readily deployed to respond to HIV outbreaks in other populations, including MSM and persons who engage in transactional sex, among others.

MASS AND CASS

Within the city of Boston, a small area of land is known as a place for people who inject drugs or use non-injection drugs to access services, purchase drugs, find community in its varied forms, and, for some, to live on a short- or long-term basis. The area is known as "Mass/Cass" because it is located near the intersection of Massachusetts Avenue and Melnea Cass Boulevard. The neighborhood had long attracted people who use drugs due to the location of multiple substance use disorder treatment programs, as well as the only Public Health Hospital in Massachusetts with its inpatient, outpatient, and emergency department services.

However, the closure of the bridge to Long Island, site of several SUD treatment programs and shelters, in 2014 increased both the number of people visiting the Mass/Cass area and the setting up of temporary shelters (i.e., tents.). Inevitable clashes between the occupants of the area and neighboring businesses and residents precipitated an increased call for shelter, services, and security to address the problem. Politicians, police, behavioral and physical health services providers, housing and human rights advocates and other interested groups have coalesced over many years to bring humane and holistic best practices to assisting people at Mass/Cass with shelter/housing, security, health care, harm reduction services, while respecting calls to heed the people's human rights and dignity.

One strategy to reduce new infections among people who inject would be to increase PrEP update. According to the CDC, PrEP is an effective means of preventing acquisition of HIV among people who inject. In their document "Pre-exposure Prophylaxis for the Prevention of HIV Infection in the United States - 2021 Update," they describe the sexual risk of people who inject drugs:

> "Data from NHBS also demonstrate that most persons who inject drugs report sexual behaviors that confer risk of HIV acquisition. Among HIV-negative persons who use drugs who identify as male, 69% reported having had condomless vaginal sex in the prior 12 months, and 4% reported having had condomless anal sex with a male partner. Among HIV-negative persons who use drugs who identify as female, 79% reported having had condomless

vaginal sex, and 27% reported having had condomless anal sex. 33% of HIV negative persons who use drugs reported their most recent sex was condomless sex with a partner known to have HIV."[26]

STRATEGIES TO ADDRESS HIV

DIAGNOSE ALL PEOPLE WITH HIV AS EARLY AS POSSIBLE

The COVID-19 pandemic presented unique challenges in engaging PLWH, particularly the most vulnerable populations. The disproportionate impact of COVID-19 and Monkeypox infections on vulnerable, at-risk populations has been well documented, both in terms of reduced access to HIV testing, increased infection rates as well as secondary economic and emotional well-being effects.

Public health staff continue to support programs during this time, through continued engagement via contract management staff, COVID supplemental relief funds, and other resources. Furthermore, the pandemic presents opportunities to enhance the model of engagement for people at risk and with HIV as well as to implement new strategies for early intervention and care completion services, through expansion of telehealth capabilities. Additionally, strengthening of MassHealth during the pandemic through coverage protections, emergency waivers, and self-attestation for eligibility requests will continue to complement efforts to engage and retain people with HIV in care.

Engagement of people at risk to get tested for HIV is hampered by several factors. These include a lack of trust in the healthcare system, access to routine testing in convenient settings, and the stability of lifestyle required to return for test results. These challenges are addressed in the goals/objectives section which address expanding HIV screening pilots in hospital emergency departments and outpatient urgent care settings, deployment of mobile clinics that collaborate with local public health partners, in oral health settings, use of Peer Advocates/CHWs to bridge the "trust gap" to reach the homeless population as well as to increase bi- and multilingual capacity of HIV testing and counseling services.

TREAT PEOPLE WITH HIV RAPIDLY AND EFFECTIVELY TO REACH SUSTAINED VIRAL SUPPRESSION

Many of the challenges to expand access to treatment services are similar to the challenges facing the entire system of care for HIV in Massachusetts and the Boston EMA. These include cultural competency and the need to acknowledge and address structural racism, the issue of homelessness and housing instability making linkage to and maintenance in care difficult, mistrust and lack of positive experiences with the medical system, and the need to address social determinants of health including poverty, malnutrition, and lack of transportation. These factors often interfere with keeping medical appointments, maintaining consistent access to and use of ART, and the ability to reach and maintain viral suppression.

Some of the goals/objectives to improve treatment outcomes include the expansion of the Rapid Start model, ongoing work to Increase cultural awareness, competency and humility in care and treatment services, efforts to Increase access to housing and behavioral health services and increased opportunities for peer interactions for people with HIV. By December 31, 2026, these goals/objectives, and the activities to implement them, are intended to improve rates of viral suppression by 10% for all people with HIV, while

[26] Pre-exposure Prophylaxis for the Prevention of HIV Infection in the United States - 2021 Update p.26. Accessed online at https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

improving viral suppression rates for racial/ethnic minorities to be equivalent to rates in white (non-Hispanic) populations.

PREVENT NEW HIV TRANSMISSIONS BY USING PROVEN INTERVENTIONS, INCLUDING PRE-EXPOSURE PROPHYLAXIS (PREP) AND SYRINGE SERVICES PROGRAMS (SSPS)

The Prevent strategy will focus on addressing racial equity for the priority population groups of Black and Latinx people including gay, bisexual, and other men who have sex with men, transgender, nonbinary, and gender expansive people, cisgender women, and Black women who have recently immigrated to the United States.

Assessments within both the Black and Latinx communities are needed to gauge current understanding of HIV, HIV risk, how concern about HIV ranks against social determinants of Health (education, employment, housing, transportation, etc.), and what messages and messengers are most effective. This information can be used to develop updated materials for both the Black (non-Hispanic) and Latinx communities at risk for acquiring HIV.

For Black women who have recently immigrated to Massachusetts and the Boston EMA, prevention services need to focus on secondary prevention as many are HIV+ prior to arriving in the United States. An important strategy is to engage recent Black women immigrants in the HIV care and treatment services so that their viral load is undetectable and the virus is untransmittable.

One strategy to do this include use of community health workers with lived experience in communities similar or parallel to the countries of origin to the Black women. Another strategy is to develop materials that stress the importance of HIV treatment to achieve viral suppression by way of messages and messengers that reflect their culture, and especially their language (Haitian Creole, Luganda, etc.). These materials should provide clear guidance on how to obtain HIV treatment services and should reach them through the locations and media sources they frequent.

RESPOND QUICKLY TO POTENTIAL HIV OUTBREAKS TO GET NEEDED PREVENTION AND TREATMENT SERVICES TO PEOPLE WHO NEED THEM

Young, often homeless, people who inject drugs are difficult to reach and difficult to link to and retain in care due in part to the changeable and inconsistent conditions in which they live. They are a mobile population moving throughout Massachusetts as well as the entire Boston EMA.

RESPONDING TO MONKEYPOX AND OTHER INFECTIOUS DISEASES

Much of the infrastructure development in Massachusetts by the OHA has been built upon by BIDLS (the Bureau within which OHA exists) to help with both COVID-19 and, more recently, monkeypox. The importance of strengthening and building upon this infrastructure has been recognized by the Commonwealth of Massachusetts. Each State Budget Year, the line item for HIV needs to be renewed and some years additional language accompanies the funding allocation to help direct its use. This year the language explicitly has been expanded to include infectious diseases that also affect people with HIV.

Specifically, the HIV line item included this language:

> For human immunodeficiency virus and acquired immune deficiency syndrome, or HIV/AIDS, services, programs, and related services for persons affected by the associated conditions of viral hepatitis, sexually transmitted

> infections, tuberculosis, and other infections of public health importance; provided, that funding shall be provided to proportionately serve each of the demographic groups afflicted by HIV/AIDS and associated conditions…. (emphasis added) - Massachusetts FY23 Budget Line 4512-0103 HIV/AIDS Prevention Treatment and Services

This language points to a model of service by OHA that can sufficiently respond to HIV and infectious diseases outbreaks to the degree they impact populations of focus. This includes, in addition to the named diseases, monkeypox. In terms of monkeypox, the community most affected has been Black gay, bisexual and other men who have sex with men. Thus, not only has the state's "Respond" infrastructure been activated to respond to monkeypox prevention (including vaccination) and treatment, but the provider and community networks have been a key source of information on how this community has been impacted and have also provided service models to reach those most at risk.

SECTION V: 2022-2026 GOALS AND OBJECTIVES

GOALS AND OBJECTIVES DESCRIPTION

OHA and the BPHC's Ryan White Divisions are responsible for overseeing a significant amount of state and federal funds on an annual basis. Together they support an HIV prevention and care system for over 23,000 people with HIV or roughly 2% of the estimated 1.2 million people with HIV in the United States. In addition, both OHA and BPHC provide prevention services to reduce the number of new HIV infections across Massachusetts. To accomplish this, both jurisdictions administer contracts with many subrecipients and work with community engagement groups to set programmatic and policy direction. Therefore, there are a substantial number of goals/objectives in this Integrated Plan, representing an ambitious agenda to address all components of HIV across the five strategies: diagnose, treat, prevent, respond, and workforce.

Based on needs assessment findings, including the SCSN, extensive consultation with community engagement and population advisory groups, and building on previous plans, racial equity emerged as a key issue to be addressed. As described in the Situational Analysis, the disparity in infection rates for both the Black population and the Latinx population have been persistent in Massachusetts and the Boston EMA since the beginning of the epidemic. To continue addressing these disparities, the goals/objectives and associated activities in this Integrated Plan will focus specifically on these two populations. In response to recent epidemiological data, the plan will also address the HIV prevention and care needs of immigrant women of color, including Black and Latinx women.

UPDATES TO OTHER STRATEGIC PLANS USED TO MEET REQUIREMENTS

This Integrated Plan builds upon other strategic plans the goals/objectives of the EHE Plan for Suffolk County Massachusetts, the most recent of these plans. Many of the objectives in the EHE plan are included in this plan and have been expanded to encompass the entire State and EMA. For each of the goals/objectives in this plan, it is noted what goal of the National HIV/AIDS Strategy is supported, as well as which, if any, previous goal/objective builds upon.

2022-2026 GOALS AND OBJECTIVES

DIAGNOSE – GOAL A: INCREASE THE ABILITY TO IDENTIFY NEW HIV CASES

- **Objective A1:** Move the MA-Boston HIV System to a 100% Status Neutral Approach
- **Objective A2:** Expand a Syndemic Approach to Diagnosis of HIV and other Infectious Diseases among 100% of funded providers
- **Objective A3:** Implement strategies to ensure equitable access to HIV testing/counseling services by sexual and racial/ethnic communities made vulnerable to HIV across the State and EMA (urban-rural)
- **Objective A4:** Consult with stakeholders about rapid HIV testing
- **Objective A5:** Increase access to testing for individuals lacking medical and personal homes
- **Objective A6:** By 2021, achieve a reduction in the proportion of cases reported to Massachusetts HIV Surveillance Program with No Identified Risk (NIR), from 30% to 15% of all reported cases

OBJECTIVE A1: BY DECEMBER 31, 2026, MOVE THE MA-BOSTON HIV SYSTEM TO A 100% STATUS NEUTRAL APPROACH

A.1.2 Develop guidance on a Status Neutral Approach so that there is "no wrong door" for OHA and BPHC Ryan White-funded service providers.

A.1.3 Integrate guidance on Status Neutral Approach into subsequent procurements for HIV prevention and care services.

A.1.4 Monitor implementation of Status Neutral Approach in HIV prevention and care services.

- **Outcomes (reported annually, locally monitored):** Status neutral approach is implemented in all OHA and BPHC funded HIV prevention and care settings.
- **Monitoring Data Source:** Status Neutral Approach is described in procurements, competitive funding opportunities, applied in annual work plan submissions from contracted prevention and care vendors, as part of training and capacity building initiatives, and in federal applications and reports.
- **Expected impact on the HIV Care Continuum:** Improve identification of people at risk and living with HIV, increase linkage to care, and expand access to testing, linkage, and adherence support services.
- **Expected impact racial/ethnic and other inequities:** Reduce racial and ethnic disparities across all modes of transmission with respect to access to diagnostic services.
- **Links to which goal/s of the NHAS and/or other previous plans:** Links to Goal 1 of NHAS
- **Responsible party or parties/key partners:** OHA and BPHC, funded prevention and care providers, and members of community engagement and population health advisory groups, Boston EMA Planning Council.
- **Potential funding sources:** State, CDC, HRSA

OBJECTIVE A2: BY DECEMBER 31, 2026, EXPAND A SYNDEMIC APPROACH TO DIAGNOSIS OF HIV AND OTHER INFECTIOUS DISEASES TO 100% OF FUNDED PROVIDERS

A.2.1 Throughout the course of this Integrated Plan, the OHA will consult with population health advisory groups and impacted populations on ways to promote access to integrated HIV/HCV/STI, and tuberculosis (TB) testing for Black and Latinx populations, gay men, persons who inject drugs, transgender, nonbinary, and gender expansive people, and non-US born individuals.

A.2.2 By December 31, 2026, the OHA and funded capacity building providers will ensure training plans for the workforce address integrated infectious disease testing including (at a minimum) HIV, syphilis, and Hepatitis C.
A.2.3 By December 31, 2026, expand laboratory services to include viral load for Hepatitis C.
A.2.4 Adopt a syndemic approach that includes emerging health threats such as monkeypox.
A.2.5 Incorporate a syndemic approach into subsequent procurement of HIV prevention and care services.

- Outcomes (reported annually, locally monitored more frequently): All serum samples are screened for HIV, all urine and extra-genital samples have been co-tested for gonorrhea and chlamydia.
- Monitoring Data Source: Annual work plan submissions, service utilization data, State Public Health Laboratory reports
- Expected impact on the HIV Care Continuum: Impact on diagnoses of HIV, syphilis, Hep C and other STIs
- Expected impact racial/ethnic and other inequities: Increased diagnoses of HIV and other STIs that disproportionately impact Black and Latinx people, and increased access to prevention, care, and treatments
- Links to which goal/s of the NHAS and/or other previous plans: NHAS Goal 1, builds upon Objectives 1.1 and 3:5 of the MA EHE Plan for Suffolk County
- Responsible party or parties/key partners: State Public Health Laboratory, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, NEAETC, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- Potential funding sources: State, CDC

OBJECTIVE A3: IMPLEMENT STRATEGIES TO ENSURE EQUITABLE ACCESS TO HIV TESTING/COUNSELING SERVICES BY SEXUAL AND RACIAL/ETHNIC POPULATIONS, ESPECIALLY BLACK PEOPLE AND LATINX PEOPLE, WHO HAVE BEEN MADE VULNERABLE TO HIV

A.3.1 Develop education program to reduce provider stigma regarding best practices in taking a sexual history, including for Black women (especially those who are foreign born).
A.3.2 Develop education program on transgender, nonbinary, and gender expansive people and sexual practices to support appropriate screening for HIV and other STIs.
A.3.3 Increase HIV outreach in physical spaces such as clubs, sexual cultures, Pride events and festivals as well as Social Networking Model for testing (and/or linkage to care.)

- Outcomes (reported annually, locally monitored more frequently): Increase in testing of Black and Latinx gay, bisexual, and other men who have sex with men, Black and Latinx transgender, nonbinary, and gender expansive people, women, and immigrant women of color
- Monitoring Data Source: Service utilization data
- Expected impact on the HIV Care Continuum: Increase in percentage of people with HIV and STIs who are aware of their status and are linked to care
- Expected impact racial/ethnic and other inequities: Reduce or eliminate inequities in access to HIV and STI testing, and counseling based on race, ethnicity, sexual orientation, gender identity, and immigration status
- Links to which goal/s of the NHAS and/or other previous plans: NHAS Goals 1 and 3

- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, NEAETC, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC

OBJECTIVE A4: CONSULT WITH STAKEHOLDERS ABOUT RAPID HIV TESTING

A.4.1 Convene an advisory consultation with clinicians, harm reduction, LGBTQIA+, program manager, and consumer representatives to discuss serum and rapid HIV test technologies in the context of ending transmissions.

A.4.2 Summarize and report findings and recommendations from ad hoc group to BIDLS, BSAS, OHA leadership, and to members of OHAs advisory groups.

- **Outcomes (reported annually, locally monitored more frequently):** A diverse and representative c advisory consultation is conducted with a summary and key points shared with BIDLS, BSAS, OHA leadership, and OHAs advisory groups
- **Monitoring Data Source:** Completed standardized meeting summary template for advisory meetings and consultations
- **Expected impact on the HIV Care Continuum:** Improved access to HIV and integrated infectious disease testing, and linkage to care and treatments for newly identified people with HIV
- **Expected impact racial/ethnic and other inequities:** Improve access to HIV testing among vulnerable population groups to identify and link people at risk for HIV and people with HIV to prevention, care, and treatments
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 1, 2 and 3
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, BSAS, community-based organizations, including LGBTQIA+ organizations, healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC, HRSA

OBJECTIVE A5: INCREASE ACCESS TO TESTING FOR INDIVIDUALS LACKING MEDICAL AND PERSONAL HOMES, PEOPLE IN RURAL AREAS, AND OLDER INDIVIDUALS

A.5.1 By December 31, 2026, the OHA will expand an HIV screening pilot program in health care setting emergency departments to 10 high prevalence communities.

A.5.2 By December 31, 2026, OHA will assess the feasibility and mechanism through which to offer HIV screening in a pharmacy-based setting, urgent care centers, and dental care settings, in five or more high prevalence communities.

A.5.3 Establish a deployment protocol for mobile clinics (including serving rural areas), and fund at least five programs, that includes local collaboration with public health partners, and ensuring inclusion of cultural and linguistic capacities (cross-cutting activity).

A.5.4 Build strategies to increase trust including use of Peer Advocates/CHWs to bridge the "trust gap" to reach the homeless or marginally populations.
A.5.5 Increase capacity of PCPs to treat HIV to reduce need for referrals to specialty care which may reduce access to care/more patient education on value of Rapid Start.

- **Outcomes (reported annually, locally monitored more frequently):** Competitive procurement initiated and completed, vendors identified, increased HIV testing among persons at risk for HIV in communities with high HIV prevalence, increased number of persons who are aware of their HIV status, increased identification of HIV-negative persons at risk for HIV infection referred for nPEP, PrEP, and PrEPDAP, and increased participation in HIV partner services among persons diagnosed with HIV infection.
- **Monitoring Data Source:** Service utilization reports
- **Expected impact on the HIV Care Continuum:** Increase number of people with HIV who are aware of their status, and are linked and retained in care
- **Expected impact racial/ethnic and other inequities:** Reduces racial and other health inequities by reaching Black, Latinx, Black and Latinx gay and bisexual men, other men who have sex with men, including transgender, nonbinary, and gender expansive people, people who inject drugs who are disproportionately homeless or unstably housed, people in geographic areas with limited access to HIV testing in traditional health care settings, and older people (60+) at risk for HIV
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 1, 2 and 3, Objectives 1.2, 1.3 and 1.4 of the MA EHE Plan for Suffolk County
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC

OBJECTIVE A6: BY DECEMBER 31, 2026, ACHIEVE A REDUCTION IN THE PROPORTION OF CASES REPORTED TO MASSACHUSETTS HIV SURVEILLANCE PROGRAM WITH NO IDENTIFIED RISK (NIR), FROM 30% TO 15% OF ALL REPORTED CASES.

- **Outcomes (reported annually, locally monitored more frequently):** Reduced percentage of newly diagnosed cases with NIR as exposure
- **Monitoring Data Source:** HIV surveillance data
- **Expected impact racial/ethnic and other inequities:** NIR cases are disproportionately among people of color. Reducing the %NIR cases will improve ability to link and retain people in care.
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goal 3,
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA

community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers

- **Potential funding sources:** State, CDC, HRSA

TREAT – GOAL B: IMPROVE HEALTH OUTCOMES FOR PEOPLE LIVING WITH HIV

- **Objective B1:** Build upon the EHE effort to boost the Rapid Start model with a goal of making it universal and available in all health services regions (urban-rural) to achieve improvements in ART uptake, viral suppression, and retention in care
- **Objective B2:** Increase cultural awareness, competency and humility in care and treatment services to support linkage to and maintenance in care
- **Objective B3:** Increase access to housing and behavioral health services to support linkage to and maintenance in care
- **Objective B.4:** By December 31, 2026, improve rates of viral suppression by 10% for all people with HIV while improving viral suppression rates for Black and Latinx residents to be equivalent to rates in white (non-Hispanic) populations
- **Objective B.5** Increase opportunities for peer interaction for people with HIV

OBJECTIVE B1: BUILD UPON THE EHE EFFORT TO BOOST THE RAPID START MODEL WITH A GOAL OF MAKING IT UNIVERSAL AND AVAILABLE IN ALL HEALTH SERVICE REGIONS (URBAN-RURAL) TO ACHIEVE IMPROVEMENTS IN ART UPTAKE, VIRAL SUPPRESSION, AND RETENTION IN CARE

B.1.1 Increase the capacity of PCPs to treat HIV to reduce need for referrals to specialty care which may reduce access to care/more patient education on value of Rapid Start.
B.1.2 Develop patient education materials on value of Rapid Start.
B.1.3 Require use of Rapid Start model in subsequent procurement of HIV care services (see Prevent goal for incorporation of Rapid Start into prevention services to ensure a status neutral approach).

- **Outcomes (reported annually, locally monitored more frequently):** Procurement for services that includes Rapid Start model funded across all health service regions
- **Monitoring Data Source:** Annual work plans, service utilization reports of funded organizations
- **Expected impact on the HIV Care Continuum:** Improve linkage and retention in care
- **Expected impact racial/ethnic and other inequities:** Reduce racial/ethnic disparities, treatment interruptions by linking newly diagnosed and out of care people with HIV who are disproportionately Black or Latinx
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goal 2
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, NEAETC, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC, HRSA

OBJECTIVE B2: INCREASE CULTURAL AWARENESS, COMPETENCY, AND HUMILITY IN PREVENTION, CARE, AND TREATMENT SERVICES TO SUPPORT LINKAGE TO AND MAINTENANCE IN CARE

B.2.1 By Dec 31, 2026, the OHA and funded capacity building providers will ensure training plans for the workforce address client-centered and culturally responsive care for Black and Latinx and non-US born populations. To accomplish this, OHA will systematically review all training plans and update as needed to ensure that they are client-centered and anti-racist.

B.2.2 By December 31, 2026, the OHA will expand Community Health Worker (CHW)/Peer service models by adding CHWs and/or Peers to interdisciplinary prevention and care teams across MA and the EMA.

B.2.3 Work with BSAS to increase cultural competency on transgender, nonbinary, and gender expansive people among those working in SUD treatment programs.

B.2.4 By December 31, 2026, OHA will expand Correctional Linkage to Care (CLTC) services for individuals diagnosed with HIV and/or hepatitis C (HCV) who are incarcerated in correctional facilities across MA and the Boston EMA.

- Outcomes (reported annually, locally monitored more frequently): Improved rates of Black and Latinx people with HIV retained in care and virally suppressed
- Monitoring Data Source: State public health laboratory viral load reports, examples of training materials and notes that explicitly address anti-racist and transgender, nonbinary, and gender expansive educational content, and services inventory identifying CHWs in prevention and care teams
- Expected impact on the HIV Care Continuum: Increase rates of people with HIV retained in care and virally suppressed
- Expected impact racial/ethnic and other inequities: Reduction of inequities between Black, Latinx and non-Hispanic whites with respect to retention in care and viral suppression
- Links to which goal/s of the NHAS and/or other previous plans: NHAS Goals 2 and 3, Objectives 2.1, 2.3 and 3.5 of the MA EHE Plan for Suffolk County
- Responsible party or parties/key partners: State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, NEAETC, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- Potential funding sources: State, CDC, HRSA

OBJECTIVE B3: INCREASE ACCESS TO HOUSING AND BEHAVIORAL HEALTH SERVICES TO SUPPORT LINKAGE TO AND RETENTION IN CARE

B.3.1 Work collaboratively with HOPWA, and other entities to increase the availability of low-threshold housing available to people with HIV made vulnerable by poverty, racial and linguistic discrimination, prior arrest, or criminal record.

B.3.2 Work collaboratively with BSAS to increase availability of low-threshold housing including sober housing and housing for transgender, nonbinary, and gender expansive people.

B.3.3 By December 31, 2026, the OHA will increase programmatic investments in rapid-response housing and stabilization service models for newly diagnosed homeless and unstably housed people with HIV who inject drugs.

B.3.4 Increase access to mental health treatment that is culturally and linguistically competent and accessible, notably to existing treatment programs including SSPs.
B.3.5 Ensure CHWs involved with mental health care are adequately trained and supported through ongoing training and clinical supervision.
B.3.6 In subsequent procurement, OHA will purchase CHW, MH/BH support via FTE as staff of the integrated prevention and care team.

- **Outcomes (reported annually, locally monitored more frequently):** Increase linkage to and retention in HIV care, increased wellness
- **Monitoring Data Source:** Service utilization reports
- **Expected impact on the HIV Care Continuum:** Improve linkage to care, retention in care
- **Expected impact racial/ethnic and other inequities:** Strategies are intended to reach people with HIV who are experiencing homelessness or housing instability and those with behavioral health issues which both disproportionately impact Black and Latinx people
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goal 2, Objective 2.2 of the MA EHE Plan for Suffolk County
- **Responsible party or parties/key partners:** OHA, BPHC, BSAS, SAMHSA, HOPWA, community-based organizations, including LGBTQIA+ organizations, healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC, HRSA, SAMHSA, HOPWA

OBJECTIVE B.4 BY DECEMBER 31, 2026, IMPROVE RATES OF VIRAL SUPPRESSION BY 10% FOR ALL PEOPLE WITH HIV WHILE IMPROVING VIRAL SUPPRESSION RATES FOR RACIAL/ETHNIC MINORITIES TO BE EQUIVALENT TO RATES IN WHITE (NON-HISPANIC) POPULATIONS

B.4.1 By December 31, 2026, the OHA will utilize electronic laboratory reporting surveillance data to identify people with HIV who are out of care, to increase HIV care retention rates.
B.4.2 Increase rates of viral suppression through education about U=U; medications and side effects, housing access programs and medication assistance programs.
B.4.3 Initiate discussion regarding new and emerging prevention and treatment modalities (injectable, long-term treatment options, including injectable PrEP).
B.4.4 Utilize community-based education models that enhance acceptance and access to integrated testing and linkage to care.
B.4.5 OHA will provide expected models of service with tailored activities to increase role of local decision making in how services are delivered and therefore to engage and build trust in services.
B.4.6 Increase education on aging with HIV for providers, integrated prevention and care team staff, consumers, and others, to ultimately improve health outcomes.
B.4.7 Support people with HIV and dementia at long-term care facilities through education about HIV and LGBTQIA+ (and especially transgender, nonbinary, and gender expansive people) issues.
B.4.8 By December 31, 2026, the OHA will launch a new data dashboard for MA and EMA counties in MA that displays key indicators including rates of retention in care and viral suppression stratified by race, ethnicity, gender identity, age, mode of exposure, and geography.

- **Outcomes (reported annually, locally monitored more frequently):** Improved viral suppression rates
- **Monitoring Data Source:** State public health laboratory viral load reports

- **Expected impact on the HIV Care Continuum:** Increase rates of people with HIV retained in care and virally suppressed
- **Expected impact racial/ethnic and other inequities:** Reduction of inequities between Black, Latinx and non-Hispanic whites with respect to retention in care and viral suppression
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 2 and 3, Objectives 3.2 and 3.3 of the MA EHE Plan for Suffolk County
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, NEAETC, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC, HRSA

OBJECTIVE B.5 INCREASE OPPORTUNITIES FOR PEER INTERACTION AMONG PEOPLE WITH HIV

B.5.1 Increase both virtual and in-person resources for peer support to increase linkage to and maintenance in care while developing guidance for preserving privacy for individuals as needed.

B.5.2 For Boston EMA: Consider support groups for women (and others) who are survivors of sexual and domestic violence; sex workers; parents/moms who need support to increase linkage to and maintenance in care.

- **Outcomes (reported annually, locally monitored more frequently):** Number of support groups offered with sufficient attendance
- **Monitoring Data Source:** Service utilization reports
- **Expected impact on the HIV Care Continuum:** Retain people with HIV in care and virally suppressed
- **Expected impact racial/ethnic and other inequities:** Help Black and Latinx people find support to help them stay in care, virally suppressed, with improved overall health and wellness
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goal 2
- **Responsible party or parties/key partners:** OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, HRSA

Adapted from MA EHE Application for Suffolk County and expanded to include the entire jurisdiction (state and EMA):

OBJECTIVE 2:4: BY JUNE 30, 2026, THE OHA WILL HAVE SUSTAINED CONSULTATIONS WITH THE BOSTON PUBLIC HEALTH COMMISSION ON THE DEVELOPMENT AND IMPLEMENTATION OF A RED-CARPET ENTRY MODEL OF SERVICE THAT EXPEDITES LINKAGE TO HIV MEDICAL CARE AND TREATMENT

PREVENT – GOAL C: REDUCE NUMBER OF NEW HIV INFECTIONS AND INCREASE HIV AWARENESS AND KNOWLEDGE AMONG THE PUBLIC

- **Objective C1:** By December 31, 2026, reduce new HIV infections among US born-and foreign-born Black populations by 20%
- **Objective C2:** By December 31, 2026, reduce new HIV infections among native- and foreign-born Latinx populations by 20%
- **Objective C3:** By December 31, 2026, reduce new HIV infections among people who inject drugs by 20%
- **Objective C4:** By December 31, 2026, reduce new HIV infections among native Americans and native- and foreign-born people from Asia including East Asia, South Asia, the Middle East, and Eastern Europe by 20%
- **Objective C5:** By December 31, 2026, increase PrEP uptake by 35%
- **Objective C6:** Increase targeted prevention efforts through increased assessments and partnerships
- **Objective C7:** Develop and conduct HIV prevention education campaigns to increase HIV awareness and reduce stigma
- **Objective C8:** Develop resource to improve access to information about prevention and other HIV services

OBJECTIVE C1: BY DECEMBER 31, 2026, REDUCE NEW HIV INFECTIONS AMONG NATIVE- AND FOREIGN-BORN BLACK POPULATIONS BY 20%

C.1.1 By December 31, 2026, the OHA will award funding for up to ten organizations that include peers and others in the role of community health workers (CHWs) as well as behavioral health providers on interdisciplinary prevention and care teams.

C.1.2 By December 31, 2026, OHA will develop tailored health communications and educational materials to promote effective prevention strategies and health promotion topics relevant for Black people at risk for HIV including Black gay, bisexual and other men who have sex with men, including transgender, nonbinary, and gender expansive people, as well as Black people made vulnerable by substance use and mental health disorders, homelessness and housing instability, and poverty. Education efforts will also focus on Black partners of people with HIV.

C.1.3 Develop prevention messages and materials for immigrant women of color, and translate prevention messages in languages of these communities including Haitian Creole and Luganda.

- **Outcomes (reported annually, locally monitored more frequently):** Reduce new HIV infections
- **Monitoring Data Source:** HIV Surveillance program
- **Expected impact on the HIV Care Continuum:** Reducing number of new HIV infections
- **Expected impact racial/ethnic and other inequities:** Reduce new infections among the Black population in MA and the Boston EMA including immigrant women of color
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goal 1, Objectives 1.5, 1.7 and 1.11 of the MA EHE Plan for Suffolk County
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA

community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- OHA, Boston Public Health Commission/Ryan White Division
- **Potential funding sources:** State, CDC

OBJECTIVE C2: BY DECEMBER 31, 2026, REDUCE NEW HIV INFECTIONS AMONG NATIVE- AND FOREIGN-BORN LATINX POPULATIONS BY 20%

C.2.1 By December 31, 2026, the OHA will award funding for up to ten organizations that include peers and others in the role of community health workers (CHWs) as well as behavioral health providers on interdisciplinary prevention and care teams.

C.2.2 By December 31, 2026, OHA will develop tailored health communications and educational materials to promote effective prevention strategies and health promotion topics relevant for Latinx people at risk for HIV including Latinx gay, bisexual, and other men who have sex with men, including transgender, nonbinary, and gender expansive people, as well as Latinx transgender, nonbinary, and gender expansive people made vulnerable by stigma, discrimination, and poverty. Education efforts will also focus on Latinx partners of people with HIV.

- **Outcomes (reported annually, locally monitored more frequently):** Reduce new HIV infections
- **Monitoring Data Source:** HIV Surveillance program
- **Expected impact on the HIV Care Continuum:** Reducing number of new HIV infections
- **Expected impact racial/ethnic and other inequities:** Reduce new infections among the Hispanic/Latinx population in MA and the Boston EMA
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goal 1, Objectives 1.7 and 1.11 of the MA EHE Plan for Suffolk County
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC, HRSA

OBJECTIVE C3: BY DECEMBER 31, 2026, REDUCE NEW HIV INFECTIONS AMONG PEOPLE WHO INJECT DRUGS BY 20%

C.3.1 By December 31, 2026, expand syringe service programming to five or more cities/towns that have not yet approved it (addressing stigma, role of local authority, and procedure for funding syringe services).

C.3.2 Develop a strategy to expand access to PrEP among people who inject drugs and are eligible for PrEP based on needle sharing or condomless sex. The strategy should focus on several communities where there is a concentration of people who inject drugs including Mass/Cass.

- **Outcomes (reported annually, locally monitored more frequently):** Reduce new HIV infections
- **Monitoring Data Source:** HIV/STD Surveillance program
- **Expected impact on the HIV Care Continuum:** Reducing number of new HIV infections
- **Expected impact racial/ethnic and other inequities:** Reduce new infections among people who inject drugs in MA and the Boston EMA

- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goal 1, Objectives 1.5, 1.7 and 1.11 of the MA EHE Plan for Suffolk County
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, Office of Local and Regional Public Health, MA-based harm reduction providers, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC

OBJECTIVE C4: BY DECEMBER 31, 2026, REDUCE NEW HIV INFECTIONS AMONG NATIVE AMERICANS AND NATIVE- AND FOREIGN-BORN PEOPLE FROM ASIA INCLUDING EAST ASIA, SOUTH ASIA, THE MIDDLE EAST, AND EASTERN EUROPE BY 20%

C.4.1 By December 31, 2026, engage at-risk and vulnerable Native American and native-and foreign-born individuals from Asia, including Ease Asia, South Asia, the Middle East, and Eastern Europe in integrated testing services.

C.4.2 Utilize culturally tailored and effective venues and strategies to provide integrated testing alongside holistic approaches to care services.

- **Outcomes (reported annually, locally monitored more frequently):** Reduce new HIV infections
- **Monitoring Data Source:** HIV Surveillance program
- **Expected impact on the HIV Care Continuum:** Reducing number of new HIV infections
- **Expected impact racial/ethnic and other inequities:** Reduce new infections among foreign-born people from Asia including East Asia, South Asia, the Middle East, and Eastern Europe in MA and the Boston EMA
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goal 1, Objective 1.11 of the MA EHE Plan for Suffolk County
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC

OBJECTIVE C5: INCREASE PREP PRESCRIPTIONS BY 35% BY DECEMBER 31, 2026

C.5.1 By December 31, 2026, collaborate with area health service and capacity building partners to assess provider prescribing practices for biomedical prevention services and increase PrEP and nPEP prescriptions to MA and EMA-based residents.

C.5.2 Increase provider education to reduce HIV-related stigma, hesitancy and improve screening process in prescribing PrEP, increase utilization of PrEP assistance programs, and limit patient costs (co-pays, monitoring tests) related to PrEP receiving a Grade; classification by the USPSTF.

C.5.3 Expand marketing of PrEP to reach cisgender women, transgender, nonbinary, and gender expansive people, and gay/bi/MSM of color.
C.5.4 Identify strategy to increase same-day PrEP modeled upon Rapid Start for people with HIV.

- **Outcomes (reported annually, locally monitored more frequently):** Increase in PrEP prescriptions among populations disproportionately impacted by HIV, including those in rural communities
- **Monitoring Data Source:** Pharmacies, patient assistance programs
- **Expected impact on the HIV Care Continuum:** Fewer people diagnosed
- **Expected impact racial/ethnic and other inequities:** Reduce disparities in use of PrEP between white non-Hispanic population and Black and Latinx populations.
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 1 and 3
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC, HRSA

OBJECTIVE C6: INCREASE TARGETED PREVENTION EFFORTS THROUGH INCREASED ASSESSMENTS AND PARTNERSHIPS

C.6.1 Implement an acuity scale (including an abbreviated version) for prevention to account for people at risk for multiple conditions as well as understand the impact of social determinants of health and trauma in relationship to implementation of HIV prevention strategies (as well as Hepatitis C, other STIs, SUD, etc.).
C.6.2 Partner with Black Lives Matter and Black excellence movements to promote HIV prevention into Black spaces.
C.6.3 Reduce risk for women who have sex with men by increasing prevention among men who have sex with men but may not identify as gay or bisexual.

- **Outcomes (reported annually, locally monitored more frequently):** Reduced HIV infections and promote sexual health
- **Monitoring Data Source:** OHA contract managers, including annual work plans, and end of year report summary
- **Expected impact on the HIV Care Continuum:** Reduce number of people diagnosed with HIV
- **Expected impact racial/ethnic and other inequities:** Expand the types and numbers of partners from Black communities involved in community-wide prevention, linkage, and retention services
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS goals 1 and 3
- **Responsible party or parties/key partners:** OHA, BPHC Ryan White Program, CBOs serving Black communities across MA and EMA
- **Potential funding sources:** State, CDC

OBJECTIVE C7: DEVELOP AND CONDUCT HIV PREVENTION EDUCATION CAMPAIGNS TO INCREASE HIV AWARENESS AND REDUCE STIGMA

C.7.1 Create a targeted education campaign for older adolescents and young adults (ages 16-24) regarding the health impact of HIV infection despite the availability of effective treatment.
C.7.2 For Boston EMA: Collaborate with the Boston public school system to increase HIV education in the schools.

C.7.3 By December 31, 2026, work collaboratively with school-based health centers and school-based sexual health programs, and MA Commission on LGBTQ+ Youth to support youth and young adults with access to medically accurate and developmentally informed sexual health services, including access to nPEP and PrEP, etc.
C.7.4 Pool resources to support prevention activity on dating sites (Jack'd, Scruff, Grindr) to enable agencies to utilize this important space to provide HIV prevention messages to gay, bisexual, transgender, nonbinary, and gender expansive people, and other men who have sex with men.
C.7.5 For Boston EMA: Continue to promote and utilize Someone You Know video and messages to combat stigma and increase HIV awareness.

- Outcomes (reported annually, locally monitored more frequently): Increased HIV awareness, access to prevention methods, reduced HIV incidence, and decreased stigma
- Monitoring Data Source: Community health needs assessments, BRFSS, YRBS, school-based health center monitoring and data collection
- Expected impact on the HIV Care Continuum: Reduction in new HIV cases
- Expected impact racial/ethnic and other inequities: Decreased HIV infections among Black and Latinx youth and young adults
- Links to which goal/s of the NHAS and/or other previous plans: NHAS Goals 1 and 3, Objective 3.4 of the MA EHE Plan for Suffolk County
- Responsible party or parties/key partners: State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, school-based health centers, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- Potential funding sources: State, CDC

OBJECTIVE C8: DEVELOP RESOURCES TO IMPROVE ACCESS TO INFORMATION ABOUT PREVENTION AND OTHER HIV SERVICES

C.8.1 Improve access to basic information about available services (and be specific about which services) (cross-cutting goal/objective) and how to access them, including Spanish language information, and transgender, nonbinary, and gender expansive competency.
C.8.2 Create web portal or other mechanism to increase community-facing information related to HIV prevention services, stakeholder meetings, and other opportunities for engagement.

- Outcomes (reported annually, locally monitored more frequently): Increase knowledge about HIV services and how to access them as well as opportunities for community engagement
- Monitoring Data Source: Input from community engagement and population advisory groups, MIPCC, Boston EMA Planning Council
- Expected impact on the HIV Care Continuum: Improvement across entire continuum
- Expected impact racial/ethnic and other inequities: Overall improvement in outcomes should disproportionately benefit Black people and Latinx people
- Links to which goal/s of the NHAS and/or other previous plans: NHAS Goals 1, 2, 3
- Responsible party or parties/key partners: OHA, BPHC Ryan White Program, community engagement and population advisory groups
- Potential funding sources: State, CDC, HRSA

RESPOND – GOAL D: IMPROVE HIV RESPOND FUNCTIONS THROUGH SYSTEMS STRENGTHENING

- **Objective D1:** Implement and improve upon cluster and outbreak detection and response plans
- **Objective D2:** Conduct assessments to create new data sources, strengthen existing data sources, and monitor data sources to anticipate needs of populations vulnerable to outbreaks
- **Objective D3:** Strengthen response function at community level and in rural areas
- **Objective D4:** Increase equity in response to outbreaks by reducing structural racism and strengthening programs that address social determinants of health
- **Objective D5:** Address monkeypox epidemic and ensure vaccine equity to build trust in response system

OBJECTIVE D1: IMPLEMENT AND IMPROVE UPON CLUSTER AND OUTBREAK DETECTION AND RESPONSE PLANS

D.1.1 Build Health Department infrastructure and local HD partner model (as local capacity permits) to respond to emergent outbreaks by establishing dedicated personnel and response protocol in OHA to respond sufficiently, including ensuring dedicated community-based capacities and resources to meet the need.

D.1.2 By December 31, 2026, the OHA will engage members from its Community Engagement and Population Health Advisory Groups to address concerns regarding data confidentiality, including the use of molecular surveillance, client-level data, rationale for data collection, and protocols for consent, data storage, and analysis.

D.1.3 By December 31, 2026, in partnership with the Boston Public Health Commission, update HIV cluster detection and outbreak response policies and protocols, including review of partnerships, processes and data systems to improve real-time cluster detection and response to improve sharing of data between state and local public health and providers.

D.1.4 Move toward more digitized solutions, including virtual meetings and online appointment booking to support a more rapid response.

D.1.5 Support availability of high quality and timely data for decision making (cross-cutting into other areas).

D.1.6 Continue and expand use of molecular surveillance while utilizing person-centered language when utilizing this resource to avoid stigmatizing language. This includes the use of molecular, socioeconomic, and demographic data (including information about sub-populations at risk, such as country of origin, social determinants of health and relevant outcomes) to investigate and intervene in networks with active transmission.

D.1.7 Include "Respond" in subsequent OHA and BPHC procurements with development of guidance for service providers, including who should be involved in the "Respond" function and a description of their responsibilities.

- **Outcomes (reported annually, locally monitored more frequently):** More effective response to HIV clusters, successful procurement of integrated respond function into programs of funded contractors
- **Monitoring Data Source:** After action reports of HIV outbreaks, successful procurement, and funding of contractors
- **Expected impact on the HIV Care Continuum:** Reduce new HIV infections, identify people with HIV who do not know it, linkage to and retention in care

- **Expected impact racial/ethnic and other inequities:** Reduce impact of HIV outbreaks which disproportionately impact Black people and Latinx people
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS goals 1 and 2; Objectives 2.5, 2.6 and 3.7 of the MA EHE Plan for Suffolk County
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC, HRSA

OBJECTIVE D2: CONDUCT ASSESSMENTS TO CREATE NEW DATA SOURCES, STRENGTHEN EXISTING DATA SOURCES, AND MONITOR DATA SOURCES TO ANTICIPATE NEEDS OF POPULATIONS VULNERABLE TO OUTBREAKS

D.2.1 Conduct assessment of size of populations of transgender, nonbinary, and gender expansive people in MA including size of population living with HIV (consider same for Black people, Native Americans, and at-risk women).

D.2.2 Identify gaps in knowledge and infectious disease service assessment of Black (and other) populations to learn what they know about HIV and other STIs.

D.2.3 Monitor substance use among gay and bisexual men, other MSM, and transgender, nonbinary, and gender expansive people about risks associated with injecting meth (slamming).

- **Outcomes (reported annually, locally monitored more frequently):** Increase in current information regarding areas currently requiring additional assessment
- **Monitoring Data Source:** HIV needs assessments including surveys, stakeholder groups, Boston EMA Planning Council input and other sources to be determined
- **Expected impact on the HIV Care Continuum:** Reduce HIV outbreaks by increasing ability to interfere with transmission in communities disproportionately impacted by HIV
- **Expected impact racial/ethnic and other inequities:** Increase ability to address HIV outbreaks among Black people, Latinx people, transgender, nonbinary, and gender expansive people, and people who inject drugs
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 1 and 3
- **Responsible party or parties/key partners:** OHA, BPHC Ryan White Program, funded contractors, community engagement and population advisory groups, Boston EMA Planning Council
- **Potential funding sources:** State, CDC, HRSA

OBJECTIVE D3: STRENGTHEN RESPONSE FUNCTION AT COMMUNITY LEVEL AND IN RURAL AREAS

D.3.1 Increase use of Community Health Centers (CHCs) for Respond activities.

D.3.2 Improve collaboration between CHCs and community-based organizations through data sharing and other agreements to help strengthen service provision to identified people with HIV or people at risk for HIV.

D.3.3 Implement strategies, such as telehealth and improved transportation, to support equal access to care for people living in rural areas.

- **Outcomes (reported annually, locally monitored more frequently):** Number of CHCs engaged in Respond activities, improved coordination among CHCs, community-based organizations and others in response activities
- **Monitoring Data Source:** After action reports
- **Expected impact on the HIV Care Continuum:** Reduce new infections, linkage, and retention in HIV care
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 1 and 2
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Mass League of CHCs, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC

OBJECTIVE D4: INCREASE EQUITY IN RESPONSE TO OUTBREAKS BY STRENGTHENING PROGRAMS THAT ADDRESS SOCIAL DETERMINANTS OF HEALTH TO REDUCE IMPACT OF STRUCTURAL RACISM IN HIV OUTBREAKS

D.4.1 Identify opportunities to reduce disparities in response to outbreaks in all aspects of the HIV prevention and care system through use of trusted messengers including CHWs, treating people holistically, and being transparent in use of molecular surveillance and privacy protections.

D.4.2 Integrate social determinants of health (housing, education, transportation, childcare, etc.) into all parts of the HIV care continuum to strengthen response to outbreaks.

- **Outcomes (reported annually, locally monitored more frequently):** Racial equity in response to outbreaks
- **Monitoring Data Source:** After action reports
- **Expected impact on the HIV Care Continuum:** Reduce new infections, linkage, and retention in HIV care
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 1 and 3
- **Responsible party or parties/key partners:** State Public Health Laboratory, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, case reporters in healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Mass League of CHCs, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State, CDC

OBJECTIVE D5: ADDRESS MONKEYPOX EPIDEMIC AND ENSURE VACCINE EQUITY TO BUILD TRUST IN RESPONSE SYSTEM

D.5.1 Ensure protocols for vaccine distribution and tracking reach communities in greatest need, notably the population of Black gay men, bisexual men and other men who have sex with men.

D.5.2 Engage with new stakeholders, sexual subcultures and affinity groups and spaces, including media/social media, and others with a stake in reducing monkeypox infections and impact among Black gay men, Black bisexual men, Black transgender, nonbinary, and gender expansive people.

D.5.3 Collect demographic data for those receiving monkeypox vaccine, specifically race/ethnicity data.

- **Outcomes (reported annually, locally monitored more frequently):** Number and race/ethnicity of people vaccinated for monkeypox, race and ethnicity of people reported infected with monkeypox
- **Monitoring Data Source:** MAVEN, MIIS, service intervention plans
- **Expected impact on the HIV Care Continuum:** Reduce new infections, linkage to care
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 1 and 3
- **Responsible party or parties/key partners:** OHA, BPHC Ryan White Program, funded subrecipients, Massachusetts League of Community Health Centers, BIDLS infections disease reporting system (MAVEN) Massachusetts Immunization Information System (MIIS)
- **Potential funding sources:** State, CDC, HRSA

WORKFORCE – GOAL E: STRENGTHEN AND EXPAND HIV WORKFORCE

- **Objective E1:** Increase HIV workforce participation and satisfaction through various strategies
- **Objective E2:** Increase racial and ethnic equity in the HIV workforce
- **Objective E3:** Increase equity in the HIV workforce for the transgender, nonbinary, and gender expansive communities

OBJECTIVE E1: INCREASE HIV WORKFORCE PARTICIPATION AND SATISFACTION THROUGH VARIOUS STRATEGIES

E.1.1 Dedicate an OHA staff person to focus on workforce issues.
E.1.2 Increase opportunities, including tuition reimbursement, for professional development of existing staff and new staff entering field.
E.1.3 Continue to preferentially support full-time work at competitive wages through policy, including utilizing procurements and workforce development initiatives.
E.1.4 Re-establish provider networks for support, knowledge exchange, and better care coordination through strategies like Communities of Practice.
E.1.5 Work with professional licensing boards in MA to include training in HIV care as part of continuing education (alternative: as part of licensure requirements).
E.1.6 Support hiring of qualified individuals with both lived (living with HIV, living Black, Latinx, transgender, gay, and immigrant in the US) and learned experiences as well as those who've received prevention and care services.
E.1.7 Require funded organizations to review hiring practices and job descriptions for biases, prioritize compensation for language skills, and support organizations to shift from retributive supervision/HR paradigms to more restorative options.

- **Outcomes (reported annually, locally monitored more frequently):** Increase in staff representation of affected populations, retention, increase in worker satisfaction
- **Monitoring Data Source:** Job postings, OHA contract manager records, input from stakeholder groups
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 1 and 2
- **Responsible party or parties/key partners:** OHA, BPHC Ryan White Program, funded contractors, capacity building and training providers, MA professional licensure boards, academic partners, HIV/AIDS Surveillance Program, Division of STD Prevention, OHA, BPHC, community-based organizations, including LGBTQIA+ organizations, healthcare settings, including hospitals, community health centers, private physician practices, reproductive health settings, health care facilities in correctional settings, mobile units, AccessHealth MA, Mass League of CHCs, NEAETC, Ryan White Planning Council, OHA community engagement and population health advisory groups, Getting to Zero Coalition, and behavioral health providers
- **Potential funding sources:** State

OBJECTIVE E2: INCREASE RACIAL AND ETHNIC EQUITY IN THE HIV WORKFORCE

E.2.1 By December 31, 2026, the OHA, in collaboration with its funded capacity building providers, will identify training topics to improve staff retention and improve opportunities for career advancement, particularly for gay men, gay men of color, persons with history of addiction, Black, Latinx, and non-US born people, transgender, nonbinary, and gender expansive people, and people with HIV who are part of the workforce.
E.2.2 By December 31, 2026, the OHA and funded capacity building providers will ensure training plans for the workforce addresses integrated infectious disease testing, client-centered and culturally responsive

care, delivery of stigma-free sexual histories and behavioral health assessments, trauma-informed care, and referral to community resources for both at-risk and people with HIV and their partners.
E.2.3 Identify more providers with linguistic and cultural competency in Spanish, ideally creating a statewide Latino HIV serving organization.
E.2.4 Conduct more training for providers in Spanish.
E.2.5 Hire and professionalize peer navigators through integration with certification of community health workers.
E.2.6 Work to increase staff who are reflective of the community we are serving, including people with lived experience (rather than just degrees) as well as people who have experienced incarceration.
E.2.7 Provide more training on meeting people with intersectional identities, i.e., gay Black men, transgender, nonbinary, and gender expansive people of color.
E.2.8 Implement justice, equity, and inclusion metrics in procurements and monitor programs when funded

- **Outcomes (reported annually, locally monitored more frequently):** More diverse workforce at OHA, BPHC, and among those working in program manager, coordinator, and direct service settings
- **Monitoring Data Source:** Staffing demographic charts, provider staffing chart and service reports
- **Expected impact on the HIV Care Continuum:** Improvement across the HIV Care Continuum resulting from the delivery of tailored and culturally responsive services
- **Expected impact racial/ethnic and other inequities:** Reduce racial/ethnic disparities through greater trust of an invested HIV services workforce
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 1, 2, and 3, Objectives 2.7 and 3.6 of the MA EHE Plan for Suffolk County
- **Responsible party or parties/key partners:** OHA, BPHC Ryan White Program, funded contractors, capacity building and training providers, academic partners
- **Potential funding sources:** State, CDC, HRSA

OBJECTIVE E3: INCREASE EQUITY IN THE HIV WORKFORCE FOR THE TRANSGENDER, NONBINARY, AND GENDER EXPANSIVE COMMUNITIES

E.3.1 Assess and build capacity of providers to serve the transgender, nonbinary, and gender expansive communities.
E.3.2 Identify best practices or standards for providing culturally competent services for transgender, nonbinary, and gender expansive people.
E.3.3 Develop document on best practices or standards of care for HIV prevention and care services for transgender, nonbinary, and gender expansive diverse communities to build competency in transgender, nonbinary, and gender expansive care across the HIV workforce.
E.3.4 Support training and integration of transgender, nonbinary, and gender expansive staff into HIV service organizations.
E.3.5 Work with MassHealth specifically around competency and gender-affirming care in treating the transgender, nonbinary, and gender expansive community.

- **Outcomes (reported annually, locally monitored more frequently):** More diverse workforce at funded contractors across all program capacities
- **Monitoring Data Source:** Provider work plans, staffing charts, and service reports
- **Expected impact on the HIV Care Continuum:** Improvement across the HIV Care Continuum
- **Expected impact racial/ethnic and other inequities:** Create improved system of HIV care for transgender, nonbinary, and gender expansive people through greater trust of the HIV services workforce
- **Links to which goal/s of the NHAS and/or other previous plans:** NHAS Goals 1, 2, 3

- **Responsible party or parties/key partners:** OHA, BPHC Ryan White Program, funded subrecipients, capacity building and training providers, academic partners, community-based organizations working with transgender, nonbinary, and gender expansive people, and OHAs population health advisory groups, including the Transgender Advisory Group
- **Potential funding sources:** CDC, HRSA

SECTION VI: 2022-2026 INTEGRATED PLAN IMPLEMENTATION, MONITORING, AND JURISDICTIONAL FOLLOW UP

2022-2026 INTEGRATED PLANNING IMPLEMENTATION

The Integrated Plan includes a range of objectives, strategies, and associated activities. MDPH and BPHC are committed to deep collaboration with partners and community stakeholders to implement activities of the plan, frequent assessment of our progress in implementing planned strategies, and the extent to which these activities achieve our objectives. MDPH and BPHC have robust public health infrastructures and mechanisms to support the implementation, monitoring, evaluation, quality improvement, reporting and dissemination of the Integrated Plan's goals and objectives.

MDPH and BPHC staff are already responsible for oversight of HIV prevention, care, treatment, and community engagement activities, in addition to MDPH's oversight of the HIV/STD Surveillance Program. This, along with the existing robust capacity of the HIV prevention and care workforce in Massachusetts, will support the successful implementation of the Integrated Plan activities.

OFFICE OF HIV/AIDS

OHA is the division within BIDLS that is responsible for administering state and federal resources for HIV prevention, care, and treatment services. OHA works with medical and non-medical organizations, community-based programs, people with HIV/AIDS, and other stakeholders to advance HIV prevention and care services. This includes needs assessment, community engagement and HIV service planning, awarding contracts for services, capacity building assistance, and service monitoring and evaluation.

OHA funds a range of services in medical, non-medical, and community-based settings across the Commonwealth for persons living with or at risk for HIV infection. These services include prevention and risk reduction services; integrated testing for HIV, hepatitis C, sexually transmitted infections, and TB; and linkage to care and treatment; as well as opioid overdose education and naloxone distribution (OEND) activities, syringe services programs (SSP), non-occupational post-exposure prophylaxis (nPEP) and pre-exposure prophylaxis (PrEP). OHA funds a range of health promotion and disease prevention services for people living with HIV, with the aim of supporting engagement and retention in care and improving health outcomes. Medical case management programs assist in the coordination of medical care and support services, and either directly provide or coordinate access to HIV treatment, adherence counseling, health systems navigation, peer support, nutrition, housing search and advocacy, rental/utility assistance, legal services, and benefits counseling services.

Within OHA, the Behavioral Health and Infectious Disease Prevention unit is responsible for all stakeholder engagement and community advisory activities. This unit integrates behavioral health and infectious disease frameworks, and population health data to inform service models to better meet the needs of individuals disproportionately impacted by HIV. Public health interventions are planned and coordinated with stakeholders to effectively address complex health conditions to maximize outcomes in the OHA-contracted prevention and care service system. Coordination of community engagement and advisory activities are an integral component of this work. Staff within this unit routinely participate in several local and national meetings, as well as planning and advisory groups, including recent participation in the National Alliance of State and Territorial AIDS Director's Health Equity Regional Meeting during which the use of dashboards to track EHE efforts were discussed.

BOSTON PUBLIC HEALTH COMMISSION

BPHC, the local health department for the City of Boston, administers Ryan White Part A HIV funding to the Boston Eligible Metropolitan Area (EMA). The Boston EMA is home to 85% of persons with HIV in Massachusetts, and the work of BPHC supports delivery of responsive, highly effective services to people with HIV in Suffolk County. Awards from BPHC support the following services: medical case management, psychosocial support, medical transportation, housing search and advocacy, and nutritional programs. BPHC staff provides programmatic support to Ryan White-funded agencies in Suffolk County, including contract management, monitoring client demographics and service utilization data, and providing technical assistance on grant management and reporting requirements. BPHC also awards municipal funds within the City of Boston to support evidence-based interventions for HIV-negative individuals at high risk for HIV, HCV, and STI acquisition.

HIV/STD SURVEILLANCE

The Massachusetts HIV/AIDS Surveillance Program (MAHASP) is responsible for providing a comprehensive picture of the HIV/AIDS epidemic to support prevention and health service activities delivered by the MDPH and a statewide system of health care and social service organizations. Epidemiologists are responsible for the collection, analysis, and interpretation of adult and pediatric HIV/AIDS case data. HIV/AIDS Surveillance data are disseminated widely throughout the Commonwealth, to governmental agencies, public and private providers, advocacy groups and consumers. MAHASP staff work collaboratively with planning and policy groups, health care providers and other Bureaus within MDPH, providing surveillance information and assisting with assessment of resource distribution and ongoing planning to ensure that the needs of people living with or at risk for HIV infection are met. HIV Surveillance staff routinely perform analyses to identify increases in new HIV diagnoses in particular agencies, cities, regions, or populations, and are vigilant to the emergence of HIV infection clusters or potential outbreaks.

CAPACITY OF THE HIV PREVENTION AND CARE WORKFORCE

In Massachusetts, HIV prevention and care services are delivered in community based medical and non-medical agencies by a highly skilled and experienced workforce. The comprehensive healthcare system in Massachusetts provides people living with HIV, and those at elevated risk, with a wide range of access to medical providers, including internal medicine and specialty and sub-specialty providers; these providers are in community health centers, hospitals, academic medical centers, family planning agencies, substance use disorder treatment programs, and other community-based health and social service programs.

Programs include a range of clinical and non-clinical staff, including HIV testing and linkage providers, phlebotomists, medical case managers, behavioral health specialists, and peers with HIV. These individuals often work directly, or in collaboration with, registered nurses, nurse practitioners, infectious disease physicians, and primary care providers.

MPDH has a robust internal capacity building system to support the development of the HIV prevention and care workforce. Capacity building staff utilizes several different modalities to deliver trainings and provide technical assistance, including, individual agency and/or program level TA, coaching sessions, classroom trainings, and webinars. Capacity building and technical assistance efforts are supported by staff from the Office of Health Care Planning (OHCP). OHCP oversees capacity building activities for all the programs/divisions of BIDLS. OHCP offers trainings and other capacity building services to local partners in collaboration with OHA, the New England Prevention Training Center (PTC), and external TA providers such

as the New England AIDS Education and Training Center (NEATC) and others. Contracts with capacity building providers and technical assistance consultants will also be leveraged as necessary.

KEY DATA SOURCES FOR EVALUATION

Available data sources are described below, along with a description of the feasibility of collecting the required data for evaluation of the activities outlined in the Goals and Objectives section of this Integrated Plan. We do not anticipate any substantial barriers to collecting data for the outcomes outlined.

ELECTRONIC HEALTH RECORDS SUPPORT FOR PUBLIC HEALTH

Electronic Health Records Support for Public Health (ESP) uses specific case detection algorithms consisting of diagnosis codes, laboratory tests, prescriptions, and clinical indicators to accurately identify health conditions. Data sent to MDPH includes procedures, laboratory results, medications, clinical visits, missed appointments, as well as patient information such as demographics, insurance information, and housing status. BIDLS currently receives data through ESP on a variety of conditions including chlamydia, gonorrhea, syphilis, and acute hepatitis A, B, and C. ESP implementation will be incrementally expanded to include health care facilities funded by BIDLS for provision of integrated HIV, HCV, STI, and TB prevention, screening, linkage, and care coordination services.

Expansion of ESP will facilitate reporting of enhanced surveillance data including HIV treatment and health status (e.g., retention in care, sustained viral suppression). Importantly, expansion of ESP will enhance capacity for data to care activities; notably, it will facilitate streamlining identification of patients who are out of care or sub-optimally engaged in care, and thereby increase the timeliness and efficiency of public health intervention to re-engage patients in HIV medical care. Timely data from ESP provides a mechanism to measure and monitor disparities in health outcomes and will be a component of Integrated Planning efforts to identify and prioritize clinical interventions to optimize health outcomes.

COMMUNICABLE DISEASE SURVEILLANCE DATA

Surveillance data including case reports and laboratory results on all reportable infectious diseases, including HIV, STIs and HCV, are reported to MDPH and are managed through the Massachusetts Virtual Epidemiologic Network (MAVEN). MAVEN is a web-based disease surveillance and case management system that enables state and local health departments to collect and share public health, laboratory, clinical, and case management data securely over the Internet. Data generated from these sources include updated HIV epidemiologic and laboratory data that inform federal reporting via eHARS. These data will be important for efforts to characterize the incidence of HIV co-infections (e.g., HIV/syphilis, HIV/HCV, and HIV/TB in particular), to understand how co-infections affect populations, and to inform and refine prevention and care planning efforts.

OHA SERVICE UTILIZATION DATA

All OHA-supported providers of prevention, testing and linkage, medical case management, and care and treatment services submit data to OHA including client demographics, exposure mode category, and service utilization (e.g., testing, medical case management, treatment). Data are maintained in multiple databases. Testing and linkage services data are submitted by providers via electronic forms; data collected from these forms are uploaded into the secure testing and linkage to care database (TLC) for ongoing analysis and submission to federal funders. Data related to health education, materials distribution, and syringe services (e.g., number of syringes distributed and collected) are similarly submitted to MDPH by contracted agencies for entry into a dedicated database (i.e., the Risk Reduction Activities database). Direct

services delivered to persons diagnosed with HIV, including referrals made and confirmation of linkages are entered into a local installation of CAREWare (CAREWare Massachusetts), a client-level data collection system supported by HRSA to evaluate Ryan White- funded services that have been tailored to the Massachusetts services system.

Boston Public Health Commission: Service Data and Funding Streams Overview

Members of the Ryan White Part A Planning Council, as well as staff at the Boston Public Health Commission, contributed valuable information to the needs assessment process relative to HIV/AIDS services funded through RWHAP Part A funds and the City of Boston. This information includes an annual review of funding streams and the availability of HIV/AIDS services within the Boston Eligible Metropolitan Area (EMA). This review describes the types and amounts of federal, state, and local funds available for HIV-related services in the Boston EMA. Data for this assessment is collected using a survey completed by various HIV/AIDS payers and providers in the Boston EMA. BPHC collects service utilization data for people with HIV in the Boston EMA through a system called e2Boston, which generates analytic reports that will contribute to planning processes.

IMPLEMENTATION

In developing the Integrated Plan, goals/objectives were written based on input from community engagement and population-based advisory groups. This included the Massachusetts Integrated Plan Coordination Committee (MIPCC) and the Boston EMA Ryan White Services Planning Council. Previous goals/objectives from the 2020 EHE Plan for Suffolk County Massachusetts were then re-examined by OHA and BPHC and, where it made sense, incorporated into the Integrated Plans goals/objectives, and expanded to encompass the entirety of OHA's jurisdiction, the Commonwealth of Massachusetts and BPHC's Ryan White Division's jurisdiction, the Boston Eligible Metropolitan Area.

Once finalized, MDPH and BPHC will create an annual work plan based on the Integrated HIV Prevention and Care Plan outlined in Section V, and which will include detailed tasks, responsible party, timelines, and measurable outcomes. As part of the implementation approach, MDPH and BPHC will review and update as necessary the structure and process for collaboration between planning bodies, recipients, and contractors/subrecipients, including communication protocols to support implementation and mechanisms to share progress and challenges.

OHA and the BPHC Ryan White Program are committed to continuing the collaborative relationships established during the development of the EHE Plan for Suffolk County Massachusetts throughout the implementation of this Integrated Plan. This is especially important, as synergy is needed between this plan and the EHE plan, and the collaborative approach will continue beyond initial implementation through the monitoring, evaluation, and improvement of the Plan. After submission of the plan, both OHA and BPHC plan to develop processes to create collaboration between OHA and BPHC for the purpose of monitoring, evaluating, and improving the plan. This will help to ensure that what has been done to accomplish the EHE plan will be replicated in the Integrated Plan and expanded into the full geographic area covered by both entities (OHA and BPHC).

MDPH and BPHC will perform frequent assessment of Integrated Plan progress in implementing planned strategies. Successful implementation will include:

- Monitoring of programmatic investments;

- Ongoing community engagements with the Boston EMA Planning Council, OHAs Community Engagement and Population Health Advisory Groups and residents from impacted populations;
- Regular communications with existing and new partners;
- Timely review of service utilization and MDPH HIV Data Dashboard data; and
- Contract monitoring performance information.

MONITORING AND EVALUATION

MDPH and BPHC will monitor and evaluate the Integrated Plan based on the goals, objectives, activities, data indicators, timeline, and responsible parties, as outlined in Section V. These indicators alongside other variables provide a roadmap for monitoring and evaluating the Commonwealth's response to HIV, specifically the strategies and associated activities outlined in the Integrated Plan. MIPCC and the Boston EMA Planning Council will also provide input on the monitoring and evaluation plan.

This monitoring and evaluation process will articulate the data collection, management, and analytic resources, tools and processes needed to implement the monitoring and evaluation plan, including identification of gaps and opportunities for improvement (including HOWPA). Specific measurable outcomes associated with identified strategies and activities have been identified. In this way, implementation of the monitoring and evaluation plan will promote and facilitate provision of high-quality, evidence-based prevention, care, and treatment services for HIV.

This process will be the primary mechanism to monitor our coordinated efforts across multiple actors and initiatives, and to remain accountable to stakeholders for priority commitments to reduce the impacts of HIV infection in the Commonwealth. Ongoing assessment of progress will enable adjustments to program plans, including ramping up strategies that are proven effective and reducing or re-directing investments from those that do not meet expectations. Evaluation of the plan will occur on an annual basis to assess whether the process of implementation and monitoring calls for improvement to the Integrated Plan. This may include readjustment of goals, objectives, timelines, measures, data sources, parties responsible or other factors.

To create a participatory process for monitoring and evaluation, OHA and BPHC will integrate their primary Integrated Plan workgroups, MIPCC and the Boston EMA Planning Council, into the process through periodic updates and discussion regarding progress on the IP's goals/objectives. In addition, progress on specific goals and objectives will be reviewed and discussed with community engagement and population advisory groups as part of the process of collecting input for the purpose of monitoring and evaluating the Integrated Plan.

IMPROVEMENT

This Integrated Plan is a living document that will be updated annually to include new or revised goals, objectives, and key strategies and activities. MDPH and BPHC will seek input from our existing recipients, subrecipients, the Boston EMA Planning Council, and OHA's Community Engagement and Population Advisory Groups regarding the local-level issues and challenges impacting progress as well as strategies to refine and improve efforts to respond to HIV and other STDs.

REPORTING AND DISSEMINATION

MDPH and BPHC are committed to transparency and accountability, and vows to report regularly on its progress towards achieving the objectives presented in this plan. We will report to key stakeholders and

advisory bodies on progress toward implementing the Integrated Plan, achievement of benchmarks, challenges encountered, and changes to the plan.

We will work with the MDPH Media Office to prepare a press release and collaborate with the Boston Public Health Commission and the local health agencies on coordinated communications about the Integrated Plan. MDPH and BPHC will distribute this plan to BIDLS staff, the Boston EMA Planning Council, and members of OHAs Community Engagement and Population Health Advisory Groups. The Integrated Plan will be posted on both the MPDH website and the Boston EMA Planning Council website for all community stakeholders to read and/or download. Updates and progress will be shared through these same venues.

The Executive Summary of the Integrated HIV Prevention and Care Plan serves as a stand-alone summative document highlighting the depth and breadth of community engagement, the future of prevention and care services priorities. It will be disseminated to internal and external partners of MDPH and the BPHC, corrections and mental health partners, researchers, academic partners, and MassHealth (the State's Medicaid agency) as well as local public health departments, elected officials, and advocacy organizations.

CONTRIBUTORS

The Bureau of Infectious Disease and Laboratory Sciences (BIDLS), Office of HIV/AIDS (OHA), and the Bureau of Infectious Diseases, Ryan White Services Division, gratefully acknowledges the many advisors and contributors to this plan. Each member of the Massachusetts Integrated Prevention and Care Committee (MIPCC), Statewide Consumer Advisory Group, Ryan White Planning Council members and Consumer Committee, Getting to Zero Coalition, The EHE Steering Committee, BIDLS and OHA staff, and participants of population advisory groups brought a wealth of experience, recommendations, insights, passion, and commitment, directed the content, feedback, and value to this joint city and state plan.

SECTION VII: LETTERS OF CONCURRENCE

APPENDIX 1: CHECKLIST

Requirement:	New Material and/or Existing Material Used to Meet Requirement:	Document Title/File Name of Existing Material Attached to Meet Requirement	Page Number(s) Where Requirement is Addressed in Existing Material	Notes (If Applicable)
Section I: Executive Summary of Integrated Plan and SCSN				
1. Executive Summary of Integrated Plan and SCSN	New Material			
a. Approach	New Material			
b. Documents Submitted to Meet Requirements	New Material			
Section II: Community Engagement and Planning Process				
1. Jurisdiction Planning Process				
a. Entities Involved in Process	Existing Material	Massachusetts DPH CDC PS19-1906: Strategic Partnerships and Planning to Support Ending the Epidemic in the United States Grant Application	pp. 5-7	NA
b. Role of the RWHAP Part A Planning Council/Planning Body (not required for state only plans)	New Material	NA	NA	NA
c. Role of Planning Bodies and Other	New Material	NA	NA	NA

Requirement:	New Material and/or Existing Material Used to Meet Requirement:	Document Title/File Name of Existing Material Attached to Meet Requirement	Page Number(s) Where Requirement is Addressed in Existing Material	Notes (If Applicable)
Entities				
d. Collaboration with RWHAP Parts – SCSN Requirement	New Material	NA	NA	NA
e. Engagement of People with HIV – SCSN Requirement	New Material	NA	NA	NA
f. Priorities	New Material	NA	NA	NA
g. Updates to Other Strategic Plans Used to Meet Requirements	NA	NA	NA	NA
Section III: Contributing Data Sets and Assessments				
1. Data Sharing and Use	New Material	NA	NA	NA
2. Epidemiologic Snapshot	Existing Materials	Massachusetts HIV/AIDS Epidemiologic Profiles (Statewide and Population-specific used)	Multiple throughout the various Massachusetts Epi documents	Refer to https://www.mass.gov/lists/hivaids-epidemiologic-profiles and footnotes throughout section for specific reports
3. HIV Prevention Care and Treatment Resource Inventory	New Material	NA	NA	NA
a. Strengths and Gaps	New Material	NA	NA	NA
b. Approaches and Partnerships	New Material	NA	NA	NA
4. Needs Assessment	New Material	NA	NA	NA

Requirement:	New Material and/or Existing Material Used to Meet Requirement:	Document Title/File Name of Existing Material Attached to Meet Requirement	Page Number(s) Where Requirement is Addressed in Existing Material	Notes (If Applicable)
a. Priorities	New Material	NA	NA	NA
b. Actions Taken	New Material	NA	NA	NA
c. Approach	New Material	NA	NA	NA
Section IV: Situational Analysis				
1. Situational Analysis	New Material	NA	NA	NA
a. Priority Populations	New Material	NA	NA	NA
Section V: 2022-2026 Goals and Objectives				
Goals and Objectives Description	New Material	NA	NA	Some objectives were taken from the MA EHE Plan for Suffolk County. The specific objectives from the EHE plan are noted throughout the section
a. Updates to Other Strategic Plans used to Meet Requirements	No updates to other plans	NA	NA	NA
Section VI: 2022-2026 Integrated Planning Implementation, Monitoring and Jurisdictional Follow Up				
1. 2022-2026 Integrated Planning Implementation Approach	New Material	NA	NA	NA
a. Implementation	New Material	NA	NA	NA
b. Monitoring	New Material	NA	NA	NA

Requirement:	New Material and/or Existing Material Used to Meet Requirement:	Document Title/File Name of Existing Material Attached to Meet Requirement	Page Number(s) Where Requirement is Addressed in Existing Material	Notes (If Applicable)
c. Evaluation	New Material	NA	NA	NA
d. Improvement	New Material	NA	NA	NA
e. Reporting and Dissemination	New Material	NA	NA	NA
f. Updates to Other Strategic Plans Used to Meet Requirements	New Material	NA	NA	NA
Section VII: Letters of Concurrence				
1. CDC Prevention Program Planning Body Chair(s) or Representative(s)	NA (Integrated Planning Body)			
2. RWHAP Part A Planning Council/Planning Body(s) Chair(s) or Representative(s) (Boston EMA PC)	New Material			
3. RWHAP Part B Planning Body Chair or Representative	NA (Integrated Planning Body)			
4. Integrated Planning Body (MIPCC)	New Material			
5. EHE Planning Body	NA (Integrated Planning Body)			

APPENDIX 2: MASSACHUSETTS AND BOSTON EMA HIV PREVENTION, CARE AND TREATMENT RESOURCE INVENTORY

Organization Name	Funding Source	Services / Activities	Priority Populations Served
Action for Boston Community Development (ABCD) Health Services	Boston HIV Prevention Subrecipient	Health Education and Risk Reduction	MSM of Color, Black Women, Youth
AccessHealth MA (formerly Community Research Initiative – CRI)	Part A Subrecipient	ADAP	All
AIDS Project Worcester	Part A Subrecipient	Emergency Financial Assistance, Food Bank and Home-Delivered Meals, Health Education and Risk Reduction, Medical Transportation, Non-Medical Case Management, Psychological Support Services	All
AIDS Response of the Seacoast	Part A Subrecipient	Non-Medical Case Management	All
Beth Israel Deaconess Medical Center - Plymouth	RWHAP Part C Recipient; Part A Subrecipient	Part C: Community-Based Early Intervention; Part A: Medical Case Management, Medical Transportation	All
Boston Children's Hospital	Part A Subrecipient; Boston HIV Prevention Subrecipient	Part A: Medical Nutritional Therapy, Health Education and Risk Reduction; Prevention: Health Education and Risk Reduction	Youth
Boston Health Care for	RWHAP Part C	Part C: Community-	All

Organization Name	Funding Source	Services / Activities	Priority Populations Served
the Homeless Program	Recipient; Part A Subrecipient	Based Early Intervention; Part A: Medical Case Management, Medical Transportation	
Boston Medical Center	RWHAP Part D Recipient; Boston HIV Prevention Subrecipient	Part D: Core and Support Services for Families and Youth Prevention: Health Education and Risk Reduction	Women, Youth, People Who Inject Drugs
Boston Public Health Commission	RWHAP Part A / MAI Recipient; Boston HIV Prevention Recipient	Part A: Community Planning, Grant Administration, Quality Management, Dental; Prevention: Community Planning, Grant Administration	All
Boston University	RWHAP Part F Recipient - Dental and SPNS	Dental / Oral Health	All
Brockton Neighborhood Health Center	RWHAP Part C Recipient	Community-Based Early Intervention	All
Cambridge Health Alliance	RWHAP Part C Recipient; Part A Subrecipient	Part C: Community-Based Early Intervention; Part A: Medical Case Management	All
Cape Cod Hospital	RWHAP Part C Recipient	Community-Based Early Intervention	All
Casa Esperanza	Part A Subrecipient	Medical Case Management, Health Education and Risk Reduction, Medical Transportation	All
Catholic Charities	Part A Subrecipient	Non-Medical Case Management, EF, Linguistics	All

Organization Name	Funding Source	Services / Activities	Priority Populations Served
Codman Square Health Center	Part A Subrecipient; Boston HIV Prevention Subrecipient	Part A: Medical Case Management, Medical Transportation, Psychological Support Services (MAI), Emergency Financial Assistance; Prevention: Health Education and Risk Reduction	All
City of Lowell, -- Community Development Department	HOPWA Recipient	Housing	All
Community Servings	Part A Subrecipient	Medical Nutritional Therapy	All
Dimock Community Health Center	RWHAP Part C/D Recipient; Part A Subrecipient	Part C: Community-Based Early Intervention; Part D: Core and Support Services for Families and Youth Part A: Medical Case Management, Medical Transportation, Psychological Support Services (MAI)	All
East Boston Neighborhood Health Center	RWHAP Part C Recipient; Part A Subrecipient; Boston HIV Prevention Subrecipient	Part C: Community-Based Early Intervention; Part A: Medical Case Management (MAI), Psychological Support Services (MAI) Prevention: Health Education and Risk Reduction	All
Edward M. Kennedy Health Center	Part A Subrecipient	Medical Case Management, Medical	All

Organization Name	Funding Source	Services / Activities	Priority Populations Served
		Transportation	
Worcester Executive Office of Economic Development	HOPWA Recipient	Housing	All
Family Health Center of Worcester	RWHAP Part C Recipient	Community-Based Early Intervention	All
Father Bill's and Mainspring	Part A Subrecipient	Housing	All
Fenway Community Health Center	RWHAP Part C and F - SPNS Recipient; Part A Subrecipient; Boston HIV Prevention Subrecipient	Part C: Community-Based Early Intervention; Part F: SPNS; Part A: Medical Case Management, Emergency Financial Assistance, Medical Transportation, Housing, Other Professional Services-Legal (MAI), Psychological Support Services; Prevention: Health Education and Risk Reduction	All
Greater Lawrence Family Health Center	RWHAP Part C Recipient; Part A Subrecipient	Part C: Community-Based Early Intervention; Part A: Medical Case Management, Medical Transportation, Emergency Financial Assistance	All
Greater New Bedford Community Health Center	RWHAP Part C/D Recipient	Part C: Community-Based Early Intervention; Part D: Core and Support Services for Families and Youth	All

Organization Name	Funding Source	Services / Activities	Priority Populations Served
Harbor Care (Harbor Homes)	Part A Subrecipient	Medical Case Management, Psychological Support Services	All
Harbor Health Center	RWHAP Part C Recipient; Part A Subrecipient	Part C: Community-Based Early Intervention; Part A: Medical Case Management, Housing, Emergency Financial Assistance (MAI)	All
Harvard College	RWHAP Part F Recipient - Dental	Dental / Oral Health	All
Holyoke Health Center	RWHAP Part C Recipient	Community-Based Early Intervention	All
Jordan Health Systems	RWHAP Part C Recipient	Community-Based Early Intervention	All
JRI (Justice Resource Institute, Inc.) Health	Part A Subrecipient; Boston HIV Prevention Subrecipient	Medical Transportation, Housing, Psychological Support Services, Other Professional Services-Legal; Prevention: Health Education and Risk Reduction	All
Lynn Community Health Center	RWHAP Part C Recipient; Part A Subrecipient	Part C: Community-Based Early Intervention; Part A: Medical Case Management, Medical Transportation	All
Making Opportunity Count	Part A Subrecipient	Emergency Financial Assistance, Food Bank and Home-Delivered Meals, Health Education and Risk Reduction, Medical Transportation, Non-	All

Organization Name	Funding Source	Services / Activities	Priority Populations Served
		Medical Case Management, Psychological Support Services	
Massachusetts Alliance of Portuguese Speakers (MAPS)	Part A Subrecipient	Non-Medical Case Management (MAI), Emergency Financial Assistance, Health Education and Risk Reduction	All
Massachusetts Department of Public Health	RWHAP Part B & D Recipient; CDC High-Impact Prevention Recipient; HOPWA Recipient	Part B: Community Planning, Grant Administration, Quality Management; Part D: Dental; CDC: Community Planning, Grant Administration; HOPWA: Housing	All
Massachusetts Department of Mental Health	SAMHSA Substance Abuse Prevention and Treatment Block Grant Recipient	Grant Administration and Coordination	All
Massachusetts General Hospital - Boston	Part A Subrecipient	Medical Case Management, Medical Transportation	All
Massachusetts General Hospital - Chelsea	Part A Subrecipient	Medical Case Management, Medical Transportation	All
Merrimack Valley Assistance Program	Part A Subrecipient	Non-Medical Case Management	All
Multicultural AIDS Coalition (MAC)	Part A Subrecipient; Boston HIV Prevention Subrecipient	Non-Medical Case Management, Medical Transportation, Psychological Support Services (MAI), Emergency Financial Assistance, Health	All

Organization Name	Funding Source	Services / Activities	Priority Populations Served
		Education and Risk Reduction; Prevention: Health Education and Risk Reduction	
Neighborhood Development (Boston)	HOPWA Recipient	Housing	All
New England AIDS Education and Training Center (NEAETC)	RWHAP Part F Recipient - AETC	Capacity Building and Technical Assistance	NA
New Hampshire Department of Public Health	Part A Subrecipient	ADAP	All
Office of Housing & Neighborhood Services (Springfield)	HOPWA Recipient	Housing	All
Sociedad Latina	Boston HIV Prevention Subrecipient	Health Education and Risk Reduction	Youth
Tufts University School of Dental Medicine	RWHAP Part F Recipient - Dental	Dental / Oral Health	All
University of Massachusetts Medical School	RWHAP Part C Recipient	Community-Based Early Intervention	All
Upham's Community Health Center	Part A Subrecipient	Medical Case Management (MAI), Emergency Financial Assistance	All
Victory Programs	Part A Subrecipient; Boston HIV Prevention Subrecipient	Non-Medical Case Management, Housing, Medical Transportation, Food Bank and Home-Delivered Meals, Psychological Support Services, Health Education and Risk Reduction; Prevention: Health	All

Organization Name	Funding Source	Services / Activities	Priority Populations Served
		Education and Risk Reduction	
Whittier Street Health Center	Part A Subrecipient; Boston HIV Prevention Subrecipient	Part A: Medical Case Management (MAI), Medical Transportation, Psychological Support Services, Emergency Financial Assistance; Prevention: Health Education and Risk Reduction	All

APPENDIX 3: MASSACHUSETTS HIV FINANCIAL INVENTORY

FEDERAL GRANTS AND CONTRACTS FEDERAL FISCAL YEAR 2022

Funding Source	Funded Service Providers	Funded Services
Ryan White HIV/AIDS Program Part A	Resources are administered by the Boston Public Health Commission Resources support service contracts at community-based medical and non-medical agencies in the Boston EMA.	• Medical case management • Medical transportation • Nutrition programs • Client advocacy (legal services) • Peer services • Dental ombudsman
Ryan White HIV/AIDS Program Part B	Resources support health department personnel, direct service contracts with 22 agencies that provide HIV services, and a contract with 1 agency that operates the HIV Drug Assistance Program.	• HDAP: Coverage for the full cost of drugs for uninsured people with HIV; Health insurance premium assistance; HIV medication copayment assistance • HIV Drug Assistance Program • HIV Medical case management • HIV ARCH services (high-acuity MCM) • HIV Medical transportation • HIV Home-delivered meals • HIV Housing search and advocacy • HIV Legal services • HIV Peer support services • HIV dental ombudsperson services
Ryan White HIV/AIDS Program Part C	Resources support personnel and costs associated with the delivery of services at 16 community health center and hospital programs	• Early Intervention Services • Core medical services • Support services • Clinical quality management
Ryan White HIV/AIDS Program Part D	Resources support health department personnel, 3 direct service contracts, 1 contract to provide consumer activities, and 1 contract to provide training and technical assistance through the MassCARE Program. Services are for women, infants, children, and	• Medical case management • Peer support • Consumer activities • Training and technical assistance

Funding Source	Funded Service Providers	Funded Services
	youth. HRSA also directly awards funds for this population to 1 hospital and 2 community health centers in Massachusetts.	
Ryan White HIV/AIDS Program Part F	Resources support personnel and costs associated with administering direct awards to oral health service providers and the New England AIDS Education and Training Center (NEAETC).	• Dental reimbursement program • Community based dental partnership program • AIDS Education and Training Center programs
CDC High-Impact HIV Prevention Programs for Health Depts. (PS18-1802)	Resources support health department personnel, health communications, training and capacity building, and direct service contracts with 20 agencies.	• HIV/HCV/STI testing • Comprehensive prevention services for people living with HIV and at risk for HIV
EHE Funding (PS 20-2020)	Resources support health department personnel, health communications, training, technical assistance, and direct service contracts with 9 agencies to provide HIV services in Suffolk County.	• HIV, HCV, and STI testing and linkage services • HIV Housing search and advocacy • HIV Legal services • HIV Peer navigation/support
Housing Opportunities for Persons with HIV/AIDS (HOPWA)	Resources fund service delivery at 4 agencies.	• HIV Medical case management • HIV Housing search and advocacy
Bureau of Substance Addiction Services (BSAS) Block Grant	Resources fund service delivery at 11 agencies.	• Overdose Education/Naloxone Distribution (OEND)

Funding Source	Funded Service Providers	Funded Services
SAMHSA State Opioid Response (SOR)	Resources fund service delivery at 23 agencies.	• HIV/HCV/STI testing and linkage services • Overdose Education/Naloxone Distribution (OEND) • HCV and PrEP clinical capacity and health navigation • HIV/HCV Correctional Linkage to Care • HIV ARCH services • Housing search and advocacy • Legal services
Bureau of Substance Addiction Services (BSAS) CDC Overdose 2 Action (OD2A)	Resources fund service delivery at 4 agencies.	• HIV/HCV/STI testing and linkage services at substance use disorder treatment sites • Overdose Education/Naloxone Distribution (OEND) • Recovery Coaching

MASSACHUSETTS STATE PROGRAMS AND RESOURCES FISCAL YEAR 2023

Funding Source	Funded Service Providers	Funded Services
MassHealth (MA Medicaid)	MassHealth resources are managed by the Commonwealth of Massachusetts.	• Medical care and treatment services • Expanded access to Medicaid for non-disabled PLWH under 200% FPL under an 1115 Medicaid waiver
State Budget Appropriations	Resources support direct service contracts with medical and non-medical providers: - 40 contracts to provide HIV prevention and screening services - 27 contracts to provide Medical Case Management and health-related support services - One contract to administer the Infectious Disease Drug Assistance Program	• Integrated HIV, HCV, STI, TB testing and linkage to care and treatment • Drug user health services/harm reduction services • HIV/HCV Correctional Linkage to Care Services • HCV, TB, and PrEP Health Navigation • HIV Medical case management, HIV ARCH (high-acuity MCM), medical transportation, HIV/HCV home-delivered meals, housing search and advocacy, rental assistance (rental start-up, eviction prevention, and utilities assistance), legal services, and peer support services. • HIV Disease Drug Assistance Program
Retained Revenue	Resources fund 21 agencies to provide HIV services, and fund 1	• HDAP: Coverage for the full cost of drugs for uninsured people with HIV; Health insurance

Funding Source	Funded Service Providers	Funded Services
Account (Pharmaceutical manufacturer rebates)	agency to operates the HIV Drug Assistance Program (HDAP)	premium assistance; HIV medication copayment assistance • HIV Medical Case Management • HIV Home-delivered meals • HIV housing search and advocacy, • HIV legal services • HIV dental ombudsperson services • HIV peer support
Bureau of Substance Addiction Services (BSAS) State Line	Resources fund 12 agencies to provide HIV services	• Overdose Education/Naloxone Distribution (OEND)
Bureau of Substance Addiction Services (BSAS) Harm Reduction Line	Resources fund 3 agencies to provide HIV services.	• Overdose Education/Naloxone Distribution (OEND) • Syringe services • Clinical capacity and health navigation

APPENDIX 4: PEOPLE WITH HIV AND KEY STAKEHOLDER REPRESENTATION IN PLANNING

#	Key Stakeholder Group	Name/Agency/Affiliation	Involvement Mechanism
1	Health Department staff (RW Part A)	Eileen Merisola Greg Lanza	MIPCC, EHE Steering Committee (SC), and Boston PC, representing: Boston Public Health Commission (BPHC)
2	Health Department staff (RW Part B)	Dawn Fukuda Linda Goldman Annette Rockwell Barry Callis Emile Day Eduardo Nettle (Massachusetts) Cynthia Bell (New Hampshire)	MIPCC and EHE Steering Committee, representing: Massachusetts Department of Public Health (MDPH); Boston PC, representing: New Hampshire Department of Public Health
3	People with HIV, including members of a Federally recognized Indian tribe as represented in the population, and individuals co-diagnosed with hepatitis B or C	Yes (names excluded for confidentiality)	MIPCC, Boston PC, EHE Steering Committee, and OHA Population Health Advisory Groups
4	Populations at-risk or with HIV representing priority populations	Yes (names excluded for confidentiality)	MIPCC, Boston PC, EHE Steering Committee, and OHA Population Health Advisory Groups
5	Behavioral or social scientists	Brianne Olivieri Mui Oscar Mairena Serena Rajabiun	MIPCC, representing: Northeastern University, Harvard University Boston PC, representing: University of Massachusetts, Lowell
6	Epidemiologist(s), HIV Prevention and Surveillance	Betsey John Laura Kersanske	MIPCC, EHE SC, MDPH HIV/AIDS and STD Surveillance Program

#	Key Stakeholder Group	Name/Agency/Affiliation	Involvement Mechanism
7	HIV clinical care providers (can include those funded by RW)	Alysse Wurcel Jeffrey Schaffer Anthony Silva Helene Bednarsh Norm Deschaine-Bonfiglio Emily DeMartino Michael Swaney Susana Medeiros Glory Ruiz	MIPCC, representing: Tufts Medical Center, Outer Cape Health Center Dental Program, BPHC, Dental Health Consultant, Baystate Medical Center Transgender Health Program of Western Massachusetts, Family Health Services, Health Innovations, Boston Medical Center
8	RWHAP Part C recipient	Leah Ward Meelyn Wong Chris Furtek Norm Deschaine-Bonfiglio Cecilio Orta Sarah Dupont Michael Swaney	MIPCC, representing: Brockton Neighborhood Health Center UMASS Medical Center BayState Medical Center Holyoke Health Center Lowell CHC Greater New Bedford Community Health Center; Boston PC, representing: Family Health Center of Worcester
9	RWHAP Part D recipient	Margarita Diaz Mahara Pinheiro	MIPCC, representing: MDPH, Bureau of Family Health and Nutrition, MassCARE, Boston PC, representing: Boston Medical Center
10	RWHAP Part F recipient (AETC)	Vanessa Carson-Sasso Debra Winters Amanda Hart	MIPCC, EHE SC, and Boston PC, representing: New England AIDS Education and Training Center
11	STD clinics and programs	Catherine Weerts David Goudreau	Boston PC, representing: Massachusetts General Hospital Division of STD Prevention
12	Non-elected community leaders including faith community members and business/labor representatives	Paul Glass Shirley Royster Lea Ward Kim Wilson Darian Hendricks Oscar Mairena	MIPCC, EHE SC, representing: Community Leaders and Advocates; Boston PC, representing: Boston University

#	Key Stakeholder Group	Name/Agency/Affiliation	Involvement Mechanism
		Richard Johnson George Henry-Hastie David Huckle Chris Wittke Margaret Lombe	
13	Community-based organizations serving populations affected by HIV as well as HIV services providers	Alysse Wurcel Jeffrey Schaffer Anthony Silva Helene Bednarsh Norm Deschaine-Bonfiglio Emily DeMartino Michael Swaney Susana Medeiros Glory Ruiz Ericka Olivera Nate Ross Lamar Brown-Noguera Manuel Pires	MIPCC, representing: Tufts Medical Center, Outer Cape Health Center Dental Program, BPHC, Dental Health Consultant, Baystate Medical Center, Transgender Health Program of Western Massachusetts, Family Health Services Health Innovations, Boston Medical Center Boston PC, representing: Edward M. Kennedy Community Health Center Community Servings AIDS Project Worcester Catholic Charities
14	Community health care center representatives including FQHCs	Michael Swaney Jorgette Theophilis Jeffrey Schaffer Edward Kayondo Joey Carlesimo	MIPCC, representing Family Health Center, Brockton Neighborhood Health Center, Outer Cape Health Services, Lowell Community Health Center Boston PC, representing: Massachusetts General Hospital
15	Substance use treatment providers	Brittni Reilly Carla Whitlow Connie Rocha-Mimosa Catherine Weerts	MIPCC, representing: Bureau of Substance Addiction Services (BSAS), AIDS Project Worcester, Seven Hills Behavioral Health Boston PC, representing: Massachusetts General Hospital
16	Hospital planning agencies and health care planning agencies	Melissa Hector Stewart Landers Julie Hook Travis Barnhart Celicia Boykin	Boston PC, representing: Boston PHC Consultants on Integrated HIV Prevention and Care Plan:

#	Key Stakeholder Group	Name/Agency/Affiliation	Involvement Mechanism
		Anna Laurence	JSI Research and Training Institute, Inc.
17	Intervention specialist(s)	Betsey Shally-Jensen Chi-Chi Ibili Jill Northrop	MIPCC, representing: Cooley Dicken Hospital, Whittier Street Neighborhood Health Center EHE SC: representing: MDPH School Based Health Center Program
18	Jurisdictions with CDC-funded local education agencies /academic institutions	Lenore Maniaci	Massachusetts Department of Elementary and Secondary Education
19	Mental health providers	Kym Kroeger Jamie Sprague Chris Furtuk Ruth Cooper Justin Alves	MIPCC, representing: Manet Community Health Center, River Valley Counseling Services, Beth Israel Deaconess Medical Center (Plymouth) Boston PC, representing: Boston Medical Center
20	Individuals (or representatives) with an HIV diagnosis during a period of incarceration (within the last three years) at a federal, state, or local correctional facility	Bishop Garet Reid Richard Johnson Carla Whitlow Kathy Creehan	MIPCC, representing: Massachusetts Department of Corrections, New North Citizens Council, AIDS Project Worcester Victory Programs
21	Representatives for state or local law enforcement and/or correctional facilities	Bishop Garet Reid	MIPCC, representing: Massachusetts Department of Corrections
22	Social services providers including housing and homeless services representatives (HOPWA)	Kathy Crehan Ismael Rivera Wendy LeBlanc	MIPCC, representing: Victory Programs, JRI Health Boston PC, representing: Harbor Care
23	Local, regional, and school-based clinics; healthcare facilities; clinicians; and other medical providers	Alysse Wurcel Jeffrey Schaffer Anthony Silva Helene Bednarsh Norm Deschaine Emily DeMartino	MIPCC, representing: Tufts Medical Center, Outer Cape Health Center Dental Program, BPHC, Dental Health Consultant, Baystate Medical Center, Transgender Health Program of

#	Key Stakeholder Group	Name/Agency/Affiliation	Involvement Mechanism
		Michael Swaney Susana Medeiros Glory Ruiz	Western Massachusetts, Family Health Services Health Innovations, Boston Medical Center
24	Medicaid/Medicare partners	Alison Kirchgasser	Boston PC, representing: Massachusetts Office of Medicaid
25	Member(s) of a Federally Recognized Indian Tribe	Aaron Gonzalez	MIPCC, representing: Boston Alliance of Gay and Lesbian Youth
26	Faith Community Representative(s)	Bishop Garet Reid	MIPPC, representing: Massachusetts Department of Corrections

EXHIBIT B

Boston EMA Ryan White Part A

Integrated HIV Prevention and Care Plan 2017-2021





Contributions and Acknowledgements

The Boston EMA Integrated HIV Prevention and Care Plan stems from the work of the Boston EMA Planning Council and the Boston Public Health Commission (Ryan White Part A Recipient).

Special thanks to the Comprehensive Plan Working Group Members for their work and input that contributed to the development of the Integrated Plan:

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- Massachusetts Integrated Prevention and Care Committee (MIPCC)
- Statewide Consumer Advisory Board (SWCAB)
- Massachusetts Department of Public Health, Office of HIV/AIDS
- New Hampshire Department of Health and Human Services
- New Hampshire HIV Planning Group

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Lexicon

ADAP	AIDS Drug Assistance Program
AETC	AIDS Education and Training Center
AIDS	Acquired Immunodeficiency Syndrome
ASO	AIDS Service Organization
BRFSS	Behavioral Risk Factor Surveillance System
BPHC	Boston Public Health Commission
CBA	Capacity Building Assistance
CBO	Community-based Organization
CDC	Centers for Disease Control and Prevention
DHAP	CDC's Division of HIV/AIDS Prevention
DPHS	New Hampshire Department of Public Health Services
eHARS	Enhanced HIV AIDS Reporting System
EMA	Eligible metropolitan area
HAB	HRSA's HIV/AIDS Bureau
HASD	HIV/AIDS Services Division
HDAP	HIV Drug Assistance Program
HCBC	Home and Community Based Care
HIV	Human Immunodeficiency Virus
HOPWA	Housing Opportunities for Persons with AIDS
HPG	HIV Planning Group
HRSA	Health Resources and Services Administration
IDB	Infectious Disease Bureau
IDU	Injecting drug user
IHP	Integrated HIV Prevention and Care Plan
IHW	Integrated HIV Work Group
MA	Massachusetts
MAI	Minority AIDS Initiative
MCM	Medical Case Management
MDPH	Massachusetts Department of Public Health
MSM	Men who have sex with men
NH	New Hampshire
NH HIV ICP	New Hampshire Integrated HIV Prevention and Care Plan
NH DHHS	New Hampshire Department of Health & Human Services
NSDUH	National Surveys of Drug Use and Health
OHA	MDPH Office of HIV/AIDS
PLWA	People living with AIDS
PLWH	People living with HIV, also known as consumers
PLWHA	People living with HIV/AIDS
PCS	Planning Council Support
PWID	People who inject drugs
RWHAP	Ryan White HIV/AIDS Program
SAMHSA	Substance Abuse and Mental Health Services Administration
SCSN	Statewide Coordinated Statement of Need
STD	Sexually transmitted disease
STDMIS	Sexually Transmitted Disease Management Information System
SSP	Syringe Services Programs
US	United States
VL	Viral load

BOSTON EMA PART A INTEGRATED HIV PREVENTION AND CARE PLAN INTRODUCTION

In 2015, the Centers for Disease Control and Prevention (CDC) and the Health Resources and Services Administration (HRSA) released guidance to support the submission of an Integrated HIV Prevention and Care Plan (IHP), including the Statewide Coordinated Statement of Need (SCSN), a legislative requirement for Ryan White HIV/AIDS Program (RWHAP) Part A and B recipients. The IHP provides a roadmap for implementing the goals of the National HIV/AIDS Strategy, which has recently been updated up to 2020. The overarching NHAS goals include: 1.) preventing new HIV infections, 2.) increasing access to care and improving health outcomes, and 3.) reducing HIV-related health disparities.

Jurisdictions funded by the CDC's Division of HIV/AIDS Prevention (DHAP) and HRSA's HIV/AIDS Bureau (HAB) were charged with developing the IHP. A unique aspect of the guidance and the process to develop the plan is the option for jurisdictions to not only integrate previously separate HIV prevention and care services into one planning process, but also the potential for government agencies that served as funders of these services to better coordinate federal, state, and local funds to improve service delivery and health outcomes.

Unlike many other areas in the country, stakeholders in the Boston EMA have had a long history of collaboration. The Boston Public Health Commission (BPHC) works closely with the Boston EMA HIV Services Planning Council, including past work to develop a Part A Comprehensive Plan. Massachusetts Department of Public Health (MDPH) and New Hampshire Department of Health & Human Services (NH DHHS) have mandated seats on the Planning Council and are essential partners in designing and sustaining the region's HIV service delivery system. The three agencies are also national leaders in addressing the changing healthcare landscape through comprehensive health insurance coverage for all residents and a cleary focus on achieving and maintaining HIV viral suppression among PLWH.

In recognition of the longstanding role that MDPH and NH DHHS play in funding critical HIV prevention and care services, BPHC entered into the IHP process with the goal of supporting state health departments in their efforts to carry out the NHAS goals and collaboratively develop IHP workplans. This meant cross-participation in each agency's respective community planning groups/events, frequent communication on progress in developing the IHP, and demonstration of mutual support via letters of concurrence.

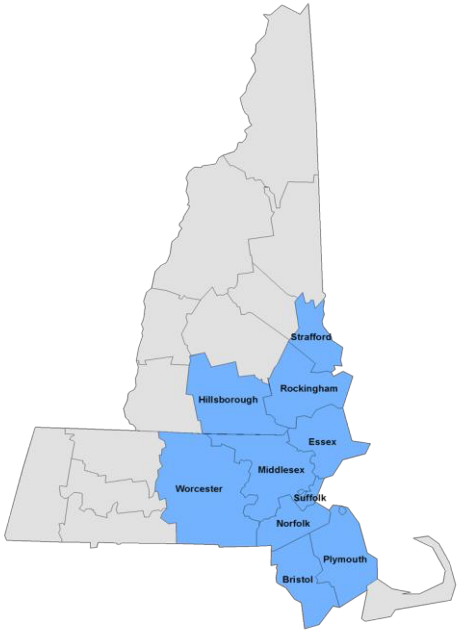
The Boston EMA Part A IHP represents a culmination of over a year of collaborative effort across government agencies and community planning group. It is a living document and will continually be updated to reflect the most current needs among PLWH in the EMA. This provides the best opportunity to achieve the NHAS goal of eliminating the HIV epidemic in the United States.

SECTION I: STATEWIDE COORDINATED STATEMENT OF NEED/NEEDS ASSESSMENT

A. Epidemiologic Overview

This section describes the geography of the Boston EMA and the demographic characteristics (socio-economic and ethnic composition) of both the overall general EMA region and its respective specific counties served by Part A funds.

Figure 1: Map of the Boston EMA



Geography

The Boston EMA includes ten counties: seven in Massachusetts (Bristol, Essex, Middlesex, Norfolk, Plymouth, Suffolk, and Worcester) and three in New Hampshire (Hillsborough, Rockingham, and Strafford). (Figure1). These ten counties in the Boston EMA cover an area of 6,451 square miles and a have total population of 6,411,521 [1] as of 2014.

Suffolk County is the smallest county, covering only 59 square miles; Worcester County is the largest county, covering 1,513 square miles. Despite being a small area, Suffolk County includes the city of Boston and is home to 747,928 [1] people, which constitutes a little over 11% of the total population of the Boston EMA. Middlesex County, MA has an area of 823 square miles, yet it has the largest population in the Boston EMA with 1,539,832 people. Strafford County has an area of 369 square miles and is home to 124,387 people, the smallest population in the Boston EMA.

Overview of HIV/AIDS in the Boston EMA

Data for this section were collected by MDPH and the NHDHHS, according to CDC surveillance criteria. De-identified data were then provided to the BPHC. BPHC also collects Ryan White Part A data through e2Boston, an electronic client level data system.

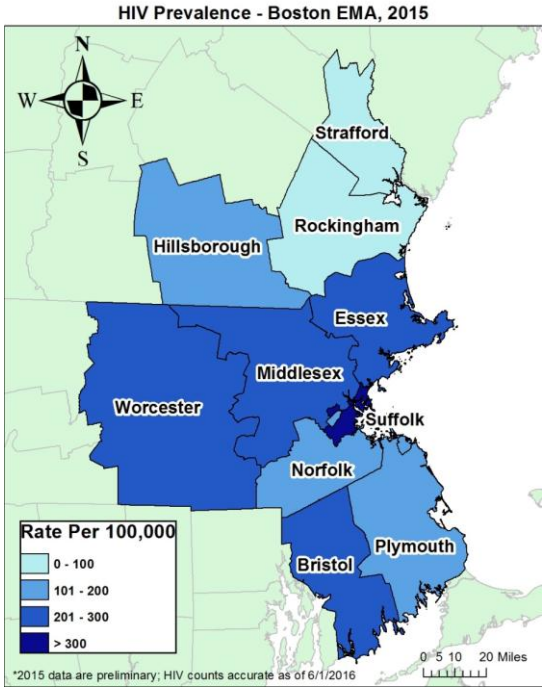
Prevalence and Incidence: As of December 31, 2014, there were 16,875 people living with HIV (PLWH) in the Boston EMA. This represents a 9% increase in PLWH from 2011 to 2014 [2] [3]. Among these PLWH, there were 9,397 individuals who also had an AIDS diagnosis, a 6% increase from 2011 to 2014. HIV incidence remained relatively stable from 2011 to 2013, with 604, 634, and 601 cases reported in 2011, 2012, and 2013, respectively. HIV incidence decreased from 2013 to 2014, dropping by over 5%. AIDS incidence also decreased from 379 cases in 2011 to 229 cases in 2014. In MA, the number of deaths among individuals reported with HIV/AIDS declined by 31%, from 333 in 2005 to 231 deaths in 2014 [4].

Table 1: Incident and Prevalent Cases – Boston EMA 2011-2014

	CY 2011		CY 2012		CY 2013		CY 2014	
	Inc.	Prev.*	Inc.	Prev.*	Inc.	Prev.*	Inc.	Prev.*
HIV	604	6,557	634	6,778	601	7,154	570	7,478
AIDS	379	8,902	344	9,077	309	9,310	229	9,397

Geographic concentrations by county: The majority of MA and NH HIV cases are located within the 10 counties that make up the Boston EMA. Eighty-one percent of all PLWH in MA live within the Boston EMA. Similarly, 69% of all PLWH in NH live in the Boston EMA [2] [3].

The burden of disease was highest in Suffolk County, where the prevalence rate was 883 PLWH per 100,000 people. This was substantially higher than Middlesex County, which has the second highest HIV prevalence rate at 238 PLWH per 100,000 people.



Characteristics of PLWH in the Boston EMA

Table 2: PLWH in the Boston EMA N = 16,875		
Gender	**EMA**	**%**
Male	**11,957**	71
Female	**4,918**	29
Race	**EMA**	
White (non-Hispanic)	**7,528**	45
Black (non-Hispanic)	**5,280**	31
Hispanic	**3,571**	21
Asian/Pacific Islander	**358**	2
Other/Unknown	**138**	1
Age	**EMA**	
0-12	**40**	0
13-19	**70**	0
20-44	**4,558**	27
45-64	**10,570**	63
65+	**1,637**	10
Risk	**EMA**	
MSM	**6,732**	40
IDU	**2,426**	14
MSM/IDU	**544**	3
Heterosexual Sex	**2,498**	15
Presumed Heterosexual	**1,609**	10
Unknown	**2,688**	16
Pediatric	**311**	2
Other	**67**	0
Country of Birth	**EMA**	
USA	**10,713**	63
US-Dependency	**1,226**	7
Non-US	**4,907**	29
Unknown	**29**	0

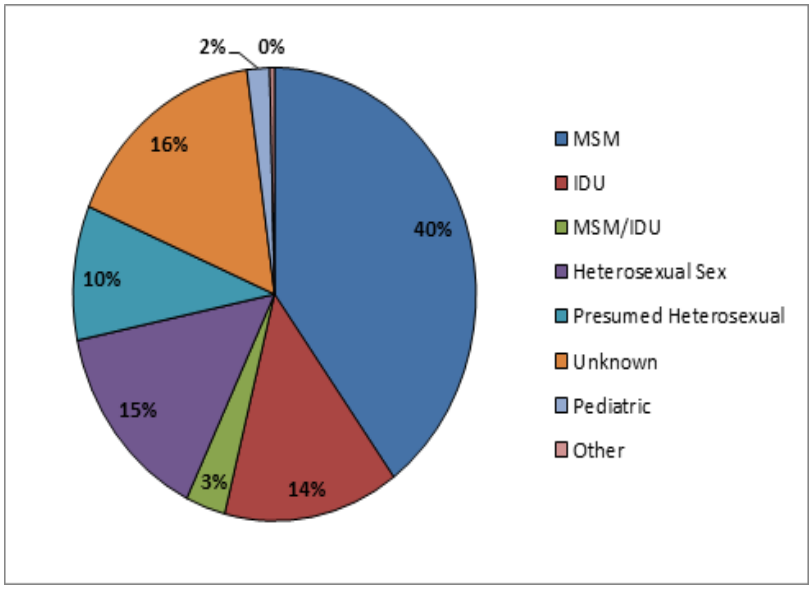
Race: HIV in the Boston EMA disproportionately affects Black and Latino residents. Though Black residents only make up 6% of the overall population of the Boston EMA, they represented 31% of PLWH in the same area in 2014 [2] [3]. This trend can also be seen in the most recent HIV diagnoses, where Black residents accounted for 36% of all cases diagnosed from 2011 to 2014. Similarly, Hispanic residents make up only 9% of the overall Boston EMA population, but accounted for 21% of PLWH in the same area in 2014. Hispanic residents represented an even larger proportion of recent HIV cases, accounting for 25% of all diagnoses from 2011 to 2014. Black and Hispanic residents were also more likely to be concurrently diagnosed with both HIV and AIDS from 2011 to 2014, a marker of lateness-to-care; 39% of those concurrently diagnosed from 2012 to 2014 were Black, and 26% were Hispanic, accounting for a combined 66% of total concurrent diagnoses in that time period.

Age: PLWH in the Boston EMA represent an aging population. As of 12/31/2014, 73% were ages 45 or older. This is in stark contrast to recent cases, where the majority (62%) of those reported in 2014 were diagnosed at ages 20 to 44 [2] [3].

Gender: Both nationally and in the Boston EMA, men account for a disproportionately large proportion of PLWH. In 2014, the majority (71%) of PLWH in the EMA were male and a similar proportion (75%) of new cases were men [2] [3].

Risk Exposure: A major reason for these gender disparities is due in large part to the fact that men who have sex with men (MSM) represent such a high risk group. In 2014, 40% of all PLWH in the Boston EMA identified MSM as a risk, more than any other risk group. MSM represented an even larger proportion of recent HIV cases, accounting for 45% of all cases diagnosed from 2011 to 2014 [2] [3]. The second most common risk group was those who were likely exposed through heterosexual sex (including presumed heterosexual), accounting for 25% of PLWH in the EMA. Fourteen percent were likely exposed through injection drug use, while 16% had unknown modes of exposure.

Figure 2: Percentage Distribution of PLWH by Risk Exposure



Among new cases reported in 2014, 30% had an unknown mode of exposure, a much larger proportion compared to 16% of all PLWH in the EMA. Another major difference in risk categories between PLWH and recent cases is that only 4% of cases reported in 2014 identified injecting drug use as a risk, whereas 14% of PLWH overall have this risk. This difference is probably due in large part to the success of needle exchange programs throughout the Boston EMA, and also may be due to shifting population networks among IDU.

Intersection of Risk Exposure, Gender and Race: White PLWH have historically accounted for the majority of MSM living with HIV in the Boston EMA, although more recent data indicate a demographic shift in this risk group. In 2014, 68% of all MSM living with HIV in the Boston EMA were White but a substantially smaller proportion (47%) of MSM diagnosed with HIV in 2014 were White [2] [3].

Twenty-eight percent of men diagnosed with HIV from 2011 to 2014 had an unknown mode of exposure. This represents the second largest risk category behind only MSM. Men exposed through injection drug use (IDU) represented 4% of all male cases during this time period, equal to the proportion exposed through heterosexual sex and through MSM/IDU. All other risk groups represented 3% or less of all male cases diagnosed from 2011 to 2014.

Table 3: Risk Exposure By Gender in the Boston EMA		
	N	%
Male Risk		
MSM	**6,732**	56
IDU	**1,487**	12
MSM/IDU	**544**	5
Heterosexual Sex	**746**	6
Presumed Heterosexual	**0**	0
Unknown	**2,240**	19
Pediatric	**160**	1
Other	**48**	0
Female Risk		
MSM	**0**	0
IDU	**939**	19
MSM/IDU	**0**	0
Heterosexual Sex	**1,752**	36
Presumed Heterosexual	**1,609**	33
Unknown	**448**	9
Pediatric	**151**	3
Other	**19**	0

For women, heterosexual sex is the primary mode of HIV exposure in the Boston EMA. Seventy-one percent of all women diagnosed from 2011 to 2014 fall into the heterosexual sex or presumed heterosexual sex risk groups. Black and Hispanic women account for the vast majority of these cases. In 2014, Black women accounted for 55% of new HIV cases in women, and the majority of these women were exposed to HIV through heterosexual contact. In 2014, Black women also represented nearly 14% of all PLWH in the Boston EMA, yet make up only 3% of the overall population of the Boston EMA [2] [3].

From 2011 to 2014, 18% of all women diagnosed with HIV in the Boston EMA had an unknown mode of exposure. While this constituted the second largest risk group for women behind heterosexual and presumed heterosexual sex, this was smaller than the proportion of men with an unknown risk during the same time period. Ten percent of the female cases from 2011 to 2014 were IDU, and no other risk group accounted for more than 1% of female cases from 2011 to 2014.

One risk group that has decreased substantially over the past couple of decades in the Boston EMA is IDU. Whereas 24% of all incident HIV cases were due to IDU in 1999, in 2014 this risk group accounted for only 4% of incident cases in the Boston EMA [2] [3]. This reduction is probably due in large part to the success of needle exchange programs throughout the Boston EMA, and also may be due to shifting population networks among IDU. Men made up the majority of IDU cases in 2014 at 60%.

Country of Origin: While most PLWH in the EMA were born in the United States or in U.S. territories, 29% were born outside of the United States. Foreign born individuals made up a larger proportion of recent cases, accounting for 38% of cases reported in 2014 [2] [3].

Concurrent Diagnosis: 126 of 553 (23%) new Boston EMA resident HIV cases in 2014 were concurrently diagnosed with AIDS. This means that these cases received both an HIV diagnosis and an AIDS diagnosis within 2 months of each other. Concurrent diagnoses may be a marker of late presentation to HIV care. This may be partly explained by new arrivals to the EMA from overseas who have an AIDS diagnoses when they arrive [2] [3].

Table 4: Socioeconomic status of newly diagnosed Part A clients*	
	N =206
Federal Poverty Level	%
0–99%	59
100-199%	22
200-299%	7
>300%	6
Unknown	6
Medical Insurance Provider	
Medicaid	54
Uninsured	10
Other, Public Insurance	9
Private Insurance, Individual	8
Private Insurance, Employer	4
Health Safety Net	10
Medicare	5

*Data represents only Part A clients reported in e2Boston during March 1, 2015- February 29,2016. BPHC does not have income or insurance information of non-Part A clients.

Socioeconomic data: Based on 2014 census data, an estimated 11**%** of residents in the EMA are living below 100% FPL, 23.5% live below 200% FPL, and 36.7% live below 300% FPL [1]. Compared to the EMA population, e2Boston data show that majority of Part A clients (59%) live below 100% FPL, showing that Part A serves populations most in need [5].

Indicators of Risk for HIV Infection

MDPH and NHDHHS are responsible for collecting risk behavior data from behavioral risk factor surveillance, STD surveillance, Hepatitis C surveillance and substance use data. The following is a summary description of indicators of risk for HIV infection in MA and NH as described in the respective state plans [4] [6]:

MA

- Among 3,543 male and female respondents to the 2013 and 2014 MA Behavioral Risk Factor Surveillance System (BRFSS) surveys, 9% reported two or more sexual partners in the previous year, 69% reported one partner, and 22% reported no sexual partners. A larger proportion of men, as well as 18 to 24 year olds reported two or more partners in the previous year. All respondents were between 18–64 years of age,
- Of the 2,512 18–64 year old sexually active respondents to the 2013 and 2014 MA BRFSS, only 25% reported using a condom at last sexual encounter (27% of male respondents and 24% of female respondents).
- According to the Massachusetts Youth Risk Behavior Survey (MYRBS) collected in 2013, 58% of respondents reported condom use at last intercourse, 38% reported

ever having had sexual intercourse and 3% reported sexual intercourse before age 13. Nine percent reported four or more lifetime sexual partners. In addition, 28 % and 24% reported alcohol or drug use at last intercourse, respectively.

- MA publicly funded HIV Counseling, Testing and Referral (CTR) sites conducted 66,426 HIV tests of which 0.5% were positive. Testing identified 276 new diagnoses, representing 44% of individuals newly diagnosed with HIV infection (N=629) in the state.
- In MA state fiscal year 2014, 42% of 5,436 participants in state-funded Syringe Service Programs (SSP) reported being under age 20 years at first injection. Agencies providing SSP distributed over 650,000 syringes and collected over 640,000 syringes.
- The percentage of admissions to state-licensed substance abuse treatment programs for heroin addiction increased from 37% to 53% of total admissions, comparing state fiscal year 2006 to fiscal year 2015

NH

- 31% of NH adults have been tested for HIV test at some point compared to 34% of all US adults [7]. This lower percentage, indicates the need to increase HIV testing services in NH.
- An estimated 3% of adults in NH were at risk for HIV transmission in the 12 months prior to the BRFSS survey. Being "at risk for HIV transmission" included any of the following: used injection drugs in the past year; treated for an STD in the past year; had given or received money or drugs in exchange for sex in the past year; or had anal sex without a condom in the past year.
- STDs represent the highest burden for reportable diseases in NH. Rates of Chlamydia increased over the past decade from 140.7 per 100,000 in 2005 to 236.3 per 100,000 in 2013 (all rates are per 100,000). Over the same time period, gonorrhea incidence was ranging from a high of 13.7 in 2005 to a low of 7.6 in 2008. The rate was 8.9 in 2013 (the latest available year of data). Syphilis rates were also low (< 6 per 100,000), but increased slightly with rates of 5.4 and 5.7 in 2012 and 2013 respectively [6].
- Limited data were available to identify the scope of injection drug use in the general NH population or to describe the IDU population at risk for HIV. However, the NSDUH estimates show that from 2013 to 2014, 3.7% of NH residents 12 years or older and 2.6% of those 26 years and older reported using illicit drugs other than marijuana in the past month [8].

Information on these risk factors enables our state partners to implement effective HIV prevention strategies targeting those of highest risk. The Boston EMA Part A recipient also

utilizes this information to develop an action plan for its Early Identification of Individuals with HIV (EIIHA) strategies. As part of the Part A grant application, BPHC produces an EIIHA data table summarizing all HIV testing conducted at publically funded sites in the EMA (Table 5).

Table 5: EIIHA Data – Newly Diagnosed Test Events in the Boston EMA

Newly diagnosed positive HIV test events at Boston EMA publicly funded sites:							
	Between January 1, 2015 and June 30, 2015	Total	MSM	IDU	MSM/ IDU	Het. Sex (Women)	Unknown
(a)	Number of test events	20,961	3,035	3,135	152	4,419	10,220
(b)	Number of newly diagnosed positive test events	91	34	10	4	15	28
(c)	Number of newly diagnosed positive test events with client linked to HIV medical care	38	20	1	4	4	9
(d)	Number of newly diagnosed confirmed positive test events	68	33	5	4	9	17
(e)	Number of newly diagnosed confirmed positive test events with client interviewed for Partner Services	30	18	0	1	1	8
(f)	Number of newly diagnosed confirmed positive test events with client referred to prevention services	39	21	3	3	3	9
(g)	Total number of newly diagnosed confirmed positive test events who received CD4 cell count and viral load testing	81	36	6	2	16	21

The EIIHA data also identifies any services the newly diagnosed person may receive, such as linkage to medical care or partner notification services. Ensuring rapid engagement in care after initial diagnosis is one of many small steps to improve viral suppression in the EMA. The overarching goal of the EIIHA Plan is to reduce the number of undiagnosed and late diagnosed individuals and to ensure they are accessing HIV care and treatment.

Ryan White Part A Client Level Outcomes Information

Summary of Performance Measure Data: BPHC Quality Management staff conducted an in depth review of client level outcomes data following the conclusion of FY15. Outpatient ambulatory health services is not funded with Part A funds in the Boston EMA, so only primary achievements and characteristics among Part A medical case management clients and providers are listed below:

- 64% of clients indicated the presence of mental health issues (ranging from mild to severe)
- 94% had received a medical visit within 12 months of their most recent Part A service
- 54% are always able to attend HIV care visits
- 66% are stably housed, white the remaining 34% indicated need of some housing services

Many of the outcome scores of MCM clients were worse than clients who did not receive Part A funded MCM, presumably because clients active in Part A MCM have more initial needs. Trends will be monitoring in the future once more data is collected. JSI previously gathered outcomes data, but it is not possible to link the data sets.

Use of Data to Address Disparities: An in depth review of outcomes data from clients served in FY15 identified the following factors significantly associated with unsuppressed viral load in the EMA.

- Clients < 45 years old
- Unstably housed clients or those who need housing services
- Clients with non-MSM risk exposure
- Clients with reported mental health problems
- Black clients compared to other races
- Clients with no or a limited support network

These factors were identified through a multivariate regression analysis, using client level data from 92% of all clients served in FY15. Cross-sectional views of data continue to provide information about continuing disparities, such as the higher burden of HIV among Black and Hispanic communities in the EMA. The outcomes level data is already being used for an upcoming housing RFP and will be presented to the Planning Council later this year to assist with the allocations process.

Co-morbidities Affecting PLWH in the EMA:

BPHC specifically collects comorbidity information such as mental illness, substance abuse, sexually transmitted infections (STIs), hepatitis B (HBV), hepatitis C (HCV), and tuberculosis which greatly increase the cost and complexity of providing care to PLWH in the EMA. Many clients face multiple co-morbidities, particularly PLWH over the age of 45, requiring providers to prioritize and manage a number of conditions simultaneously.

Sexually Transmitted Infections: STI rates in the EMA are high, including PLWH. While Chlamydia remained by far the most common STI in the EMA in 2014, the incidence rate has decreased by 14% since 2012 [2] [3]. However, gonorrhea incidence rose sharply during this same time period, increasing by 41%. The incidence of primary and secondary (P&S) Syphilis increased by over 100% from 2012 to 2014. Despite this increase, case counts for Chlamydia and Gonorrhea still far exceeded those of P&S Syphilis, (18,449 and 3,432 vs. 567, respectively). The burden of STIs is not uniformly shared in the EMA, with MA counties of the EMA accounting for 89% of all reported STIs in the EMA in 2014. In 2014, Black residents represented only 6% of the EMA's population, but accounted for 14% of Chlamydia cases, 23% of Gonorrhea cases, and 15% of Syphilis cases. Also, Hispanic residents (only 9% of the EMA's population) accounted for nearly 19% of Syphilis cases.

Adolescents and young adults continue to be disproportionately impacted by Chlamydia, with the highest burden of disease reported in ages 15-24, while Gonorrhea mostly impacts a slightly older population. MSM accounted for 62% of reported Syphilis cases in the EMA in 2014. STIs are of particular concern due to the increased risk of HIV transmission. 32% of syphilis cases reported in 2014 were known to be co-infected with HIV, and another 17% did not know or declined to share their HIV status [2].

A recent John Snow, Inc. (JSI) Clinical Chart Review Project focuses on HAB Performance Measures and collects STI screening data [9]. In the most recent 2013 chart abstraction review year, the rates of STI screening among sampled PLWH at the 22 sites surveyed were as follows: Chlamydia 58%, Gonorrhea 58%, syphilis 63%, Pap or colposcopy 59% (Eligible populations varied by STI, but included about 1,000 people each, about 400 of whom were women eligible for a Pap smear).

Hepatitis: In 2014, there were 255 chronic cases of hepatitis B (HBV) reported in the Boston EMA, and 30 cases of acute HBV. The majority of chronic cases were reported in people 25 to 44 years old, with males accounting for slightly more cases than females. In the same time period, there were 4,613 cases of HCV confirmed in the MA counties of the EMA [2]. Case counts were highest in the 20-34 and 50-64 age ranges. In 2015, 65% of individuals (under 40 years) living with HIV and HCV co-infection in MA reported an IDU-related exposure mode, compared to only 7% among individuals infected with HIV only [4]. Shared transmission risk behaviors, such as unprotected sex and sharing of injection drug paraphernalia, have resulted in higher incidence of both HBV and HCV among PLWH than those not infected with HIV.

B. HIV Care Continuum

Using the diagnosis-based approach, the Boston EMA developed its HCC to identify barriers to achieving HIV viral suppression among PLWH in the Boston EMA. The surveillance data used to produce the HCC was obtained from MDPH and NH DHHS. In addition to these sources, the BPHC also uses e2Boston, a data system used to track demographic information and outcome measures for clients of Part A funded services, as well as information from the Clinical Chart Review (CCR), a report produced by John Snow Inc. The CCR project reviews a sample of HIV/AIDS clients receiving clinical care and/or case management among Part A and B funded clinics in MA. Figure 3 represents the HCC for all PLWH living in the Boston EMA in 2014. Table 6 explains how each stage is defined.

Figure 3: 2014 HIV Care Continuum in the Boston EMA

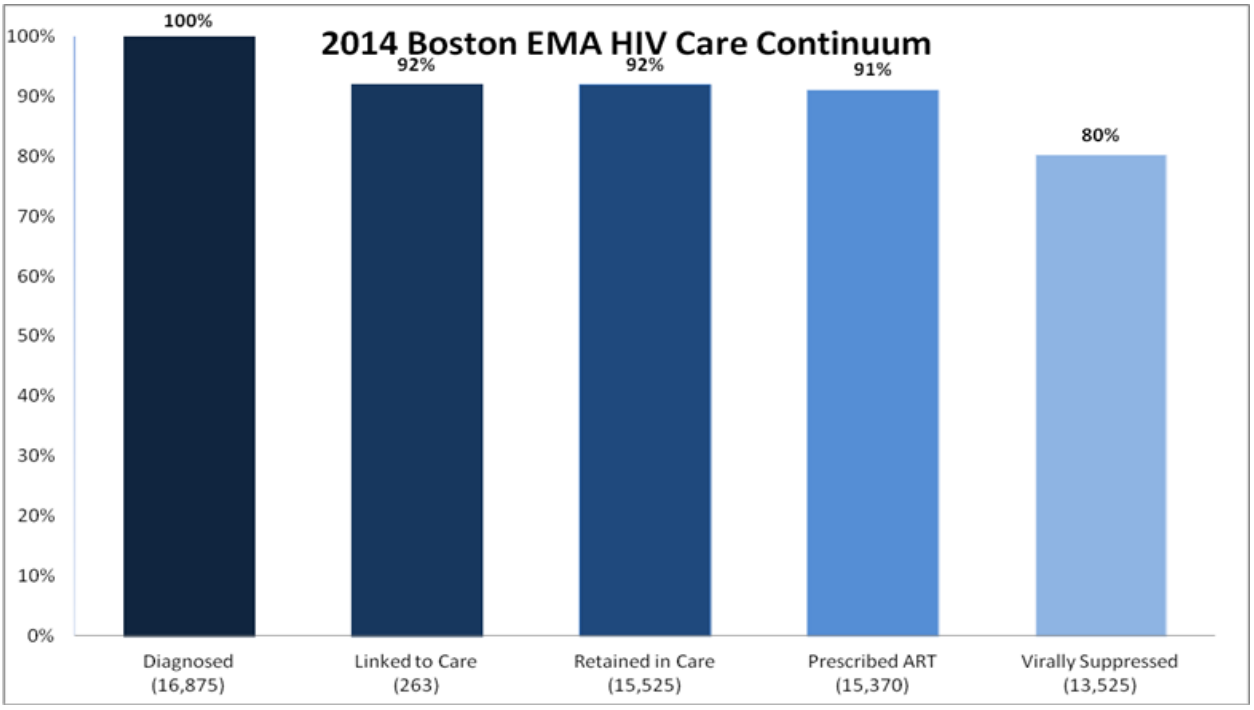


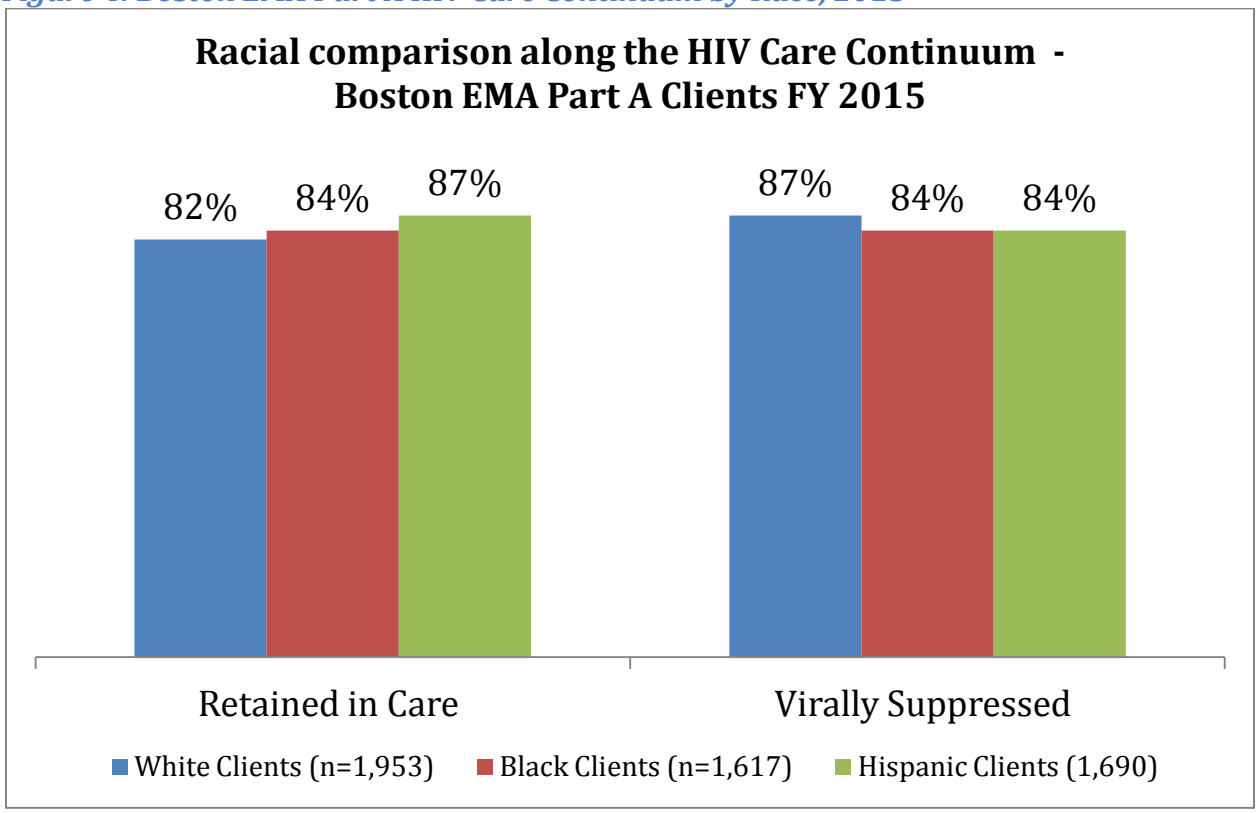
Table 5: HIV Care Continuum Narrative and Definitions	
Diagnosed:	16,875 estimated prevalent cases reside in the EMA. The diagnosed category represents the HIV prevalence in the Boston EMA as of December 31, 2014. MDPH and NHDHHS report the number of diagnosed individuals.
Linkage to Care:	This is defined as a medical visit within three months of their initial diagnosis (n=236). Linkage to care was identified through EIIHA data from MDPH and NHDHHS.
Retention in Care*:	According to the 2014 CCR, an estimated 15,525 PLWH had two or more medical visits at least 90 days apart during the measurement year.
Prescribed ART*:	An estimated 15,370 diagnosed PLWH were on ART in 2015. This measure was estimated with data from the 2014 CCR, which looked at presence of an ART prescription in medical records.
Virally Suppressed*:	An estimated 13,525 PLWH were virally suppressed in 2015. Viral suppression is defined as a viral load less than 200 copies/mL, data was used from the 2014 CCR.

* CCR data does not include PLWH living in the EMA counties of NH.

The Boston EMA HCC shows that 92% of PLWH who were diagnosed in 2014 are linked to care, 91% of those diagnosed are on ART, and 80% are virally suppressed. The Boston EMA has a higher percentage of PLWH who are linked to each stage of care in comparison to the national average. This may suggest that the Boston EMA's healthcare system has a greater capacity to support PLWH in comparison to other U.S. states and regions. However, significant barriers remain for many PLWH who are disproportionately affected by health disparities, which will be discussed under the *Assessing, Needs, Gaps, and Barriers* section.

*Disparities in Engagement among Key Populations along the HIV Care Continuum**

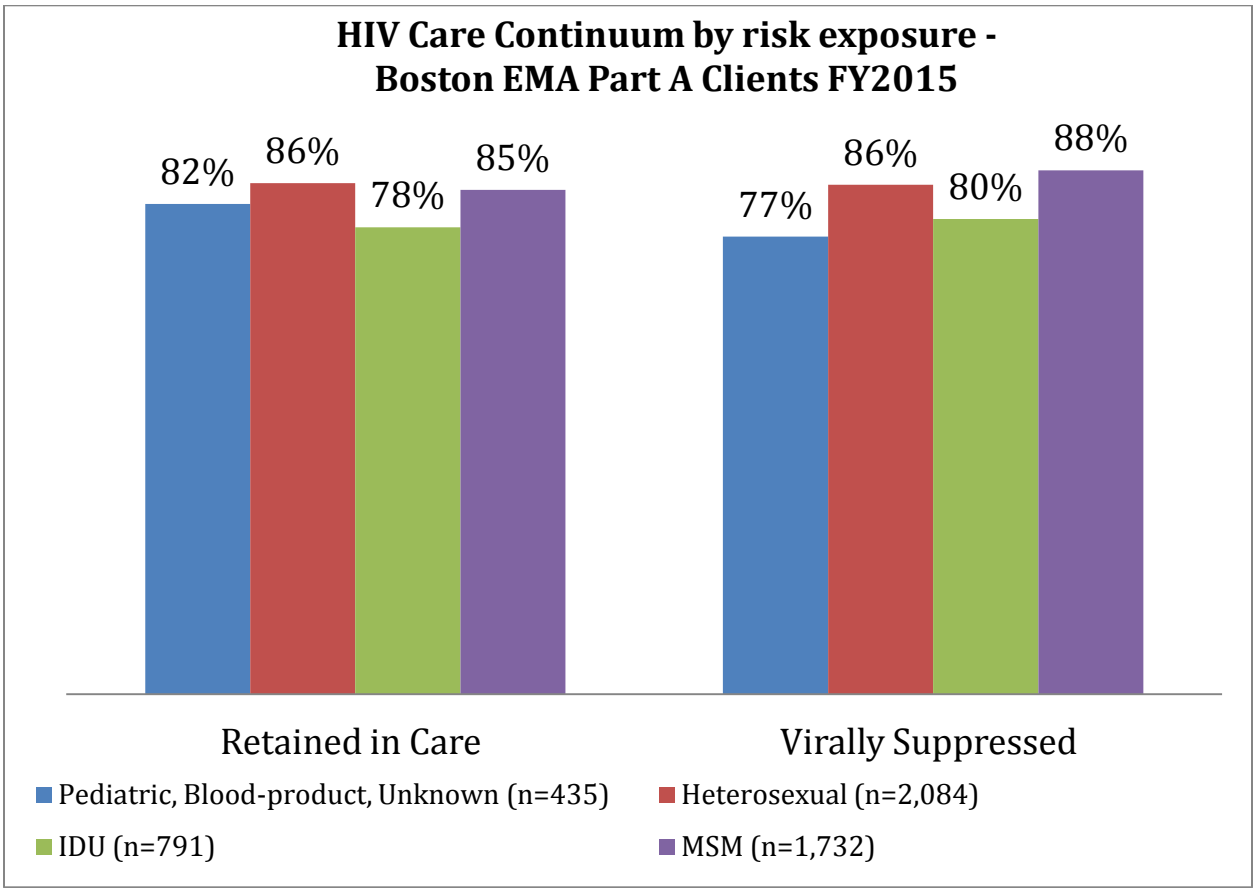
Figure 4: Boston EMA Part A HIV Care Continuum by Race, 2015



- More white clients were virally suppressed than retained in care
- An equal percentage of black clients were retained in care and virally suppressed
- Less Hispanic clients were virally suppressed than retained in care
- Retention in care is highest among Hispanic clients, and lowest among white clients
- Viral suppression is highest among white clients

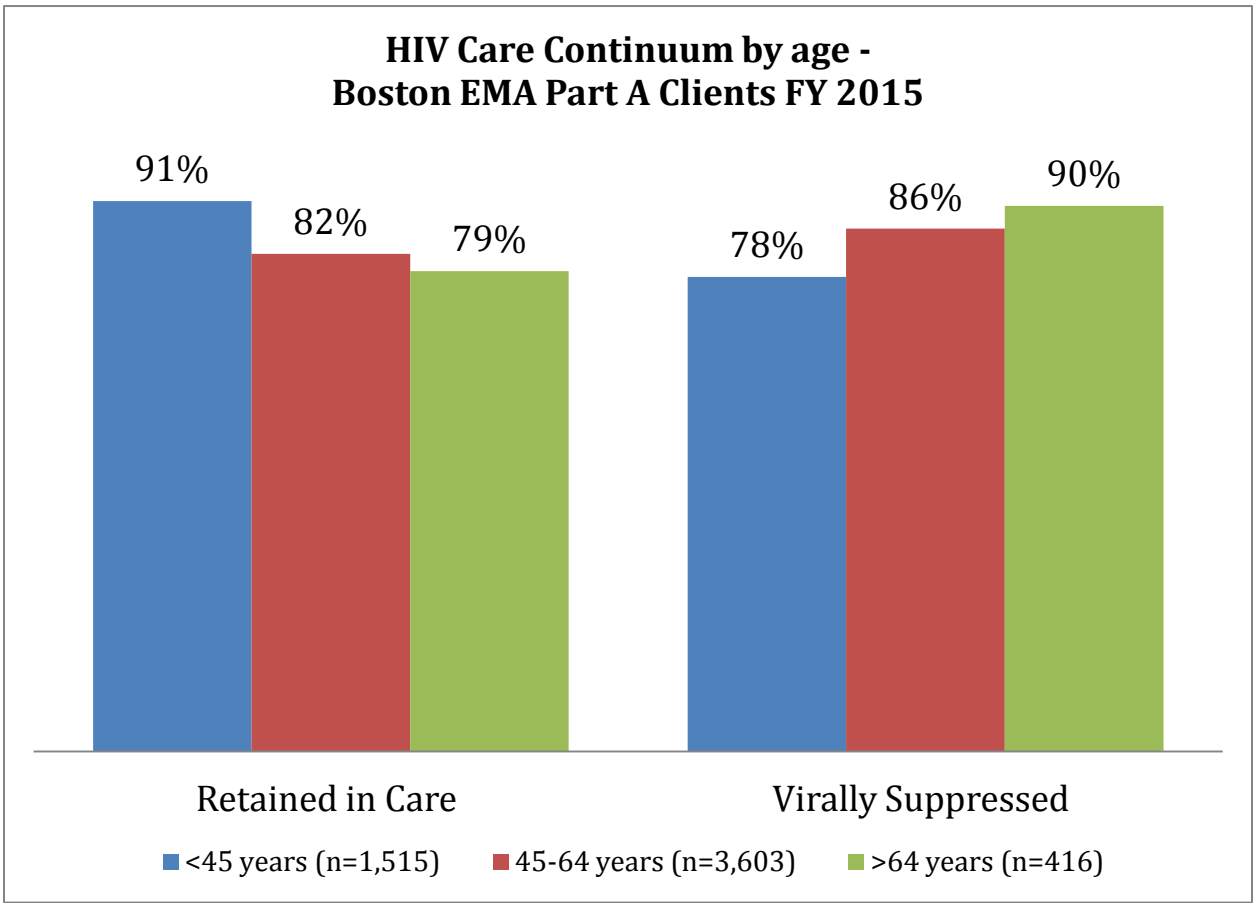
**Figures 4-8 use a different definition for retention than the previous continuum. Retention in care is defined as having at least one medical visit within the last 12 months.*

Figure 5: Boston EMA Part A HIV Care Continuum by Risk Exposure, 2015



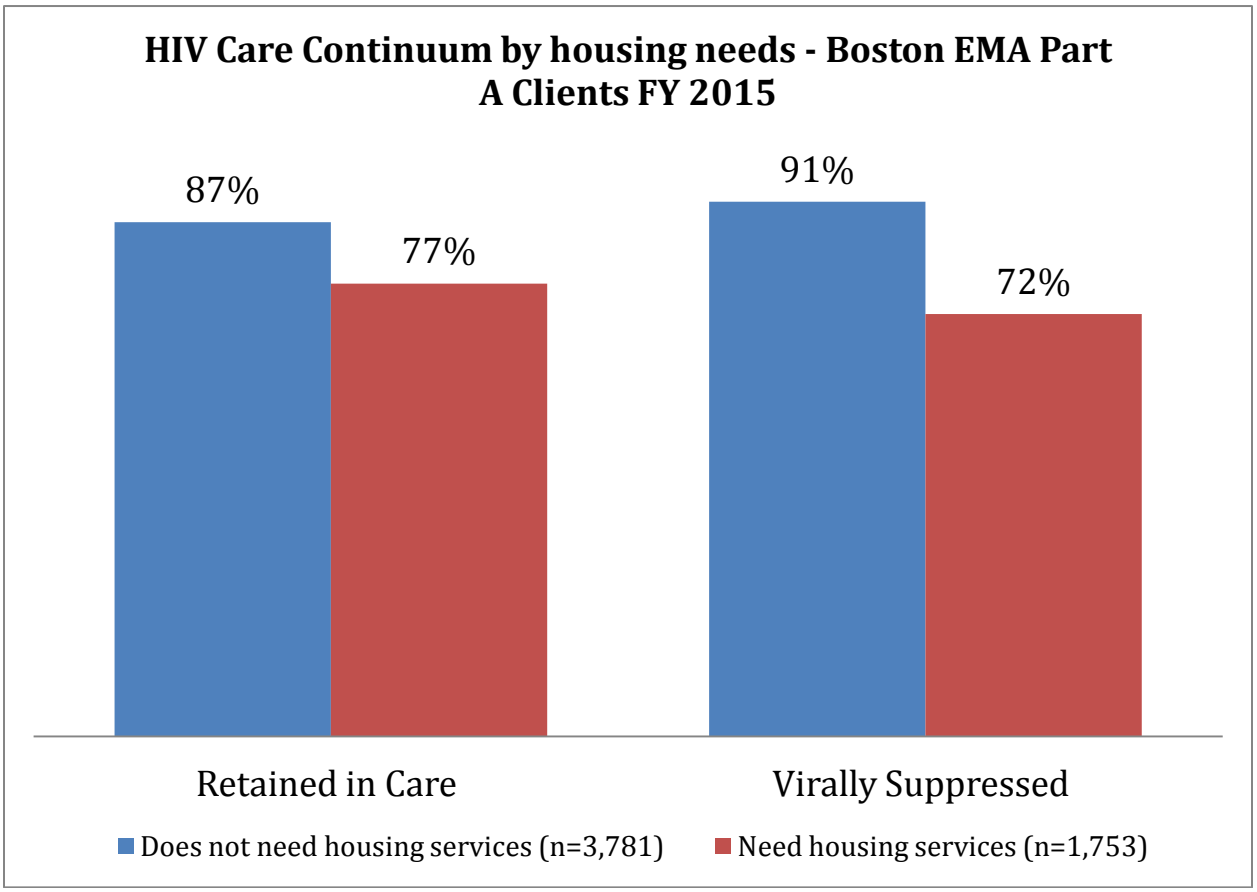
- Retention in care was highest among heterosexual clients
- Retention in care lowest among IDU clients
- Viral suppression was highest among MSM clients
- Viral suppression was lowest among pediatric/other risk exposed clients
- More clients were virally suppressed and not retained among MSM and IDU clients

Figure 6: Boston EMA Part A HIV Care Continuum by Age, 2015



- Retention in care was highest among clients less than 45 years old
- Viral suppression was highest among clients over 64 years old
- Older clients are less likely to be retained in care, but more likely to be virally suppressed
- Younger clients are more likely to be retained in care but less likely to be virally suppressed

Figure 7: Boston EMA Part A HIV Care Continuum by Housing Needs, 2015



Housing needs were determined by outcome reports submitted for clients, not by utilization data. In the outcome reports, providers were asked to report the clients housing status. Options included: stably housed, stably housed but need assistance, unstable housing, homeless/recently evicted.

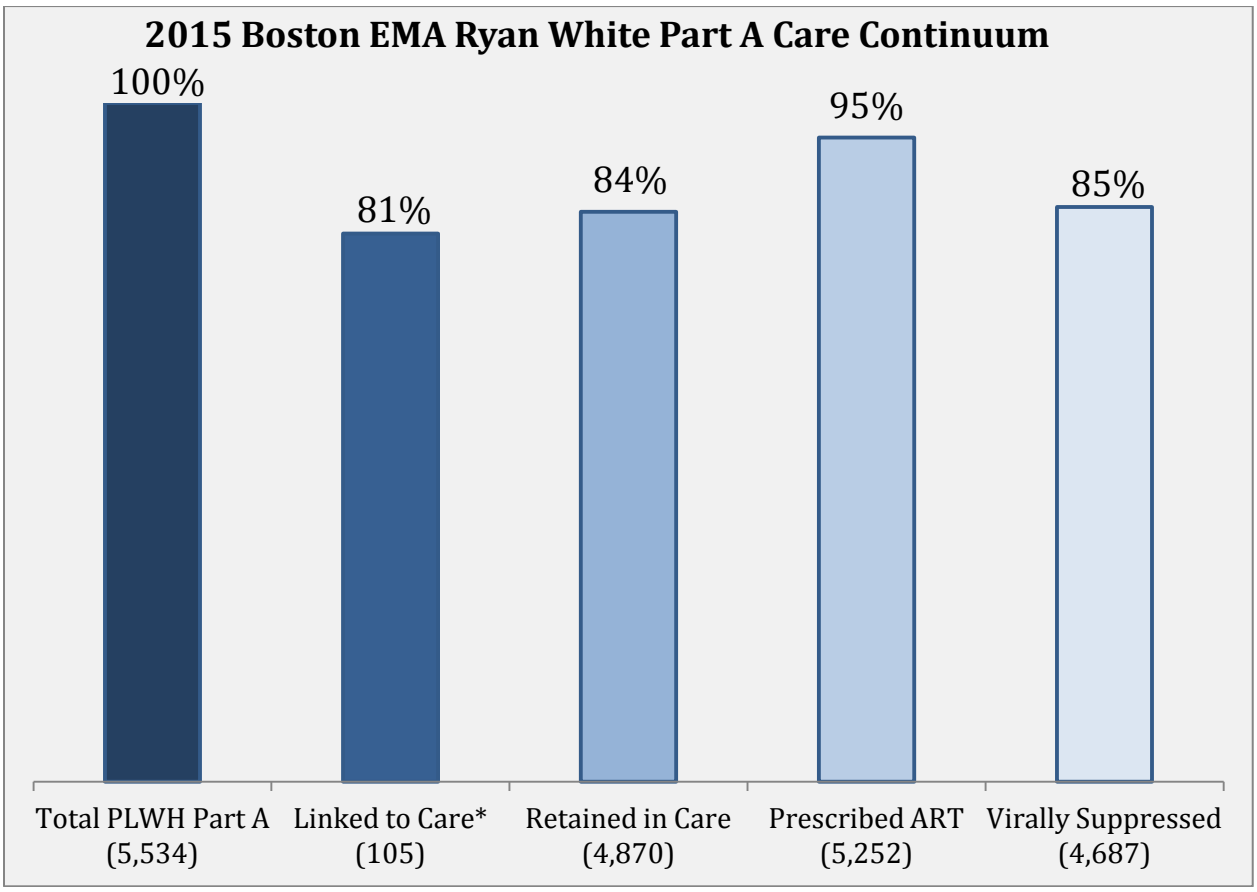
- Clients that indicated no housing needs were more likely to be retained in care and virally suppressed than clients who have housing needs
- More clients without housing needs were virally suppressed than retained in care

More clients with housing needs were retained in care than virally suppressed

Utilizing the HIV Care Continuum in the Boston EMA

Figure 8 provides information on the HCC PLWH who are receiving Part A funded services, only using data from e2Boston. The figure shows 16% of clients are not retained in care, 5% are not on ART and 15% are not virally suppressed. This suggests the need to invest in more services that keep clients retained in care such as medical case management and psychosocial support.

Figure 8: HIV Care Continuum for PLWH Receiving Part A Funded Services



The Planning Council (PC) utilizes the Part A and broader EMA HCC in several ways. Since FY13, members have received a presentation on the national, MA, and NH care continuums as part of the National HIV/AIDS Strategy (NHAS). This information, part of data to care efforts, helps members prioritize and allocate funding towards key services to have PLWH achieve viral suppression. In addition to the information in the HCC, BPHC, in conjunction with the PC, has unpacked in greater depth factors associated with lack of viral suppression through the Unmet Need Project. This project identified homelessness, mental health and substance use disorder as major barriers to viral suppression.

C. Financial and Human Resources Inventory

PLWH in the Boston EMA utilize a range of HIV prevention and care services to ensure there are no gaps in services. There are many sources of funding for these services. The funding amounts reported in the table below are from an annual funding streams report conducted by BPHC and the Boston EMA Planning Council. The Funding Streams Report identifies funding for HIV services, particularly public funds available throughout the EMA. It describes federal, state and local resources available for HIV-related services. Data for this assessment are collected using a form completed by various HIV/AIDS payers and providers. The form requested a description of available services and funding information on their most recent fiscal year. This report also includes limited information on funding from the private and philanthropic sectors[1].

Table 7 lists all the (1) public and private funding sources for HIV prevention, care, and treatment services in the Boston EMA, (2) the dollar amount and the percentage of the total available funds in fiscal year 2015 for each funding source; (3) a description of services provided; and (4) impacted steps of the HIV Care Continuum. Supplemental information on funded agencies and service category funding are included in Appendices 1 and 2.

1 Most data consist of public funding; available private sources are limited.

Table 7: Boston EMA HIV Resource Inventory [10]

Funding Source	Direct Funding Allocation	Number of Provider Agencies*	Funded Services Delivered	Impacted Step of HIV Care Continuum
Ryan White Part A	$12,438,406	35	AIDS Drug Assistance Program (ADAP), Medical Case Management Medical Nutrition Therapy, Oral Health Care, Food Bank/Home-delivered Meals, Housing Services, Medical Transportation Services, Non-medical Case Management, Psychosocial Support Services, Substance Abuse Residential	Linkage to Care; Retained in Care; Antiretroviral Use; Viral Load Suppression
Ryan White Part B (MA&NH)	$14,006,000	MA: 57 NH: 21	ADAP, Early Intervention Services, Health Insurance Premium/ Cost-Sharing Assistance, Home Health Care, Medical Case Management, Mental Health Services, Oral Health Care. Outpatient/Ambulatory Medical Care, Substance Abuse Services – Outpatient	Diagnosed; Linkage to Care; Retained in Care; Antiretroviral Use; Viral Load Suppression
Ryan White Part C (MA&NH)	$5,244,451	MA: 16 NH: 1	Early Intervention Services, Medical Case Management, Medical Nutrition Therapy, Mental Health Services, Oral Health Care, Outpatient/Ambulatory Medical Care, Substance Abuse Services – Outpatient, Health Education/Risk Reduction, Legal Services, Linguistic Services, Medical Transportation Services, Non-Medical Case Management, Outreach Services, Psychosocial Support Services, Referral for Health Care/Supportive Services, Treatment Adherence Counseling	Diagnosed; Linkage to Care; Retained in Care; Antiretroviral Use; Viral Load Suppression
Ryan White Part D (MA &NH)	$1,731,342	MA: 4 NH: 1	Early Intervention Services, Medical Case Management, Mental Health Services, Oral Health Care, Outpatient/Ambulatory Medical Care, Emergency Financial Assistance, Food Bank/Home-delivered Meals, Health Education/Risk Reduction, Medical Transportation Services, Non-medical Case Management, Outreach Services, Psychosocial Support Services	Diagnosed; Linkage to Care; Retained in Care; Antiretroviral Use; Viral Load Suppression
Ryan White Part F (Dental, SPNS, AETC)	$1,078,892		Oral Health Services	Linkage to Care; Retained in Care; Viral Load Suppression
CDC Prevention	$2,366,491		Early Intervention Services	Diagnosed; Linkage to Care

Funding Source	Direct Funding Allocation	Number of Provider Agencies*	Funded Services Delivered	Impacted Step of HIV Care Continuum
Medicaid (Federal and State contributions)	$181,234,770	MA: 21,537 NH: 344	Home & Community-based Health Services, Home Health Care Hospice Services Medical Case Management Mental Health Services, Oral Health Care, Outpatient/Ambulatory Medical Care, Substance Abuse Services – Outpatient	Linkage to Care; Retained in Care; Antiretroviral Use; Viral Load Suppression
HUD/ Housing Opportunities for Persons with HIV/AIDS (HOPWA)	$7,097,201	MA: 11 NH: 4	Medical Case Management (MA and NH), Mental Health Services (MA and NH), Substance Abuse Services – Outpatient (MA and NH),, Emergency Financial Assistance (MA and NH), Employment Services* (MA and NH), Food Bank/Home-delivered Meals (MA) Health Education/Risk Reduction (MA), Housing Services (MA and NH), Linguistic Services (NH) Medical Transportation Services (MA and NH), Non-medical Case Management (MA), Referral for Health Care/ Supportive Services(MA and NH), Substance Abuse Services – Residential (MA)	Retained in Care; Antiretroviral Use; Viral Load Suppression
SAMHSA (BSAS and BDAS)	$312,213		Substance Abuse Services – Outpatient, Non-medical Case Management, Psychosocial Support Services, Substance Abuse Services – Residential	Retained in Care; Antiretroviral Use; Viral Load Suppression
MA State AIDS Line Item	$25,850,364		AIDS Drug Assistance Program (ADAP), Early Intervention Services, Medical Case Management, Oral Health Care, Food Bank/Home-delivered Meals, Housing Services, Psychosocial Support Services	Diagnosed; Linkage to Care; Retained in Care; Antiretroviral Use; Viral Load Suppression
Private Funds	$333,989		Early Intervention Services, Health Insurance Premium & Cost Sharing Assistance, Medical Nutrition Therapy, Outpatient Ambulatory Medical Care, Case Management, Non-medical, Emergency Financial Assistance, Food Bank/ Home Delivered Meals, Housing Services, Medical Transportation, Psychosocial Support (Peer Support), Referral for Health Care / Supportive Services	Diagnosed; Linkage to Care; Retained in Care; Antiretroviral Use; Viral Load Suppression

*Appendix 1 has the full list of provider agencies.

HIV Workforce Capacity

The comprehensive healthcare system in Massachusetts provides PLWH, and those at risk, with a wide range of access to medical providers located in community health centers, hospitals, academic medical centers, family planning agencies, substance abuse treatment programs, and other community-based health and social service programs. These programs include a range of clinical and non-clinical staff, including HIV testing counselors, phlebotomists, medical case managers, behavioral health providers, and HIV+ peers, all working in collaboration with, registered nurses, nurse practitioners, infectious disease physicians, and primary care providers. All MDPH-funded HIV service providers are required to comply with MDPH expectations to provide clinically and linguistically appropriate services (CLAS) [4].

NH DPHS developed a resource inventory describing the service providers available to PLWH in NH. The resource inventory includes HIV medical care providers, New Hampshire Ryan White CARE program information, AIDS Service Organizations (ASOs), and counseling and testing sites. Most HIV service providers are concentrated in the southern and eastern part of the state, which constitutes part of the Boston EMA [6].

A comprehensive workforce capacity assessment for MA has also been developed by the New England AIDS Education and Training Center (NEAETC), and is available in the MA IHP. The assessment cited specific findings from regional focus groups:

NEAETC Workforce Capacity Assessment Findings [11]	
MA	The knowledge gaps and training needs of providers include: • PrEP implementation in rural and urban settings, • Strategies to improve adherence to PrEP in the substance use population, • Sexual health history taking • Addressing cultural barriers
NH	Potential training topics based on perceived providers' needs: • Transgender issues and HIV • Transplant issues • Pregnancy and HIV • Aging with HIV • Cardiovascular disease • Prison issue • Treatment of pain and opioid users • Addiction issues with HIV • Non-alcoholic Hepatitis • PrEP The NH IHP recommends training around HIV, LGBTQ, and racial and ethnic minorities.

Coordination of HIV Prevention, Care, and Treatment Services

Coordination of resources and services between BPHC, the Planning Council, and other federal, state and local funders assures that Part A funds are used as the payer of last resort, that duplication of services is prevented and that the continuum of care meets the needs of PLWH. The Council tracks these funding sources as an annual activity related to resource reallocation. A Funding Streams expo took place on December 9, 2015 to introduce Planning Council members to major sources of public funding for HIV services including, Ryan White Parts A, B, C, D, and F, MA and NH Office of Medicaid, New Hampshire Bureau of Drug and Alcohol Services (NH BDAS), Massachusetts Bureau of substance Abuse Services (MA BSAS), Housing Opportunities for Persons with HIV/AIDS (HOPWA), Centers for Disease Prevention and Control (CDC), Special Projects of National Significance (SPNS), and AIDS Education and Training Centers (AETCs). A survey was also sent out to all funders and funded agencies to provide up-to-date information on programs and services within their respective funding streams. In the FY15-16 funding streams report, Ryan White funding in the EMA included information from the following:

- 2 Part B programs (MA and NH, including ADAP funding)
- 17 Part C programs,
- 5 Part D programs,
- 3 Part F Dental Reimbursement programs,
- 1 AIDS Education and Training Center, and
- 1 Special Projects of National Significance (SPNS).

Ryan White funding accounted for only 13% of funding for HIV services in the EMA [10]. Other federal and state resources, such as Medicaid, BSAS, BDAS, HOPWA, and Boston Housing Authority (BHA) made up a majority of payers for services for PLWH in the EMA. The funding streams report also sought funding information from Medicare, Department of Veterans Affairs (VA), and non-public funding sources (including foundation grants and private insurance). However, there was limited success in obtaining funding information from these organizations and agencies. Only $333,989 that directly supported HIV services was identified. Many institutions were reluctant to release any fiscal information.

Needed Resources and Services

Mental health has consistently been raised as a needed service, with clients and providers both citing lack of access and a limited number of providers. However, many mental health services are reimbursable by third parties and thus not eligible for Part A funds. In response, the Planning Council designates funds for non-traditional mental health services under Psychosocial Support. These services are non-traditional in that they are intended to serve clients in agencies and settings that are not certified to bill third party payers such as

Medicaid or other insurers. The Planning Council also does not allocate any funds to Early Intervention Services due to availability of funding from other sources with respect to HIV testing and referrals. The Council recognizes the importance of these services and they remain part of our full list of prioritized services within the Boston EMA.

D. Assessing Needs, Gaps, and Barriers

For this Integrated Plan, the Planning Council, along with the help of the PCS staff, utilized five resources to understand the needs of PLWH and groups that are at risk of HIV infection:

1.) ***2015 Unmet Need Project:*** This project utilized focus groups with PLWH (N=35) and surveys that were completed by infectious disease physicians who provided HIV care (N=23) to identify service gaps and barriers among PLWH who were out of care.
   a. Focus groups were held in different geographic regions of the EMA, and included sites where a variety of services were provided such as food banks, homeless shelters, substance abuse treatment sites, and a corrections facility
   b. The anonymous physician survey was sent electronically and asked participants to prioritize common barriers and identify services that would address unmet needs among their at-risk patients living with HIV

2.) ***2015-2016 Boston EMA Client Outcome Report:*** During FY15, Ryan White Part A funded agencies served 5,534 clients through 12 service categories and 34 unique agencies. Client level outcome data was collected through e2Boston, a data system used by all Part A funded providers in the Boston EMA. The report analyzes a sub-population of clients on outcome measures such as their viral suppression, housing status, mental health status, and medical visits.

3.) ***Needs Assessment data published by MDPH and NHDHHS:*** Since Ryan White Part A does not fund or track information about prevention efforts, data on risk populations were gathered from our Ryan White Part B partners.

4.) ***2016 Priority Setting Exercise:*** The Planning Council conducts a priority setting exercise each year to establish top service priorities. Members identify these priorities based on presentations and reports provided by PCS staff, and their personal experiences as PLWH, HIV service providers, and other stakeholders.

Populations at Risk for HIV Infection- Service Needs and Gaps

According to the MDPH, groups that have a higher risk of HIV infection include MSM, racial and ethnic minorities, non-US born immigrants and refugees, persons who inject drugs, and transgender individuals. Common service gaps among these groups include a lack of

service capacity (e.g. agency closures or insufficient resources), lack of culturally and linguistically appropriate services (e.g. low knowledge of risk group or lack of translation services), lack of access to behavioral and mental health services, and insufficient access to PrEP.

People Living with HIV- Service Needs and Service Gaps

Housing

Part A data suggest there is a need for housing services within the EMA, as 29% of reported FY2015 clients indicated a housing related need. These needs ranged from financial assistance for rent or utilities to housing search and advocacy. In addition, focus group participants within the Unmet Need Project indicated the need for more housing options as well as services to help them find housing, enroll in subsidized housing, and obtain vouchers. Planning Council members ranked housing services as the third most important service need during the 2016 Priority Setting exercise.

Mental Health

Part A data show that 54% of Part A clients reported having mental health problems. Of those clients, 41% were not receiving mental health services. Focus group respondents identified the need for more therapists, and in particular therapists who were bilingual and empathetic. Among physicians, access to mental health services and lack of mental health resources was the most frequently reported service need to address the challenges among their highest risk and non-adherent patients.

HIV Education

Focus group participants in the Unmet Need Project overwhelmingly reported the need for more HIV education for various groups including:

a.) PLWH: Participants expressed needing more information on how their body is affected by missing a medication dosage and substance use while taking ART. They also wanted to learn about pregnancy and reducing risk of vertical transmission, as well as nutrition guidelines for PLWH.

b.) HIV Providers: Some focus group participants felt that providers needed basic HIV information as well as empathy training.

c.) General Public: Participants mentioned the need to educate students, older adults, and immigrants on safe sex practices, HIV testing, and STIs to prevent future transmission and reduce stigma.

Transportation

The Unmet Need Project Focus group respondents felt that transportation services were needed specifically for PLWH to get to their medical appointments. Based on an

assessment of need among PLWH in NH, transportation to get to medical appointments was cited as the most common challenge among a sample of HIV positive survey participants. Despite Part A funding medical transportation services, the need for transportation may be an indication that PLWH may not know how to access or qualify for medical transportation services.

ADAP and Medical Case Management were ranked as the two most important services for PLWH based on the Priority Setting exercise done by the Planning Council. There are no data suggesting an unmet need for these categories, which may indicate that PLWH are able to obtain the services.

Barriers to HIV Prevention and Care

Evidence provided by the 2015 Boston EMA Ryan White Part A HCC (Figure 8) suggests that approximately 26% of PLWH in the Boston EMA experience barriers that prevent them from engaging in continuous HIV care. In addition, an estimated 5% of PLWH are not taking ART, and 15% are not virally suppressed in the Boston EMA. Below is a list of common barriers that contribute to gaps in the continuum of care:

Social and Structural Barriers

Poverty- During FY15, 59% of newly diagnosed Part A clients reported living at or below 100% FPL, 81% reported living below 200% FPL, and 88% lived below 300% FPL [5]. These data continue to demonstrate that many PLWH are challenged by economic and societal stresses. As a result, healthcare, including that for HIV, competes with needs such as housing, food, transportation, and clothing. Provision of care to this population is complex, as providers must address these tangible needs and assist clients in navigating the system of benefits and entitlements to keep them engaged in care.

Stigma- Stigma and public misperceptions of HIV can have a severely negative impact on PLWH. Focus group participants discussed various types of stigma that prevented them from seeking HIV care including stigma associated with substance abuse, immigration status, and fear of a partner finding out about their HIV status. In addition, 93% of physicians agreed that HIV stigma is a barrier to care with at least some of their clients.

Homelessness and Housing Instability – Homelessness in the EMA is driven by some of the highest housing costs in the nation, accompanied by low rental vacancy rates and a large share of renting households paying more than 30% of their income toward rent [12] [13]. The prevalence of homelessness is high among PLWH; an estimated 40% to 60% will experience homelessness at least once in their lifetime [14]. During FY14, 11% of Part A clients were non-permanently housed, reflecting the high prevalence of housing instability

among PLWH BPHC [5]. Homelessness was a constant concern raised by all respondents in the Unmet Need Project. For PLWH who experience homelessness, the lack of storage space created challenges with taking medication. In addition, going to medical appointments became problematic if the time of the appointment conflicted with the time they needed to be at a shelter to secure a bed for the night. When PLWH are focusing on securing basic needs such as a place to live or sleep for the night, their HIV care becomes a lower priority.

Service Provider Barriers

Service Provider Capacity - Lack of access to mental health services and inadequate mental health services were a frequently reported concern in the Unmet Need Project. Respondents reported long wait times for intake appointments and follow-up visits, as well as high turnover among mental health providers. Mental health service locations and eligibility requirements also limited clients' access to services. Respondents also reported a lack of system capacity for both inpatient and outpatient substance abuse facilities. Addressing these system capacity concerns will be critical for successful HIV treatment.

Client Barriers

Substance Use- According to data provided through the Drug and Alcohol Services Information System, in 2014 there were 84,719 new enrollments to substance abuse treatment services, or approximately 1.3 new enrollments per 100 MA residents [15]. In 2014, 218 Part A clients accessed substance abuse services [5]. Substance use disorder was frequently cited as a barrier to HIV care in the Unmet Need Project. Prioritization of substance use over HIV care was a common theme among focus group participants. Eighty-two percent of physicians providing HIV care also cited substance use as a common barrier to care for PLWH and that patients with substance use issues were less likely to respond to phone calls or emails from providers.

Other reported barriers from the Unmet Need Project include having a negative experience with a provider, being in denial about or not wanting to deal with their HIV, and fear of others finding out about their HIV status.

E. Data: Access, Sources, and Systems

Main Sources of Data

Table 8 outlines the data sources and data systems used to conduct the needs assessment and develop the HIV Care Continuum

Table 8: Data Sources and Data Systems

Data Systems/Data Source	Data
e2Boston	Client demographics, Service Utilization and Outcomes
Clinical Chart Review	Client demographics, Service Utilization and Outcomes
2015 Unmet Need Project (Focus Groups, Surveys, Emergency Department Data)	Needs, Gaps and Barriers
MDPH HIV Surveillance	Prevalence, Incidence, Viral Load Monitoring and HIV Testing data
NHenhanced HIV/AIDS Reporting System (eHARS) database (2005-2014) (Surveillance Data)	HIV Infections, HIV diagnoses, HIV prevalence, including by transmission status, race/ethnicity, gender, country of origin; HIV Care Continuum
NH 2014 and 2015 Quantitative Survey of Assessment of Need, Gaps, and Barriers	Needs, Gaps and Barriers
NH 2014 Qualitative Focus Groups	Needs, Gaps and Barriers

Data Policies

The Boston EMA relies on its state partners, MDPH and NHDHHS to provide HIV surveillance data. Release of this information is usually delayed.

Obtaining New Sources of Data

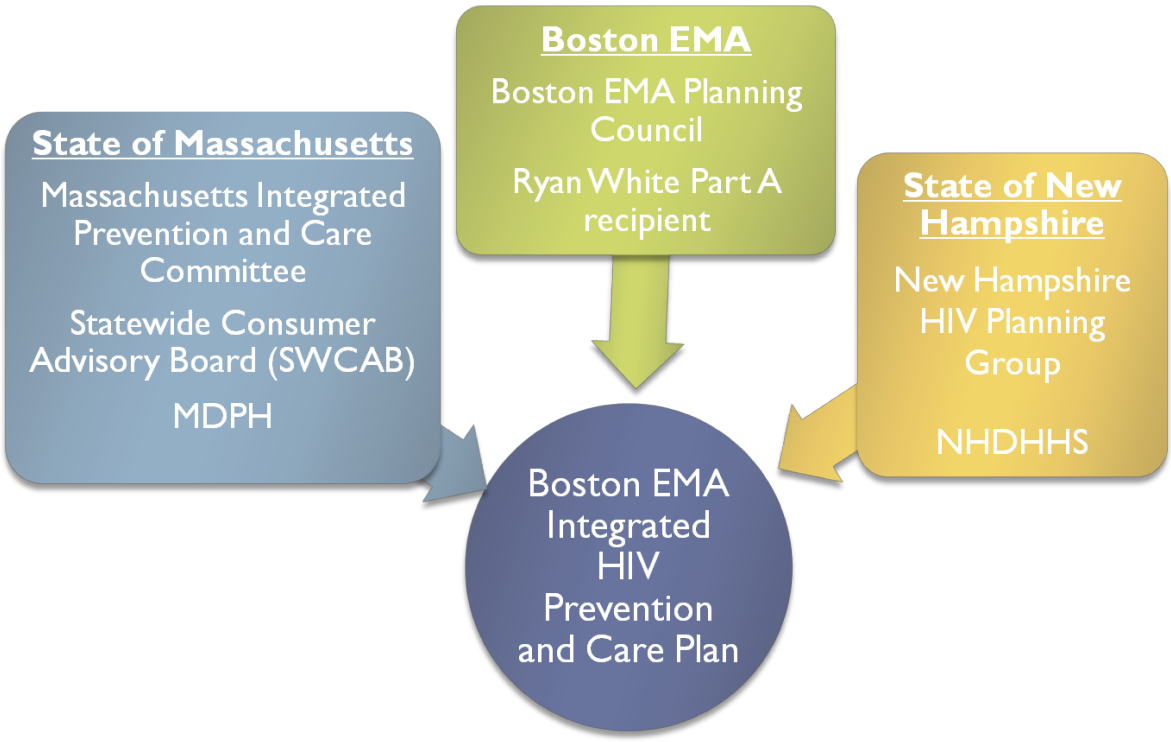
Direct access to HIV data for analysis is not available to BPHC. Access to the HIV surveillance dataset would allow BPHC to perform additional analyses of interest without having to burden MDPH and NHDHHS.

In addition, both the Boston EMA Unmet Need Project and the NH Needs Assessment study had low numbers of participants who were not in care. BPHC and the Planning Council are currently conducting a new study to identify barriers that prevent PLWH both in and out of care from receiving needed services or from continuing in care, including an assessment of unmet needs for PLWH who know their HIV status but are not in care and strategies to reach out to those unaware of their status. This new study is targeting a higher sample size of participants and should provide more current information on the needs of the Boston EMA population.

Section II: Integrated HIV Prevention and Care Plan

A. Integrated HIV Prevention and Care Plan

As a directly funded agency with a jurisdiction overlapping two states, the Part A IHP represents a combination of three distinct jurisdictions: MA, NH and the Boston EMA. Representatives from the Planning Council and BPHC attended planning meetings convened between 2015 – 2016 by the NH Integrated HIV Prevention and Care Work Group (IHW) and MDPH OHA to develop and prioritize the goals and objectives of the state plans. The Planning Council also convened its own Comprehensive Plan working group which consisted of key stakeholders such as members of the MDPH Statewide Consumer Advisory Board, representatives from MDPH and NHDHHS, a representative from BPHC, the City of Boston's Mayor's representative, and Planning Council members, including PLWH, to examine progress on previous Comprehensive Plans and adapt them for an EMA-specific IHP.



Based on these state planning meetings and community planning process, the Boston EMA developed an Integrated Care and Prevention Plan that compliments the two state plans while highlighting specific EMA objectives that can address the unique needs of EMA residents. Table 9 (included under the Section III: Monitoring & Improvement) provides the Boston EMA goals and objectives along with corresponding strategies, activities, target populations, responsible parties and metrics to monitor progress. Copies of MA and NH IHP workplans are included in Appendix 3 and 4.

Boston EMA Part A Integrated HIV Prevention and Care Plan – Goals and Objectives

The 2017 – 2021 IHP includes at least three strategies in each objective. Each objective utilizes a SMART format that identifies the timeframe, responsible parties, activity/action step, target population or stakeholder, and data indicators. As a Part A jurisdiction, the EMA's IHP identifies numerous projects that involve the Planning Council and particularly its consumer membership.

The plan also features short and long-term strategies and activities that allow more complicated, intensive initiatives to be completed and evaluated closer towards 2021. Conversely, short term activities allow BPHC to update the Planning Council on current goals to implementing the IHP. Similarly, new strategies and activities may be adopted in collaboration with MDPH and NH DHHS based on lessons learned from implementation of their state plans.

A workplan with all goals, SMART objectives, and strategies is included in Section III.

IHP Goal 1: Reduce New HIV Infections

Objective A: By 2021, ensure 100% of all Part A funded sites provide internal linkages to comprehensive HIV services for PLWH and their significant contacts or can demonstrate appropriate linkages in the community

Strategies and activities include:

- Complete a comprehensive needs assessment on current HIV positive prevention and care needs of PLWH residents in the Boston EMA, comprising a literature review, consumer survey, focus groups, and interviews with healthcare providers and case managers
- Implement contract language to require comprehensive HIV services to be made available to PLWH accessing Part A case management & peer support programs and ensure access to a range of "treatment as prevention" services, including access to partner notification services, family & reproductive health services, and risk/harm reduction services
- Re-procure all Part A service categories and incorporate language in contracts that require providers to directly deliver or make available through linkages access to comprehensive HIV services for PLWH and their significant contacts.

Objective B: By 2021, expand entry points or specialized staffing that serve individuals at high-risk for HIV infection or those that do not know their status.

Strategies and activities include:

- Submit an application to HRSA requesting a Syringe Services Program (SSP) Waiver to utilize Part A funds to support engagement of PLWH affected by substance abuse, particularly those at risk for co-occurring Hepatitis C infection and opiate overdose
- Expand collaboration with partners, including embedding and integration with existing Part A program sites, to identify newly diagnosed individuals who may be seeking care for HIV, TB, HCV and other STI's
- Develop a coalition/network of providers and government agencies dedicated to expanding the presence and awareness of comprehensive HIV services for chronically homeless individuals seen at homeless/transitional shelters, drop-in centers, and environments where they can be engaged for services
- Implement a training program to expand the number of community health workers in the EMA with expertise in providing comprehensive HIV services targeting PLWH and high-risk negatives, particularly in developing community-based needs assessments, home-based service delivery, and linkage to primary care services

IHP Goal 2: Increase access to care and improve health outcomes for PLWH

Objective A: By 2021, improve viral suppression rates from 85% to 90% for PLWH who currently utilize Part A services in the Boston EMA.

Strategies and activities include:

- Utilize case managers, peer advocates, and community health workers targeting virally non-suppressed PLWH for community-based services, including those delivered in the home, such as directly observed therapy, accompaniment to medical appointments, and other support
- Expand funding for high acuity case manager positions at agencies with >10% virally unsuppressed client populations to improve PLWH utilization of essential services that improve viral suppression
- Expand services that address persistent challenges to viral suppression, such as mental health, substance abuse, and homelessness, including usage of community health workers; referrals to syringe exchange/recovery services; housing search & advocacy

Objective B: By 2021, improve percentage of Part A clients who have health insurance from 92% to 97%.

Strategies and activities include:

- Ensure all funded Medical Case Management (MCM) and (Peer Support) PS staff are trained and consistently providing health insurance enrollment and recertification activities to any RW eligible PLWH
- Ensure uninsured or under-insured PLWH are aware, referred, and enrolled in health insurance premium and co-pay assistance services funded by MA and NH Part B

- Reduce number of clients that have lapses in coverage due to failure to recertify or payment of insurance premiums

IHP Goal 3: Reducing HIV related disparities and health inequities

Objective A: By 2021, reduce the gap in viral suppression rates among White (87%) versus non-Hispanic Black (84%) and Hispanic (84%) PLWH who currently utilize Part A services in the Boston EMA.

Strategies and activities include:

- Design training and capacity building activities that utilize current viral suppression data for Black and Hispanic PLWH to improve providers' abilities to deliver high quality, culturally competent HIV services to virally non-suppressed PLWH
- Support the NH anti-stigma campaign, which will focus on communities of color
- Invest in high acuity case management and peer support services that target Black and/or Hispanic PLWH through Part A MAI funding, including funding at least one new agency/program targeting an area with high HIV incidence among Black and/or Hispanic PLWH
- Implement data-to-care quality improvement activities for agencies and programs with >10% virally unsuppressed Black and/or Hispanic PLWH

Objective B: By 2021, decrease the percentage of Part A clients who need housing services from 34% to 29%.

Strategies and activities include:

- Conduct annual priority setting and resource allocation processes that identify new HRSA service categories that can be added to the EMA's list of funded categories in order to address housing needs among PLWH EMA residents.
- Invest in comprehensive housing services that successfully place PLWH into permanent housing, including funding additional housing search & advocacy programs
- Provide ongoing support for PLWH in maintaining their housing, including case management and emergency assistance.
- Improve collaboration with HUD HOPWA grantees in the region to:
    - Better maximize federal resources that provide housing subsidies for PLWH
    - Identify PLWH that require RW assistance as a result of not meeting HUD HOPWA-defined 80% area median income (AMI) limit.
    - Identify new service components that can be delivered in residential settings that enhance viral suppression among PLWH

Anticipated Challenges in Implementing the Plan

Since BPHC only receives Part A funding and is not directly funded by CDC for HIV prevention, developing objectives that meet the NHAS goal of reducing new infections must be constructed in a manner that does not utilize Part A funds for HIV uninfected individuals. This is one major reason why collaboration with state health departments receiving Part B and CDC prevention funds is so critical when developing the region's IHP. Through the states' own IHP strategies, actvities are able to simultaneously reach PLWH and uninfected individuals through concurrent activities that seek to reduce disease burden for highest risk communities and individuals, while addressing factors that place all residents at risk for infection potentially contributing to lateness to care.

Due to funding limitations, BPHC is utilizing the IHP as a way to initiate system change through a variety of structural interventions and quality improvement activities that allow Part A funds to support many non-HIV-specific environments where PLWH may access services. This includes bridging gaps and silos that have existed between traditional HIV service settings and providers with those that serve residents that experience highest HIV risk. Successful implementation must involve better collaboration and integration with homeless/transitional shelters, substance abuse recovery programs, mental health providers, and housing assistance resources.

Many of these non-HIV-specific settings and providers have access to PLWH who are unlikely to access services at RW funded sites. However, PLWH at some of these sites would benefit from infusion of new resources brought by Parts A and B. BPHC has a demonstrated track record in expanding availability of Part A services and resources into these types of settings.

For example, no RW funded services were available for TB/HIV co-infected individuals receiving care at a state run hospital in Boston where inpatient TB care and aftercare is provided. Many of these co-infected individuals were struggling with substance use disorder, mental illness, and homelessness. BPHC recruited an existing Part A MCM provider and successfully negotiated with the hospital in 2015 to embed case managers at the hospital to assist physicians in providing high acuity case management services post-discharge. As of September 2016, 20 PLWH continue to be followed for primary care and case management services at the facility.

B. Collaborations, Partnerships, and Stakeholder Involvement

The Boston EMA IHP represents the collaborative work of two states and one Part A jurisdiction. Each Ryan White recipient has their own community planning bodies that assisted and guided the development of plans. Groups, such as the Planning Council (Boston EMA Part A), MIPCC (MA Part B), and NH HPG (NH Part B) were also previously involved in developing multi-year Comprehensive Plans and the related Statewide Coordinated Statements of Need (SCSN). Components of those previous major undertakings, such as a comprehensive needs assessment and resource inventory, are essential components of the IHP. Rather than entirely reinventing the system of care or approaches to HIV service delivery, developers of the IHP were sensitive to retain the strengths and assets previously identified through activities, such as comprehensive planning, and incorporating NHAS directives and goals in order to provide the most modern, science-based and data-driven plan to reduce the impact of HIV in the two-state region.

For Part A, the Planning Council and PCS staff took the leadership role in starting the IHP development process. A special Comprehensive Working Group was formed to utilize the historic and institutional knowledge of community members, current and former Planning Council members, and representatives from health departments. Members of this committee also had cross-membership with MIPCC/SWCAB and NH HPG that were responsible for state IHP development activities. These cross-participants were able to report at committee meetings on MA and NH's progress in completing and submitting their plans. The committee met monthly until July 2016 to work on key components of the IHP, including special/emerging populations for a needs assessment, the HIV resource inventory, and the IHP workplan. The group successfully completed their work in time for a presentation at the September 2016 Council meeting to review the proposed goals and objectives for the Part A IHP.

MDPH worked in tandem with Part A through their two main community planning bodies, MIPCC and SWCAB. MIPCC is an integrated planning group, which existed prior to the release of the IHP guidance; SWCAB is a consumer-led advisory body, which also participated in MIPCC. Membership within these groups includes PLWH, advocates, funded providers, and other advisors from across the state. Through its meetings between September 2015 and February 2016, MDPH convened three separate meetings to identify planning priorities, outline service needs, and identify gaps and barriers. In June 2016, the final results of the Integrated SCSN/Needs Assessment were reviewed and confirmed with the members of the MIPCC and SWCAB. MDPH also held a special statewide meeting, convening 172 attendees to review the state's current progress in developing the MA IHP and solicit feedback on critical areas of focus for the state vision and strategy to end the

HIV epidemic.

NH DHHS operated on a smaller scale compared to MA and worked very intimately with their existing NH HPG, a group historically involved in prioritizing both HIV prevention and care services, and formed a special Integrated HIV Work Group (IHW). Membership within this group included NH health department officials, HIV medical providers, ASO's, and PLWH; JSI Research & Training Institute was contracted to assist the planning process and to generate the final report to submit to HRSA and CDC. The NH IHW met regularly for four months to develop and prioritize the goals and objectives for the NH IHP. They reviewed results from the 2013 NH Comprehensive Needs Assessment, developed priority areas and strategies for the plan, and created objectives and activities for the workplan.

Engagement of Stakeholders

It would be helpful to bridge the non-HIV-specific payers that have historically been under-recognized as significant contributors to the HIV care system. While a Medicaid representative is and has been an extremely active participant on the Planning Council, not as much is understood regarding the role of Medicare, particularly as the Boston EMA's aging PLWBH population being increasingly more likely to be dual-eligible Medicare recipients. As this is likely to be an issue not just in MA and NH, support from HRSA would be beneficial.

Similarly, the changing healthcare landscape requires more information and participation from the private insurance industry. The Blue Cross Blue Shield Foundation contributes to frequent special reports on private insurance trends in MA, but little else tends to be available on the impact of private insurance for PLWH. This will become more relevant over time as younger PLWH and those who are working are more likely to be covered under employer-based private health insurance plans, which are affected by changes to the Affordable Care Act and any future national legislation on healthcare access.

SAMHSA and HUD/HOPWA are two major funders of services utilized by PLWH in the EMA. However, there is no representation from either office on the current Planning Council. Substance abuse and the associated opiate epidemic has gained prominence in recent years; HUD also provides a major housing infrastructure through its HOPWA housing subsidies, an essential resource in the Greater Boston region where rental prices are significantly above national averages. As outlined in the IHP workplan, BPHC and the Planning Council are committed to furthering relationships with the two federal agencies and better coordinate with agencies that receiving SAMSHA and HOPWA funding.

Letters of Concurrence

BPHC has received a letter from the Planning Council for the Part A IHP based on a vote of concurrence occurring on September 8, 2016. MDPH received support from their state planning bodies through a letter of concurrence following their MIPCC on September 15, 2016. NH DHHS received their letter of concurrence from the NH HPG following their final planning group before the summer of 2016. In addition, the Chair of the Boston EMA Planning Council reviewed the IHP workplans for both MA and NH and provided letters of concurrence supporting the state plans. Copies of letters are included within Appendix 4.

C. People Living With HIV (PLWH) and Community Engagement

The Comprehensive Plan Working Group (CPWG) was the primary group initially developing the Part A IHP. Based on EMA epidemiological data, the working group's composition met the reflectiveness of the HIV/AIDS epidemic. The group consisted of 10 members, 80% of which were PLWH. The group was 50%male, 50% people of color, and included three MSM. The current Planning Council, which reviewed and approved the IHP goals and objectives, is similarly reflective of the EMA epidemiological profile and has the HRSA-mandated 33% PLWH representation.

The CPWG met monthly to review progress made on the 2012-2015 Comprehensive Plan, discuss emerging consumer needs and specific populations of interest, and brainstorm relevant goals and objectives for the IHP. After the plan is submitted, members of the working group will then continue the community planning process by also updating the previous Comprehensive Plan. Council members felt that while the IHP provides a good five-year roadmap on the integrated prevention and care needs, many elements of the Comprehensive Plan, including examination of special PLWH populations (e.g. long-term HIV survivors) should be updated. This work will also be synthesized into the annual updates and adjustments to the Part A IHP over the next five years.

Engaging PLWH and Impacted Communities

BPHC and the Planning Council place significant value on the involvement of PLWH in all of its work. The goal-setting processes for the IHP could not have been completed without the aid of consumers of HIV services who personally understand the impact of funding on the quality of care they receive. Their input validates the need for strong epidemiologic data that accurately identifies areas and communities most disproportionately affected, and including information on how disparities in healthcare have an impact on health outcomes, especially viral suppression.

As one of the original first Title I grantees funded by HRSA in the 1990's, the Boston EMA has been fortunate to have many longtime PLWH advocates that remain committed to having their consumer voices heard by government officials and policymakers. Many working group members have passionately discussed the acute and emerging needs of long-term survivors and the service gaps experienced due to the current Ryan White HIV/AIDS Program model. At the same time, the group also is aware of the need to adjust to changes in the epidemic as HIV incidence in the EMA skews significantly and disproportionately towards young MSM of color, and new infections due to IDU and perinatal transmission continue to decline.

Section III: Monitoring and Improvement

Process of Updating the Boston EMA Part A IHP

BPHC will report back to the Planning Council on progress towards achieving the IHP objectives. This will be accomplished through annual presentations conducted during one of the monthly meetings during the Council year to review the workplan, implemented activities, and observable outcomes seen. Viral suppression data, which is an indicator identified for two of IHP goals, are regularly reported in Council documents and presentations. Similarly, racial/ethnicity health disparities are identified by reviewing client demographic and outcomes data to show any potential gaps in viral suppression between different PLWH served via Part A programs.

In addition, BPHC will introduce the IHP at the FY 2017 Annual Provider Training, outlining the EMA's workplan and how agencies are contributing to the overall plan. Many of the special initiatives described in the plan, such as expansion of community health workers in RW settings, will present major opportunities for providers to gain new or additional resources that will ultimately help their clients achieve viral suppression and address persistent challenges, such as homelessness, mental illness, or substance abuse. In subsequent years, BPHC will review progress with providers at future provider gatherings and through smaller work groups to collaborate more intimately with agencies to address regional or local issues or concerns.

Depending on priorities and available resources, the Council may also decide to maintain the Comprehensive Plan Work Group as an ongoing activity to monitor and evaluate the IHP. It is unique from the Council's other committees in that non-Council members, such as community advocates, RW providers, and other consumers, can volunteer and participate in the group's activities. The group proved to be highly productive in assisting in the creation of the IHP workplan and many of the members were interested in potential opportunities to continue their volunteer work.

Both MDPH and NH DHHS have already planned on reconvening with their community planning bodies to review their respective workplans. BPHC and the Planning Council have been invited to participate in those meetings as guests and partners. There is the potential to host joint meetings in upcoming years, where members of the various planning bodies can engage in cross-conversations about the separate IHP's and how additional opportunities for collaboration can be facilitated by BPHC, MDPH, and NH DHHS. The Planning Council remains to be the central place, where Part B representatives can update on IHP implementation through dedicated time on the agenda allotted at every monthly meeting.

Monitoring and Evaluation of the Boston EMA Part A IHP

As BPHC/Planning Council, MDPH, and NH DHHS individually submit their IHP to HRSA and CDC, all recipients/grantees will re-convene with their community planning bodies to report back. Full copies of the plans will be available for planning body members and posted online for all community stakeholders to read and/or download.

BPHC, MDPH, and NH DHHS will meet shortly after their respective plans are submitted to identify overlaps within the workplans and discuss how to properly track and report progress in achieving the range of long and short term objectives and activities proposed in the plans. Each goal of the Part A IHP has at least one objective which overlaps with the objective, strategies, and activities from either state plan. This intentional overlap will also encourage cross-participating members of the planning bodies to communicate and collaborate across the groups to accomplish shared goals and objectives.

For the development of the IHP, all three government agencies focused and prioritized in-person participation in order to maximize opportunity to gather feedback to develop the plans. Moving forward, webinars and conference calls will be used as an additional method to include individuals that may not participated in the previous planning process and bring new voices into the conversation. The Part A IHP features many 1-2 year activities that also offer opportunities for interested individuals to become involved for a shorter time duration and see incremental accomplishments, which contribute the overall vision and goals as put forth by the various plans.

Table 9: Boston EMA Integrated HIV Prevention and Care Plan – Goals and Objectives

Goal 1: Reducing New HIV Infections				
Timeframe	**Responsible parties**	**Activity**	**Target Population or Stakeholder**	**Data Indicators**
Objective 1A: By 2021, ensure 100% of all Part A funded sites provide internal linkages to comprehensive HIV services for PLWH and their significant contacts or can demonstrate appropriate linkages in the community				
2016 - 2018:	Boston EMA Planning Council	Complete a comprehensive needs assessment on current HIV positive prevention and care needs of PLWH residents in the Boston EMA, comprising a literature review, consumer survey, focus groups, and interviews with healthcare providers and case managers	• PLWH currently receiving a Part A service • PLWH currently out of care • HIV service providers located in the EMA	• Representativeness of the sample of of PLWH reached for consumer survey • Number of consumers, providers, and experts interviewed
2016 - 2018:	BPHC HASD	Implement contract language to require comprehensive HIV services to be made available to PLWH accessing Part A case management & peer support programs and ensure access to a range of "treatment as prevention" services, including access to partner notification services, family & reproductive health services, and risk/harm reduction services	Part A sub-recipients funded to deliver MCM & PS services	Number of programs that demonstrate internal and/or external linkages to comprehensive HIV services
By the end of 2021:	BPHC HASD	Re-procure all Part A service categories and incorporate language in contracts that require providers to directly deliver or make available through linkages access to comprehensive HIV services for PLWH and their significant contacts.	All sub-recipients of Part A funds	Number of agencies that demonstrate internal and/or external linkages to comprehensive HIV services

Objective 1B: By 2021, expand entry points or specialized staffing that serve individuals at high-risk for HIV infection or those that do not know their status				
2017 – 2018:	• Boston EMA Planning Council • BPHC HASD	Submit an application to HRSA requesting a Syringe Services Program (SSP) Waiver to utilize Part A funds to support engagement of PLWH affected by substance abuse, particularly those at risk for co-occurring Hepatitis C infection and opiate overdose	• PLWH affected by substance abuse, including those at high risk for opiate overdose • PLWH co-infected with HCV • Program sites involved with delivering potential SSP services	• Number of Part A clients accessing substance abuse treatment services • Number of new SSP sites receiving Part A funds
2016 – 2018:	• BPHC • MDPH • NH DHHS	Expand collaboration with partners, including embedding and integration with existing Part A program sites, to identify newly diagnosed individuals who may be seeking care for HIV, TB, HCV and other STI's	• Newly diagnosed PLWH and their contacts • Part A sub-recipients funded to deliver MCM and PS services	• Number of PLWH reached at non-HIV specific settings • Percentage of PLWH linked to MCM, primary care, or ADAP
By the end of 2018:	• BPHC HASD • HOPWA funded agencies in the EMA	Develop a coalition/network of providers and government agencies dedicated to expanding the presence and awareness of comprehensive HIV services for chronically homeless individuals seen at homeless/transitional shelters, drop-in centers, and environments where they can be engaged for services	• Homeless or unstably housed PLWH in the Boston EMA • Homeless/transitional shelter programs • HOPWA funded agencies • Part A sub-recipients that have >25% client population that are homeless/unstably housed	• Percentage of Part A clients reported as homeless or unstably housed • Number of PLWH served through programs funded by HOPWA and other housing services • Number of new sites that offer HIV services not currently receiving Part A funding
By the end of 2019	• BPHC HASD • BPHC Comm. Health Education Center	Implement a training program to expand the number of community health workers in the EMA with expertise in providing comprehensive HIV services targeting PLWH and high-risk negatives, particularly in developing community-based needs assessments, home-based service delivery, and linkage to primary care services	• Agencies with existing community health worker staff or those desiring to create such positions	• Number of new community health workers trained • Number of new community health worker positions funded by Part A

Goal 2: Increasing Access to Care and Improving Health Outcomes for PLWH				
Timeframe	**Responsible parties**	**Activity**	**Target Population or Stakeholder**	**Data Indicators**
Objective 2A: By 2021, improve viral suppression rates from 85% to 90% for PLWH who currently utilize Part A services in the Boston EMA.				
2016 - 2018:	• BPHC HASD • Part A funded MCM and PS programs	Utilize case managers, peer advocates, and community health workers targeting virally non-suppressed PLWH for community-based services, including those delivered in the home, such as directly observed therapy, accompaniment to medical appointments, and other support	• Part A client reported as virally non-suppressed during the last 6 months from most recent service	• Percentage of PLWH with an undetectable VL
By the end of 2018:	BPHC HASD	Expand funding for high acuity case manager positions at agencies with >10% virally unsuppressed client populations to improve PLWH utilization of essential services that improve viral suppression	• Part A client reported as virally non-suppressed during the last 6 months from most recent service	• Number of agencies with a client population with >10% virally unsuppressed clients • Percentage of PLWH with an undetectable VL
By the end of 2021:	BPHC HASD	Expand services that address persistent challenges to viral suppression, such as mental health, substance abuse, and homelessness, including usage of community health workers; referrals to syringe exchange/recovery services; housing search & advocacy	• PLWH identified during intake & assessment as needing mental health, substance abuse, and/or housing services	• Number of Part A clients accessing substance abuse treatment services • Percentage of Part A clients with a reported mental health status requiring referral to counseling • Percentage of Part A clients reported as homeless or unstably housed

Objective 2B: By 2021, improve percentage of Part A clients who have health insurance from 92% to 97%.				
By the end of 2018:	• BPHC HASD • Part A funded MCM & PS programs	Ensure all funded Medical Case Management (MCM) and (Peer Support) PS staff are trained and consistently providing health insurance enrollment and recertification activities to any RW eligible PLWH	Uninsured PLWH or those requiring assistance with recertification	• Percentage of uninsured PLWH or those with unknown insurance status
By the end of 2018:	• BPHC HASD • MDPH • NH DHHS	Ensure uninsured or under-insured PLWH are aware, referred, and enrolled in health insurance premium and co-pay assistance services funded by MA and NH Part B	Uninsured PLWH that are ineligible for Medicaid or have inadequate insurance coverage	• Percentage of uninsured PLWH • Number of EMA PLWH currently accessing Part B ADAP/HDAP services
By the end of 2021:	BPHC HASD	Reduce number of clients that have lapses in coverage due to failure to recertify or payment of insurance premiums	PLWH currently enrolled in Medicaid, private insurance, or Part B sponsored health insurance	• Percentage of insured PLWH

Goal 3: Reducing HIV Related Disparities and Health Inequities				
Timeframe	**Responsible parties**	**Activity**	**Target Population or Stakeholder**	**Data Indicators**
Objective 3A: By 2021, reduce the gap in viral suppression rates among White (87%) versus non-Hispanic Black (84%) and Hispanic (84%) PLWH who currently utilize Part A services in the Boston EMA.				
By the end of 2017:	BPHC	Design training and capacity building activities that utilize current viral suppression data for Black and Hispanic PLWH to improve providers' abilities to deliver high quality, culturally competent HIV services to virally non-suppressed PLWH	• Part A sub-recipients funded to deliver MCM and PS services	• Number of trainings delivered • Number of case managers and peer advocates trained
2017 – 2018:	• Boston EMA Planning Council • BPHC	Support the NH anti-stigma campaign, which will focus on communities of color	• Black and/or Hispanic PLWH residents in NH EMA • Part A sub-recipients in NH	• Social media metrics related to stigma campaign (views, likes, shares)
By the end of 2019:	BPHC HASD	Invest in high acuity case management and peer support services that target Black and/or Hispanic PLWH through Part A MAI funding, including funding at least one new agency/program targeting an area with high HIV incidence among Black and/or Hispanic PLWH	• Black and Hispanic PLWH currently utilizing at least one Part A service reported as virally unsuppressed • Out of care Black and/or Hispanic PLWH	• Percentage of virally suppressed Black PLWH that received a Part A service • Number of face-to-face encounters delivered by MCM and PS providers
By the end of 2021:	BPHC HASD	Implement data-to-care quality improvement activities for agencies and programs with >10% virally unsuppressed Black and/or Hispanic PLWH	• Virally unsuppressed Black and/or Hispanic PLWH currently receiving a Part A service	• Percentage of virally suppressed Black and/or Hispanic PLWH that received a Part A service • Number of agencies with a client population with >10% virally unsuppressed Black PLWH

Objective 3B. By 2021, decrease the percentage of Part A clients who need housing services from 34% to 29%.				
2016- 2018:	• Boston EMA Planning Council • BPHC HASD	Conduct annual priority setting and resource allocation processes that identify new HRSA service categories that can be added to the EMA's list of funded categories in order to address housing needs among PLWH EMA residents.	Homeless or unstably housed PLWH in the Boston EMA	Percentage of Part A clients reported as homeless or unstably housed
By the end of 2018:	BPHC HASD	Invest in comprehensive housing services that successfully place PLWH into permanent housing, including funding additional housing search & advocacy programs	Homeless or unstably housed PLWH in the Boston EMA	Percentage of Part A clients reported as homeless or unstably housed
By the end of 2018:	BPHC HASD	Provide ongoing support for PLWH in maintaining their housing, including case management and emergency assistance.	Homeless or unstably housed PLWH in the Boston EMA	Percentage of Part A clients reported as homeless or unstably housed
By the end of 2021:	• Boston EMA Planning Council • BPHC HASD • HOPWA funded agencies in the EMA	Improve collaboration with HUD HOPWA grantees in the region to: • Better maximize federal resources that provide housing subsidies for PLWH • Identify PLWH that require RW assistance as a result of not meeting HUD HOPWA-defined 80% area median income (AMI) limit. • Identify new service components that can be delivered in residential settings that enhance viral suppression among PLWH	• Homeless or unstably housed PLWH in the Boston EMA • PLWH that are above 80% of HUD HOPWA-defined area median income limit and therefore ineligible for HOPWA services	• Percentage of Part A clients reported as homeless or unstably housed • Number of PLWH served through programs funded by HOPWA and other housing services • Number of HOPWA funded agencies and programs

Assessing Outcomes Along the HIV Care Continuum

BPHC and MPDH collaboratively fund a clinical chart review project conducted by JSI. Since neither MPDH nor BPHC directly uses RW funds for Outpatient Ambulatory Health Services, this project provides essential information on quality of medical care and most current clinical practices for HIV patients at selected sites. The majority of the sites are health centers and hospitals that also receive Parts C and D funding and JSI reviews on average about 1,200 records per cycle at over 30 sites. With increased emphasis on collection of health outcome data for the IHP, BPHC has already added two additional BPHC sites to the chart review project.

State regulations require that HIV viral load results be reported to MDPH. The state health department uses this information to provide feedback to selected healthcare sites on whether a PLWH seen at that site has had a laboratory result reported within six month. Those without a lab result are assumed to be lost to care. That information is given to the healthcare site using a line list that is periodically sent. Providers, including those funded by Part A, have found this service incredibly useful as a way to determine if a client is lost to care. Since these line lists are automatically generated for sites based on the patients they have previously reported to surveillance, primary care staff can then apply the lists towards their routine care planning within the site's primary care team to contact patients that have been seen and to schedule appointments. Although this service is not available to all providers in the state at this point, there is significant potential to enhance efforts to improve retention in care and viral load monitoring efforts if more providers are able to access the line list.

Internally, BPHC will monitor and evaluate progress within its Contract Management and Quality Management units. A majority of the data indicators, including viral suppression data, are tracked using the e2Boston system. Contract Management will review at agency level progress related to achievement and maintenance of viral suppression. The Quality Management unit will also assist in the development of agency level continuua of care, an exciting way (and highly requested by providers) to highlight successes and challenges faced by providers in meeting NHAS goals. Similarly, Quality Management will also create an HIV Continuum of Care model using Part A data for all clients served and continue to present the data annually to the Planning Council.

APPENDIX

1. List of Provider Agencies
2. Coordination of Services and Funding Table
3. Massachusetts Integrated Prevention and Care Plan – Goals and Objectives
4. New Hampshire Integrated Prevention and Care Plan
5. Letters of Concurrence

Appendix 1: List of Provider Agencies within the Boston EMA

Boston EMA– HIV Service Inventory
(Sorted alphabetically by Service Category funded by the Boston EMA Planning Council)

Types of Funders:

Ryan White	**Other Federal:**	**State Funding:**
Ryan White Part A	Medicaid (MassHealth & NH Medicaid)	Medicaid (MassHealth & NH Medicaid)
Ryan White Part B	Medicare	MA Bureau of Substance Abuse
Ryan White Part C	HOPWA	NH Bureau of Drug, Alcohol, & Substances
Ryan White Part D	SAMSHA	MA State AIDS Line
Ryan White Part F		
HRSA SPNS		

Core Medical Services Available	**Providers**	**Funding Source**
AIDS Drug Assistance Program	Community Research Initiative of New England	Ryan White Part A, B, & MA State AIDS Line
	NH Department of Health and Human Services (NH DHHS)	Ryan White Part A, B
Early Intervention Services	Cambridge Health Alliance	Ryan White Part C
	Beth Israel Deaconess Hospital-Plymouth	Ryan White Part C
	Boston Health Care for the Homeless	Ryan White Part C
	Brockton Neighborhood Health Center, Inc.	Ryan White Part C
	Dartmouth-Hitchcock (NH)	Ryan White Part C
	Dimock Community Health Center	Ryan White Part C
	East Boston Neighborhood Health Center	Ryan White Part C
	Family Health Center Of Worcester, Inc.	Ryan White Part C
	Fenway Community Health Center	Ryan White Part C
	Greater Lawrence Family Health Center, Inc.	Ryan White Part C
	Greater New Bedford Community Health Center	Ryan White Part C
	Harbor Health Services, Inc.	Ryan White Part C
	Lynn Community Health Center	Ryan White Part C
	University Of Massachusetts - Medical	Ryan White Part C
Medical Case Management, including treatment adherence services	AIDS Project Worcester	Ryan White Part B
	AIDS Response Seacoast	Ryan White Part A, B
	Beth Israel Deaconess Hospital-Plymouth	Ryan White Part A, B
	Boston Medical Center – Pediatric AIDS Program	Ryan White Part A
	Boston Health Care for the Homeless	Ryan White Part A
	Boston Medical Center	Ryan White Part B
	BPHC – Homeless Services/ Safe Harbor	Ryan White Part A
	Brockton Area Multi-Services	Ryan White Part B
	Brockton Neighborhood Health Center, Inc.	Ryan White Part B
	Cambridge Health Alliance	Ryan White Part A
	Catholic Charitable Bureau of the Archdiocese of Boston	Ryan White Part A
	Commonwealth Land Trust	Ryan White Part B

	Community Counseling of Bristol County	Ryan White Part B
	Community Health Link	Ryan White Part B
	Dimock Community Health Center	Ryan White Part A
	Dorchester House Multi Service Center	Ryan White Part A
	East Boston Neighborhood Health Center	Ryan White Part A
	Edward M. Kennedy Community Health Center	Ryan White Part A
	Father Bill's Place / Mainspring	Ryan White Part A
	Fenway Community Health Center	Ryan White Part A
	Greater Lawrence Family Health Center, Inc.	Ryan White Part A
	Greater New Bedford Community Health Center	Ryan White Part B
	Harbor Health Services, Inc.	Ryan White Part A
	Justice Resource Institute	Ryan White Part B
	Lowell Community Health Center	Ryan White Part B
	Lynn Community Health Center	Ryan White Part A
	Massachusetts Alliance of Portuguese Speakers	Ryan White Part A, B
	Merrimack Valley Assistance Program	Ryan White Part A, B
	MetroWest Medical Center	Ryan White Part B
	MGH Chelsea Healthcare Center	Ryan White Part A
	Montachusett Opportunity Council	Ryan White Part A
	Pine Street Inn/Paul Sullivan Housing	Ryan White Part B
	Seven Hills Behavioral Health	Ryan White Part B
	South Middlesex Opportunity Council	Ryan White Part B
	Southern NH HIV/AIDS Task Force	Ryan White Part A, B
	Stanley Street Treatment & Resources	Ryan White Part B
	Steppingstone, Inc.	Ryan White Part B
	University Of Massachusetts - Medical	Ryan White Part B
	Victory Programs, Inc	Ryan White Part B
	Vinfen Corporation	Ryan White Part B
	Whittier Street Health Center	Ryan White Part A
	Community Servings	Ryan White Part A& B
Medical Nutrition Therapy	AIDS Action Committee	Ryan White Part B, HOPWA, & MassHealth
Mental Health Services	AIDS Project Worcester	Ryan White Part B, HOPWA, & MassHealth
	Cambridge Health Alliance	MassHealth, Medicare, SAMHSA
	Casa Esperanza	MassHealth, Medicare, SAMHSA
	City of Nashua, NH	HOPWA, SAMHSA
	Community Healthlink	HOPWA, MassHealth, Medicare, SAMHSA
	Dimock Community Health Center	MassHealth, Medicare
	Dorchester House Multi Service Center	MassHealth, Medicare
	East Boston Neighborhood Health Center	MassHealth, Medicare
	Edward M. Kennedy Community Health Center	MassHealth, Medicare

	Fenway Community Health Center	MassHealth, Medicare
	Greater Lawrence Family Health Center, Inc.	MassHealth, Medicare
	Harbor Health Services, Inc.	MassHealth, Medicare
	Justice Resource Institute	HOPWA, MassHealth &SAMHSA
	Lynn Community Health Center	MassHealth, Medicare
	Manet Community Health Center	MassHealth, Medicare
	Span, Inc.	Ryan White Part B & SAMHSA
	Boston University Goldman School of Dental Medicine	Ryan White Part F & MassHealth
Oral Health	BPHC – HIV Dental Ombudsperson Program	Ryan White Part A, MA State AIDS Line
	Harvard School of Dental Medicine	Ryan White Part F & MassHealth
	Tufts University School of Dental Medicine	Ryan White Part F & MassHealth
	Beth Israel Deaconess Hospital - Boston	MassHealth, Medicare
Outpatient and ambulatory medical care	Boston Children's Hospital	MassHealth, Medicare
	Boston Health Care for the Homeless	Ryan White Part C, MassHealth, Medicare
	Boston Medical Center	MassHealth, Medicare
	Brigham & Women's Hospital	MassHealth, Medicare
	Brockton Neighborhood Health Center, Inc.	Ryan White Part C, MassHealth, Medicare
	Cambridge Health Alliance	Ryan White Part C, MassHealth, Medicare
	Codman Square Health Center	HRSA SPNS, MassHealth, Medicare
	Dartmouth-Hitchcock (NH)	Ryan White Part B, C, D, NH Medicaid, Medicare
	Dimock Community Health Center	Ryan White Part C, D, MassHealth, Medicare
	East Boston Neighborhood Health Center	Ryan White Part C, MassHealth, Medicare
	Edward M. Kennedy Community Health Center	Ryan White Part C, MassHealth, Medicare
	Family Health Center Of Worcester, Inc.	Ryan White Part C, MassHealth, Medicare
	Fenway Community Health Center	Ryan White Part C, D, MassHealth, Medicare
	Greater Lawrence Family Health Center, Inc.	Ryan White Part C, MassHealth, Medicare
	Greater New Bedford Community Health Center	Ryan White Part C, MassHealth, Medicare
	Harbor Health Services, Inc.	Ryan White Part C, MassHealth, Medicare
	Lowell Community Health Center	MassHealth, Medicare
	Lynn Community Health Center	Ryan White Part C, MassHealth, Medicare
	Manet Community Health Center	MassHealth, Medicare
	Mattapan Health Center	HRSA SPNS, MassHealth, Medicare
	MGH Chelsea Healthcare Center	MassHealth, Medicare
	Morton Hospital	MassHealth, Medicare
	University Of Massachusetts - Medical	MassHealth, Medicare
	Whittier Street Health Center	HRSA SPNS, MassHealth, Medicare
	Casa Esperanza, Inc.	MA BSAS & SAMHSA
Substance Abuse Outpatient Care	Catholic Charitable Bureau of the Archdiocese of Boston	MA BSAS
	Community Healthlink	MA BSAS

	Dartmouth-Hitchcock (NH)	NH BDAS & SAMHSA
	Dimock Community Health Center	MA BSAS & SAMHSA
	Dorchester House Multi Service Center	SAMHSA
	East Boston Neighborhood Health Center	MA BSAS & SAMHSA
	Edward M. Kennedy Community Health Center	MA BSAS & SAMHSA
	Harbor Health Services, Inc.	MA BSAS & SAMHSA
	Justice Resource Institute	MA BSAS
	Lynn Community Health Center	MA BSAS
	NH Department of Health and Human Services (NH DHHS)	SAMHSA
	Span, Inc.	SAMHSA

Appendix 2 - Coordination of Services and Funding Table

Funding Source		Part A	Part B	Part C	Part D	Part F	Medicaid Federal	CDC	HUD/ HOPWA	SAMHSA	MA Medicaid	MA AIDS	NH Medicaid	NH AIDS	MA Substance Abuse	Private Funding +
Total 2015 Funding: $342,770,607	Dollar Amount	$14,228,418	$14,034,927	$6,132,850	$2,169,299	$1,402,487	$131,235,663	$2,566,915	$6,310,490	$144,709	$129,816,159	$28,482,270	$1,419,505	$3,329,443	$1,183,403	$314,069
	%	4.15%	4.09%	1.79%	0.63%	0.41%	38.29%	0.75%	1.84%	0.04%	37.87%	8.31%	0.41%	0.97%	0.35%	0.09%
Total Anticipated 2016 Budget*: $342,770,607	Dollar Amount	$14,228,418	$14,034,927	$6,132,850	$2,169,299	$1,402,487	$131,235,663	$2,566,915	$6,310,490	$144,709	$129,816,159	$28,482,270	$1,419,505	$3,329,443	$1,183,403	$314,069
	%	4.15%	4.09%	1.79%	0.63%	0.41%	38.29%	0.75%	1.84%	0.04%	37.87%	8.31%	0.41%	0.97%	0.35%	0.09%
Core Medical-related Services																
AIDS Drug Assistance Program		X	X									X		X		
AIDS Pharmaceutical Assist.																
Early Intervention Services			X	X	X			X				X				
Health Insurance Premium/ Cost-Sharing Assistance			X											X		X
Home & Community-based Health Services							X				X		X			
Home Health Care			X				X				X		X	X		
Hospice Services							X				X					
Medical Case Management		X	X	X	X		X		X		X	X	X	X		X
Medical Nutrition Therapy		X		X												X
Mental Health Services			X	X	X		X		X		X		X	X		X
Oral Health Care		X	X	X	X	X	X				X	X	X	X		
Outpatient/Ambulatory Medical Care			X	X	X		X				X		X	X		
Substance Abuse Services – Outpatient			X	X			X		X	X	X		X	X	X	
Support Services																
Child Care Services																
Emergency Financial Assistance									X							X
Food Bank/Home-delivered Meals		X	X						X			X		X		X
Health Education/Risk Reduction				X	X				X							X
Housing Services		X	X						X			X		X		X
Legal Services			X									X				X
Linguistic Services				X												
Medical Transportation Services		X	X	X	X		X		X		X		X	X		
Non-medical Case Management		X		X	X				X	X					X	X
Outreach Services				X	X											
Psychosocial Support Services		X	X	X	X					X		X			X	
Referral for Health Care/ Supportive Services				X					X							X
Rehabilitation Services							X				X					
Respite Care																
Substance Abuse Services – Residential		X							X	X					X	
Treatment Adherence Counseling				X												
HIV Testing				X		X										

Appendix 3 - Massachusetts Integrated HIV Prevention and Care Plan Goals and Objectives

Goal 1: Reduce the Impact of HIV

Objectives

- By 2021, reduce newly diagnosed HIV infections among MSM by 30%
- By 2021, eliminate newly diagnosed HIV infections among PWID
- By 2021, eliminate perinatal HIV transmission
- By 2021, Achieve a reduction in the proportion of cases reported to Massachusetts HIV Surveillance Program with No Identified Risk (NIR), from 25% to 15% of all reported cases
- By 2021, establish a baseline understanding of new infections among transgender-identified individuals, and set health outcomes benchmarks to improve the quality and effectiveness of prevention and care services

Goal 2: Improve Health Outcomes For Persons Living With HIV

Objectives

- By 2021, 90% of newly diagnosed HIV+ individuals will be successfully linked to care within 45 days of the date of diagnosis
- By 2021, improve Massachusetts HIV Care Continuum outcomes to 90/90/90 (90% diagnosed; 90% retained in care; and 90% of PLWH virally suppressed)
- By 2021, eliminate progression to AIDS among PLWH.
- By 2021, reduce HIV related mortality among PLWH by 10%
- By 2021, 90% of individuals co-infected with HIV and HCV will be linked to HCV treatment
- By 2021, l00% of clients diagnosed with acute HIV infection will be linked to care within 72 hours
- By 2021, improve the rates of STD testing among sexually active PLWH

Goal 3: Reduce Persistent HIV-Related Health Disparities

Objectives

- By 2021, reduce the disparity in relative rates of new HIV infection diagnoses between black (non-Hispanic) and white (non-Hispanic) residents by 20%.
- By 2021, reduce the disparity in relative rates of new HIV infection diagnoses between Hispanic/Latino and white (non-Hispanic) residents by 25%.
- By 2021, improve rates of viral suppression for racial/ethnic minorities to be equivalent to rates in white (non-Hispanic) populations
- By 2021, reduce rates of new HIV diagnoses among young MSM (under age 30) by 50%

Appendix 4 – New Hampshire Integrated Prevention and Care Plan

New Hampshire Integrated HIV Prevention and Care Plan					
Goal 1: Reducing New HIV Infections					
	Activities (Strategies only)	**Time Phased Resources**	**Responsible Entity**	**Target Population**	**Metrics**
Objective 1A: By 2021, lower the new AIDS/Concurrent diagnoses by 5%					
Strategy a) Expand the availability of routine HIV testing of all patients between 15 and 65 who seek primary or urgent care, based on CDC recommendations.	- Promote increased awareness of CDC recommendations - Assess and address perceived barriers to routine HIV testing	Federal HIV Prevention program (add new FOA time period)	DPHS	- Adult population 15-65 y/o - Routine and emergency medical care sites	Number of HIV tests performed
Strategy b) By 2021, establish a syringe-exchange program in the state with an HIV/referral/testing service component.	- Identify potential entities willing to establish syringe exchange program - Identify resources to support HIV/referral/testing service component	Other funds, Public funds as allowed 2017-2021	HPG, in coordination with CBO/ other funders	- Syringe using adults	Number of HIV tests performed
Strategy c) Develop a comprehensive HIV service provider training program/series/plan, utilizing multiple learning modalities (web portal, public health detailing, conferences, meetings).	- Review existing training programs - Identify best modalities for delivering training - Identify resources for implementing training - Implement training	Adapt ANAC or other existing module MPH Intern 2016-2018	DPHS, AETC, HPG	- HIV Service Providers	Number of HIV tests performed
Strategy d) Expand 4th generation testing to help identify recent infections.	- Promote increased use of 4th generation testing - Identify resources to support use of 4th generation test if needed	Federal HIV Prevention funds (add new FOA time period)	DPHS	- HIV Testing/Counseling Programs	Number of HIV tests performed
Objective 1B: By 2021, increase access to PrEP for all people in NH who meet the CDC guidelines by identifying 5-10 new prescribing providers/organizations					
Strategy a) By 2018, improve access to PrEP in	- Review current information about providers who see at-risk populations - Identify which	HRSA CDC	DPHS AETC	HIV medical providers in Hillsborough County	Number of providers that

New Hampshire Integrated HIV Prevention and Care Plan					
Hillsborough County through identification of additional prescribing providers/organizations or a new PrEP clinic.	providers might benefit from additional education/training with respect to PrEP - Promote use of PrEP for eligible clients among providers receiving additional education/training	CBA 2016-2018	HPG		prescribe PrEP
Strategy b) Identify performance metrics for PrEP utilization by 2018.	- Review possible options for tracking prescribing and or utilization of PrEP - Identify which option provides the most efficient and effective data source for monitoring PrEP uptake	NASTAD 2016-2018	DPHS & HPG	Individuals at risk for HIV/AIDS	Metric TBD
Strategy c) Assess barriers to uptake of and adherence to PrEP	- Include questions regarding barrier to PrEP utilization on next needs assessment	NASTAD 2018-2021	DPHS	Individuals potentially eligible for PrEP	Number of people taking PrEP
Goal 2: Increasing Access to Care and Improving Health Outcomes for People Living with HIV					
	Activities (Strategies only)	**Time Phased Resources**	**Responsible Entity**	**Target Population**	**Metrics**
Objective 2A: By 2021, increase viral suppression from 87% to 92%.					
Strategy a) Link new cases to care within 90 days.	- Train providers to follow the International Association of Physicians in AIDS Care guidelines for improving entry into care for persons with HIV (brief strengths-based case management interventions, intensive outreach for individuals not engaged in care within six months of a new HIV diagnosis, and use of peer patient navigators)	ID Care Coordinators 2016-2021	DPHS Medical Advisory Board	Newly identified individuals with HIV diagnosis; HIV medical providers	Number linked to medical care
Strategy b) Ensure access to ART For NH CARE Program clients.	- Screen all CARE program clients for access to ART on a periodic basis (i.e. every 6 months) - Work with clients and case managers to select insurance plans that include comprehensive ART Coverage	NH Ryan White CARE Program 2016-2021	DPHS	NH CARE Program clients	ART among persons in HIV medical care
Strategy c) Identify an available measure of HIV medication adherence for RW Care program clients	- Review existing quality indicators for adherence	NH CARE Program 2017-2018	DPHS	HIV CARE Program clients	Measure identified
Objective 2B: By 2021, reduce the number of people on the unmet need/out of care list in NH by 20%.					

New Hampshire Integrated HIV Prevention and Care Plan					
Strategy a) Build upon Care Engagement Program to improve understanding of those out of care.	- Analyze data from Care Engagement Program to develop strategies to target those out of care	Care Engagement Program 2016-2017	DPHS	Out of care list	Percentage of persons with an HIV diagnosis retained in medical care
Strategy b) Assess strategies to include peer to peer options to identify out of care individuals.	- Utilize peer mentors to identify and engage out of care individuals	Dartmouth-Hitchcock 2016-2021	DHMC	Consumers in care	Percentage of persons with an HIV diagnosis retained in medical care
Strategy c) Assess HIV medical provider workforce and develop plan to increase the number of providers	- Survey providers for HIV service capacity - Survey existing HIV service provider current capacity to take additional clients, when going to retire - Develop plan to increase number of providers	AETC 2016-2018	HPG	Medical providers	Percentage of persons with an HIV diagnosis retained in medical care
Objective 2C: By 2021, increase utilization of dental, mental health and substance abuse services of NH CARE Program clients.					
Strategy a) Expand list of contracted dental providers for NH CARE Program clients in geographically underserved areas.	- Update at least annually and maintain list of contracted dental providers on the CARE Program website - Engage and contract with additional dental providers	NH CARE Program 2016-2021	DPHS DHMC	Dental providers in NH	Number of contract providers Number of total dental visits
Strategy b) Identify mechanism to assess need, referral and utilization of mental health and substance abuse services among CARE Program clients.	- Conduct consumer based assessment of mental health and substance abuse service's needs, barriers, and utilization - Develop recommendations based on the assessment - Utilize CAREWare to collect referral information	NH CARE Program 2017-2018	HIV CARE program	HIV CARE Program clients	Number of total mental health and substance abuse services visits
Goal 3: Reducing HIV-Related Disparities and Health Inequities					
	Activities (Strategies only)	**Time Phased Resources**	**Responsible Entity**	**Target Population**	**Metrics**
Objective 3A: By 2021, reduce disparities in prevalence rates of HIV between non-hispanic white and non-white individuals by 5%.					
Strategy a) Research & adopt an anti-stigma messaging campaign	- Research the demographic most affected and specific issues to tailor media outlets to have the broadest reach - Select campaign, social media campaign, print media materials or other	DPHS 2016-2018	HPG DPHS	- PLWHA - Providers - Public (depends on campaign)	Number of HIV tests

New Hampshire Integrated HIV Prevention and Care Plan					
Strategy b) Develop resource for community by identifying LGBTQ-friendly providers	- Create web resource on HPG website	Rhode Island web template 2017-2021	DPHS HPG	- HIV/AIDS service providers	Number of HIV tests Number of newly diagnosed
Strategy c) Assess use of quality management data to monitor/track disparities and increase ability of providers to collect racial/ethnicity and linguistic data accurately and consistently.	- Survey providers for capacity to monitor/track disparities - Survey providers for capacity on collecting racial/ethnic and linguistic data - Develop plan to increase number of providers who monitor/track disparities/data	NH Health and Equity Partnership 2017	DPHS	- HIV/AIDS service providers	Rate of diagnosis by race and ethnicity
Objective 3B: Reduce geographically based disparities of care by providing more support services to PLWHA living north of Concord, NH by 2021.					
Strategy a) By 2018, establish a pilot tele-medicine site in NH to link hard-to-reach HIV+ clients to care.	- Identify tele-medicine partners - Identify location of need for pilot - Identify tele-medicine model to be piloted	Dartmouth-Hitchcock 2018	HPG	- PLWHA outside of urban areas	Number of tele-medicine visits for HIV medical care
Strategy b) By 2021, assess and map service needs and gaps in NH.	- Use results of future needs assessment and mapping of services to identify areas of need	DPHS Surveillance Mapping Software 2021	DPHS	- PLWHA outside of urban areas - HIV/AIDS service providers	Number medical visits Number of visits to ASOs
Strategy c) By 2021, disseminate information on available resources by region.	- Use results of mapping to disseminate resources by region - Create web resource on HPG website - Promote resources through the ASOs	DPHS Surveillance Mapping Software 2021	HPG DPHS	- PLWHA outside of urban areas - HIV/AIDS service providers	Number medical visits Number of visits to ASOs



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Boston EMA HIV Health Services Planning Council

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Lawrence Vison II
Arthur Weeks
Timothy Young

September 12, 2016

Steven Young, Director
Division of Metropolitan HIV/AIDS Programs
HIV/AIDS Bureau, HRSA
5600 Fishers Lane
Rockville, Maryland 20857

Dear Mr. Young:

The Boston Eligible Metropolitan Area (EMA) Planning Council ***concurs*** with the following submission by the Boston Public Health Commission (BPHC) in response to the guidance set forth for health departments and HIV planning groups funded by the CDC's Division of HIV/AIDS Prevention (DHAP) and HRSA's HIV/AIDS Bureau (HAB) for the development of an Integrated HIV Prevention and Care Plan (IHP). The Council serves as the mandated community planning body overseeing the priority setting and resource allocation process for Ryan White Part A funding for people living with HIV (PLWH) in the EMA. In partnership with the Boston Public Health Commission (BPHC), the Council has worked with various stakeholders, including the Massachusetts Department of Public Health (MDPH) and the New Hampshire Department of Public Health, to develop coordinated IHP workplans that outline the needs of PLWH residents in our region.

A representative from BPHC serves as a mandated member serving as the Ryan White Part A recipient. During the last year, BPHC has worked collaboratively with Planning Council Support (PCS) staff to develop the IHP. Updates were given on a monthly basis during the monthly Council and Executive Committee meetings on progress in developing and the plan to submit the IHP by the September 30th deadline. Members of the Planning Council also serve as members of state planning bodies that worked on MA and NH IHP development and reported back to the Council periodically on the states' progress.

The Council also created an ad-hoc committee called the Comprehensive Plan Work Group (CPWG), which was responsible for drafting the Boston EMA's Part A IHP with support from PCS staff and BPHC. The group met every month between January and August 2016 to review the HRSA/CDC guidance and focus on essential components that relate to the Council's role and involvement of PLWH. In the September 2016 meeting, an overview of the Part A IHP goals and objectives were presented and the Council proceeded to vote in support of the proposed plan.

The Planning Council concurs that the Boston EMA Part A Integrated HIV Prevention and Care Plan submission fulfills the requirements put forth by the Funding Opportunity Announcement PS12-1201 and the Ryan White HIV/AIDS Program legislation and program guidance.

I hereby provide this letter of concurrence of the Planning Council with the Boston EMA's Part A Integrated HIV Prevention and Care Plan.

Sincerely,

Darren Sack
2016-2017 Boston EMA HIV Health Services Planning Council Chair

Ryan White HIV/AIDS Treatment Extension Act
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September 19, 2016

Amy Griffin,
Division of Metropolitan HIV/AIDS Programs
HIV/AIDS Bureau, HRSA
5600 Fishers Lane
Rockville, Maryland 20857

Dear Ms. Griffin:

The Boston EMA HIV Health Services Planning Council concurs with the following submission by the Massachusetts Department of Public Health in response to the guidance set forth for health departments and HIV planning groups funded by the CDC's Division of HIV/AIDS Prevention (DHAP) and HRSA's HIV/AIDS Bureau (HAB) for the development of an Integrated HIV Prevention and Care Plan (IHP). The Council serves as the mandated community planning body overseeing the priority setting and resource allocation process for Ryan White Part A funding for people living with HIV (PLWH) in the EMA. In partnership with the Boston Public Health Commission (BPHC), the Council has worked with various stakeholders, including Massachusetts Department of Public Health, to develop coordinated IHP workplans that outline the needs of PLWH in our region.

A representative from Massachusetts Department of Public Health serves as a mandated member representing state health departments and as a Ryan White Part B recipient. During the last year, updates were given on a monthly basis on progress in developing and the plan to submit the IHP by the September 30th deadline.

Between August and September 2016, Massachusetts Department of Public Health also shared drafts with BPHC and the Council's Comprehensive Plan Work Group, which was responsible for drafting the Boston EMA's Part A IHP. On September 8, 2016, the Council received a presentation outlining coordinated efforts between shared goals and objectives in the jurisdictions respective plans and proceeded to vote in support of the proposed plan. The Planning Council will continue to work collaboratively with MDPH to implement the plan and review progress on tasks.

The Planning Council concurs that the MA Integrated HIV Prevention and Care Plan submission fulfills the requirements put forth by the Funding Opportunity Announcement PS12-1201 and the Ryan White HIV/AIDS Program legislation and program guidance.

I hereby provide this letter of concurrence of the Planning Council with the Massachusetts Integrated HIV Prevention and Care Plan.

Sincerely,

Darren Sack
2016-2017 Boston EMA HIV Health Services Planning Council Chair

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September 12, 2016

Kenya L. Young, MPH
Public Health Analyst
Division of Metropolitan HIV/AIDS Programs
HIV/AIDS Bureau, HRSA
5600 Fishers Lane
Rockville, Maryland 20857

Dear Ms. Young:

The Boston EMA HIV Health Services Planning Council concurs with the following submission by the New Hampshire Department of Health and Human Services in response to the guidance set forth for health departments and HIV planning groups funded by the CDC's Division of HIV/AIDS Prevention (DHAP) and HRSA's HIV/AIDS Bureau (HAB) for the development of an Integrated HIV Prevention and Care Plan (IHP). The Council serves as the mandated community planning body overseeing the priority setting and resource allocation process for Ryan White Part A funding for people living with HIV (PLWH) in the EMA. In partnership with the Boston Public Health Commission (BPHC), the Council has worked with various stakeholders, including New Hampshire Department of Health and Human Services, to develop coordinated IHP workplans that outline the needs of PLWH in our region.

A representative from New Hampshire Department of Health and Human Services serves as a mandated member representing state health departments and as a Ryan White Part B recipient. During the last year, updates were given on a monthly basis on progress in developing and the plan to submit the IHP by the September 30th deadline.

Between August and September 2016, New Hampshire Department of Health and Human Services also shared drafts with BPHC and the Council's Comprehensive Plan Work Group, which was responsible for drafting the Boston EMA's Part A IHP. On September 8, 2016, the Council received a presentation outlining coordinated efforts between shared goals and objectives in the jurisdictions respective plans and proceeded to vote in support of the proposed plan. The Planning Council will continue to work collaboratively with the NH IHP working group to implement the plan and review progress on tasks.

The Planning Council concurs that the NH Integrated HIV Prevention and Care Plan submission fulfills the requirements put forth by the Funding Opportunity Announcement PS12-1201 and the Ryan White HIV/AIDS Program legislation and program guidance.

I hereby provide this letter of concurrence of the Planning Council with the New Hampshire Integrated HIV Prevention and Care Plan.

Sincerely,

Darren Sack
2016-2017 Boston EMA HIV Health Services Planning Council Chair



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September 12, 2016

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Centers for Disease Control and Prevention
NCHHSTP/DHAP/PPB
Funding Opportunity Announcement PS12-1201
2920 Brandywine Road, Room 3000
Atlanta, GA 30341-4146

Dear Ms. Hampton:

The Boston EMA HIV Health Services Planning Council concurs with the following submission by the New Hampshire Department of Health and Human Services in response to the guidance set forth for health departments and HIV planning groups funded by the CDC's Division of HIV/AIDS Prevention (DHAP) and HRSA's HIV/AIDS Bureau (HAB) for the development of an Integrated HIV Prevention and Care Plan (IHP). The Council serves as the mandated community planning body overseeing the priority setting and resource allocation process for Ryan White Part A funding for people living with HIV (PLWH) in the EMA. In partnership with the Boston Public Health Commission (BPHC), the Council has worked with various stakeholders, including New Hampshire Department of Health and Human Services, to develop coordinated IHP workplans that outline the needs of PLWH in our region.

A representative from New Hampshire Department of Health and Human Services serves as a mandated member representing state health departments and as a Ryan White Part B recipient. During the last year, updates were given on a monthly basis on progress in developing and the plan to submit the IHP by the September 30th deadline.

Between August and September 2016, New Hampshire Department of Health and Human Services also shared drafts with BPHC and the Council's Comprehensive Plan Work Group, which was responsible for drafting the Boston EMA's Part A IHP. On September 8, 2016, the Council received a presentation outlining coordinated efforts between shared goals and objectives in the jurisdictions respective plans and proceeded to vote in support of the proposed plan. The Planning Council will continue to work collaboratively with the NH IHP working group to implement the plan and review progress on tasks.

The Planning Council concurs that the NH Integrated HIV Prevention and Care Plan submission fulfills the requirements put forth by the Funding Opportunity Announcement PS12-1201 and the Ryan White HIV/AIDS Program legislation and program guidance.

I hereby provide this letter of concurrence of the Planning Council with the New Hampshire Integrated HIV Prevention and Care Plan.

Sincerely,

Darren Sack
2016-2017 Boston EMA HIV Health Services Planning Council Chair

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE; HIV MEDICINE ASSOCIATION of the INFECTIOUS DISEASES SOCIETY OF AMERICA; INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE; JENNIFER K. BRODY, MD; and CHRISTOPHER B. FOX, NP, *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION; THOMAS J. ENGELS, in his official capacity as the Administrator of the Health Resources and Services Administration; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., in his official capacity as Secretary of the U.S. Department of Health and Human Services, *Defendants*.	Case No.

DECLARATION OF MICHELLE COLLINS-OGLE, MD

I, Michelle Collins-Ogle, MD, hereby declare and state as follows:

1. I am over 18 years of age, of sound mind, and in all respects competent to testify.

2. I have personal knowledge of the facts set forth in this declaration and would testify competently to those facts if called to do so.

3. I am offering this declaration as a member of the American Academy of HIV Medicine, the International Association of Providers of AIDS Care, and the HIV Medicine Association, which are bringing claims on behalf of their members, like me, and on behalf of the transgender patients of their members, like mine.

4. I submit this declaration in support of Plaintiffs' Motion for Preliminary Relief under 5 U.S.C. § 705 and for a Preliminary Injunction, which seeks to prevent Defendants from giving effect to certain conditions relating to transgender people and gender-affirming medical care set forth in Ryan White HIV/AIDS Program ("Ryan White Program" or "RWHAP") Notices of Funding Opportunity issued or forecasted to be issued in 2026 and the 2026 Updated HRSA General Terms and Conditions, issued on March 11, 2026 (collectively, "the Challenged Conditions").

5. I am a longtime HIV provider who directs a Ryan White-funded HIV clinic serving medically underserved rural communities in North Carolina. The clinic relies on Ryan White to provide integrated HIV care. I have been providing services under Ryan White since the program began in 1990. Ryan White has evolved into a comprehensive "wraparound" model designed to address co-occurring medical and social needs that affect HIV outcomes and retention in care, particularly for medically underserved populations. Integrated gender-affirming medical care and affirming treatment environments are critical to maintaining patient trust, adherence to antiretroviral therapy, retention in care, and sustained viral suppression among transgender patients living with HIV. Further, in rural communities like the ones my clinic serves, patients often have no realistic alternative source of affirming HIV care or gender-affirming medical care because of provider shortages, transportation barriers, poverty, stigma, and geographic isolation. The Challenged Conditions would disrupt this integrated care model, cause patients to disengage from care, increase reliance on unsafe or informal treatment sources, worsen health outcomes, undermine public health efforts to control HIV transmission, and threaten the continued operation of Ryan White-supported HIV programs in rural communities.

I. Background

6. I am a physician specializing in infectious diseases and HIV care. I serve as the Medical Director of the Warren Vance Community Health Center, Inc. ("the Clinic") in rural North Carolina. I have held this position for approximately twenty-five years.

7. I also hold an administrative role in my clinic. I am the clinic's Ryan White Part C Principal Investigator. In this role, I oversee all administrative Ryan White grant responsibilities.

8. I split my time as Medical Director of the Warren Vance Community Health Center, Inc. with my role as the Director of the MAYS Specialty Care Clinic at The Children's Hospital at Montefiore in New York, where I provide care to infants, children and adolescents living with HIV/AIDS.

9. I have over thirty years of experience providing HIV care, beginning in the early years of the epidemic in the late 1980s, including treating infants and pediatric patients. Since 2008, I have also provided comprehensive gender-affirming medical care, including hormone therapy, to my transgender patients as part of my clinical practice.

10. The Warren Vance Community Health Center, Inc. was the first clinic in North Carolina to integrate gender-affirming healthcare services including hormone therapy into an HIV care program in 2008. Ryan White Part B funding was and is used to provide medically necessary gender-affirming treatment for transgender women with HIV. Transgender women, like all other patients receiving Ryan White Program services receive their primary care in our programs. This integration arose out of medical necessity and patient need.

11. The Clinic primarily serves communities that are medically underserved. We serve 241 individuals. 87% of my patients are Black, 13% are White and a significant portion are low-income with 2% being unhoused. Approximately 3% of my patients at the Clinic are transgender,

all of whom are Black women. At the Clinic, our patient population is largely composed of adults living with HIV, many of whom are over the age of twenty-four.

12. At present, the Clinic receives funds under Ryan White Parts B and C, as well Supplemental Part B.

II. The Ryan White Program

12. I have specialized in HIV/AIDS care and have treated patients who received funding under Ryan White since the program's inception. The Ryan White Program was established in 1990 to provide services to individuals and families living with HIV, particularly those who lacked access to adequate care.

13. When the program was first created and I was providing services under it, effective HIV medications were limited and patients required extensive supportive services. In the early years of the epidemic—before the advent of effective antiretroviral therapy—care was often focused on hospice, palliative care, and supporting patients and their families through serious illness and death. The Ryan White CARE Act became a critical safety net, particularly for under-resourced communities, ensuring equitable access to care and helping communities and families cope with the devastating impact of the HIV/AIDS epidemic.

14. Over time, the program evolved to meet the needs of the epidemic. As effective antiretroviral therapy emerged in the mid-1990s, the focus of the program shifted from end-of-life care to long-term disease management, with an emphasis on helping patients access and adhere to life-saving medications. The program expanded to include prescription drug assistance, most notably through ADAP, and increasingly prioritized retention in care and viral suppression.

15. In the decades since and as HIV treatment advanced, the Ryan White Program further evolved to include a deliberate expansion beyond traditional medical care for HIV to a

holistic, "wraparound" model that addresses the full range of needs affecting health outcomes of patients with HIV. As such, the program now funds not only HIV treatment and medications, but also treatment for co-occurring conditions as well as a broad array of supportive services, including case management, mental health care, substance use treatment, housing support, and transportation, recognizing that social and structural factors directly affect a patient's ability to access and remain in care, especially populations most disproportionately impacted by HIV.

16. Ryan White programs are the "Gold Standard" other healthcare programs use to provide chronic medical care. The Ryan White Program is the first model for the "Medical Home" which ensures patients receive comprehensive care related to their primary disease. Patients with HIV have other co-morbidities, some associated with the virus and others not, and experience side effects of the medications they take through their lifespan. Transgender people are no different. They too have complications from the medications we prescribe and co-morbidities. Providing transgender patients with HIV with gender-affirming hormone therapy when medically indicated ensures they remain in care and monitored closely as we do for all of our patients.

17. This integrated approach reflects the understanding that successful HIV treatment requires more than prescribing HIV-related medications. It depends on addressing the social determinants of health and maintaining sustained engagement in care, particularly for low-income and medically underserved populations.

18. The Ryan White Program is widely regarded in the medical community as a model for integrated healthcare delivery. Other areas of medicine, including oncology and community health center systems, have adopted aspects of its approach. In my view, the program has been nothing short of a success story. Having witnessed its evolution over the decades, I have seen firsthand how its effectiveness is rooted in core public health principles: prioritizing access,

continuity of care, and addressing the social determinants that shape health outcomes, which has enabled it to achieve remarkable success in improving the health and longevity of people living with HIV. HIV is no longer a death sentence but rather a manageable disease.

19. Today, the Ryan White Program serves as a payer of last resort, filling gaps for uninsured and underinsured patients and ensuring access to services that other payors do not cover.

III. The Clinic's Use of Ryan White Funds

20. My clinic receives funding under Parts B, B Supplemental, and C of the Ryan White Program, which we use to provide holistic HIV care.

21. Part B and its supplemental funding provides access to medications and other critical services, including diagnostic testing and specialty care.

22. Part C funding supports the provision of comprehensive outpatient medical care for people living with HIV, including clinical services and support staff such as Physicians, Nurse Practitioners, Physician Assistants, Nurses, case managers, and behavioral health professionals.

23. Together, Parts B and C allow us to provide holistic, integrated care to all our HIV patients, including those who are transgender. For example, Part C supports clinical visits and mental health services, while Part B enables access to medications and additional services not otherwise covered.

24. In reliance on Ryan White's longstanding directives and funding structure prioritizing this integrated healthcare model, we have intentionally developed and structured our model of care to meet the needs of transgender and gender-diverse people living with HIV, including gender-affirming healthcare.

25. We carefully track and allocate staff time and services through established systems, including CAREWare, to ensure compliance with Ryan White requirements.

IV. Importance of Affirming HIV Care and Gender-Affirming Treatment for Our Transgender Patients with HIV

26. Gender-affirming medical care is healthcare that is medically necessary for many our transgender patients and that is essential to ensuring adherence to effective HIV treatment as well as addressing the health needs and wellbeing of our transgender patients living with HIV.

27. In my experience, providing comprehensive gender-affirming medical care improves patient retention in care, treatment of co-morbidities, and adherence to HIV medications. Similarly, being able to acknowledge, affirm, and respect the identity of a transgender patient is crucial to patient retention in care, treatment of co-morbidities, and adherence to HIV medications. This builds trust between patients and providers and reduces mental health barriers, including depression, dysphoria, and suicidality.

28. My experience integrating comprehensive gender-affirming medical care into HIV treatment arose from clinical and medical necessity. I first began treating transgender women with HIV who presented with advanced disease and had delayed seeking care due to lack of access to affirming providers. Before the Ryan White Program covered gender-affirming medical care and medication, many of my patients faced significant barriers to obtaining such care through the formal healthcare system, including lack of insurance coverage, cost, lack of understanding how to provide medical care for transgender people, and discrimination.

29. In my professional experience, when patients are unable to access gender-affirming medical care through licensed providers, some turn to non-prescribed or informal sources of hormones, including online or underground markets, in order to meet their basic healthcare needs. These alternatives are often medically unsupervised and can carry significant health risks, but patients may nonetheless pursue them because the alternative is going without care altogether.

These underground markets had limited access to medical supplies, which lead to needle sharing, thus increasing the risk of HIV transmission.

30. In my professional experience, prohibiting access to gender-affirming medical care as well as prohibiting acknowledgement, affirmation, and respect of the identities of transgender patients are not neutral actions; they each actively drive patients away from the healthcare system or into unsafe pathways, further delaying engagement in HIV care and worsening clinical outcomes requiring hospitalization which increase financial burden on the healthcare system which is already strained.

31. By affirming and respecting my transgender patients and providing gender-affirming medical care within the HIV treatment setting, I built trust, reduced unsafe practices, and improved health outcomes of patients, including achieving sustained viral suppression. In my clinical experience, patients explicitly linked their willingness to engage in HIV care to whether they feel seen, respected, and affirmed in their gender identity. For example, patients told me that they avoided or delayed care in the past because providers dismissed or stigmatized their gender identity, but that they felt safe returning to our clinic once they could receive gender-affirming medical services in the same setting.

32. Our Clinic tracks engagement in care, including appointment adherence, retention in treatment, and viral suppression rates. Consistent with broader clinical experience, I observed that patients who begin receiving gender-affirming medical care alongside HIV treatment are more likely to attend appointments, adhere to their medications, and remain engaged in care over time. In our clinical practice, all our transgender patients remain consistently engaged in their care, sustain viral suppression, reduced unsafe practices which would put them at risk for other types of infections and co-morbidities like Hepatitis C.

33. Conversely, when gender-affirming medical care is unavailable or disrupted, patients are more likely to miss appointments, disengage from care, or seek services outside the healthcare system. Integrating these services is therefore not ancillary; it is a critical component of effective HIV treatment for many transgender patients.

34. In my opinion, as informed by my clinical experience, treating the "whole person," including providing gender-affirming medical care, is essential to effective HIV care as it is for all people receiving Ryan White services.

V. Impact of the Challenged Conditions on Our Transgender Patients

35. By prohibiting acknowledgement, affirmation, and respect of the identities of our transgender patients as well as prohibiting provision of gender-affirming medical care using Ryan White-supported services, the Challenged Conditions will have severe consequences for our Clinic and our patients.

36. As noted, it is likely that many transgender patients will disengage from HIV care if they cannot receive HIV care that is affirming and cannot access gender-affirming medical care as part of their care. Many of our transgender patients come regularly as needed to treat their HIV only because they receive comprehensive care for all their medical needs, including gender-affirming hormone therapy and treatment for other co-morbidities, at our Clinic. For many patients, even a short disruption can result in missed appointments, loss of trust, medication non-adherence, and lack of follow-up. Once that occurs, it can be difficult to reverse.

37. This disengagement will—likely result in reduced adherence to HIV medications, which leads to increased viremia which over time progresses to AIDS. It also leads to worsening mental health, including depression and suicidality.

38. All people with HIV are at increased risk for cardiovascular disease, diabetes, and kidney disease which result from not only living with a chronic viral infection but results from the medications they must take through out their lifespan. Transgender people are no different. For transgender people with HIV, managing their medical treatment may actually decrease their risks for some of these diseases. For example, providing appropriate medical treatment allows for better monitoring of heart disease, and for some transgender women less likelihood of early cardiovascular complications.

39. Disengagement with care is particularly dangerous in the context of HIV care because interruptions in antiretroviral therapy can lead to viral rebound, immune decline, and clinical progression to AIDS. Federal HIV treatment guidelines recognize that stopping or interrupting antiretroviral therapy may result in viral rebound, immune decompensation, and clinical progression to AIDS, and studies show that viral rebound often occurs within weeks after treatment interruption.

40. This issue is particularly acute for rural areas. Patients in our practice have extremely limited, and often nonexistent, alternatives for obtaining gender-affirming medical care if it is not available through my clinic. In rural areas, providers with experience delivering gender-affirming medical care are scarce. In states such as North Carolina, most providers offering gender-affirming medical care are concentrated in large metropolitan areas, leaving rural patients with HIV without meaningful local access.

41. For our patients, there are no metropolitan areas within a 60-mile radius of the Clinic's location. Many lack reliable transportation, cannot afford the cost of travel, or are unable to take time away from work or caregiving responsibilities. In our rural community, there is no public transportation coupled with a paucity of providers with the clinical skills to provide gender

affirming medical care for transgender people with HIV. Others face housing instability or live in circumstances that make long-distance travel logistically impossible. In addition, the stigma and discrimination that transgender patients frequently encounter in unfamiliar healthcare settings create further barriers to seeking care outside of a trusted provider-patient relationship.

42. As a result, if gender-affirming medical care is not available within our Clinic for transgender people with HIV who require Ryan White medical services, many of our patients will not be able to obtain care at all. In my clinical judgment, this lack of access would lead to delays in care, reliance on unsafe or informal alternatives, or complete disengagement from the healthcare system altogether.

43. Such a policy would set comprehensive HIV care back decades, undoing progress made in engaging and retaining vulnerable populations in care and in turn reducing the human, social, and financial impact of HIV on the larger community.

44. Patients who cannot access medically necessary gender-affirming hormone therapy may again turn to informal and unsafe sources, including shared needle networks, increasing the risk of HIV and other infections, namely endocarditis.

45. Gender-affirming medical care is grounded in established medical science. Removing access to this care destabilizes the entire treatment framework for transgender patients with HIV who rely on Ryan White funding.

VI. The Challenged Conditions' Impact on Our Ability to Provide Comprehensive Care for People with HIV

46. Prohibitions on acknowledgement, affirmation, and respect for the identities of our transgender patients and the provision of gender-affirming medical care using Ryan White funds would place me and colleagues at the Clinic in an untenable position as physicians and healthcare providers.

47. We would be forced to deny medically necessary care to our patients and go against our clinical judgment in ways that conflict with accepted standards of care, including the ethical obligations of the medical profession and the clinical guidance set forth by the American Academy of HIV Medicine.

48. This would create a profound ethical conflict, as we would be unable to fulfill our duty to provide appropriate medical treatment.

49. Our relationships with patients are built on trust developed over many years. Being forced to deny care or to refuse to acknowledge and respect our patients' identities would undermine that trust and permanently damage those relationships. It would also have concrete consequences for patient engagement and retention into medical care. Many of our transgender patients seek care at the Clinic specifically because they trust that their identities and medical needs, including gender-affirming hormone therapy, will be respected and treated as legitimate. If we are no longer able to provide such care, some patients will reasonably perceive that we are unwilling to meet their full medical needs, which will erode that trust.

50. As a result, I expect that some patients would reduce or altogether stop coming to the Clinic, including for HIV treatment. Others may delay care, miss appointments, or become less adherent to HIV treatment. In my experience, once that trust is damaged, particularly for patients who have previously experienced stigma or discrimination in healthcare settings, it is difficult to rebuild, and patients may disengage from care entirely rather than seek services in settings they do not perceive as affirming or safe.

51. As a provider, I have a professional and ethical obligation to treat all aspects of my patients' health. Being prohibited from doing so would be deeply distressing and inconsistent with my oath as a physician.

VII. Financial and Programmatic Impact of the Challenged Conditions on the Clinic

52. The Clinic relies heavily on Ryan White funding to sustain its HIV care program and the broader services that support our patients. A substantial portion of our patients are uninsured or underinsured, and Ryan White funding allows us to provide care that would otherwise not be reimbursed, including medications, clinical services, and critical support services such as case management, outreach, and care coordination. Without this funding, we would not be able to maintain the current scope of services we provide.

53. Our clinic and our transgender patients also rely on Ryan White to continue to cover gender-affirming medical care as it has done for years.

54. Combined, Ryan White Parts B and C provide over 70% of our Clinic's HIV directed funding. The combined funding streams allows us to provide medical care for all people with HIV including those with co-morbidities that are a result of taking medications for decades like cardiovascular disease, renal dysfunction as well as infections like Hepatitis C. Medications used to treat these chronic diseases are provided with funding through Ryan White Part B. Transgender people with HIV suffer from these same chronic diseases making it germane to the integration of their gender-affirming medical care.

55. If Ryan White funding were reduced or lost, the impact on our Clinic would be immediate and severe and impact patients who rely on us to treat other co-morbidities as well. We would be forced to scale back services, reduce staffing, and limit the number of patients we are able to serve. In a rural setting like mine, there are no alternative funding sources or providers that could absorb this loss. As a result, all patients would lose access to care, and the Clinic's ability to continue operating its HIV program would be significantly threatened.

56. The loss of transgender patients from care would reduce patient volume and negatively impact funding tied to Ryan White program participation. Ryan White funding is distributed through federal grants to states, local jurisdictions, and clinics based in part on the number of people living with HIV who are served and retained in care, as well as demonstrated service needs. As a result, reductions in patient engagement and retention can directly affect the level of funding a clinic or jurisdiction receives or is able to sustain over time.

57. This would result in reduced funding, staff layoffs, and cuts to essential services. Ryan White funds support not only medical care, but also the staffing, infrastructure, and support services necessary to maintain patient engagement and achieve viral suppression. If patient volume declines, our Clinic would lose financial capacity to maintain these services, leading to reductions in clinical staff, case management, and other critical programs that are necessary to keep patients in care.

58. These impacts would be particularly severe in rural communities like mine, where Ryan White programs often serve as the primary, and sometimes only, source of HIV care. For the Clinic, based in North Carolina, there are limited alternative funding streams to replace lost Ryan White resources, and clinics like ours operate with thin margins, making them especially vulnerable to reductions in patient volume and associated funding.

59. In North Carolina, a significant portion of people living with HIV reside in rural areas – including all of our patients – making the Ryan White Program a critical lifeline.

VIII. The Public Health Impact of the Challenged Conditions

60. Limiting access to gender-affirming medical care and prohibiting affirming HIV care would have particularly severe public health consequences in rural areas like the communities

we serve. In these settings, HIV care infrastructure is limited, and a small number of providers and clinics are responsible for treating large geographic regions.

61. Because of this limited infrastructure, maintaining consistent patient engagement is essential. When patients disengage from care in rural areas, there are often no alternative providers or systems to bring them back into treatment. As a result, even small disruptions in care can have outsized and lasting effects on population health.

62. Based on my experience leading the American Academy of HIV Medicine's Southeast Region committee and working extensively with rural clinics, these harms would be especially acute in rural communities, where HIV providers are limited and often serve as the sole source of comprehensive care.

63. Integrated care models supported by the Ryan White Program are especially critical in rural settings, where patients face significant barriers including transportation challenges, provider shortages, and stigma. These models are designed to keep patients connected to care over time. Disrupting one component of that model, such as access to gender-affirming hormone therapy, can destabilize the entire system of care for this vulnerable population.

64. At the population level, reduced engagement in care leads to lower rates of viral suppression, which in turn increases the likelihood of HIV transmission within the community. In rural areas, where healthcare resources are already constrained, increases in untreated or poorly managed HIV place additional strain on limited medical infrastructure and public health systems.

65. Over time, these effects would undermine efforts to control the HIV epidemic in rural regions and reverse progress made through decades of targeted public health interventions. In my clinical judgment, the loss of integrated, accessible care in rural communities would have

immediate and compounding consequences for both individual patients and the broader public health system.

IX. Conclusion

66. Based on my decades of clinical experience in providing comprehensive HIV care, as well as my training and familiarity with the research and medical literature pertaining to HIV care, being able to care for my transgender patients with HIV in an affirming manner and to provide them with gender-affirming medical care when so indicated is essential to my ability to effectively treat patients living with HIV.

67. Prohibiting such care would harm my patients, undermine public health, and prevent me from fulfilling my obligations as a physician.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: June 9, 2026

Michelle Collins-Ogle

Michelle Collins-Ogle, MD

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE; HIV MEDICINE ASSOCIATION, a division of the INFECTIOUS DISEASES SOCIETY OF AMERICA; INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE; JENNIFER K. BRODY, MD; and CHRISTOPHER B. FOX, NP, *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION; THOMAS J. ENGELS, in his official capacity as the Administrator of the Health Resources and Services Administration; U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES; and ROBERT F. KENNEDY, JR., in his official capacity as Secretary of the U.S. Department of Health and Human Services, *Defendants*.	Case No.

DECLARATION OF RACHEL ROE, MD

I, Rachel Roe, MD, hereby declare and state as follows:

1. I am over 18 years of age, of sound mind, and in all respects competent to testify.

2. I have personal knowledge of the facts set forth in this declaration and would testify competently to those facts if called to do so.

3. I am offering this declaration as a member of the HIV Medicine Association, which are bringing claims on behalf of their members like me and on behalf of the transgender patients of their members like mine.

4. Rachel Roe is a pseudonym. I am submitting this declaration under a pseudonym to protect my privacy and to protect my family and me from harassment, violence, and retaliation.

5. I submit this declaration in support of Plaintiffs' Motion for Preliminary Relief under 5 U.S.C. § 705 and for a Preliminary Injunction, which seeks to prevent Defendants from giving effect to certain conditions relating to transgender people and gender-affirming medical care set forth in Ryan White HIV/AIDS Program ("Ryan White Program") Notices of Funding Opportunity issued or forecasted to be issued in 2026 and the 2026 Updated HRSA General Terms and Conditions, issued on March 11, 2026 (collectively, "the Challenged Conditions").

6. I also submit this declaration in support of Plaintiffs' Motion for Leave to Submit Pseudonymous Declarations and for a Protective Order.

7. I am HIV physician practicing in Tennessee and my Ryan White funded clinic serves more than one thousand patients. The clinic relies on Ryan White funding to provide integrated HIV care, including clinical treatment, mental health services, case management, substance use services, and gender-affirming medical care. Integrated and affirming care is essential to maintaining trust, retention in care, treatment adherence, and viral suppression among transgender patients living with HIV. In Tennessee, a non-Medicaid expansion state, Ryan White often serves as the only realistic source of healthcare for low-income people living with HIV, making integrated care particularly critical. The challenged conditions would prevent me from offering affirming HIV care and gender-affirming medical care, causing our patients to disengage from treatment, lose viral suppression, experience worsening physical and mental health outcomes, and increase HIV transmission risk to the community. The challenged conditions would also create significant operational and financial harms for my clinic, undermine longstanding provider-patient

relationships, and threaten the viability of HIV care programs serving medically vulnerable communities.

I. Background and Professional Experience

8. I am a physician and clinical provider licensed to practice medicine in Tennessee. I have more than fifteen years of experience providing care for people living with HIV and providing gender-affirming medical care.

9. My clinic serves more than a thousand patients. Our patient population includes many low-income people, people of color, gay and bisexual men, cisgender women, transgender people, immigrants, and migrants. More than half of our patients rely on the Ryan White HIV/AIDS Program for some part of their care.

10. I am a member of the HIV Medicine Association.

11. My Ryan White clinic currently provides gender-affirming medical care to more than 50 patients.

II. Need for Pseudonymity

12. I am submitting this declaration under a pseudonym because I fear that disclosure of my identity would subject me and my patients to a substantial risk of harm, harassment, and retaliation.

13. I practice in Tennessee, where there is significant hostility toward transgender people as well as providers who offer affirming care to transgender individuals. In my experience, transgender people, including some of my patients, are subject to inordinate and disproportionate amounts of harassment and discrimination.[1] I am thus aware of the rise in anti-transgender violence

[1] James, S.E., Herman, J.L., Durso, L.E., & Heng-Lehtinen, R. (2024). Early Insights: A Report of the 2022 U.S. Transgender Survey. National Center for Transgender Equality, Washington, DC.

and harassment in the South.[2]

14. As a result, there has been a significant rise in harassment against those who care for and support transgender people, including in Tennessee. Based on media reports, I am aware of targeted online harassment, doxxing, and even bomb threats targeting gender-affirming care providers. Indeed, I am aware of media reports documenting how medical groups have urged the U.S. Department of Justice "to investigate the organizations, individuals, and entities coordinating, provoking, and carrying out bomb threats and threats of personal violence" against hospitals and physicians who provide gender-affirming care to transgender people and have been targeted as a result.[3]

15. Accordingly, I am concerned that public identification would endanger my safety as well as the safety of my family, my colleagues, and my patients.

16. Furthermore, I am concerned that public identification could expose me to retaliation that would disrupt my ability to provide care, including potential scrutiny from federal and state officials, loss of institutional support, or interference with my clinical practice. Based on media reports, I am aware that the current federal administration has targeted those who support transgender care or oppose their priorities. For example, media reports document efforts to

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[2] *See*, *e.g.*, Christopher Wiggins, *Transgender people are being killed at an alarming rate, especially in the South*, The Advocate (Feb. 13, 2024), https://tinyurl.com/5n7dj5fv [https://perma.cc/ED6P-MJ3X]; Sydney Bauer, *In the Southeast, heightened danger and few protections for trans people*, NBC News (June 11, 2021), https://tinyurl.com/3ue2cfkm [https://perma.cc/A96B-3QYU].

[3] *See* Orion Rummler, *Medical groups ask Justice Department to investigate threats against hospitals over gender-affirming care*, The 19th (Oct. 3, 2022), https://tinyurl.com/4v5cn76y; *see also* Goldberg, A.E., Boskey, E.R., & Redfield, E. (2026). The experiences of transgender providers of gender-affirming care: Scrutiny, stress, and solidarity in sociopolitically turbulent times. *Psychology of Sexual Orientation and Gender Diversity.* Advance online publication. https://tinyurl.com/3kdxjh4p [https://doi.org/10.1037/sgd0000927]; Hughes, L.D., Gamarel, K.E., Restar, A.J., Sequeira, G.M., Dowshen, N., Regan, K., & Kidd, K.M. (2023). Adolescent providers' experiences of harassment related to delivering gender-affirming care. *Journal of Adolescent Health*, *73*(4), 672-678.

pressure medical organizations to change their positions on gender-affirming care and retaliation against those who have opposed the administration's priorities.[4]

17. It would also risk drawing unwanted attention to my patients, which, as noted, are already vulnerable and might potentially deter them from seeking care or further expose them to discrimination, stigmatization, and harm.

18. I am willing to disclose my identity to the Court as directed under a protective order.

III. The Role of the Ryan White Program in Patient Care

19. The Ryan White Program is lifesaving for our patients. In Tennessee, which has not expanded Medicaid, many low-income adults living with HIV have no realistic alternative source of comprehensive care. For those patients, the Ryan White Program is not one option among many; it is often the last stop before no care at all.

20. My clinic receives Ryan White funding through Parts A, B, C, D, and F. That funding supports clinical care and the staffing infrastructure needed to provide comprehensive HIV services. In practice, Ryan White helps pay for the providers, case managers, social workers, mental-health providers, substance-use specialists, and other staff who make HIV care possible for patients who are uninsured, underinsured, poor, or medically vulnerable.

21. Ryan White funding allows us to provide holistic integrated care. Our patients do not come to us only for antiretroviral prescriptions; they come to us for primary care, HIV specialty care, sexual health care, counseling, mental-health support, medication monitoring, and assistance addressing social determinants of health such as transportation barriers, food insecurity, and

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[4] *See*, *e.g.*, Peter Charalambous, et al., *Here's a list of the individuals, including James Comey, targeted by the Trump administration*, ABC News (Apr. 28, 2026), https://tinyurl.com/ynhp24th [https://perma.cc/K5TU-R8ZA]; Samantha Riedel, *Dr. Oz Tried to Pressure Medical Societies to Oppose Trans Youth Care*, Them (Mar. 16, 2026), https://tinyurl.com/338tt5d8.

housing instability. For our transgender adult patients, this also includes access to treatment for their gender dysphoria (also known as "gender-affirming medical care").

IV. Integration of Gender-Affirming Medical Care and HIV Treatment

22. Gender-affirming medical care is a critical part of that integrated model for transgender patients living with HIV in my practice. While the Ryan White formulary in my state does not include medications specifically for gender-affirming treatment, our clinic nonetheless provides essential gender-affirming medical care as part of comprehensive HIV services. In my practice, this includes counseling patients regarding gender identity and transition-related goals, conducting clinical assessments, providing referrals to appropriate specialists, coordinating care with outside providers, supporting medication management where available through other coverage, and ensuring that care is delivered in an affirming and culturally competent environment.

23. Ryan White supports the clinical infrastructure, including provider time and care coordination, through which this care is delivered. Ryan White pays both for the care our patients receive and pays a significant percentage of the salary for my staff.

24. For my transgender patients living with HIV, gender-affirming medical care is not separate from HIV care. It is a core part of how I am able to provide effective medical treatment. In my experience, patients often come to my clinic precisely because they know they can receive both affirming HIV care and gender-affirming medical care in a single, trusted setting. Without that integration, many would not seek care at all.

25. Providing gender-affirming medical care, as well as being able to acknowledge and affirm my transgender patients' identities, is essential to building trust with transgender patients, many of whom have experienced stigma, discrimination, or mistreatment in healthcare settings. When I am able to affirm a patient's gender identity and provide care that recognizes them as a

whole person, it creates the foundation for an ongoing therapeutic relationship. That trust is what allows me to engage patients in conversations about HIV treatment, adherence, and long-term health.

26. That trust directly affects whether my patients remain in care. When patients feel safe and respected, they are far more likely to attend appointments, follow up regularly, and remain engaged in treatment over time. Conversely, when care is not affirming and gender-affirming medical care is withheld or denied, transgender patients are likely to disengage, miss appointments, or stop seeking care altogether.

27. Many of my transgender patients face profound and overlapping barriers to care, including poverty, lack of reliable transportation, unstable housing, inflexible or low-wage employment, caregiving responsibilities, and prior experiences of stigma or discrimination in healthcare settings. For example, I regularly treat patients who have issues affording even a $2.00 bus fare to attend an appointment, who must choose between missing work and seeking care, or who rely on inconsistent public transit systems that make traveling across a metropolitan area difficult or impossible.

28. Because of these constraints, it is not feasible to require my patients to obtain different aspects of their care from multiple providers across different locations and at different times. Each additional appointment creates another logistical hurdle, another day off work, another transportation cost, another opportunity for something to go wrong. For many of my patients, even one missed bus, one unexpected expense, or one scheduling conflict can mean that an appointment is missed and not rescheduled.

29. In my experience, requiring my low-income patients to navigate multiple, disconnected systems of care effectively denies them access to care altogether. Many of my

patients do not have the time, financial resources, or stability to coordinate visits across different providers for HIV care, primary care, mental health services, and gender-affirming medical care. When HIV care is not centralized and coordinated by one clinic, patients are often forced to prioritize one need over another or to forgo care entirely.

30. Integrated care in a single, trusted setting is essential. By providing multiple services in one place, during the same visit or within the same care team, we reduce the number of barriers a patient must overcome to receive care. Patients are able to address multiple health needs in one trip, with providers who understand their medical history and social circumstances. This model is particularly critical for low-income patients, for whom even small logistical burdens can become insurmountable.

31. For transgender patients in particular, access to affirming, integrated care is often the reason they remain engaged in treatment. When patients are able to receive HIV care and gender-affirming care from providers they trust, in a single setting, they are far more likely to stay in care, attend appointments, and adhere to treatment. When that integration is disrupted, patients may disengage entirely, with serious consequences for their health and for public health.

V. The Challenged Conditions' Harms to My Patients

32. If the restrictions set forth in the Challenged Conditions take effect, in my clinical experience, many transgender patients will disengage from HIV care. This disengagement will lead to missed appointments, interruptions in HIV treatment, loss of viral suppression, and worsening health outcomes.

33. My patients who fall out of care will face increased risk of opportunistic infections, hospitalization, and long-term health complications. They may also develop drug resistance if treatment is interrupted.

34. Loss of viral suppression has serious public health consequences. When patients are not virally suppressed, the risk of HIV transmission increases, including transmission of drug resistant virus strains to the community.

35. The restrictions would also undermine my patients' mental health and the trust that is essential to effective medical care. Many of my transgender patients have spent years building trust with me and with our clinic, often after prior experiences of stigma, discrimination, or mistreatment in healthcare settings. That trust is not easily earned. In some cases, it has taken years before a patient felt safe enough to fully engage in care, accept examinations, or consistently follow treatment recommendations.

36. If I am forced to discriminate against my patients or to withdraw gender-affirming medical care they need, patients are likely to experience that change as a profound betrayal. From their perspective, it communicates that their identity is not respected and that their care is conditional. That perception can be deeply destabilizing, particularly for patients who already face high rates of depression, anxiety, trauma, and social marginalization.

37. The resulting harms are both immediate and long-term. Patients who disengage from care may experience worsening mental health, including increased depression, anxiety, and suicidality. At the same time, they may interrupt or stop HIV treatment, leading to loss of viral suppression and deterioration in their physical health. These harms reinforce each other, making it more difficult for patients to re-engage in care in the future.

VI. Unique Harms in Non-Medicaid Expansion States

38. Tennessee has not expanded Medicaid, which means that there is no coverage pathway for most low-income adults. For those who do qualify, eligibility is extremely limited. For example, adults with dependent children generally must have incomes at or below

approximately 100–105% of the federal poverty level, about $15,650 annually (or roughly $1,300 per month). For adults without dependent children, there is effectively no Medicaid eligibility category at all unless they meet strict disability criteria. Even for those qualifying under disability-based programs, income limits can be as low as approximately $994 per month for an individual.

39. As a result, many of my patients fall into a "coverage gap"—they earn too much to qualify under Tennessee's extremely restrictive Medicaid categories, but far too little to afford private insurance or out of pocket care. For these patients, the Ryan White Program is their only reliable source of HIV care and, indeed, any healthcare at all.

40. In this context, restricting gender-affirming care within the Ryan White Program effectively eliminates access to that care altogether. It forces my patients to choose between receiving HIV care without affirmation or disengaging from care entirely. In my experience I believe many of my patients will choose the latter.

VII. The Challenged Conditions' Harms to Providers and Public Health

41. The restrictions set forth in the Challenged Conditions would harm me as a physician by preventing me from providing medically necessary care consistent with my clinical judgment and ethical obligations. I would be placed in the untenable position of knowing what care my patients need that is integral to their overall health while being prohibited from providing it. This is directly contrary to the standards of care I am trained to follow and to my ethical duty to do no harm.

42. The restrictions would also create significant operational disruptions within my clinic. Our model of care is built around integration: providing HIV care, primary care, behavioral health, and gender-affirming medical care in a coordinated, patient-centered way. If the restrictions take effect, we may be forced to restructure how care is delivered. This could include revising

clinical protocols, retraining staff, determining which services can be provided under which funding streams, and attempting to separate services that are currently delivered together in a single visit. That process would be complex, time-consuming, and disruptive to both providers and patients.

43. My clinic relies on Ryan White funding for a substantial portion of its operating budget, including provider salaries, clinical services, and the infrastructure necessary to deliver comprehensive HIV care. In Tennessee, there is no meaningful alternative funding stream that could replace Ryan White.

44. If my clinic were found to be out of compliance with Ryan White restrictions, we could face loss of funding. The loss of that funding would be devastating. It would require reductions in staffing, elimination of services, and potentially limiting the number of patients we are able to serve.

45. Even if funding is not immediately terminated, a restriction on gender-affirming care using Ryan White funds or being able to provide affirming HIV care by prohibiting us from acknowledging, affirming, or respecting our transgender patients would itself have financial consequences. If transgender patients disengage from care because they can no longer receive integrated services, the clinic would lose the associated Ryan White-supported encounters and programmatic funding tied to patient care. At the same time, we would face increased costs associated with attempting to retain patients, redesign care systems, and manage the fallout from disrupted care.

46. If my patients disengage from care, the clinic will face increased uncompensated care and greater strain on limited resources. Patients who fall out of routine care often return only when they are acutely ill, requiring more intensive, complex, and expensive interventions. These

episodes of care are significantly more resource-intensive than routine outpatient management and are often not fully reimbursed.

47. At a broader level, the restriction would undermine efforts to control the HIV epidemic. By disrupting engagement in care and reducing viral suppression rates, the policy would increase the likelihood of HIV transmission in the community. This reverses decades of progress made through sustained investment in evidence-based, integrated HIV care models like Ryan White.

48. The harms described above are immediate and irreparable. Loss of patient trust cannot easily be restored, and the disruption of longstanding provider-patient relationships has lasting consequences. Interruptions in HIV treatment can lead to viral rebound, drug resistance, and permanent deterioration in a patient's health.

49. Patients who disengage from care may not return. In my experience, once patients fall out of care it can take years for them to re-engage, if they return at all. During that time, their health will significantly decline, and the risk of transmission to others increases. These are harms that cannot be undone through later intervention.

VIII. Conclusion

50. If the restrictions set forth in the Challenged Conditions are enjoined, I will be able to continue providing integrated, medically appropriate affirming care to my patients. If they are not enjoined, my patients in Tennessee and those in other non-Medicaid expansion states will suffer severe and irreparable harm.

I declare under penalty of perjury that the foregoing is true and correct.

Dated: June 8, 2026

Rachel Roe

Rachel Roe, MD

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

AMERICAN ACADEMY OF HIV MEDICINE, et al., *Plaintiffs*, v. HEALTH RESOURCES AND SERVICES ADMINISTRATION, et al., *Defendants*.	Case No. 1:26-cv-12638-WGY

DECLARATION OF JOSE ABRIGO

I, Jose Abrigo, hereby state and declare as follows:

1. I am a Senior Attorney at Lambda Legal Defense and Education Fund and counsel for Plaintiffs in the above-referenced litigation. I am admitted to practice in the State of New York and have applied for admission *pro hac vice* in this matter, which remains pending.

2. I have personal knowledge of the matters stated herein and am competent to testify thereto.

3. I submit this Declaration in support of Plaintiffs' Motion for a Preliminary Injunction.

4. Attached hereto as **Exhibit A** is a true and correct copy of the Centers for Disease Control and Prevention's ("CDC") guidance titled *Sexually Transmitted Infections Treatment Guidelines: Transgender and Gender Diverse Persons* (2021), available at https://tinyurl.com/jcjskthp [https://perma.cc/PLX2-H25M].

5. Attached hereto as **Exhibit B** is a true and correct copy of the "FY 2026 HRSA General Terms and Conditions," issued by the Health Resources and Services Administration

("HRSA") on March 11, 2026 (hereafter "**Updated FY2026 General Terms**"), and available at https://www.hrsa.gov/sites/default/files/hrsa/grants/manage/fy2026-hrsa-general-terms-and-conditions-2026-03-11-update.pdf [https://perma.cc/GK9K-2FZ4].

6. Attached hereto as **Exhibit C** is a true and correct copy of HRSA's priorities webpage titled "Advancing HRSA's Mission Through Focused, Accountable Action," available at https://tinyurl.com/2j65ckdv [https://perma.cc/5TS2-8LE2] ("**HRSA Priorities**").

7. Attached hereto as **Exhibit D** is a true and correct copy of the *Notice of Funding Opportunity, AIDS Drug Assistance Program (ADAP) Emergency Relief Funds (ERF)*, Opportunity No. HRSA-26-012, issued by HRSA on November 3, 2025 (hereafter "**ADAP NOFO"**).

8. Attached hereto as **Exhibit E** is a true and correct copy of Executive Order No. 14168, *Defending Women From Gender Ideology Extremism and Restoring Biological Truth to the Federal Government*, 90 Fed. Reg. 8615 (Jan. 20, 2025) (hereafter "**Gender Order**").

9. Attached hereto as **Exhibit F** is a true and correct copy of the GLAAD webpage titled "Medical Association Statements Supporting Trans Youth Health Care and Against Discriminatory Bills," available at https://tinyurl.com/3n2tp54t [https://perma.cc/WV6P-F9PC].

10. Attached hereto as **Exhibit G** is a true and correct copy of the Advocates for Trans Equality webpage titled "Medical Organization Statements," available at https://tinyurl.com/4tnf3ny4 [https://perma.cc/A78N-DQMP].

11. Attached hereto as **Exhibit H** is a true and correct copy of the article titled "Making a Statement: Positions of Professional Medical Organizations on Gender-Affirming Care," published in the *Annals of Surgery* in February 2025, available at https://tinyurl.com/yhndcw5t [https://perma.cc/QG8B-V5BC].

12. Attached hereto as **Exhibit I** is a true and correct copy of the *Notice of Funding Opportunity, Ryan White HIV/AIDS Program Part B States/Territories Supplemental Grant Program*, Opportunity No. HRSA-26-074, issued by HRSA on June 8, 2026.

13. Attached hereto as **Exhibit J** is a true and correct copy of the *Notice of Funding Opportunity: Ryan White HIV/AIDS Program Part C Capacity Development Program*, Opportunity No. HRSA-26-061, issued by HRSA on June 5, 2026.

14. Attached hereto as **Exhibit K** is a true and correct copy of the *Notice of Funding Opportunity: Ryan White HIV/AIDS Program Part F Dental Reimbursement Program*, Opportunity No. HRSA-26-085, issued by HRSA on June 8, 2026.

15. Attached hereto as **Exhibit L** is a true and correct copy of an excerpt of the transcript of the preliminary injunction hearing held on May 22, 2025 before the Honorable Jon S. Tigar in *San Francisco AIDS Foundation, et al. v Trump, et al.,* No. 25-cv-01824-JST, in the U.S. District Court for the Northern District of California.

Pursuant to 28 U.S.C. § 1746, I declare under the penalty of perjury that the foregoing is true and correct.

Executed on June 10, 2026.

/s/ Jose Abrigo
Jose Abrigo

EXHIBIT A

Per a court order, HHS is required to restore this website to its version as of 12:00 AM on January 29, 2025. Information on this page may be modified and/or removed in the future subject to the terms of the court's order and implemented consistent with applicable law. Any information on this page promoting gender ideology is extremely inaccurate and disconnected from truth. The Trump Administration rejects gender ideology due to the harms and divisiveness it causes. This page does not reflect reality and therefore the Administration and this Department reject it.

Transgender and Gender Diverse Persons

Transgender persons often experience high rates of stigma and socioeconomic and structural barriers to care that negatively affect health care usage and increase susceptibility to HIV and STIs (*326–332*). Persons who are transgender have a gender identity that differs from the sex that they were assigned at birth (*333*,*334*). Transgender women (also known as trans women, transfeminine persons, or women of transgender experience) are women who were assigned male sex at birth (born with male anatomy). Transgender men (also known as trans men, transmasculine persons, or men of transgender experience) are men who were assigned female sex at birth (i.e., born with female anatomy). In addition, certain persons might identify outside the gender binary of male or female or move back and forth between different gender identities and use such terms as "gender nonbinary," "genderqueer," or "gender fluid" to describe themselves. Persons who use terms such as "agender" or "null gender" do not identify with having any gender. The term "cisgender" is used to describe persons who identify with their assigned sex at birth. Prevalence studies of transgender persons among the overall population have been limited and often are based on small convenience samples.

Gender identity is independent of sexual orientation. Sexual orientation identities among transgender persons are diverse. Persons who are transgender or gender diverse might have sex with cisgender men, cisgender women, or other transgender or gender nonbinary persons.

Clinical Environment Assessment

Providers should create welcoming environments that facilitate disclosure of gender identity and sexual orientation. Clinics should document gender identity and sex assigned at birth for all patients to improve sexual health care for transgender and gender nonbinary persons. Assessment of gender identity and sex assigned at birth has been validated among diverse populations, has been reported to be acceptable (*335*,*336*), and might result in increased patients identifying as transgender (*337*).

Lack of medical provider knowledge and other barriers to care (e.g., discrimination in health care settings or denial of services) often result in transgender and gender nonbinary persons avoiding or delaying preventive care services (*338–340*) and incurring missed opportunities for HIV and STI prevention services. Gender-inclusive and trauma-guided health care might increase the number of transgender patients who seek sexual health services, including STI testing (*341*), because transgender persons are at high risk for sexual violence (*342*).

Primary care providers should take a comprehensive sexual history, including a discussion of STI screening, HIV PrEP and PEP, behavioral health, and social determinants of sexual health. Clinicians can improve the experience of sexual health screening and counseling for transgender persons by asking for their choice of terminology or modifying language (e.g., asking patients their gender pronouns) to be used during clinic visits and history taking and examination (*343*). Options for fertility preservation, pregnancy potential, and contraception options should also be discussed, if indicated. For transgender persons who retain a uterus and ovaries, ovulation might continue in the presence of testosterone therapy, and pregnancy potential exists (https://transcare.ucsf.edu).

Transgender Women

Doxy PEP as an STI Prevention Strategy – Guidelines on the use of doxycycline post-exposure prophylaxis (doxy PEP) to prevent some bacterial STIs.

A systematic review and meta-analysis of HIV infection among transgender women estimated that HIV prevalence in the United States is 14% among transgender women, with the highest prevalence among Black (44%) and Hispanic (26%) transgender women (*344*). Data also demonstrate high rates of HIV infection among transgender women worldwide (*345*). Bacterial STI prevalence varies among transgender women and is based largely on convenience samples. Despite limited data, international and U.S. studies have indicated elevated incidence and prevalence of gonorrhea and chlamydia among transgender women similar to rates among cisgender MSM (*346–348*). A recent study using data from the STD Surveillance Network revealed that the proportions of transgender women with extragenital chlamydial or gonococcal infections were similar to those of cisgender MSM (*349*).

Providers caring for transgender women should have knowledge of their patients' current anatomy and patterns of sexual behavior before counseling them about STI and HIV prevention. The majority of transgender women have not undergone genital-affirmation surgery and therefore might retain a functional penis; in these instances, they might engage in insertive oral, vaginal, or anal sex as well as receptive oral or anal sex. In the U.S. Transgender Survey, 12% of transgender women had undergone vaginoplasty surgery, and approximately 50% more were considering surgical intervention (*350*). Providers should have knowledge about the type of tissue used to construct the neovagina, which can affect future STI and HIV preventive care and screening recommendations. The majority of vaginoplasty surgeries conducted in the United States use penile and scrotal tissue to create the neovagina (*351*). Other surgical techniques use intestinal tissue (e.g., sigmoid colon graft) or split-skin grafts (*352*). Although these surgeries involve penectomy and orchiectomy, the prostate remains intact. Transgender women who have had a vaginoplasty might engage in receptive vaginal, oral, or anal sex.

Neovaginal STIs have infrequently been reported in the literature and include HSV and HPV/genital warts in penile-inversion vaginoplasty, *C. trachomatis* in procedures that involved penile skin and grafts with urethra mucosa or abdominal peritoneal lining (*353*), and *N. gonorrhoeae* in both penile-inversion and colovaginoplasty (*354–359*). If the vaginoplasty used an intestinal graft, a risk also exists for bowel-related disease (e.g., adenocarcinoma, inflammatory bowel disease, diversion colitis, and polyps) (*360–362*).

Transgender Men

The few studies of HIV prevalence among transgender men indicated that they have a lower prevalence of HIV infection than transgender women. A recent estimate of HIV prevalence among transgender men was 2% (*344*). However, transgender men who have sex with cisgender men might be at elevated risk for HIV infection (*332*,*363*,*364*). Data are limited regarding STI prevalence among transgender men, and the majority of studies have used clinic-based data or convenience sampling. Recent data from the STD Surveillance Network demonstrated higher prevalence of gonorrhea and chlamydia among transgender men, similar to rates reported among cisgender MSM (*365*).

The U.S. Transgender Survey indicated that the proportion of transgender men and gender diverse persons assigned female sex at birth who have undergone gender-affirmation genital surgery is low. Providers should consider the anatomic diversity among transgender men because a person can undergo a metoidioplasty (a procedure to increase the length of the clitoris), with or without urethral lengthening, and might not have a hysterectomy and oophorectomy and therefore be at risk for bacterial STIs, HPV, HSV, HIV, and cervical cancer (*366*). For transgender men using gender-affirming hormone therapy, the decrease in estradiol levels caused by exogenous testosterone can lead to vaginal atrophy (*367*,*368*) and is associated with a high prevalence of unsatisfactory sample acquisition (*369*). The impact of these hormonal changes on mucosal susceptibility to HIV and STIs is unknown.

Transgender men who have not chosen to undergo hysterectomy with removal of the cervix remain at risk for cervical cancer. These persons often avoid cervical cancer screening because of multiple factors, including discomfort with medical examinations and fear of discrimination (*338*,*370*). Providers should be aware that conducting a speculum examination can

be technically difficult after metoidioplasty surgery because of narrowing of the introitus. In these situations, high-risk HPV testing using a swab can be considered; self-collected swabs for high-risk HPV testing has been reported to be an acceptable option for transgender men (*371*).

Screening Recommendations

The following are screening recommendations for transgender and gender diverse persons:

- Because of the diversity of transgender persons regarding surgical gender-affirming procedures, hormone use, and their patterns of sexual behavior, providers should remain aware of symptoms consistent with common STIs and screen for asymptomatic infections on the basis of the patient's sexual practices and anatomy.
- Gender-based screening recommendations should be adapted on the basis of anatomy (e.g., routine screening for *trachomatis* and *N. gonorrhoeae)* as recommended for all sexually active females aged <25 years on an annual basis and should be extended to transgender men and nonbinary persons with a cervix among this age group.
- HIV screening should be discussed and offered to all transgender persons. Frequency of repeat screenings should be based on level of risk.
- For transgender persons with HIV infection who have sex with cisgender men and transgender women, STI screening should be conducted at least annually, including syphilis serology, HCV testing, and urogenital and extragenital NAAT for gonorrhea and chlamydia.
- Transgender women who have had vaginoplasty surgery should undergo routine STI screening for all exposed sites (e.g., oral, anal, or vaginal). No data are available regarding the optimal screening method (urine or vaginal swab) for bacterial STIs of the neovagina. The usual techniques for creating a neovagina do not result in a cervix; therefore, no rationale exists for cervical cancer screening (*368*).
- If transgender men have undergone metoidioplasty surgery with urethral lengthening and have not had a vaginectomy, assessment of genital bacterial STIs should include a cervical swab because a urine specimen will be inadequate for detecting cervical infections.
- Cervical cancer screening for transgender men and nonbinary persons with a cervix should follow current screening guidelines (see Human Papillomavirus Infections).

Next

Last Reviewed: July 22, 2021

Was this page helpful?

Yes Partly No

EXHIBIT B

March 11, 2026

FY 2026 HRSA General Terms and Conditions

These terms and conditions apply to all discretionary awards with funds and award modifications with funds made on or after March 11, 2026.

Compliance with Court Orders: Any term or condition in this Notice of Award (NOA), including those incorporated by reference, that HHS is enjoined by court order from imposing or enforcing shall not apply or be enforced as to any recipient or subrecipient to which that court order applies and while that court order is in effect.

1. Administrative Requirements

You must comply with the laws, policies, and terms and conditions included in your Notice of Award (NOA).

This includes:

- Requirements of the authorizing statutes and implementing regulations for the programs under which your award is funded.
- Appropriations acts provisions.
- Terms and conditions included in the HHS Grants Policy Statement (HHS GPS), which HHS revised with an effective date of October 01, 2025.This includes the requirements of applicable HHS regulations and the Uniform Administrative Requirements, Cost Principles and Audit Requirements for Federal Awards codified at 2 CFR 200 and any successor regulations, policies and requirements.
    - The HHS GPS applies to monetary actions only, including non-competing continuation awards and award modifications that add funding made on or after October 01, 2025. This includes supplements to awards, competing and non-competing continuations. The GPS applies to all HRSA discretionary awards and the requirements flow down to subrecipients.
    - Until a monetary action is processed, the July 24, 2025 GPS applies to your award.
- The HHS Administrative and National Policy Requirements (Appendix D, revised to ensure consistency with all administration policies.
- Requirements included in the Notice of Funding Opportunity (NOFO); and
- Policies specific to the award.

Applicable Regulatory Provisions. This award is subject to any applicable provisions of 2 CFR 200 and 2 CFR 300.

In case of conflicting or inconsistent requirements, follow the order of precedence indicated in the HHS Administrative and National Policy Requirements. This document provides statutory, regulatory, and executive requirements that apply to HHS awards.

We may list exceptions to individual requirements stated above in the NOA.

Use of the terms “federal award,” “award,” and “grant” refers collectively and separately to federal assistance awards, grants, and cooperative agreements, unless otherwise indicated.

Per 2 CFR 25, SAM.gov and Unique Entity Identifier (UEI) registration are required throughout the lifecycle of all HRSA awards.

a. Termination

This award is subject to the termination provisions at 2 CFR 200.340. Pursuant to 2 CFR 200.340, the recipient agrees by accepting this award that continued funding for the award is contingent upon the availability of appropriated funds, recipient satisfactory performance, compliance with the Terms and Conditions of the award, and to the extent authorized by law, a decision by the agency that the award continues to effectuate program goals or agency priorities.

b. Appeals

HRSA affords appeal rights for remedies for non-compliance, including terminations for compliance reasons. See 2 CFR 200.342 for opportunities to object, hearings, and appeals.

c. Subrecipients and Recipients (Pass-Through Entities) Responsibilities

The recipient is the entity that receives a federal award directly from HRSA.

The recipient can give a portion of the direct award to other organizations, called subrecipients, to accomplish the goals and objectives of the award.

In this case, the recipient becomes a pass-through entity and the subrecipient's award is called a subaward.

As a recipient, you must ensure the applicable general terms and conditions stated in this document flow down to subrecipients. See the HHS Administrative and National Policy Requirements.

d. Prior Approval

You must get prior approval for certain items, as stated in 2 CFR 200.308 and 2 CFR 200.407. Examples of items requiring prior approval include:

- Significant rebudgeting of project costs. Significant budget changes require prior approval when:
    - The award exceeds the simplified acquisition threshold (currently $350,000), and
    - The cumulative amount of the transfer exceeds 25 percent of the total budget, including cost share, of the most recent approved award (budget period).
        - Due to programmatic need, HRSA is using the 25 percent threshold for prior approval, instead of the 10 percent threshold cited in the HHS GPS Section 3.1.2.2 (Significant Budget Changes)
- Change of scope. A change in scope can occur when a recipient makes a budget change that cause a project to change substantially.
    - If you are not sure your budget change is beyond the scope, contact your Grants Management Specialist (GMS).
- Rebudgeting funding into a direct cost category not previously requested.

We do not automatically authorize prior approvals under 2 CFR 200.308(g) or 2 CFR 200.308(h):

- We do not waive cost-related or administrative prior approvals unless specifically stated in your NOA. You must submit these as a Prior Approval action via HRSA Electronic Handbooks (EHBs) or GrantSolutions (when HRSA transitions to GrantSolutions).
- Only responses to prior approval requests signed by the Grants Management Officer (GMO) are valid.

If you act based on responses from other officials, you do so at your own risk. We do not consider these responses binding.

f. Funding Restrictions

See your NOA and the HHS Administrative and National Policy Requirements for funding restrictions such as:

- Salary Cap (also see Salary Rate Limitation)
- Gun control
- Anti-lobbying
- Restrictions on abortion
- Ban on funding embryo research
- Limitation on use of funds for promotion of legalization of controlled substances
- Restriction of pornography on computer networks
- Restriction on the purchase of sterile needles
- Prohibition on certain telecommunications and video surveillance services or equipment.

g. Roles and Responsibilities.

To see the roles and responsibilities of the GMS and the Program Official (PO) for your award, visit Manage Your Grant - Administrative Management.

i. Antidiscrimination Laws and Requirements Compliance Certification

By applying for or accepting federal funds from HHS, recipients certify compliance with all federal antidiscrimination laws and these requirements and that complying with those laws is a material condition of receiving federal funding streams. Recipients are responsible for ensuring subrecipients, contractors, and partners also comply.

2. Policy Requirements

The HHS Administrative and National Policy Requirements provide a list of requirements applicable to HHS awards.

a. Conflict of Interest

See the HRSA Federal Financial Assistance Conflict of Interest Policy (COI Policy)

3. Financial Requirements

a. Salary rate limitation (SRL)

See the Salary Cap Summary Table for the latest salary rate limitation.

The HHS salary rate limitation applies to both direct and indirect costs for all applicable HHS awards.

b. Payments

Grant funds must be drawn and Federal Financial Reports (FFR) filed using the HHS Payment Management System (PMS).

The Division of Payment Management, Financial Management Services, Program Support Center, manages PMS and has instructions for obtaining payments.

Submit direct inquiries about payments:
ONE-DHHS Help Desk for PMS Support at 1-877-614-5533 or PMSSupport@psc.hhs.gov.

If you do not have access, complete a PMS Access Form (PMS/FFR Form). If you have any questions about accessing PMS, contact the PMS Liaison Accountant.

c. Program income

Per 2 CFR 200.307, HRSA awards use the additive method for program income earned from your award.

Program income requirements for for-profit recipients are governed by 2 CFR 300.318.

4. Reporting Requirements

Review your NOA, HHS Administrative and National Policy Requirements, and HRSA Manage Your Grant for required reports and method of submission.

a. General Reports may include:

- Federal Financial Reports (FFR)
- Noncompeting Continuation (NCC) Progress Reports
- Tangible Personal Property Report (SF-428) for Equipment and Supplies
- Real Property Report (SF-429)
- Subaward Reporting under the Federal Funding Accountability and Transparency Act (FFATA) reporting at SAM.gov.
- Recipient integrity and performance

b. Audit Reports

- If your organization is a nonprofit organization and is required to have audits in accordance with 2 CFR 200, Subpart F (See 2 CFR 200.501) because it spends $1,000,000 or more in federal funds in one fiscal year, submit the audit reports to the Federal Audit Clearinghouse.
- For-profit organizations required to have audits should submit the audit reports directly to HRSA.

c. Reporting Fraud, Waste, Abuse, and Mismanagement

- The HHS Office of the Inspector General (OIG) maintains a toll-free number (1-800- HHS-TIPS [1-800-447-8477]; TTY: 1-800-377-4950) and website for receiving information concerning fraud, waste, abuse, and mismanagement under HHS programs.

  Additionally, information may be submitted by mail to:

  Office of the Inspector General
  Department of Health and Human Services
  Attn: HOTLINE
  330 Independence Ave., SW
  Washington DC 20201

- Such reports are treated as sensitive material. You can decline to give your name if you choose to remain anonymous.

5. Alignment with HRSA funding priorities

a. General Alignment with HRSA Mission and Strategic Priorities

As a condition of this award, you must ensure that all activities funded under this award are implemented in a manner consistent with HRSA's mission and strategic priorities as authorized by law.

Funded activities must advance HRSA's mission of protecting and improving the health and well-being of Americans. The particular focus is on those who are underserved, medically vulnerable, or live in areas with limited access to care. HRSA's duty is to serve wisely, effectively, and with measurable results that justify every taxpayer dollar invested.

Consistent with HRSA's priorities, in carrying out any funded project, the recipient must adhere to the following principles, where they are consistent with the authority and scope of the award and its activities:

- **Gold Standard Science:** Design and deliver services using gold standard evidence-based and evidence-informed approaches, establish measurable performance goals, and use data to monitor outcomes and drive continuous improvement.
- **Program Integrity and Fiscal Stewardship:** Administer all funds in accordance with applicable federal statutes, regulations, and award conditions. You must maintain strong internal controls to prevent waste, fraud, abuse, and mismanagement of taxpayer dollars.
- **Partnership and Local Leadership:** Coordinate with state, tribal, territorial, local, and community partners to ensure services are tailored to community-identified needs while respecting local decision-making authority.

b. Alignment with Administration Objectives

Recipients must manage any awarded project in accordance with the following objectives in programs authorized to advance them:

Make America Healthy Again (MAHA): HRSA prioritizes the health and well-being of all Americans by supporting common-sense, evidence-based health policies that promote:

- Personal responsibility.
- Strong families and communities.
- Proper nutrition.
- The prevention and management of chronic disease, while ensuring access to high-quality, affordable physical and mental health care.

Child protections, biological integrity, parental rights, and lawful use of funds: HRSA prioritizes safeguarding children's health and safety by:

- Not supporting medical interventions for gender dysphoria in minors that lack a strong evidence base.
- Applying sex-based definitions grounded in biological reality.
- Supporting parental authority, transparency, and choice in education, including school-based health centers that respect parental rights and religious upbringing.
- Ensuring taxpayer funds are not used to promote or support elective abortions, consistent with federal law and the Hyde Amendment.

Advancing evidence-based, merit-driven, and ethically grounded health care: HRSA will prioritize unbiased, transparent science; merit-based workforce opportunities; and programs that demonstrate measurable outcomes, while deprioritizing organizations with:

- Conflicts of interest.
- Ineffective "harm reduction" models.
- Housing-first approaches lacking accountability.
- Activities that facilitate illegal drug use or unsafe medical practices.

Promoting public safety, lawful use of federal funds, and national health priorities: To the extent permitted by law, HRSA will align funding with administration priorities by:

- Supporting ending the HIV epidemic through authorized, evidence-based care.
- Reserving benefits for eligible individuals.
- Discouraging illegal immigration and unsafe community practices.
- Prioritizing recipients that enforce public safety, address serious mental illness and substance use through treatment and recovery, and reduce homelessness responsibly.

c. Enforcement Standards

To the extent permitted by law, HRSA gives priority to states and municipalities for programs to:

- Enforce prohibitions on open illicit drug use.
- Enforce prohibitions on urban camping and loitering.
- Enforce prohibitions on urban squatting.
- Enforce, and where necessary, adopt, standards that address individuals who are a danger to themselves or others and suffer from serious mental illness or substance use disorder, or who are living on the streets and cannot care for themselves. The approach must be through assisted outpatient treatment or by moving them into treatment centers or other appropriate facilities through civil commitment or other available means, to the maximum extent permitted by law.

d. Compliance, Monitoring, and Termination

HRSA will implement these priorities consistent with applicable laws, regulations, court orders, and any required procedures.

- **Ongoing Compliance:** You must demonstrate continuous alignment with these priorities through program design, implementation, reporting, and evaluation throughout the period of performance.
- **Corrective Action:** Failure to meaningfully align funded activities with these requirements may result in the imposition of specific award conditions, additional reporting requirements, or corrective action plans.
- **Termination:** In accordance with 2 CFR § 200.340(a)(4), HRSA may terminate this award in whole or in part, to the extent permitted by law, if it determines that the award no longer effectuates the program goals or agency priorities outlined in these terms.

EXHIBIT C

Advancing HRSA's Mission Through Focused, Accountable Action

As stewards of federal resources, the Health Resources and Services Administration (HRSA) remains firmly committed to protecting and improving the health and well-being of Americans, particularly those who are medically vulnerable, or live in areas where access to care is limited. Our duty is not just to serve, but to serve wisely, effectively, and with measurable results that justify every taxpayer dollar invested.

In alignment with the current administration's focus on outcomes-driven governance and responsible spending, HRSA is emphasizing targeted investments that strengthen the nation's core healthcare infrastructure, address pressing health challenges, and deliver real results for communities across the country.

HRSA is committed to prioritizing gold-standard science and the mission outlined in the *Make America Healthy Again Commission Report* to deliver better health outcomes. Through its critical public health and workforce programs, HRSA intends to address the nation's most pressing health challenges, including the chronic disease epidemic, the mental health crisis, obesity, nutritional deficiencies, exposure to chemical and environmental toxins, and overreliance on medical interventions.

HRSA is committed to supporting programs and initiatives that will focus on the underlying causes of disease, including lifestyle modifications and other modalities that are shown to be effective in improving health outcomes. HRSA will preference programs, partnerships, grants, cooperative agreements, contracts, and other funding mech[illegible] that prioritize these objectives.

By narrowing our focus to high-impact, data-supported interventions, HRSA is reinforcing the programs that work, cutting inefficiencies, and directing resources to areas of greatest need. From rural towns to tribal nations, and from health centers to home visiting programs, our goal is clear: improve health outcomes while honoring the trust placed in us by the American people.

Our strategy is rooted in time-tested principles: responsible governance, fiscal restraint, local empowerment, and accountability. Through stronger oversight, partnerships with community-based providers, and support for innovation in care delivery, HRSA is advancing its mission while ensuring that federal dollars are not wasted, misdirected, or overextended.

We understand that taxpayer dollars are not unlimited. Every investment must be justified by results. By focusing on measurable outcomes, emphasizing efficiency, and ensuring transparency at every level of operations, HRSA is fulfilling its charge not only to improve healthcare access, but to do so in a way that reflects respect for American taxpayers and the limits of federal responsibility.

This commitment to focused, accountable action drives every policy we craft, every program we fund, and every reform we implement. We are proud to serve the American people and equally proud to do so with discipline, integrity, and impact.

Thomas J. Engels
Administrator, HRSA

About the Health Resources and Services Administration

HRSA, an agency of the U.S. Department of Health and Human Services, plays a vital role in improving access to care for Americans who are uninsured, isolated, or medically underserved. With a focus on strengthening local healthcare capacity, HRSA funds community health centers, supports health workforce development, invests in maternal and child health programs, sustains HIV/AIDS care, and promotes rural and telehealth services.

HRSA's goal is to support and empower existing healthcare systems, helping communities serve their own people with long-term, cost-effective solutions. Our programs are designed not to expand bureaucracy but to reinforce self-sufficiency, resilience, and responsible stewardship of public health resources. To learn more, visit www.hrsa.gov.

HRSA's Strategic Priority Areas

This document has been prepared in furtherance of the HRSA Administrator's responsibility to provide the overall direction of HRSA, to establish and implement general policies respecting the management and operation of programs and activities, and to coordinate and oversee the operation of the agency's bureaus and offices. Several HRSA's authorities permit HRSA to exercise a certain level of discretion and judgment in making federal financial assistance awards. This document is intended to clarify HRSA's Strategic Priority Areas in areas subject to HRSA's discretion.

HRSA is prioritizing the following areas:

- We believe the health and safety of children must be the highest priority. HHS released a comprehensive review (PDF - 68 KB) of the evidence and best practices for promoting the health of children and adolescents with gender dysphoria. This review, informed by an evidence-based medicine approach, found medical interventions, such as puberty blockers, cross-sex hormones, and surgeries, that attempt to transition minors away from their sex are supported by extremely weak evidence base and have an unfavorable risk/benefit profile. It is a HRSA priority to protect children from these practices, and, to the extent allowable by law. HRSA programs will deprioritize programs that engage in these practices. HRSA funds will also not support the costs of such practices where not required by law or relevant court order. On March 6, 2025, a letter was issued (PDF - 285 KB) outlining that HRSA may begin taking steps to update its policies in order to strengthen protections for children against harmful chemical and surgical interventions.
- HHS released guidance (PDF - 232 KB) promulgating sex-based definitions rooted in biological truth. It is a HRSA priority to recognize that a person's sex as either male or female is unchangeable and determined by objective biology, and to ensure its programs accurately reflect science, including the biological reality of sex.

- Where permitted by law, HRSA will deprioritize unlawful diversity, equity, and inclusion initiatives, which prioritize group identity over individual merit. We believe opportunities should be based on character, effort, and ability, not race or other group identity. HRSA is committed to restoring merit-based opportunities and removing unlawful discriminatory practices (including unlawful proxies for racial discrimination), including in HRSA's health care workforce programs.

HRSA believes parents are the primary decision-makers in their children's education and should have full authority over what their children are taught. School policies should include transparency and choice, and curricula should emphasize knowledge, critical thinking, and civic responsibility, without imposing ideas that may conflict with parents' political, religious, or social beliefs. To the extent allowable by law, HRSA will also prioritize School Based Health Centers that respect parental rights and authority to direct the religious upbringing of their children.

Make America Healthy Again is a call to prioritize the well-being of all Americans through common-sense health policies, personal responsibility, and strong community support. HRSA believes in empowering individuals and families to take charge of their physical and mental health, with a focus on proper nutrition and the prevention and management of chronic diseases, while ensuring access to high-quality, affordable care.

The public must know that unbiased science—evaluated through a transparent process and insulated from conflicts of interest—guides the recommendations of our health agencies, and HRSA-funded programs and activities carried out by HRSA's partners. HRSA will deprioritize organizations which present conflicts of interest or otherwise compromise their objectivity or integrity in carrying out HRSA-funded programs.

HRSA supports the President's Ending the HIV Epidemic in the US initiative and will not provide funding under the Ryan-White HIV/AIDS Program (RWHAP) for purposes unrelated to the statute, including for medications that are used without proper authorization or outside of approved medical guidelines. Public resources should support safe, evidence-based care, ensuring that treatments are used appropriately and responsibly to protect patient health and public trust. In a letter dated April 7, 2025, the Trump Administration reaffirmed its commitment to 'Make America Healthy Again (PDF - 322 KB),' calling on RWHAP recipients and subrecipients to align with this vision while emphasizing training, technical assistance, and culturally competent care to strengthen antiretroviral adherence and viral suppression in the fight to end HIV.

Federal law prohibits the use of HHS funds for elective abortions. Accordingly, HRSA programs will not use taxpayer funds to promote elective abortions. Taxpayer dollars should be used to protect life and support alternatives to abortion that honor the dignity of every mother and unborn child. Our commitment is to uphold the values of life and, consistent with the Hyde Amendment, ensure public funds are not used for elective abortions.

It is a priority of HRSA to ensure that federal public benefits are reserved for American citizens and qualified aliens, in compliance with the Personal Responsibility and Work Opportunity Reconciliation Act and other federal laws. Consistent with applicable law, Federal funds should not be used to encourage or support illegal immigration. HRSA will prioritize programs that further the administration's priority to end illegal immigration.

HRSA grants will prioritize evidence-based programs and not fund programs that fail to achieve adequate outcomes, including so-called "harm reduction" or "safe consumption" efforts that only facilitate illegal drug use and its attendant harm. HRSA funds will not be used to support poorly defined so-called "harm reduction" activities, consistent with guidance on July 29, 2025 published by the Substance Abuse and Mental Health Services Administration (SAMHSA) (PDF - 272 KB).

It is a priority of HRSA to end support for "housing first" policies that deprioritize accountability and fail to promote treatment, recovery, and self-sufficiency. Where applicable, HRSA will increase competition among grantees through broadening the applicant pool and hold grantees to higher standards of effectiveness in reducing homelessness and increasing public safety. HRSA will ensure that Federal funds for Federally Qualified Health Centers reduce rather than promote homelessness by supporting, to the maximum extent permitted by law, comprehensive services for individuals with serious mental illness and substance use disorder, including crisis intervention services.

It is a priority of HRSA not to support programs that subsidize drug injection sites for illegal drugs or so-called "safe consumption sites," knowingly distribute drug paraphernalia, or permit use or distribution of illegal drugs on property under their control.

To the extent allowable by law, HRSA will give priority to grantees in States and municipalities that actively meet the below criteria: (i) enforce prohibitions on open illicit

drug use; (ii) enforce prohibitions on urban camping and loitering; (iii) enforce prohibitions on urban squatting; (iv) enforce, and where necessary, adopt, standards that address individuals who are a danger to themselves or others and suffer from serious mental illness or substance use disorder, or who are living on the streets and cannot care for themselves, through assisted outpatient treatment or by moving them into treatment centers or other appropriate facilities via civil commitment or other available means, to the maximum extent permitted by law; or (v) substantially implement and comply with, to the extent required, the registration and notification obligations of the Sex Offender Registry and Notification Act, particularly in the case of registered sex offenders with no fixed address, including by adequately mapping and checking the location of homeless sex offenders.

HRSA will implement these priorities consistent with applicable laws, regulations, court orders, and any required procedures.

Date Last Reviewed: May 2026

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EXHIBIT D

Notice of Funding Opportunity

Application due Monday, November 3, 2025

HRSA
Health Resources & Services Administration

HIV/AIDS Bureau
Division of State HIV/AIDS Programs

AIDS Drug Assistance Program (ADAP) Emergency Relief Funds (ERF)

Opportunity number: HRSA-26-012

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Before you begin

If you believe you are a good candidate for this funding opportunity, secure your SAM.gov and Grants.gov registrations now. If you are already registered, make sure your registrations are active and up-to-date.

SAM.gov registration (this can take several weeks)

You must have an active account with SAM.gov. This includes having a Unique Entity Identifier (UEI).

See Step 2: Get Ready to Apply

Grants.gov registration (this can take several days)

You must have an active Grants.gov registration. Doing so requires a Login.gov registration as well.

See Step 2: Get Ready to Apply

Apply by the application due date

Applications are due by 11:59 p.m. Eastern Time on Monday, November 3, 2025.

To help you find what you need, this NOFO uses internal links. In Adobe Reader, you can go back to where you were by pressing Alt + Left Arrow (Windows) or Command + Left Arrow (Mac) on your keyboard.

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Step 1:
Review the Opportunity

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Basic information

Health Resources and Services Administration (HRSA)

HIV/AIDS Bureau

Division of State HIV/AIDS Programs

Summary

The purpose of the AIDS Drug Assistance Program (ADAP) Emergency Relief Funds (ERF) is to provide funding to states/territories to prevent, reduce, or eliminate ADAP waiting lists or to address shortfalls in ADAP funding for medications and/or the purchase of health care coverage. Recipients will use these funds along with the Ryan White HIV/AIDS Program (RWHAP) Part B ADAP base award.

Funding details

Application Types: Competing continuation, New

Expected total available funding in FY 2026: $75,000,000

Expected number and type of awards: Up to 25 grants

Funding range per award: $100,000 to $10,000,000

- If you have a current ADAP waiting list, you may apply for up to $10,000,000. If you do not have a waiting list, you may apply for up to $7,000,000. The minimum award amount is $100,000.

We plan to fund awards in one 12-month budget period from April 1, 2026, to March 31, 2027.

The program and awards depend on the appropriation of funds and are subject to change based on the availability and amount of appropriations.

Have questions?
Go to Contacts and Support.

Key facts

Opportunity name: AIDS Drug Assistance Program (ADAP) Emergency Relief Funds (ERF)

Opportunity number: HRSA-26-012

Announcement version: New

Federal assistance listing: 93.917

Key dates

NOFO issue date: October 2, 2025

Informational webinar: October 15, 2025

Application deadline: November 3, 2025

Expected award date is by: April 1, 2026

Expected start date: April 1, 2026

See other submissions for other time frames that may apply to this NOFO.

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Eligibility

Who can apply

You can only apply if you are a state/territory that receives RWHAP Part B funding and needs additional funding to:

- Reduce or eliminate an existing ADAP waiting list.
- Actively prevent an ADAP waiting list.
- Address a reduction in available resources to fund ADAP.
- Address a current or projected increase in treatment needs to end the HIV epidemic in the U.S.
- Address other increases in the number of clients in the program due to new diagnosis, re-engagement in care, loss of income, and/or loss of health care coverage.

Types of eligible organizations

These types of domestic* organizations may apply:

- State governments, including the District of Columbia, domestic territories, and freely associated states.

* “Domestic” means the 50 states, the District of Columbia, the Commonwealth of Puerto Rico, the Northern Mariana Islands, American Samoa, Guam, the U.S. Virgin Islands, the Federated States of Micronesia, the Republic of the Marshall Islands, and the Republic of Palau.

Tribes and tribal organizations are not eligible for this funding. Individuals are not eligible for this funding.

Completeness and responsiveness criteria

We will review your application to make sure it meets these basic requirements to move forward in the competition.

We will not consider an application that:

- Is from an organization that does not meet all eligibility criteria.
- Requests funding above the award ceiling shown in the funding range.
- Is submitted after the deadline.

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Application limits

You may not submit more than one application. If you submit more than one application, we will only accept the last on-time submission.

Cost sharing

This program has no cost-sharing requirement. If you choose to share in the costs of the project, we will not consider it during merit review. We will hold you accountable for any funds you add, including through reporting

Post-award requirements

Before you apply, make sure you understand the requirements that come with an award.

See Step 6: Learn What Happens After Award for information on regulations that apply, reporting, and more.

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Program description

Purpose

This notice announces the opportunity to apply for funding under the Ryan White HIV/AIDS Program (RWHAP) Part B AIDS Drug Assistance Program (ADAP) Emergency Relief Funds (ERF).

ADAP ERF awards are intended for states/territories that need additional resources to prevent, reduce, or eliminate ADAP waiting lists or to address shortfalls in ADAP funding for medications or health care coverage. HRSA will base ADAP ERF awards upon your ability to successfully demonstrate the need for additional funding.

At the time of this NOFO publication, there are no ADAP waiting lists. States/territories that establish a waiting list after this NOFO is published must report the waiting list to HRSA immediately and use funding awarded under this NOFO to remove clients from the waiting list.

HRSA anticipates increases in clients who need ADAP services due to reductions in program income or rebates, loss of health care coverage among people with HIV, and increased case finding. States/territories may use ERF funds to address current or projected increases in treatment needs aligned with ending the HIV epidemic in the U.S. or other increases in the number of clients in their ADAP.

Background

ADAPs ensure access to medication to treat HIV for eligible clients by directly purchasing medication and covering the costs of health care coverage premiums, deductibles, co-payments, and co-insurance. The state/territory determines client eligibility and ADAPs are expected to confirm client eligibility on a timely basis. Eligibility criteria include documented diagnosis of HIV, financial eligibility, and residence eligibility.

The Ryan White HIV/AIDS Program

The HRSA Ryan White HIV/AIDS Program has five statutory funding parts that provide a comprehensive system of medical care, support, and medications for low-income people with HIV. The goal is to improve health outcomes and to prevent HIV transmission.

The HIV care continuum is a key strategy to meet the goals of the program. It shows the journey of someone with HIV from diagnosis to effective treatment, leading to viral

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suppression. Achieving viral suppression boosts the individual's quality of life and prevents HIV transmission.

This continuum also helps programs and planners measure progress and use resources effectively. We require you to assess your outcomes and work with your community and public health partners to improve outcomes across the HIV care continuum. To assess your program, review HRSA's Performance Measure Portfolio.

Expanding the effort

There have been significant accomplishments:

- From 2010 to 2023, HIV viral suppression among RWHAP clients improved from 87.1% to 90.6%. For more, see the 2023 Ryan White Services Report (RSR).
- In 2020, the Ending the HIV Epidemic in the U.S. (EHE) initiative launched to further expand federal efforts to reduce HIV transmission. For the RWHAP, the EHE initiative expands the program's ability to meet the needs of clients, specifically focusing on linking people with HIV who are either newly diagnosed, diagnosed but currently not in care, or are diagnosed and in care but not yet virally suppressed, to the essential HIV care, treatment, and support services needed to help them reach viral suppression.

Program requirements and expectations

The steady growth in the number of eligible clients combined with rising costs of complex HIV treatments can result in states/territories experiencing greater demand for ADAP services than available resources can cover. As a last resort, a state/territory may implement an ADAP waiting list when available funding cannot provide medications to all eligible people requesting enrollment in their ADAP and after they have used all other feasible cost-containment strategies.

HRSA HAB defines a waiting list as a register of individuals who have applied for and been deemed eligible for a state's/territory's ADAP, but whom the state cannot immediately serve due to insufficient resources. If an ADAP is proposing to implement a waiting list, the ADAP must be able to clearly demonstrate to HRSA HAB the need for the list before they establish one.

An ADAP must have written policies and procedures for managing a waiting list that include:

- Fair and equitable criteria.
- Compliance with relevant state/territory laws and regulations.
- A means for public input and communication to the public.

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- Methods for monitoring the waiting list to make sure that policies and procedures are consistently followed across the state/territory.
- A revisions and appeals process.

An ADAP must assess each applicant for ADAP eligibility before putting them on the waiting list. The ADAP must confirm eligibility according to a pre-established schedule outlined in a waiting list policy and procedure. An ADAP must prioritize individuals by predetermined criteria and bring clients into the program as soon as funding becomes available. Clients on waiting lists should be given information about:

- Why a waiting list is necessary.
- Waiting list criteria.
- The estimated length of time they might remain on the waiting list.
- Options for getting their medications in the meantime, including:
  - Recommendations or requirements for clients to work with a case manager.
  - Patient Assistance Programs (PAPs) applications and help applying.
  - Other available options, such as the RWHAP Part A Local Pharmacy Assistance Program (LPAP).
  - Continuous assistance applying and re-applying for other programs, as needed.

We strongly discourage the use of a waiting list to contain costs, unless absolutely necessary. If you establish a waiting list, the DSHAP project officer will monitor the RWHAP Part B grant more closely, and you will need to report waiting list data to us.Statutory authority

Statutory authority:

42 U.S.C. §§ 243(c) and 300ff-26 (§§ 311(c) and 2616 of the Public Health Service Act)

Award information

Funding policies and limitations

Changes in HHS regulations

As of October 1, 2025, HHS will adopt 2 CFR 200, with some modifications included in 2 CFR 300. These regulations replace those in 45 CFR 75.

Policies

- We will only make awards if this program receives funding. If Congress appropriates funds for this purpose, we will move forward with the review and award process.
- Award amounts are subject to demonstrated need and the availability of funds. Total cost includes both direct and indirect costs per year.
- HAB will base the amount of your award on your showing the need for funding to:
  - Reduce or eliminate an existing ADAP waiting list.
  - Actively prevent implementing an ADAP waiting list.
  - Address a reduction in available resources to fund ADAP.
  - Address a current or projected increase in treatment needs aligned with ending the HIV epidemic in the U.S.
  - Address other increases in the number of clients in the program due to new diagnosis, re-engagement in care, loss of income, and/or loss of health care coverage.
- HRSA will base funding decisions on review by an external merit review panel (MRP) review and scoring of the criteria listed in the merit review section of this notice.
- HRSA places significant importance on eliminating waiting lists, so:
  - We will use the MRP scores to establish the rank order for awarding funds.
  - If sufficient funding is available, we will make awards to all applicants that request funds to address an existing waiting list, as long as the MRP recommends them for an award based on their MRP score. See the funding preference section.
  - After we provide funds to address existing waiting lists, we will award funds to remaining applicants that the MRP recommends for an award based on their MRP scores.

ADAPs are required to secure the best price available for all products on their ADAP formularies to achieve maximum results with these funds. As covered entities, ADAPs are eligible to participate in the 340B Drug Pricing Program under Section 340B of the PHS Act. Rebates and program income generated from these funds must be applied to the RWHAP Part B program, with priority given to ADAP (see Policy Clarification Notices 15-03 and 15-04 for more information).

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General limitations

- For guidance on some types of costs we do not allow or restrict, see Project Budget Information in Section 3.1.4 of the Application Guide. You can also see 2 CFR Part 200 Subpart E - General Provisions for Selected Items of Cost ..
- You cannot earn profit from the federal award. See 2 CFR 200.400(g)..
- Congress's current appropriations act includes a salary limitation, which applies to this program. As of January 2025, the salary rate limitation is $225,700. This limitation may be updated. You may pay salaries at a rate higher than Executive Level II if the amount beyond the salary rate limit is paid with non-HHS funds not associated with the HHS awarded project.

Program-specific statutory or regulatory limitations

As outlined under applicable statute, regulation, or policy, you cannot use funds under this notice for the following purposes:

- Any costs unallowable under the ADAP service category (as defined in PCN 16-02: RWHAP Services Eligible Individuals and Allowable Uses of Funds).
- Payment for any item or service to the extent that payment has been made (or reasonably can be expected to be made), with respect to that item or service, under any state compensation program, insurance policy, federal or state benefits program, or any entity that provides health services on a prepaid basis (except for a program administered by or providing the services of the Indian Health Service).
- Planning and evaluation activities as defined by the RWHAP Part B.
- Cash payments to intended recipients of RWHAP services.
- Clinical quality management.
- International travel.
- Construction. (Minor alterations and renovations to an existing facility to make it more suitable for the purposes of the award program are allowable with prior HRSA approval.)
- Syringe Services Programs (SSPs). Some aspects of SSPs are allowable with HRSA's prior approval and in compliance with HHS and HRSA policy.
- Development of materials designed to directly promote or encourage intravenous drug use or sexual activity, whether homosexual or heterosexual.
- Pre-exposure prophylaxis (PrEP) medications and related medical services or post-exposure prophylaxis (PEP), as the person using PrEP or PEP is not diagnosed with HIV and therefore is not eligible for RWHAP-funded medication.

See Manage Your Grant for other information on costs and financial management.

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Indirect costs

Indirect costs are costs you charge across more than one project that cannot be easily separated by project. For example, this could include utilities for a building that supports multiple projects.

To charge indirect costs you can select one of two methods:

Method 1 – Approved rate. You currently have an indirect cost rate approved by your cognizant federal agency at the time of award.

Method 2 – *De minimis* rate. Per 2 CFR 200.414(f), if you have never received a negotiated indirect cost rate, you may elect to charge a *de minimis* rate. If you choose this method, costs included in the indirect cost pool must not be charged as direct costs.

This rate is up to 15% of modified total direct costs (MTDC). See 2 CFR 200.1 for the definition of MTDC. You can use this rate indefinitely for all your federal awards or until you choose to receive a negotiated rate.

Consider your indirect costs when developing your budget.

Program income and rebates

Program income is money earned as a result of your award-supported project activities. You must use any program income you generate from awarded funds for allowable project-related activities. Find more about program income at 2 CFR 200.307. Rebates generated because of awarded funds must be used for the statutorily permitted purposes under the RWHAP Part B with a priority for ADAP.

Per 2 CFR 200.305(b)(5), to the extent available, you must disburse funds available from program income and rebates before requesting grant funds. Please see HAB PCNs 15-03: Clarifications Regarding the Ryan White HIV/AIDS Program and Program Income and 15-04: Utilization and Reporting of Pharmaceutical Rebates for more information.

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Step 2:
Get Ready to Apply

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Get registered

SAM.gov

You must have an active account with SAM.gov to apply. This includes having a Unique Entity Identifier (UEI). SAM.gov registration can take several weeks. Begin that process today.

To register, go to SAM.gov Entity Registration and select Get Started. From the same page, you can also select the Entity Registration Checklist to find out what you'll need to register.

When you register or update your SAM.gov registration, you must agree to the financial assistance general certifications and representations. You must agree to those for grants specifically, as opposed to contracts, because the two sets of agreements are different. You will have to maintain your registration throughout the life of any award.

Grants.gov

You must also have an active account with Grants.gov. You can see step-by-step instructions at the Grants.gov Quick Start Guide for Applicants.

Find the application package

The application package has all the forms you need to apply. You can find it online. Go to Grants Search at Grants.gov and search for opportunity number HRSA-26-012.

After you select the opportunity, we recommend that you click the Subscribe button to get updates.

Application writing help

Visit HHS Tips for Preparing Grant Proposals.

Visit HRSA's How to Prepare Your Application page for more guidance.

See Apply for a Grant for other help and resources.

Join the webinar

For more information about this opportunity, join the webinar on Wednesday, October 15, 2025 at 2 PM ET.

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Join on: Microsoft Teams

If you are not able to join through your computer, you can call in:

- Phone number: 240-800-7959
- Meeting ID: 264 408 003#

Have questions? Go to Contacts and Support.

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Step 3:
Build Your Application

In this step

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Application contents and format 20

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Application checklist

Make sure that you have everything you need to apply:

Narratives

Component		Included in page limit*?
☐ Project narrative	Use the Project Narrative Attachment form.	Yes
☐ Budget narrative	Use the Budget Narrative Attachment form.	Yes

Attachments

Insert each in the Attachments Form in this order.

Component	Included in page limit*?
☐ 1. Work plan	Yes
☐ 2. Agreement Compliance Assurances	Yes
☐ 3. ADAP Organizational Chart	Yes
☐ 4. ADAP Funding Utilization Summary for FY 2024	Yes

Other required forms

Upload using each required form in Grants.gov.

Component	Included in page limit*?
☐ Application for Federal Assistance (SF-424)	No

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☐ Budget Information for Non-Construction Programs (SF-424A)	No
☐ Project Abstract Summary Form	No
☐ Disclosure of Lobbying Activities (SF-LLL), optional	No
☐ Project/Performance Site Location(s)	No
☐ Grants.gov Lobbying Form	No
☐ Key Contacts	No

*Only what you attach in these forms counts toward the page limit. The forms themselves do not count.

Application contents and format

Applications include 5 main components. This section includes guidance on each.

Application page limit: 40 pages.

Submit your information in English and express whole number budget figures using U.S. dollars.

Required format

You must format your narratives and attachments using our required formats for fonts, size, color, format, and margins. See the formatting guidelines in Section 3.2 of the Application Guide.

Project narrative

In this section, you will describe all aspects of your project.

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Use the section headers and the order listed.

Introduction

See merit review criterion 1: Need

Briefly describe the purpose of your project.

Need

See merit review criterion 1: Need

The purpose of this section is to show that you need additional resources to meet the projected ADAP client service needs for FY 2026. Provide the following information to show that you are eligible for this award and explain the structure, functions, and operational processes of the ADAP and its clients.

State/territory's ADAP profile

ADAP funding and utilization summary for FY 2024

In table format, please list:

- All the following sources of funding for ADAP (1 through 12),
- The amount received.
- The amount expended.
- The amount of unspent funds and unobligated balances during the FY 2024 period of performance (April 1, 2024 through March 31, 2025)
- The estimated number of unduplicated clients served with each funding source.

If you did not receive funding from one or more of the categories listed below, please list the source and enter zero. Please include the table as **Attachment 4**. A sample table format is provided in **Appendix B**.

The funding sources are:

1. ADAP base
2. ADAP supplemental
3. RWHAP Part B Base Contribution to ADAP
4. RWHAP Part B Supplemental Contribution to ADAP
5. ADAP ERF Award
6. RWHAP Part A Contribution to ADAP
7. State funds
8. Pharmaceutical rebates
9. Carryover

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10. Program income
11. Other sources (describe)
12. Total ADAP funding

Cost-cutting measures for FY 2024 and FY 2025

Please identify which, if any, of the following cost-cutting measures you were using or began using in FY 2024 and FY 2025 for your ADAP:

- Enrollment cap—specify the maximum number of enrollees.
- Capped number of prescriptions per month—specify the cap.
- Capped expenditure—specify the amount and timeframe.
- Drug-specific enrollment caps for antiretroviral medication—specify the cap.
- Reduction in formulary—specify the reduction.
- Decrease in financial eligibility criteria—specify the decrease.
- Other—please specify.

Cost-Saving Measures for FY 2024 and FY 2025

Please identify which, if any, of the following cost-saving measures you were using or began using in FY 2024 and FY 2025 for your ADAP:

- Expansion of health care coverage assistance—specify the services you currently offer.
- Enrolling eligible clients in health care coverage—specify how many were enrolled and how they were enrolled.
- Enrolling eligible clients into Medicaid.
- Improved client eligibility confirmation processes—specify improvements.
- Decrease in administrative expenditures—specify decreases.
- Other—please specify.

Factors affecting state/territory ADAP capacity to meet need

Provide a detailed description of any key factors affecting the ADAP's need for additional resources for the approved purposes. Describe:

- Why the ADAP cannot meet the need with existing resources.
- Any anticipated funding shortfalls for ADAP.
- The cost-cutting measures you would take if your ADAP was not awarded additional funding.

If you reported any unspent funds or unobligated balances in the ADAP Funding Summary for FY 2024, please explain why you need emergency funds, given these other available resources.

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Examples of factors that could create need for additional resources include, but are not limited to:

- Trends or changes in the HIV disease prevalence over the past two calendar years (January 1, 2023, through December 31, 2024) have affected the ADAP.
- Increases in clients engaged in care.
- Changes to the state/territory's service delivery system may increase client need or administrative burden as a result of the changing health care landscape.
- Changes in client population or demographics over the last two calendar years, including:
  - More eligible clients.
  - Higher percentage of eligible clients below 100% of the FPL.
  - High unemployment rates.
  - Increased co-morbidities, such as substance use disorder.
  - Increased number of out-of-care clients seeking treatment.
- Increased program costs, including the cost of ADAP medications or cost to ADAP for health care coverage premiums, deductibles, or cost sharing.
- Decreased or level funding from state or RWHAP resources for ADAP and/or HIV services.
- Decreased program income or pharmaceutical rebates.

You should include data sources when discussing trends and changes (including environmental changes) that have resulted in this need.

Approach

See merit review criterion 2: Response

ADAP average annual client costs and forecasting

Calculate the projected average cost per client for medication assistance and/or health care coverage for the FY 2026 ADAP ERF period of performance (April 1, 2026, to March 31, 2027). Important note: You only need to provide average costs for clients for the types of assistance you are requesting funding for.

Determine the average cost per client through your own calculations, or through the formula in **Appendix A**. Whichever method you use, provide the step-by-step calculations you used to find the average cost per client. Use this calculation to develop the proposed budget for the ADAP ERF funds. Show how you multiplied the average cost per client by the projected number of clients to be served to determine the budget request for medication assistance and/or health care coverage assistance.

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ADAP average annual client costs

- If you are requesting funding for **medication costs**, please provide current projected annual average medication cost per client and all calculations used to determine the cost.
- If you are requesting funding for **health care coverage**, please provide current projected annual average health care coverage assistance cost per client and all calculations used to determine the cost.

Forecasting

- If you have an existing ADAP waiting list, provide the current number of people on the list.
- Describe the projected impact of ADAP ERF and any other projected resources in addressing any of these:
  - Your projected/potential ADAP waiting list.
  - Your current waiting list.
  - Your other increases in the number of clients in the program.

High-level work plan

See merit review criteria 2: Response and 4: Impact

Work plan

Provide a workplan, uploaded as **Attachment 1,** that lists each planned ADAP ERF service—for example, purchase of ADAP medications, purchase of health care coverage premiums, or payment of medication co-payments, deductibles, or co-insurance. Only costs allowed under the ADAP service category (as defined in PCN 16-02 RWHAP Services Eligible Individuals and Allowables Uses of Funds) can be funded through ADAP ERF. If you have any unallowable costs in your proposed budget, we will deduct them before award.

HRSA encourages you to use a table format with the following sections:

- **Planned Expenditures Summary** listing the amount budgeted by service category and recipient administrative costs.
- **Planned Expenditures by Service Category** with columns for Planned Service, Service Unit Description, Number of Service Units, Number of Clients, and amount budgeted for each service.
- **Service Unit Description** with the definition of the unit of service for the planned service category.

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Work plan narrative

Provide a narrative that describes the following for each planned service and recipient administrative cost identified in the work plan:

- How you will ensure that you will spend funds allocated for each service/activity within the 12-month period of performance.
- If you have an existing ADAP waiting list, how the services/activities will reduce the number of people on the waiting list.
- If you do not have an existing waiting list, how the services/activities will prevent an ADAP waiting list in FY 2026, address a reduction in available resources to fund ADAP, or address a current or projected increase in treatment needs or in the number of clients in the program.

Anticipated impact of ADAP ERF

Briefly describe the anticipated impact of the proposed ADAP ERF-funded planned service(s).

- Describe how you'll monitor progress toward meeting the goals and objectives of the proposed project.
- Describe how these activities will support the continued function of the ADAP.
- Describe the anticipated outcomes resulting from ADAP ERF supported activities.

Monitoring

Briefly describe your methods to monitor and assess the effectiveness of the activities proposed on the ADAP ERF work plan. Describe how the ADAP will measure and monitor progress on outcomes and address problems identified through monitoring.

Important note: We expect you to use your current RWHAP Part B clinical quality management program when implementing services funded through the ADAP ERF award.

Resolving challenges

See merit review criterion 2: Response

State/territory actions to address ADAP challenges

Please describe for each of the following sections how the program has addressed the specific challenges and barriers facing the ADAP through cost-cutting and/or cost-saving strategies in FY 2024 and FY 2025. Support each section with data showing how these strategies benefit the ADAP.

Program efficiencies:

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Please describe any challenges regarding program efficiencies and how your program has addressed challenges, including by using ADAP ERF funding or improving operations to reduce costs and improve efficiency. Support your decision with data showing how the improved operational efficiencies will benefit ADAP.

Ability to enroll clients in other payor sources

Please describe any challenges enrolling clients in other payor sources, and how your program has addressed challenges by improving systems to increase enrollment in Medicare Part D, Medicaid, and other health care coverage options. Be sure to support your decision with data showing how improved enrollment in other payor sources will benefit your ADAP.

Reallocation of ADAP resources

Please describe any challenges or limits with ADAP resources, and whether or how you have reallocated funds to address ADAP challenges. Be sure to indicate whether this reallocation is a one-time augmentation to the program or an expected long-term, sustainable reallocation of funds.

Generation and collection of rebates and program income

Please describe any challenges generating or collecting rebates and program income. Include how your ADAP has modified its processes or monitoring of processes to ensure that you purchase drugs at the best possible cost and/or that you fully collect rebates or program income and apply them back to the RWHAP Part B program, with priority given to ADAP.

Sustainability

See merit review criterion 4: Impact

We expect you to sustain key project elements that improve practices and outcomes for the target population. Propose a plan for project sustainability after the period of federal funding ends.

- Highlight key elements of your projects. Examples include training methods or strategies that have been effective in improving practices.
- Describe the actions you'll take to obtain future sources of funding.
- Determine the timing to become self-sufficient.
- Discuss challenges that you'll likely encounter in sustaining the program. Include how you will resolve these challenges.

Organizational information

See merit review criterion 5: Resources and capabilities

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ADAP oversight and administration

Provide a brief narrative that describes the organizational structure and resources that help the ADAP maintain compliance with legislative requirements and program expectations, including those of ADAP ERF funding. Include an organizational chart for the ADAP as **Attachment 3**.

Compliance with reporting requirements

Describe how you will meet reporting requirements by tracking and reporting ADAP ERF specific expenditures and client utilization.

Budget and budget narrative

See merit review criterion 6: Support requested

Your **budget** should follow the instructions in Section 3.1.4 Project Budget Information – Non-Construction Programs (SF-424A) of the Application Guide and the instructions listed in this section. Your budget should show a well-organized plan.

HHS now uses the definitions for equipment and supply in 2 CFR 200.1. The new definitions change the threshold for equipment to the lesser of the recipient's capitalization level or $10,000 and the threshold for supplies to below that amount.

The total project or program costs are all allowable (direct and indirect) costs used for the HRSA award activity or project. This includes costs charged to the award and non-federal funds used to satisfy a matching or cost-sharing requirement (which may include maintenance of effort, if applicable).

The **budget narrative** supports the information you provide in Standard Form 424-A. See other required forms. It includes an itemized breakdown and a clear justification of the costs you request. The merit review committee reviews both.

As you develop your budget, consider:

- If the costs are reasonable and consistent with your project's purpose and activities.
- The restrictions on spending funds. See funding policies and limitations.

ADAP ERF applicants must also consider the following:

- **Caps on expenses:** Administrative costs for ADAP ERF funding recipients may not exceed 10% of the total grant award. For further guidance , see PCN 15-01: Treatment of Costs under the 10% Administrative Cap for Ryan White HIV/AIDS Program Part A, B, C, and D.
- **Staffing:** Due to the emergent nature of this award, if you need any additional personnel to administer this award, their salaries must fit within the

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administrative cost cap. Usual and ordinary expenses for salaries associated with RWHAP awards must be allocated to the RWHAP Part B award and therefore cannot be allocated to this award.

- **Payor of last resort:** Charges that are billable to third-party payors are unallowable. Third-party payors include Medicaid, Children's Health Insurance Programs (CHIP), Medicare (including Medicare Part D), basic health plans, and private insurance, including those purchased through the Health Insurance Marketplace. The RWHAP is the payor of last resort, and recipients must vigorously pursue alternate sources of payments. HRSA expects recipients to determine eligibility for all clients and to confirm eligibility on a timely basis (please see HAB PCN 21-02: Determining Client Eligibility & Payor of Last Resort in the Ryan White HIV/AIDS Program). Recipients are required to use effective strategies to coordinate with third-party payers that are ultimately responsible for covering the cost of services provided to eligible or covered people.

To create your budget narrative, see detailed instructions in Section 3.1.5 of the Application Guide.

Attachments

See Section 3.2.6 of the Application Guide.

Place your attachments in this order in the Attachments Form. See application checklist to determine if they count toward the page limit.

Attachment 1: Work plan

Attach the project's work plan. Make sure it includes everything required in the work plan section of the project narrative.

Attachment 2: Agreement and compliance assurances

Please complete and include **Appendix D**: Agreements and compliance assurances.

Attachment 3: ADAP organizational chart

Provide a one-page diagram that shows the project's organizational structure.

Attachment 4: ADAP funding and utilization summary for FY 2024

In table format, please provide all information requested in the Need section of the project narrative. A sample table format is provided in **Appendix B**.

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Other required forms

You will need to complete some other forms. Upload the following forms at Grants.gov. You can find them in the NOFO application package or review them and any available instructions at Grants.gov Forms.

Component	Included in page limit*?
☐ Application for Federal Assistance (SF-424)	No
☐ Budget Information for Non-Construction Programs (SF-424A)	No
☐ Project Abstract Summary Form	No
☐ Disclosure of Lobbying Activities (SF-LLL), optional	No
☐ Project/Performance Site Location(s)	No
☐ Grants.gov Lobbying Form	No
☐ Key Contacts	No

Form instructions

Follow the instructions for Application for Federal Assistance in section 3.1 of the Application Guide and any additional instructions provided here.

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Project abstract summary form instructions. Complete the information in the Project Abstract Summary form. Include a short description of your proposed project. Include the needs you plan to address, the proposed services, and the population groups you plan to serve. In addition, provide brief up-to-date information, in this order:

- Brief description of the state ADAP and key environmental factors impacting the program.
- Description of the need for additional resources to:
- Prevent, reduce, or eliminate an ADAP waiting list.
- Address a reduction in available resources to fund ADAP.
- Address a current or projected increase in treatment needs aligned with ending the HIV epidemic in the U.S.
- Address other increases in the number of clients in the program due to new diagnosis, re-engagement in care, loss of income, and/or loss of health care coverage.
- Description of how you plan to use the ADAP ERF, if awarded.

For more information, see Section 3.1.2 of the Application Guide.

Important: public information

When filling out your SF-424 form, pay attention to Box 15: Descriptive Title of Applicant's Project.

We share what you put there with USAspending. This is where the public goes to learn how the federal government spends their money.

Instead of just a title, insert a short description of your project and what it will do.

See instructions and examples.

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Step 4: Understand Review, Selection, and Award Application review

In this step

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Initial review

We will review your application to make sure that it meets eligibility criteria, including the completeness and responsiveness criteria. If your application does not meet these criteria, it will not be funded.

We will not review any pages that exceed the page limit.

Merit review

A panel reviews all applications that pass the initial review. The members use these criteria.

Criterion	Total number of points = 100
1. Need	50 points
2. Response	25 points
3. Impact	10 points
4. Resources and capabilities	5 points
5. Support requested	10 points

Criterion 1: Need

50 points

See the project narrative Introduction and Need sections.

The panel will review your application for how well it:

- Demonstrates the need for additional resources to prevent, reduce, or eliminate a waiting list, to address a reduction in available resources to fund ADAP, or to address a current or projected increase in treatment needs aligned with ending the HIV epidemic in the U.S. or other increases in the number of clients in the program due to new diagnosis, re-engagement in care, loss of income, and/or loss of health care coverage.

Introduction (5 points)

- Describes a feasible plan for how the state/territory will use RWHAP ADAP ERF to prevent, reduce, or eliminate a waiting list, address a reduction in available resources to fund ADAP, or address a current or projected increase in treatment needs or the number of clients in the program.

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State/territory's ADAP profile (20 points)

- Provides a strong, complete, and clear ADAP profile.
- Provides a strong, clear demonstration of need for additional resources by presenting data, including the complete use of available resources, the implementation of cost-cutting and/or cost-saving measures, and/or an increase in clients utilizing the ADAP.

Factors affecting the state/territory ADAP capacity to meet need (25 points)

- Provides a strong, clear narrative (and supporting data) describing the demonstrated need for additional resources to prevent, reduce, or eliminate a waiting list, address a reduction in available resources to fund ADAP, or address a current or projected increase in treatment needs or the number of clients in the program. **(10 points)**
- Provides a strong, clear description of why the ADAP cannot meet the need with existing resources (especially if you report any unobligated or unspent funds), any anticipated funding shortfalls for ADAP, and the cost-cutting measures you would need to implement if you do not receive additional funding. **(15 points)**

Criterion 2: Response

25 points

See the project narrative Approach, High-level work plan, and Resolving challenges sections.

ADAP average annual client costs and forecasting (5 points)

The panel will review your application for the extent to which it provides clear, complete, and compelling descriptions of the following:

- A step-by-step methodology for calculating average cost per client for medication assistance and/or health care coverage assistance, depending on the type of assistance requested.
- Accurate calculations of annual client costs, reflected in your plan and budget.
- The impact of the requested funding on preventing, reducing, or eliminating a waiting list or addressing a current or projected increase in treatment needs or in the number of clients in the program.

Note: If the calculations are incorrect, we will note the error along with its impact on your average client cost calculations and budget request.

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Work plan and work plan narrative (10 points)

The panel will review your application for the extent to which it provides strong and feasible descriptions of:

- The proposed services and projected expenditures to address the problem and align with the project objectives
- Evidence that funds allocated for each service/activity will be spent within the 12-month period of performance.
- For applicants with an ADAP waiting list, proposed services/activities to reduce the number of persons on the waiting list:
  - Proposed services/activities to improve ADAP operations and maximize ADAP resources.
  - Proposed services/activities to prevent a waiting list in FY 2026.

State/territory actions to address ADAP challenges (10 points)

The panel will review your application for the extent to which it provides:

- A strong, clear description of the challenges facing the ADAP in the following areas:
  - Program efficiencies.
  - The ability to enroll clients in other payor sources.
  - Reallocation of ADAP resources.
  - Generation or collection of rebates and program income.
- A strong, clear description of the cost-cutting or cost-saving strategies you have taken in response to these challenges and the extent to which they could achieve program objectives.
- Data demonstrating how these strategies benefit the ADAP.

Criterion 3: Impact

10 points

See the project narrative High-level work plan and Sustainability sections.

The panel will review your application for the extent to which the application provides strong and feasible descriptions of:

- The methods in place to monitor and assess the effectiveness of the activities proposed on the ADAP ERF work plan.
- How the applicant will monitor progress toward meeting the proposed goals and objectives.

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- How the proposed activities support the continued function of the ADAP.
- The anticipated outcomes of the ADAP ERF.

Criterion 4: Resources and capabilities

5 points

See the project narrative Organizational information and Performance reporting and evaluation sections.

The panel will review your application to determine the extent to which it provides a strong and complete description of your ability to implement the ADAP ERF, as evidenced by:

- The organizational structure and resources that administer the ADAP to maintain compliance with legislative requirements and program expectations, including those of ADAP ERF funding.
- The organizational chart for the ADAP in **Attachment 3**.

Criterion 5: Support requested

10 points

See the Budget and budget narrative section.

The panel will review your application to determine:

- How reasonable the proposed budget is for the one-year period of performance.
- How reasonable costs are and how well they align with the project's scope.
- Whether key staff have allotted sufficient time to spend on the project to achieve project objectives.

We do not consider **voluntary** cost sharing during merit review.

Risk review

Before making an award, we review your award history to assess risk. We need to ensure all prior awards were managed well and demonstrated sound business practices. We:

- Review any applicable past performance.
- Review audit reports and findings.
- Analyze the budget.
- Assess your management systems.
- Ensure you continue to be eligible.
- Make sure you comply with any public policies.

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We may ask you to submit additional information.

As part of this review, we use SAM.gov Entity Information Responsibility/Qualification to check your history for all awards likely to be more than $250,000 over the period of performance. You can comment on your organization's information in SAM.gov. We'll consider your comments before making a decision about your level of risk.

If we find a significant risk, we may choose not to fund your application or to place specific conditions on the award.

For more details, see 2 CFR 200.206.

Selection process

When making funding decisions, we consider:

- The amount of available funds.
- Assessed risk.
- Merit review results. These are key in making decisions but are not the only factor.
- The larger portfolio of HRSA-funded projects, project types and geographic distribution.
- The funding preference listed.

We may:

- Fund out of rank order.
- Fund applications in whole or in part.
- Fund applications at a lower amount than requested.
- Decide not to allow a recipient to subaward if they may not be able to monitor and manage subrecipients properly.
- Choose to fund no applications under this NOFO.

Funding preferences

This program includes an ADAP waiting list funding preferences if you demonstrate within the application that you have a current ADAP waiting list, or if you notify the director of DSHAP in writing via EHBs that you have started a waiting list by January 15, 2026. If DSHAP determines that your application meets these criteria, we will move it up in our ranking of fundable applications. Qualifying for a funding preference does not guarantee that you will receive funding.

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Award notices

We issue Notices of Award (NOA) on or around the start date listed in the NOFO. See Section 4 of the Application Guide for more information.

By drawing down funds, you accept the terms and conditions of the award.

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Step 5: Submit Your Application

In this step

Application submission and deadlines 39

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Application submission and deadlines

Your organization's authorized official must certify your application. See the section on finding the application package to make sure you have everything you need.

Make sure you are current with SAM.gov and UEI requirements. When you register or update your SAM.gov registration, you must agree to the financial assistance general certifications and representations, and specifically with regard to grants.

Make sure that your SAM.gov registration is accurate for both contracts and grants, as these registrations differ. See information on getting registered. You will have to maintain your registration throughout the life of any award.

Application Deadlines

You must submit your application by November 3, 2025, at 11:59 p.m. ET.

Grants.gov creates a date and time record when it receives applications.

Submission method

Grants.gov

You must submit your application through Grants.gov. You may do so using Grants.gov Workspace. This is the preferred method. For alternative online methods, see Applicant System-to-System.

For instructions on how to submit in Grants.gov, see the Quick Start Guide for Applicants. Make sure that your application passes the Grants.gov validation checks, or we may not get it. Do not encrypt, zip, or password protect any files.

Have questions? Go to Contacts and Support.

Other submissions

Click or tap here to enter text.

Intergovernmental review

This NOFO is not subject to Executive Order 12372, Intergovernmental Review of Federal Programs. No action is needed.

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Step 6: Learn What Happens After Award

In this step

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Post-award requirements and administration

Administrative and national policy requirements

There are important rules you need to know if you get an award. You must follow:

- All terms and conditions in the Notice of Award (NOA). We incorporate this NOFO by reference.
- The regulations at 2 CFR 200, Uniform Administrative Requirements, Cost Principles, and Audit Requirements for HHS Awards, modifications at 2 CFR 300, and any superseding regulations.
- The HHS Grants Policy Statement (GPS) [PDF]. Your NOA will reference this document. If there are any exceptions to the GPS, they'll be listed in your NOA.
- All federal statutes and regulations relevant to federal financial assistance, including those highlighted in HHS Administrative and National Policy Requirements.
- The requirements for performance management in 2 CFR 200.301 (before October 1, 2025: 45 CFR 75.301).
- HRSA reminds States that therapeutics funded under the ADAP may only be provided "to treat HIV/AIDS or prevent the serious deterioration of health arising from HIV/AIDS in eligible individuals, including measures for the prevention and treatment of opportunistic infections." Section 2616(a) of the Public Health Service (PHS) Act (42 U.S.C. § 300ff–26 (a)). For example, if an ADAP provides sex hormones, it may only allow such hormones to be dispensed to treat HIV/AIDS or prevent the serious deterioration of health arising from HIV/AIDS, rather than for non-statutory purposes such as specified sex-trait modification procedures. HRSA will prioritize funding to States that require clinical documentation and the use of a prior authorization process before sex hormones, are approved for dispensing to ADAP clients.
- HRSA also reminds States that the RWHAP legislation states: "A State shall ensure that any drug rebates received on drugs purchased from funds provided pursuant to this section [ADAP] are applied to activities supported under this subpart [RWHAP Part B], with priority given to activities described under this section [ADAP]." Section 2616(g) of the PHS Act (42 U.S.C. § 300ff–26(g)). As such, all 340B rebates directly generated by a federal dollar are subject to HRSA HAB's rebate policies and rules for expenditure. All rebates generated through ADAP must be

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used for RWHAP Part B activities, with priority given to ADAP, rather than diverted for unsupported activities that exceed the RWHAP's limited statutory purpose, such as for specified sex-trait modification procedures.

Cybersecurity

If awarded, you must develop plans and procedures, modeled after the NIST Cybersecurity framework, to protect HHS systems and data. See details here.

Reporting

If you are funded, you will have to follow the reporting requirements in Section 4 of the Application Guide. The NOA will provide specific details.

You must also follow these program-specific reporting requirements:

- Progress reports semi-annually.
- Other required reports and/or products.
  - **ADAP Data Report (ADR).** If you accept this award, you are indicating that you will comply with data requirements of the ADR and will require that your contractors and subcontractors also comply. The ADR captures information necessary to demonstrate program performance and accountability. Further information will be available in the NOA.
  - **Program Terms Report.** You must submit a Program Terms Report using the format provided in that system. Further information will be available in the NOA.

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Contacts and Support

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Agency contacts

Program and eligibility

Glenn Clark

AIDS Drug Assistance Program (ADAP) Advisor

Attn: Division of State HIV/AIDS Programs

HIV/AIDS Bureau

Health Resources and Services Administration

glclark@hrsa.gov

301-443-6745

Financial and budget

Marie Mehaffey

Grants Management Specialist

Division of Grants Management Operations, OFAAM

Health Resources and Services Administration

mmehaffey@hrsa.gov

301-945-3934

HRSA Contact Center

Open Monday – Friday, 7 a.m. – 8 p.m. ET, except for federal holidays.
Call: 877-464-4772 / 877-Go4-HRSA
TTY: 877-897-9910

Electronic Handbooks Contact Center

Grants.gov

Grants.gov provides 24/7 support. You can call 800-518-4726, search the Grants.gov Knowledge Base, or email Grants.gov for support. Hold on to your ticket number.

SAM.gov

If you need help, you can call 866-606-8220 or live chat with the Federal Service Desk.

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Helpful websites

- HRSA Grants page
- HHS Tips for Preparing Grant Proposals

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Appendices

Appendix A: Model for calculating average client costs

Calculate your projected average cost per client for medication assistance and/or health care coverage assistance for the FY 2026 ADAP ERF period of performance (April 1, 2026, to March 31, 2027). **Important Note:** You only need to provide average costs for clients for the types of assistance you are requesting funding for.

Determine the average cost per client through your own calculations or through the cost calculation template here. Use this calculation to develop your proposed budget for the ADAP ERF funds and/or to project the impact of proposed cost-containment measures. **States/territories must provide the step-by-step calculations and clearly identify all data elements used to complete the calculations, not just the resulting average client cost.**

Due to the timing of this NOFO, the calculations in this model are based on client utilization and ADAP cost data for the January 1, 2025, to June 30, 2025, period. The calculations should include all clients who received at least one medication through ADAP during this period, including clients who were enrolled in ADAP temporarily or for part of the year (for example, because they experienced changes in their health care coverage, moved out of state, or died).

Average cost per client to provide medications

Step 1: Baseline average annual client medication cost

Determine the total amount spent to purchase prescription medications (not health care coverage) from January 1, 2025, to June 30, 2025, period. Divide this amount by the total number of ADAP clients who received at least one prescription medication in that period. Multiply that amount by two to determine the ADAP's baseline average annual medication cost per client.

$$\left(\frac{Total\ amount\ spent\ on\ prescription\ medications\ from\ January\ 1\ to\ June\ 30,\ 2025}{Number\ of\ ADAP\ clients\ who\ received\ at\ least\ 1\ prescription\ medication}\right) \times 2$$

Step 2: Average Annual Client Rebate Reduction:

Determine the total amount of rebate income received by the state/territory.

- If you operate a 340B Rebate State ADAP, this includes all 340B rebates and other negotiated rebates (e.g., ADAP Crisis Task Force rebates) you received in the January 1, 2025 to June 30, 2025 period.

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- If you operate a 340B State Direct Purchase ADAP, this includes all negotiated rebates (e.g., ADAP Crisis Task Force rebates) you received in the January 1, 2025, to June 30, 2025, period.

Divide the total amount of rebate income by the total number of ADAP clients that received at least one prescription medication in the January 1, 2025, to June 30, 2025, period. Multiply that amount by two to determine the average rebate reduction per client.

Note: The health care coverage section below addresses the impact of rebates for health care coverage deductibles and co-payments.

Step 3: Adjusted Average Client Medication Cost:

Subtract the Average Annual Client Rebate Reduction amount determined in Step 2 from the Baseline Average Annual Client Medication Cost determined in Step 1.

Step 4: Average Annual Client Dispensing Fee:

Determine the total number of prescriptions filled in the January 1, 2025, to June 30, 2025, period. Multiply that number by the dispensing fee for a single pharmacy prescription in the January 1, 2025, to June 30, 2025, period. Divide the resulting product by the total number of ADAP clients that received at least one prescription in the same period. Multiply that amount by two for the average annual dispensing fee cost per client.

Step 5: Average Annual Medication Cost per Client:

Add the Average Annual Client Dispensing Fee cost determined in Step 4 to the Adjusted Average Annual Medication Cost calculated in Step 3. The sum of these two amounts will be your State's Average Medication Cost per Client.

Example:

Step	Description	Calculation	Result
Step 1	In the January 1, 2025, to June 30, 2025, period, the ADAP spent a total of $7,410,000 for prescription drugs; a total of 1,000 clients received at least one prescription medication.	$7,410,000 ÷ 1,000 = $7,410 $7,410 × 2 = $14,820	Baseline Average 6-Month Client Medication Cost Baseline Average Annual Client Medication Cost
Step 2	In that same period, the ADAP received $555,000 in total 340B rebates and $100,000 in negotiated rebates.	$555,000 + $100,000 = $655,000 $655,000 ÷ 1,000 = $655 $655 × 2 = $1,310	Total Rebates Received by the ADAP Average 6-Month Client Rebate Reduction

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Step	Description	Calculation	Result
			Average Annual Client Rebate Reduction
Step 3	Adjusted Average Annual Cost per Client: Baseline Average Annual Client Medication Cost minus Average Annual Client Rebate Reduction	$14,820 – $1,310 = $13,510	Adjusted Average Annual Cost per Client
Step 4	The ADAP filled 10,000 prescriptions in the January 1, 2025, to June 30, 2025, period of CY 2025 and the dispensing fee per prescription was $10; 1,000 ADAP clients received at least 1 ADAP prescription.	$10 × 10,000 = $100,000 $100,000 ÷ 1,000 = $100 $100 × 2 = $200	Total Dispensing Fee Expenditures Average 6-Month Client Dispensing Fee Average Annual Client Dispensing Fee
Step 5	Add amount calculated in Step 3 to amount calculated in Step 4.	$13,510 + $200 = $13,710	Average Annual Medication Cost per Client

Note: For States/Territories with Hybrid/Dual ADAPs:

Step 1: *Determine the number and percentage of clients who received medications through the 340B Rebate model and the number and percentage who received medications through the 340B Direct Purchase model.*

Step 2: *For each cohort of clients, determine the total amount spent to provide medications for that cohort.*

Step 3: *Determine the average client costs for the rebate cohort, follow the instructions above in Steps 2 through 5. For the direct purchase cohort, follow the instructions above in Steps 2 through 5.*

II. Average Cost per Client to Provide Health Care Coverage Assistance

All ADAPs providing access to prescription medications through health care coverage assistance must provide step-by-step calculations of average costs per client, making sure all required data elements for each calculation are clearly identified.

Step 1: Total Health Care Coverage Expenditures:

Add the total amount spent on health care coverage premiums, deductibles, and co-payments/co-insurance in the January 1, 2025, to June 30, 2025, period. This includes

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amounts spent for ADAP eligible clients who are also eligible for Medicare Part D, including payments for Part D premiums, deductibles, and co-payments.

Step 2: Rebate Reduction:

Determine the total amount of manufacturer's rebates received in the January 1, 2025, to June 30, 2025, period on health care coverage deductibles and co-payments/co-insurance expenditures.

Step 3: Adjusted 6-Month Total Insurance Cost:

Subtract the total amount of manufacturers' rebates received from the Total Health Care Coverage Expenditures calculated in Step 1. This is your Adjusted 6-Month Total Health Care Coverage Cost.

Step 4: Average Annual Cost per Client for Health Care Coverage Assistance (including COBRA, High Risk Health Insurance Pools, private insurance, State-sponsored insurance, and Medicare Part D):

Divide results from Step 3 by the total number of clients on whose behalf the ADAP paid at least one premium, co-payment/co-insurance or deductible in the January 1, 2025, to June 30, 2025, period. Multiply by two for average annual cost per client for health care coverage assistance.

Example:

The ADAP spent $1,500,000 in the January 1, 2025, to June 30, 2025, period to pay for health care coverage premiums and $300,000 on co-payments/co-insurance and deductibles, providing assistance to 300 ADAP eligible clients.

Step	Description	Calculation	Result
Step 1	Add health care coverage premiums expenditures to expenditures for co-payments/ co-insurance, and deductibles.	$1,500,000 + $300,000 = **$1,800,000**	Total 6-Month Health Care Coverage Expenditures
Step 2	Determine the total amount of rebates received by adding the manufacturers rebates received from January 1, 2025 to June 30, 2025 on health care coverage co-payments/co-insurance/deductibles.	**$50,000**	Total 6-Month Rebates Received
Step 3	Total 6-Month Health Care Coverage Expenditures minus Total 6-Month Rebates Received	$1,800,000 - $50,000 = **$1,750,000**	Adjusted Total Health Care Coverage Cost

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Step	Description	Calculation	Result
Step 4	Divide Adjusted Total Health Care Coverage Cost by total clients served. Multiply the Average 6-Month Cost per Client by two to calculate the Average Annual Cost per Client.	$1,750,000 / 300 = $5,833 $5,833 × 2 = **$11,666**	Average 6-Month Cost Per Client Health Care Coverage Assistance Average Annual Cost Per Client for Health Care Coverage Assistance

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Appendix B: Sample format for ADAP funding and utilization summary for FY 2024

Funding source	Amount received	Amount expended	Amount of unspent funds	Number of undupl. clients served
ADAP base				
ADAP supplemental				
RWHAP Part B base				
RWHAP Part B supplemental				
ADAP ERF				
Part A				
State funds				
Pharmaceutical rebates				
Carryover				
Program oncome				
Other sources (describe)				
Totals for each column				

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Appendix C: Sample format for FY 2026 ADAP Emergency Relief Funds work plan

Section A. Identifying information

Recipient name:	
Person preparing this report:	
Preparer's phone number:	

Section B. Planned expenditure summary

Expenditure type	Amount budgeted
1. Planned expenditures by service category (Section C)	$0
2. Recipient administrative costs (capped at 10%)	
Total amount requested:	**$0**

Section C. Planned expenditures by service category

Services	Service unit description	Number of service units	Number of clients	Amount budgeted
1. Purchase of ADAP medications	1 prescription			
2. Purchase of health insurance premiums	1 coverage month			
3. Payment of medication co-payments, deductibles, or co-insurance	1 payment			

Total Planned Expenditures by Service Category (Reported in Section B): $0

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Appendix D: Agreements and compliance assurances

FY 2026 Ryan White HIV/AIDS Program ADAP Emergency Relief Funds Awards agreements and compliance assurances

I, the Governor of the State or Territory or his/her official designee for the Ryan White HIV/AIDS Part B Program Grant, _____, pursuant to Title XXVI of the Public Health Service Act as amended by the Ryan White HIV/AIDS Treatment Extension Act of 2009, hereby certify that:

Pursuant to §§ 2616 and 311 of the PHS Act, these funds will be used specifically for the provision of medications and the purchase of health care coverage to prevent, reduce, or eliminate an ADAP waiting list or to address shortfalls in ADAP funding for medications and/or the purchase of health care coverage in the State or Territory.

These funds and services will be allocated and administered in accordance with the *FY 2026 Part B Ryan White HIV/AIDS Program Agreements and Compliance Assurances* submitted to the Health Resources and Services Administration.

SIGNED: _____ **Title:** _____

Governor or Official Designee

Date: _____

EXHIBIT E

Presidential Documents

Executive Order 14168 of January 20, 2025

Defending Women From Gender Ideology Extremism and Restoring Biological Truth to the Federal Government

By the authority vested in me as President by the Constitution and the laws of the United States of America, including section 7301 of title 5, United States Code, it is hereby ordered:

Section 1. *Purpose.* Across the country, ideologues who deny the biological reality of sex have increasingly used legal and other socially coercive means to permit men to self-identify as women and gain access to intimate single-sex spaces and activities designed for women, from women's domestic abuse shelters to women's workplace showers. This is wrong. Efforts to eradicate the biological reality of sex fundamentally attack women by depriving them of their dignity, safety, and well-being. The erasure of sex in language and policy has a corrosive impact not just on women but on the validity of the entire American system. Basing Federal policy on truth is critical to scientific inquiry, public safety, morale, and trust in government itself.

This unhealthy road is paved by an ongoing and purposeful attack against the ordinary and longstanding use and understanding of biological and scientific terms, replacing the immutable biological reality of sex with an internal, fluid, and subjective sense of self unmoored from biological facts. Invalidating the true and biological category of ''woman'' improperly transforms laws and policies designed to protect sex-based opportunities into laws and policies that undermine them, replacing longstanding, cherished legal rights and values with an identity-based, inchoate social concept.

Accordingly, my Administration will defend women's rights and protect freedom of conscience by using clear and accurate language and policies that recognize women are biologically female, and men are biologically male.

Sec. 2. *Policy and Definitions.* It is the policy of the United States to recognize two sexes, male and female. These sexes are not changeable and are grounded in fundamental and incontrovertible reality. Under my direction, the Executive Branch will enforce all sex-protective laws to promote this reality, and the following definitions shall govern all Executive interpretation of and application of Federal law and administration policy:

(a) ''Sex'' shall refer to an individual's immutable biological classification as either male or female. ''Sex'' is not a synonym for and does not include the concept of ''gender identity.''

(b) ''Women'' or ''woman'' and ''girls'' or ''girl'' shall mean adult and juvenile human females, respectively.

(c) ''Men'' or ''man'' and ''boys'' or ''boy'' shall mean adult and juvenile human males, respectively.

(d) ''Female'' means a person belonging, at conception, to the sex that produces the large reproductive cell.

(e) ''Male'' means a person belonging, at conception, to the sex that produces the small reproductive cell.

(f) ''Gender ideology'' replaces the biological category of sex with an ever-shifting concept of self-assessed gender identity, permitting the false claim that males can identify as and thus become women and vice versa, and requiring all institutions of society to regard this false claim as true.

Gender ideology includes the idea that there is a vast spectrum of genders that are disconnected from one's sex. Gender ideology is internally inconsistent, in that it diminishes sex as an identifiable or useful category but nevertheless maintains that it is possible for a person to be born in the wrong sexed body.

(g) ''Gender identity'' reflects a fully internal and subjective sense of self, disconnected from biological reality and sex and existing on an infinite continuum, that does not provide a meaningful basis for identification and cannot be recognized as a replacement for sex.

Sec. 3. *Recognizing Women Are Biologically Distinct From Men.* (a) Within 30 days of the date of this order, the Secretary of Health and Human Services shall provide to the U.S. Government, external partners, and the public clear guidance expanding on the sex-based definitions set forth in this order.

(b) Each agency and all Federal employees shall enforce laws governing sex-based rights, protections, opportunities, and accommodations to protect men and women as biologically distinct sexes. Each agency should therefore give the terms ''sex'', ''male'', ''female'', ''men'', ''women'', ''boys'' and ''girls'' the meanings set forth in section 2 of this order when interpreting or applying statutes, regulations, or guidance and in all other official agency business, documents, and communications.

(c) When administering or enforcing sex-based distinctions, every agency and all Federal employees acting in an official capacity on behalf of their agency shall use the term ''sex'' and not ''gender'' in all applicable Federal policies and documents.

(d) The Secretaries of State and Homeland Security, and the Director of the Office of Personnel Management, shall implement changes to require that government-issued identification documents, including passports, visas, and Global Entry cards, accurately reflect the holder's sex, as defined under section 2 of this order; and the Director of the Office of Personnel Management shall ensure that applicable personnel records accurately report Federal employees' sex, as defined by section 2 of this order.

(e) Agencies shall remove all statements, policies, regulations, forms, communications, or other internal and external messages that promote or otherwise inculcate gender ideology, and shall cease issuing such statements, policies, regulations, forms, communications or other messages. Agency forms that require an individual's sex shall list male or female, and shall not request gender identity. Agencies shall take all necessary steps, as permitted by law, to end the Federal funding of gender ideology.

(f) The prior Administration argued that the Supreme Court's decision in *Bostock* v. *Clayton County* (2020), which addressed Title VII of the Civil Rights Act of 1964, requires gender identity-based access to single-sex spaces under, for example, Title IX of the Educational Amendments Act. This position is legally untenable and has harmed women. The Attorney General shall therefore immediately issue guidance to agencies to correct the misapplication of the Supreme Court's decision in *Bostock* v. *Clayton County* (2020) to sex-based distinctions in agency activities. In addition, the Attorney General shall issue guidance and assist agencies in protecting sex-based distinctions, which are explicitly permitted under Constitutional and statutory precedent.

(g) Federal funds shall not be used to promote gender ideology. Each agency shall assess grant conditions and grantee preferences and ensure grant funds do not promote gender ideology.

Sec. 4. *Privacy in Intimate Spaces.* (a) The Attorney General and Secretary of Homeland Security shall ensure that males are not detained in women's prisons or housed in women's detention centers, including through amendment, as necessary, of Part 115.41 of title 28, Code of Federal Regulations and interpretation guidance regarding the Americans with Disabilities Act.

(b) The Secretary of Housing and Urban Development shall prepare and submit for notice and comment rulemaking a policy to rescind the final rule entitled ''Equal Access in Accordance with an Individual's Gender Identity in Community Planning and Development Programs'' of September 21, 2016, 81 FR 64763, and shall submit for public comment a policy protecting women seeking single-sex rape shelters.

(c) The Attorney General shall ensure that the Bureau of Prisons revises its policies concerning medical care to be consistent with this order, and shall ensure that no Federal funds are expended for any medical procedure, treatment, or drug for the purpose of conforming an inmate's appearance to that of the opposite sex.

(d) Agencies shall effectuate this policy by taking appropriate action to ensure that intimate spaces designated for women, girls, or females (or for men, boys, or males) are designated by sex and not identity.

Sec. 5. *Protecting Rights.* The Attorney General shall issue guidance to ensure the freedom to express the binary nature of sex and the right to single-sex spaces in workplaces and federally funded entities covered by the Civil Rights Act of 1964. In accordance with that guidance, the Attorney General, the Secretary of Labor, the General Counsel and Chair of the Equal Employment Opportunity Commission, and each other agency head with enforcement responsibilities under the Civil Rights Act shall prioritize investigations and litigation to enforce the rights and freedoms identified.

Sec. 6. *Bill Text.* Within 30 days of the date of this order, the Assistant to the President for Legislative Affairs shall present to the President proposed bill text to codify the definitions in this order.

Sec. 7. *Agency Implementation and Reporting.* (a) Within 120 days of the date of this order, each agency head shall submit an update on implementation of this order to the President, through the Director of the Office of Management and Budget. That update shall address:

(i) changes to agency documents, including regulations, guidance, forms, and communications, made to comply with this order; and

(ii) agency-imposed requirements on federally funded entities, including contractors, to achieve the policy of this order.

(b) The requirements of this order supersede conflicting provisions in any previous Executive Orders or Presidential Memoranda, including but not limited to Executive Orders 13988 of January 20, 2021, 14004 of January 25, 2021, 14020 and 14021 of March 8, 2021, and 14075 of June 15, 2022. These Executive Orders are hereby rescinded, and the White House Gender Policy Council established by Executive Order 14020 is dissolved.

(c) Each agency head shall promptly rescind all guidance documents inconsistent with the requirements of this order or the Attorney General's guidance issued pursuant to this order, or rescind such parts of such documents that are inconsistent in such manner. Such documents include, but are not limited to:

(i) ''The White House Toolkit on Transgender Equality'';

(ii) the Department of Education's guidance documents including:

(A) ''2024 Title IX Regulations: Pointers for Implementation'' (July 2024);

(B) ''U.S. Department of Education Toolkit: Creating Inclusive and Nondiscriminatory School Environments for LGBTQI+ Students'';

(C) ''U.S. Department of Education Supporting LGBTQI+ Youth and Families in School'' (June 21, 2023);

(D) ''Departamento de Educación de EE.UU. Apoyar a los jóvenes y familias LGBTQI+ en la escuela'' (June 21, 2023);

(E) ''Supporting Intersex Students: A Resource for Students, Families, and Educators'' (October 2021);

(F) ''Supporting Transgender Youth in School'' (June 2021);

(G) ''Letter to Educators on Title IX's 49th Anniversary'' (June 23, 2021);

(H) ''Confronting Anti-LGBTQI+ Harassment in Schools: A Resource for Students and Families'' (June 2021);

(I) ''Enforcement of Title IX of the Education Amendments of 1972 With Respect to Discrimination Based on Sexual Orientation and Gender Identity in Light of Bostock v. Clayton County'' (June 22, 2021);

(J) ''Education in a Pandemic: The Disparate Impacts of COVID–19 on America's Students'' (June 9, 2021); and

(K) ''Back-to-School Message for Transgender Students from the U.S. Depts of Justice, Education, and HHS'' (Aug. 17, 2021);

(iii) the Attorney General's Memorandum of March 26, 2021 entitled ''Application of *Bostock* v. *Clayton County* to Title IX of the Education Amendments of 1972''; and

(iv) the Equal Employment Opportunity Commission's ''Enforcement Guidance on Harassment in the Workplace'' (April 29, 2024).

Sec. 8. *General Provisions.* (a) Nothing in this order shall be construed to impair or otherwise affect:

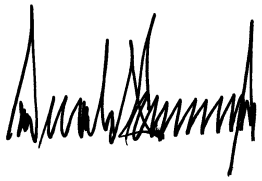
(i) the authority granted by law to an executive department or agency, or the head thereof; or

(ii) the functions of the Director of the Office of Management and Budget relating to budgetary, administrative, or legislative proposals.

(b) This order shall be implemented consistent with applicable law and subject to the availability of appropriations.

(c) This order is not intended to, and does not, create any right or benefit, substantive or procedural, enforceable at law or in equity by any party against the United States, its departments, agencies, or entities, its officers, employees, or agents, or any other person.

(d) If any provision of this order, or the application of any provision to any person or circumstance, is held to be invalid, the remainder of this order and the application of its provisions to any other persons or circumstances shall not be affected thereby.



THE WHITE HOUSE,
January 20, 2025.

[FR Doc. 2025–02090
Filed 1–29–25; 11:15 am]
Billing code 3395–F4–P

EXHIBIT F

TRANSGENDER

Medical Association Statements in Support of Health Care for Transgender People and Youth

By **GLAAD** - June 26, 2024 23 Mins Read



Transgender Flag, Getty

Original article posted June 21,2023

Every major medical association and leading world health authority supports health care for transgender people and youth. They are also increasingly speaking out against the disinformation being spread by opponents of this care. Below are excerpts from 30+ organizations' statements.

Reporters covering state bills and other discussions about this care have an obligation to note that every major medical association supports health care for transgender people and youth as safe and lifesaving.

The following have issued statements in support of health care for transgender people and youth:

American Academy of Child and Adolescent Psychiatry

American Academy of Dermatology

American Academy of Pediatrics

American Academy of Physician Assistants

American Medical Association

American Nurses Association

American Association of Clinical Endocrinology

American Association of Geriatric Psychiatry

American College Health Association

American College of Nurse-Midwives

American College of Obstetricians and Gynecologists

American College of Physicians

American Counseling Association

American Heart Association

American Medical Student Association

American Psychiatric Association

American Psychological Association

American Society of Plastic Surgeons

American Society for Reproductive Medicine

American Urological Association

Endocrine Society

Federation of Pediatric Organizations

GLMA: Health Professionals Advancing LGBTQ Equality

The Journal of the American Medical Association

National Association of Nurse Practitioners in Women's Health

National Association of Social Workers

Ohio Children's Hospital

Pediatric Endocrine Society

Pediatrics (Journal of the American Academy of Pediatrics) and Seattle Children's Hospital

Texas Medical Association

Texas Pediatric Society

United States Professional Association for Transgender Health (USPATH)

World Health Organization (WHO)

World Medical Association

World Professional Association for Transgender Health

In the December 23 issue of the journal Pediatrics, doctors from Seattle Children's Hospital published an article that describes bans on care for transgender youth as a form of child abuse.

In *"Prohibition of Gender-Affirming Care as a Form of Child Maltreatment: Reframing the Discussion,"* the authors write: "These legislative efforts operate under the guise of protecting children. In reality, they punish caregivers and physicians when they choose to support children. They deny children access to routine health care that has been shown to decrease dramatically high rates of suicide and depression for TGD (transgender and gender diverse) youth. They fuel discriminatory rhetoric, which negatively impacts the mental health of TGD children and imperils their safety."

Ohio Children's Hospital submitted testimony to the Ohio state Senate in December 2023 in defense of transgender health care for youth and against Ohio's HB68, which sought to ban it:

"It is so unfathomable to hear the statements made regarding what pediatric providers do and don't do when treating youth who are expressing a conflict between the sex they were assigned at birth and the gender with which they identify. This false narrative is intended to incite fear in order to take away parental rights and restrict health care," wrote Associate Chief Medical Officer for Behavioral Health at Ohio Children's Hospital-Dayton, Kelly Blankenship.

"At Dayton Children's Hospital, all service lines within our hospital follow national standards of care to ensure quality, safety, and deliver best outcomes," Blankenship continued. "All care delivered is age-appropriate, and aligned with clinical practice guidelines based on research… Our health care providers evaluate all symptoms, and patients are screened and evaluated for all comorbid mental health conditions before determining if treatment is needed. We seek to ensure that the decision of each parent is informed by medically sound information and is free from coercion or undue influence. Again, Dayton Children's does not perform hysterectomies, or any genital surgeries, as part of gender affirming medical care. The care provided by the medical and mental health professionals at Dayton Children's is all evidence-based. We believe all young people should have access to comprehensive, developmentally appropriate, mental health care

and gender-affirming health care provided in a safe and inclusive environment. Transgender children, adolescents, and their families deserve care that is grounded in science, compassion and ethics."

Nick Lashutka, President and CEO of the Ohio Children's Hospital, submitted additional testimony in May 2023: "The allegations made against children's hospitals by supporters of HB 68 are deeply offensive and disappointing. Children's hospitals across Ohio are filled with pediatric experts who have dedicated their lives to caring for kids."

"Here are the facts." Lashutka continued, "1. Children's hospitals in Ohio have responded to a need in the community to serve a very small, but complex population. 2. All medical gender dysphoria treatment requires parental consent. It is supported by a multi-disciplinary team of professionals, including pediatric specialists in psychiatry, adolescent medicine, and endocrinology. 3. Again, we DO NOT perform surgeries on minors for the condition of gender dysphoria. 4. Individuals diagnosed with gender dysphoria are consistent, persistent, and insistent for a lengthy period of time. The notion that kids declare a feeling and are immediately medicated at one of our clinics is false. 5. Patients do not self-diagnose their gender dysphoria; they present with symptoms of gender dysphoria. Their health care providers evaluate these symptoms, and only their health care providers make diagnoses. 6. All comorbid mental health conditions are screened and evaluated before determining if additional treatment is needed. 7. Patients do not receive blockers or hormones at their first appointment."

On June 12, 2023, The American Medical Association passed a resolution drafted by The Endocrine Society to protect access to evidence-based care for transgender and gender-diverse youth, noting "it is the responsibility of the medical community to speak out in support of evidence-based care. Medical decisions should be made by patients, their relatives and health care providers, not politicians."

The resolution was cosponsored by:

- The American Academy of Pediatrics
- The American College of Obstetricians and Gynecologists
- The American Urological Association
- The American Society for Reproductive Medicine
- The American College of Physicians

- The American Association of Clinical Endocrinology
- GLMA: Health Professionals Advancing LGBTQ+ Equality
- the AMA's Medical Student Section

The resolution stated the widespread misinformation and bans on care "do not reflect the research landscape. More than 2,000 scientific studies have examined aspects of gender-affirming care since 1975, including more than 260 studies cited in the Endocrine Society's Clinical Practice Guideline."

Additional excerpts from organization statements:

American Academy of Child and Adolescent Psychiatry: "The AAP's 2018 policy statement 'Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents' defines gender affirmation as developmentally appropriate, nonjudgmental, supportive care provided in a safe clinical space. The policy states that pediatric providers, often the first medical professionals to discover a child's gender identity concerns, have a special role in caring for these patients who have a high risk of depression, anxiety and suicide. The care model is not one-size-fits-all, said Brittany Allen, M.D., FAAP, a member of the AAP Section on LGBTQ Executive Committee. It recognizes the wide spectrum of normal, healthy gender identities." *(January 6, 2022)*

American Academy of Child and Adolescent Psychiatry: "(AACAP) supports the use of current evidence-based clinical care with minors. AACAP strongly opposes any efforts – legal, legislative, and otherwise – to block access to these recognized interventions. Blocking access to timely care has been shown to increase youths' risk for suicidal ideation and other negative mental health outcomes. Consistent with AACAP's policy against conversion therapy, AACAP recommends that youth and their families formulate an individualized treatment plan with their clinician that addresses the youth's unique mental health needs under the premise that all gender identities and expressions are not inherently pathological." *(November 8, 2019)*

American Academy of Dermatology: "The AADA recognizes the dignity and identity of transgender individuals and advocates for dermatologists' ability to provide therapy and procedures that help the mental and physical well-being of these and all patients. Transgender and gender-diverse individuals can benefit greatly from medical and surgical gender-affirming treatments. These treatments are often medically necessary for the health and well-being of

these patients and are not to be considered as cosmetic or elective. Decisions about care should remain within the confines of the physician-patient relationship, guided by strong medical evidence and the best interests of the individual patient." *(June 1, 2021)*

American Medical Association: "Empirical evidence has demonstrated that trans and non-binary gender identities are normal variations of human identity and expression. For gender diverse individuals, standards of care and accepted medically necessary services that affirm gender or treat gender dysphoria may include mental health counseling, non-medical social transition, gender-affirming hormone therapy, and/or gender-affirming surgeries. Clinical guidelines established by professional medical organizations for the care of minors promote these supportive interventions based on the current evidence and that enable young people to explore and live the gender that they choose. Every major medical association in the United States recognizes the medical necessity of transition-related care for improving the physical and mental health of transgender people." *(April 26, 2021)*

The American Medical Association passed a resolution drafted by The Endocrine Society to protect access to evidence-based gender-affirming care for transgender and gender-diverse youth. *(June 12, 2023)*

American Nurses Association: "The American Nurses Association strongly opposes any legislation or policy action that places restrictions on transgender health care and that criminalizes gender-affirming care. Due to recent state legislative efforts, transgender and gender-diverse youth and their parents or guardians who choose to access gender-affirming care may come under legal assault in many states. Health care professionals, including nurses and advanced practice registered nurses (APRNs) who provide gender-affirming care, may also be subject to judicial process or other legal action. These restrictive laws interfere with the trust and confidentiality between patients, parents or guardians, and clinicians in the delivery of evidence-based care. The legislative intent and medical claims behind these laws are not grounded in reputable science and conflict with the nurse's obligation to promote, advocate, and protect the rights, health, and safety of patients. ANA's Position Statement Nursing Advocacy for LGBTQ+ Populations (2018) underlines the mandate that nurses "must deliver culturally congruent care and advocate for lesbian, gay, bisexual, transgender, queer, or questioning (LGBTQ+) populations." *(October 26, 2022)*

American Academy of Pediatrics*:* "There is strong consensus among the most prominent medical organizations worldwide that evidence-based, gender-affirming care for transgender

children and adolescents is medically necessary and appropriate. It can even be lifesaving. The decision of whether and when to start gender-affirming treatment, which does not necessarily lead to hormone therapy or surgery, is personal and involves careful consideration by each patient and their family." *(August 10, 2022)*

American Academy of Pediatrics: "The American Academy of Pediatrics recommends that youth who identify as transgender have access to comprehensive, gender-affirming, and developmentally appropriate health care that is provided in a safe and inclusive clinical space. We also recommend that playing on sports teams helps youth develop self-esteem, correlates positively with overall mental health, and appears to have a protective effect against suicide. These bills not only ignore these recommendations, they undermine them." *(March 16, 2021)*

American Academy of Physician Assistants*:* "All the undersigned associations have adopted policies or otherwise support addressing the specific health concerns of LGBTQ people, including opposition to discrimination in health care and insurance coverage based on an individual's sexual orientation or gender identity. As part of that commitment, our organizations support public and private health insurance coverage for the treatment of gender dysphoria when medically necessary." *(Signatories: American Academy of Nursing, American Academy of PAs, American Academy of Pediatrics, American Academy of Psychiatry and The Law American Association for Geriatric Psychiatry, American College Health Association, American College of Physicians, American Medical Association, American Medical Student Association, American Medical Women's Association, American Nurses Association, American Pediatric Surgical Association) (May 24, 2019)*

American Association of Clinical Endocrinology: "Transgender and gender diverse people represent a sizable and growing segment of the U.S. and world Population. It is estimated that over 1 million people in the U.S. alone are transgender or gender diverse. Many transgender and gender diverse people seek hormone therapy under the supervision of an endocrinologist or other medically trained health care professional to better align their bodies with their gender identities. Being transgender is widely accepted to require medical treatment for those patients who seek it. Medical treatment may include behavioral assessment, hormone therapy, and surgery. These treatments are well established in the relevant established, international professional society guidelines including those from the Endocrine Society co-sponsored by the American Association of Clinical Endocrinology (AACE) and the World Professional Association for Transgender Health (WPATH)." *(March 7, 2022)*

American Association of Geriatric Psychiatry: "With the overarching goals of improving the healthcare of older transgender individuals and of inspiring pertinent clinical research, a session at the 2017 American Association for Geriatric Psychiatry Annual Meeting focused on an interdisciplinary approach to transgender aging. The older the transgender adult, the more likely the individual grew up in a historical context when there was greater social stigma towards their gender identity, even among mental health professionals... In spite of notable health disparities, some evidence points to resilience among transgender older adults. The mental health professional often serves as the first contact for a patient who is struggling with gender identity." *(February 7, 2018)*

American College Health Association: "As a society, we have made significant strides in removing barriers and improving health care and outcomes for transgender and gender diverse patients. Individuals feel more comfortable disclosing their authentic gender and are doing so at younger ages. Health care services should be made universal to all and should not discriminate in any way, whether this be on age; race/ethnicity, sex; sexual orientation; gender (including gender identity); marital status; physical size; religious, spiritual or cultural identity; psychological/physical/learning disability; socioeconomic status; or veteran status. This is consistent with the long-held values of cultural inclusion, respect, equality, and equity that ACHA has advocated for. Therefore, ACHA opposes any legislation, both state or federal, that would restrict or limit access to gender-related medically necessary services for transgender youth and adults." *(February 8, 2023)*

American College of Nurse-Midwives: The American College of Nurse-Midwives (ACNM) supports efforts to provide transgender and gender non-binary (TGNB) people with access to safe, comprehensive, culturally-responsive, and respectful health care. ACNM is committed to taking the following actions: Incorporating gender-inclusive language into ACNM documents. Offering educational opportunities to members of the midwifery community on how to care for TGNB people. Advancing legislation and policies that prohibit discrimination based on gender expression and/or identity. Supporting measures to ensure TGNB people have comprehensive and unrestricted access to health insurance coverage. *(March 2021)*

American College of Obstetricians and Gynecologists: "The American College of Obstetricians and Gynecologists opposes discrimination on the basis of gender identity, urges public and private health insurance plans to cover necessary services for individuals with gender dysphoria, and advocates for inclusive, thoughtful, and affirming care for transgender individuals." *(January 2017)*

American College of Physicians*:* "A growing number of states are banning gender-affirming health care and pursuing anti-LGBTQ+ legislation, contrary to ACP policy, which urges non-discrimination in health care. ACP opposes these restrictions on health care for transgender individuals, who already may face extreme barriers to accessing care, and strongly objects to any unnecessary government interference with any health care services." *(April 24, 2023)*

American Counseling Association: "The American Counseling Association (ACA) is committed to nondiscrimination and prevention of harassment in all forms (verbal, physical, sexual, emotional, and psychological), including protections for all diverse groups including protections for transgender and nonbinary individuals. ACA recognizes the stress and psychological impact of discrimination and is committed to helping counselors advocate for nondiscrimination policies and practices in their schools, colleges/universities, clinical mental health settings, communities, and in the nation." *(March 29, 2019)*

American Heart Association: The AHA opposed the repeal of transgender-specific protections under Section 1557 of the Affordable Care Act noting: "Transgender people also face a high degree of insurance discrimination. Historically, many plans have used transgender-specific exclusions to deny transgender people coverage for medically necessary care—including hormone therapy, mental health counseling, and surgeries—even though the same services are routinely covered for non-transgender individuals... These experiences of healthcare and health insurance discrimination contribute to significant health disparities." *(September 2019)*

American Medical Student Association: "AMSA adamantly opposes treatment policies that discriminate against patients based on their sexual orientation and gender identity, or that inhibit their access to quality care. Health care for transgender people should be individualized, holistic, and comprehensive – including, but not limited to surgical treatment– and transgender persons in the military should be allowed to openly undergo gender transition and be eligible for the equitable benefits and rights afforded to cisgender service personnel, including health care." *(August 2017)*

American Medical Women's Association: The American Medical Women's Association (AMWA) supports the US Department of Health and Human Services adopting revisions to Section 1557 of the Affordable Care Act that codify protections for LGBTQ+ people from mistreatment by physicians, other clinicians, and insurers. Adopting this rule will restore and strengthen protections for LGBTQ+ people by clarifying that the definition of "sex" discrimination applies to discrimination based on sex characteristics, intersex traits, and pregnancy and pregnancy

termination, and aligns with federal court decisions prohibiting discrimination based on gender identity and sexual orientation. AMWA urges adoption of these crucial protections.

American Psychiatric Association: "Our organizations, which represent nearly 600,000 physicians and medical students, oppose any laws and regulations that discriminate against transgender and gender-diverse individuals or interfere in the confidential relationship between a patient and their physician. That confidentiality is critical to allow patients to trust physicians to properly counsel, diagnose and treat. Our organizations are strongly opposed to any legislation or regulation that would interfere with the provision of evidence-based patient care for any patient, affirming our commitment to patient safety. We recognize health as a basic human right for every person, regardless of gender identity or sexual orientation." *(Joint statement with the American Academy of Family Physicians, American Academy of Pediatrics, American College of Physicians, American College of Obstetricians and Gynecologists, American Osteopathic Association; April 2, 2021)*

American Society of Plastic Surgeons: "The delivery of gender affirming care is not a political issue, but rather a health care issue – Gender dysphoria is a medical diagnosis, not a political choice. ASPS firmly believes that plastic surgery services can help gender dysphoria patients align their bodies with whom they know themselves to be and improve their overall mental health and well-being. The Society will continue its efforts to advocate for full access to medically necessary transition care and stand up to those who oppose it – from the board rooms of big tech to Capitol Hill." *(June 22, 2021)*

American Urological Association: "The AUA is committed to the principle that medical decision-making for transgender children is the responsibility of parents acting in their child's best interest to ensure their physical and mental health, safety and well-being, and that consultation with medical professionals and education via medically safe (respected, peer-reviewed) resources must not be legislated or criminalized."

Federation of Pediatric Organizations: "We stand with pediatricians who partner with families every day to make the best possible decision for each individual child based on available research and evidence pertinent to that child's care. Transgender and gender-diverse children and youth deserve to lead safe, healthy lives in environments that allow them to be their authentic selves. That can only happen if physicians are allowed to treat these children in the same manner, and with the same respect, that we expect them to treat every other child. Our

mission to advance child health will succeed only if we work to improve health outcomes for all children." *(March 28, 2022*)

GLMA: Health Professionals Advancing LGBTQ Equality: Many but not all transgender people experience gender dysphoria, a medical condition defined by the American Psychiatric Association as a "conflict between a person's physical or assigned gender and the gender with which he/she/they identify." Standards of care and accepted medically necessary services that affirm gender or treat gender dysphoria may include but are not limited to mental health counseling, non-medical social transition, gender-affirming hormone therapy, and/or gender-affirming surgeries. Every major medical association in the United States recognizes the medical necessity of transition-related care for improving the physical and mental health of transgender people and has called for health insurance coverage for treatment of gender dysphoria." *(March 2019)*

The Journal of the American Medical Association: "Transgender and gender diverse patients should receive nonjudgmental care from appropriately trained health care professionals. Gender-affirming primary care includes preventive care, mental health and substance use disorder screening, hormone therapy, and education about nonmedical/nonsurgical gender-affirming interventions. *(September 15, 2022)*

National Association of Nurse Practitioners in Women's Health: "The National Association of Nurse Practitioners in Women's Health (NPWH) affirms each individual's right to quality, evidence-based sexual and reproductive healthcare and celebrates diversity of sexuality, gender identity, and gender expression. NPWH is committed to providing quality sexual and reproductive healthcare to all individuals, regardless of gender identity or expression... Transgender and Gender Diverse individuals have a right to care that aligns with and affirms their gender identity." *(May 2022)*

National Association of Social Workers: Gender-Affirming Health Care Saves Lives: "The National Association of Social Workers (NASW) asserts that discrimination and prejudice directed against any individuals on the basis of gender identity or expression are damaging to the social, emotional, psychological, physical and economic well-being of transgender and gender diverse (TGD) people and society as a whole. The unprecedented increase in legislation focused on TGD youth seeking affirming health care, the professionals who provide their medical care, and the families and social supports that offer resources to them is an unfortunate indicator of the lack of understanding and misinformation that currently exists... NASW will work to repeal

discriminatory legislation and regulations that do not honor someone's self-identified gender identity, transgender-inclusive health care access, health insurance options, or use of language promoting health equity and inclusive communication."

Pediatric Endocrine Society: "Bills that threaten the health of transgender and gender diverse (TGD) youth have been introduced in multiple state legislatures across the United States. These bills undermine medical recommendations and seek to criminalize health care professionals who provide gender-affirming care such as puberty suppressing medications and gender-affirming hormone therapy. We caution legislators and the public that the support and implementation of these bills will worsen mental health, increase the risk of suicide, and contribute to poorer overall health in our TGD patients. Such bills contradict evidence-based Standards of Care recommendations from the Pediatric Endocrine Society as well as Position Statements from several national and international medical associations with expertise in the care of TGD youth, such as the American Academy of Pediatrics, the Endocrine Society, the American Academy of Child and Adolescent Psychiatry, the American Psychiatric Association and the World Professional Association for Transgender Health. The Pediatric Endocrine Society recommends an affirmative model of care that supports one's gender identity, and follows a multidisciplinary approach that includes involvement of mental health professionals, patients and their families. Puberty suppression and/or gender-affirming hormone therapy is recommended within this evidence-based approach on a case-by-case basis as medically necessary and is potentially lifesaving. The implementation of these recommendations has been demonstrated to improve the psychological health and well-being of TGD youth." *(April 2021)*

Texas Medical Association: "filed friend-of-the-court brief in the case in support of medically necessary, gender-affirming care, and opposing the criminalization of such treatment... TMA's brief addresses "the acceptance and medical necessity of gender-affirming care for adolescents with gender dysphoria" and raises concerns the state actions "will create barriers in access to care for transgender adolescents, a vulnerable population that already faces barriers in access to care. The full range of evidence and the current recommendations developed by the American Academy of Pediatrics, and affirmed by every major American medical association, supports the medical necessity and appropriateness of providing gender-affirming support and care to transgender youth and adolescents. Medical care for transgender youth and adolescents is evidence-based and has proven effectiveness." *(March 10, 2022)*

Texas Pediatric Society: Statement opposing Actions in Texas Threatening Health of Transgender Youth: **"**TPS has long-advocated against prohibitions on gender-affirming care in

Texas. For young people who identify as transgender, studies show that gender-affirming care can reduce emotional distress, improve their sense of well-being and reduce the risk of suicide. "Evidence-based medical care for transgender and gender diverse children is a complex issue that pediatricians are uniquely qualified to provide. This directive undermines the physician-patient-family relationship and will cause undue harm to children in Texas. TPS opposes the criminalization of evidence-based, gender-affirming care for transgender youth and adolescents. We urge the prioritization of the health and well-being of all youth, including transgender youth."

United States Professional Association for Transgender Health (USPATH): "USPATH and the World Professional Association for Transgender Health (WPATH) denounces the emergency regulation halting gender-affirming healthcare for transgender and gender diverse (TGD) children and adolescents issued by Missouri Attorney General Andrew Bailey as lacking scientific grounding. The WPATH Standards of Care for the Health of Transgender and Gender Diverse People, now in its 8th version (SOC8), is the foremost evidence-based guideline for the provision of TGD healthcare. SOC8 is based on the best available science with input from over 100 global medical professionals and experts and represents best-practice guidelines for the provision of gender-affirming healthcare. Gender-affirming interventions are based on decades of clinical experience and research and are not considered experimental. Gender affirming hormone therapy (GAHT) is a component of widely accepted medically necessary care for TGD people." *(March 22, 2023)*

World Health Organization (WHO): "WHO's role, to promote health for all, means it is committed to inclusive healthcare and equitable access for trans, gender diverse and all other people... Our fight is for #HealthForAll" (28), demonstrating WHO's highest level commitment to support countries to attend to the health needs of transgender and gender diverse people."

World Medical Association: "The WMA emphasizes that everyone has the right to determine one's own gender and recognizes the diversity of possibilities in this respect. The WMA calls for physicians to uphold each individual's right to self-identification with regard to gender. The WMA asserts that gender incongruence is not in itself a mental disorder; however, it can lead to discomfort or distress, which is referred to as gender dysphoria (DSM-5). The WMA affirms that, in general, any health-related procedure or treatment related to an individual's transgender status, e.g. surgical interventions, hormone therapy or psychotherapy, requires the freely given informed and explicit consent of the patient. The WMA urges that every effort be made to make individualized, multi-professional, interdisciplinary and affordable transgender healthcare (including speech therapy, hormonal treatment, surgical interventions and mental healthcare)

available to all people who experience gender incongruence in order to reduce or to prevent pronounced gender dysphoria." *(October 2015)*

World Professional Association for Transgender Health: "Both the World Professional Association for Transgender Health (WPATH) and the US affiliate, the United States Professional Association for Transgender Health (USPATH), vehemently oppose the broad and sweeping legislation being introduced and ratified in states across the country to ban access to gender-affirming health care to transgender and gender diverse (TGD) people. WPATH's long-standing Standards of Care for Transgender and Gender Diverse People, now in its eighth version (SOC8), explain in detail the science- and evidence-based benefits of gender affirming care for TGD people. Any legislation that restricts or prohibits access to this care is against best practice medical standards and is condemned by WPATH and USPATH." (March 8, 2023)

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EXHIBIT G

Medical Organization Statements

Leading medical groups recognize the medical necessity of treatments for gender dysphoria and endorse such treatments. Most of these groups have also explicitly rejected insurance exclusions for transgender-related care.

Expand all Collapse all

American Academy of Child and Adolescent Psychiatry

About the organization:

The mission of the 9,600-member American Academy of Child and Adolescent Psychiatry is to promote the healthy development of children, adolescents, and families through advocacy, education, and research, and to meet the professional needs of child and adolescent psychiatrists throughout their careers.

Statements:

- **Florida's "Don't Say Gay or Trans" Law Stigmatizes LGBTQ+ Youth and Families**

  "Harmful legislation like the 'Don't Say Gay or Trans' bill not only endangers the LGBTQ+ community, but it also jeopardizes their ability to reach their full potential. This action sends a dangerous message that certain voices don't deserve to be heard. Additionally, this bill is a big step backwards for all marginalized communities, their families, and for the appreciation and understanding of diversity."

  "AACAP opposes policies that stigmatize normal and healthy expressions of sexual and gender identity... This bill exacerbates the stigma that many LGBTQ+ youth already experience and paves the way for other groups to similarly be targeted... This law grossly undermines the basic tenets of education policy by denying students

access to and support from some of the most important and influential adults in their lives. This regressive approach to education and development will have devastating consequences for all, especially for LGBTQ+ youth and families."

Date: March 18, 2022

- **AACAP Statement Opposing Actions in Texas Threatening the Health, Mental Health and Well-Being of Transgender and Gender Diverse Youth and Their Families**

  "The American Academy of Child and Adolescent Psychiatry (AACAP) supports the healthy development of all children, adolescents, and their families, including transgender and gender-diverse youth and families. Recent state attacks on gender-affirming support and care for transgender and gender-diverse youth endanger the welfare of many young people across the country. These attacks undermine the right of parents and caregivers to access evidence-based and developmentally appropriate treatment"

  Date: March 1, 2022

- **AACAP Statement Responding to Efforts to ban Evidence-Based Care for Transgender and Gender Diverse Youth**

  "The American Academy of Child and Adolescent Psychiatry (AACAP) supports the use of current evidence-based clinical care with minors. AACAP strongly opposes any efforts – legal, legislative, and otherwise – to block access to these recognized interventions. Blocking access to timely care has been shown to increase youths' risk for suicidal ideation and other negative mental health outcomes. Consistent with AACAP's policy against conversion therapy (2), AACAP recommends that youth and their families formulate an individualized treatment plan with their clinician that addresses the youth's unique mental health needs under the premise that all gender identities and expressions are not inherently pathological."

  Date: November 8, 2019

- **Practice Parameter on Gay, Lesbian, or Bisexual Sexual Orientation, Gender Nonconformity, and Gender Discordance in Children and Adolescents**

  Stewart L. Adelson & American Academy of Child and Adolescent Psychiatry Committee on Quality Issues, Practice parameter on gay, lesbian, or bisexual sexual orientation, gender nonconformity, and gender discordance in children and adolescents, 51 J. Am. Acad. of Child & Adolesc. Psychiatry 957 (2012).

  "Children and adolescents who are growing up gay, lesbian, bisexual, gender nonconforming, or gender discordant experience unique developmental challenges.

They are at risk for certain mental health problems, many of which are significantly correlated with stigma and prejudice. Mental health professionals have an important role to play in fostering healthy development in this population. Influences on sexual orientation, gender nonconformity, and gender discordance, and their developmental relationships to each other, are reviewed. Practice principles and related issues of cultural competence, research needs, and ethics are discussed."

Date: Sept. 1, 2012

American Academy of Dermatology

About the organization:

The American Academy of Dermatology, founded in 1938, is the largest, most influential, and most representative of all dermatologic associations. With a membership of more than 20,500 physicians worldwide, the AAD is committed to: advancing the diagnosis and medical, surgical, and cosmetic treatment of the skin, hair, and nails; advocating high standards in clinical practice, education, and research in dermatology; and supporting and enhancing patient care for a lifetime of healthier skin, hair, and nails.

Statements:

- **American Academy of Dermatology Association statement on legislative interference in health care for transgender patients**

  The American Academy of Dermatology

  - Strongly opposes recent efforts by state legislatures to restrict physicians' ability to provide care to transgender youths.
  - Recognizes the dignity and identity of transgender individuals and advocates for dermatologists' ability to provide therapy and procedures that help the mental and physical well-being of these and all patients.

  "Evidence has shown that transgender individuals who are forced to forgo gender-affirming care face an increased risk of mental health disorders including substance

abuse disorders, and have higher rates of suicide. Transgender and gender-diverse individuals can benefit greatly from medical and surgical gender-affirming treatments. Treatments are often medically necessary for the health and well-being of these patients and are not to be considered as cosmetic or elective."

Date: June 1, 2021

- **Position Statement on Sexual and Gender Minority Health in Dermatology**

  The American Academy of Dermatology

  - "Recognizes that transgender and gender diverse individuals can benefit greatly from medical and surgical gender-affirming treatments.
  - Supports evidence-based coverage of all gender-affirming therapy and procedures which help the mental and physical well-being of gender diverse individuals.
  - Recognizes that gender-affirming procedures and treatments are not “cosmetic” or “elective” or for the mere convenience of the patient. These procedures are not optional in any meaningful sense, but are understood to be medically necessary for the health and well-being of the individual.
  - Advocates for removal of barriers to care and supports both public and private health insurance coverage of gender transition treatment."

  Date: March 4, 2019

American Academy of Family Physicians

About the organization:

Founded in 1947, the American Academy of Family Physicians represents 136,700 physicians and medical students nationwide. It is the only medical society devoted solely to primary care.

Statements:

- **NCCL Delegates Concern for Anti-Transgender Legislation**

  "The reference committee heard strong support for a resolution to oppose state legislation banning adolescent transgender care and to offer an advocacy toolkit on the subject, which delegates adopted.

  Member testimony noted the sharp increase in anti-transgender legislation across the states and discussed how these bills are a direct interference in evidence-based care, and the denial of gender-affirming care is linked to adverse outcomes," the committee reported. Members expressed particular concern that some of the bills "seek to penalize and criminalize physicians for medically necessary care."

  Date: 2021

- **Frontline Physicians Oppose Legislation That Interferes in or Penalizes Patient Care**

  AAFP joined the American Academy of Pediatrics, The American College of Obstetricians and Gynecologists, the American College of Physicians, the American Osteopathic Association, and the American Psychiatric Association in opposing legislation that interferes in or penalizes patient care for transgender individuals.

  "Our organizations, which represent nearly 600,000 physicians and medical students, oppose any laws and regulations that discriminate against transgender and gender-diverse individuals or interfere in the confidential relationship between a patient and their physician. That confidentiality is critical to allow patients to trust physicians to properly counsel, diagnose and treat.

  Our organizations are strongly opposed to any legislation or regulation that would interfere with the provision of evidence-based patient care for any patient, affirming our commitment to patient safety. We recognize health as a basic human right for every person, regardless of gender identity or sexual orientation. For gender-diverse individuals, including children and adolescents, this means access to gender-affirming care that is part of comprehensive primary care.

  Further, we strongly oppose any effort to criminalize or penalize physicians for providing necessary care for their patients. Physicians must be able to practice medicine that is informed by their years of medical education, training, experience, and the available evidence, freely and without threat of punishment. Patients and their physicians, not policymakers, should be the ones to make decisions together about what care is best for them."

  Date: April 2, 2021

- **Policy: Discrimination, Patient**

"The AAFP opposes all discrimination in any form, including but not limited to, on the basis of actual or perceived race, color, religion, gender, sexual orientation, gender identity, ethnic affiliation, health, age, disability, economic status, body habitus or national origin."

Date: 2020

- **Coverage Equity for Drugs, Testing, Procedure, Preventive Services, and Reproductive Technologies**

  "Employers and health plans should not discriminate by the patient's birth gender, sexual orientation, or marital status in the provision of health care benefits including a) prescription drugs and devices, b) elective sterilization procedures, c) diagnostic testing, d) medically indicated surgical procedures, and e) assisted reproductive technologies. These benefits should be covered under the same terms and conditions as other prescription drugs, devices, elective surgeries, diagnostic testing, and medically indicated surgical procedures.

  Coverage should include medically appropriate services for individuals requiring transition or transgender care as determined by best practice standards, the patient, and the attending physician. Further, this coverage should extend to the medically-appropriate, sex-specific recommended preventive services determined appropriate by the patient's primary care physician."

  Date: 2018

American Academy of Nursing

About the organization:

The American Academy of Nursing serves the public and the nursing profession by advancing health policy and practice through the generation, synthesis, and dissemination of nursing knowledge. The Academy's more than 2,800 fellows are nursing's most accomplished leaders in policy, research, administration, practice, and academia.

Statements:

- **Health Care Services for Transgender Individuals: Position Statement**

  Carol A. Sedlak & Carol J. Boyd, Health Care Services for Transgender Individuals: Position Statement, 64 Nursing Outlook 510-12 (Sept./Oct. 2016).

  "The American Academy of Nursing supports initiatives to address the health needs of transgender individuals (TI) and supports policy initiatives that reduce the heath care barriers that most TI encounter. There is a great need for the development of strategies and policies to eliminate the health care disparities of approximately 700,000 TI in the United States."

  Date: 2016

- **AAN Comments HHS Sec 1557 Nondiscrimination Proposed Rule**

  The AAN opposed the repeal of transgender-specific protections under Section 1557 of the Affordable Care Act noting: "The proposed rule would eliminate the definition of sex discrimination from the Section 1557 regulation, inviting insurers to deny treatment to transgender and gender nonconforming patients, including the denial of treatments such as hormone therapy, counseling and surgery that are essential to transgender patients, as they see fit. ... Since the implementation of Section 1557, 18 states have implemented affirmative coverage protocols in their respective Medicaid programs to ensure coverage of medically necessary transition-related care. These coverage improvements and any future progress will be in jeopardy if this rule is finalized as proposed."

  Date: 2019

- **Amicus Brief to Call for VA Support of Surgical Treatment for Transgender Veterans with Gender Dysphoria**

  AAN joined an amicus brief in Fulcher v. Secretary of Veterans Affairs, which challenged the U.S. Department of Veterans Affairs' refusal to engage in rulemaking to reconsider its ban on providing transgender-related surgery to veterans.

  Date: 2017

American Academy of Pediatrics

About the organization:

The American Academy of Pediatrics (AAP), a non-profit professional organization of 67,000 primary care pediatricians, pediatric medical subspecialists, and pediatric surgical specialists dedicated to the health, safety and well-being of infants, children, adolescents, and young adults,

Statements:

- **AAP SAHM Comments on Nondiscrimination in Health and Health Education Programs or Activities**

  The AAP opposed the repeal of transgender-specific protections under Section 1557 of the Affordable Care Act noting: "The proposal would also eliminate the provision that prohibits a health plan from categorically or automatically excluding or limiting coverage for health services related to gender transition. The rollback of these protections could have a devastating impact on access to medically necessary services for youth who identify as TGD and adversely affect self-esteem and contribute to the perception that they are undervalued by society and the health care system. Furthermore, insurance denials can reinforce a socioeconomic divide between those who can finance the high costs of uncovered care and those who cannot."

  Date: 2019

- **Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents**

  Jason Rafferty et al., Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents, 142 Pediatrics e20182162 (2018).

  The AAP works toward all children and adolescents, regardless of gender identity or expression, receiving care to promote optimal physical, mental, and social well-being. Any discrimination based on gender identity or expression, real or perceived, is damaging to the socioemotional health of children, families, and society.

  The AAP recommends that youth who identify as transgender and gender diverse have access to comprehensive, gender-affirming, and developmentally appropriate health care that is provided in a safe and inclusive clinical space and that insurance plans offer coverage for health care that is specific to the needs of youth

who identify as transgender and gender diverse, including coverage for medical, psychological, and, when indicated, surgical gender-affirming interventions.

Date: 2018

American Academy of Physician Assistants

About the organization:

Founded in 1968, the American Academy of Physician Assistants is the national professional society for PAs. It represents a profession of more than 140,000 PAs across all medical and surgical specialties in all 50 states, the District of Columbia, U.S. territories, and the uniformed services.

Statements:

- **Letter Opposing Changes to Section 1557 Regulation**

  All the undersigned associations have adopted policies or otherwise support addressing the specific health concerns of LGBTQ people, including opposition to discrimination in health care and insurance coverage based on an individual's sexual orientation or gender identity. As part of that commitment, our organizations support public and private health insurance coverage for treatment of gender dysphoria when medically necessary.

  Date: 2019

- **Guidelines for Ethical Conduct for the PA Profession**

  PAs should not discriminate against classes or categories of patients in the delivery of needed healthcare. Such classes and categories include gender, color, creed, race, religion, age, ethnic or national origin, political beliefs, nature of illness, disability, socioeconomic status, physical stature, body size, gender identity, marital status, or sexual orientation.

  Date: 2018

- **Amicus Brief to Call for VA Support of Surgical Treatment for Transgender Veterans with Gender Dysphoria**

The Lesbian Bisexual Gay & Transgender PA (LBGT PA) Caucus joined an amicus brief in Fulcher v. Secretary of Veterans Affairs, which challenged the U.S. Department of Veterans Affairs' refusal to engage in rulemaking to reconsider its ban on providing transgender-related surgery to veterans.

Date: 2017

American College Health Association

About the organization:

Since 1920, the American College Health Association (ACHA) has served as the voice for student health and wellness. Through advocacy, research and education, ACHA stands at the forefront of issues that impact the health and wellness of our college students. ACHA represents over 1,100 institutions of higher education, representing the collective health and wellness needs of 10 million college students. ACHA serves nearly 3,000 individual college health and wellness professionals and leaders of all disciplines united together to advance the health and wellness of college students.

Statements:

- **Statement on Legislation Affecting Medically Necessary Services for Transgender Patients**

  "As a society, we have made significant strides in removing barriers and improving health care and outcomes for transgender and gender diverse patients. Individuals feel more comfortable disclosing their authentic gender and are doing so at younger ages. Health care services should be made universal to all and should not discriminate in any way, whether this be on age; race/ethnicity, sex; sexual orientation; gender (including gender identity); marital status; physical size; religious, spiritual or cultural identity; psychological/physical/learning disability; socioeconomic status; or veteran status. This is consistent with the long held values of cultural inclusion, respect, equality, and equity that ACHA has advocated for.

  Therefore, ACHA opposes any legislation, both state or federal, that would restrict or limit access to gender-related medically necessary services for transgender youth and adults."

  Date: 2020

- **Non-Discrimination Policy**

  ACHA rejects all forms of discriminatory conduct with respect to: age; race/ethnicity; sex; sexual orientation; gender, including gender identity and expression; marital status; physical size; psychological/physical/learning ability; religious, spiritual or cultural identity; socioeconomic status; or veteran status.

  Date: 2019

American College of Nurse-Midwives

About the organization:

The American College of Nurse-Midwives (ACNM) is the professional association that represents certified nurse-midwives (CNMs) and certified midwives (CMs) in the United States.

Statements:

- **American College of Nurse-Midwives Strongly Opposes Reversal of Gender Identity and Sexual Orientation Protections in Health Care**

  "The American College of Nurse-Midwives (ACNM) strongly opposes the U.S. Department of Health and Human Services' (HHS) recent decision to finalize a rule removing non-discrimination protections established under the Affordable Care Act for LGBTQ people when it comes to health care providers and health insurance coverage. ACNM champions access to comprehensive sexual and reproductive health care services for every person, and as midwives we believe everyone has the right to make choices that meet their individual needs. Every person has the right to safe, supportive, and affirming health care in which providers demonstrate respect for human dignity."

  Date: June 19, 2020

- **Health Care for Transgender and Gender Non-Binary People**

  It is the position of ACNM that midwives should:

  ● Respect transgender and gender non-binary (TGNB) people. This includes becoming familiar with terminology related to gender identities and expression and endeavoring to use correct names, pronouns, and preferred anatomical language.

● Understand TGNB identity as a normal human variation rather than pathology.

● Be knowledgeable about the health care needs of TGNB people, including the individual and systematic barriers to care, as well as the options and benefits of gender-affirming treatment within a framework of shared decision-making and harm reduction.

● Provide or identify appropriate referral for reproductive and sexual health and primary care, including gender-affirming hormone therapy. Match treatment approaches to the specific needs of TGNB people, particularly their goals for gender affirmation and expression.

● Provide resources and referrals to support and advocate for patients within their families and communities (eg, schools, workplaces, and other settings).

● Advocate for, and work to create welcoming and inclusive health care settings for TGNB people (eg, gender-neutral bathrooms and gender inclusive forms, signage, education materials, and electronic health records).

Date: 2021

American College of Obstetricians and Gynecologists —

About the organization:

The American College of Obstetricians and Gynecologists is the nation's leading group of professionals providing health care for women.

Statements:

- **Committee Opinion No. 512: Health Care for Transgender Individuals, 118 Obstet Gynecol 1454 (2011).**

  "Within the medical community, transgender individuals face significant barriers to health care. This includes the failure of most health insurance plans to cover the cost of mental health services, cross-sex hormone therapy, or gender affirmation surgery. This barrier exists despite evidence that such treatments are safe and effective and that cross-gender behavior and gender identity issues are not an issue of choice for the individual and cannot be reversed with psychiatric treatment."

"The American College of Obstetricians and Gynecologists, therefore, urges public and private health insurance plans to cover the treatment of gender identity disorder."

Date: 2011

- **Committee Opinion No. 685: Care for Transgender Adolescents**

  American College of Obstetricians and Gynecologists, Committee Opinion No. 685: Care for transgender adolescents, 129 Obstet Gynecol e11 (2017).

  Date: 2017

American College of Physicians

About the organization:

The American College of Physicians recommends that public and private health benefit plans include comprehensive transgender health care services and provide all covered services to transgender persons as they would all other beneficiaries.

Statements:

- **Lesbian, Gay, Bisexual, and Transgender Health Disparities: Executive Summary of a Policy Position Paper From the American College of Physicians**

  Hilary Daniel & Renee Butkus, for the Health and Public Policy Committee of the American College of Physicians, Lesbian, Gay, Bisexual, and Transgender Health Disparities: Executive Summary of a Policy Position Paper From the American College of Physicians, 163 Annals of Internal Medicine 135 (2015).

  Date: 2015

- **Amicus Brief to Call for VA Support of Surgical Treatment for Transgender Veterans with Gender Dysphoria**

  ACP joined an amicus brief in Fulcher v. Secretary of Veterans Affairs, which challenged the U.S. Department of Veterans Affairs' refusal to engage in rulemaking to reconsider its ban on providing transgender-related surgery to veterans.

Date: 2017

American Counseling Association

About the organization:

The American Counseling Association is a not-for-profit, professional and educational organization that is dedicated to the growth and enhancement of the counseling profession. Founded in 1952, ACA is the world's largest association exclusively representing professional counselors in various practice settings.

Statements:

- **Competencies for Counseling Transgender Clients**

  The American Counseling Association's Association of Lesbian, Gay, Bisexual, and Transgender Issues in Counseling has issued competencies for counseling transgender clients that include "affirm[ing] transgender mental and medical health care (e.g., hormone therapies, sexual reassignment surgery, safe and trans-positive general medical services) through the entire lifespan."

  Date: Nov. 7, 2011

- **Nondiscrimination: Position Statement**

  The American Counseling Association is committed to nondiscrimination and to the prevention of harassment in all forms—verbal, physical, sexual, emotional, and psychological—including protections for transgender, gender non-conforming, and LGBTQ+ individuals.

  Date: Undated

American Heart Association

About the organization:

The American Heart Association (AHA) is a nonprofit and nonpartisan organization that represents more than 100 million patients with cardiovascular disease (CVD) and includes more than 33 million volunteers and supporters committed to our goal of improving the cardiovascular health of all human beings. As the nation's oldest and largest voluntary organization dedicated to building healthier lives free from cardiovascular disease and stroke, the AHA has long advocated for health equity, access to quality health insurance coverage, and evidence-based medical services and treatment for all individuals.

Statements:

- **AHA Comments on Proposed Rule on Nondiscrimination in Health and Health Education Programs or Activities**

  The AHA opposed the repeal of transgender-specific protections under Section 1557 of the Affordable Care Act noting: "Transgender people also face a high degree of insurance discrimination. Historically, many plans have used transgender-specific exclusions to deny transgender people coverage for medically necessary care—including hormone therapy, mental health counseling, and surgeries—even though the same services are routinely covered for non-transgender individuals. While the 2016 rule resulted in the elimination of transgender-specific exclusions from many private health insurance policies, transgender people continue to face a high number of denials for transition-related care. ...

  This discrimination is not limited to transition-related care and, rather, affects all health care access for transgender people. ... These experiences of health care and health insurance discrimination contribute to significant health disparities. The LGBTQI community faces higher rates of substance use, including tobacco; higher rates of mental health issues; a higher risk of HIV and other sexually transmitted diseases; and a higher risk of certain types of cancer (due in part to reduced access to cancer screening). Relative to heterosexual people, lesbian, gay, and bisexual individuals are more likely to rate their overall and cardiovascular health as poor, have more chronic health conditions, have higher prevalence and earlier onset of disabilities, and have a heightened risk for CVD."

  Date: 2019

American Medical Association

About the organization:

The American Medical Association, the largest association of physicians and medical students in the United States, articulates in H-185.950 that an "established body of medical research" shows both the medical effectiveness and necessity of "mental health care, hormone therapy, and sex reassignment surgery" in treating gender dysphoria. The AMA has resolved "[t]hat our American Medical Association support public and private health insurance coverage for treatment of gender identity disorder as recommended by the patient's physician."

Statements:

- **Clarification of Evidence-Based Gender-Affirming Care**

  The AMA:

  - Recognizes that treatments for gender dysphoria and gender incongruence are medically necessary
  - Will work with stakeholders to advocate for laws and policies that protect access to care, oppose laws and policies that impede the provision of care, support protections against liability for physicians and institutions who provide care and patients who seek it, and communicate about the importance of gender-affirming care
  - Will advocate for coverage of gender-affirming care by public and private health insurer

  Date: 2023

- **AMA opposes effort to allow discrimination against patients**

  "This proposal marks the rare occasion in which a federal agency seeks to remove civil rights protections. It legitimizes unequal treatment of patients by not only providers, health care organizations, and insurers, but also by the government itself—and it will harm patients. Such policy should not be permitted by the U.S. government, let alone proposed by it."

  Date: June 12, 2020

- **AMA statement on U.S. Supreme Court's ruling on Title VII cases**

"As physicians, and as leaders in medicine, we believe that LGBTQ+ individuals must be protected from workplace discrimination in order to prevent negative health outcomes. The AMA supports everyone's access to quality, evidence-based health care regardless of gender or sexual orientation, and will continue to work diligently at the state and federal levels to expand access to medical services, reduce stigma in treating patients with unique needs and break down discriminatory barriers to care."

Date: June 15, 2020

- **Transgender prisoners have fundamental right to appropriate care**

  "Prisoners have a fundamental right to access necessary and effective medical care, and that includes the full range of treatments for gender dysphoria. So argues a strongly worded friend-of-the-court brief filed by the AMA and other medical and mental health professional organizations."

  Date: May 2019

- **Health Insurance Coverage for Gender-Affirming Care of Transgender Patients**

  "The AMA opposes any discrimination based on an individual's sex, sexual orientation or gender identity, opposes the denial of health insurance on the basis of sexual orientation or gender identity, and supports public and private health insurance coverage for treatment of gender dysphoria as recommended by the patient's physician."

  Date: 2019

- **Removing Financial Barriers to Care for Transgender Patients H-185.950**

  "Our AMA supports public and private health insurance coverage for treatment of gender dysphoria as recommended by the patient's physician."

  Date: 2016

American Medical Student Association

About the organization:

The American Medical Student Association is the oldest and largest independent association of physicians-in-training in the United States. Founded in 1950, AMSA is a student-governed, non-profit organization committed to representing the concerns of physicians-in-training.

Statements:

- **AMSA Joins Amicus Brief to Call for VA Support of Surgical Treatment for Transgender Veterans with Gender Dysphoria**

  "AMSA adamantly opposes treatment policies that discriminate against patients based on their sexual orientation and gender identity, or that inhibit their access to quality care. Health care for transgender people should be individualized, holistic, and comprehensive – including, but not limited to surgical treatment– and transgender persons in the military should be allowed to openly undergo gender transition and be eligible for the equitable benefits and rights afforded to cisgendered service personnel, including health care."

  Date: 2017

American Nurses Association

About the organization:

"The American Nurses Association (ANA) is the premier organization representing the interests of the nation's 4 million registered nurses. ANA is at the forefront of improving the quality of health care for all. Founded in 1896, and with members in all 50 states and U.S. territories, ANA is the strongest voice for the profession."

Statements:

- **ANA Comment Letter to HHS on 1557 Revisions**

  The ANA opposed the repeal of transgender-specific protections under Section 1557 of the Affordable Care Act noting: "The proposed rule would substantially alter HHS' current approach to discrimination in health care, removing a number of safeguards built into the 2016 regulations. Among the significant revisions proposed, HHS seeks to eliminate provisions clarifying the health care rights of LGBTQ+ individuals. If

finalized, the rule's definition of sex discrimination under Section 1557 would no longer include discrimination based on gender identity or sex-stereotyping. Additionally, there would be no prohibition to insurance plans denying or limiting health care coverage based on gender identity. Without these protections, providers and payers can deny care to transgender persons and to other LGBTQ+ patients based on sex-stereotyping."

Date: 2019

- **Nursing Advocacy for LGBTQ+ Populations**

  "ANA is committed to the elimination of health disparities and discrimination based on sexual orientation, gender identity, and/or expression within health care. LGBTQ+ populations face significant obstacles accessing care such as stigma, discrimination, inequity in health insurance, and denial of care because of an individual's sexual orientation or gender identity. ...

  ANA condemns any discrimination based on sexual orientation, gender identity, and/or gender expression in access to or provision of health care."

  Date: 2018

- **Amicus Brief to Call for VA Support of Surgical Treatment for Transgender Veterans with Gender Dysphoria**

  ANA joined an amicus brief in Fulcher v. Secretary of Veterans Affairs, which challenged the U.S. Department of Veterans Affairs' refusal to engage in rulemaking to reconsider its ban on providing transgender-related surgery to veterans.

  Date: 2017

American Osteopathic Association

About the organization:

The American Osteopathic Association represents more than 137,000 osteopathic physicians and medical students, promotes public health and serves as the primary certifying body for DOs.

Statements:

- **American Osteopathic Association policy compendium H445-A/15 Gender Identity Non-Discrimination**

  "The American Osteopathic Association supports the provision of adequate and medically necessary treatment for transgender and gender-variant people and opposes discrimination on the basis of gender identity."

  Date: 2015

American Psychiatric Association

About the organization:

The American Psychiatric Association is the world's largest psychiatric organization and publisher of the Diagnostic and Statistical Manual.

Statements:

- **APA Official Actions: Position Statement on Access to Care for Transgender and Gender Variant Individuals**

  Jack Drescher, M.D., Ellen Haller, M.D., APA Caucus of Lesbian, Gay and Bisexual Psychiatrists. Revised 2017 Eric Yarbrough, M.D., APA Caucus of LGBTQ Psychiatrists and the Council on Minority Mental Health and Health Disparities, APA Official Actions: Position Statement on Access to Care for Transgender and Gender Variant Individuals (2018).

  "Significant and long-standing medical and psychiatric literature exists that demonstrates clear benefits of medical and surgical interventions to assist gender variant individuals seeking transition. ... Access to medical care (both medical and surgical) positively impacts the mental health of transgender and gender variant individuals," and states the following:

  1. Recognizes that appropriately evaluated transgender and gender variant individuals can benefit greatly from medical and surgical gender transition treatments.

2. Advocates for removal of barriers to care and supports both public and private health insurance coverage for gender transition treatment.
3. Opposes categorical exclusions of coverage for such medically necessary treatment when prescribed by a physician.
4. Supports evidence-based coverage of all gender-affirming procedures which would help the mental well-being of gender diverse individuals"

Date: 2018

American Psychological Association

About the organization:

The American Psychological Association is the largest association of psychologists worldwide.

Statements:

- **APA Policy Statement on Affirming Evidence-Based Inclusive Care for Transgender, Gender Diverse, and Nonbinary Individuals, Addressing Misinformation, and the Role of Psychological Practice and Science**

  “This policy statement affirms APA’s support for unobstructed access to healthcare and evidence-based clinical care for transgender, gender-diverse, and nonbinary children, adolescents, and adults.

  Furthermore, this policy statement addresses the spread of misleading and unfounded narratives that mischaracterize gender dysphoria and affirming care, likely resulting in further stigmatization, marginalization, and lack of access to psychological and medical supports for transgender, gender-diverse, and nonbinary individuals.”

  Date: February 2024

- **APA adopts resolution opposing biased or coercive efforts to change individuals’ gender identity**

  "The American Psychological Association has adopted a resolution opposing efforts to change people’s gender identity, citing scientific research showing that such actions may be harmful.

The resolution, adopted by APA's governing Council of Representatives on Feb. 26, aligns with the association's stance against similar efforts aimed at changing people's sexual orientation.

"There is a growing body of research that shows that transgender or nonbinary gender identities are normal variations in human expression of gender," said APA President Jennifer F. Kelly, PhD. "Attempts to force people to conform with rigid gender identities can be harmful to their mental health and well-being."

The Resolution on Gender Identity Change Efforts (PDF, 105KB) emphasizes that "individuals who have experienced pressure or coercion to conform to their sex assigned at birth or therapy that was biased toward conformity to one's assigned sex at birth have reported harm resulting from these experiences, such as emotional distress, loss of relationships, and low self-worth."

At the same meeting, the council also adopted an updated Resolution on Sexual Orientation Change Efforts (PDF, 222KB), which reiterates APA's opposition to using nonscientific explanations to frame same-gender and multiple-gender orientations as unhealthy. APA adopted its first resolution discouraging efforts to change people's sexual orientation in 1997 and a second in 2009, when it also issued a task force report with a systematic review of research on the topic. The new resolution now specifically opposes those efforts."

Date: March 2021

- **APA RESOLUTION on Gender Identity Change Efforts**

  "WHEREAS APA opposes discrimination on the basis of gender identity, gender expression, and transgender and gender nonbinary identities, and actively opposes the adoption of discriminatory legislation (APA, 2008) .... BE IT FURTHER RESOLVED that the APA opposes the dissemination of inaccurate information about gender identity, gender expression, and the efficacy of GICE, including the claim that gender identity can be changed through treatment, the characterization of transgender or gender nonbinary identity as a mental disorder and the promotion of treatments that prescribe gender identity or expression consistent with one's birth-assigned sex as effective for clients with gender dysphoria..."

  Date: February 2021

- **APA Comments on Nondiscrimination in Health and Health Education Programs or Activities**

  The APA opposed the repeal of transgender-specific protections under Section 1557 of the Affordable Care Act noting: "We are especially concerned about the discrimination many transgender people experience in the healthcare system

because the proposed rule eliminates the general prohibition of discrimination based on gender identity, as well as specific health insurance coverage protections for transgender people. ...

APA practice guidelines recognize that care for transgender persons can include assessment, psychotherapy or surgery." Even though these treatments may be clinically necessary, providers or insurance plans under the proposed rule may refuse to provide or pay for them. ...

Additionally, after publication of the rule implementing Section 1557, one study showed that over 95% of insurers removed exclusions for gender dysphoria treatments from their 2017 plans, ensuring that a greater number of transgender consumers can have access to treatment. If the proposed rule were implemented, positive gains made in improving transgender health outcomes in recent years would be lost."

Date: 2019

- **Transgender, Gender Identity & Gender Expression Non-Discrimination**

  Anton, B. S., Proceedings of the American Psychological Association for the legislative year 2008: Minutes of the annual meeting of the Council of Representatives. American Psychologist, 64, 372–453 (2009).

  "Therefore be it resolved that APA opposes all public and private discrimination on the basis of actual or perceived gender identity and expression and urges the repeal of discriminatory laws and policies; ...

  Therefore be it further resolved that APA calls upon psychologists in their professional roles to provide appropriate, nondiscriminatory treatment to transgender and gender variant individuals and encourages psychologists to take a leadership role in working against discrimination towards transgender and gender variant individuals; ...

  Therefore be it further resolved that APA supports the provision of adequate and necessary mental and medical health care treatment for transgender and gender variant individuals;

  Therefore be it further resolved that APA recognizes the efficacy, benefit and medical necessity of gender transition treatments for appropriately evaluated individuals and calls upon public and private insurers to cover these medically necessary treatments;

  Therefore be it further resolved that APA supports access to appropriate treatment in institutional settings for people of all gender identities and expressions; including access to appropriate health care services including gender transition therapies; ..."

Date: 2008

American Public Health Association

About the organization:

The American Public Health Association is the nation's leading public health organization with 25,000 members and works to advance the health of all people and all communities.

Statements:

- **Promoting Transgender and Gender Minority Health through Inclusive Policies and Practices**

  APHA:

  - Urges Congress and state legislatures to enact legislation to protect the rights, legal benefits, and access to services of people of all gender identities and expressions. ...
  - Urges public and private workplaces to institute nondiscriminatory policies and practices inclusive of transgender and gender-nonconforming people. ...
  - Encourages public health and health care practices that are inclusive of transgender and gender-nonconforming people.
  - Encourages public and private entities to adopt policies and practices inclusive of transgender and gender-nonconforming people in different settings and across all sectors.

  Date: 2016

- **Amicus Brief to Call for VA Support of Surgical Treatment for Transgender Veterans with Gender Dysphoria**

  The Lesbian, Gay, Bisexual, and Transgender (LGBT) Caucus of the APHA joined an amicus brief in Fulcher v. Secretary of Veterans Affairs, which challenged the U.S.

Department of Veterans Affairs' refusal to engage in rulemaking to reconsider its ban on providing transgender-related surgery to veterans.

Date: 2017

American Society of Plastic Surgeons

About the organization:

The American Society of Plastic Surgeons (ASPS) is the world's largest organization of board-certified plastic surgeons. Representing more than 7,000 Member Surgeons, the Society is recognized as a leading authority and information source on aesthetic and reconstructive plastic surgery. ASPS comprises more than 94 percent of all board-certified plastic surgeons in the United States. Founded in 1931, the Society represents physicians certified by The American Board of Plastic Surgery or The Royal College of Physicians and Surgeons of Canada. ASPS advances quality care to plastic surgery patients by encouraging high standards of training, ethics, physician practice and research in plastic surgery.

Statements:

- **Public comments on CMS Hospital Inpatient Prospective Payment Systems proposed rule for FY18**

  American Society of Plastic Surgeons to Seema Verma, Comment Letter on Proposed Rule on Medicare Program; Hospital Inpatient Prospective Payment System for Acute Care Hospitals and the Long-Term Care Hospital Prospective Payment System and Proposed Policy Changes and Fiscal Year 2018 Rates (June 13, 2017).

  "We would be remiss to not also ask the Agency to review current policy for breast implant placement for trans females. As we are sure you are aware, in the typical patient, estrogen therapy alone does not result in what would be considered adequate growth of breast tissue. Augmentation procedures are necessary, and should be included as a reimbursable service.

  We would encourage CMS to review the nuances of CPT coding for breast prosthesis, and adjust existing policy that excludes augmentation mammoplasty (CPT 19325) as a covered service for MtF patients undergoing gender confirmation surgery."

  Date: June 13, 2017

Endocrine Society

About the organization:

Founded in 1916, The Endocrine Society is the world's oldest, largest, and most active organization devoted to research on hormones and the clinical practice of endocrinology. They have published clinical guidelines, Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. The Guideline is co-sponsored by the American Association of Clinical Endocrinologists, American Society of Andrology, European Society for Pediatric Endocrinology, European Society of Endocrinology, Pediatric Endocrine Society, and World Professional Association for Transgender Health.

Statements:

- **Transgender Health Position Statement**
    - "There is a durable biological underpinning to gender identity that should be considered in policy determinations.
    - Medical intervention for transgender youth and adults (including puberty suppression, hormone therapy and medically indicated surgery) is effective, relatively safe (when appropriately monitored), and has been established as the standard of care. Federal and private insurers should cover such interventions as prescribed by a physician as well as the appropriate medical screenings that are recommended for all body tissues that a person may have.
    - Increased funding for national pediatric and adult transgender health research programs is needed to close the gaps in knowledge regarding transgender medical care and should be made a priority."

  Date: December 2020

- **Proper Care of Transgender and Gender Diverse Persons in the Setting of Proposed Discrimination: A Policy Perspective**

  Abby Walch, Caroline Davidge-Pitts, Joshua D Safer, Ximena Lopez, Vin Tangpricha, Sean J Iwamoto, Proper Care of Transgender and Gender Diverse Persons in the

Setting of Proposed Discrimination: A Policy Perspective, The Journal of Clinical Endocrinology & Metabolism, dgaa816, https://doi.org/10.1210/clinem/dgaa816.

Date: December 2020

- **Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline**

  Wylie C. Hembree et al., Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline, Journal of Clinical Endocrinology & Metabolism, November 2017, 102(11):1–35.

  Date: 2017

Federation of Pediatric Organizations

About the organization:

The Federation of Pediatric Organizations (FOPO) is an umbrella organization made up of the leadership of the Academic Pediatric Association, the American Academy of Pediatrics, the American Board of Pediatrics, the American Pediatric Society, the Association of Medical School Pediatric Department Chairs, the Association of Pediatric Program Directors, and the Society for Pediatric Research. The purpose of the Federation of Pediatric Organizations (FOPO) is to promote optimal health for children by building on the efforts and expertise of the member organizations, and on the relationships between the member organizations to accomplish shared goals.

Statements:

- **Statement in Support of Transgender Children and Youth, their Families, and Health Care Providers**

  "We stand with pediatricians who partner with families every day to make the best possible decision for each individual child based on available research and evidence pertinent to that child's care. Transgender and gender diverse children and youth deserve to lead safe, healthy lives in environments that allow them to be their

authentic selves. That can only happen if physicians are allowed to treat these children in the same manner, and with the same respect, that we expect them to treat every other child. Our mission to advance child health will succeed only if we work to improve health outcomes for all children."

Date: March 28, 2022

GLMA: Health Professionals Advancing LGBTQ Equality

About the organization:

GLMA is a national organization committed to ensuring health equity for lesbian, gay, bisexual, transgender, queer (LGBTQ) and all sexual and gender minority (SGM) individuals, and equality for LGBTQ/SGM health professionals in their work and learning environments. To achieve this mission, GLMA utilizes the scientific expertise of its diverse multidisciplinary membership to inform and drive advocacy, education, and research.

Statements:

- **GLMA 127-18-101: Transgender Healthcare**

  "Therapeutic treatment, including hormone therapy, mental health therapy and gender affirming surgeries, are medically necessary for the treatment of gender dysphoria. These gender-affirming medical and surgical treatments should be covered by all public and private insurance plans."

  Date: 2018

- **Health Insurance Coverage for Gender-Affirming Care of Transgender Patients**

  "GLMA: Health Professionals Advancing LGBTQ Equality recognizes that mental healthcare, hormone replacement therapy, and/or gender-affirming surgery are medically necessary for the treatment of transgender people who meet the criteria for gender dysphoria and advocates that these services not be excluded from any public or private insurance programs."

  Date: 2018

- **Amicus Brief to Call for VA Support of Surgical Treatment for Transgender Veterans with Gender Dysphoria**

GLMA joined an amicus brief in Fulcher v. Secretary of Veterans Affairs, which challenged the U.S. Department of Veterans Affairs' refusal to engage in rulemaking to reconsider its ban on providing transgender-related surgery to veterans.

Date: 2017

National Association of Nurse Practitioners in Women's Health

About the organization:

The National Association of Nurse Practitioners in Women's Health's (NPWH) mission is to ensure the provision of quality primary and specialty healthcare to women of all ages by women's-health and women's-health-focused nurse practitioners.

Statements:

- **Healthcare for Transgender and Gender Non-Conforming Individuals**

  "NPWH encourages all NPs who provide sexual and reproductive healthcare to seek out learning opportunities to improve their ability to provide evidence-based, culturally competent care for transgender and GNC individuals. NPWH supports the role of NPs in providing gender-affirming hormone therapy and pre- and post-gender-affirming surgery care for individuals who desire such treatment."

  Date: Oct. 2017

National Association of Social Workers

About the organization:

Founded in 1955, the National Association of Social Workers (NASW) is the largest membership organization of professional social workers in the world, with more than 120,000 members. NASW works to enhance the professional growth and development of its members, to create and maintain professional standards, and to advance sound social policies.

Statements:

- **Transgender and Gender Identity Issues**

  National Association of Social Workers, Transgender and Gender Identity Issues, in Social Work Speaks: National Association of Social Workers Policy Statements 2009-2012, 347 (8th ed. 2009).

  NASW "supports the rights of all individuals to receive health insurance and other health coverage without discrimination on the basis of gender identity, and specifically without exclusion of services related to transgender or transsexual transition (or sex change), to receive medical and mental health services through their primary care physician and the appropriate referrals to medical specialists, which may include hormone replacement therapy, surgical interventions, prosthetic devices, and other medical procedures."

  Note: the current version can be found in Social Work Speaks: National Association of Social Workers Policy Statements 2018–2020 (11th ed. 2018).

  Date: 2009

National Commission on Correctional Health Care

About the organization:

The mission of the National Commission on Correctional Health Care is to improve the quality of health care in jails, prisons and juvenile confinement facilities. NCCHC establishes standards for health services in correctional facilities, operates a voluntary accreditation program for institutions that meet those standards, produces resource publications, conducts educational conferences and offers certification for correctional health professionals. NCCHC is supported by the major national organizations representing the fields of health, mental health, law and corrections. Each supporting organization has named a liaison to the NCCHC board of directors to create a robust, multidisciplinary governing structure that reflects the complexities of correctional health care.

Statements:

- **Transgender, Transsexual, and Gender Nonconforming Health Care in Correctional Settings**

  "Because jails, prisons, and juvenile confinement facilities have a responsibility to ensure the physical and mental health and well-being of inmates in their custody, correctional health staff should manage transgender patients in a manner that respects their biomedical and psychological needs. The National Commission on Correctional Health Care recommends that the following principles guide correctional health professionals in addressing the needs of transgender patients: ...

  1. Because transgender patients may be under different stages of care prior to incarceration, there should be no blanket administrative or other policies that restrict specific medical treatments. Policies that make treatments available only to those who received them prior to incarceration or that limit transition and/or maintenance are inappropriate and out of step with medical standards and should be avoided. ...
  2. Accepted treatments for gender dysphoria should be made available to people with gender dysphoria. Providing mental health care, while necessary, is not sufficient. ...
  3. When determined to be medically necessary for a particular patient, hormone therapy should be initiated and regular laboratory monitoring should be conducted according to community medical standards.
  4. Sex reassignment surgery should be considered on a case-by-case basis and provided when determined to be medically necessary for a patient."

  Date: 2015

Pediatric Endocrine Society

About the organization:

The Pediatric Endocrine Society (PES) is the leading professional society for this specialty in the United States. The mission of PES is to advance and promote the endocrine health and

well-being of children and adolescents. The PES has over 1,400 members representing the multiple disciplines of Pediatric Endocrinology.

The PES Transgender and Gender Non-Conforming Youth Special Interest Group is dedicated to providing safe, comprehensive and evidence based medical care to transgender and gender nonconforming youth.

Statements:

- **Transgender Health Position Statement**

  "Medical intervention for transgender youth and adults (including puberty suppression, hormone therapy and medically indicated surgery) is effective, relatively safe (when appropriately monitored), and has been established as the standard of care. Federal and private insurers should cover such interventions as prescribed by a physician as well as the appropriate medical screenings that are recommended for all body tissues that a person may have."

  Date: December 2020

- **Pediatric Endocrine Society/Endocrine Society Joint Position Statement on Transgender Health**

  "There is a durable biological underpinning to gender identity that should be considered in policy determinations.

  Medical intervention for transgender youth and adults (including puberty suppression, hormone therapy, and medically indicated surgery) is effective, relatively safe (when appropriately monitored), and has been established as the standard of care.6 Federal and private insurers should cover such interventions as prescribed by a physician as well as the appropriate medical screenings that are recommended for all body tissues that a person may have.

  Increased funding for national pediatric and adult transgender health research programs is needed to close the gaps in knowledge regarding transgender medical care and should be made a priority."

  Date: December 2020

- **Proper Care of Transgender and Gender Diverse Persons in the Setting of Proposed Discrimination: A Policy Perspective**

  Abby Walch, Caroline Davidge-Pitts, Joshua D Safer, Ximena Lopez, Vin Tangpricha, Sean J Iwamoto, Proper Care of Transgender and Gender Diverse Persons in the

Setting of Proposed Discrimination: A Policy Perspective, The Journal of Clinical Endocrinology & Metabolism, dgaa816, https://doi.org/10.1210/clinem/dgaa816.

Date: December 2020

- **Discriminatory policies threaten care for transgender, gender diverse individuals**

  "The Endocrine Society and the Pediatric Endocrine Society oppose legislative efforts to block transgender and gender diverse individuals from accessing gender-affirming medical and surgical care, the two medical societies said in a joint policy perspective published in The Journal of Clinical Endocrinology & Metabolism."

  Date: December 2020

- **PES Fact Sheet: Introduction to Health for Transgender Youth**

  Date: June 17, 2020

- **PES Fact Sheet: Masculinizing Treatment for Transgender Males**

  Date: 2018

- **PES Fact Sheet: Feminizing Treatment for Transgender Females**

  Date: 2018

- **Statement on Gender Affirmative Approach to Care from the Pediatric Endocrine Society Special Interest Group on Transgender Health**

  Ximena Lopez, Maja Marinkovic, Toni Eimicke, Stephen M. Rosenthal & Jerrold S. Olshan, “Statement on gender-affirmative approach to care from the pediatric endocrine society special interest group on transgender health.” Current opinion in pediatrics vol. 29,4 (2017): 475-480. doi:10.1097/MOP.0000000000000516

  "[T]ransgender youth have optimal outcomes when affirmed in their gender identity, through support by their families and their environment, as well as appropriate mental health and medical care. For this reason, the Pediatric Endocrine Society Special Interest Group on Transgender Health joins other academic societies involved in the care of children and adolescents in supporting policies that promote a safe and accepting environment for gender nonconforming/transgender youth, as well as adequate mental health and medical care."

  Date: May 27, 2017

- **PES Statement Promoting Safety of Transgender Youth**

"The Pediatric Endocrine Society (PES), the leading professional society for this specialty in the United States, strongly opposes the guidance issued on February 22, 2017, by the Departments of Justice and Education, which eliminates protection of the rights of transgender youth."

Date: March 2017

Society for Adolescent Health and Medicine

About the organization:

Founded in 1968, the Society for Adolescent Health and Medicine (SAHM) is a multidisciplinary organization committed to improving the physical and psychosocial health and well-being of all adolescents through advocacy, clinical care, health promotion, health service delivery, professional development and research.

Statements:

- **AAP SAHM Comments on Nondiscrimination in Health and Health Education Programs or Activities**

  SAHM opposed the repeal of transgender-specific protections under Section 1557 of the Affordable Care Act noting: "The proposal would also eliminate the provision that prohibits a health plan from categorically or automatically excluding or limiting coverage for health services related to gender transition. The rollback of these protections could have a devastating impact on access to medically necessary services for youth who identify as TGD [transgender and gender diverse] and adversely affect self-esteem and contribute to the perception that they are undervalued by society and the health care system. Furthermore, insurance denials can reinforce a socioeconomic divide between those who can finance the high costs of uncovered care and those who cannot."

  Date: 2019

World Medical Association

About the organization:

The World Medical Association (WMA) is an international organization representing physicians. The organization was created to ensure the independence of physicians, and to work for the highest possible standards of ethical behavior and care by physicians, at all times. Membership consists of 114 National Medical Associations.

Statements:

- **Statement on Transgender People**

  The WMA recommends, among other things, the following:

  1. "The WMA emphasises that everyone has the right to determine one's own gender and recognises the diversity of possibilities in this respect. The WMA calls for physicians to uphold each individual's right to self-identification with regards to gender.
  2. The WMA asserts that gender incongruence is not in itself a mental disorder; however it can lead to discomfort or distress, which is referred to as gender dysphoria (DSM-5).
  3. The WMA affirms that, in general, any health-related procedure or treatment related to an individual's transgender status, e.g. surgical interventions, hormone therapy or psychotherapy, requires the freely given informed and explicit consent of the patient.
  4. The WMA urges that every effort be made to make individualised, multi-professional, interdisciplinary and affordable transgender healthcare (including speech therapy, hormonal treatment, surgical interventions and mental healthcare) available to all people who experience gender incongruence in order to reduce or to prevent pronounced gender dysphoria. [...]"

  Date: Oct. 2015

World Professional Association for Transgender Health

About the organization:

The World Professional Association for Transgender Health (WPATH) is an international, interdisciplinary, professional association devoted to the understanding and treatment of individuals with Gender Dysphoria (GD). Founded in 1979, and currently with over 1500 medical, mental health, social scientist, and legal professional members, all of whom are engaged in clinical practice and/or research that affects the lives of transgender and transsexual people, WPATH is the oldest professional association in the world that continuously has been concerned with this clinical specialty.

Recognized by the American Medical Association as "leading international, interdisciplinary professional organization devoted to the understanding and treatment of gender identity disorders," WPATH issues the widely followed Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People.

Statements:

- **Transgender Medical Benefits**

  Listing procedures that should be covered by insurance plans based on the Standards of Care.

  Date: June 28, 2018

- **Position Statement on Medical Necessity of Treatment, Sex Reassignment, and Insurance Coverage in the U.S.A.**

  "The WPATH Board of Directors urges health insurance carriers and healthcare providers in the United States to eliminate transgender or transsexual exclusions from their policy documents and medical guidelines, and to provide coverage for transgender patients; also to include in their policy documents and medical guidelines the medically prescribed sex reassignment or gender affirming/confirming services necessary for subscribers' treatment and well-being; and to ensure that ongoing healthcare, both routine and specialized, is readily accessible and affordable to all their subscribers on an equal basis."

  Date: Dec. 21, 2016

- **WPATH Standards of Care for the Health of Transsexual, Transgender, and Gender Nonconforming People, 7th ed.**

  Date: 2011

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EXHIBIT H

Making a Statement

Positions of Professional Medical Organizations Towards Gender-Affirming Care

Myles N. LaValley, BS, Danielle J. Eble, MD,† William M. Kuzon Jr, MD, PhD,‡ Blair R. Peters, MD,§ Alexander J. Skokan, MD,†‖ Russell E. Ettinger, MD,† and Shane D. Morrison, MD, MS†‖✉*

Objective: Despite politically charged media coverage and legislation surrounding gender-affirming care (GAC), many organizations have released position statements to provide scientifically backed clinical practice standards, combat misinformation, and inform medicolegal policies. The purpose of this study is to objectively assess the availability and the content of the official position statements of relevant medical professional organizations regarding GAC.

Summary Background Data: A list of US medical professional organizations with likely involvement in GAC based on medical or surgical specialties was compiled.

Methods: For included organizations, we evaluated the availability, content, and publication year of positions on GAC through October 2023. When available, formal positions were categorized as supportive or unsupportive.

Results: A total of 314 professional medical organizations were screened for our study based on specialty, relevance to GAC, and issuance of patient guidelines or position statements. Inclusion criteria were met by 55 organizations. Most organizations (35, 63.6%) had formal position statements on GAC. Support for GAC was described in 97.1% (n = 34). Further, 94.2% (n = 33) of available statements explicitly addressed GAC in individuals less than 18 years old and were largely supportive (96.9%, n = 32).

Conclusions: This cross-sectional analysis demonstrates that a majority of multidisciplinary professional medical organizations with relevance to GAC have issued formal position statements on the topic. Available positions were overwhelmingly supportive of individualized access to gender-affirming therapies in adult and adolescent populations. However, silence from some organizations continues to represent a modifiable disparity in the provision of GAC.

Keywords: gender affirmation, position statements, gender affirming surgery

(*Ann Surg* 2025;281:219–220)

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The authors report no conflicts of interest.

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DOI: 10.1097/SLA.0000000000006342

BACKGROUND

Based on the body of available evidence, there is consensus among medical professionals that gender-affirming care is medically necessary and effective.[1] Many organizations have released supportive position statements to provide scientifically backed clinical practice standards, combat misinformation, and inform medicolegal policies.[2,3] Despite this concordance, treatment has become politically charged in both media coverage and legislation advocating for restrictions or criminal penalties on the provision of care.[4] As consequences escalate, US hospitals and physicians now endure increased harassment and targeted threats.[5,6] The purpose of this study is to objectively assess the availability and the content of the official position statements of relevant medical professional organizations regarding gender-affirming care (GAC).

METHODS

A list of US medical professional organizations with likely involvement in GAC based on medical or surgical specialties was compiled. Eligible disciplines included endocrinology, psychiatry, gynecology, urology, otolaryngology, oral and maxillofacial surgery, plastic surgery, pediatrics, and speech-language pathology. Umbrella nursing, medicine, and surgical organizations were also included for overarching context. Organizations meeting inclusion criteria encompassed those focused on specialties involved in GAC that issue position statements or clinical guidelines on any topic within their scope of practice. For included organizations, we evaluated the availability, content, and publication year of positions on GAC through October 2023 using an online search and direct email inquiry. Those with educational materials surrounding GAS without explicitly delineating the organization's stance were also noted. If ambiguities arose, materials were reviewed independently by 2 authors (M.N.L. and D.J.E.). When available, formal positions were categorized as supportive or unsupportive. The largest organizations in each field were identified based on reported membership size. Results were analyzed using Pearson χ^2 tests performed with John Macintosh Project, version 16.0 (SAS Institute Inc., Cary, NC), and a significance level of $P < 0.5$.

RESULTS

A total of 314 professional medical organizations were screened for our study based on specialty, relevance to GAC, and issuance of patient guidelines or position statements (Fig. 1). Inclusion criteria were met by 55 organizations. Most organizations (35, 63.6%) had formal position statements

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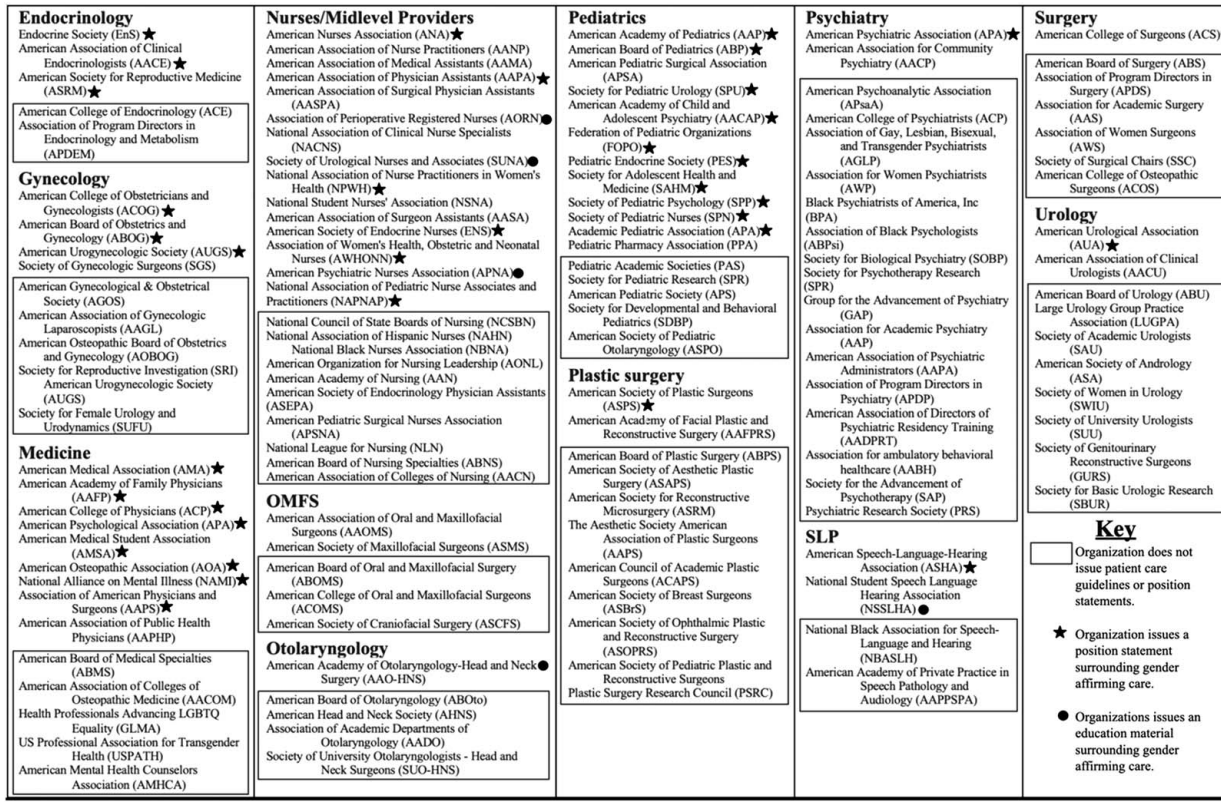


FIGURE 1. Included US medical professional organizations. For each specialty or field, the first organization listed comprises the largest membership size within that field.

on GAC (Supplemental Figure 1, Supplemental Digital Content 1, http://links.lww.com/SLA/F110). An additional 6 (10.9%) organizations provided educational materials without offering a formal position. Available positions were published between 2016 and 2023, with the greatest number issued in 2022 (n = 11, 31.4%). Support for GAC was described in 97.1% (n = 34). Further, 94.2% (n = 33) of available statements explicitly addressed GAC in individuals less than 18 years old and were largely supportive (96.9%, n = 32). There was no statistically significant correlation observed between the issuance of positional statements and organization size ($P = 0.31$) or specialty ($P = 0.18$), but the single largest organization in each field provided a position statement except for the American College of Surgeons (ACS), American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS), and the American Association of Oral and Maxillofacial Surgeons (AAOMS).

DISCUSSION

This cross-sectional analysis demonstrates that a majority of multidisciplinary professional medical organizations with relevance to GAC have issued formal position statements on the topic. Available positions were overwhelmingly supportive of individualized access to gender-affirming therapies in adult and adolescent populations. However, the most influential bodies representing fields of surgery, otolaryngology, and oral and maxillofacial surgery are silent despite the routine issuance of guidelines on other topics, which may highlight a modifiable disparity in the provision of GAC as consistent medical recommendations provide more reliable standards. Limitations of our study include the potential bias of unblinded organization material review and a limited representation of the varying degrees of statement visibility as well as discrepancies across organization communications or fluctuating dissent among members. Furthermore, we have not captured actions taken in accordance with voiced positions, including opposing anti-trans legislation and condemning provider harassment. Given the risks posed to patient and provider safety, future studies should expound on current statements to further improve their quality and impact on professional guidance.

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EXHIBIT I

[1]Notice of Funding Opportunity

Application due Friday, July 10, 2026

HRSA
Health Resources & Services Administration

HIV/AIDS Bureau
Division of State HIV/AIDS Program (DSHAP)

Ryan White HIV/AIDS Program Part B States/Territories Supplemental Grant Program

Opportunity number: HRSA-26-074

1


DEPARTMENT OF HEALTH & HUMAN SERVICES · USA

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Before you begin

If you believe you are a good candidate for this funding opportunity, secure your SAM.gov and Grants.gov registrations now. If you are already registered, make sure your registrations are active and up-to-date.

SAM.gov registration (this can take several weeks)

You must have an active account with SAM.gov. This includes having a Unique Entity Identifier (UEI).

See Step 2: Get Ready to Apply

Grants.gov registration (this can take several days)

You must have an active Grants.gov registration. Doing so requires a Login.gov registration as well.

See Step 2: Get Ready to Apply

Apply by the application due date

Applications are due by 11:59 p.m. Eastern Time on Friday, July 10, 2026.

To help you find what you need, this NOFO uses internal links. In Adobe Reader, you can go back to where you were by pressing Alt + Left Arrow (Windows) or Command + Left Arrow (Mac) on your keyboard.

All activities proposed in your application and budget narrative must align with applicable law, including but not limited to statutes, executive orders, federal regulations and applicable judicial holdings. Accordingly, discretionary awards shall not be used to fund, promote, encourage, subsidize, or facilitate: racial preferences or other forms of racial discrimination by the recipient, including activities where race or intentional proxies for race will be used as a selection criterion for employment or program participation; denial by the recipient of the sex binary in humans, or the belief that sex is a chosen or mutable characteristic; illegal immigration; or any other initiatives that compromise public safety. If an application does not align, the application will not receive funding to the extent permitted by law and applicable court orders.

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Step 1:
Review the Opportunity

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Basic Information

Health Resources Services Administration

HIV/AIDS Bureau

Division of State HIV/AIDS Program (DSHAP)

Providing additional funding for HIV/AIDS programs.

Summary

The purpose of the Ryan White HIV/AIDS Program Part B States/Territories Supplemental Grant Program is to provide funding for HIV/AIDS care. Specifically, it adds to formula-based funding provided through the HIV Care Grant Program – RWHAP Part B States/Territories Formula, AIDS Drug Assistance Program (ADAP) Formula, and the ADAP Supplemental Awards Notice of Funding Opportunity (HRSA-22-033).

Funding details

Application types: Competing continuation, New

Expected total available funding in FY 2026: $48,000,000

Expected number and type of awards: 30 grants

Funding range per award: $500,000 to $9,000,000

We plan to fund awards in one 12-month budget period for a total one-year period of performance from September 30, 2026, to September 29, 2027.

The program and awards depend on the appropriation of funds and are subject to change based on the availability and amount of appropriations.

Have questions?
Go to Contacts and Support.

Key facts

Opportunity name: Ryan White HIV/AIDS Program Part B States/Territories Supplemental Grant Program

Opportunity number: HRSA-26-074

Announcement version: Initial

Federal assistance listing: 93.917

Key dates

NOFO issue date: March 11, 2026

Informational webinar: TBD

Application deadline: Friday, July 10, 2026

Expected award date is by: September 30, 2026

Expected start date: September 30, 2026

See other submissions for other time frames that may apply to this NOFO.

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Eligibility

Who can apply

You can apply if you are a state government, including the District of Columbia, domestic territories, and the Freely Associated States, unless your state/territory had an unobligated balance (UOB) of more than 5% of a prior year's formula funds.

Types of eligible organizations

These types of domestic* organizations may apply:

- State governments

*"Domestic" means the 50 states, the District of Columbia, the Commonwealth of Puerto Rico, the Northern Mariana Islands, American Samoa, Guam, the U.S. Virgin Islands, the Federated States of Micronesia, the Republic of the Marshall Islands, and the Republic of Palau.

Individuals are not eligible applicants under this NOFO.

Completeness and responsiveness criteria

We will review your application to make sure it meets these basic requirements to move forward in the competition.

We will not consider an application that:

- Is from an organization that does not meet all eligibility criteria.
- Requests funding above the award ceiling shown in the funding range.
- Is submitted after the deadline.

Application limits

You may not submit more than one application. If you submit more than one application, we will only accept the last on-time submission.

Cost sharing

Post-award requirements

Before you apply, make sure you understand the requirements that come with an award.

See Step 6: Learn What Happens After Award for information on regulations that apply, reporting, and more.

This program has no cost-sharing requirement. If you choose to share in the costs of the project, we will not consider it during merit review. Recipients agree that once committed, cost sharing amounts are enforceable and subject to reporting and auditing requirements under 2 CFR 200.

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Program description

Purpose

This program provides funding under the Ryan White HIV/AIDS Program (RWHAP) Part B States/Territories Supplemental Grant Program. The purpose of this program is to supplement formula-based funding provided through the HIV Care Grant Program — RWHAP Part B States/Territories Formula, AIDS Drug Assistance Program (ADAP) Formula, and the ADAP Supplemental Awards Notice of Funding Opportunity (HRSA-22-033).

States/territories use this supplemental funding in conjunction with RWHAP Part B HIV Care Grant Program funding to develop or increase access to a comprehensive continuum of high-quality care and treatment services for low-income people with HIV.

Background

The Ryan White HIV/AIDS Program

The Ryan White HIV/AIDS Program (RWHAP) has five statutorily defined parts that provide grants to states, cities, counties, local clinics, and community-based organizations. The grants fund medical care, medication, and essential support services, to meet the needs of people with HIV and family members affected by HIV. Together these grants provide a comprehensive system of care to ensure low-income people with HIV have access to services for early diagnosis of HIV, linkage to care, medically appropriate treatment, retention in care, and sustained viral suppression (a very low or undetectable amount of HIV in the blood).

For nearly four decades, the RWHAP has funded services to provide HIV primary health care, medication, and essential support services, including mental health care, transportation, case management, nutrition, and housing. These services support clients to enter and remain in care, access medications, and reach viral suppression, reducing transmission and lowering health care costs.

Ending the HIV Epidemic

Launched in 2020, the Ending the HIV Epidemic in the U.S. (EHE) initiative further expands federal efforts to reduce HIV transmission. For the RWHAP, the EHE initiative expands the program's ability to meet the needs of clients, specifically focusing on linking people with HIV who are either newly diagnosed, diagnosed but currently not in care, or are diagnosed and in care but not yet virally suppressed, to the essential HIV care, treatment, and support services needed to help them reach viral suppression.

Making America Healthy Again

The Ryan White HIV/AIDS Program helps advance the Making America Healthy Again (MAHA) priorities by:

- **Expanding access to primary care** for people with HIV, particularly those with low incomes, and by Strengthening the health workforce.
- **Fighting the chronic disease epidemic** by providing HIV medical care, treatment, and support services to people with HIV.
- **Supporting improved nutrition** by providing patient-centered focused medical nutrition therapy and food services.
- **Supporting disease prevention** through HIV care and treatment services that help people reach viral suppression, so they live longer, healthier lives and do not transmit HIV.

Key accomplishments

- **Nearly 602,000 people with HIV** in the U.S. received life-saving care, medication, and essential support services through the RWHAP, representing over half of all people diagnosed with HIV in the U.S. This is an increase of nearly 26,000 clients.
- **More than 91%** of Ryan White HIV/AIDS Program patients receiving HIV medical care were virally suppressed in 2024. This is up from 69.5% of patients virally suppressed in 2010 and significantly higher than the 67.2% virally suppressed nationally among all people with diagnosed HIV.
- **More than 47%** of Ryan White HIV/AIDS Program clients are aged 50 years and older, demonstrating the program's success in supporting older clients and its commitment to addressing the unique needs of people aging with HIV.

Program requirements and expectations

Your state/territory should conduct activities to provide core medical and/or support services, as defined in HAB Policy Clarification Notice (PCN) 16-02: RWHAP Services: Eligible Individuals and Allowable Uses of Funds. Your project should address unmet needs among HIV-positive people and improve client-level health outcomes across the HIV care continuum, including viral suppression.

Eligible RWHAP Part B states/territories that are focus areas, or have counties that are focus areas, for the Ending the HIV Epidemic in the U.S. (EHE) initiative should consider if they still need supplemental funding.

As required in section 2620(b) of the Public Health Service (PHS) Act, states/territories must demonstrate the severity of the need for RWHAP Part B supplemental funding, using quantifiable data in one or more of these areas:

- The unmet need for such services, as determined under section 2617(b) of the PHS Act.
- An increasing need for HIV/AIDS-related services, including relative rates of increase in the number of HIV/AIDS cases.

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- The relative rates of increase in the number of HIV/AIDS cases within subpopulations.
- The current prevalence of HIV/AIDS.
- Relevant factors related to the cost and complexity of delivering health care to individuals with HIV/AIDS in the eligible area.
- The impact of comorbid factors, including co-occurring conditions, determined relevant by the Secretary.
- The prevalence of homelessness.
- The prevalence of individuals who were released from federal, state, or local prisons during the past three years and had HIV/AIDS when they were released.
- Factors that limit access to health care, including geographic variation, adequacy of health insurance coverage, and language barriers.
- The impact of a decline in the amount of RWHAP Part B funding received on services available to all individuals with HIV/AIDS identified and eligible under this title.

Statutory authority

42 U.S.C. § 300ff-29a (Title XXVI, § 2620 of the Public Health Service Act)

Award information

Funding policies and limitations

Changes in HHS regulations

As of October 1, 2025, HHS has adopted 2 CFR Part 200, with some modifications included in 2 CFR Part 300. These regulations replace those in 45 CFR Part 75.

Policies

- To make an award, funding must be available and allocated for this program and purpose, at which point we will move forward with the review and award process.
- Have clear policies and good financial practices to avoid spending HRSA funds on unallowable activities. Like other award rules, we may audit your policies, procedures, and controls.
- If we receive more funding for this program, we may:
  - Fund more applicants from the rank order list.
  - Extend the period of performance.
  - Award supplemental funding.

General limitations

- For guidance on some types of costs we do not allow or restrict, see:
  - Project Budget Information in the Application Guide [PDF].
  - 2 CFR Part 200 Subpart E — General Provisions for Selected Items of Cost.
  - Allowable and Unallowable Costs and Activities, in the HHS Grants Policy Statement.
- All costs must be reasonable, necessary, allocable to the award, and adequately documented (2 CFR 200.403).
- You cannot earn profit from the federal award. See 2 CFR § 200.400(g).
- Current appropriations law includes a salary limit of $228,000 as of January 2026 that applies to this program. You may pay salaries at a higher rate if the rate beyond the salary rate limit (Executive Level II) is paid with non-HHS funds. For help calculating salaries under this limit, read more at “salary rate limitation” in the application guide.

Program-specific statutory or regulatory limitations

- Pursuant to section 2620(c) of the PHS Act, the Secretary prioritizes funds to states/territories to address the reduction or disruption of services due to a decline in the amount of formula funding. To determine whether funding has declined, we compare the amount of formula funding received in the current fiscal year (FY) to the amount received in FY 2006.
- If your state/territory has current or potential shortfalls in ADAP resources, you should prioritize using RWHAP Part B supplemental funds to augment ADAP resources if your state/territory has any of these conditions:
  - Existing or anticipated ADAP waiting list.
  - Capped enrollment.
  - Reductions in ADAP formulary.
  - Reduction in the percentage of federal poverty level (FPL) eligibility requirement.
  - Other ADAP restrictions within your state/territory.
- Payor of Last Resort: Charges that are billable to third party payers are unallowable. Third party payers include Medicaid, Children's Health Insurance Programs (CHIP), Medicare (including Medicare Part D), basic health plans, or private insurance, including those purchased through the Health Insurance Marketplace. The RWHAP is the payor of last resort, and recipients must vigorously pursue alternate sources of payments.
  - HRSA expects you to determine eligibility for all clients and to confirm eligibility on a timely basis (please see HAB PCN 21-02).
  - You must coordinate with third-party payers that are ultimately responsible for covering the cost of services provided to eligible or covered people.
- As outlined under applicable statutes, regulation, or policy, you cannot use funds under this notice for the following purposes:
  - Payment for any item or service to the extent that payment has been made, or reasonably can be expected to be made, with respect to that item or service, under any state compensation program, insurance policy, federal or state benefits program, or any entity that provides health services on a prepaid basis (except for a program administered by or providing the services of the Indian Health Service).
  - Cash payment to intended recipients of RWHAP services.
  - International travel.

- Construction (minor alterations and renovations to an existing facility to make it more suitable for the purposes of the award program are allowable with prior HRSA approval).
-
- Development of materials designed to directly promote or encourage intravenous drug use or sexual activity, whether homosexual or heterosexual.
- Pre-Exposure Prophylaxis (PrEP) medications and related medical services or Post-Exposure Prophylaxis (PEP). This is because a person using PrEP or PEP is not diagnosed with HIV and therefore is not eligible for RWHAP-funded medication.

See Manage Your Grant for other information on costs and financial management.

Indirect costs

Indirect costs are costs you charge across more than one project that cannot be easily separated by project. For example, this could include utilities for a building that supports multiple projects.

To charge indirect costs, you can select one of two methods:

Method 1 – Approved rate. You currently have an indirect cost rate approved by your cognizant federal agency at the time of award.

Method 2 – *De minimis* rate. Per 2 CFR § 200.414(f), if you don't have a current negotiated indirect cost rate, you may elect to charge a *de minimis* rate. If you choose this method, costs included in the indirect cost pool must not be charged as direct costs.

This rate is up to 15% of modified total direct costs (MTDC). See 2 CFR § 200.1 for the definition of MTDC. You can use this rate indefinitely for all your federal awards or until you choose to receive a negotiated rate.

Consider your indirect costs when developing your budget.

Program income

Program income is money earned as a result of your award-supported project activities. You must use any program income you generate from awarded funds for approved project-related activities. Find more about program income at 2 CFR 200.307.

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Step 2:
Get Ready to Apply

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Get registered

SAM.gov

You must have an active account with SAM.gov to apply. SAM.gov registration can take several weeks. Begin that process today.

To register:

- Go to SAM.gov Entity Registration and select Get Started. From the same page, you can also select the Entity Registration Checklist for the information you will need to register.
- You must agree to the financial assistance general certifications and representations [PDF] specifically. Those for contracts are different.

When you register, you will also receive your required Unique Entity Identifier (UEI).

Once you register:

- You will have to maintain your registration throughout the life of any award.
- If your organization has multiple UEIs, use the one associated with your physical location.

If you need additional information about user roles in SAM.gov, see “Get registered: SAM.gov user roles” in the application guide.

Grants.gov

You must also have an active account with Grants.gov. You can see step-by-step instructions at the Grants.gov Quick Start Guide for Applicants and How to Apply for Grants.

Find the application package

The application package has all the forms you need to apply. You can find it online. Go to Grants Search at Grants.gov and search for opportunity number HRSA-26-074.

After you select the opportunity, we recommend that you select the Subscribe button to get updates.

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Application writing help

Visit HHS Tips for Preparing Grant Proposals.

Visit HRSA's How to Prepare Your Application page for more guidance.

See Apply for a Grant for other help and resources.

Join the webinar

For more information about this opportunity, join the webinar: Webinar information will be posted to the Related Documents tab on Grants.gov. We recommend you "Subscribe" to the NOFO on Grants.gov to receive updates when documents are posted.

Have questions? Go to Contacts and Support.

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Step 3:
Build Your Application

In this step

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Application checklist

There are two types of forms in Grants.gov:

- Some forms allow you to upload components of your application to the form. These include components like your project narrative, budget and budget narrative, and attachments.
- Other forms are more typical, fill-in-the-blank forms.

Make sure that you have everything you need to apply.

Narratives

Component	Grants.gov form	Included in page limit*?
☐ Project narrative	Project Narrative Attachment form.	Yes
☐ Budget narrative	Budget Narrative Attachment form.	Yes

Attachments

Insert each in the Attachments Form in this order.

Component	Included in page limit*?
☐ 1. Staffing plan and job descriptions	Yes
☐ 2. Biographical sketches	No
☐ 3. Project organizational chart	Yes
☐ 4. Tables and charts	No
☐ 5. Core medical services waiver	No
☐ 6. Epidemiological data snapshot	Yes
☐ 7. Unmet need framework and narrative	No
☐ 8-15. Other relevant documents	Yes

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Other required forms

Upload using each required form in Grants.gov.

Component	Included in page limit*?
☐ Application for Federal Assistance (SF-424)	No
☐ Budget Information for Non-Construction Programs (SF-424A)	No
☐ Project Abstract Summary form	No
☐ Disclosure of Lobbying Activities (SF-LLL), optional	No
☐ Project/Performance Site Location(s)	No
☐ Grants.gov Lobbying form	No
☐ Key Contacts	No

*Only what you attach in these forms counts toward the page limit. The forms themselves do not count.

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Application contents and format

This section includes guidance on each component found in the application checklist.

Application page limit: 60

Submit your information in English and express whole number budget figures using U.S. dollars.

Required format

Required format for project summary, project narrative, budget narrative, and attachments:

Font: A readable font like Arial, Courier, CG Times, or Times New Roman.

File format: We only accept the following document formats:

- .PDF — Adobe Portable Document Format
- .DOC/.DOCX — Microsoft Word
- .RTF — Rich Text Format
- .TXT — Text
- .WPD — Word Perfect Document
- .XLS/.XLSX — Microsoft Excel
- .VSD — Microsoft Visio

Size: 12-point font
Footnotes, charts, graphics, and budget tables may be 10-point or higher.

Ink color: Black

Spacing: Single-spaced, including all text and tables.

Alignment: Left

Headings: Bold all headings and align left.

Size: 8.5 x 11 (Make sure the print area is set and allows printing to 8.5 x 11.)

Margins: 1-inch on all sides.

Footer: On each page as the footer, include your organization's name and page numbers. If a competing continuation or competing supplement, also include your 10-digit award number.

Page numbering:

- Do not number the standard OMB-approved forms.
- Number each attachment page sequentially (that is, 1, 2, 3).
- Reset the numbering for each attachment.
- Treat each attachment as a separate section.

File names: You can find guidance for naming our files in the application guide.

Project narrative

Introduction

See merit review criterion 1: Need.

Briefly describe how you will use RWHAP Part B supplemental funding to support a comprehensive system of high-quality care and treatment for people with HIV.

- Describe how the comprehensive system of care and treatment will improve outcomes across the HIV care continuum.
- Provide a snapshot of epidemiological data as Attachment 6. Describe the current prevalence of HIV/AIDS in your state/territory using data tables or figures. The page limit is 4 pages.

Need

See merit review criterion 1: Need.

Need for HIV-related services, including augmenting ADAP

Explain why you need funds to address issues such as:

- Unmet need.
- An increased need due to an increase in relative rates or prevalence of HIV/AIDS cases.
- A decline in available funding for HIV services, including ADAP.

Note: If you are requesting funds specifically for unmet need, then you must submit an Unmet Need Framework and narrative as **Attachment 7**.

If you are using funds to augment ADAP services, include information on either of the following, if applicable, in a narrative format:

- An existing or anticipated ADAP waiting list.
- Other cost containment measures. These could include capped enrollment, reduction of ADAP formulary, or reduction in the percentage of FPL eligibility requirement.

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Assessment of increases in the number of cases of HIV/AIDS within new or emerging subpopulations

If you are requesting funding to address needs for new or emerging subpopulations with limited access to existing HIV/AIDS care and services, address all the following bullet points. Explain how you will use funds to meet the need. Select six or fewer subpopulations.

- Unique challenges for each subpopulation related to the service delivery system.
- Service gaps for each subpopulation.
- Estimated costs of care for delivering service to each subpopulation.
- Current HIV viral suppression for each subpopulation.

Impact of comorbidities and other factors on the cost and complexity of providing care

If you request funding to address the impact of comorbidities and other factors on the cost and complexity of providing care, include a table as **Attachment 4** that provides quantitative evidence addressing these impacts. Include data sources. In this section, you must include a narrative explaining the data you provided in the table as **Attachment 4**.

You only need to include information on comorbidities and other factors for which you are applying for funding. Where applicable, include the following information in the table:

- Rates of sexually transmitted infections (STIs), including syphilis.
- Rates of hepatitis and tuberculosis.
- Rates of substance use and mental health disorders.
- Estimated number of people who are homeless.
- Estimated number of people with HIV who were released from federal, state, or local correctional facilities (i.e., prisons and jails) in the past three (3) years.
- The number and percent of people without insurance coverage, including those without Medicaid.
- The number and percent of people with HIV living at or below 138% and 400% of the 2026 FPL. Also include information about your FPL requirements for RWHAP eligibility.

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Access to health care

You may use funds to improve access to HIV health care in your state/territory. This includes access based on either:

- Geographic variation.
- Lack of health insurance.

Discuss the factors impacting access to care. Describe how you will use the requested funds to address each factor.

Approach

See merit review criterion 2: Response.

Describe how you will do all the following to address your demonstrated needs:

- Use programmatic and fiscal forecasting tools to meet projected service needs.
- Develop, maintain, streamline, and/or diversify service delivery models, service contracts, strategic partnerships, and/or collaborations.
- Involve clients, families, and communities with and affected by HIV, as appropriate, in planning, implementing, and improving your project.

High-level work plan

See merit review criteria 2: Response and 4: Impact.

In a narrative format, describe the following.

- How funded services will be used for all the following:
  - Promoting access to high-quality HIV care.
  - Addressing gaps in services.
  - Maximizing health outcomes along the HIV care continuum.
- How you will conduct all these activities:
  - Working with internal and external stakeholders, including people with HIV, to plan program activities.
  - Using the HIV care continuum to respond to the needs of people with HIV.
  - Ensuring availability of the same services throughout your jurisdiction.

In a table or outline format, provide goals and objectives that are specific, measurable, achievable, realistic, and time-framed (SMART). Also address all of these:

- The relationship of the goals and objectives to the needs you will use the requested funds to address.
- The core medical and support services you will provide.

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- The HIV care continuum stages tied to the goals and objectives.
- The anticipated outcome measures.

Resolving challenges

See merit review criterion 2: Response.

Discuss any challenges you anticipate in planning and implementing the proposed project. Include all the following:

- Specific challenges related to each identified need area that you are requesting funding for. This could include access to health care or impact of comorbidities.
- Specific activities or strategies you will use to identify risks and mitigate or resolve these challenges.

Performance reporting and evaluation

See merit review criteria 3: Performance reporting and evaluation and 5: Resources and capabilities.

Discuss your evaluation process and describe all the following:

- How you will collect and analyze data and use it for continuous quality improvement.
- The specific staff who will implement your evaluation process for this project.
- The systems (such as software) and other resources that are available to support evaluation efforts.
- How you will share evaluation results internally and externally with key stakeholders, including people with HIV, to improve program implementation and outcomes.
- How you will determine whether the SMART objectives you proposed in your work plan have been achieved.

See the reporting section for more information.

Sustainability

See merit review criterion 4: Impact.

We expect you to sustain key project elements that improve practices and outcomes for the population of focus. Propose a plan to sustain your project after the period of federal funding ends.

- Describe the actions you'll take to obtain future sources of funding.
- Discuss challenges that you'll likely encounter in sustaining the program. Include how you will resolve these challenges.

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Organizational Information

See merit review criterion 5: Resources and capabilities.

- Briefly describe your agency's mission and structure, including personnel and facilities.
- Describe the scope of your current RWHAP activities.
- Explain how your mission, structure, and scope of RWHAP activities will help you carry out the program requirements of this project.
- If you use funds for personnel costs, you must submit all the following as attachments:
  - A staffing plan and job description for key personnel as **Attachment 1**.
  - Biographical sketches of key personnel as **Attachment 2**.
  - A project organizational chart as **Attachment 3**.

Budget and budget narrative

See merit review criterion 6: Support requested.

Your **budget** should follow the instructions in budget narrative: detailed instructions section of the Application Guide and the instructions listed in this section. Your budget should show a well-organized plan.

HHS now uses the definitions for equipment and supply in 2 CFR 200.1. The new definitions change the threshold for equipment to the lesser of the recipient's capitalization level or $10,000 and the threshold for supplies to below that amount.

The total project or program costs are all allowable (direct and indirect) costs used for the HRSA award activity or project. This includes costs charged to the award and non-federal funds used to satisfy a matching or cost-sharing requirement (which may include maintenance of effort, if applicable).

The **budget narrative** supports the information you provide in Standard Form 424-A. It includes an itemized breakdown and a clear justification of the costs you request. The merit review committee reviews both.

As you develop your budget, consider:

- If the costs are reasonable, allowable and allocable, and consistent with your project's purpose and activities.
- The restrictions on spending funds. See funding policies and limitations.

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In addition, you must:

- Submit a separate line-item budget using Section B Object Class Categories of the SF-424A. The program budget categories for the line-item budget include:
  - **Administration:** Include all funds allocated to recipient administration, planning and evaluation, and clinical quality management.
  - **ADAP:** Include all funds allocated to ADAP activities.
  - **Consortia:** Include all funds allocated to consortia.
  - **Direct services:** Include all funds allocated to state direct services, home- and community-based care, and health insurance premium and cost-sharing assistance.
- Consider the following caps on expenses:
  - Administrative costs may not exceed 10% of the total grant award.
  - Planning and evaluation costs may not exceed 10% of the total grant award.
  - Together, administration and planning and evaluation may not exceed 15% of the total award. For further guidance on the treatment of costs under the 10% administrative limit, refer to HAB PCN 15-01 Treatment of Costs under the 10% Administrative Cap for Ryan White HIV/AIDS Program Part A, B, C, and D [PDF].
- Fulfill the Core Medical Services Requirement. RWHAP Part B supplemental funding is subject to Section 2612(b)(1) of the PHS Act. This act requires that after you have reserved funding for administration, planning and evaluation, and clinical quality management, you must use at least 75% of the remaining funds to provide core medical services that are needed in the state/territory for people with HIV who are eligible under RWHAP. The core medical and support service category definition for this award can be found in HRSA HAB Policy Clarification Notice (PCN) 16-02: RWHAP Services: Eligible Individuals and Allowable Use of Funds [PDF].
  - If you are seeking a waiver for this requirement, you must submit a waiver request. You can do this either before applying, with this application (as Attachment 5, Core Medical Services Waiver), or up to four months into the award period. Submission must be in accordance with HAB Policy Notice (PN) 21-01 Waiver of the RWHAP Core Medical Services Expenditures Requirement [PDF].

To create your budget narrative, see budget narrative detailed instructions in the Application Guide [PDF].

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Attachments

Place your attachments in this order in the Attachments Form. See application checklist to determine if they count toward the page limit.

Unless the instructions below require it, do not submit organizational brochures or other promotional materials (for example, slides, films, clips).

Attachment 1: Staffing plan and job descriptions

Provide a staffing plan and job descriptions for all key personnel included in the budget.

Limit each job description to one page. Include the role, responsibilities, and qualifications of the proposed project staff.

If your program will not use RWHAP Part B supplemental funding for staffing, attach a one-page document that says, “Attachment 1: Not Applicable.”

Attachment 2: Biographical sketches

Provide biographical sketches of all key personnel included in the budget.

If your program will **not** use RWHAP Part B supplemental funding for staffing, provide a one-page document that says, “Attachment 2: Not Applicable.”

Note: Each biographical sketch should be no more than two pages. Do not include non-public, personally identifiable information. If you include someone you have not hired yet, provide a letter of commitment from that person along with the biographical sketch.

Attachment 3: Project organizational chart

Provide a one-page project organizational chart highlighting the key personnel included in the budget.

If your program will **not** use RWHAP Part B supplemental funding for staffing, provide a one-page document that says, “Attachment 3: Not Applicable.”

Attachment 4: Tables and charts

Provide the cost and complexity comorbidities table and narrative. See the full description of the comorbidities table in the need section of the project narrative.

If your program will **not** use RWHAP Part B supplemental funding due to the impact of comorbidities in the state/territory, provide a one-page document that says, “Attachment 4: Not Applicable.”

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Attachment 5: Core medical services waiver (if applicable)

You may provide a Core Medical Services Waiver request and supporting documents as Attachment 5.

If you are **not** applying for a waiver now, provide a one-page document that says, “Attachment 5: Not Applicable.”

Attachment 6: Epidemiological data snapshot

This attachment is required for all applicants.

Page limit: 4 pages

Provide data tables or figures, as described in the introduction section of the project narrative, using the most recent available epidemiological data.

Attachment 7: Unmet need framework

If you are applying for RWHAP Part B supplemental funding due to unmet need, provide the Unmet Need Framework and narrative.

If your program will **not** use RWHAP Part B supplemental funding due to unmet need, provide a one-page document that says, “Attachment 7: Not Applicable.”

Attachment 8-15: Other relevant documents

Provide any other documents that are relevant to the application. If you include letters of support, they must be dated and indicate specific commitment to the project, like in-kind services, dollars, staff, space, or equipment.

If you do **not** have any other relevant documents, provide a one-page document that says, “Attachments 8-15: Not Applicable.”

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Other required forms

You will need to complete some other forms. Upload the following forms at Grants.gov. You can find them in the NOFO application package or review them and any available instructions at Grants.gov Forms.

Forms	Submission Requirement
Application for Federal Assistance (SF-424)	With application.
Project Abstract Summary form	With application.
Grants.gov Lobbying form	With application.
Project/Performance Site Location(s)	With application.
Budget Information for Non-Construction Programs (SF-424A)	With application.
Key Contacts	With application.

Form instructions

The application guide [PDF] has detailed instructions for:

- The Application for Federal Assistance (SF-424).
- The Budget Information for Non-Construction Programs (SF-424A).

Project abstract summary form instructions

Complete the information in the Project Abstract Summary form. Include a short description of your proposed project. Include the needs you plan to address, the proposed services, and the population groups you plan to serve. For more information, see Section 3.1.2 of the Application Guide [PDF].

In this section, also describe all the following:

- Why you need RWHAP Part B supplemental funding to ensure comprehensive HIV care and treatment for people with HIV in your state/territory.
- How this supplemental funding will improve viral suppression and improve client health outcomes across the HIV care continuum.
- The severity of the HIV epidemic in your state/territory, using quantifiable data on:
  - Epidemiology.
  - Comorbidities.
  - Cost of care.
  - Service needs of emerging subpopulations.

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- Unmet need for core medical services (as defined by HAB PCN 16-02 Ryan White HIV/AIDS Program Services: Eligible Individuals and Allowable Use of Funds [PDF]).
- Unique service delivery challenges.

Important: public information

When filling out your SF-424 form, pay attention to Box 15: Descriptive Title of Applicant's Project.

We share what you put there with USAspending. This is where the public goes to learn how the federal government spends their money.

Instead of just a title, insert a short description of your project and what it will do.

See instructions and examples [PDF].

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Step 4: Understand Review, Selection, and Award

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Application review

Initial review

We will review your application to make sure that it meets eligibility criteria, including the completeness and responsiveness criteria. If your application does not meet these criteria, we will not fund it. If this is the case, we will notify your authorized official.

We will not review any pages that exceed the page limit.

Merit review

A panel reviews all applications that pass the initial review. You can find more about the merit review process in the application guide. The members use these criteria.

Criterion	Total number of points = 100
1. Need	45 points
2. Response	20 points
3. Performance reporting and evaluation	10 points
4. Impact	10 points
5. Resources and capabilities	5 points
6. Support requested	10 points

Criterion 1: Need (45 points)

See the project narrative Introduction and Need sections.

The panel will review your application for how well it does the following.

- **Comprehensive system of care and treatment (10 points) —** Details how your state/territory will use RWHAP Part B supplemental funding to support a comprehensive system of high-quality care and treatment for people with HIV and improve outcomes across the HIV care continuum.
- **Data supporting need (15 points) —** Includes data that supports the described need.
- **Severity of need (20 points) —** Demonstrates need and the relative severity of that need for the areas for which you are requesting funding. This includes all the information requested in the need section of the project narrative and its subsections.

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Criterion 2: Response (20 points)

See the project narrative Approach, High-level work plan, and Resolving challenges sections.

The panel will review your application for how well it:

- Proposes strong, appropriate goals, objectives, outcome measures, and activities that relate well to the program's purpose.
- Shows how you will engage stakeholders, including people with HIV, in planning, implementing, and improving your project.
- Details challenges likely to be encountered, and how you will resolve them and address possible risks.

Criterion 3: Performance reporting and evaluation (10 points)

See the project narrative Performance reporting and evaluation section.

The panel will review your application for the following.

Evaluation

- The appropriateness of your methods to collect, analyze, and use data to develop and carry out the project.
- The effectiveness of available resources (such as staff or software) to carry out the evaluation.
- The suitability of plans to share project evaluation results with stakeholders, including people with HIV.

Performance measurement

- Evidence that the measures you selected will assess whether you have met project goals and objectives, and to what extent the results can be attributed to the project.

Criterion 4: Impact (10 points)

See the project narrative High-level work plan and Sustainability sections.

The panel will review your application for:

- How effective the proposed project is in potentially improving the stages of the HIV care continuum. This includes your goals, objectives, outcome measures, and activities.

- How strong the project is in addressing gaps in service. This includes addressing unmet needs due to lack of funds, improving health outcomes, reducing the number of people out of care, and working toward ending the HIV epidemic.
- The strength of the proposed plan to sustain key elements of the project beyond the performance period.

Criterion 5: Resources and capabilities (5 points)

See the project narrative Organizational information and Performance reporting and evaluation sections.

The panel will review your application to determine the extent to which:

- Your agency can fulfill the needs of the proposed project.
- The project staff funded by this award (if any) have the experience necessary to carry out the project.

Criterion 6: Support requested (10 points)

See the Budget and budget narrative section.

The panel will review your application to determine:

- How reasonable costs support the objectives described in the application.
- How reasonable costs are and how well they align with the project's scope.

We do not consider **voluntary** cost sharing during merit review.

We review your application based on its technical merit.

Risk review

Before making an award, we review your award history to assess risk. We need to ensure all prior awards were managed well and demonstrated sound business practices. We:

- Review any applicable past performance.
- Review audit reports and findings.
- Analyze the budget.
- Assess your management systems.
- Ensure you continue to be eligible.
- Make sure you comply with any public policies.

We may ask you to submit additional information.

As part of this review, we use SAM.gov Entity Information Responsibility/Qualification to check your history for all awards likely to be more than $250,000 over the period of

performance. You can comment on your organization's information in SAM.gov. We'll consider your comments before making a decision about your level of risk.

If we find a significant risk, we may choose not to fund your application or to place specific conditions on the award.

For more details, see 2 CFR 200.206.

Selection process

When making funding decisions, we consider:

- The amount of available funds.
- Assessed risk.
- Alignment with HRSA Mission and Strategic Priorities
- Merit review results. These are key in making decisions but are not the only factor.
- The larger portfolio of HRSA-funded projects, including project type and geographic distribution.
- The funding priorities, funding preferences, and special considerations listed.

You cannot appeal a denial, or the amount of funds awarded" which comes above funding priorities: "Additionally, we may not make an award if you are delinquent on two or more Single Audit Report.

Funding preferences

Priority funding

Qualifications to meet the funding preferences:

Qualification 1: RWHAP Part B base formula award decreased by greater than 10% between FY 2006 and FY 2026.

You can request funding preference if:

Section 2620(c) of the PHS Act directs the Secretary to provide funds to states/territories to address the decline or disruption of services related to the decline in the amount of formula funding. We set aside a portion of the RWHAP Part B supplemental funding to award priority funds in conformance with this statutory requirement.

You will be granted priority funding if your RWHAP Part B base formula award decreased by more than 10% between FY 2006 and FY 2026. If you are determined eligible for priority funding, we will calculate the additional amount to be awarded and include that amount in the final award.

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Award notices

We issue Notices of Award (NOA) on or around the start date listed in the NOFO. See How we make awards in the Application Guide [PDF] for more information.

By drawing down funds, you accept the terms and conditions of the award.

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Step 5:
Submit Your Application

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Application submission and deadlines

Your organization's authorized official must certify your application. See the section on finding the application package to make sure you have everything you need.

Application deadline

You must submit your application by Friday, July 10, 2026, at 11:59 p.m. ET.

Grants.gov creates a date and time record when it receives applications.

If you need a deadline extension, see "requesting a waiver" in the application guide.

Submission method

Grants.gov

You must submit your application through Grants.gov. You may do so using Grants.gov Workspace. This is the preferred method. For alternative online methods, see Applicant System-to-System.

For instructions on how to submit in Grants.gov, see the Quick Start Guide for Applicants. Make sure that your application passes the Grants.gov validation checks, or we may not get it. Do not encrypt, zip, or password protect any files.

If Grants.gov rejects your application due to errors, you must correct and resubmit before the deadline.

If you want to know more about correcting errors or tracking your application, you can refer to the application guide.

Have questions? Go to Contacts and Support.

Other submissions

Intergovernmental review

This NOFO is not subject to Executive Order 12372, Intergovernmental Review of Federal Programs. No action is needed.

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Step 6: Learn What Happens After Award

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Post-award requirements and administration

Administrative and national policy requirements

There are important rules you need to know if you get an award. You must follow:

- All terms and conditions in the Notice of Award (NOA). We incorporate this NOFO by reference.
- The regulations at 2 CFR Part 200, Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards, modifications at 2 CFR Part 300, and any superseding regulations.
- The HHS Grants Policy Statement. Your NOA will reference this document. If there are any exceptions to the GPS, they'll be listed in your NOA.
- All federal statutes and regulations relevant to federal financial assistance, including those highlighted in HHS Administrative and National Policy Requirements [PDF].
- The requirements for performance reporting and evaluation in 2 CFR 200.301.
- All anti-discrimination laws: By applying for or accepting federal funds from HHS, you certify compliance with all federal antidiscrimination laws and these requirements. Complying with those laws is a material condition of receiving federal funding streams. You are responsible for ensuring subrecipients, contractors, and partners also comply.

Required Alignment with Health Resources and Services Administration (HRSA) Mission and Strategic Priorities

Recipients must use funds awarded under this NOFO to implement program goals or agency priorities in accordance with the HRSA vision, mission, core values, and strategic priorities, where authorized by law.

In administering programs under this and all funding announcements, HRSA prioritizes:

- **Evidence-based healthcare:** Funding activities supported by rigorous scientific evidence, particularly for programs serving children and adolescents, where HRSA is committed to approaches that reflect the highest standards of clinical care and child safety.
- **Biological and physiological integrity:** Recognizing the relevance of biological sex to health outcomes, HRSA encourages applicants to account for sex-based health factors

in program design, data collection, and service delivery where scientifically appropriate.

HRSA will implement these priorities consistent with applicable laws, regulations, court orders, and all required administrative procedures. Applicants are encouraged to describe how their proposed programs align with these priorities in their project narratives.

Funded activities must advance HRSA's vision of protecting and improving the health and well-being of Americans. The particular focus is on those who are medically vulnerable or live in areas with limited access to care. HRSA's duty is to serve wisely, effectively, and with measurable results that justify every taxpayer dollar invested.

Consistent with HRSA's priorities, in carrying out any project funded under this NOFO, the recipient must adhere to the following principles, where they are consistent with the authority and scope of the award and its activities:

- **Gold standard science:** Design and deliver services using gold standard evidence-based and evidence-informed approaches, establish measurable performance goals, and use data to monitor outcomes and drive continuous improvement.
- **Program integrity and fiscal stewardship:** Recipients must:
    - Administer funds in accordance with all applicable federal statutes, regulations, and award conditions.
    - Maintain strong internal controls.
    - Prevent waste, fraud, and abuse.
- **Partnership and local leadership:** Coordinate with state, tribal, territorial, local, and community partners, as appropriate, and tailor services to meet community-identified needs while respecting local decision-making authority.

Recipients must manage any project awarded under this NOFO in accordance with the following objectives in programs authorized to advance them:

- **Make America Healthy Again (MAHA):** While ensuring access to high-quality, affordable physical and mental health care, HRSA prioritizes the health and well-being of all Americans by supporting common-sense, evidence-based health policies that promote:
    - Personal responsibility.
    - Strong families and communities.
    - Proper nutrition.
    - The prevention and management of chronic disease.
- **Child protections, biological integrity, parental rights, and lawful use of funds:** HRSA prioritizes safeguarding children's health and safety by:
    - Not supporting medical interventions for gender dysphoria in minors that lack a

strong evidence base.

- Applying sex-based definitions grounded in biological reality.
- Supporting parental authority, transparency, and choice in education, including school-based health centers that respect parental rights and religious upbringing.
- Ensuring taxpayer funds do not promote or support elective abortions, consistent with federal law and the Hyde Amendment.

- **Advancing evidence-based, merit-driven, and ethically grounded health care**: HRSA will prioritize unbiased, transparent science; merit-based workforce opportunities; and programs that demonstrate measurable outcomes. HRSA will deprioritize organizations with:
  - Conflicts of interest.
  - "Harm reduction" models.
  - Housing-first approaches.
  - Activities that facilitate illegal drug use or unsafe medical practices.
- **Promoting public safety, lawful use of federal funds, and national health priorities:** To the extent permitted by law, HRSA will align funding with administration priorities by:
  - Supporting ending the HIV epidemic through authorized, evidence-based care.
  - Reserving benefits for eligible individuals.
  - Discouraging illegal immigration and unsafe community practices.
  - Prioritizing recipients that enforce public safety, address serious mental illness and substance use through treatment and recovery, and reduce homelessness responsibly.

To the extent allowable by law, under awards, HRSA will give priority to states and municipalities for programs to:

- Enforce prohibitions on open illicit drug use.
- Enforce prohibitions on urban camping and loitering.
- Enforce prohibitions on urban squatting.
- Enforce, and where necessary, adopt, standards that address individuals who are a danger to themselves or others and suffer from serious mental illness or substance use disorder, or who are living on the streets and cannot care for themselves. The approach must be through assisted outpatient treatment or by moving them into treatment centers or other appropriate facilities through civil commitment or other available means, to the maximum extent permitted by law.

HRSA will implement these priorities consistent with applicable laws, regulations, court orders, and any required procedures.

The recipient must demonstrate ongoing compliance with these priorities, in all programs that are authorized to advance them, through program design, implementation, reporting, and evaluation.

Failure to meaningfully align funded activities with the applicable requirements may result in corrective action, additional reporting requirements, or other actions consistent with federal grant regulations at 2 CFR. part 200 and the terms and conditions of this award. This includes termination under CFR. 200.340(a)(4) if an award no longer effectuates the program goals or agency priorities.

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Cybersecurity

- If awarded, you must develop plans and procedures, modeled after the NIST Cybersecurity framework, to protect HHS systems and data.

Successful applicants under this NOFO agree that:

Where award funding involves:	Recipients and subrecipients are required to:
Implementing, acquiring, or upgrading health IT for activities funded by any entity.	Use health IT that meets standards and implementation specifications adopted in 45 CFR 170, Subpart B, if such standards and implementation specifications can support the activity. Visit 45 CFR 170, Subpart B to learn more.
Implementing, acquiring, or upgrading health IT for activities by eligible clinicians in ambulatory settings, or hospitals, eligible under Sections 4101, 4102, and 4201 of the HITECH Act.	Use health IT certified under the ONC Health IT Certification Program if certified technology can support the activity. Visit Certification of Health IT to learn more.

If standards and implementation specifications adopted in 45 CFR part 170, Subpart B cannot support the activity, recipients and subrecipients are encouraged to use health IT that meets non-proprietary standards and implementation specifications developed by consensus-based standards development organizations. This may include standards identified in the ONC Interoperability Standards Advisory.

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Reporting

If you are funded, you will have to follow the reporting requirements in the reporting section of the Application Guide [PDF]. The NOA will provide specific details.

You must also follow these program-specific reporting requirements:

- Progress reports at the end of the period of performance.
- Annual performance reports.
- NOFO-specific reporting requirements:
  - **Federal Financial Report (SF-425).** You must account for your expenditures under the project for the year. We will provide more specific information in the notice of award (NoA). You can also see Reporting Requirements on HRSA's website.
  - **Program Terms Report (PTR).** You must submit a program terms report, which will be described in the NoA.
  - **RWHAP Services Report (RSR).** You must comply with the RSR data requirements and make sure your subrecipients also comply. The RSR captures information to show program performance and accountability.
    - All RWHAP core medical service and support service providers must submit client-level data, as instructed in the RSR manual.
    - We will provide further information in the NoA. You can also refer to the HIV/AIDS Program Client-Level Data website for additional information.
  - **ADAP Data Report (ADR).** If you spend any of the RWHAP Part B supplemental award on ADAP, you must comply with ADR data reporting requirements. You must also make sure your subrecipients comply. We will provide further information in the NoA. You can also refer to the HIV/AIDS Program ADAP Data Report website for additional information.

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Agency contacts

Program and eligibility

Kibibi Matthews-Brown
Senior Program Advisor
Attn: Division of State HIV/AIDS Programs (DSHAP)
Ryan White HIV/AIDs Program Part B States/Territories Supplemental Grant Program
Health Resources and Services Administration
KMatthews-Brown@hrsa.gov
301-443-1035

Financial and budget

Olusola Dada
Grants Management Specialist
Division of Grants Management Operations
Office of Financial Assistance and Acquisition Management (OFAAM)
Health Resources and Services Administration
ODada@hrsa.gov
301-443-0195

HRSA Contact Center

Open Monday – Friday, 7 a.m. – 8 p.m. ET, except for federal holidays.
Call: 877-464-4772 / 877-Go4-HRSA
TTY: 877-897-9910

Electronic Handbooks Contact Center

Help with systems

Grants.gov

Grants.gov provides 24/7 support. You can call 800-518-4726, search the Grants.gov Knowledge Base, or email Grants.gov for support. Hold on to your ticket number.

SAM.gov

If you need help, you can call 866-606-8220 or live chat with the Federal Service Desk.

Helpful websites

- Application Guide [PDF]
- HRSA Grants page
- HHS Tips for Preparing Grant Proposals
- Grants.gov Frequently Asked Questions
- Grants.gov Applicant Training

EXHIBIT J

Notice of Funding Opportunity

Application due 07/08/2026

HRSA
Health Resources & Services Administration

HIV/AIDS Bureau

Ryan White HIV/AIDS Program Part C Capacity Development Program

Opportunity number: HRSA-26-061

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Before you begin

If you believe you are a good candidate for this funding opportunity, secure your SAM.gov and Grants.gov registrations now. If you are already registered, make sure your registrations are active and up-to-date.

SAM.gov registration (this can take several weeks)

You must have an active account with SAM.gov. This includes having a Unique Entity Identifier (UEI).

See Step 2: Get Ready to Apply

Grants.gov registration (this can take several days)

You must have an active Grants.gov registration. Doing so requires a Login.gov registration as well.

See Step 2: Get Ready to Apply

Apply by the application due date

Applications are due by 11:59 p.m. Eastern Time on 07/08/2026.

To help you find what you need, this NOFO uses internal links. In Adobe Reader, you can go back to where you were by pressing Alt + Left Arrow (Windows) or Command + Left Arrow (Mac) on your keyboard.

All activities proposed in your application and budget narrative must align with applicable law, including but not limited to statutes, executive orders, federal regulations and applicable judicial holdings. Accordingly, discretionary awards shall not be used to fund, promote, encourage, subsidize, or facilitate racial preferences or other forms of racial discrimination by the recipient, including activities where race or intentional proxies for race will be used as a selection criterion for employment or program participation; denial by the recipient of the sex binary in humans, or the belief that sex is a chosen or mutable characteristic; illegal immigration; or any other initiatives that compromise public safety. If an application does not align, the application will not receive funding to the extent permitted by law and applicable court orders.

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Step 1:
Review the Opportunity

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Basic information

Health Resources Services Administration

HIV/AIDS Bureau

Strengthening the capacity of community-based organizations to improve health outcomes and reduce HIV transmission, especially for people not yet in regular HIV care.

Summary

The Ryan White HIV/AIDS Program (RWHAP) provides a comprehensive system of HIV care that improves health outcomes and supports HIV viral suppression.

The purpose of the RWHAP Part C Capacity Development Program is to strengthen the capacity of community-based organizations to improve health outcomes and reduce HIV transmission, especially for people not yet in regular HIV care. The focus of this Part C program is on infrastructure.

This capacity development funding offers a one-year opportunity to carry out one short-term activity in FY 2026.

Funding details

Application types: New

Expected total available funding in FY26: $9,000,000

Expected number and type of awards: 60 G (Grants)

Funding range per award: Up to $150,000

We plan to fund awards in one 12-month budget period for a total one-year period of performance from 09/01/2026 to 08/31/2027.

The program and awards depend on the appropriation of funds and are subject to change based on the availability and amount of appropriations.

Have questions?
Go to Contacts and Support.

Key facts

Opportunity name:
Ryan White HIV/AIDS Program Part C Capacity Development Program

Opportunity number:
HRSA-26-061

Announcement version:
Initial

Federal assistance listing:
93.918

Key dates

NOFO issue date:

06/05/2026

Informational webinar:
See Join the webinar

Application deadline:
07/08/2026

Expected award date is by:
09/01/2026

Expected start date:
09/01/2026

See other submissions for other time frames that may apply to this NOFO.

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Eligibility

You can apply if your organization is in the United States.

Types of eligible organizations

These types of domestic organizations may apply:

- State governments.
- County governments.
- City or township governments.
- Special district governments.
- Public and State controlled institutions of higher education.
- Native American tribal governments (Federally recognized).
- Native American tribal organizations (other than Federally recognized tribal governments).
- Nonprofits having a 501(c)(3) status with the IRS, other than institutions of higher education.
- Nonprofits without 501(c)(3) status with the IRS, other than institutions of higher education.
- Private institutions of higher education.

Additional information on eligibility

Individuals are not eligible applicants under this NOFO.

Completeness and responsiveness criteria

We will review your application to make sure it meets these basic requirements to move forward in the competition.

We will not consider an application that:

- Is from an organization that does not meet all eligibility criteria.
- Requests funding above the award ceiling shown in the funding range.
- Is submitted after the deadline.
- Does not propose one of the three activities listed as described in the Program Requirements and Expectations section. The three available activities in this announcement are: 1. Electronic Health Record and Data Integration, 2. Telehealth, or 3. Office dental equipment for expanding service capacity.

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Application limits

You may not submit more than one application. If you submit more than one application, we will only accept the last on-time submission.

Cost sharing

This program has no cost-sharing requirement. If you choose to share in the costs of the project, we will not consider it during merit review. Recipients agree that once committed, cost sharing amounts are enforceable and subject to reporting and auditing requirements under 2 CFR 200.

Post-award requirements

Before you apply, make sure you understand the requirements that come with an award.

See Step 6: Learn What Happens After Award for information on regulations that apply, reporting, and more.

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Program description

Purpose

This one-year capacity development funding opportunity is intended to strengthen organizational capacity to develop, enhance, or expand access to high quality HIV care and treatment for low-income people with HIV, especially for people not yet in regular HIV care.

HRSA intends to fund one short-term activity under this program that can be completed by the end of the one-year period of performance.

Goal alignment

Proposed projects must:

- Align with program goals.
- Address unmet needs or gaps in care for people with HIV.
- Establish activities that represent a meaningful addition to your existing program.
- Support improved health outcomes for people with HIV.

For additional information, please refer to Policy Clarification Notice (PCN) 16-02 for a list of RWHAP allowable services and use of funds.

For more details, see Program requirements and expectations.

Background

The Ryan White HIV/AIDS Program

The Ryan White HIV/AIDS Program (RWHAP) has five statutorily defined Parts that provide grants to states, cities, counties, local clinics, and community-based organizations. The grants fund medical care, medication, and essential support services, to meet the needs of people with HIV and family members affected by HIV. Together these grants provide a comprehensive system of care to ensure low-income people with HIV have access to services for early diagnosis of HIV, linkage to care, medically appropriate treatment, retention in care, and sustained viral suppression (a very low or undetectable amount of HIV in the blood).

For nearly four decades, the RWHAP has funded services to provide HIV primary health care, medication, and essential support services, including mental health care, transportation, case management, nutrition, and housing. These services support

clients to enter and remain in care, access medications, and reach viral suppression, reducing transmission and lowering health care costs.

Ending the HIV Epidemic

Launched in 2020, the Ending the HIV Epidemic in the U.S. (EHE) initiative further expands federal efforts to reduce HIV transmission. For the RWHAP, the EHE initiative expands the program's ability to meet the needs of clients, specifically focusing on linking people with HIV who are either newly diagnosed, diagnosed but currently not in care, or are diagnosed and in care but not yet virally suppressed, to the essential HIV care, treatment, and support services needed to help them reach viral suppression.

Making America Healthy Again

The Ryan White HIV/AIDS Program helps advance the Making America Healthy Again (MAHA) priorities by:

- **Expanding access to primary care** for people with HIV, particularly those with low incomes, and by strengthening the health workforce.
- **Fighting the chronic disease epidemic** by providing HIV medical care, treatment, and support services to people with HIV.
- **Supporting improved nutrition** by providing patient-centered focused medical nutrition therapy and food services.
- **Supporting disease prevention** through HIV care and treatment services that help people reach viral suppression so they live longer, healthier lives and do not transmit HIV.

Key accomplishments

- **Nearly 602,000 people with HIV** in the U.S. received life-saving care, medication, and essential support services through the RWHAP, representing over half of all diagnosed with HIV in the U.S. This is an increase of nearly 26,000 clients.
- **More than 91%** of Ryan White HIV/AIDS Program patients receiving HIV medical care were virally suppressed in 2024. This is up from 69.5% of patients virally suppressed in 2010 and significantly higher than the 67.2% virally suppressed nationally among all people with diagnosed HIV.
- **More than 47%** of Ryan White HIV/AIDS Program clients are aged 50 years and older, demonstrating the program's success in supporting older clients and its commitment to addressing the unique needs of people aging with HIV.

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Program requirements and expectations

You must show:

- That the proposed activity will strengthen organizational capacity.
- Your organization's intent and ability to maintain services, activities or equipment that were either purchased by, or are a direct result of, this federal award.
- Coordinating with other relevant HHS and HRSA providers to avoid duplicating efforts.

You must select only one activity.

You may submit a proposal for only **one** activity from the list of activities below. Do not submit a proposal that includes more than one activity.

The goal of these activities is to enhance an organization's infrastructure to better serve people with HIV.

- **Activity 1:** Electronic Health Record and Data Coordination
- **Activity 2:** Telehealth
- **Activity 3:** Dental equipment for expanding dental service capacity

Brief summaries of each activity

Activity 1: Electronic Health Record and Data Coordination

Improving how Electronic Health Records (EHR) connect with HIV data systems helps reduce duplicate data entry, increases the accuracy of data collection and reporting, and improves care coordination and tracking of referrals.

If you select this activity, funding may be used to purchase software to interface CAREWare (or other HIV data collection systems) with an existing EHR system.

Activities can include:

- Improving the accuracy and efficiency of data collection.
- Creating workflows to reduce administrative burden.
- Verifying and cleaning data.
- Testing historical and new data.
- Integrating oral health and primary care EHR systems.
- Securing consultant services for system integration and coordination.
- Enhancing interoperability to streamline RWHAP eligibility across Parts using existing data sources (e.g., Medicaid, health information exchanges, or marketplace records).

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All activities must be used to enhance or expand an existing EHR system to improve the:

- Quality.
- Pharmacological safety.
- Efficiency.

Funds cannot be used to purchase a brand-new EHR system. Any component purchased with federal funds must meet certification requirements set by the Assistant Secretary for Technology Policy and be configured to report clinical data electronically for HRSA reporting. More information is available at HealthIT.gov.

Activity 2: Telehealth

Telehealth improves access to care. It does this by reducing or eliminating the time needed to travel to and from appointments, and by lessening other social barriers such as caregiving responsibilities and lack of transportation that can cause people to miss their appointments.

Telehealth allows care delivery across any distance, expanding access to quality primary health.

If you select this activity, you must develop and acquire, through lease or purchase:

- Computer hardware and software.
- Audio and video equipment.
- Computer network equipment.
- Interactive equipment.
- Data terminal equipment.
- Other equipment that furthers the objectives of the proposed telehealth activity.

You must describe technology requirements and each type of equipment to be employed.

Include a concise description of the equipment's:

- Relevance to the project.
- Cost-effectiveness.
- Timeliness.
- Accuracy of care.
- Ease of use.

Discuss the telehealth reimbursement environment and whether Medicare, Medicaid, or private insurance in your state(s) cover telehealth services.

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For resources addressing this topic, access HRSA's Office for the Advancement of Telehealth and HHS's Telehealth for providers.

Activity 3: Dental Equipment for Expanding Dental Service Capacity

Personnel salaries for the provision of dental care (positions such as hygienist, dental assistant, dentist, etc.), purchase of a mobile unit, or construction are **not** allowable under this activity.

Oral health care is one of the core medical service categories in the RWHAP and can be a part of all clinical care plans for people with HIV. A large proportion of people with HIV have unmet dental care needs due to lack of available dental providers, limited transportation, costs of care, or other barriers.

RWHAP Part C supports a comprehensive approach to oral health care for low-income people with HIV, including the co-location of oral health care services with outpatient ambulatory health care.

If you select this activity, you must purchase dental equipment for the purpose of developing, enhancing, or expanding oral health care services for people with HIV.

Specifically, this activity involves creating or expanding a dental operatory in a clinic or in a mobile unit (e.g., van) through purchasing equipment such as:

- Dental patient chairs.
- Sterilization units.
- X-ray imaging instruments.
- Dental operating lights.
- Operatory cabinets.
- Hand pieces.

Statutory authority

42 U.S.C. §§ 300ff-54(c)(1)(B) and (Title XXVI, §§ 2654(c)(1(B) and 2693 of the Public Health Service Act).

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Award information

Funding policies and limitations

Changes in HHS regulations

As of October 1, 2025, HHS has adopted 2 CFR Part 200, with some modifications included in 2 CFR Part 300. These regulations replace those in 45 CFR Part 75.

Policies

- To make an award, funding must be available and allocated for this program and purpose, at which point we will move forward with the review and award process.
- Have clear policies and good financial practices to avoid spending HRSA funds on unallowable activities.
- Like other award rules, we may audit your policies, procedures, and controls.
- If we receive more funding for this program, we may:
  - Fund more applicants from the rank order list.
  - Extend the period of performance.
  - Award supplemental funding.

General limitations

- For guidance on some types of costs we do not allow or restrict, see
  - Project Budget Information in Section 3.1. of the Two-Tier Application Guide [PDF].
  - 2 CFR Part 200 Subpart E - General Provisions for Selected Items of Cost.
  - Allowable and Unallowable Costs and Activities, in the HHS Grants Policy Statement.
- All costs must be reasonable, necessary, allocable to the award, and adequately documented (2 CFR 200.403).
- You cannot earn profit from the federal award. See 2 CFR § 200.400(g).
- Current appropriations law includes a salary limit of $228,000 as of January 2026 that applies to this program. You may pay salaries at a higher rate if the rate beyond the salary rate limit (Executive Level II) is paid with non-HHS funds. For help calculating salaries under this limit, read more at “salary rate limitation” in the Two-Tier Application Guide [PDF].

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Program-specific statutory or regulatory limitations

You cannot use funds under this notice for the following:

- Funding restrictions included in Policy Clarification Notice 16-02 *Ryan White HIV/AIDS Program Services: Eligible Individuals and Allowable Uses of Funds*.
- Charges that are billable to third party payors (e.g., private health insurance, prepaid health plans, Medicaid, Medicare, Department of Housing and Urban Development (HUD) funding for housing services, other RWHAP funding including AIDS Drug Assistance Program).
- To directly provide housing or health care services (e.g., HIV care, counseling and testing) that duplicate existing services.
- Payments for clinical research.
- Payments for nursing home care.
- Cash payments to intended clients of RWHAP services.
- Purchase or improvement to land.
- Purchase, construction, or major alterations or renovations on any building or other facility (see 2 CFR 200 – subpart A Definitions).
- PrEP or non-occupational Post-Exposure Prophylaxis (nPEP) medications or the related medical services. As outlined in the updated November 16, 2021 RWHAP and PrEP program letter.
- Purchase of sterile needles and syringes for the purpose of hypodermic injection of any illegal drug use. Some aspects of syringe services programs are allowable with HRSA's prior approval and in compliance with HHS and HRSA policy. See Syringe Services Programs.
- Development of materials designed to directly promote or encourage intravenous drug use or sexual activity, whether homosexual or heterosexual.
- Research.
- Foreign travel.
- Long-term activities.
    - Instead, the activities should be short-term in nature with a targeted completion by the end of the one-year period of performance.

You must have policies, procedures, and financial controls in place. Anyone who receives federal funding must comply with legal requirements and restrictions, including those that limit specific uses of funding.

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Follow the list of statutory restrictions on the use of funds in Section 4.1 (Funding Restrictions) of the Application Guide. We may audit the effectiveness of these policies, procedures, and controls. 2 CFR § 200.216 prohibits certain telecommunications and video surveillance services or equipment. For details, see the HRSA Grants Policy Bulletin Number: 2021-01E.

See Manage Your Grant for other information on costs and financial management.

Indirect costs

Indirect costs are costs you charge across more than one project that cannot be easily separated by project. For example, this could include utilities for a building that supports multiple projects.

To incur indirect costs, you can select one of two methods:

Method 1 – Approved rate. You currently have an indirect cost rate approved by your cognizant federal agency at the time of award.

Method 2 – *De minimis* rate. Per 2 CFR § 200.414(f), if you do not have a current negotiated indirect cost rate, you may elect to charge a *de minimis* rate. If you choose this method, costs included in the indirect cost pool must not be charged as direct costs.

This rate is up to 15% of modified total direct costs (MTDC). See 2 CFR § 200.1 for the definition of MTDC. You can use this rate indefinitely for all your federal awards or until you choose to receive a negotiated rate.

Consider your indirect costs when developing your budget.

Program income

Program income is money earned as a result of your award-supported project activities. You must use any program income you generate from awarded funds for approved project-related activities. Find more about program income at 2 CFR 200.307.

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Step 2:
Get Ready to Apply

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Get registered

SAM.gov

You must have an active account with SAM.gov to apply. SAM.gov registration can take several weeks. Begin that process today.

To register:

- Go to SAM.gov Entity Registration and select Get Started. From the same page, you can also select the Entity Registration Checklist for the information you will need to register.
- You must agree to the financial assistance general certifications and representations specifically. Those for contracts are different.

When you register, you will also receive your required Unique Entity Identifier (UEI).

Once you register:

- You will have to maintain your registration throughout the life of any award.
- If your organization has multiple UEIs, use the one associated with your physical location.

If you need additional information about user roles in SAM.gov, see “Get registered: SAM.gov user roles” in the Application Guide [PDF].

Grants.gov

You must also have an active account with Grants.gov. You can see step-by-step instructions at the Grants.gov Quick Start Guide for Applicants and How to Apply for Grants.

Find the application package

The application package has all the forms you need to apply. You can find it online. Go to Grants Search at Grants.gov and search for opportunity number HRSA-26-061.

After you select the opportunity, we recommend that you click the Subscribe button to get updates.

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Application writing help

Visit HHS Tips for Preparing Grant Proposals.

Visit HRSA's How to Prepare Your Application page for more guidance.

See Apply for a Grant for other help and resources.

FAQs will be posted on our TA webpage after the webinar.

Join the webinar

Webinar information will be posted to the Related Documents tab on Grants.gov. We recommend you "Subscribe" to the NOFO on Grants.gov to receive updates when documents are posted.

Have questions? Go to Contacts and Support.

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Step 3: Build Your Application

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Application checklist

There are two types of forms in Grants.gov.

- Some forms allow you to upload components of your application to the form. These include components like your project narrative, budget and budget narrative, and attachments, as applicable.
- Other forms are more typical, fill-in-the-blank forms.

Make sure that you have everything you need to apply.

Narratives

Component	Grants.gov form	Included in page limit*?
☐ **Project narrative**	Project Narrative Attachment form.	Yes
☐ **Budget narrative**	Budget Narrative Attachment form.	Yes

Attachments

Insert each in the Attachments Form in this order.

Component	Included in page limit*?
☐ 1. Proof of non-profit status	No
☐ 2. Funding preference	No
☐ 3. Federally negotiated indirect cost rate	No
☐ 4. Biographical sketches	No
☐ 5. Program specific line-item budget	Yes
☐ 6. Work plan	Yes
☐ 7. Staffing plan job descriptions	Yes
☐ 8. Agreements with other entities and memoranda of understanding	Yes
☐ 9-15. Other relevant documents	Yes

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Other required forms

Upload using each required form in Grants.gov.

Forms	Submission requirement
Application for Federal Assistance (SF-424)	With application.
Project Abstract Summary form	With application.
Grants.gov Lobbying form	With application.

*Only what you attach in these forms counts toward the page limit. The forms themselves do not count.

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Application contents and format

This section includes guidance on each component found in the application checklist.

Application page limit: 25

Submit your information in English and express whole number budget figures using U.S. dollars.

Required format

Required format for project summary, project narrative, budget narrative, and attachments.

Font: A readable font like Arial, Courier, CG Times, or Times New Roman

File format: We only accept the following document formats:

- .PDF - Adobe Portable Document Format
- .DOC/.DOCX - Microsoft Word
- .RTF - Rich Text Format
- .TXT - Text
- .WPD - Word Perfect Document
- .XLS/.XLSX - Microsoft Excel
- .VSD - Microsoft Visio

Size: 12-point font
Footnotes, charts, graphics, and budget tables may be 10-point or higher.

Ink color: Black

Spacing: Single-spaced, including all text and tables.

Alignment: Left

Headings: Bold all headings and align left.

Size: 8.5 x 11 (Make sure the print area is set and allows printing to 8.5 x 11.)

Margins: 1-inch on all sides

Footer: On each page as the footer, include your organization's name and page numbers. If a competing continuation or competing supplement, also include your 10-digit award number.

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Page numbering:

- Do not number the standard OMB-approved forms.
- Number each attachment page sequentially (that is, 1, 2, 3).
- Reset the numbering for each attachment.
- Treat each attachment as a separate section.

File names: You can find guidance for naming your files in the Application Guide [PDF].

Project narrative

Introduction

See merit review criterion 1: Need

- Indicate the **one activity** you will implement:
  - Electronic Health Record and Data Coordination.
  - Telehealth.
  - Dental equipment for expanding office capacity.
- Describe the need for capacity development funding within your community and organization.
- Explain how the proposed activity will improve access to high-quality, HIV primary care for low-income people with HIV.
- Demonstrate how this is a **brand-new activity** and does not duplicate nor repeat any infrastructure development activities previously funded under the RWHAP Part C Capacity Development program.
- It also cannot duplicate activities of the RWHAP Part D Women, Infants, Children and Youth (WICY) Supplemental program (HRSA-24-061; HRSA-24-062) or FY 2025 (HRSA-25-050; HRSA-25-049).

Need

See merit review criterion 1: Need

For your proposed activity:

- Outline the equipment or data system needs you plan to address.
  - Describe the gaps in organizational capacity due to limitations in the current system infrastructure.
  - Include changes you have made to the current service delivery system.
  - Describe how the lessons you have learned will be applied to this activity.

- Provide information specific to the selected activity and describe how these gaps or limitations are affecting the optimal provision of quality HIV primary care services.
    - Include how health care gaps or limitations are affecting your organization's ability to optimize HIV outcomes.
- Discuss the relevant barriers to successfully carry out the project. Include the steps you will take to minimize or overcome them.

Approach

See merit review criterion 2: Response

- Provide a clear description of the approach.
    - Include specific action steps.
    - Describe how actions will address the need and attain project objectives.
    - Include how the activity will be used to expand or improve client care.
    - Include the person(s) responsible for putting your proposed project in place (both staff and partners).
- Describe plans to share any information or products developed with the people and communities disproportionately impacted by HIV.
    - You should also plan to share lesson learned with these people and communities.
    - This should include community providers and project partners so they are made aware of the additional capability created by this proposed project.

Work plan

See merit review criteria 2: Response

Provide a detailed work plan for the 12-month period of performance of September 1, 2026 to August 31, 2027. For all activities, the work plan must:

- Describe the activity's goal and objectives.
- Describe how you'll achieve each of the objectives during the period of performance.
- List the key action steps needed to reach the goal.
    - Include when each step will be completed and who is responsible for each.
- Provide a timeline showing when each step will be completed and name the staff responsible for each step.
- Identify the measures you will use to evaluate success.
- Describe the expected outcomes that will show the impact of the activity.

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    - Outcomes may include changes in quality of service, service delivery type, treatment outcomes, knowledge, skills, practices, or other improvements.

Provide the above information in a table format with the following sections outlined:

- Goal and objectives.
- Action steps.
- Timeline.
- Person responsible.
- Evaluation measures.
- Outcomes.

You will also include a more detailed work plan that you will submit as Attachment 6.

Resolving challenges

See merit review criterion 4: Impact

- Discuss challenges that you are likely to encounter in your work plan and explain approaches that you'll use to resolve them.
- Describe the specific activities or strategies you will use to mitigate or resolve anticipated challenges. Include your plan to overcome any barriers to full implementation

Performance reporting and evaluation

See merit review criteria 3: Performance reporting and evaluation and 5: Resources and capabilities

Performance measurement and reporting

- Describe how you will collect and manage data in a way that helps you improve the way you carry out your activity.
- Track the goals and objectives identified in the work plan.

Program evaluation

- Describe how you will evaluate the effectiveness of your proposed capacity development project.
- Describe how you will share evaluation results internally with program staff and externally with key stakeholders (including people with HIV).

See the reporting section for more information.

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Sustainability

See merit review criterion 4: Impact

- Show that the activities outlined in the work plan can be reasonably completed within 12 months.
- Describe the organizational resources that you will use to sustain, without additional funds from the federal government, the project activities or enhancements supported by this award beyond the one-year period of performance.

Organizational information

See merit review criterion 5: Resources and capabilities

- Briefly describe the organizational skills, capabilities, and resources, including staff that will contribute to your organization's ability to carry out the proposed activity.
- Highlight key staff with relevant expertise and experience with similar work.
  - This information should align with the staffing plan provided in Attachment 7 and the biographical sketches of key personnel provided in Attachment 4.
- Discuss the organization's ability to secure agreements or contracts with community-based organizations, health care providers, and consultant services to achieve this project.
- Describe your plan to purchase equipment and execute contracts for services for this project within a reasonable timeframe.

Budget and budget narrative

See merit review criterion 6: Support requested

Your **budget** should follow the instructions in budget narrative: detailed instructions section of the Application Guide [PDF] and the instructions listed in this section. Your budget should show a well-organized plan.

HHS now uses the definitions for equipment and supply in 2 CFR 200.1. The new definitions change the threshold for equipment to the lesser of the recipient's capitalization level or $10,000 and the threshold for supplies to below that amount.

The total project or program costs are all allowable (direct and indirect) costs used for the HRSA award activity or project. This includes costs charged to the award and non-federal funds used to satisfy a matching or cost-sharing requirement (which may include maintenance of effort, if applicable).

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The **budget narrative** supports the information you provide in Standard Form 424-A. It includes an itemized breakdown and a clear justification of the costs you request. The merit review committee reviews both.

As you develop your budget, consider:

- If the costs are reasonable, allowable and allocable, and consistent with your project's purpose and activities.
- The restrictions on spending funds. See funding policies and limitations.

Line-Item budget:

- In addition to the SF-424 Application Guide requirements, you must also provide the line-item budget and budget narrative according to each object class category (e.g., Personnel, Fringe Benefits, Travel).
    - The budget allocations on the line-item budget must relate to the activities proposed in the project narrative, including the work plan.
- To evaluate your adherence to RWHAP Part C Capacity Development statutory budget requirements, submit a program-specific line-item budget for the one-year period of performance (September 1, 2026 – August 31, 2027).
    - Highlight any administrative costs by making them **bold**.

The budget narrative supports the information you provide in Standard Form 424-A. See other required forms. It includes an itemized breakdown and a clear justification of the requested costs. The merit review committee reviews both.

As you develop your budget, also consider the **restrictions on spending funds**. See Funding policies & limitations.

To create your budget narrative, see detailed instructions in Section 3.1.5 of the Application Guide [PDF].

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Attachments

Place your attachments in this order in the Attachments Form. See application checklist to determine if they count toward the page limit.

Unless the instructions below require it, do not submit organizational brochures or other promotional materials (for example, slides, films, clips).

Attachment 1: Proof of non-profit status

If your organization is non-profit, you need to attach proof. We will accept any of the following:

- A copy of a current tax exemption certificate from the IRS.
- A letter from your state's tax department, attorney general, or another state official saying that your group is non-profit and that none of your net earnings go to private shareholders or others.
- A certified copy of your certificate of incorporation. This document must show that your group is non-profit.
- Any of the listed documents for a parent organization. Also include a statement signed by an official of the parent group that your organization is a non-profit affiliate.

Attachment 2: Funding preference documentation

Provide information, including supporting documentation, data, and other details according to the instructions for funding preferences for either rural areas or underserved populations. **HRSA will review the information to determine whether you qualify for a funding preference.** See funding preferences for more information.

Attachment 3: Federally negotiated indirect cost rate (if applicable)

Provide any documents that describe working relationships between your organization and others you mention in your project narrative. If you include documents that confirm actual or pending contracts or agreements, the documents should clearly describe the roles of subrecipients and contractors and any deliverables. It is not necessary to include the entire contents of lengthy agreements, so long as the portions you include describe the working relationship between you and the other organization. Make sure letters of agreement are signed and dated.

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Attachment 4: Biographical sketches

Include biographical sketches for the principal investigator/principal director, project coordinator (if different) and any staff directly responsible for implementing the proposed projects that you describe in Attachment 7.

For key personnel, the biographical sketch should be no more than 1-page. Do not include personally identifiable information.

Attachment 5: Program specific line-item budget

Submit as a PDF document a program-specific line-item budget for the 1-year period of performance. SF-424A Section B is not counted toward the page limit; however, the line-item budget itself does count toward the page limit. Reference section See Section 3.4.1. of the Application Guide [PDF].

Attachment 6: Work plan

Attach the project's work plan for the 12-month period of performance of September 1, 2026 to August 31, 2027. Make sure it includes everything required in the project narrative section.

Attachment 7: Staffing plan and job descriptions

See Section 3.1.7 of the Application Guide [PDF].

Include a staffing plan that provides key information about the staff positions. Include: name, position title, brief background, and the role and responsibilities of the person in your proposed project. For each staff, include the sources of funding for your proposed project and corresponding time and effort. It is recommended to supply this information in the form of a table.

Attachment 8: Agreements with other entities

Provide any documents that describe working relationships between your organization and others you refer to in the proposal. Documents that confirm actual or pending contracts or agreements should clearly describe the roles of the contractors and any deliverable. Make sure you sign and date any letters of agreement.

Attachment 9-15: Other relevant documents

You may use attachments 9 through 15 for any other relevant documentation.

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Other required forms

You will need to complete some other forms. Upload the following forms at Grants.gov. You can find them in the NOFO application package or review them and any available instructions at Grants.gov Forms.

Forms	Submission requirement
Application for Federal Assistance (SF-424)	With application.
Project Abstract Summary form	With application.
Grants.gov Lobbying form	With application.

Form instructions

The application guide has detailed instructions for:

- The Application for Federal Assistance (SF-424).
- The Budget Information for Non-Construction Programs (SF-424A).

Project abstract summary form instructions

Complete the information in the Project Abstract Summary form. Include a short description of your proposed project. Include the needs you plan to address, the proposed services, and the population groups you plan to serve. Indicate the funding amount requested and the name the specific activity.

For more information, see Section 3.1.2 of the Application Guide [PDF].

Important: Public information

When filling out your SF-424 form, pay attention to Box 15: Descriptive Title of Applicant's Project.

We share what you put there with USAspending. This is where the public goes to learn how the federal government spends their money.

Instead of just a title, insert a short description of your project and what it will do.

See instructions and examples.

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Step 4: Understand Review, Selection, and Award

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Application review

Initial review

We will review your application to make sure that it meets eligibility criteria, and the requirements in this NOFO. If your application does not meet eligibility criteria, it will not be funded. If your application does not meet other criteria, we will not fund it.

Merit review

A panel reviews all applications that pass the initial review. You can find more about the merit review process in the Application Guide [PDF]. The members use these criteria.

Criterion	Total number of points = 100
1. Need	10 points
2. Response	35 points
3. Performance reporting and evaluation	15 points
4. Impact	10 points
5. Resources and capabilities	20 points
6. Support requested	10 points

Criterion 1: Need (10 points)

See the project narrative Introduction and Need sections.

The panel will review your application for how well it:

Introduction (3 points)

- States the proposed activity.
- Describes the overall purpose of the proposed project and the need for capacity development funding.
- Explain how the proposed activity will improve access to high-quality primary care for low-income people with HIV.
- Demonstrates that the proposed activity is a brand-new activity that introduces innovative approaches, services, or strategies to the program.

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Need (7 points)

- Justifies the need for capacity development funding to address the gaps in organizational capacity or the limitations of current infrastructure.
- Describes the relevant barriers to successfully carry out the project, and the steps to be taken to minimize or overcome the stated barriers.
- Outlines equipment or data system needs.
- Includes proposed changes to the current service delivery system.
- Describes how the lessons learned will be applied.

Criterion 2: Response (35 points)

See the project narrative Approach, and Work plan sections.

The panel will review your application for:

Approach (15 points)

- Clarity of the approach, including specific action steps and the roles of responsible staff or partners, to ensure effective implementation of the proposed activity.
- The extent to which the activities described in the application can address the need and attain the project objectives.
- The description of intent to share or disseminate relevant information and products developed through the funded activity and lessons learned with other providers in the community and collaborators to this project.

Work plan (20 points)

- Clarity of the goal, objectives, and action steps for the 12-month work plan (Attachment 6).
- The structure and completeness, including when each step will be completed and who is responsible for implementation.
- The extent to which the activities described in the application can address the problem and attain the project objectives.

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Criterion 3: Performance reporting and evaluation (15 points)

See the project narrative Performance reporting and evaluation section.

The panel will review your application for:

- Clearness of the evaluation plan to monitor progress towards project goals and objectives, and efficiency of plan to address barriers to implementation.

Criterion 4: Impact (10 points)

See the project narrative Resolving challenges and Sustainability sections.

The panel will review your application for:

Resolving challenges (5 points)

- The clarity of the outline of challenges likely to be encountered in designing and carrying out the activities in the work plan.
- Describes the specific activities or strategies used to mitigate or resolve anticipated challenges in implementing the proposed activity.

Sustainability (5 points)

- The extent to which activities outlined in the work plan can reasonably be completed in the 12-month period of performance.
- The strength of the applicants proposed plan for sustaining activities, without additional federal funds, beyond the federal funding period

Criterion 5: Resources and capabilities (20 points)

See the project narrative Organizational information and Performance reporting and evaluation sections.

The panel will review your application to determine the extent to which:

Organizational information (10 points)

- The organization demonstrates the ability to secure agreements with community-based organizations, health care providers, and consultant services needed to successfully achieve the proposed project.
- The organization demonstrates the ability to purchase equipment and execute contracts for services for this project within a reasonable timeframe to complete project activities.

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Staffing plan (10 points)

- The staffing plan (Attachment 7) is consistent with the proposed activity.
- Staffing plan is adequate or sufficient for meeting the proposed project goals and objectives.

Criterion 6: Support requested (10 points)

See the Budget and budget narrative section.

The panel will review your application to determine:

- How reasonable the proposed budget is for the period of performance.
- How reasonable costs are and how well they align with the project's scope.
- How sufficient the time is for key staff to spend on the project to achieve project objectives.

We do not consider **voluntary** cost sharing during merit review.

Risk review

Before making an award, we review your award history to assess risk. We need to ensure all prior awards were managed well and demonstrated sound business practices. We:

- Review any applicable past performance.
- Review audit reports and findings.
- Analyze the budget.
- Assess your management systems.
- Ensure you continue to be eligible.
- Make sure you comply with any public policies.

We may ask you to submit additional information.

As part of this review, we use SAM.gov Entity Information Responsibility/Qualification to check your history for all awards likely to be more than $250,000 over the period of performance. You can comment on your organization's information in SAM.gov. We'll consider your comments before making a decision about your level of risk.

If we find a significant risk, we may choose not to fund your application or to place specific conditions on the award.

For more details, see 2 CFR 200.206.

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Funding priorities

A funding priority adds points to merit review scores if we determine that the application meets the listed criteria. Qualifying for a funding priority does not guarantee that your application will be successful.

Priority 1: Not currently funded by this opportunity (2 Points)

We will give you a funding priority if:

Your organization does not hold an active award under this opportunity at the time you apply.

Priority 2: Never funded by this opportunity (2 Points)

We will give you a funding priority if:

Your organization has never received an award under this opportunity.

Priority 3: Alignment with Ending the HIV Epidemic in the U.S. (EHE) initiative (2 points)

We will give you funding priority if the following is met:

Your proposal is in an EHE priority state.

Selection process

When making funding decisions, we consider:

- The amount of available funds.
- Assessed risk.
- Merit review results. These are key in making decisions but are not the only factor.
- The larger portfolio of HRSA-funded projects, including project type and geographic distribution.
- The funding priorities, funding preferences, and special considerations listed.
- Alignment with HRSA Mission and Strategic Priorities

We may:

- Fund out of rank order.
- Fund applications in whole or in part.
- Fund applications at a lower amount than requested.
- Decide not to allow a recipient to subaward if they may not be able to monitor and manage subrecipients properly.
- Choose to fund no applications under this NOFO.

Additionally, we may not make an award if you are delinquent on two or more Single Audit Reports.

You cannot appeal a denial, or the amount of funds awarded.

Funding preferences

This program includes funding preferences, based on section 2654(c)(3) of the PHS Act. If we determine that your application meets these criteria, we will move it up in our ranking of fundable applications. Qualifying for a funding preference does not guarantee that you will receive funding.

HRSA will grant only **one** funding preference to any qualified applicant that justifies its qualification.

Qualifications to meet the funding preferences:

- **Attachment 2 is required for all applicants.**
  - HRSA will review the information and determine whether your application qualifies for a funding preference.
  - Receipt of a funding preference is not a guarantee of funding.

Qualification 1: Rural areas

The criterion for this funding preference is based on the provision of HIV primary care services in a rural area including:

- RWHAP recipients are defined as rural if their service area (in part or in whole) or main organizational address is in a HRSA Federal Office of Rural Health Policy (FORHP)-designated rural area.
- FORHP classifies all non-metropolitan counties, as defined by the Office of Management and Budget, as rural.
- FORHP uses Rural-Urban Commuting Area (RUCA) codes to identify other rural areas.
- For more information about **what defines a rural area**, visit FORHP's website.
- To determine if your organization **serves a rural area**, refer to FORHP's Rural Health Analyzer.
    - If your service area (either in part or in whole) or main organizational address **is defined as rural**, print out a screenshot of the result and include the printout as supporting documentation in .pdf format in Attachment 2.
    - If your organization **does not provide HIV primary care services in a rural area**, you can indicate "Not applicable" in Attachment 2.

Qualification 2: Underserved populations

The criterion for this funding preference is the provision of HIV primary care services to underserved populations including:

- Underserved populations include communities and subpopulations that do not have access to adequate HIV primary care services, as defined by HAB PCN 16-02.
- These gaps in the provision of HIV primary care services must be defined and documented in Attachment 2.
- State in Attachment 2 whether your organization provides HIV primary care services for underserved populations.
- You must provide all information to be considered for this funding preference:
    - Data and information on overall HIV primary care gaps, including any inadequate or unavailable HIV primary care services, as defined by HAB PCN 16-02.
    - Data and information on specific HIV subpopulations served by your organization that are disproportionately affected by inadequate or unavailable HIV primary care services, as defined by HAB PCN 16-02.
- If your organization does not provide HIV primary care services to underserved populations, you can indicate "Not applicable" on Attachment 2.

Award notices

We issue Notices of Award (NOA) on or around the start date listed in the NOFO. See "how we make awards" in the Application Guide [PDF] for more information.

By drawing down funds, you accept the terms and conditions of the award.

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Step 5: Submit Your Application

In this step

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Application submission and deadlines

Your organization's authorized official must certify your application. See the section on finding the application package to make sure you have everything you need.

Application deadline

You must submit your application by 06/01/2026, at 11:59 p.m. ET.

Grants.gov creates a date and time record when it receives applications.

If you need a deadline extension, see "requesting a waiver" in the Application Guide [PDF].

Submission method

Grants.gov

You must submit your application through Grants.gov. You may do so using Grants.gov Workspace. This is the preferred method. For alternative online methods, see Applicant System-to-System.

For instructions on how to submit in Grants.gov, see the Quick Start Guide for Applicants. Make sure that your application passes the Grants.gov validation checks, or we may not get it. Do not encrypt, zip, or password protect any files.

If Grants.gov rejects your application due to errors, you must correct and resubmit before the deadline.

If you want to know more about correcting errors or tracking your application, you can refer to the Application Guide [PDF].

Have questions? Go to Contacts and Support.

Other submissions

Intergovernmental review

This NOFO is not subject to Executive Order 12372, Intergovernmental Review of Federal Programs. No action is needed.

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Step 6: Learn What Happens After Award

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Post-award requirements and administration

Administrative and national policy requirements

There are important rules you need to know if you get an award. You must follow:

- All terms and conditions in the Notice of Award (NOA). We incorporate this NOFO by reference.
- The regulations at 2 CFR Part 200, Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards, modifications at 2 CFR Part 300, and any superseding regulations.
- The HHS Grants Policy Statement. Your NOA will reference this document. If there are any exceptions to the GPS, they'll be listed in your NOA.
- All federal statutes and regulations relevant to federal financial assistance, including those highlighted in HHS Grants Policy Statement, Appendix D: HHS Administrative and National Policy Requirements.
- The requirements for performance management in 2 CFR 200.301.
- All anti-discrimination laws: By applying for or accepting federal funds from HHS, you certify compliance with all federal antidiscrimination laws and these requirements. Complying with those laws is a material condition of receiving federal funding streams. You are responsible for ensuring subrecipients, contractors, and partners also comply.
- Any applicable statutory provisions.
- The Assurances (standard certification and representations) included in the annual SAM registration.

Required alignment with HRSA mission and strategic priorities

Recipients must use funds awarded under this NOFO to implement program goals or agency priorities in accordance with the HRSA vision, mission, core values, and strategic priorities, where authorized by law.

Funded activities must advance HRSA's vision of protecting and improving the health and well-being of Americans. The particular focus is on those who are medically vulnerable or live in areas with limited access to care. HRSA's duty is to serve

wisely, effectively, and with measurable results that justify every taxpayer dollar invested.

Consistent with HRSA's priorities, in carrying out any project funded under this NOFO, the recipient must adhere to the following principles, where they are consistent with the authority and scope of the award and its activities:

- **Gold standard science:** Design and deliver services using gold standard evidence-based and evidence-informed approaches, establish measurable performance goals, and use data to monitor outcomes and drive continuous improvement.
- **Program integrity and fiscal stewardship:** Recipients must:
  - Administer funds in accordance with all applicable federal statutes, regulations, and award conditions.
  - Maintain strong internal controls.
  - Prevent waste, fraud, and abuse.
- **Partnership and local leadership:** Coordinate with state, tribal, territorial, local, and community partners, as appropriate, and tailor services to meet community-identified needs while respecting local decision-making authority.

Recipients must manage any project awarded under this NOFO in accordance with the following objectives in programs authorized to advance them:

Make America Healthy Again (MAHA): HRSA prioritizes the health and well-being of all Americans by supporting common-sense, evidence-based health policies that promote:

- Personal responsibility.
- Strong families and communities.
- Proper nutrition.
- The prevention and management of chronic disease, while ensuring access to high-quality, affordable physical and mental health care.

Child protections, biological integrity, parental rights, and lawful use of funds: HRSA prioritizes safeguarding children's health and safety by:

- Not supporting medical interventions for gender dysphoria in minors that lack a strong evidence base.
- Applying sex-based definitions grounded in biological reality.
- Supporting parental authority, transparency, and choice in education, including school-based health centers that respect parental rights and religious upbringing.
- Ensuring taxpayer funds are not used to promote or support elective abortions, consistent with federal law and the Hyde Amendment.

Advancing evidence-based, merit-driven, and ethically grounded health care: HRSA will prioritize unbiased, transparent science; merit-based workforce opportunities; and programs that demonstrate measurable outcomes, while deprioritizing organizations with:

- Conflicts of interest.
- "Harm reduction models."
- Housing-first approaches.
- Activities that facilitate illegal drug use or unsafe medical practices.

Promoting public safety, lawful use of federal funds, and national health priorities: To the extent permitted by law, HRSA will align funding with administration priorities by:

- Supporting ending the HIV epidemic through authorized, evidence-based care.
- Reserving benefits for eligible individuals.
- Discouraging illegal immigration and unsafe community practices.
- Prioritizing recipients that enforce public safety, address serious mental illness and substance use through treatment and recovery, and reduce homelessness responsibly.

To the extent allowable by law, under awards, HRSA will give priority to states and municipalities for programs to:

- Enforce prohibitions on open illicit drug use.
- Enforce prohibitions on urban camping and loitering.
- Enforce prohibitions on urban squatting.
- Enforce, and where necessary, adopt, standards that address individuals who are a danger to themselves or others and suffer from serious mental illness or substance use disorder, or who are living on the streets and cannot care for themselves. The approach must be through assisted outpatient treatment or by moving them into treatment centers or other appropriate facilities through civil commitment or other available means, to the maximum extent permitted by law.

HRSA will implement these priorities consistent with applicable laws, regulations, court orders, and any required procedures.

The recipient must demonstrate ongoing compliance with these priorities, in all programs that are authorized to advance them, through program design, implementation, reporting, and evaluation.

Failure to meaningfully align funded activities with the applicable requirements may result in corrective action, additional reporting requirements, or other actions consistent with federal grant regulations at 2 CFR. part 200 and the terms and

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conditions of this award. This includes termination under CFR. 200.340(a)(4) if an award no longer effectuates the program goals or agency priorities.

Cybersecurity

If awarded, you must develop plans and procedures, modeled after the NIST Cybersecurity framework, to protect HHS systems and data. See details here.

HIT

Successful applicants under this NOFO agree that:

Where award funding involves:	Recipients and subrecipients are required to:
Implementing, acquiring, or upgrading health IT for activities funded by any entity	Use health IT that meets standards and implementation specifications adopted in 45 CFR 170, Subpart B, if such standards and implementation specifications can support the activity. Visit to 45 CFR 170, Subpart B learn more.
Implementing, acquiring, or upgrading health IT for activities by eligible clinicians in ambulatory settings, or hospitals, eligible under Sections 4101, 4102, and 4201 of the HITECH Act	Use health IT certified under the ONC Health IT Certification Program if certified technology can support the activity.

If standards and implementation specifications adopted in 45 CFR part 170, Subpart B cannot support the activity, recipients and subrecipients are encouraged to use health IT that meets non-proprietary standards and implementation specifications developed by consensus-based standards development organizations. This may include standards identified in the ONC Interoperability Standards Advisory.

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Reporting

If you are funded, you will have to follow the reporting requirements in “reporting” section of the Application Guide [PDF]. The NOA will provide specific details.

You must also follow these program-specific reporting requirements:

- Information relevant to program-specific goals and progress on the work plan (for example, number of clients served, partnerships)
- Impact of the overall project
- The degree to which the recipient achieved the mission, goal, and objectives outlined in the program
- Recipient accomplishments
- Barriers encountered
- Responses to summary questions regarding the recipient’s overall experiences during the 1-year period of performance.
- Recipients will be expected to provide end-of-the-period of performance outcome data and demonstrate the impact of the project’s activity.

Further information will be available in the NOA.

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Agency contacts

Program and eligibility

Brian Fitzsimmons
Public Health Advisor
Attn: Ryan White HIV/AIDS Program Part C Capacity Development Program
Health Resources and Services Administration
AskPartCCapacity@hrsa.gov
301-945-9820

Financial and budget

Bria Haley
Grants Management Specialist
Division of Grants Management Operations
Office of Financial Assistance and Acquisition Management (OFAAM)
Health Resources and Services Administration
BHaley@hrsa.gov
301-443-3778

HRSA Contact Center

Open Monday through Friday, 7 a.m. to 8 p.m. ET, except for federal holidays.
Call: 877-464-4772 / 877-Go4-HRSA
TTY: 877-897-9910

Electronic Handbooks Contact Center

Help with systems

Grants.gov

Grants.gov provides 24/7 support. You can call 800-518-4726, search the Grants.gov Knowledge Base, or email Grants.gov for support. Hold on to your ticket number.

SAM.gov

If you need help, you can call 866-606-8220 or live chat with the Federal Service Desk.

Helpful websites

- Application Guide [PDF]
- HRSA Grants page
- HHS Tips for Preparing Grant Proposals
- Frequently Asked Questions
- Applicant Training

EXHIBIT K

Notice of Funding Opportunity

Application due 07/10/2026

HRSA
Health Resources & Services Administration

HIV/AIDS Bureau
Division of Community HIV/AIDS Programs

Ryan White HIV/AIDS Program Part F Dental Reimbursement Program

Opportunity number: HRSA-26-085

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Before you begin

If you believe you are a good candidate for this funding opportunity, secure your SAM.gov and Grants.gov registrations now. If you are already registered, make sure your registrations are active and up-to-date.

SAM.gov registration (this can take several weeks)

You must have an active account with SAM.gov. This includes having a Unique Entity Identifier (UEI).

See Step 2: Get Ready to Apply

Grants.gov registration (this can take several days)

You must have an active Grants.gov registration. Doing so requires a Login.gov registration as well.

See Step 2: Get Ready to Apply

Apply by the application due date

Applications are due by 11:59 p.m. Eastern Time on 07/10/2026.

To help you find what you need, this NOFO uses internal links. In Adobe Reader, you can go back to where you were by pressing Alt + Left Arrow (Windows) or Command + Left Arrow (Mac) on your keyboard.

All activities proposed in your application and budget narrative must align with applicable law, including but not limited to statutes, executive orders, federal regulations and applicable judicial holdings. Accordingly, discretionary awards shall not be used to fund, promote, encourage, subsidize, or facilitate: racial preferences or other forms of racial discrimination by the recipient, including activities where race or intentional proxies for race will be used as a selection criterion for employment or program participation; denial by the recipient of the sex binary in humans, or the belief that sex is a chosen or mutable characteristic; illegal immigration; or any other initiatives that compromise public safety. If an application does not align, the application will not receive funding to the extent permitted by law and applicable court orders.

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Step 1:
Review the Opportunity

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Basic information

Health Resources Services Administration

HIV/AIDS Bureau

Division of Community HIV/AIDS Programs

Dental reimbursement program.

Summary

The Dental Reimbursement Program reimburses certain costs incurred by eligible entities that have provided uncompensated or partially uncompensated oral health care to people with HIV during a specified one-year period. Funds will be distributed among eligible applicants by comparing each eligible applicant's number of patients with HIV served and unreimbursed oral health care costs to the total number of patients served and costs incurred by all eligible applicants.

Funding details

Application Types: New

Expected total available funding in FY 2026: $9,000,000

Expected number and type of awards: 50 grants

Funding range per award: Amount varies.

We plan to fund awards in a single six-month budget period. The period of performance is 9/1/2026 to 2/28/2027.

Have questions?
Go to Contacts and Support.

Key facts

Opportunity name:
Ryan White HIV/AIDS Program Part F Dental Reimbursement Program

Opportunity number:
HRSA-26-085

Announcement version:
Initial

Federal assistance listing:
93.924

Key dates

NOFO issue date:
06/08/2026

Informational webinar:
Join the Webinar

Application deadline:
07/10/2026

Expected award date:
09/01/2026

Expected start date:
09/01/2026

See other submissions for other time frames that may apply to this NOFO.

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Eligibility

You can apply if you are an accredited domestic dental school and other accredited domestic dental education program, such as dental hygiene program, or those sponsored by a school of dentistry, a hospital with a dental education program that is accredited by the Commission on Dental Accreditation, or a public or private institution that offers postdoctoral training in the specialties of dentistry, advanced education in general dentistry, or a dental-general practice residency. Dental education programs must be accredited by the Commission on Dental Accreditation.

Types of eligible organizations

These types of domestic organizations may apply:

- Public and State controlled institutions of higher education.
- Private institutions of higher education.
- Others. (See text field entitled “Additional Information on Eligibility” for clarification.)

Additional information on eligibility

“Domestic” means the 50 states, the District of Columbia, the Commonwealth of Puerto Rico, the Northern Mariana Islands, American Samoa, Guam, the U.S. Virgin Islands, the Federated States of Micronesia, the Republic of the Marshall Islands, and the Republic of Palau.

Individuals are not eligible applicants under this NOFO.

Completeness and responsiveness criteria

We will review your application to make sure it meets these basic requirements to move forward in the competition.

We will not consider an application that:

- Is from an organization that does not meet all eligibility criteria.
- Is submitted after the deadline.
- **Applications that do not meet the following requirements may be deemed ineligible**:
    - Failure to include the total unreimbursed costs of oral health care provided to low-income people with HIV from July 1, 2024, through June 30, 2025, in fields 18a and 18g of the SF-424 application.

- Failure to submit the required Dental Services Report information on or before the application deadline on the Dental Services Report website.
- Discrepancies between the unreimbursed costs reported on the Dental Services Report and the SF-24 application. HRSA will verify these amounts, and if they do not match, the application may be deemed ineligible.

Application limits

You may not submit more than one application. If you submit more than one application, we will only accept the last on-time submission.

Cost sharing

This program has no cost-sharing requirement. If you choose to share in the costs of the project, we will not consider it during merit review. Recipients agree that once committed, cost sharing amounts are enforceable and subject to reporting and auditing requirements under 2 CFR 200.

Maintenance of effort

Federal funds must add to any existing non-federal funds for your proposed activities. If you receive an award, you will have to spend at least as much as you spent in the last fiscal year before the award. Section 2692(b)(4) of the PHS Act requires this. We will enforce these statutory requirements through all available mechanisms. You must provide supporting documentation of your maintenance of effort in your attachments.

RWHAP Part F DRP funds are not intended to be the sole source of support for oral health care services for people with HIV. The RWHAP statute requires DRP recipients to maintain expenditures of state funds (if any) for DRP-related activities at a level equal to or greater than the fiscal year preceding the DRP reimbursement period. The maintenance of effort (MOE) requirement is important in ensuring that RWHAP funds are used to supplement, not supplant, state funds allotted for oral health care services for people with HIV.

Post-award requirements

Before you apply, make sure you understand the requirements that come with an award.

See Step 6: Learn What Happens After Award for information on regulations that apply, reporting, and more.

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Program description

Purpose

Our purposes are to:

1. Improve access to oral health care services for low-income people with HIV.
2. Support related education and training for the delivery of dental care to people with HIV.

This program will reimburse certain costs incurred by eligible entities that have provided uncompensated or partially uncompensated oral health care to people with HIV from July 1, 2024, through June 30, 2025.

Funding opportunity goals

- Reduce the new HIV infections in the U.S. by focusing on HIV care and treatment strategies so that people with HIV reach viral suppression and therefore do not sexually transmit HIV.
- Help low-income people with HIV by providing: medical care, medications , and support service to help them stay in care .
- Reach people with HIV who are out of care by leveraging partnerships, focusing interventions, and engaging communities.

Background

The Ryan White HIV/AIDS Program

The Ryan White HIV/AIDS Program (RWHAP) has five statutorily defined Parts that provide grants to states, cities, counties, local clinics, and community-based organizations. The grants fund medical care, medication, and essential support services, to meet the needs of people with HIV and family members affected by HIV. Together these grants provide a comprehensive system of care to ensure low-income people with HIV have access to services for early diagnosis of HIV, linkage to care, medically appropriate treatment, retention in care, and sustained viral suppression (a very low or undetectable amount of HIV in the blood).

For nearly four decades, the RWHAP has funded services to provide HIV primary health care, medication, and essential support services, including mental health care, transportation, case management, nutrition, and housing. These services support clients to enter and remain in care, access medications, and reach viral suppression, reducing transmission and lowering health care costs.

Ending the HIV Epidemic

Launched in 2020, the Ending the HIV Epidemic in the U.S. (EHE) initiative further expands federal efforts to reduce HIV transmission. For the RWHAP, the EHE initiative expands the program's ability to meet the needs of clients, specifically focusing on linking people with HIV who are either newly diagnosed, diagnosed but currently not in care, or are diagnosed and in care but not yet virally suppressed, to the essential HIV care, treatment, and support services needed to help them reach viral suppression.

Making America Healthy Again

The Ryan White HIV/AIDS Program helps advance the Making America Healthy Again (MAHA) priorities by:

- **Expanding access to primary care** for people with HIV, particularly those with low incomes, and by strengthening the health workforce.
- **Fighting the chronic disease epidemic** by providing HIV medical care, treatment, and support services to people with HIV.
- **Supporting improved nutrition** by providing patient-centered focused medical nutrition therapy and food services.
- **Supporting disease prevention** through HIV care and treatment services that help people reach viral suppression so they live longer, healthier lives and do not transmit HIV.

Key accomplishments

- **Nearly 602,000 people with HIV** in the U.S. received life-saving care, medication, and essential support services through the RWHAP, representing over half of all diagnosed with HIV in the U.S. This is an increase of nearly 26,000 clients.
- **More than 91%** of Ryan White HIV/AIDS Program patients receiving HIV medical care were virally suppressed in 2024. This is up from 69.5% of patients virally suppressed in 2010 and significantly higher than the 67.2% virally suppressed nationally among all people with diagnosed HIV.
- **More than 47%** of Ryan White HIV/AIDS Program clients are aged 50 years and older, demonstrating the program's success in supporting older clients and its commitment to addressing the unique needs of people aging with HIV.

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Program requirements and expectations

- **Dental Services Report** — You must submit a Dental Services Report electronically. For detailed instructions, see Appendix.
- **Patient payment for services** — Recipients must have consistent policies and procedures related to verification of patients' financial status.
- **Payor of last resort and eligibility determination** — With the exception of programs administered by or providing the services of the Indian Health Service, the RWHAP is the payor of last resort. Recipients may not use RWHAP Part F DRP funds for a service if payment has been made, or reasonably can be expected to be made, by a state compensation program, under an insurance policy, under a Federal or State health benefits program, or by an entity that provides health services on a pre-paid basis.
    - Eligibility and confirmation should be determined in accordance with guidelines in HAB PCN 21-02 Determining Client Eligibility & Payor of Last Resort [PDF] in the RWHAP. HRSA HAB expects all RWHAP recipients and subrecipients to establish, implement, and monitor policies and procedures to determine client eligibility.
    - To extend finite RWHAP grant resources to low-income people with HIV, recipients and subrecipients must vigorously pursue and rigorously document enrollment into, and subsequent reimbursement from, health care coverage for which their clients may be eligible. Examples include Medicaid, Medicare, Children's Health Insurance Program (CHIP), state-funded HIV programs, employer-sponsored health insurance coverage, and health plans offered through other private health insurers.
- **Recipients cannot use RWHAP Part F DRP funds to supplement the maximum cost allowance for services reimbursed by third party payments such as Medicaid, Medicare, or other insurance programs.** Please note that recipients cannot use direct or indirect federal funds such as RWHAP Parts A, B, C, D and Part F Community Based Dental Partnership Program (CBDPP) to duplicate reimbursement for services funded under Part F DRP. Additionally, recipients cannot bill RWHAP Parts A, B, C, D or Part F CBDPP for services reimbursed by RWHAP Part F DRP.
- **Other financial management issues** — Funds received from DRP must be allocated to the accredited dental schools and other accredited dental education programs (see Eligibility section that provide oral health services to low-income people with HIV. HRSA expects that these reimbursement funds will provide expanded access to oral health care for people with HIV.

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- **Education and training** — RWHAP Part F DRP awarded applicants must ensure HIV-related oral health education and training for dental students, dental hygiene students, dental residents, or other dental providers. Education and training curricula should focus on the provision of comprehensive oral health care for people with HIV.

Statutory authority

42 U.S.C. § 300ff-111(b) (Title XXVI, § 2692(b) of the Public Health Service (PHS) Act).

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Award information

Funding policies and limitations

Changes in HHS regulations

As of October 1, 2025, HHS has adopted 2 CFR Part 200, with some modifications included in 2 CFR Part 300. These regulations replace those in 45 CFR Part 75.

Policies

- To make an award, funding must be available and allocated for this program and purpose, at which point we will move forward with the review and award process.
- Have clear policies and good financial practices to avoid spending HRSA funds on unallowable activities. Like other award rules, we may audit your policies, procedures, and controls.

General limitations

- For guidance on some types of costs we do not allow or restrict, see
  - Project Budget Information in Section 3.1. of the Two-Tier Application Guide [PDF].
  - 2 CFR Part 200 Subpart E - General Provisions for Selected Items of Cost.
  - Allowable and Unallowable Costs and Activities, in the HHS Grants Policy Statement.
- All costs must be reasonable, necessary, allocable to the award, and adequately documented (2 CFR 200.403).
- You cannot earn profit from the federal award. See 2 CFR § 200.400(g).
- Current appropriations law includes a salary limit of $228,000 as of January 2026 that applies to this program. You may pay salaries at a higher rate if the rate beyond the salary rate limit (Executive Level II) is paid with non-HHS funds. For help calculating salaries under this limit, read more at “salary rate limitation” in the Two-Tier Application Guide [PDF].

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Program-specific statutory or regulatory limitations

You cannot use funds under this notice for the following:

- Funding restrictions included in PCN 16-02.
- Services that must be paid for by other sources, consistent with the RWHAP payor of last resort requirement in PCN 21-02.
- Payments for inpatient hospitals, nursing homes, and other long-term care facilities.
- Cash payments to intended clients of RWHAP services.
- Purchase of, or improvement to land.
- Purchase, construction, or major alterations or renovations on any building or other facility (see 2 CFR 200 – subpart A Definitions).
- PrEP or non-occupational Post-Exposure Prophylaxis (nPEP) medications or the related medical services. As outlined in the updated November 16, 2021 RWHAP and PrEP program letter.
- Purchase of sterile needles and syringes for the purpose of hypodermic injection of any illegal drug use. Some aspects of syringe services programs are allowable with HRSA's prior approval and in compliance with HHS and HRSA policy. See Syringe Services Programs.
- Development of materials designed to directly promote or encourage intravenous drug use or sexual activity, whether homosexual or heterosexual.
- Research.
- Foreign travel.

You must have policies, procedures, and financial controls in place. Anyone who receives federal funding must comply with legal requirements and restrictions, including those that limit specific uses of funding.

- Follow the list of statutory restrictions on the use of funds in Section 4.1 (Funding Restrictions) of the Application Guide.
    - We may audit the effectiveness of these policies, procedures, and controls. 2 CFR § 200.216 prohibits certain telecommunications and video surveillance services or equipment.
    - For details, see the HRSA Grants Policy Bulletin Number: 2021-01E.

See Manage Your Grant for other information on costs and financial management.

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Indirect costs

Indirect costs are costs you charge across more than one project that cannot be easily separated by project. For example, this could include utilities for a building that supports multiple projects.

To incur indirect costs, you can select one of two methods:

Method 1 – Approved rate. You currently have an indirect cost rate approved by your cognizant federal agency at the time of award.

Method 2 – *De minimis* rate. Per 2 CFR § 200.414(f), if you do not have a current negotiated indirect cost rate, you may elect to charge a ***de minimis*** rate. If you choose this method, costs included in the indirect cost pool must not be charged as direct costs.

This rate is up to 15% of modified total direct costs (MTDC). See 2 CFR § 200.1 for the definition of MTDC. You can use this rate indefinitely for all your federal awards or until you choose to receive a negotiated rate.

Consider your indirect costs when developing your budget.

Program income

Program income is money earned as a result of your award-supported project activities. You must use any program income you generate from awarded funds for approved project-related activities. Find more about program income at 2 CFR 200.307.

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Step 2:
Get Ready to Apply

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Get registered

SAM.gov

You must have an active account with SAM.gov to apply. SAM.gov registration can take several weeks. Begin that process today.

To register:

- Go to SAM.gov Entity Registration and select Get Started. From the same page, you can also select the Entity Registration Checklist for the information you will need to register.
- You must agree to the financial assistance general certifications and representations specifically. Those for contracts are different.

When you register, you will also receive your required Unique Entity Identifier (UEI).

Once you register:

- You will have to maintain your registration throughout the life of any award.
- If your organization has multiple UEIs, use the one associated with your physical location.

If you need additional information about user roles in SAM.gov, see “Get registered: SAM.gov user roles” in the Application Guide [PDF].

Grants.gov

You must also have an active account with Grants.gov. You can see step-by-step instructions at the Grants.gov Quick Start Guide for Applicants and How to Apply for Grants.

Find the application package

The application package has all the forms you need to apply. You can find it online. Go to Grants Search at Grants.gov and search for opportunity number HRSA-26-085.

After you select the opportunity, we recommend that you click the Subscribe button to get updates.

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Application writing help

Visit HHS Tips for Preparing Grant Proposals.

Visit HRSA's How to Prepare Your Application page for more guidance.

See Apply for a Grant for other help and resources.

FAQs will be posted on our TA webpage after the webinar.

Join the webinar

Webinar Information will be posted to the Related Documents tab on Grants.gov. We recommend you "Subscribe" to the NOFO on Grants.gov to receive updates when documents are posted.

Have questions? Go to Contacts and Support.

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Step 3: Build Your Application

In this step

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Application checklist

There are two types of forms in Grants.gov.

- Some forms allow you to upload components of your application to the form. These include components like your project narrative, budget and budget narrative, and attachments, as applicable.
- Other forms are more typical, fill-in-the-blank forms.

Make sure that you have everything you need to apply.

Narratives

Component	Grants.gov form	Included in page limit*?
☐ Attachments	Insert each in the Other Attachments form	Yes, unless marked otherwise
☐ Other required forms	Upload using each required form	No
☐ Dental Services Report	Submit this on the Dental Services Report website	No

Attachments

Insert each in the Attachments form in this order.

Component	Included in page limit*?
☐ 1. Maintenance of effort	Yes
☐ 2. Other relevant documents (if applicable)	Yes

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Other required forms

Upload using each required form in Grants.gov.

Forms	Submission requirement
☐ Application for federal assistance (SF-424)	With application.
☐ Project/Performance site location(s)	With application.
☐ Project abstract summary form	With application.
☐ Grants.gov lobbying form	With application.
☐ Key contacts	With application.

*Only what you attach in these forms counts toward the page limit. The forms themselves do not count.

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Application contents and format

This section includes guidance on each component found in the application checklist.

Application page limit: 10

Submit your information in English and express whole number budget figures using U.S. dollars.

Required format

Required format for project summary, project narrative, budget narrative, and attachments.

Font: A readable font like Arial, Courier, CG Times, or Times New Roman.

File format: We only accept the following document formats:

- .PDF - Adobe Portable Document Format
- .DOC/.DOCX - Microsoft Word
- .RTF - Rich Text Format
- .TXT - Text
- .WPD - Word Perfect Document
- .XLS/.XLSX - Microsoft Excel
- .VSD - Microsoft Visio

Size: 12-point font
Footnotes, charts, graphics, and budget tables may be 10-point or higher.

Ink color: Black

Spacing: Single-spaced, including all text and tables.

Alignment: Left

Headings: Bold all headings and align left.

Size: 8.5 x 11 (Make sure the print area is set and allows printing to 8.5 x 11.)

Margins: 1-inch on all sides

Footer: On each page as the footer, include your organization's name and page numbers. If a competing continuation or competing supplement, also include your 10-digit award number.

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Page numbering:

- Do not number the standard OMB-approved forms.
- Number each attachment page sequentially (that is, 1, 2, 3).
- Reset the numbering for each attachment.
- Treat each attachment as a separate section.

File names: You can find guidance for naming your files in the Application Guide.

See the reporting section for more information.

Attachments

Place your attachments in this order in the Attachments Form. See application checklist to determine if they count toward the page limit.

Unless the instructions below require it, do not submit organizational brochures or other promotional materials (for example, slides, films, clips).

Attachment 1: Maintenance of effort documentation

Counts toward page limit.

You must maintain state funds (if any) that support proposed activities. These include cash, in-kind, and other contributions. If there were no state funds expended, enter zero. Do not include any federal funds. See maintenance of effort requirement.

You must provide a baseline aggregate expenditure of state funds for the most recently completed fiscal year prior to the application deadline and estimates for the following fiscal year using a chart like the one shown in this section.

As an example, if your fiscal year begins July 1, you report actual expenditures of state funds for oral health care services for people with HIV from July 1, 2024, through June 30, 2025, in column one. In column two, you report estimated expenditures for the next fiscal year (July 1, 2025, through June 30, 2026).

Additionally, provide a brief description of the methodology your institution or program used to calculate MOE for oral health care services for low-income people with HIV. Provide a description of consistent data set(s) of state expenditures for oral health care services for low-income people with HIV and a brief narrative of any changes from the previous FY and the projected FY spending.

Use this sample format to provide the maintenance of effort documentation.

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FY before application: Actual nonfederal expenditures	First FY of award: Estimated nonfederal expenditures
$	$

Attachment 2: Other relevant documents (if applicable)

Include here any other documents that are relevant to your application.

Other required forms

You will need to complete some other forms. Upload the following forms at Grants.gov. You can find them in the NOFO application package or review them and any available instructions at Grants.gov Forms.

Forms	Submission requirement
Application for federal assistance (SF-424)	With application.
Project/performance site location(s)	With application.
Project abstract summary form	With application.
Grants.gov lobbying form	With application.
Key contacts	With application.

Form instructions

The application guide has detailed instructions for:

- The Application for Federal Assistance (SF-424).

Project abstract summary form instructions

Complete the information in the Project Abstract Summary form. For more information, see Section 3.1.2 of the Application Guide [PDF] .

Please name your project title “FY 2026 RWHAP Part F Dental Reimbursement Program” and include the following information:

- The total unreimbursed costs of oral health care provided to people with HIV from July 1, 2024, through June 30, 2025, that are entered in fields 18a and 18g of the SF-424 Application for Federal Assistance. This amount should also match the unreimbursed cost reported on Tab Two of the DSR.

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Important: Public information

When filling out your SF-424 form, pay attention to Box 15: Descriptive Title of Applicant's Project.

We share what you put there with USAspending. This is where the public goes to learn how the federal government spends their money.

Instead of just a title, insert a short description of your project and what it will do.

See instructions and examples.

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Step 4: Understand Review, Selection, and Award

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Application review

Initial review

We will review your application to make sure that it meets eligibility criteria, and the requirements in this NOFO. If your application does not meet eligibility criteria, it will not be funded. If your application does not meet other criteria, we will not fund it.

Risk review

Before making an award, we review your award history to assess risk. We need to ensure all prior awards were managed well and demonstrated sound business practices. We:

- Review any applicable past performance.
- Review audit reports and findings.
- Analyze the budget.
- Assess your management systems.
- Ensure you continue to be eligible.
- Make sure you comply with any public policies.

We may ask you to submit additional information.

As part of this review, we use SAM.gov Entity Information Responsibility/Qualification to check your history for all awards likely to be more than $250,000 over the period of performance. You can comment on your organization's information in SAM.gov. We'll consider your comments before making a decision about your level of risk.

If we find a significant risk, we may choose not to fund your application or to place specific conditions on the award.

For more details, see 2 CFR 200.206.

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Selection process

When making funding decisions, we consider:

- The amount of available funds.
- Assessed risk.
- Alignment with HRSA Mission and Strategic Priorities

We may:

- Fund applications in whole or in part.
- Fund applications at a lower amount than requested.
- Choose to fund no applications under this NOFO.

- Additionally, we may not make an award if you are delinquent on two or more Single Audit Reports.

You cannot appeal a denial, or the amount of funds awarded.

Award notices

We issue Notices of Award (NOA) on or around the start date listed in the NOFO. See "how we make awards" in the Application Guide [PDF] for more information.

By drawing down funds, you accept the terms and conditions of the award.

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Step 5: Submit Your Application

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Application submission and deadlines

Your organization's authorized official must certify your application. See the section on finding the application package to make sure you have everything you need.

Application deadline

You must submit your application by 07/10/2026, at 11:59 p.m. ET.

Grants.gov creates a date and time record when it receives applications.

If you need a deadline extension, see "requesting a waiver" in the Application Guide [PDF] .

Submission method

Grants.gov

You must submit your application through Grants.gov. You may do so using Grants.gov Workspace. This is the preferred method. For alternative online methods, see Applicant System-to-System.

For instructions on how to submit in Grants.gov, see the Quick Start Guide for Applicants. Make sure that your application passes the Grants.gov validation checks, or we may not get it. Do not encrypt, zip, or password protect any files.

If Grants.gov rejects your application due to errors, you must correct and resubmit before the deadline.

If you want to know more about correcting errors or tracking your application, you can refer to the Application Guide [PDF] .

Have questions? Go to Contacts and Support.

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Other submissions

Intergovernmental review

This NOFO is not subject to Executive Order 12372, Intergovernmental Review of Federal Programs. No action is needed.

Dental Services Report

Dental Services Report : You must submit this report electronically. Complete and submit the Dental Reimbursement Program Dental Services Report in the Dental Services Report website. You'll need to request access to the website the first time you visit it by completing the registration form on the Dental Services Report website.

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Step 6: Learn What Happens After Award

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Post-award requirements and administration

Administrative and national policy requirements

There are important rules you need to know if you get an award. You must follow:

- All terms and conditions in the Notice of Award (NOA). We incorporate this NOFO by reference.
- The regulations at 2 CFR Part 200, Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards, modifications at 2 CFR Part 300, and any superseding regulations.
- The HHS Grants Policy Statement. Your NOA will reference this document. If there are any exceptions to the GPS, they'll be listed in your NOA.
- All federal statutes and regulations relevant to federal financial assistance, including those highlighted in HHS Grants Policy Statement, Appendix D: HHS Administrative and National Policy Requirements.
- The requirements for performance management in 2 CFR 200.301.
- All anti-discrimination laws: By applying for or accepting federal funds from HHS, you certify compliance with all federal antidiscrimination laws and these requirements. Complying with those laws is a material condition of receiving federal funding streams. You are responsible for ensuring subrecipients, contractors, and partners also comply.
- Any applicable statutory provisions.
- The Assurances (standard certification and representations) included in the annual SAM registration.

Required Alignment with HRSA Mission and Strategic Priorities

Recipients must use funds awarded under this NOFO to implement program goals or agency priorities in accordance with the HRSA vision, mission, core values, and strategic priorities, where authorized by law.

In administering programs under this and all funding announcements, HRSA prioritizes:

- **Evidence-based healthcare:** Funding activities supported by rigorous scientific evidence, particularly for programs serving children and adolescents, where HRSA is committed to approaches that reflect the highest standards of clinical care and child safety.

- **Biological and physiological integrity:** Recognizing the relevance of biological sex to health outcomes, HRSA encourages applicants to account for sex-based health factors in program design, data collection, and service delivery where scientifically appropriate.

HRSA will implement these priorities consistent with applicable laws, regulations, court orders, and all required administrative procedures. Applicants are encouraged to describe how their proposed programs align with these priorities in their project narratives.

Funded activities must advance HRSA's vision of protecting and improving the health and well-being of Americans. The particular focus is on those who are medically vulnerable or live in areas with limited access to care. HRSA's duty is to serve

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wisely, effectively, and with measurable results that justify every taxpayer dollar invested.

Consistent with HRSA's priorities, in carrying out any project funded under this NOFO, the recipient must adhere to the following principles, where they are consistent with the authority and scope of the award and its activities:

- **Gold standard science:** Design and deliver services using gold standard evidence-based and evidence-informed approaches, establish measurable performance goals, and use data to monitor outcomes and drive continuous improvement.
- **Program integrity and fiscal stewardship:** Recipients must:
  - Administer funds in accordance with all applicable federal statutes, regulations, and award conditions.
  - Maintain strong internal controls.
  - Prevent waste, fraud, and abuse.
- **Partnership and local leadership:** Coordinate with state, tribal, territorial, local, and community partners, as appropriate, and tailor services to meet community-identified needs while respecting local decision-making authority.

Recipients must manage any project awarded under this NOFO in accordance with the following objectives in programs authorized to advance them:

Make America Healthy Again (MAHA): HRSA prioritizes the health and well-being of all Americans by supporting common-sense, evidence-based health policies that promote:

- Personal responsibility.
- Strong families and communities.
- Proper nutrition.
- The prevention and management of chronic disease, while ensuring access to high-quality, affordable physical and mental health care.

Child protections, biological integrity, parental rights, and lawful use of funds: HRSA prioritizes safeguarding children's health and safety by:

- Not supporting medical interventions for gender dysphoria in minors that lack a strong evidence base.
- Applying sex-based definitions grounded in biological reality.
- Supporting parental authority, transparency, and choice in education, including school-based health centers that respect parental rights and religious upbringing.
- Ensuring taxpayer funds are not used to promote or support elective abortions, consistent with federal law and the Hyde Amendment.

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Advancing evidence-based, merit-driven, and ethically grounded health care: HRSA will prioritize unbiased, transparent science; merit-based workforce opportunities; and programs that demonstrate measurable outcomes, while deprioritizing organizations with:

- Conflicts of interest.
- "Harm reduction" models.
- Housing-first approaches.
- Activities that facilitate illegal drug use or unsafe medical practices.

Promoting public safety, lawful use of federal funds, and national health priorities: To the extent permitted by law, HRSA will align funding with administration priorities by:

- Supporting ending the HIV epidemic through authorized, evidence-based care.
- Reserving benefits for eligible individuals.
- Discouraging illegal immigration and unsafe community practices.
- Prioritizing recipients that enforce public safety, address serious mental illness and substance use through treatment and recovery, and reduce homelessness responsibly.

To the extent allowable by law, under awards, HRSA will give priority to states and municipalities for programs to:

- Enforce prohibitions on open illicit drug use.
- Enforce prohibitions on urban camping and loitering.
- Enforce prohibitions on urban squatting.
- Enforce, and where necessary, adopt, standards that address individuals who are a danger to themselves or others and suffer from serious mental illness or substance use disorder, or who are living on the streets and cannot care for themselves. The approach must be through assisted outpatient treatment or by moving them into treatment centers or other appropriate facilities through civil commitment or other available means, to the maximum extent permitted by law.

HRSA will implement these priorities consistent with applicable laws, regulations, court orders, and any required procedures.

The recipient must demonstrate ongoing compliance with these priorities, in all programs that are authorized to advance them, through program design, implementation, reporting, and evaluation.

Failure to meaningfully align funded activities with the applicable requirements may result in corrective action, additional reporting requirements, or other actions consistent with federal grant regulations at 2 CFR. part 200 and the terms and

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conditions of this award. This includes termination under 2 CFR. 200.340(a)(4) if an award no longer effectuates the program goals or agency priorities.

Cybersecurity

If awarded, you must develop plans and procedures, modeled after the NIST Cybersecurity framework, to protect HHS systems and data. See details here.

Health IT

Successful applicants under this NOFO agree that:

Where award funding involves:	Recipients and subrecipients are required to:
Implementing, acquiring, or upgrading health IT for activities funded by any entity.	Use health IT that meets standards and implementation specifications adopted in 45 CFR 170, Subpart B, if such standards and implementation specifications can support the activity. Visit to 45 CFR 170, Subpart B learn more.
Implementing, acquiring, or upgrading health IT for activities by eligible clinicians in ambulatory settings, or hospitals, eligible under Sections 4101, 4102, and 4201 of the HITECH Act.	Use health IT certified under the ONC Health IT Certification Program if certified technology can support the activity. Visit the Certification of Health IT site to learn more.

If standards and implementation specifications adopted in 45 CFR part 170, Subpart B cannot support the activity, recipients and subrecipients are encouraged to use health IT that meets non-proprietary standards and implementation specifications developed by consensus-based standards development organizations. This may include standards identified in the ONC Interoperability Standards Advisory.

Reporting

If you are funded, you will have to follow the reporting requirements in “reporting” section of the Application Guide. The NOA will provide specific details.

You must also follow these program-specific reporting requirements:

- Progress reports, Federal Financial Report, and the final report noted under Section 6 of HRSA’s SF 424 Application Guide are not required for DRP.

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Contacts and Support

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Agency contacts

Program and eligibility

Catishia Mosley
Public Health Advisor
Attn: Ryan White HIV/AIDS Program Part F Dental Reimbursement Program
Health Resources and Services Administration
AskPartFDental@hrsa.gov
301-945-0903

Financial and budget

Patryce Peden
Grants Management Specialist
Division of Grants Management Operations
Office of Financial Assistance and Acquisition Management (OFAAM)
Health Resources and Services Administration
PPeden@hrsa.gov
301-443-2277

HRSA contact center

Open Monday to Friday, 7 a.m. to 8 p.m. ET, except for federal holidays.
Call: 877-464-4772 / 877-Go4-HRSA
TTY: 877-897-9910

Electronic Handbooks Contact Center

Help with systems

Grants.gov

Grants.gov provides 24/7 support. You can call 800-518-4726, search the Grants.gov Knowledge Base, or email Grants.gov for support. Hold on to your ticket number.

SAM.gov

If you need help, you can call 866-606-8220 or live chat with the Federal Service Desk.

Helpful websites

- Application Guide
- HRSA Grants page
- HHS Tips for Preparing Grant Proposals
- Frequently Asked Questions
- Applicant Training

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Appendix

Dental Services Report

Instructions

For instructions on completing the report, see reporting requirements on our website under “Dental Services Report.”

We will only accept actual counts of people with HIV who received oral health care services from your institution or program as the basis of your application for DRP funding.

- **Funding and payment coverage:** You should only report direct reimbursements from third party payers (public and private) as payment for services provided in Section 2 Tabs 1 & 2. You should not report funding from the RWHAP or other federal grant programs as reimbursements in these items.
- **Unreimbursed costs:** The total unreimbursed costs of oral health care provided to people with HIV from July 1, 2024, through June 30, 2025, that are entered in fields 18a and 18g of the SF-424 Application for Federal Assistance must match the amount reported in Section 4 Tab 2 on the Dental Reimbursement Program Dental Services Report. We may verify the unreimbursed costs listed on the DSR and SF-424 application for Federal Assistance if there are differences. ***If these amounts do not match, we may deem your application ineligible.**
- **Narratives:** Please include narrative responses in Section 4 Tab 3, not to exceed one page in length for each item. Your responses will better inform us about your institution or program; your collaborations in the larger community; your training of students, residents, and providers; and other accomplishments. Your responses will also help us target technical assistance activities, document the value of funds expended, and demonstrate the importance of continued RWHAP funding for oral health care.

EXHIBIT L

Pages 1 - 72

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

Before The Honorable Jon S. Tigar, Judge

SAN FRANCISCO AIDS FOUNDATION, et al.,	)	
Plaintiffs,	)	
VS.	)	**NO. 25-CV-01824-JST**
TRUMP, et al.,	)	
Defendants.	)	

Oakland, California
Thursday, May 22, 2025

TRANSCRIPT OF PROCEEDINGS

APPEARANCES:

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(APPEARANCES CONTINUED ON THE NEXT PAGE.)

REPORTED REMOTELY BY: Kendra A. Steppler, RPR, CRR
Official United States Reporter

APPEARANCES: (Continued)

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ASSISTANT UNITED STATES ATTORNEY

Thursday - May 22, 2025 **2:06 p.m.**

P R O C E E D I N G S

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THE COURTROOM DEPUTY: All rise. U.S. District Court is now in session, the Honorable Jon S. Tigar presiding.

Please be seated.

Calling Civil Case Number 25-1824-JST, San Francisco AIDS Foundation, et al. v. Trump, et al.

Parties, please state your appearance, beginning with the plaintiff.

MS. TAYLOR: Thank you, Your Honor. Camilla Taylor for the plaintiffs.

MR. ABRIGO: Jose Abrigo for the plaintiffs.

MR. GONZALEZ-PAGAN: Good afternoon, Your Honor. Omar Gonzalez-Pagan for the plaintiffs.

MS. PELECANOS: Good afternoon, Your Honor. Pelecanos for the plaintiffs.

MS. GHEIBI: Good afternoon, Your Honor. Pardis Gheibi for the Government.

MR. JEU: Christopher Jeu on behalf of the Government.

THE COURT: Welcome. And good afternoon to those of you in the audience.

As you all know, the matter is on calendar to consider San Francisco AIDS Foundation and the other plaintiffs' motion for a preliminary injunction.

vague. Again --

THE COURT: I know you wouldn't say "so what" to a judge, but I'm just trying to summarize.

MS. GHEIBI: But what we're saying is we're not putting forth a definition for it. And we're saying, under the case law, that's okay. The same way the Government didn't have to put forth a definition of what it means to be "excellent" or "decent," it doesn't have to put forth a definition for "equity."

THE COURT: Let's take another word from these orders. This is from the gender order. And it's a word that Ms. Taylor focused on a few minutes ago, which is what it means to, quote, "promote," closed quote, gender ideology. And this time, rather than ask you what something means, I'm going to give you some specific examples and ask if you can tell me whether doing the action that I'm describing would promote gender ideology. And these are all things that I could see one of the plaintiff agencies doing --

MS. GHEIBI: Mm-hm.

THE COURT: -- in the day-to-day conduct of their work.

So, for example, would referring to someone -- a client perhaps or an agency employee -- by a pronoun other than Mr., Ms., Mrs., or Miss promote gender ideology?

MS. GHEIBI: I want to -- I want to make something

clear here, that Plaintiffs are assuming that just because their entity promotes gender ideology, that means they're going to lose all the funds. And I want to be very clear that that's not what the executive order says. I think that the relevant provision --

THE COURT: I'm sorry, Ms. Gheibi.

Madame Reporter, would you read my question back, please?

(Reporter read back.)

MS. GHEIBI: Under the executive order, yes. But it does not mean they automatically lose funding if the funding does not go to a program that promotes gender ideology. So the question is, is it -- is the entity just doing it outside of the scope of the program versus within the scope of the program?

And I think Plaintiffs -- from their declarations -- they seem very concerned that just because their entity sort of either respects --

THE COURT: Yeah. I appreciate the clarity.

MS. GHEIBI: Yes.

THE COURT: What if an agency trained its employees to ask clients which pronoun they use? Would that promote gender ideology?

MS. GHEIBI: I think it would fall within the scope -- yes, it would promote gender ideology. But, again, the question is, is the --

THE COURT: Again, I appreciate the --

MS. GHEIBI: -- funding going to it?

THE COURT: Again, I appreciate the clarity. This is in some relatively stark contrast to our earlier conversation. What if a facility designated its restrooms, quote, "all gender," closed quote, even if the agency had more than one restroom and could designate specific genders if it wanted to? Would that be promoting gender ideology?

MS. GHEIBI: I'm sorry, could you repeat that?

THE COURT: Sure. I want you to imagine an agency that has at least two bathrooms. And it designates each of them, quote, "all gender," closed quote, even though it doesn't have to because it has two bathrooms. It could identify or it could designate a men's bathroom and a women's bathroom if it wanted to. But it chooses not to do that. It just puts a sign outside each bathroom that says "all gender." Would that promote gender ideology, in your view?

MS. GHEIBI: I don't know the answer to that question -- I don't know if the answer to that question is yes or no under the executive order. I can't answer that --

THE COURT: A little closer to the line.

MS. GHEIBI: -- hypothetical.

THE COURT: Okay. Does the Government make any argument in its brief regarding legitimate Government interests advanced by the gender order? I ask because I didn't see such

CERTIFICATE OF REPORTER

I certify that the foregoing is a correct transcript from the record of proceedings in the above-entitled matter.

DATE: Tuesday, June 10, 2025

Kendra Steppler

Kendra A. Steppler, RPR, CRR

Official Reporter, U.S. District Court