JAMA | Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV in Adults: 2024 Recommendations of the International Antiviral Society–USA Panel

Rajesh T. Gandhi, MD; Raphael J. Landovitz, MD; Paul E. Sax, MD; Davey M. Smith, MD; Sandra A. Springer, MD; Huldrych F. Günthard, MD; Melanie A. Thompson, MD; Roger J. Bedimo, MD; Constance A. Benson, MD; Susan P. Buchbinder, MD; Brenda E. Crabtree-Ramirez, MD; Carlos del Rio, MD; Ellen F. Eaton, MD; Joseph J. Eron Jr, MD; Jennifer F. Hoy, MBBS; Clara Lehmann, MD; Jean-Michel Molina, MD; Donna M. Jacobsen, BS; Michael S. Saag, MD

IMPORTANCE New data and new antiretroviral drugs and formulations continue to become available for the prevention and management of HIV infection.

OBJECTIVE To provide updated recommendations for HIV treatment and clinical management and HIV prevention.

METHODS A panel of volunteer expert physician scientists were appointed to provide updated consensus recommendations for 2024. Relevant evidence in the literature since the last report was identified from PubMed and Embase searches (which initially yielded 3998 unique citations, of which 249 were considered relevant); from ongoing monitoring of the literature by the panel members; from data submitted by product manufacturers; and from studies presented at peer-reviewed scientific conferences between June 2022 and October 2024.

FINDINGS Antiretroviral therapy continues to be recommended for all individuals with HIV. For most people with HIV, initial regimens composed of an integrase strand transfer inhibitor (InSTI), specifically bictegravir or dolutegravir, with 2 (and in some cases 1) nucleoside or nucleotide reverse transcriptase inhibitors are recommended. Recommendations are made for those with particular clinical circumstances, such as pregnancy and active opportunistic diseases, as well as for those unable to take InSTIs. Regimens may need to be changed for virologic failure, adverse effects, convenience, or cost, among other reasons. Long-acting injectable therapy is available for those who prefer not to take daily oral medications and for people struggling with adherence to daily therapy. Recommendations are provided for laboratory monitoring, management of substance use disorders and weight changes, as well as use of statins for cardiovascular disease prevention. For HIV prevention, oral (daily or intermittent) and injectable long-acting medications are effective options for people at increased likelihood of HIV exposure. Further, new tools for maintaining health and well-being among people with HIV, such as doxycycline postexposure prophylaxis to avert sexually transmitted infection, and strategies to treat substance use disorders, are recommended. Disparities in HIV acquisition and care access are discussed and solutions proposed.

CONCLUSIONS New approaches for treating and preventing HIV offer additional tools to help end the HIV epidemic, but achieving this goal depends on addressing disparities and inequities in access to care.

Editorial
Multimedia
Supplemental content
CME at jamacmelookup.com

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Rajesh T. Gandhi, MD (panel chair), Massachusetts General Hospital, GRB 504, Infectious Disease, 55 Fruit St, Boston, MA 02114 (RGANDHI@mgh.harvard.edu).

JAMA. doi:10.1001/jama.2024.24543
Published online December 1, 2024.

Because of effective antiretroviral therapy (ART), many people with HIV will live a normal or near-normal lifespan.[1] Management of HIV continues to improve, with increasing options for initial therapy, novel approaches for switching therapy, and effective strategies for managing co-infections. In addition, there are new tools for preventing cardiovascular disease in people with HIV and for reducing the incidence of sexually transmitted infections (STIs). HIV prevention through preexposure prophylaxis (PrEP) remains a dynamic field, with several recent advances. However, improving care of people with HIV who have substance use disorder (SUD) and addressing HIV care disparities remain challenges and high priorities. Here, updated recommendations for HIV treatment and clinical management as well as HIV prevention based on the latest data are provided, and challenges that need additional attention and dedicated resources are highlighted.

Methods

Appointment of the Panel

A volunteer international panel of experts in HIV research and clinical care and the panel leadership were appointed by the International Antiviral (formerly AIDS) Society-USA (IAS-USA). Panel members were screened for expertise, involvement in research and clinical care, financial relationships with commercial entities, and ability to work toward consensus. The panel convened in person and by video conference calls from November 2023 to October 2024. Teams and a team leader were appointed for each primary section and evaluated relevant evidence and drafted recommendations for full-panel review. Details of the recommendations development process, along with members of the volunteer leadership board, recommendations panel, and working sections, are available in the eMethods and eBoxes 1 through 3 in the Supplement.

Identification of the Evidence

New evidence on antiretroviral drugs was identified in the literature (published between June 2022 and July 2024), major scientific conference presentations, and safety reports.[2] Literature searches were conducted using Pubmed and Embase by a panel member (C.d.R), which identified 2998 unique citations. These were reviewed by another panel member (M.S.S.), who identified 249 possibly relevant publications. The relevant citations were categorized by section of the paper for review by each section lead. After July 2024, the panel closely monitored the literature through October 2024 for new evidence that informed the recommendations. Abstracts presented at scientific conferences between June 2022 and October 2024 were identified by panel members and teams. In addition, antiretroviral drug manufacturers were asked to submit a list of relevant publications and abstracts (same criteria as above), which were reviewed by section leads. Details of the evidence collection are available in eTables 1 through 3 in the Supplement.

Process

The recommendations address antiretroviral drugs for prevention and management of HIV in adults in settings in which most antiretroviral drugs are available. Recommendations are rated for the strength of the recommendation and the quality of the supporting evidence (**Table 1**).[2,3] For recommendations that have not changed substantially or for which few new data have become available since 2022, the previous iterations of the recommendations provide background information and relevant evidence.[2] Key recommendations for each section are listed in a text box, with new or updated recommendations highlighted. Abbreviations used for antiretroviral drugs are available in eTable 4 in the Supplement. Antiretroviral drug combinations that are coformulated are noted with slashes (eg, drug A/drug B/drug C). Tables and further details about the process, panel, evidence identification, and the IAS-USA and its policies are available in the Supplement.

Table 1. Strength of Recommendation and Quality of Evidence Rating Scale[a]

Category, rating	Definition
Strength of recommendation	
A	Strong panel support for the recommendation
B	Moderate panel support for the recommendation
C	Limited or weak panel support for the recommendation
Quality of evidence	
Ia	Evidence from 1 or more randomized clinical trials published in the peer-reviewed literature
Ib	Evidence from 1 or more randomized clinical trials presented in abstract form at peer-reviewed scientific meetings
IIa	Evidence from nonrandomized clinical trials or cohort or case-control studies published in the peer-reviewed literature
IIb	Evidence from nonrandomized clinical trials or cohort or case-control studies presented in abstract form at peer-reviewed scientific meetings
III	Recommendation based on the panel's analysis of the accumulated available evidence

[a] Adapted in part from the Canadian Task Force on Periodic Health Examination.[2,3]

ART for Individuals With HIV

All individuals with HIV should receive ART (**Box 1**).[2] Recommended initial ART regimens remain as described in the last publication (**Box 2**).[2,4] Regimens composed of the integrase strand transfer inhibitors (InSTIs) bictegravir (BIC) or dolutegravir (DTG) are recommended as initial treatment for most people with HIV due to high viral suppression rates, excellent tolerability, infrequent toxicity, limited drug-drug interactions, a high barrier to resistance, and a low pill burden (evidence rating: AIa).

Tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF) (herein TXF) and emtricitabine (FTC) or lamivudine (3TC) (herein XTC) remain the recommended nucleoside or nucleotide reverse transcriptase inhibitor (NRTI) components of an initial ART regimen (evidence rating: AIa).[2]

The single recommended 2-drug regimen for initial ART is DTG/3TC (evidence rating: AIa). However, it should not be used if lamivudine resistance is detected on HIV genotyping, HIV RNA level is 500 000 copies/mL or higher, or hepatitis B (HBV) co-infection is present (evidence rating: AIa). Thus, DTG/3TC is not recommended for ART initiation in the absence of those laboratory results. DTG/3TC also should not be initiated during pregnancy because of limited data in

this setting. There are limited data on using DTG/3TC for initial therapy in people who have CD4+ cell counts below 200/μL.

Initial boosted darunavir (DRV)–containing regimens are recommended when InSTI resistance is suspected before the results of resistance testing are returned, particularly when there has been prior exposure to long-acting cabotegravir (CAB-LA) as PrEP (evidence rating: AIIb).[2] The treatment can be modified to an InSTI or nonnucleoside reverse transcriptase inhibitor (NNRTI)–based therapy once results of the test excludes resistance to these drug classes.

In a person who acquires HIV-1 while taking TXF/XTC for PrEP, dolutegravir or bictegravir in combination with TXF/XTC can be started before resistance testing results are available. However, results of resistance testing (when available) should inform which regimen is continued.

ART and Pregnancy

Immediate initiation of ART is recommended for all individuals with HIV who are pregnant for reasons of maternal health and to prevent perinatal and sexual transmission (evidence rating: AIa). Dolutegravir with TAF/FTC (or TDF/XTC if TAF/FTC is not available) is the recommended ART regimen in pregnancy and in persons who plan to become pregnant[5] because of high antiviral efficacy[6] and low rates of adverse birth outcomes (evidence rating: AIa).[7] BIC/TAF/FTC is an alternative regimen (evidence rating: BIIa). Recent pharmacokinetic studies found that bictegravir levels were sufficient during pregnancy, and the low rates of birth defects in infants born to persons with first-trimester exposure are reassuring.[8,9] Persons found to be pregnant while receiving BIC/TAF/FTC should continue this regimen if it is tolerated and effective (evidence rating: AIIa). When dolutegravir is not an option or when HIV has been acquired after receiving long-acting cabotegravir for preexposure prophylaxis, TXF/XTC plus twice-daily darunavir (600 mg) plus ritonavir 100 mg is recommended (see Box 2) (evidence rating: AIa). Recommended regimens to use if dolutegravir, darunavir, or bictegravir are not an option are summarized in **Table 2**.

Cobicistat (COBI)-containing treatment regimens should not be used during pregnancy owing to low drug levels that can reduce efficacy (AIIb). So far there are insufficient data to recommend doravirine (DOR)-containing regimens, injectable long-acting cabotegravir plus long-acting rilpivirine, or DTG/3TC during pregnancy (evidence rating: AIII). If pregnancy occurs in someone receiving long-acting cabotegravir plus long-acting rilpivirine, switching to an oral triple-drug regimen is recommended (evidence rating: AIII).[10]

Considerations for Other Initial ART Regimens

Other initial regimen options appear in Table 2. Despite the fact that InSTI-based regimens are recommended as initial regimens for the majority of individuals, there are circumstances in which other regimens need to be used.

ART in the Setting of Opportunistic Infections

Recommendations for ART in this setting appear in Box 1. As previously recommended for persons with an opportunistic infection,[2] ART should be initiated within 2 weeks of starting treatment for most opportunistic infections. Exceptions to this recommendation are tuberculous meningitis and cryptococcal meningitis as detailed below. For people with HIV and active tuberculosis excluding tuberculous meningitis, ART initiation is recommended within 2 weeks after starting treatment for tuberculosis, particularly if the CD4+ cell count is below 50/μL (evidence rating: AIa). For those with tuberculous meningitis, treatment for tuberculosis and high-dose corticosteroids should be initiated immediately at diagnosis of tuberculous meningitis, and ART initiation is recommended when tuberculous meningitis is under control, based on clinical improvement and changes toward normal in CSF parameters, generally 2 to 4 weeks thereafter (evidence rating: BIa).[11]

For persons with cryptococcal meningitis who can be closely monitored and treated for increased intracranial pressure and immune reconstitution inflammatory syndrome, ART initiation is recommended within 2 to 4 weeks after starting antifungal therapy, with earlier initiation at 2 weeks after starting antifungal therapy for those who have clinically improved, have control of intracranial pressure, have negative CSF cultures with use of antifungal therapy, and can

Box 1. Recommendations for When to Start Antiretroviral Therapy

- Initiation of ART is recommended as soon as possible after diagnosis, ideally within 7 days, including on the same day as diagnosis or at the first clinic visit if the individual is ready and there is no suspicion for a concomitant opportunistic infection (evidence rating: AIII).
- Structural barriers that could delay receipt of ART (including same-day) and impede care engagement, continuous ART access, and ART adherence should be addressed using evidence-informed strategies (evidence rating: AIIa).
- Initiation of ART at the time of diagnosis of acute HIV infection or in a person who is pregnant is recommended (evidence rating: AIIa).
- Initiation of ART is recommended within 2 weeks of initiation of treatment for most opportunistic infections:
  - For persons with active tuberculosis without evidence of tuberculous meningitis, ART should be initiated within 2 weeks after initiation of tuberculosis treatment, especially for those with CD4+ cell count below 50/μL (evidence rating: AIa).
  - For those with tuberculous meningitis, high-dose corticosteroids and tuberculosis treatment should be initiated immediately at diagnosis, and ART initiation is recommended when tuberculous meningitis is under control, based on clinical improvement and changes toward normal in CSF parameters, within 2 to 4 weeks thereafter (evidence rating: BIa).
  - For persons with cryptococcal meningitis who can be closely monitored and treated for increased intracranial pressure and immune reconstitution inflammatory syndrome, ART initiation is recommended 2 to 4 weeks after starting antifungal therapy, with earlier initiation at 2 weeks after starting antifungal therapy for those who have clinically improved, have control of intracranial pressure, have negative CSF cultures with use of antifungal therapy and can continue to be closely monitored, and 4 weeks after starting antifungal therapy for those who do not meet these criteria (evidence rating: BIII).
  - For ART-naive individuals with asymptomatic cryptococcal antigenemia and a negative lumbar puncture, immediate ART and preemptive fluconazole are recommended (evidence rating: BIII).
- Initiation of ART is recommended immediately in the setting of a new diagnosis of cancer with attention to drug-drug interactions (evidence rating: AIIa).

Adapted from Gandhi et al.[2] ART indicates antiretroviral therapy; CSF, cerebrospinal fluid.

Box 2. Recommended Initial Antiretroviral Therapy Regimens

Recommended for Most People With HIV

- The following are recommended (in alphabetical order by anchor drug) for most people with HIV:
  - BIC/TAF/FTC (evidence rating: AIa)
  - Dolutegravir plus TXF/XTC (evidence rating: AIa)
  - DTG/3TC (only if HIV RNA level <500 000 copies/mL, if lamivudine resistance is not present, and if HBV co-infection not present)(evidence rating: AIa). There are limited data on using DTG/3TC for initial therapy in people who have CD4$^+$ cell counts below 200/μL. This regimen should not be used for rapid ART initiation when genotype, HIV RNA, and HBV serology results are not yet available (evidence rating: AIII).
- Persons who acquired HIV while receiving preexposure prophylaxis with TAF/FTC or TDF/FTC should have a blood sample for genotyping drawn prior to initiating therapy and a 3-drug regimen, preferably dolutegravir or bictegravir plus TXF/XTC, should be initiated if ART is to be started before genotype results are available (evidence rating: AIII).
- Persons who acquired HIV after exposure to cabotegravir for preexposure prophylaxis should have a blood sample for InSTI genotyping drawn prior to beginning therapy with an InSTI-based regimen (evidence rating: AIII).
  - If therapy is desired before genotype results are available or if InSTI resistance is present or suspected, ritonavir- or cobicistat-boosted darunavir and TXF/XTC should be used (evidence rating: AIIb).

Recommended During Pregnancy

- TAF/XTC plus dolutegravir (evidence rating: AIa), with TDF/XTC plus dolutegravir a suitable alternative if tenofovir alafenamide is not available (evidence rating: AIa).
- The following drugs may be used if dolutegravir is not an option:
  - Darunavir (600 mg) plus ritonavir (100 mg), both given twice daily (evidence rating: AIa) with TAF/XTC or TDF/XTC; in people who have previously received long-acting cabotegravir for preexposure prophylaxis, this regimen is recommended over InSTI-based regimens.
  - BIC/TAF/FTC (evidence rating: BIIb)
  - Persons found to be pregnant while receiving effective BIC/TAF/FTC should continue this regimen if it is tolerated (evidence rating: AIIa).
  - When dolutegravir, darunavir, and bictegravir are not options during pregnancy, other options are available (**Table 2**).
  - If pregnancy is diagnosed in an individual receiving long-acting cabotegravir plus long-acting rilpivirine, switching to an oral triple-drug regimen is recommended (evidence rating: AIII).

Not Recommended to Initiate During Pregnancy Because of Inadequate Data to Support Use (Evidence Rating: AIII for All)

- Doravirine-containing regimens
- Long-acting cabotegravir plus long-acting rilpivirine
- DTG/3TC
- DTG/RPV

If an individual is stable with use of a doravirine-containing regimen, or a 2-drug regimen such as DTG/3TC or DTG/RPV, and wishes to continue the treatment during pregnancy, counsel patient about uncertainties regarding safety and efficacy during pregnancy and switch to a recommended regimen or monitor HIV RNA levels more frequently.

Should Not Be Used During Pregnancy Because of Inadequate Drug Levels

- Cobicistat-containing regimens (evidence rating: AIIb)

Recommended During Latent or Active Tuberculosis Treatment (in Alphabetical Order by Anchor Drug)

- TXF/XTC is recommended with 1 of the following[a]:
  - Dolutegravir (50 mg once daily) during tuberculosis preventive therapy with 3HP (evidence rating: AIa)
  - Dolutegravir (50 mg twice daily) (evidence rating: BIa) during tuberculosis preventive therapy with 1HP
  - Dolutegravir (50 mg twice daily) (evidence rating: AIa) during treatment for active tuberculosis with a rifamycin-containing regimen
  - Efavirenz (600 mg) (evidence rating: AIa)
- A ritonavir-boosted protease inhibitor regimen with TXF/XTC may be used only if it is not possible to use any of the above regimens; in that case, rifabutin (150 mg) should be substituted for rifampin (evidence rating: AIII).
- Darunavir boosted with ritonavir or cobicistat, doravirine, EVG/COBI, long-acting cabotegravir plus long-acting rilpivirine, etravirine, and rilpivirine are not recommended with rifampin due to drug-drug interactions (evidence rating: AIIa).
- DTG/3TC and BIC/TAF/FTC are not currently recommended with rifampin due to drug-drug interactions and inadequate data (evidence rating: AIII).

Regimens are listed in alphabetical order by first drug in the regimen. Drug components separated with a virgule (/) indicate these are available as co-formulations. ART indicates antiretroviral therapy; BIC, bictegravir; COBI, cobicistat; DTG, dolutegravir; EVG, elvitegravir; FTC, emtricitabine; HBV, hepatitis B virus; InSTI, integrase strand transfer inhibitor; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TXF, tenofovir alafenamide or tenofovir disoproxil fumarate; XTC, emtricitabine or lamivudine; 1 HP, daily rifapentine + isoniazid for 1 month; 3HP, weekly rifapentine + isoniazid for 3 months; 3TC, lamivudine.

[a] There is a pharmacokinetic interaction between rifampin and tenofovir alafenamide; clinical data with coadministration are limited; however, in a healthy volunteer study of tenofovir alafenamide and emtricitabine with rifampin, intracellular tenofovir-diphosphate concentrations were higher than those achieved by tenofovir disoproxil fumarate, suggesting that tenofovir alafenamide can be used with caution and close monitoring of HIV RNA levels.[4]

continue to be closely monitored; those who do not meet these criteria should initiate ART 4 weeks after starting antifungal therapy (evidence rating: BIII).[11,12] All patients should be closely monitored and treated for increased intracranial pressure. For individuals who are ART-naive with asymptomatic cryptococcal antigenemia and negative findings on CSF examination, immediate ART and preemptive fluconazole are recommended (evidence rating: BIII).[13]

Careful attention to the potential for drug-drug interactions is particularly important for people receiving treatment for latent or active tuberculosis. Newer data have altered the landscape for InSTI-based ART regimens in this setting. In a phase 1/2 single-group study of individuals treated for latent tuberculosis infection with once-daily dolutegravir-based regimens and once-weekly isoniazid and rifapentine for 3 months (3HP) as preventive therapy for tuberculosis, rifapentine decreased dolutegravir exposure by 26%, but trough concentrations remained above the dolutegravir 90% minimum inhibitory concentration for all but 1 participant, and all participants maintained undetectable viral loads.[14] In another recent study, once-daily

dolutegravir-based ART and 3HP were initiated simultaneously in persons who required preventive therapy for tuberculosis, with similar results.[15] In a pharmacokinetic study of daily isoniazid and rifapentine given for 1 month (1HP) for tuberculosis preventive therapy, dolutegravir was administered twice daily with dolutegravir trough concentrations higher than when dolutegravir was dosed once daily without rifapentine; all but 1 participant had viral load levels below 50 copies/mL at the end of the 1HP treatment.[16] Last, data from an ongoing phase 3 trial of standard once-daily dolutegravir plus tenofovir disoproxil fumarate and lamuvudine administered with 1HP, 92.6% of participants evaluated had dolutegravir concentrations above the protein binding adjusted inhibitory concentration. Of the 252 participants enrolled, proportions with HIV RNA levels below 50 copies/mL were 95.2% at week 24 and 97.7% at week 48.[17]

New but less robust data are also available for bictegravir. In a single-group study, 48 people with HIV and latent tuberculosis infection virally suppressed with use of BIC/TAF/FTC were treated with 1HP; 44 (91.7%) remained virally suppressed on day 15 of 1HP treatment, and all were suppressed at months 3 and 6 after completion of 1HP treatment.[18] Bictegravir trough concentrations remained above the 95% effective concentration for 56% of participants with measurements on day 15 and 37% of those with measurements on day 29 but returned to threshold levels above the 95% effective concentration thereafter; all participants remained virally suppressed at 52 weeks. Last, in a randomized trial in persons with HIV and active tuberculosis receiving a rifampin-containing tuberculosis treatment regimen for up to 8 weeks, BIC/TAF/FTC given twice daily was compared with dolutegravir given twice daily plus once-daily TDF/FTC. Viral suppression to HIV RNA levels below 50 copies/mL at week 24 was observed for 97% of participants in both groups, and tuberculosis outcomes were the same.[19]

In aggregate, these studies support the use of dolutegravir-containing regimens for ART in the setting of latent or active tuberculosis. For treatment of latent tuberculosis infection, persons with HIV receiving 1HP treatment should receive dolutegravir at a dosage of 50 mg twice daily (evidence rating: BIa), and those receiving 3HP treatment should receive dolutegravir at a standard 50-mg once-daily dose (evidence rating: AIa). For active tuberculosis, persons with HIV being treated with a rifamycin-containing regimen should receive dolutegravir at a dosage of 50 mg twice daily (evidence rating: AIa) until longer-term follow-up data from studies evaluating once-daily dolutegravir in this setting become available. The data with bictegravir are less robust at this point, but emerging information suggests that bictegravir-containing ART might be considered an alternative in these settings if dolutegravir-containing regimens cannot be used. If none of these regimens can be used, ritonavir-boosted atazanavir or lopinavir with TXF/XTC may be used with rifabutin (150 mg daily) (evidence rating: AIII).

HIV and Cancer

As deaths from AIDS-defining diseases have declined in people with HIV, there has been an increase in the proportion of deaths due to cancer.[20,21] People with HIV have an increased incidence of non–AIDS-defining malignancies, primarily due to factors such as smoking, alcohol consumption, and low CD4$^+$ cell counts.[22] Cancer presently contributes to 20% to 30% of all HIV-related deaths[23,24]; therefore, prioritizing cancer screening, including for cervical and anal cancer, in people with HIV is recommended (evidence rating: AIa).[11]

Table 2. Other Recommended Initial Antiretroviral Therapy[a]

Regimens[b,c]	Potential uses and cautions
DRV/COBI/TAF/FTC[d]	Recommended for individuals with prior long-acting cabotegravir PrEP exposure when an InSTI genotype is not available or before the results are returned
Darunavir plus cobicistat or ritonavir plus TXF/XTC	Recommended for those with prior long-acting cabotegravir PrEP exposure when an InSTI genotype is not available or before the results are returned Darunavir plus ritonvir plus TXF/FTC is recommended during pregnancy when there has been prior exposure to long-acting cabotegravir for PrEP
DOR/TDF/3TC[d] or doravirine plus TXF/XTC	May be useful in people with HIV who have intolerance to InSTIs
EFV (600 or 400 mg)/TDF/FTC[d] or lamivudine[d]	Potential use in people with HIV receiving tuberculosis treatment Potential use in people with pregnancy or pregnancy intention, if dolutegravir, darunavir, or bictegravir are not an option
Raltegravir plus TXF/XTC	Potential use in people who are pregnant or have pregnancy intention, if dolutegravir, darunavir, or bictegravir are not an option
RPV/TAF/FTC[d] or rilpivirine plus TDF/3TC[e]	Small pill size Only use if pretreatment HIV RNA level is <100 000 copies/mL and CD4$^+$ cell count is >200/μL Potential use in people who are pregnant or have pregnancy intention, if dolutegravir, darunavir, or bictegravir are not an option
Ritonavir plus atazanavir plus TXF/XTC	Potential use in people who are pregnant or have pregnancy intention, if dolutegravir, darunavir, or bictegravir are not an option

Abbreviations: 3TC, lamivudine; COBI, cobicistat; DOR, doravirine; DRV, darunavir; EFV, efavirenz; FTC, emtricitabine; InSTI, integrase strand transfer inhibitor; PrEP, preexposure prophylaxis; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; TXF, tenofovir alafenamide or tenofovir disoproxil fumarate; XTC, emtricitabine or lamivudine.

[a] Adapted from Gandhi et al.[2]

[b] The recommended initial antiretroviral regimens appear in Box 2.

[c] The regimens are listed in alphabetical order by first drug in the regimen. Drug components separated with a virgule (/) indicate that these are available as coformulations.

[d] Available as a single-tablet coformulation.

[e] Available in generic formulations in many countries.

For people with HIV without prior ART who have cancer, immediate initiation of ART is recommended (evidence rating: AIIa). The management of cancer in people with HIV requires careful assessment of potential drug-drug interactions between ART and various anticancer agents (eg, chemotherapy, immunotherapy) and other commonly prescribed drugs for people with cancer (eg, antifungals, antivirals, immunosuppressive agents). Guidance on drug-drug interactions is available through the University of Liverpool and Toronto General Hospital (https://www.hiv-druginteractions.org/checker; https://hivclinic.ca/app/#drugInt).[25,26]

Some cancer treatments may be associated with a decline in CD4$^+$ cell count, even in individuals stable while receiving ART. The need for opportunistic infection prophylaxis varies depending on the cancer, the treatment regimen, and the CD4$^+$ cell count and should be discussed with the oncologist and other members of the care team.

When and How to Switch Antiretroviral Regimens

Recommendations for switching regimens are listed in **Box 3**.

Switching Therapy in the Setting of Virologic Suppression

People with HIV and virologic suppression may be receiving regimens that are no longer recommended due to short- and long-term

Box 3. Key Recommendations for Switching Antiretroviral Therapy Regimens

Switching Therapy in the Setting of Virologic Suppression

People with HIV and virologic suppression may be receiving regimens that are no longer recommended due to short- and long-term adverse effects, inconvenience, regimen complexity, anticipated drug-drug interactions, progressive kidney disease, risk of cardiovascular disease, or cost. Switching ART to one of the recommended initial ART regimens in these circumstances is frequently the optimal strategy, provided that virologic suppression can be maintained (evidence rating: AIa).

Individuals with virologic suppression receiving regimens that contain a boosted protease inhibitor and 2 NRTIs can be switched to dolutegravir plus TXF/XTC or BIC/FTC/TAF regardless of known or likely prior resistance to the NRTI pair and provided there is no history of InSTI resistance (evidence rating: AIa).

Switching individuals receiving boosted protease inhibitors plus 2 NRTIs to NNRTI or first-generation InSTI regimens (raltegravir or elvitegravir) plus 2 NRTIs is not recommended in the presence of previous NRTI resistance (evidence rating: AIa).

Individuals with NRTI resistance who switch to dual NRTI plus dolutegravir or bictegravir regimens should be monitored more closely in the first year after the switch, especially if there are concerns about taking the new regimen regularly (evidence rating: AIII).

Injectable long-acting cabotegravir plus long-acting rilpivirine is recommended for persons who experience stigma or other adverse consequences of taking pills daily or in response to strong patient preference (evidence rating: AIb).

Long-acting cabotegravir plus long-acting rilpivirine is not recommended in individuals with documented or suspected resistance to either agent (evidence rating: AIIa) or with chronic hepatitis B (evidence rating: AIa).

Switching Therapy With Blips, Low-Level Viremia, or Virologic Failure

Virologic failure occurs when ART fails to achieve or maintain an HIV RNA level below 200 copies/mL (evidence rating: AIIa).

Intermittent detection of HIV RNA at levels between 20 and 200 copies/mL (often referred to as a "blip") and persistent low-level viremia at this level should not prompt changing treatment (evidence rating: AIIa). Evaluation should include review of ART adherence and the possibility of interacting drugs or supplements. Ideally, the patient should be receiving a treatment that has a high barrier to resistance, such as those including bictegravir, dolutegravir, or boosted darunavir.

For people who have stopped ART, resuming the most recent dolutegravir- or bictegravir-based regimen is recommended even before the results of the resistance genotype test have been returned, provided adherence is good and the individual is amenable (evidence rating: AIIb).

In individuals with virologic failure with extensive multiclass resistance (including to InSTIs), agents with novel mechanisms of action such as ibalizumab, fostemsavir, or lenacapavir are recommended, ideally in combination to allow for 2 fully active drugs (evidence rating: AIa).

For those unable to take oral ART with advanced HIV disease, long-acting cabotegravir plus long-acting rilpivirine in conjunction with intensive case management and adherence support may be considered for people with viremia who meet the criteria below when no other treatment options are effective (evidence rating: AIIa under the conditions described):

- Unable to take oral ART consistently despite extensive efforts and clinical support
- High risk of HIV disease progression ($CD4^+$ cell count <200/μL or history of AIDS-defining complications)
- Virus susceptible to both cabotegravir and rilpivirine

If applicable, individuals should also be referred for treatment of substance use disorders or mental illness.

ART indicates antiretroviral therapy; BIC, bictegravir; FTC, emtricitabine; InSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside or nucleotide reverse transcriptase inhibitor; TAF, tenofovir alafenamide; TXF, tenofovir alafenamide or tenofovir disoproxil fumarate; XTC, emtricitabine or lamivudine.

adverse effects, inconvenience, regimen complexity, anticipated drug-drug interactions, progressive kidney disease, risk of cardiovascular disease, or cost. Switching ART to one of the recommended initial ART regimens in these circumstances is frequently the optimal strategy, provided that virologic suppression can be maintained. Successful ART switches require a detailed review of prior treatment history, resistance testing (if available), comorbid medical conditions, the potential for drug-drug interactions, presence of chronic hepatitis B virus (HBV) infection (which requires continuing a tenofovir-containing regimen), and potential financial barriers to obtaining the new treatments. Many patients without previous documented virologic failure or drug resistance can switch to either DTG/3TC or DTG/RPV, 2-drug regimens that were highly effective in clinical trials. Both are available in coformulated single tablets and are particularly attractive options for those who cannot take tenofovir and do not have chronic HBV infection. When such switches are undertaken, short-term increased frequency of clinical and laboratory monitoring is warranted to avoid unanticipated toxicities, pharmacy dispensing errors, or inadvertent misunderstanding from the patient regarding the correct dosing.

Prospective clinical trials indicate that individuals with virologic suppression who are receiving regimens that contain a boosted protease inhibitor and 2 NRTIs can be switched to dolutegravir plus TXF/XTC or BIC/FTC/TAF regardless of likely prior resistance to the NRTI pair (evidence rating: AIa), provided there is no history of InSTI resistance.[27-29] This switch may be particularly advantageous in people with HIV who require medications that interact with boosted protease inhibitors or have cardiovascular risk factors or hyperlipidemia that may be exacerbated by boosted protease inhibitors. By contrast, switching those receiving boosted protease inhibitors plus 2 NRTIs to NNRTI or first-generation InSTI regimens (raltegravir or elvitegravir) plus 2 NRTIs is not recommended in the presence of previous NRTI resistance due to increased risk of virologic failure and emergent resistance to the NNRTI and InSTI classes (evidence rating: AIa).

The increased use of dolutegravir-containing regimens globally has raised concerns that InSTI resistance would become more frequent. Although observational studies show an association between NRTI resistance and subsequent virologic failure and InSTI resistance, thus far the incidence of this resistance occurring is uncommon and related to poor medication adherence and viremia at the time of switch.[30-32] People with NRTI resistance who switch to dual NRTI plus dolutegravir or bictegravir regimens should be monitored more closely in the first year after the switch, especially if there are concerns about taking the new regimen regularly (evidence rating: AIII). As with other switches, a viral load checked at 1 month and then every 3 months for a year is reasonable to ensure ongoing viral suppression.

Long-acting cabotegravir plus long-acting rilpivirine provides an option that may be particularly attractive for persons who experience stigma or other adverse consequences of taking pills daily (evidence rating: AIb). Since the injections are administered in outpatient clinics, this regimen is more resource intensive for clinicians and clinic staff than self-administered oral ART. As a result, clinical sites that offer this option must have the personnel available for obtaining the medications, administering the injections, and scheduling the follow-up. In addition, since long-acting cabotegravir plus long-acting rilpivirine and other tenofovir-sparing regimens do not provide treatment for or protection against HBV infection, rescreening for HBV may be warranted, along with immunization if indicated. Patients unable to attend their scheduled injections need additional close attention and interventions to bring them back to care. Long-acting cabotegravir plus long-acting rilpivirine should only be used in persons with chronic HBV infection if HBV treatment is also continued.

An important limitation of injectable cabotegravir and rilpivirine is a low (1%-2%) incidence of virologic failure with emergence of 2-class resistance even with adherence to the scheduled injections, a risk not observed with adherence to currently available oral ART.[33-35] In prospective clinical trials, risk factors for virologic failure included rilpivirine-associated resistance at baseline as detected by proviral DNA genotyping, viral subtype A6, and a body mass index greater than 30 (calculated as weight in kilograms divided by square of height in meters).[36] Clinicians should discuss the possibility of treatment failure with patients prior to switching to long-acting cabotegravir plus long-acting rilpivirine, including the potential for viral transmission if virologic rebound occurs and future limitations of treatment options. To minimize the risk of treatment failure, long-acting cabotegravir plus long-acting rilpivirine is not recommended in individuals with documented or suspected resistance to either agent (evidence rating: AIIa).

Definition and Management of Virologic Failure

Virologic failure occurs when ART fails to achieve or maintain an HIV RNA level below 200 copies/mL. Intermittent detection of HIV RNA at levels between 20 and 200 copies/mL (often referred to as a "blip") is common with the current quantitative HIV polymerase chain reaction assays and should not prompt changing treatment, although ART adherence should be discussed and the possibility of interacting drugs or supplements, such as those containing multivalent cations (including calcium, magnesium, iron, or zinc), which impair absorption of InSTIs, should be evaluated. Less often, some people with HIV may have persistent low-level viremia between 20 and 200 copies/mL despite confirmed excellent adherence to ART, which may be caused by a large HIV reservoir, clonal expansion of long-lived resting $CD4^+$ cells with latent HIV, or impaired immune responses to the virus.[37] In addition, people with low-level viremia may have more adverse virologic and clinical outcomes than those who do not.[38,39] Patients with low-level viremia and confirmed adherence are unlikely to benefit from ART intensification (evidence rating: AIa). Studies in such individuals show no reduction in low-level viremia by changing therapy or intensifying their ART regimen.[40] As a result, such changes are not recommended (evidence rating: AIa) provided the patient is already receiving a regimen that has a high barrier to resistance, such as those including bictegravir, dolutegravir, or boosted darunavir.

The most common cause of virologic failure is suboptimal adherence to ART. While assessing potential causes of a patient's difficulty taking ART regularly, clinicians should order a genotype test to assess for drug resistance that might warrant a regimen change. Due to the high resistance barrier in most contemporary regimens that contain dolutegravir or bictegravir, many individuals will have no drug resistance detected. Prospective studies suggest that resuming the most recent regimen will have high rates of virologic suppression, provided adherence is good. As a result, resuming these treatments if people are amenable is recommended, even before the results of the resistance genotype test have been returned (evidence rating: AIIa).[41,42]

Contemporary clinical trials of virologic failure have consisted of 2 distinct patient populations. In the first, individuals with virologic failure receiving an initial regimen of 2 NRTIs plus 1 NNRTI received new regimens with or without real-time resistance testing. In aggregate, these studies demonstrated that use of dolutegravir along with TXF/XTC provided rates of virologic suppression comparable or superior to those of a boosted protease inhibitor plus 2 NRTIs.[29,43,44] These favorable results were observed even in the presence of NRTI resistance at the time of treatment failure. In 1 study, however, there was a low risk of emergent dolutegravir resistance in the dolutegravir-treated groups.[43]

Other studies evaluated the role of novel agents in managing virologic failure with multiclass drug resistance, often including resistance to InSTIs.[45] This degree of multidrug resistance is uncommon and often reflects years of nonsuppressive regimens in people treated in the early ART era, or those with perinatal HIV and long periods of intermittent medication adherence. In this setting, newer agents with novel mechanisms of action such as ibalizumab, fostemsavir, or lenacapavir (LEN) are recommended, ideally in combination to allow for 2 fully active drugs (evidence rating: AIa). Also, continued treatment with NRTIs such as TXF/XTC is recommended, since they retain partial activity even in the presence of extensive resistance mutations (evidence rating: AIIa).

Persistent Virologic Failure in the Setting of Poor Oral Medication Adherence

A small proportion of people in HIV care have difficulty taking oral ART despite the availability of simple, highly effective regimens and consequently have persistent virologic failure. Some clinical programs have reported success in caring for such individuals using injectable long-acting cabotegravir plus long-acting rilpivirine every 4 weeks initially (and subsequently every 8 weeks), in conjunction with intensive case management services, as a way to achieve and maintain virologic control.[46,47] As recommended recently,[48] based on the high risk of disease progression or death in persons with advanced HIV disease who are not taking ART, injectable long-acting cabotegravir plus long-acting rilpivirine in conjunction with intensive case management and adherence support may be considered for people with viremia who meet the criteria below when no other treatment options are effective (AIIa under the conditions described):

- Unable to take oral ART consistently despite extensive efforts and clinical support
- High risk of HIV disease progression ($CD4^+$ cell count <200/μL or history of AIDS-defining complications)
- A virus susceptible to both cabotegravir and rilpivirine

If applicable, individuals should also be referred for treatment of SUD or mental health concerns.

Table 3. Laboratory Monitoring Recommendations for Persons With HIV[a]

Laboratory test	At HIV diagnosis and start of ART	During ART	At virologic failure
HIV RNA level	✓	Four to 6 wk after ART initiation; then every 3 mo until suppressed; then every 6 mo	✓
$CD4^+$ cell count	✓	Every 6 mo until >250/μL for 1 y, then stop	✓
HIV reverse transcriptase-protease (RT-pro) genotype	✓		✓
HIV integrase genotype	If partner is known to have HIV and receiving a failing ART regimen that includes an InSTI or when a person acquires HIV after exposure to cabotegravir for PrEP		If failing ART regimen included an InSTI
Viral tropism			Before start of maraviroc
CrAG screening if $CD4^+$ cell count ≤100 cells/μL	✓		
Age-appropriate cancer screening	✓	✓	
Safety laboratory tests, lipid profiles, and co-infection screening (STIs, viral hepatitis)	✓	✓	✓

Abbreviations: ART, antiretroviral; CrAG, serum cryptococcal antigen; InSTI, integrase strand transfer inhibitor; PrEP, preexposure prophylaxis; STI, sexually transmitted infection.

[a] See text for strength of the recommendation, quality of the evidence, and frequency.

Further support for the use of injectable long-acting cabotegravir plus long-acting rilpivirine in people who struggle taking oral medications comes from a randomized trial in those with virologic failure.[49] After providing economic incentives for participants to achieve viral suppression with oral ART, the trial then randomly assigned them to continue oral therapy or switch to injectable therapy. At a preplanned interim review by an independent data and safety monitoring board, the study results demonstrated that the injectable therapy was superior to oral ART in rates of virologic and treatment failure. As a result, the randomization was stopped, and participants were notified of the outcome and offered the option to continue or switch to long-acting therapy with continued follow-up.

An additional study evaluating long-acting cabotegravir and long-acting rilpivirine in individuals with viremia is planned. When the trial is available, clinicians are encouraged to refer eligible individuals to generate more robust data on the risks and benefits of this strategy.

Laboratory Monitoring in Individuals With Established HIV

Recommendations for laboratory monitoring are summarized in **Table 3**.

At HIV Diagnosis and Starting ART

Prior to initiating ART, recommended laboratory tests should assess (1) HIV RNA level; (2) $CD4^+$ cell count (evidence rating: AIIa); (3) general health (lipid levels, kidney and liver function, complete blood cell count, glucose level and, in people of childbearing potential, pregnancy status) (evidence rating: AIa); (4) ART resistance (reverse transcriptase–protease genotype) (evidence rating: AIIa); and (5) potential co-infections (ie, viral hepatitis A, B, and C; latent tuberculosis; and STIs) (evidence rating: AIIa). Considering the continued low frequency of transmitted InSTI resistance, testing for InSTI resistance is not recommended in people newly diagnosed with HIV unless the person has previously taken cabotegravir-containing PrEP or there is reason to believe that the person's HIV was acquired from a partner with an InSTI-resistant virus (evidence rating: BIII). If the initial $CD4^+$ cell count is less than 100 cells/μL, then testing for cryptococcal antigen is recommended (evidence rating: AIa). If there are symptoms consistent with acute infections (eg, STIs, *Mycobacterium avium* complex, tuberculosis, cryptococcus), then testing is recommended (evidence rating: AIIa). Immediate follow-up of these results is recommended to maximize safety, but the results of these diagnostic tests should not delay starting ART (evidence rating: AIII).

During ART

At 4 to 6 weeks after starting ART, HIV RNA levels should be measured, and adherence and tolerability of ART should be assessed (evidence rating: AIII) (Table 3). A genotype based on the person's regimen is advised if, after 12 to 24 weeks of therapy, HIV RNA levels have not decreased to below 200 copies/mL and adherence seems adequate (evidence rating: AIIa).

Every clinical encounter should include an evaluation for medication toxicity, general health maintenance assessments, need for vaccinations, and age- and risk-appropriate screening for cancer (evidence rating: AIa). If there are potential exposures or there is clinical concern, testing should be performed for co-infections such as STIs (at all exposed mucosal sites), tuberculosis, and viral hepatitis (evidence rating: AIII). Regular screening and treatment for anal and cervical cancer should follow established guidelines (evidence rating: AIa).[11,50,51] Monitoring of urine glucose and protein levels should be performed in individuals starting tenofovir disoproxil fumarate and at least once a year after that (evidence rating: BIII). If the person remains clinically stable, virally suppressed, and adherent to ART, then HIV RNA levels should be monitored every 3 months until suppressed for at least 1 year (evidence rating: AIa). Following viral suppression with ART, $CD4^+$ cell counts should be assessed every 6 months until they are consistently above 250 cells/μL for a minimum of a year; after that, no further $CD4^+$ assessments are warranted unless virologic failure is identified or if the person experiences

an immunosuppressive condition (evidence rating: BIII). If the person remains clinically stable, virologically suppressed, and adherent for greater than a year, then safety laboratory and HIV RNA monitoring can be reduced to every 6 months (evidence rating: AIa); if greater than 5 years and the person prefers less monitoring, viral and ART safety laboratory monitoring can be reduced to once per year (evidence rating: BIII), although other health maintenance visits should occur as needed. Viral load and CD4$^+$ cell count testing should occur any time a person is clinically unstable, not virally suppressed, or nonadherent to ART (evidence rating: AIIa).

For people who are virologically suppressed and do not have a documented pre-ART reverse transcriptase-protease genotype or who have an incomplete treatment history and wish to start long-acting cabotegravir plus long-acting rilpivirine, proviral RT-protease genotype is an option but of unclear benefit since proviral genotyping has not been validated. If rilpivirine-associated mutations are present on genotypic testing, long-acting cabotegravir plus long-acting rilpivirine should be avoided (evidence rating: AIa).

At the Time of Virologic Failure and Before Starting New ART Regimen

If an HIV RNA level above 50 copies/mL is detected during ART following previous suppression (<50 copies/mL), a repeat measurement of HIV RNA level is recommended in 2 to 4 weeks, and adherence to medication and tolerability should be assessed (evidence rating: AIa). If HIV RNA level is above 200 copies/mL on 2 consecutive measurements, then an HIV RNA reverse transcriptase–protease genotype should be obtained, and if the person is receiving an InSTI, an InSTI genotype assay should be ordered (evidence rating: AIII). Some commercial HIV genotype assays require an HIV RNA level above 500 to 1000 copies/mL to be performed. (See the Definition and Management of Virologic Failure section above for discussion on management of intermittent or persistent low-level viremia between 50 and 200 copies/mL.) Before starting maraviroc, testing for viral tropism should be performed, and maraviroc should not be used if at any time X4 or dual-tropic virus is detected (evidence rating: AIa). If abacavir use is being considered, testing for HLA-B*5701 should be done first and, if present, abacavir avoided (evidence rating: AIa).[2]

Box 4. Recommendations for Weight Gain and Cardiometabolic Comorbidities

- Documentation of weight and body mass index at baseline and every 6 months is recommended for individuals initiating or switching to an InSTI- or tenofovir alafenamide–based regimen to identify those with excessive weight gain (evidence rating: AIIa).
- Monitoring blood pressure at each clinical visit is recommended to diagnose and treat incident hypertension (evidence rating: AIII).
- Changing regimens because of weight gain (evidence rating: BIa), hypertension (evidence rating: BIII), or insulin resistance (evidence rating: BIII) is not recommended.
- People with or at high risk for cardiovascular disease who are receiving an abacavir-containing regimen should switch to a non–abacavir-containing regimen if an active regimen is available (evidence rating: AIIb).
- Counseling about potential cardiometabolic complications and the importance of lifestyle changes (exercise and diet) is recommended for all persons beginning ART, especially those at increased likelihood of weight gain with use of InSTI- and tenofovir alafenamide–based regimens (evidence rating: AIII) and for those at increased risk for cardiovascular disease due to hypertension, insulin resistance/diabetes, smoking, or other factors (evidence rating: AIII).
- Persons with HIV and 10-year ASCVD risk above 20% or low-density lipoprotein cholesterol level of 190 mg/dL (4.92 mmol/L) or higher should receive a high-intensity statin; those with diabetes should receive at least a moderate-intensity statin (evidence rating: AIa).
- Persons with HIV aged 40 to 75 years with low to intermediate (5% to <20%) 10-year ASCVD risk should receive at least a moderate-intensity statin (pitavastatin [4 mg] [evidence rating: AIa], atorvastatin [20 mg] [evidence rating: AIIa], or rosuvastatin [10 mg] [evidence rating: AIIa]).
- Among those with 10-year ASCVD risk below 5%, a moderate-intensity statin also is recommended (evidence rating: CIa) and, in this group, considerations supporting starting a statin include the presence of traditional factors that increase ASCVD risk as well as HIV risk–enhancing factors (history of delayed ART initiation, current/nadir CD4$^+$ count <350 cells/μL, HIV treatment failure, metabolic syndrome, lipodystrophy, fatty liver disease, and hepatitis C co-infection).

ART indicates antiretroviral therapy; ASCVD, atherosclerotic cardiovascular disease; InSTI, integrase strand transfer inhibitor.

Weight Gain and Cardiometabolic Comorbidities

Recommendations for weight gain and cardiometabolic comorbidities are summarized in **Box 4**.

There is large variability in weight change associated with antiretroviral drugs, with the majority of people receiving ART having weight change of less than 5% of body weight and a minority gaining more than 10% of their body weight.[52] Weight gain can occur following ART initiation or after switching regimens. Some studies show greater weight gain with regimens containing InSTIs than those containing boosted protease inhibitors or NNRTIs.[2,53] Greater weight gain with regimens containing tenofovir alafenamide than with those containing tenofovir disoproxil fumarate also has been observed.[2] Of note, tenofovir disoproxil fumarate and efavirenz are associated with less weight gain as initial therapy and with weight loss when switching to these drugs, complicating comparisons using these agents. Weight gain with use of ART is more likely to occur in women and Black persons and mostly occurs within the first year following initiation or switch.[2] Weight gain in some patients is not solely a "return to health" phenomenon. Mechanisms, predictors, and determinants of weight gain are being investigated.[54]

The reversibility of weight gain with use of antiretroviral drugs also is being studied, with a return to pretherapy weight being rarely observed. In the DEFINE study,[55] switching to DRV/COBI/TAF/FTC following weight gain with use of InSTI-based ART resulted in no significant change in weight. Mean changes in weight and fat also were similar after switching to the investigational combination doravirine/islatravir,[56] compared with continuing BIC/FTC/TAF. Conversely, women (but not men) in the ADVANCE trial who were randomly assigned to initial TAF/FTC plus dolutegravir and who later switched to TDF/3TC/DTG had reductions in weight,[57] likely due to the weight suppressive effect of tenofovir disoproxil fumarate. Likewise, weight loss was seen in the Swiss HIV Cohort Study when people switched from tenofovir alafenamide to tenofovir disoproxil fumarate.[58]

Documentation of weight and body mass index every 6 months is recommended for individuals initiating or switching to an InSTI- or tenofovir alafenamide–based regimen to identify those with excessive weight gain (evidence rating: AIIa). Currently, because of the known toxicities of tenofovir disoproxil fumarate and lack of benefit seen when changing from an InSTI to a boosted protease inhibitor, changing regimens because of weight gain is not recommended (evidence rating: BIa). Lifestyle changes should be emphasized, including diet and exercise, especially for those at increased likelihood of weight gain with use of InSTI- and tenofovir alafenamide–based regimens (evidence rating: AIII). The efficacy of glucagon-like peptide-1 receptor agonists for weight loss among people with HIV is similar to that seen in the general population. Loss of muscle mass, a particular concern in older people at risk for sarcopenia, may occur with glucagon-like peptide-1 receptor agonist therapy.[59-62] In persons with HIV and lipohypertrophy, a randomized clinical trial found that once-weekly semaglutide is associated with decreased abdominal visceral and subcutaneous adipose tissue, and overall body fat, compared with placebo.[63]

Cardiovascular Disease and Antiretroviral Therapy

Although reductions over time in age-standardized atherosclerotic cardiovascular disease (ASCVD)–related mortality have been reported from 2 large cohorts,[23,64] a 1.5- to 2-fold excess risk of ASCVD persists in people with HIV, compared with the general population, likely associated with chronic immune activation and inflammation. Rates of traditional ASCVD risk factors remain high in people with HIV, including smoking, hypertension, dyslipidemia, insulin resistance and diabetes, body composition changes, and SUDs.[65] ASCVD risk calculators have consistently been shown to underestimate ASCVD risk in people with HIV, particularly for women and Black/African American individuals.[66]

Some individual antiretroviral drugs and classes have been associated with cardiometabolic adverse effects leading to an increased risk of ASCVD. Of the antiretroviral drugs currently in use, boosted darunavir and recent or current abacavir use have been associated with increased cardiovascular events.[2,67,68] People with or at high risk for cardiovascular disease who are receiving an abacavir-containing regimen should switch to a non–abacavir-containing regimen if an active regimen is available (evidence rating: AIIb). Data suggesting an association between cardiovascular disease and InSTIs are conflicting.[69,70] No association with ASCVD events was found in people without prior treatment who initiated an InSTI-based regimen compared with other regimens in 2 different simulated clinical trial analyses,[69,71] although an observational cohort found that initiation of InSTI-based regimens was associated with increased ASCVD events in the first 2 years of InSTI-based therapy.[70]

Prevention of Cardiovascular Disease

Data from the REPRIEVE trial have changed the approach to primary prevention of ASCVD for people with HIV. REPRIEVE, a placebo-controlled trial of pitavastatin (4 mg daily) in people with HIV, aged 40 to 75 years, receiving ART, and with low to intermediate (median, 4.5%) 10-year ASCVD event risk,[72] demonstrated a 36% reduction in major adverse cardiovascular events for the pitavastatin group (hazard ratio, 0.64 [95% CI, 0.48-0.84]).[73,74] Although benefit also was seen for persons with lower risk estimates, the number who need to be treated to prevent 1 major adverse cardiovascular event was lower (53 or below) for those with a 10-year risk score of at least 5%, compared with 149 or higher for those with risk scores of 5% or below. Based on existing recommendations for the general population, persons with a risk estimate of 20% or higher, or a low-density lipoprotein cholesterol level of 190 mg/dL (4.92 mmol/L) or higher, should receive a high-intensity statin, and those with diabetes should receive at least a moderate-intensity statin (evidence rating: AIa). Based on results from the REPRIEVE trial, a statin of at least moderate intensity is recommended for persons with HIV aged 40 to 75 years with ASCVD risk estimates of 5% or higher (evidence rating: AIa). Among those with risk estimates below 5%, a moderate-intensity statin also is recommended (evidence rating: CIa) and, in this group, considerations supporting starting a statin include the presence of traditional factors that increase ASCVD risk as well as HIV risk–enhancing factors (history of delayed ART initiation, current or nadir $CD4^+$ cell count <350/μL, HIV treatment failure, metabolic syndrome, lipodystrophy, fatty liver disease, and hepatitis C virus [HCV] co-infection). People with HIV younger than 40 years were not included in the REPRIEVE trial. General population guidelines should be followed when considering statin initiation in people with HIV younger than 40 years. In this population, HIV risk–enhancing factors or long-standing HIV infection due to perinatal acquisition may increase risk for ASCVD; however, there currently are limited data to inform decision-making for individualized statin therapy in this group. In REPRIEVE, adverse events that were more frequent in the pitavastatin group than in the placebo group included incident diabetes (5.3% vs 4.0%, respectively) and muscle-related symptoms (2.3% vs 1.4%, respectively). Counseling on modifiable lifestyle changes is essential, regardless of whether a statin is used.

Moderate-intensity doses of atorvastatin (20 mg) (evidence rating: AIIa) or rosuvastatin (10 mg) (evidence rating: AIIa) may be substituted for pitavastatin. When prescribing statins, especially to people taking an HIV protease inhibitors or cobicistat, attention must be paid to drug-drug interactions associated with cytochrome P-450 metabolism and drug transporter interactions (although less frequent with pitavastatin).[56,75]

Increased prevalence of hypertension has been reported with InSTI use in some analyses.[76] However, data supporting an association between dolutegravir and hypertension are inconclusive, and data on bictegravir are lacking. In several cohorts and a post hoc analysis of the ADVANCE and NAMSAL trials, dolutegravir-based regimens were associated with higher rates of hypertension than NNRTI- or protease inhibitor–based regimens.[25,77,78] However, dolutegravir-based regimens were associated with greater weight gain, which might contribute to a higher incidence of hypertension. In a subset analysis from the REPRIEVE trial, hypertension was more common among persons receiving dolutegravir than those receiving non-InSTI regimens.[79] In contrast, no significant difference in incident hypertension was seen in the NEAT022 study, in which people 50 years or older with viral suppression and a Framingham Risk Score above 10% were randomly assigned to continue their protease inhibitor–based regimen or to switch to a dolutegravir-based regimen.[80] Likewise, an analysis from the African Cohort Study of 2935 participants with and without HIV showed no association between dolutegravir and incident hypertension among those receiving dolutegravir compared with participants without HIV.[81] In a US retrospective study of more than 5500 PrEP initiators,[82] incidence

Box 5. Recommendations for Persons at Risk for and With HIV Who Use Substances and Who Have Substance Use Disorders

- Provide screening, diagnosis and treatment for SUDs to all persons at risk for and with HIV (evidence rating: AIa).
- SUD treatment should be integrated into HIV prevention and treatment services (evidence rating: AIa).
- Rapid HIV testing and linkage to rapid ART or preexposure prophylaxis provision, when indicated, are recommended for persons who use substances and who have SUDs (evidence rating: AIa).
- Harm reduction services, including naloxone, safe injection education, fentanyl and xylazine drug test strips, and referral to syringe service programs and safe injection sites should be offered to all persons who report drug use (evidence rating: AIa).
- Persons who use drugs should be offered either oral TDF/FTC for injection drug use risk or oral (TDF/FTC or TAF/FTC) or injectable PrEP (long-acting cabotegravir) to reduce sexual risk of HIV acquisition (evidence rating: AIa).
- Persons with SUDs and HIV infection or at risk for HIV should receive integrated SUD treatment with
  - pharmacotherapy for opioid, alcohol, and tobacco use disorders (evidence rating: AIa)
  - contingency management for stimulant use disorders and in certain situations medication treatment (evidence rating: AIa)
- Persons with opioid use and alcohol use disorders should be offered timely initiation of medications for SUD, regardless of HIV and HCV treatment plans (evidence rating: AIa).
- Peer/patient support staff, telehealth, extended hours, mobile clinics, mobile pharmacies, pharmacy delivery services and walk-in clinic options should be available to persons who use substances and/or have SUDs who are receiving HIV treatment or prevention (evidence rating: AIIb).

ART indicates antiretroviral therapy; FTC, emtricitabine; HCV, hepatitis C virus; PrEP, preexposure prophylaxis; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; SUD, substance use disorder.

of hypertension was low and similar between the tenofovir alafenamide and tenofovir disoproxil fumarate groups. Monitoring blood pressure at each clinical visit is recommended to diagnose and treat incident hypertension (evidence rating: AIII).

In persons who initiate ART in the US, the overall incidence of diabetes in 1 large cohort was almost twice that of the general population.[83] InSTI-based regimens are associated with new-onset diabetes and hyperglycemia in some cohort studies; however, the data are inconclusive.[84] As with weight gain, changing regimens due to hypertension or insulin resistance is not recommended (evidence rating: BIII); instead, lifestyle modifications, exercise, and diet intervention are recommended (evidence rating: AIII).

Substance Use in Persons at Risk for and With HIV

Recommendations for persons at risk for and with HIV who use substances and who have SUDs are summarized in **Box 5**. Substance use (eg, opioids, stimulants, alcohol) and SUD can interfere with HIV prevention and HIV care. Persons who use such substances have increased risk of acquiring HIV through sharing injection drug use (IDU) equipment and condomless sexual intercourse. Substance use may also adversely affect HIV outcomes by interfering with ART adherence and HIV RNA suppression.[2]

People with HIV are more likely to have SUDs than the general population. Despite the high prevalence, only a small number of people with HIV are referred for and receive treatment for SUD or harm reduction. Integration of SUD screening, diagnosis, and treatment into HIV prevention and treatment services is recommended (evidence rating: AIa) (eTables 5 and 6 in the Supplement).[2] Reducing substance use (even if abstinence is not achieved) is associated with improved HIV outcomes. Therefore, addiction treatment, including pharmacotherapy, behavioral-based therapies, and harm reduction are recommended for all persons (evidence rating: AIa).

All US Food and Drug Administration (FDA)–approved medications for opioid use disorder (buprenorphine, methadone, and extended-release naltrexone) reduce nonmedical opioid use and risk of HIV and HCV acquisition (eTable 7 in the Supplement).[85,86] Similarly, FDA-approved medications for alcohol use disorder (eg, extended-release naltrexone, oral naltrexone) reduce alcohol use and risk of HIV acquisition (eTable 8 in the Supplement). Medication treatment of opioid use disorder and alcohol use disorder improves ART adherence and viral suppression and is recommended with ART (eFigures 1 and 2 in the Supplement) (evidence rating: AIa).[2]

Medications for SUDs have few clinically significant drug-drug interactions with ART and HCV direct-acting antivirals[2]; therefore, medication treatments for SUDs should not be withheld for those receiving ART or direct-acting antivirals (evidence rating: AIa). Clinical guidelines recommend pharmacotherapies for stimulant use disorders in certain situations, although there are no FDA-approved medications to treat stimulant use disorders (eg, cocaine use disorder, amphetamine-type use disorder). Currently the most efficacious form of treatment for stimulant use disorders is contingency management, a behavioral form of incentivized treatment, such as financial incentives (cash or gift cards) for periods of recovery from stimulants or other nonmedical substances. Contingency management is recommended for stimulant use disorders (evidence rating: AIa).[87] Tobacco use is common among people with HIV and contributes to an excess risk of cardiovascular disease; therefore, strategies to promote tobacco cessation are recommended, including pharmacotherapies (evidence rating: AIa).[88]

Harm reduction services, including naloxone dispensation, safe use education, fentanyl and xylazine drug test strips, and referral to syringe services and safe injection sites, should be offered to all who report drug use (evidence rating: AIa).[89,90]

Interventions that reduce substance use, including medications for opioid use disorder and alcohol use disorder, may improve HIV prevention. TAF/FTC and injectable long-acting cabotegravir PrEP have not yet been fully evaluated for IDU-related HIV prevention among persons who inject drugs (PWID), but TDF/FTC is approved for IDU-related HIV prevention. However, for PWID who are at sexual risk of HIV acquisition, oral or injectable PrEP to reduce sexual risk is recommended (evidence rating: AIa).[91]

Substance use and SUDs can create an additional hurdle for retention in HIV prevention and treatment services. Screening for barriers to retention in care, including lack of transportation, insurance, and housing—as well as criminal legal barriers, poverty, mental illness, and stigma—should all be addressed. Innovative service delivery options, including extended hours, mobile clinics and pharmacies, walk-in clinics, telehealth, pharmacy delivery options, and

Box 6. Recommendations for HIV and Sexually Transmitted Infection Prevention[a]

Generally Recommended HIV Prevention Approach
- Adopt a serostatus-neutral approach to reduce HIV stigma, ensuring rapid care linkage for individuals diagnosed and PrEP navigation for those who test negative (evidence rating: AIIa).
- Offer PrEP to all sexually active individuals, anyone requesting it, and those using nonprescription drugs or substances, without specific risk criteria or screening tools (evidence rating: AIII).
- Offer PrEP to all sexual partners of individuals with HIV and to those who share injection drug works with individuals with HIV or of unknown HIV status (evidence rating: AIa). For monogamous sexual partners of persons with HIV who are known to be receiving ART and have viral loads below 200 copies/mL, it is a reasonable and appropriate decision to defer PrEP; if such a patient requests PrEP; however, it is also reasonable to provide it because of the possibility that there are undisclosed exposures occurring.
- Condoms are recommended for all penetrative sexual acts (evidence rating: AIII).

Rapid PrEP Start
- If HIV test results from within the past 7 days are negative, initiate PrEP while awaiting further diagnostics and safety assessments (evidence rating: AIIa).
- If no recent HIV test result is available, conduct testing and initiate PrEP once results are negative, assuming good remote communication (evidence rating: BIII).
- For substantial HIV exposure within 72 hours, initiation of a 3-drug PEP regimen is recommended (evidence rating: AIIa).
  - Transition to PrEP after PEP completion if HIV test results are negative is recommended (evidence rating: AIIa).

Laboratory Testing
- At initiation or after a long hiatus, HIV screening should include an HIV RNA test and a laboratory-based antigen-antibody test (evidence rating: AIIa).
  - If RNA testing is unavailable, initiation of PrEP after a rapid HIV antibody test and while awaiting a laboratory-based antigen/antibody test result is recommended (evidence rating: BIII).
- For long-acting cabotegravir PrEP follow-up, a rapid HIV antibody test and laboratory-based antigen/antibody test, not routine RNA testing, is recommended (evidence rating: AIIb).
- If RNA testing is not available, repeat antigen/antibody testing 1 month after starting or resuming tenofovir-based oral PrEP (evidence rating: AIII).

Bacterial STI Prevention[b]
- DoxyPEP (doxycycline [200 mg]) is recommended within 72 hours after condomless sex for cisgender men who have sex with men and transgender women, regardless of HIV status (evidence rating: AIa).
  - Dosing is recommended no more frequently than daily (evidence rating: BIa).
- Pharmacokinetic modeling suggests that doxyPEP is effective for vaginal exposures and is recommended on a case-by-case basis for cisgender women at risk (evidence rating: BIII).
- Prescribe 30 doses (60 tablets or capsules) of doxyPEP at a time (evidence rating: BIII).
- Quarterly STI screening of contact sites and blood syphilis testing is recommended (evidence rating: AIa).

ART indicates antiretroviral therapy; PEP, postexposure prophylaxis; PrEP, preexposure prophylaxis; STI, sexually transmitted infection.

[a] See text for recommended PrEP regimens.

[b] See text for details.

staff who are patient navigators, peers, near-peers, or community health workers are recommended (evidence rating: AIIb).[92,93] Rapid HIV testing and linkage to rapid ART or PrEP provision, when indicated, are recommended for persons who use substances and who have SUDs (evidence rating: AIa).[2]

Prevention of HIV Infection

Recommendations for PrEP with currently available agents are outlined in **Box 6**.

Biomedical tools to prevent HIV acquisition are highly effective. To reduce stigma associated with HIV testing, treatment, and prevention efforts, a serostatus-neutral approach is recommended (evidence rating: AIIa). This approach ensures that people diagnosed with HIV are rapidly linked to care and those who test negative are informed about and navigated to receive PrEP services if desired or indicated. Rapid viral suppression for persons with HIV has substantial health benefits for the individual and eliminates sexual transmission of HIV (undetectable = untransmittible, or U = U). Condoms are a cornerstone of prevention for all penetrative sex acts to reduce the acquisition of STIs, including HIV, and are recommended (evidence rating: AIII). Other effective HIV prevention strategies for applicable populations include medical circumcision for heterosexual males in high-prevalence settings, medications for opioid use disorder, and syringe service programs.

PrEP should be discussed and offered to all sexually active persons, all persons requesting PrEP, and anyone who injects nonprescription drugs, uses substances (alcohol, stimulants, opioids), or who has an SUD, without need to limit access to specific criteria for sexual or drug use behavior, or required use of screening tools (evidence rating: AIII).[94] Populations with disproportionately high HIV incidence rates should be particularly encouraged to consider PrEP as part of their HIV prevention plans. These populations include cisgender men, transgender persons, and nonbinary persons who have sex with cisgender men; young adults and adolescents (up to age 24 years); people whose sexual partners are from regions with high HIV incidence; individuals who report transactional sex; persons who use or inject drugs; incarcerated persons and their partners; and anyone with an STI acquired in the past year (evidence rating: AIIa).

Recommended PrEP Regimen

Current PrEP agent options for a given individual based on population and risk behavior are provided in Box 6 and **Table 4**.

The optimal PrEP regimen for a given person is the one that is most acceptable and congruent with their routes of potential HIV exposure; preference for modality of administration, including ability to take oral tablets reliably; ability to plan sexual or IDU activity; and adverse effect profile of the regimen. The initially chosen PrEP regimen, and whether ongoing PrEP is needed or of interest, should be reevaluated based on ongoing assessments of the same issues.

Table 4. Recommendations for Currently Approved Biomedical HIV Prevention by Type of Exposure[a]

Type of exposure	Daily TDF/FTC	On-demand ("2-1-1") TDF/FTC	Daily TAF/FTC	Every-other-month intramuscular long-acting cabotegravir[b]
Insertive anal/vaginal sex	✓	✓	✓	✓
Receptive anal sex	✓	✓	✓	✓
Receptive vaginal sex	✓			✓
Receptive neovaginal sex	✓			✓
Injection drug use[c]	✓			
Recommended for pregnant and breastfeeding women	✓			✓
Initiate with a double dose	✓	✓		
Recommended for individuals with reduced creatinine clearance (30-60 mL/min) or who have osteopenia or osteoporosis			✓	✓

Abbreviations: FTC, emtricitabine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

[a] Adapted from Gandhi et al.[2]

[b] Additional recommendations for long-acting cabotegravir: An optional 4- to 5-week oral lead-in is available before starting injections and is recommended for individuals with severe atopic histories or on request. The oral lead-in is not recommended for those who have difficulty adhering to daily oral dosing. Overlapping the first injection with 7 days of oral preexposure prophylaxis (PrEP) is recommended for maximal protection. Oral cabotegravir tablets are recommended for the overlap if an oral cabotegravir lead-in is used to initiate long-acting cabotegravir; otherwise tenofovir-containing oral PrEP can be used for the overlap. Providing a 1-month supply of tenofovir-based oral PrEP is recommended for injection delays exceeding 7 days. Administer gluteal injections at 600 mg, with the first 2 injections spaced 4 weeks apart and subsequent injections every 8 weeks. If injections are delayed by 8 weeks or more, resume with 2 injections 4 weeks apart before returning to the every-8-weeks schedule. If long-acting cabotegravir is discontinued but HIV protection is still required, transitioning to an alternative prevention method is recommended.

[c] Persons who inject drugs should also be assessed for sexual routes of exposure to HIV, and PrEP choice made considering that route of exposure as well (see text for the strength of the recommendations and quality of the data).

Oral PrEP

Daily oral TDF/FTC (including generic tenofovir disoproxil fumarate formulations) remains a recommended oral PrEP regimen for all populations likely to be exposed to HIV (evidence rating: A1a) (Box 6 and Table 4). Daily oral dosing should be initiated with a double dose of TDF/FTC followed by a single tablet thereafter. When discontinuing, daily dosing should continue until 2 doses after last sexual activity for rectal exposures. For vaginal, neovaginal, or "front-hole" exposures, a similar double dose of TDF/FTC is recommended to initiate dosing, with dosing to be continued until at least 7 days after last sexual activity (evidence rating: BIII). Recent data suggest that 4 or more doses per week on average will provide high-level protection against both rectal and vaginal HIV acquisition; for rectal exposures, 2 or more doses per week is estimated to provide 79% to 88% reduction in probability of HIV acquisition.[95,96]

TDF/FTC daily oral PrEP is also the recommended oral regimen for people who are pregnant or breast/chest feeding (evidence rating: AIIa). Long-acting cabotegravir has a growing and robust safety and pharmacokinetic profile in pregnancy and breast/chest feeding, and can be used safely in these settings (evidence rating: BIIa).[97]

On-demand (2-1-1) oral dosing of TDF/FTC is recommended for cisgender men (evidence rating: AIa) and others (evidence rating: AIII) having planned receptive anal (but not receptive vaginal or neovaginal) sex. On-demand dosing is initiated with a double dose of TDF/FTC 2 to 24 hours before sexual activity, followed by single additional doses of TDF/FTC 24 and 48 hours after the first dose. If additional sexual activity occurs after the initial sex event, daily single dosing should be continued until 2 doses after the last activity. Of note, with 2-1-1 dosing, TDF/FTC should be administered with food for transgender women using gender-affirming hormone therapy, because rectal tissue concentrations of tenofovir-diphosphate (TFV-DP) may be lower early after starting 2-1-1 regimens, which can be largely mitigated by dosing with food.[2] Insufficient data exist to support on-demand use to prevent HIV acquisition through IDU alone or through vaginal exposures.

Daily oral TAF/FTC use should be limited to cisgender men and others whose exposures do not include receptive vaginal sex (including neovaginal sex) or IDU alone (evidence rating: AIa). Daily TAF/FTC is recommended for individuals with creatinine clearance between 30 and 60 mL/min and for individuals with known osteopenia or osteoporosis (evidence rating: AIa). Bone density scans are not necessary before initiating tenofovir-based PrEP (evidence rating: AIII).

Details for prescribing oral PrEP regimens are in Table 4 of the 2022 guidelines.[2]

Rapid PrEP Start

Any delay in starting PrEP in an individual likely to be exposed to HIV may be a missed opportunity to prevent HIV acquisition. If negative HIV serologic test results are available from blood drawn within 7 days or a rapid (point-of-care) HIV antibody test result is negative on the day of PrEP initiation, PrEP initiation is recommended while awaiting additional diagnostics and safety assessments (evidence rating: AIIa); see below for details of recommended laboratory testing at PrEP initiation. Absent signs/symptoms of acute or primary HIV infection, if a rapid or laboratory-based HIV test result within the past 7 days is not available, such testing is recommended. PrEP may be initiated remotely without the need for an additional clinic visit once baseline HIV tests have been confirmed to have negative results (evidence rating: BIII). If there is a concern for substantial HIV exposure within the past 72 hours, a 3-drug postexposure prophylaxis (PEP) regimen is recommended (evidence rating: AIIa) for a duration of 28 days, with seamless transition to PrEP after PEP completion, if an

HIV test (ideally an antigen/antibody and RNA assay) result at the conclusion of PEP is negative (evidence rating: AIIa).

Injectable PrEP

Long-acting cabotegravir received regulatory approval for the prevention of sexual acquisition of HIV across populations based on 2 large randomized clinical trials and is recommended for people likely to be exposed to HIV sexually (evidence rating: AIa).[2] Data do not exist for use in injection drug exposures but PWID may also be exposed to HIV through sexual routes; therefore, the use of long-acting cabotegravir PrEP is recommended in PWID who are at risk for acquiring HIV through sexual exposures (evidence rating: AIII).

An oral cabotegravir lead-in of 4 to 5 weeks is optional prior to initiating long-acting cabotegravir injections. However, the oral lead-in is recommended for those with severe atopic histories or those who request it (evidence rating: BIII). An oral lead-in is not recommended in those challenged by adhering to daily dosing of oral tablets (evidence rating: AIa). To allow time for maximal protection from long-acting cabotegravir after first injection, an oral PrEP regimen to overlap the first injection by 7 days is recommended (evidence rating: BIII). This overlap is recommended with oral cabotegravir tablets for those transitioning to long-acting cabotegravir from an oral cabotegravir lead-in (evidence rating: BIII). For those initiating long-acting cabotegravir from no recent oral PrEP or without interruption from a tenofovir-based oral PrEP regimen, initiation or continuation of an exposure-appropriate tenofovir-based PrEP regimen is recommended for the overlap period (evidence rating: BIII). Persons receiving long-acting cabotegravir should have a 1-month supply of an appropriate tenofovir-based oral PrEP agent in hand for oral bridging in the case of injection delays of 7 days or more (evidence rating: BIII).

Injections by gluteal administration are recommended at a dose of 600 mg (3 mL), with the first 2 injections separated by 4 weeks and subsequent injections by 8 weeks (evidence rating: AIa). Because the timing of onset of protection is unknown but is likely to be approximately 7 days after first injection, barrier protection or a tenofovir-based oral regimen as noted above is recommended in the first week of the first injection cycle. There are insufficient data to recommend use of any alternative injection site; anterior thigh injections did not reach pharmacokinetic targets with repeated 2-month interval injections and had poor tolerability.[98,99] If injections are to be resumed 8 or more weeks late (that is, 12 or more weeks from previous for injection 2, or 16 or more weeks from previous for injections 3 and beyond), "reloading" is recommended, with a 4-week interval between the 2 injections after the hiatus before returning to every-8-week dosing (evidence rating: AIa). This guidance for the interval of delay requiring reloading is distinct from the current FDA package insert.[100,101]

For individuals who are stopping injectable PrEP but continue to need protection against HIV acquisition, transition is recommended to another form of HIV prevention (evidence rating: AIII), including (but not limited to) a tenofovir-based oral PrEP regimen appropriate for the individual and their exposures. That regimen, or best available nonpharmacologic HIV prevention strategies, should be continued as long as the exposures continue.

Dose adjustment of rifabutin is recommended if it is coadministered with long-acting cabotegravir, and long-acting cabotegravir should not be used with potent inducers of UGT1A1 (evidence rating: AIIa for both) (Table 4 in the 2022 guidelines).[2] Also, long-acting cabotegravir should be used with caution in individuals with gluteal implants or fillers.

The PURPOSE-1 study, in which lenacapavir was administered as an every-6-month subcutaneous injection, found no detected HIV infections among cisgender women in Southern and Eastern Africa, in a population in which the background HIV incidence was approximately 2.41 per 100 person-years. The similarly designed PURPOSE-2 trial in cisgender men, transgender people, and nonbinary individuals had only 2 incident HIV infections (HIV incidence 0.10/100 person-years) in a population with an estimated HIV incidence of 2.37 per 100 person-years (96% reduction in HIV incidence).[102,103] After approval by regulatory authorities and when available, lenacapavir is recommended for prevention of HIV infection for all routes of sexual exposure (evidence rating: AIa). The first subcutaneous injection should be overlapped with 2 daily oral doses of lenacapavir (600 mg) (evidence rating: AIa). There are ongoing trials of lenacapavir for PrEP in other populations.

Both injectable cabotegravir and injectable lenacapavir have been associated with injection site reactions, which often diminish in severity over time.

Laboratory Testing

Frequency and type of safety laboratory testing by PrEP regimen is provided in Table 4 in the 2022 guidelines,[2] with one important update. HIV screening should include a fourth- or fifth-generation laboratory-based antigen-antibody assay for all tenofovir-based PrEP regimens. HIV screening at initiation (or resumption after a hiatus of 6 months or longer with long-acting cabotegravir or of more than 14 days with tenofovir-based oral PrEP) should ideally include an HIV RNA (viral load) test with a lower limit of quantification of 50 copies/mL or lower and a laboratory-based antigen-antibody test (evidence rating: AIIa). For oral and injectable PrEP, if HIV RNA testing is not available or not feasible, PrEP is still recommended after a rapid point-of-care HIV antibody test and while awaiting a laboratory-based antigen/antibody test (evidence rating: BIII).[104] With a negative rapid antibody test result, dosing of tenofovir-based oral PrEP or long-acting cabotegravir may begin while awaiting laboratory test results. Follow-up testing for cabotegravir PrEP breakthrough infections should not routinely include HIV RNA testing but should include a point-of-care rapid HIV antibody test and a laboratory-based antigen/antibody test. RNA testing as part of routine monitoring for PrEP failure is not recommended because such testing has a low positive predictive value and false-positive results have significant negative sequelae (evidence rating: AIIb).[105] With the use of tenofovir-based oral PrEP, if an HIV RNA test is not available at PrEP initiation or resumption after a hiatus, as noted above, available antigen/antibody testing should be repeated at a visit 1 month after starting or restarting the oral PrEP regimen (evidence rating: AIII).

Diagnosis of HIV in the setting of PrEP failure can be challenging, particularly when using long-acting PrEP agents, due to delayed and inconsistent detection of viremia, antigen, and antibodies, termed *LEVI* (long-acting early viral inhibition).[100] Discordant or difficult-to-interpret HIV test results should be discussed with experts, including at the PrEP Warmline at the US National Clinician Consultation Center at 1-(855)-HIVPrEP in the US.[106] In the setting of long-acting cabotegravir PrEP, 2 sequential testing algorithm

results in which HIV RNA is detected, at any level (even if below the limit of quantification of the assay), is highly predictive of true HIV infection.[105]

Adherence and Persistence/Retention

Individuals with high likelihood of HIV exposure are also among the most challenged by adhering to and persisting with PrEP medication and services, with high rates of loss to follow-up after 12 to 18 months in key populations. Various structural barriers contribute to these findings, which appear to also be applicable to long-acting cabotegravir PrEP.[107,108] PrEP adherence and persistence/retention should be supported through techniques such as PrEP navigators where available; video telehealth; smartphone-based reminders for pill-taking or injections; use of mobile health units or mobile retail pharmacies[93,109]; peer support/administration; community health worker/visiting nurse/ pharmacy administration services to deliver PrEP; and more conventional strategies such as pill boxes and adherence check-ins by telephone or short message service.

ART Choice for PrEP Breakthrough Infections

See the Antiretroviral Therapy for Individuals With HIV section above.

Postexposure Prophylaxis

Recommendations for PEP remain the same as in the 2022 IAS-USA guidelines.[2] All individuals completing PEP for nonoccupational exposure indications should be assessed for ongoing HIV exposure. If potential for HIV exposure persists, the individual should be transitioned without interruption to PrEP.

Prevention of Bacterial STIs

Doxycycline (200 mg) taken after condomless anal or oral sex (doxyPEP) is recommended for gay, bisexual, and other men who have sex with men (MSM) and transgender women with a diagnosis of gonorrhea, chlamydia, or syphilis within the past 12 months, given data that it reduces the incidence of bacterial STIs in these populations regardless of HIV status (evidence rating: AIa). DoxyPEP is also recommended, using a shared decision-making approach, for MSM and transgender women who have not had a bacterial STI during the previous year but have a high likelihood of condomless exposure to STIs (evidence rating: AIII). Initiating oral doxyPEP is recommended as quickly as possible (but certainly within 72 hours) after condomless sexual exposure for cisgender MSM and transgender women (evidence rating: AIa).[110,111] This intervention reduces the incidence of chlamydia by 70% to 88% and early syphilis by 73% to 87%. Effects on gonorrhea are less and inconsistent, presumably due to high rates of tetracycline resistance. Dosing may be taken as frequently as daily (evidence rating: BIa). One study of doxyPEP for cisgender women in Kenya did not show a protective effect, but drug levels suggested low adherence. Pharmacokinetic modeling suggests that doxyPEP should be effective for vaginal exposures and should be considered on a case-by-case basis with individuals with likelihood of STI acquisition via vaginal exposure (evidence rating: BIII).[112]

DoxyPEP prescriptions are recommended in quantities of 30 doses (60 tablets/capsules) at a time (evidence rating: CIII). Screening of sites/orifices with sexual contact as well as blood testing for syphilis is recommended quarterly (evidence rating: AIa). It should be noted that there is concern that breakthrough syphilis infections in the setting of doxyPEP may have aberrant or attenuated rapid plasma reagin characteristics, although limited data are currently available on this topic. Complex cases should be discussed with local public health or STI experts. In the US, practitioners may contact the STI consultation service at the Centers for Disease Control and Prevention (CDC) by calling +1-800-232-4636 or via electronic submission at http://www.STDCCN.org/. The long-term effects on gonococcal (and other) bacterial resistance to tetracyclines remains an unresolved issue and should be monitored.

Although observational data suggest that the meningitis B vaccine may be associated with reduced incidence of gonorrheal infections, a randomized clinical trial did not show a statistically significant effect on gonorrhea incidence among cisgender MSM in France.[111] Additional trials are ongoing across populations, but there are insufficient data to recommend use of the meningitis B vaccine for gonorrhea prevention at this time.

Promoting Equity in HIV Treatment and Prevention

Despite a 39% reduction in new HIV diagnoses globally, new HIV infections are still on the rise in eastern Europe, Central Asia, Latin America, the Middle East, and North Africa.[113] In the US, HIV disproportionately affects Black and Hispanic people, those who live in the Southern US, cisgender gay and bisexual men and transgender individuals, and people who use drugs.[114] In a CDC analysis that included only sex assigned at birth and not gender identity,[115] from 2017 to 2021, there was a significant increase in Black-White relative disparities and for males aged 13 to 24 years and males living in the Western US. This increase over time was predominantly driven by transmission via male-to-male sexual contact (6%), injection drug use (175% in those assigned male at birth, 68% in those assigned female at birth), and those reporting male-to-male sexual contact and IDU (12%).[115] Populations born outside the US have a higher prevalence of HIV than the population born in the US and may present with advanced disease; therefore, testing for HIV and linkage to care are essential.[116] In the European Union and European Economic Area, 44% of new diagnoses in 2019 were among individuals born outside of Europe.[117,118]

Inadequate global rollout of PrEP and disparities in PrEP utilization limit its effect on reducing HIV acquisition.[119] Moreover, the lack of availability of long-acting cabotegravir for PrEP, its cost, and the implementation complexity will likely widen disparities. In middle-income countries, which are usually out of the Medicine Patent Pool, an estimated 2.4 million people who might benefit from long-acting cabotegravir will not have access to it.[119] With the advent of effective injectables for PrEP (eg, long-acting cabotegravir currently; lenacapavir in the future), a global commitment to universal access is crucial for equitable implementation and scale-up.

Criminalization laws, such as those in Uganda against LGBTQ+ individuals,[120] policies that criminalize harm reduction and drug use, and those that limit female reproductive health[121] and transgender hormone-affirming care in the US, are examples of hostile public policies that worsen inequities and disparities while restricting access to care and prevention.[122]

Ending the HIV epidemic for all will require resources as well as policies to address societal disparities, measures to reduce stigma as a root cause of HIV risk, and elimination of laws that target people with and at risk for HIV.[123]

Future Directions in ART and Prevention

Antiretroviral Therapy

New long-acting ART regimens are on the horizon. As of October 2024, only 1 long-acting injectable ART regimen (long-acting cabotegravir plus long-acting rilpivirine) is available either once monthly or every other month. Other strategies are in clinical development, including a once-weekly combination of islatravir and lenacapavir. The initial investigation of this combination was stopped when higher doses of islatravir were associated with lymphopenia.[124] In a follow-up phase 2b investigation at a lower (2 mg) weekly dose of islatravir, the combination maintained a high rate of viral suppression at 48 weeks that was similar to that of BIC/TAF/FTC, with no effect on lymphocyte count.[125] Several exploratory studies of long-acting broadly neutralizing antibodies (bNAbs) to maintain HIV RNA suppression in people with HIV switching off oral therapy have been presented, including 2 bNAbs with lenacapavir[126,127] and a single bNAb with cabotegravir.[128] The combination of the 2 bNAbs with lenacapavir is an every-6-months regimen and is now being tested in a phase 2b trial in which people with suppressed virus with use of oral ART are randomly assigned to switch to the every-6-months regimen or remain using their oral regimen (NCT05729568).

Simplifying ART has been a consistent goal over the last decade. A single daily pill of LEN/BIC is being studied in a phase 3 trial in persons with multidrug-resistant virus without known integrase resistance who are taking multiple drug/multiple pill regimens. The phase 2b study of the 2 agents given separately effectively maintained suppression at a high rate that was comparable to continued oral multiple agent therapy.[129]

Preexposure Prophylaxis

MK-8527, a nucleoside reverse transcriptase translocation inhibitor, is in phase 2 clinical trials as a monthly oral tablet. Lenacapavir is also being studied for HIV prevention in cisgender women and PWID in the US (NCT06101329, NCT06101342), but it is unclear if the data from PWID will be sufficient or available at the time of initial regulatory approvals. Combinations of intravenous and subcutaneously administered long-acting broadly neutralizing antibodies (passive immunization) are in development for HIV prevention. Vaginal rings containing tenofovir or dapivirine that would be expected to last for 3 months or more, with potential for also providing hormonal contraception in the same product, are in earlier stages of development; a 1-month dapivirine vaginal ring has not been approved by the FDA despite a recommendation by the World Health Organization. A novel formulation of long-acting cabotegravir to be administered intramuscularly at 4-month intervals is currently in clinical trials.

Limitations

There are several limitations to these recommendations. First, the recommendations were developed for high- and medium-income settings, in which most of the drugs and tools are available. The recommendations may not be applicable in all low-income settings. Second, the approach to HIV treatment and prevention continues to rapidly evolve, necessitating frequent updates to these guidelines. For example, the landscape of treatment and prevention is likely to change as additional long-acting injectable options become available.

Conclusions

HIV therapy continues to improve, with well-tolerated and highly effective oral regimens as well as long-acting injectable treatment for people who prefer to not take, or who have difficulty adhering to, daily therapy. In addition, there are new approaches to maintaining health in people with HIV, including expanded indications for statins to reduce cardiovascular events and a new biomedical strategy, doxyPEP, to decrease STIs. HIV prevention through daily oral PrEP or long-acting injectables are crucial tools for ending the HIV epidemic in the US and around the world. However, although the tools are available, efforts must be redoubled to reduce disparities and address inequities to realize the promise of ending the HIV epidemic.

ARTICLE INFORMATION

Accepted for Publication: October 31, 2024.

Published Online: December 1, 2024. doi:10.1001/jama.2024.24543

Author Affiliations: Massachusetts General Hospital and Harvard Medical School, Boston (Gandhi); University of California, Los Angeles (Landovitz); Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts (Sax); University of California San Diego School of Medicine (Smith, Benson); Yale University School of Medicine, New Haven, Connecticut (Springer); Veterans Administration Connecticut Healthcare System, West Haven (Springer); University Hospital Zurich and Institute of Medical Virology, University of Zurich, Zurich, Switzerland (Günthard); Thacker & Thompson, Atlanta, Georgia (Thompson); University of Texas Southwestern Medical Center, Dallas (Bedimo); University of California San Francisco (Buchbinder); San Francisco Department of Public Health, San Francisco, California (Buchbinder); Departamento de Infectología, Instituto Nacional de Ciencias Médicas y Nutrición, Salvador Zubirán, Mexico City (Crabtree-Ramirez); Emory University School of Medicine and Grady Health System, Atlanta, Georgia (del Rio); University of Alabama at Birmingham (Eaton, Saag); The University of North Carolina at Chapel Hill School of Medicine (Eron); The Alfred Hospital and Monash University, Melbourne, Victoria, Australia (Hoy); University Hospital of Cologne, University of Cologne, Germany (Lehmann); German Center for Infection Research, Cologne-Bonn (Lehmann); University of Paris Cité, Saint-Louis and Lariboisière Hospitals, Assistance Publique Hopitaux de Paris, France (Molina); International Antiviral Society–USA (IAS-USA), San Francisco, California (Jacobsen).

Conflict of Interest Disclosures: Dr Landovitz reported holding a significant financial interest in ViiV Healthcare; receiving scientific advisory fees from ViiV Healthcare and Merck Inc; and serving on a data and safety monitoring board for Red Queen Therapeutics during the conduct of the study. Dr Sax reported receiving grants from Gilead and ViiV and receiving personal fees from Gilead, Janssen, and ViiV outside the submitted work. Dr Smith reported receiving personal fees from Gilead, Model Medicines, Hyundai Biosciences, Red Queen Therapeutics, and Bayer outside the submitted work. Dr Springer reported receiving grants from the National Institutes of Health (NIH) and the Veterans Administration; receiving nonfinancial support from Alkermes Pharmaceutical Inc (in-kind donation of Vivitrol for National Institute on Drug Abuse [NIDA]–funded research), Indivior Pharmaceutical Inc (in-kind donation of Sublocade for NIDA- and National Center for Advancing Translational Sciences–funded research); and receiving consulting honoraria from Alkermes Inc outside the submitted work. Dr Günthard reported receiving grants (to institution) from the Swiss National Science Foundation, Swiss HIV Cohort Study, Yvonne Jacob Foundation, NIH (co-investigator), Gilead Sciences, ViiV Healthcare (co-investigator), and Bill and Melinda Gates Foundation; and serving on data and safety monitoring boards/advisory boards for Gilead, ViiV Healthcare, Merck Sharp & Dohme,

Johnson & Johnson, GlaxoSmithKline, Novartis, and Janssen outside the submitted work. Dr Thompson reported serving as chair of an independent data monitoring committee for Excision Biotherapeutics outside the submitted work. Dr Bedimo reported receiving personal fees from ViiV Healthcare, Merck, Janssen, Theratechnologies, Gilead Sciences, and Shionogi; and receiving grants from ViiV and Merck outside the submitted work. Dr Benson reported receiving grants to her institution from the National Institute of Allergy and Infectious Diseases, Gilead, and DNAe; and receiving consulting fees from NDA Partners outside the submitted work. Dr Buchbinder reported receiving nonfinancial support from Gilead, and ViiV Healthcare and receiving grants from Merck and GlaxoSmithKline outside the submitted work. Dr Crabtree-Ramírez reported receiving grants to her institution from Merck Sharp & Dohme, ViiV, and Janssen and serving as consultant for Merck Sharpe & Dohme, ViiV, and GlaxoSmithKline. Dr del Rio reported receiving consulting fees from Roche Diagnostics outside the submitted work. Dr Eron reported receiving personal fees from Merck, ViiV Healthcare, Gilead Sciences, AbbVie, and Taimed Biologics and receiving grants from ViiV Healthcare and Gilead Sciences outside the submitted work. Dr Hoy reported receiving fees to her institution from ViiV Healthcare and Gilead Sciences outside the submitted work. Dr Lehmann reported receiving grants from Gilead; receiving advisory fees from Viiv, Pfizer, Novartis, BioNTech, Merck Sharp & Dohme, and Gilead; and receiving nonfinancial support from Gilead outside the submitted work. Dr Molina reported receiving advisory fees from Gilead, Merck, and ViiV outside the submitted work and receiving research grants (to National Agency for AIDS Research [ANRS France]) from Merck and Gilead. Dr Saag reported receiving consulting fees from American Gene Technologies outside the submitted work. No other disclosures were reported.

Funding/Support: Sponsored and funded by the IAS-USA, a mission-based, nonmembership, 501(c)(3) not-for-profit organization. No private sector or government funding was used to support the work. Panel members volunteered and are not compensated for participation in the effort.

Role of the Funder/Sponsor: The IAS-USA determined the need to provide updated recommendations, selected the panel members, and provided administrative support and oversight. The panel designed and conducted the work; collected, managed, analyzed, and interpreted the data; and prepared, reviewed, and approved the text and recommendations.

Additional Contributions: We thank Michelle Valderama, BS, for assistance in managing the manuscript, Sherry Wu, BS, for administrative support, and Kimberly R. Powell, MSIS, for conducting the PubMed and Embase literature searches. Mss Valderama and Wu are salaried employees of the IAS-USA; Ms Powell is a salaried employee of Emory University.

REFERENCES

1. Edwards JK, Cole SR, Breger TL, et al. Mortality among persons entering HIV care compared with the general US population: an observational study. *Ann Intern Med*. 2021;174(9):1197-1206. doi:10.7326/M21-0065

2. Gandhi RT, Bedimo R, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2022 recommendations of the International Antiviral Society-USA panel. *JAMA*. 2023;329(1):63-84. doi:10.1001/jama.2022.22246

3. Canadian Task Force on the Periodic Health Examination. The periodic health examination. *CMAJ*. 1979;121(9):1193-1254.

4. Cerrone M, Alfarisi O, Neary M, et al. Rifampicin effect on intracellular and plasma pharmacokinetics of tenofovir alafenamide. *J Antimicrob Chemother*. 2019;74(6):1670-1678. doi:10.1093/jac/dkz068

5. Eke AC, Lockman S, Mofenson LM. Antiretroviral treatment of HIV/AIDS during pregnancy. *JAMA*. 2023;329(15):1308-1309. doi:10.1001/jama.2023.5076

6. Patel K, Huo Y, Jao J, et al; Pediatric HIV/AIDS Cohort Study; Swiss Mother and Child HIV Cohort Study. Dolutegravir in pregnancy as compared with current HIV regimens in the United States. *N Engl J Med*. 2022;387(9):799-809. doi:10.1056/NEJMoa2200600

7. Lockman S, Brummel SS, Ziemba L, et al; IMPAACT 2010/VESTED Study Team and Investigators. Efficacy and safety of dolutegravir with emtricitabine and tenofovir alafenamide fumarate or tenofovir disoproxil fumarate, and efavirenz, emtricitabine, and tenofovir disoproxil fumarate HIV antiretroviral therapy regimens started in pregnancy (IMPAACT 2010/VESTED): a multicentre, open-label, randomised, controlled, phase 3 trial. *Lancet*. 2021;397(10281):1276-1292. doi:10.1016/S0140-6736(21)00314-7

8. Zhang H, Hindman JT, Lin L, et al. A study of the pharmacokinetics, safety, and efficacy of bictegravir/emtricitabine/tenofovir alafenamide in virologically suppressed pregnant women with HIV. *AIDS*. 2024;38(1):F1-F9. doi:10.1097/QAD.0000000000003783

9. Antiretroviral Pregnancy Registry. Antiretroviral Pregnancy Registry interim report for 1 January 1989—31 July 2023. Published 2024. Accessed June 4, 2024. https://www.apregistry.com/forms/exec-summary.pdf

10. van der Wekken-Pas L, Weiss F, Simon-Zuber C, et al. Cabotegravir and rilpivirine long acting injectables in a pregnant woman living with HIV. *Clin Infect Dis*. Published online May 3, 2024. doi:10.1093/cid/ciae242

11. ClinicalInfoHIV.gov. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV. Updated July 9, 2024. Accessed August 16, 2024. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/whats-new

12. Ingle SM, Miro JM, May MT, et al. Early antiretroviral therapy not associated with higher cryptococcal meningitis mortality in people with human immunodeficiency virus in high-income countries: an international collaborative cohort study. *Clin Infect Dis*. 2023;77(1):64-73. doi:10.1093/cid/ciad122

13. National Institutes of Health, Centers for Disease Control and Prevention, and HIV Medicine Association of the Infectious Disease Society of America. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV. Updated: September 28, 2022. Accessed November 9, 2022. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections

14. Dooley KE, Savic RM, Gupte A, et al; DOLPHIN Study Team. Once-weekly rifapentine and isoniazid for tuberculosis prevention in patients with HIV taking dolutegravir-based antiretroviral therapy: a phase 1/2 trial. *Lancet HIV*. 2020;7:e401-e409. doi:10.1016/S2352-3018(20)30032-1

15. Weld ED, Perez-Solans B, Salles I, et al. Simultaneous initiation in ART-naive PWH of DTG-based ART & 3HP maintains efficacious DTG levels [abstract 156]. *Top Antivir Med*. 2024;32(1):35. Abstracts from the 2024 Conference on Retroviruses and Opportunistic Infections.

16. Imperial M, Luetkemeyer A, Dawson R, et al. DTG PK in people with HIV receiving daily 1HP for latent TB treatment (ACTG A5372) [abstract 78]. *Top Antivir Med*. 2022;30(1 suppl):29. Abstracts from the 2022 Conference on Retroviruses and Opportunistic Infections.

17. Avihingsanon A, Jirajariyavej S, Palakawong T, et al. Pharmacokinetics and HIV viral load suppression of 1 month-daily rifapentine and isoniazid (1HP) for tuberculosis preventive therapy among adults with HIV taking standard dolutegravir-based regimens [Abstract OAB1702]. Poster presented at: 25th International AIDS Conference; July 22-26, 2024; Munich, Germany.

18. Liou BH, Cheng CN, Lin YT, et al. Short-course daily isoniazid and rifapentine for latent tuberculosis infection in people living with HIV who received coformulated bictegravir/emtricitabine/tenofovir alafenamide. *J Int AIDS Soc*. 2021;24(11):e25844. doi:10.1002/jia2.25844

19. Naidoo A, Naidoo K, Letsoalo MP, et al. Efficacy, safety, and PK of BIC/FTC/TAF in adults with HIV and tuberculosis on rifampicin at week 24 [abstract 211]. *Top Antivir Ther*. 2024;32(1):57. Abstracts from the 2024 Conference on Retroviruses and Opportunistic Infections.

20. Althoff KN, Stewart CN, Humes E, et al. The shifting age distribution of people with HIV using antiretroviral therapy in the United States. *AIDS*. 2022;36(3):459-471. doi:10.1097/QAD.0000000000003128

21. Marty L, Diawara Y, Rachas A, Grabar S, Costagliola D, Supervie V. Projection of age of individuals living with HIV and time since ART initiation in 2030: estimates for France. *J Int AIDS Soc*. 2022;25(suppl 4):e25986. doi:10.1002/jia2.25986

22. Haas CB, Engels EA, Horner MJ, et al. Trends and risk of lung cancer among people living with HIV in the USA: a population-based registry linkage study. *Lancet HIV*. 2022;9(10):e700-e708. doi:10.1016/S2352-3018(22)00219-3

23. Trickey A, McGinnis K, Gill MJ, et al. Longitudinal trends in causes of death among adults with HIV on antiretroviral therapy in Europe and North America from 1996 to 2020: a collaboration of cohort studies. *Lancet HIV*. 2024;11(3):e176-e185. doi:10.1016/S2352-3018(23)00272-2

24. Weber MSR, Duran Ramirez JJ, Hentzien M, et al; Swiss HIV Cohort Study. Time trends in causes of death in people with HIV: insights from the Swiss HIV Cohort Study. *Clin Infect Dis*. 2024;79(1):177-188. doi:10.1093/cid/ciae014

25. University of Liverpool. HIV drug interactions. Accessed April 16, 2024. https://www.hiv-druginteractions.org/drug_queries/new

26. Toronto General Hospital. Drug interaction guide. Accessed April 16, 2024. https://hivclinic.ca/app/#drugInt

27. Ombajo LA, Penner J, Nkuranga J, et al. Second-line switch to dolutegravir for treatment of HIV infection. *N Engl J Med*. 2023;388(25):2349-2359. doi:10.1056/NEJMoa2210005

28. Pierre S, Marc JB, Homeus F, et al. Switching from a second-line ritonavir-boosted protease inhibitor-based regimen to bictegravir/emtricitabine/tenofovir alafenamide: results of a randomized clinical trial [abstract OAB3805]. Poster presented at: 25th International AIDS Conference; July 22-26, 2024; Munich, Germany.

29. Sivile S, Fwoloshi S, Engamba D, et al. Dolutegravir with recycled nucleoside reverse transcriptase inhibitors maintains better viral suppression than protease inhibitor based antiretroviral therapy over 144 weeks: VISEND Trial [abstract OAB3806LB]. Poster presented at: 25th International AIDS Conference; July 22-26, 2024; Munich, Germany.

30. Loosli T, Hossmann S, Ingle SM, et al. HIV-1 drug resistance in people on dolutegravir-based antiretroviral therapy: a collaborative cohort analysis. *Lancet HIV*. 2023;10(11):e733-e741. doi:10.1016/S2352-3018(23)00228-X

31. Tschumi N, Lukau B, Tlali K, et al. Emergence of acquired dolutegravir resistance in treatment-experienced people with HIV in Lesotho. *Clin Infect Dis*. Published online April 23, 2024. doi:10.1093/cid/ciae185

32. Skrivankova VW, Huwa J, Muula G, et al. Virologic failure and drug resistance after programmatic switching to dolutegravir-based first-line antiretroviral therapy in Malawi and Zambia. *Clin Infect Dis*. Published online June 7, 2024. doi:10.1093/cid/ciae261

33. Hsu RK, Sension M, Fusco JS, et al. Real-world effectiveness of cabotegravir + rilpivirine vs standard of care oral regimens in the US [Abstract 623]. *Top Antivir Med*. 2024;32(1):172. Abstracts from the 2024 Conference on Retroviruses and Opportunistic Infections.

34. Kityo C, Mambule IK, Musaazi J, et al; CARES Trial Team. Switch to long-acting cabotegravir and rilpivirine in virologically suppressed adults with HIV in Africa (CARES): week 48 results from a randomised, multicentre, open-label, non-inferiority trial. *Lancet Infect Dis*. 2024;24(10):1083-1092. doi:10.1016/S1473-3099(24)00289-5

35. van Welzen BJ, Van Lelyveld SFL, Ter Beest G, et al. Virological failure after switch to long-acting cabotegravir and rilpivirine injectable therapy: an in-depth analysis. *Clin Infect Dis*. 2024;79(1):189-195. doi:10.1093/cid/ciae016

36. Orkin C, Schapiro JM, Perno CF, et al. Expanded multivariable models to assist patient selection for long-acting cabotegravir + rilpivirine treatment: clinical utility of a combination of patient, drug concentration, and viral factors associated with virologic failure. *Clin Infect Dis*. 2023;77(10):1423-1431. doi:10.1093/cid/ciad370

37. Mohammadi A, Etemad B, Zhang X, et al. Viral and host mediators of non-suppressible HIV-1 viremia. *Nat Med*. 2023;29(12):3212-3223. doi:10.1038/s41591-023-02611-1

38. Elvstam O, Malmborn K, Elén S, et al. Virologic failure following low-level viremia and viral blips during antiretroviral therapy: results from a European Multicenter Cohort. *Clin Infect Dis*. 2023;76(1):25-31. doi:10.1093/cid/ciac762

39. Taramasso L, Magnasco L, Bruzzone B, et al. How relevant is the HIV low level viremia and how is its management changing in the era of modern ART? A large cohort analysis. *J Clin Virol*. 2020;123:104255. doi:10.1016/j.jcv.2019.104255

40. Gandhi RT, Zheng L, Bosch RJ, et al; AIDS Clinical Trials Group A5244 Team. The effect of raltegravir intensification on low-level residual viremia in HIV-infected patients on antiretroviral therapy: a randomized controlled trial. *PLoS Med*. 2010;7(8):e1000321. doi:10.1371/journal.pmed.1000321

41. Bosch B, Sokhela S, Akpomiemie G, et al. High rates of long-term HIV RNA re-suppression after virological failure on dolutegravir in the ADVANCE trial. Poster presented at: 12th IAS Conference on HIV Science; July 23-26, 2023; Brisbane, Australia.

42. Roden L, Huhn G, DeMarco CE, Keckler K, Valadez PC, Burke K. Antiretroviral (ART) virologic suppression (VS) and patient reported outcomes (PROs) at 6 months in the clinical opportunities and management to exploit bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) an asynchronous connection key (COMEBACK) study. *Open Forum Infect Dis*. 2022;9(suppl 2):ofac492.1293. doi:10.1093/ofid/ofac492.1293

43. Paton NI, Musaazi J, Kityo C, et al; NADIA Trial Team. Efficacy and safety of dolutegravir or darunavir in combination with lamivudine plus either zidovudine or tenofovir for second-line treatment of HIV infection (NADIA): week 96 results from a prospective, multicentre, open-label, factorial, randomised, non-inferiority trial. *Lancet HIV*. 2022;9(6):e381-e393. doi:10.1016/S2352-3018(22)00092-3

44. D2EFT Study Group. Dolutegravir plus boosted darunavir versus recommended standard-of-care antiretroviral regimens in people with HIV-1 for whom recommended first-line non-nucleoside reverse transcriptase inhibitor therapy has failed (D^2EFT): an open-label, randomised, phase 3b/4 trial. *Lancet HIV*. 2024;11(7):e436-e448. doi:10.1016/S2352-3018(24)00089-4

45. Segal-Maurer S, DeJesus E, Stellbrink HJ, et al; CAPELLA Study Investigators. Capsid inhibition with lenacapavir in multidrug-resistant HIV-1 infection. *N Engl J Med*. 2022;386(19):1793-1803. doi:10.1056/NEJMoa2115542

46. Gandhi M, Hickey M, Imbert E, et al. Demonstration project of long-acting antiretroviral therapy in a diverse population of people with HIV. *Ann Intern Med*. 2023;176(7):969-974. doi:10.7326/M23-0788

47. Hickey MD, Gistand N, Grochowski J, et al. 48-week viral suppression rates in people with HIV starting long-acting CAB/RPV with initial viremia. *Clin Infect Dis*. Published online October 5, 2024. doi:10.1093/cid/ciae500

48. Sax PE, Thompson MA, Saag MS; IAS-USA Treatment Guidelines Panel. Updated treatment recommendation on use of cabotegravir and rilpivirine for people with HIV from the IAS-USA guidelines panel. *JAMA*. 2024;331(12):1060-1061. doi:10.1001/jama.2024.2985

49. Rana A, Bao Y, Zheng L, et al. Long-acting injectable CAB/RPV is superior to oral ART in PWH with adherence challenges: ACTG A5359 [abstract 212]. *Top Antivir Med*. 2024;32(1):57-58. Abstracts from the CROI 2024 Conference on Retroviruses and Opportunistic Infections.

50. Stier EA, Clarke MA, Deshmukh AA, et al. International Anal Neoplasia Society's consensus guidelines for anal cancer screening. *Int J Cancer*. 2024;154(10):1694-1702. doi:10.1002/ijc.34850

51. Horberg M, Thompson M, Agwu A, et al. Primary care guidance for providers of care for persons with human immunodeficiency virus: 2024 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. Published online October 12, 2024. doi:10.1093/cid/ciae479

52. Sax PE, Erlandson KM, Lake JE, et al. Weight gain following initiation of antiretroviral therapy: risk factors in randomized comparative clinical trials. *Clin Infect Dis*. 2020;71(6):1379-1389. doi:10.1093/cid/ciz999

53. Drechsler H, Ayers C, Oboho I, et al. Choice of antiretroviral therapy has low impact on weight gain. *AIDS*. 2024;38(12):1731-1739. doi:10.1097/QAD.0000000000003950

54. Chandiwana NC, Siedner MJ, Marconi VC, et al. Weight gain after HIV therapy initiation: pathophysiology and implications. *J Clin Endocrinol Metab*. 2024;109(2):e478-e487. doi:10.1210/clinem/dgad411

55. Anderson D, Ramgopal M, Hagins DP, et al. DEFINE: a prospective, randomized, phase 4 trial to assess a protease inhibitor-based regimen switch strategy to manage integrase inhibitor-related weight gain. *Clin Infect Dis*. Published online September 24, 2024. doi:10.1093/cid/ciae449

56. McComsey GA, Molina J-M, Mills A, et al. Weight and body composition after switch to doravirine/islatravir (DOR/ISL) 100/0.75 mg once daily: week 48 results from two randomized active-controlled phase 3 trials, MK8591A-017 (P017) and MK8591A-018 (P018). Poster presented at: 12th International AIDS Society Conference on HIV Science; 2023; Brisbane, Australia.

57. Bosch B, Akpomiemie G, Chandiwana N, et al. Weight and metabolic changes after switching from tenofovir alafenamide/emtricitabine (FTC)+dolutegravir (DTG), tenofovir disoproxil fumarate (TDF)/FTC + DTG, and TDF/FTC/efavirenz to TDF/lamivudine/DTG. *Clin Infect Dis*. 2023;76(8):1492-1495. doi:10.1093/cid/ciac949

58. Damas J, Munting A, Fellay J, et al; Swiss HIV Cohort Study (SHCS). Weight, anthropometric and metabolic changes after discontinuing antiretroviral therapy containing tenofovir alafenamide in people with HIV. *Clin Infect Dis*. 2024;79(4):990-998. doi:10.1093/cid/ciae189

59. Nguyen Q, Wooten D, Lee D, et al. Glucagon-like peptide 1 receptor agonists promote weight loss among people with HIV. *Clin Infect Dis*. 2024;79(4):978-982. doi:10.1093/cid/ciae151

60. Haidar L, Crane HM, Nance RM, et al. Weight loss associated with semaglutide treatment among people with HIV. *AIDS*. 2024;38(4):531-535. doi:10.1097/QAD.0000000000003791

61. Ditzenberger GL, Lake JE, Kitch DW, et al. Effects of semaglutide on muscle structure and function in the SLIM liver study [abstract 617]. *Top Antivir Med*. 2024;32(1):237-238. Abstracts from the CROI 2024 Conference on Retroviruses and Opportunistic Infections.

62. McComsey GA, Sattar A, Albar Z, et al. Effects of semaglutide on adipose tissue in HIV-associated lipohypertrophy. *Open Forum Infect Dis*. 2023;10 (suppl 2):ofad500.111. doi:10.1093/ofid/ofad500.111

63. Eckard AR, Wu Q, Sattar A, et al. Once-weekly semaglutide in people with HIV-associated lipohypertrophy: a randomised, double-blind, placebo-controlled phase 2b single-centre clinical trial. *Lancet Diabetes Endocrinol*. 2024;12(8):523-534. doi:10.1016/S2213-8587(24)00150-5

64. Tusch E, Ryom L, Pelchen-Matthews A, et al; D:A:D Cohort Study; RESPOND Cohort Study. Trends in mortality in people with HIV from 1999 to 2020: a multi-cohort collaboration. *Clin Infect Dis*. Published online April 26, 2024. doi:10.1093/cid/ciae228

65. Zanni MV, Watanabe M, Ribaudo HJ, et al. Factors affecting risk of major adverse cardiovascular events among people with HIV in REPRIEVE [abstract 781]. *Top Antivir Med*. 2024;32 (2):231. Abstracts from the 2024 Conference on Retroviruses and Opportunistic Infections.

66. Grinspoon SK, Ribaudo HJ, Triant H, et al. Performance of the ACC/AHA polled cohort equations for risk prediction in the global RETRIEVE trial [abstract 782]. *Top Antivir Med*. 2024;31(1):231. Abstracts from the 2024 Conference on Retroviruses and Opportunistic Infections.

67. Jaschinski N, Greenberg L, Neesgaard B, et al; RESPOND Study Group. Recent abacavir use and incident cardiovascular disease in contemporary-treated people with HIV. *AIDS*. 2023;37(3):467-475. doi:10.1097/QAD.0000000000003373

68. Fichtenbaum CJ, Malvestutto CD, Watanabe MG, et al. Abacavir is associated with elevated risk for cardiovascular events in the REPRIEVE trial [abstract OAB3406LB]. Poster presented at: 25th International AIDS Conference; 2024; Munich, Germany.

69. Rein SM, Lodi S, Logan RW, et al; Antiretroviral Therapy Cohort Collaboration and the HIV-CAUSAL Collaboration. Integrase strand-transfer inhibitor use and cardiovascular events in adults with HIV: an emulation of target trials in the HIV-CAUSAL Collaboration and the Antiretroviral Therapy Cohort Collaboration. *Lancet HIV*. 2023;10(11):e723-e732. doi:10.1016/S2352-3018(23)00233-3

70. Neesgaard B, Greenberg L, Miró JM, et al. Associations between integrase strand-transfer inhibitors and cardiovascular disease in people living with HIV: a multicentre prospective study from the RESPOND cohort consortium. *Lancet HIV*. 2022;9(7):e474-e485. doi:10.1016/S2352-3018(22)00094-7

71. Surial B, Chammartin F, Damas J, et al; Swiss HIV Cohort Study. Impact of integrase inhibitors on cardiovascular disease events in people with human immunodeficiency virus starting antiretroviral therapy. *Clin Infect Dis*. 2023;77(5):729-737. doi:10.1093/cid/ciad286

72. American College of Cardiology and American Heart Association. ASCVD risk estimator plus. Accessed May 28, 20234. https://tools.acc.org/ascvd-risk-estimator-plus/#!/calculate/estimate/

73. Grinspoon SK, Fitch KV, Zanni MV, et al; REPRIEVE Investigators. Pitavastatin to prevent cardiovascular disease in HIV infection. *N Engl J Med*. 2023;389(8):687-699. doi:10.1056/NEJMoa2304146

74. Grinspoon SK, Ribaudo HJ, Douglas PS. Trial update of pitavastatin to prevent cardiovascular events in HIV infection. *N Engl J Med*. 2024;390 (17):1626-1628. doi:10.1056/NEJMc2400870

75. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents with HIV: recommendations for the use of statin therapy as primary prevention of atherosclerotic cardiovascular disease in people with HIV. Updated February 27, 2024. Accessed June 11, 2024. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/statin-therapy-people-hiv

76. Byonanebye DM, Polizzotto MN, Maltez F, et al; RESPOND Study Group. Associations between change in BMI and the risk of hypertension and dyslipidaemia in people receiving integrase strand-transfer inhibitors, tenofovir alafenamide, or both compared with other contemporary antiretroviral regimens: a multicentre, prospective observational study from the RESPOND consortium cohorts. *Lancet HIV*. 2024;11(5):e321-e332. doi:10.1016/S2352-3018(23)00328-4

77. Sokhela S, Venter WDF, Bosch B, et al. Final 192-week efficacy and safety results of the ADVANCE trial, comparing 3 first-line antiretroviral regimens. *Open Forum Infect Dis*. 2024;11(3):ofae007. doi:10.1093/ofid/ofae007

78. Brennan AT, Nattey C, Kileel EM, et al. Change in body weight and risk of hypertension after switching from efavirenz to dolutegravir in adults living with HIV: evidence from routine care in Johannesburg, South Africa. *EClinicalMedicine*. 2023;57:101836. doi:10.1016/j.eclinm.2023.101836

79. Kileel EM, Lo J, Malvestutto C, et al. Assessment of obesity and cardiometabolic status by integrase inhibitor use in REPRIEVE: a propensity-weighted analysis of a multinational primary cardiovascular prevention cohort of people with human immunodeficiency virus. *Open Forum Infect Dis*. 2021;8(12):ofab537. doi:10.1093/ofid/ofab537

80. Sempere A, Assoumou L, González-Cordón A, et al; NEAT 022 Study Group. Incidence of hypertension and blood pressure changes in persons with human immunodeficiency virus at high risk for cardiovascular disease switching from boosted protease inhibitors to dolutegravir: a post-hoc analysis of the 96-week randomised NEAT-022 trial. *Clin Infect Dis*. 2023;77(7):991-1009. doi:10.1093/cid/ciad297

81. Romo M, Frndak S, Dear N, et al. Dolutegravir-containing antiretroviral therapy and incident hypertension: findings from a prospective cohort in Kenya, Nigeria, Tanzania and Uganda [abstract OAB3404]. Poster presented at: 25th International AIDS Conference; July 22-26, 2024; Munich, Germany.

82. Rivera AS, Pak KJ, Mefford MT, Hechter RC. Use of tenofovir alafenamide fumarate for HIV pre-exposure prophylaxis and incidence of hypertension and initiation of statins. *JAMA Netw Open*. 2023;6(9):e2332968. doi:10.1001/jamanetworkopen.2023.32968

83. Herrin M, Tate JP, Akgün KM, et al. Weight gain and incident diabetes among HIV-infected veterans initiating antiretroviral therapy compared with uninfected individuals. *J Acquir Immune Defic Syndr*. 2016;73(2):228-236. doi:10.1097/QAI.0000000000001071

84. Rupasinghe D, Bansi-Matharu L, Law M, et al. Integrase strand transfer inhibitor (INSTI) related changes in BMI and risk of diabetes: a prospective study from the RESPOND cohort consortium. *Clin Infect Dis*. Published online August 9, 2024. doi:10.1093/cid/ciae406

85. Korthuis PT, Cook RR, Lum PJ, et al. HIV clinic-based extended-release naltrexone versus treatment as usual for people with HIV and opioid use disorder: a non-blinded, randomized non-inferiority trial. *Addiction*. 2022;117(7):1961-1971. doi:10.1111/add.15836

86. Mitra S, Grant C, Nolan S, Mohd Salleh NA, Milloy MJ, Richardson L. Assessing the temporality between transitions onto opioid agonist therapy and engagement with antiretroviral therapy in a cohort of HIV-positive people who use opioids daily. *AIDS Behav*. 2022;26(6):1933-1942. doi:10.1007/s10461-021-03543-y

87. American Society of Addiction Medicine (ASAM) and the American Academy of Addiction Psychiatry. (AAAP). Clinical practice guideline on the management of stimulant use disorder. Published November 7, 2023. Accessed April 18, 2024. https://www.asam.org/quality-care/clinical-guidelines/stimulant-use-disorders

88. Hoang THL, Nguyen VM, Adermark L, Alvarez GG, Shelley D, Ng N. Factors influencing tobacco smoking and cessation among people living with HIV: a systematic review and meta-analysis. *AIDS Behav*. 2024;28(6):1858-1881. doi:10.1007/s10461-024-04279-1

89. Centers for Disease Control and Prevention (CDC). Syringe services programs. Updated: February 8, 2024. Accessed August 6, 2024. https://www.cdc.gov/syringe-services-programs/php/index.html

90. New York State. Harm reduction delivered. Accessed August 6, 2024. https://oasas.ny.gov/harm-reduction-delivered

91. Beck L, Parlier-Ahmad AB, Martin CE. Pre-exposure prophylaxis (PrEP) indication and uptake among people receiving buprenorphine for the treatment of opioid use disorder. *J Subst Abuse Treat*. 2022;132:108506. doi:10.1016/j.jsat.2021.108506

92. Eaton EF, Tamhane A, Turner W, Raper JL, Saag MS, Cropsey KL. Safer in care: a pandemic-tested model of integrated HIV/OUD care. *Drug Alcohol Depend*. 2022;231:109241. doi:10.1016/j.drugalcdep.2021.109241

93. Springer SA. Ending the HIV epidemic for persons who use drugs: the practical challenges of meeting people where they are. *J Gen Intern Med*. 2023;38(12):2816-2818. doi:10.1007/s11606-023-08142-2

94. Centers for Disease Control and Prevention. Preexposure prophylaxis for the prevention of HIV infection in the United States—2021 update: a clinical practice guideline. Accessed April 18,

2024. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

95. Marrazzo J, Tao L, Becker M, et al. HIV preexposure prophylaxis with emtricitabine and tenofovir disoproxil fumarate among cisgender women. *JAMA*. 2024;331(11):930-937. doi:10.1001/jama.2024.0464

96. Anderson PL, Marzinke MA, Glidden DV. Updating the adherence-response for oral emtricitabine/tenofovir disoproxil fumarate for human immunodeficiency virus pre-exposure prophylaxis among cisgender women. *Clin Infect Dis*. 2023;76(10):1850-1853. doi:10.1093/cid/ciad021

97. Delany-Moretlwe S, Voldal E, Saidi F, et al. Initial evaluation of CAB-LA Safety during pregnancy in the HPTN 084 open-label extension. Poster presented at: 25th International AIDS Conference; 2024; Munich, Germany.

98. Han K, D'Amico R, Spreen W, Ford S. Model-based comparison of cabotegravir pharmacokinetics following thigh and gluteal infections [abstract 617]. *Top Antivir Med*. 2024;32(2):170. Abstracts from the CROI 2024 Conference on Retroviruses and Opportunistic Infections.

99. Felizarta F, D'Amico R, Wang K, et al. Thigh infections of cabotegravir+rilpirivirine in virally suppressed adults with HIV-1 [abstract 519]. *Top Antivir Med*. 2023;31(2):204. Abstracts From the CROI 2024 Conference on Retroviruses and Opportunistic Infections.

100. Landovitz RJ, Delany-Moretlwe S, Fogel JM, et al; HPTN 083 and 084 Study Teams. Features of HIV infection in the context of long-acting cabotegravir preexposure prophylaxis. *N Engl J Med*. Published online July 24, 2024. doi:10.1056/NEJMc2402088

101. Delany-Moretlwe S, Hughes JP, Bock P, et al. Cabotegravir for the prevention of HIV-1 in women: results from HPTN 084, a phase 3, randomised clinical trial. *Lancet*. 2022;399(10337):1779-1789. doi:10.1016/S0140-6736(22)00538-4

102. Bekker LG, Das M, Abdool Karim Q, et al; PURPOSE 1 Study Team. Twice-yearly lenacapavir or daily F/TAF for HIV prevention in cisgender women. *N Engl J Med*. Published online July 24, 2024. doi:10.1056/NEJMoa2407001

103. Kelley CF, Acevedo-Quinones M, Agwu AL, et al. Twice-yearly lenacapavir for HIV prevention in cisgender gay men, transgender, and gender-diverse people: Interim analysis result from the PURPOSE 2 study [oral abstract 0208]. Poster presented at: 5th HIV Research for Prevention Conference (HIVR4P 2024); October 6-10, 2024; Lima, Peru.

104. Landovitz RJ, Voldal E, Hanscom B, et al. Site-based HIV testing assay performance for cabotegravir and TDF-FTC PrEP failure in HPTN 083 [abstract 128]. *Top Antivir Med*. 2024;32(1):24-25. Abstracts from the 2024 Conference on Retroviruses and Opportunistic Infections.

105. Landovitz R, Gao F, Fogel JM, et al. Performance characteristics of HIV RNA screening with long-acting injectable cabotegravir (CAB-LA) pre-exposure prophylaxis (PrEP) in the multicenter global HIV Prevention Trials Network 083 (HPTN 083) Study [abstract OAE0406LB]. Poster presented at: 25th International AIDS Conference; July 22-26, 2024; Munich, Germany.

106. AETC National Coordinating Resources Center. National clinician consultation center. Accessed April 18, 2024. https://aidsetc.org/aetc-program/nccc

107. Landovitz R, Donnell D, Tran H, et al. Updated efficacy, safety, and case studies in HPTN 083: CAB-LA vs TDF/FTC for PrEP [abstract 96]. *Top Antiv Med*. 2022;30(1 suppl):37. Abstracts From the 2022 Conference on Retroviruses and Opportunistic Infections.

108. Psaros C, Goodman GR, Lee JS, et al. HPTN 083-02: factors influencing adherence to injectable PrEP and retention in an injectable PrEP study. *J Int AIDS Soc*. 2024;27(5):e26252. doi:10.1002/jia2.26252

109. Springer SA, Nijhawan AE, Knight K, et al. Study protocol of a randomized controlled trial comparing two linkage models for HIV prevention and treatment in justice-involved persons. *BMC Infect Dis*. 2022;22(1):380. doi:10.1186/s12879-022-07354-x

110. Luetkemeyer AF, Donnell D, Dombrowski JC, et al; DoxyPEP Study Team. Postexposure doxycycline to prevent bacterial sexually transmitted infections. *N Engl J Med*. 2023;388(14):1296-1306. doi:10.1056/NEJMoa2211934

111. Molina JM, Bercot B, Assoumou L, et al. Doxycycline prophylaxis and meningococcal group B vaccine to prevent bacterial sexually transmitted infections in France (ANRS 174 DOXYVAC): a multicentre, open-label, randomised trial with a 2 x 2 factorial design. *Lancet Infect Dis*. 2024;24(10):1093-1104. doi:10.1016/S1473-3099(24)00236-6

112. Stewart J, Oware K, Donnell D, et al; dPEP Kenya Study Team. Doxycycline prophylaxis to prevent sexually transmitted infections in women. *N Engl J Med*. 2023;389(25):2331-2340. doi:10.1056/NEJMoa2304007

113. UNAIDS. The path that ends AIDS: 2023 UNAIDS global AIDS update. Accessed May 14, 2024. https://thepath.unaids.org/

114. Sullivan PS, Satcher Johnson A, Pembleton ES, et al. Epidemiology of HIV in the USA: epidemic burden, inequities, contexts, and responses. *Lancet*. 2021;397(10279):1095-1106. doi:10.1016/S0140-6736(21)00395-0

115. Dailey A, Sumner ZG, Johnson AS, Morales JA, Reynolds S. Trends in black-white disparities in HIV diagnosis: 2017-2021, United States [abstract 192]. *Top Antivir Med*. 2024;32(1):49-50. Abstracts From the 2024 Conference on Retroviruses and Opportunistic Infections.

116. Kerani RP, Satcher JA, Buskin SE, et al. The epidemiology of HIV among people born outside the United States, 2010-2017. *Public Health Rep*. 2020;135(5):611-620. doi:10.1177/0033354920942623

117. World Health Organization (WHO). HIV/AIDS surveillance in Europe 2020: 2019 data. Accessed May 14, 2024. https://iris.who.int/bitstream/handle/10665/337037/9789289055345-eng.pdf?sequence=6&isAllowed=y

118. Palich R, Arias-Rodriguez A, Duracinsky M, et al. High proportion of post-migration HIV acquisition in migrant men who have sex with men receiving HIV care in the Paris region, and associations with social disadvantage and sexual behaviours: results of the ANRS-MIE GANYMEDE study, France, 2021 to 2022. *Euro Surveill*. 2024;29(11)2300445. doi:10.2807/1560-7917.ES.2024.29.11.2300445

119. Pepperrell T, Cross S, Hill A. Cabotegravir-global access to long-acting pre-exposure prophylaxis for HIV. *Open Forum Infect Dis*. 2023;10(1):ofac673. doi:10.1093/ofid/ofac673

120. Mujugira A, Muwonge T, Aliganyira B, Okoboi S. Uganda's Anti-Homosexuality Act undermines public health. *J Int AIDS Soc*. 2024;27(5):e26259. doi:10.1002/jia2.26259

121. Gostin LO. The US turns its back on women's reproductive rights. *BMJ*. 2022;377:o1206. doi:10.1136/bmj.o1206

122. Beyrer C, Kamarulzaman A, Isbell M, et al. Under threat: the International AIDS Society–Lancet Commission on Health and Human Rights. *Lancet*. 2024;403(10434):1374-1418. doi:10.1016/S0140-6736(24)00302-7

123. UNAIDS. Political declaration on HIV and AIDS: ending inequalities and getting on track to end AIDS by 2030. Published June 9, 2021. Accessed May 14, 2024. https://www.unaids.org/en/resources/documents/2021/2021_political-declaration-on-hiv-and-aids

124. Squires KE, Correll TA, Robertson MN, et al. Effect of islatravir on total lymphocytes and lymphocyte subset counts [abstract 192]. *Top Antivir Med*. 2023;31(2):79. Abstracts from CROI 2023 Conference on Retroviruses and Opportunistic Infections.

125. Colson A, Crofoot G, Ruane PJ, et al. Efficacy and safety of weekly islatravir plus lenacapavir in PWH at 24 weeks: a phase II study [abstract 208]. *Top Antivir Med*. 2024;32(1):56. Abstracts from the 2024 Conference on Retroviruses and Opportunistic Infections.

126. Eron JJ, Little SJ, Crofoot G, et al. Safety of teropavimab and zinlirvimab with lenacapavir once every 6 months for HIV treatment: a phase 1b, randomised, proof-of-concept study. *Lancet HIV*. 2024;11(3):e146-e155. doi:10.1016/S2352-3018(23)00293-X

127. Eron JJ, Cook PP, Mehrotra M, et al. Lenacapavir plus bNAbs for people with HIV and sensitivity to either teropavimab or zinlirvimab. *Top Antivir Med*. 2024;32(1):21.

128. Taiwo B, Zheng YE, Rodriguez K, et al. Safety and efficacy of VRC07-523LS plus long-acting cabotegravir in the phase II ACTG A5357 trial [abstract 119]. *Top Antivir Med*. 2024;32(1):20-21. Abstracts from the 2024 Conference on Retroviruses and Opportunistic Infections.

129. Mounzer K, Brunet L, Sension M, et al. Weight change after starting doravirine among ART-experienced individuals in the US [abstract 807]. *Top Antivir Med*. 2024;32(1):240-241. Abstracts From the 2024 Conference on Retroviruses and Opportunistic Infections.