JAMA | Special Communication

Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults

2022 Recommendations of the International Antiviral Society–USA Panel

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

IMPORTANCE Recent advances in treatment and prevention of HIV warrant updated recommendations to guide optimal practice.

OBJECTIVE Based on a critical evaluation of new data, to provide clinicians with recommendations on use of antiretroviral drugs for the treatment and prevention of HIV, laboratory monitoring, care of people aging with HIV, substance use disorder and HIV, and new challenges in people with HIV, including COVID-19 and monkeypox virus infection.

EVIDENCE REVIEW A panel of volunteer expert physician scientists were appointed to update the 2020 consensus recommendations. Relevant evidence in the literature (PubMed and Embase searches, which initially yielded 7891 unique citations, of which 834 were considered relevant) and studies presented at peer-reviewed scientific conferences between January 2020 and October 2022 were considered.

FINDINGS Initiation of antiretroviral therapy (ART) is recommended as soon as possible after diagnosis of HIV. Barriers to care should be addressed, including ensuring access to ART and adherence support. Integrase strand transfer inhibitor–containing regimens remain the mainstay of initial therapy. For people who have achieved viral suppression with a daily oral regimen, long-acting injectable therapy with cabotegravir plus rilpivirine given as infrequently as every 2 months is now an option. Weight gain and metabolic complications have been linked to certain antiretroviral medications; novel strategies to ameliorate these complications are needed. Management of comorbidities throughout the life span is increasingly important, because people with HIV are living longer and confronting the health challenges of aging. In addition, management of substance use disorder in people with HIV requires an evidence-based, integrated approach. Options for preexposure prophylaxis include oral medications (tenofovir disoproxil fumarate or tenofovir alafenamide plus emtricitabine) and, for the first time, a long-acting injectable agent, cabotegravir. Recent global health emergencies, like the SARS-CoV-2 pandemic and monkeypox virus outbreak, continue to have a major effect on people with HIV and the delivery of services. To address these and other challenges, an equity-based approach is essential.

CONCLUSIONS AND RELEVANCE Advances in treatment and prevention of HIV continue to improve outcomes, but challenges and opportunities remain.

Multimedia

Supplemental content

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

Corresponding Author: Rajesh T. Gandhi, MD, Cox 548, Infectious Diseases Division, Massachusetts General Hospital, 55 Fruit St, Boston, MA 02114 (RGANDHI@mgh.harvard.edu).

JAMA. 2023;329(1):63-84. doi:10.1001/jama.2022.22246
Published online December 1, 2022.

Four decades after the initial cases of HIV were reported, strategies for treating and preventing HIV infection continue to advance. People with HIV should be treated as soon as possible after diagnosis. If they have an opportunistic infection, antiretroviral therapy (ART) should be started shortly after initiation of treatment of the infection. Initial ART options include daily oral therapy, usually with a combination containing an integrase strand transfer inhibitor (InSTI). For patients who have achieved viral suppression, a long-acting injectable regimen (cabotegravir and rilpivirine [RPV]), which can be dosed every 2 months, is an option.

In addition to treatment improvements, there have been major advances in HIV prevention through preexposure prophylaxis (PrEP), including daily oral options and, for the first time, a long-acting injectable option, cabotegravir.

As treatment and prevention of HIV improve, new challenges and opportunities arise. As people with HIV live longer, there are important considerations related to aging that require an integrated approach. Multidisciplinary and holistic care of people with substance use and substance use disorder is required to achieve optimal outcomes in treating and preventing HIV. Other infectious disease outbreaks, such as COVID-19 and now monkeypox virus infection, also present rapidly evolving challenges for clinicians and people with HIV. To effectively address these and other challenges, as well as to realize the opportunity to end the HIV epidemic, efforts must be redoubled, with equity being the guiding principle.

This updated article provides current recommendations for treatment and prevention of HIV as well as an up-to-date discussion of important comorbidities and coinfections in people with HIV as they relate to the use of ART.

Methods

Appointment of the Panel

A volunteer international panel of experts in HIV research and clinical care, and the panel leadership, was appointed by International Antiviral (formerly AIDS) Society–USA (IAS-USA). Members were screened for expertise, involvement in research and care, financial relationships, and ability to work toward consensus. New members were added since the panel's last report to contribute additional expertise, particularly in substance use disorders and antiretroviral drugs. The panel convened in person and by conference calls from October 2021 to October 2022. Teams were appointed for each primary section, which evaluated relevant evidence and drafted recommendations for review by the full panel.

Identification of the Evidence

New evidence on antiretroviral drugs was identified in the published literature, major scientific conference presentations, or safety reports.[1] Literature searches were conducted by a panel member (C.d.R.) in PubMed and Embase for the period January 2020 to October 2022, and the panel monitored for new evidence thereafter. The 7891 unique citations were reviewed by a member (M.S.S.) who identified 834 possibly relevant publications. The substance use disorder team identified and reviewed additional evidence to develop this newly added section. Abstracts presented at scientific conferences between July 2020 and October 2022 were identified by panel members and teams. Additional relevant scientific publications or abstracts presented at peer-reviewed conferences were identified by the panel, and published and presented citations were obtained from drug manufacturers.

Process

The updated recommendations focus on adults with or at risk for HIV infection in settings in which most antiretroviral drugs are available. Each recommendation is rated for the strength of the recommendation and the quality of the supporting evidence (**Table 1**). For recommendations that have not changed substantially or for which few new data have become available since 2020, the previous iterations of the recommendations provide background information and relevant evidence.[1] Key recommendations for each section are listed in a Box or Table. ART drug combinations that are co-formulated are noted with slashes (eg, drug A/drug B/drug C). Detailed tables and further details about the process, panel, evidence identification, and the IAS–USA and its policies are available in the Supplement.

Initiation of ART

Recommendations for when to start ART are reported in **Box 1**. Initiating ART as soon as possible after an HIV diagnosis is a high priority to improve the health and life expectancy of people with HIV and to eliminate HIV transmission to sexual and injection drug use partners, as well as to infants.[1] Rapid ART initiation (within 7 days of diagnosis), including same-day initiation of ART on the day of diagnosis or the first clinic visit, improves the likelihood of persons linking to HIV care and the likelihood of and time to viral suppression.[3-5] In resource-limited settings, rapid ART initiation improved survival and longitudinal engagement in care.[6] In highly resourced settings, there are limited clinical and long-term outcomes from randomized clinical trials of rapid ART initiation. Based on the totality of evidence, ART initiation is recommended within 7 days of diagnosis, including on the day of diagnosis or the first clinic visit, if the patient is ready and there is no evidence of a co-occurring opportunistic infection that might affect the timing of initiation of treatment (evidence rating: AIII). Timing and choice of initial therapy in the presence of an acute opportunistic infection is discussed in the Initiating ART in the Setting of Active Opportunistic Infections and Cancer section below.

The success of ART depends on addressing barriers to care and on reliable ART access and adherence support. Identification and elimination of barriers is especially crucial to the success of rapid ART initiation programs. Barriers often include lack of transportation, housing instability,[7] food insecurity, racism,[8] out-of-pocket drug costs, pharmacy availability, restrictive clinic hours, stigma, and discrimination. Barriers that impair care engagement and ART access and adherence should be identified and addressed using evidence-informed methods (evidence rating: AIIa). These include individual-level interventions such as case management and patient/peer navigation to initiate linkage to care and social services; transportation and accompaniment to visits; appointment reminders; and psychosocial support.[9] Evidence-based structural interventions include "data to care" (using data systems to identify people who are out of care, to provide services), mobile clinics, telehealth, street medicine, use of visiting nurses, expanded clinic hours, pharmacy delivery,

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 Canadian Task Force on Periodic Health Examination.[2]

use of community health workers, and use of strategies to eliminate health care–related stigma and discrimination.[10]

The panel recommends initiating ART at the time of diagnosis for persons with acute HIV infection (evidence rating: AIIa). Immediate ART initiation leads to rapid viral suppression, thus decreasing the risk of transmission to others, and preserves immune responses.[4,11,12] Additionally, early ART initiation is associated with a lower viral reservoir.[13] People with HIV who have low or undetectable HIV RNA levels without taking ART ("elite controllers") have elevated levels of inflammation that are reduced after ART is initiated.[14,15] In addition, even those who manifest low viral loads initially often do not maintain control over time.[16] Based on the theoretical benefits of reducing inflammation in people with HIV, treating elite controllers is reasonable.

Initial ART Regimens for Individuals With HIV

Recommended initial ART regimens for individuals with HIV are reported in **Box 2**. Regimens containing the InSTIs bictegravir (BIC) or dolutegravir (DTG) are recommended as initial treatment for most individuals owing to their high efficacy, tolerability, safety, and high barrier to resistance; low pill burden; and low potential for drug-drug interactions (evidence rating: AIa). InSTI-based regimens also result in faster viral suppression than regimens containing a protease inhibitor (PI) (eg, boosted darunavir) or nonnucleoside reverse transcriptase inhibitor (NNRTI).[17]

Tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF) (herein TXF)/emtricitabine (FTC) or lamivudine (3TC) (herein XTC) are recommended as nucleoside reverse transcriptase inhibitor (nRTI) components of initial ART regimens (when DTG/3TC is not used) (evidence rating: AIa). Abacavir is no longer recommended as initial therapy in most people with HIV owing to concerns about its association with cardiovascular disease,[1,18] the risk of abacavir hypersensitivity, the burden of HLA B*5701 testing, and no substantial advantage over DTG/3TC alone.

Box 1. Key Recommendations for When to Start Antiretroviral Therapy (ART)

- 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 patient is ready and there is no suspicion for a concurrent 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 identified and addressed using evidence-informed strategies (evidence rating: AIIa)
- Initiation of ART at the time of diagnosis of acute HIV infection 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 less than 50/μL (evidence rating: AIa)
  - For those with tuberculous meningitis, high-dose steroids should be initiated along with tuberculosis treatment and ART should be initiated within 2 weeks after starting tuberculosis treatment and steroids (evidence rating: BIa)
  - For individuals with cryptococcal meningitis with access to close monitoring and supportive care for adverse events, ART should be initiated 2 to 4 weeks after starting antifungal therapy (evidence rating: BIIb); ART-naive individuals who have asymptomatic cryptococcal antigenemia and a negative lumbar puncture result with no evidence of cryptococcal meningitis should start ART immediately (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: BIIa)

DTG/3TC is the only 2-drug regimen currently recommended for initial therapy, but it should only be used when HIV RNA level is less than 500 000 copies/mL and neither hepatitis B coinfection nor lamivudine resistance is present (evidence rating: AIa). Accordingly, DTG/3TC should not be used for rapid ART initiation when these laboratory results are not yet available. Long-acting cabotegravir with rilpivirine is not recommended for initial ART, although its use has been explored in a small demonstration project (see Switches to Long-acting Cabotegravir and Rilpivirine section below).[19]

Although InSTIs and tenofovir alafenamide have been implicated in weight gain for some individuals and preliminary data raise concern about metabolic adverse effects with InSTIs, such concerns do not override the potential benefit of these drugs. Clinicians should provide resources and counsel patients regarding lifestyle changes that may ameliorate weight gain and other metabolic concerns (evidence rating: AIII) (see Weight Gain and Metabolic Complications With ART section below).

Initiation of ART in the Setting of PrEP Failure

InSTI resistance has been observed in people who acquire HIV in the setting of cabotegravir PrEP.[20,21] A pharmacokinetic study predicted that concentrations of cabotegravir may persist for up to 2.5 or 4 years in some persons assigned male or female at birth, respectively.[22] If HIV is acquired in the setting of prior cabotegravir

Box 2. Recommended Initial Antiretroviral Therapy (ART) Regimens

Recommended for Most People With HIV

- The following are recommended (in alphabetical order) for most people with HIV:
  - BIC/TAF/FTC (evidence rating: AIa)
  - Dolutegravir plus TXF/XTC (evidence rating: AIa)
  - DTG/3TC (only if HIV RNA <500 000 copies/mL and HBV coinfection not present). This regimen should not be used for rapid initiation when genotype, HIV RNA, and HBV serology results are not yet available (evidence rating: AIa)
- Persons who acquired HIV while receiving preexposure prophylaxis with tenofovir alafenamide or tenofovir disoproxil fumarate with emtricitabine 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, a boosted PI regimen containing darunavir and TXF/XTC should be used (evidence rating: AIII)

Recommended During Pregnancy

- TAF/XTC plus dolutegravir (evidence rating: AIa), withTDF/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:
  - Raltegravir (400 mg twice daily) (evidence rating: AIIa)
  - Atazanavir plus ritonavir (evidence rating: BIIa)
  - Darunavir plus ritonavir (evidence rating: BIIa)
  - Rilpivirine (evidence rating: BIIa)

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

- Bictegravir
- Doravirine
- Cabotegravir
- DTG/3TC
- DTG/RPV

If patient is already taking, and stable while taking, bictegravir- or doravirine-containing regimens or the 2-drug regimens DTG/3TC or DTG/RPV and wishes to continue, counsel patient about uncertainties regarding safety during pregnancy and monitor HIV RNA more frequently

Should Not Be Used During Pregnancy Because of Inadequate Drug Levels

- Cobicistat-containing regimens (evidence rating: AIIb)

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

- TXF/XTC is recommended with 1 of the following[a]:
  - Dolutegravir (50 mg twice daily) (evidence rating: BIa)
  - Efavirenz (600 mg) (evidence rating: AIa)
  - Raltegravir (800 mg twice daily) (evidence rating: BIa)
- A ritonavir-boosted PI 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: BIII)
- Bictegravir, darunavir boosted with ritonavir or cobicistat, doravirine, EVG/COBI, long-acting cabotegravir plus rilpivirine, etravirine, and rilpivirine are not recommended with rifampin because of drug-drug interactions (evidence rating: AIIa)
- DTG/3TC is not recommended with rifampin because of drug-drug interactions and inadequate data (evidence rating: BIII)

Abbreviations: BIC, bictegravir; COBI, cobicistat; DTG, dolutegravir; EVG, elvitegravir; FTC, emtricitabine; HBV, hepatitis B virus; InSTI, integrase strand transfer inhibitor; PI, protease inhibitor; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; 3TC, lamivudine; TXF, tenofovir alafenamide or tenofovir disoproxil fumarate; XTC, emtricitabine or lamivudine.

[a] There is a pharmacokinetic interaction between rifampin and tenofovir alafenamide; clinical data with coadministration are limited.

PrEP, the results of an InSTI genotype test should be available before starting an InSTI-based regimen (evidence rating: AIII). If ART is to be started before resistance testing results are available, or such testing is not available (owing to resource constraints or inability to amplify with a low viral load), a boosted darunavir regimen with TXF/XTC should be started (evidence rating: AIII).

In persons diagnosed with HIV while receiving TXF-based PrEP, resistance testing should be performed but initiation of ART need not be delayed while awaiting genotype results. A 3-drug regimen, preferably dolutegravir or bictegravir with TXF/XTC, is recommended until genotype results are available (evidence rating: AIII); in the rare but most extreme case of TXF/XTC-induced resistance associated with K65R and M184V mutations, TXF/XTC plus dolutegravir or bictegravir would still be expected to be active.

ART and Pregnancy

All persons with HIV who are pregnant should be receiving ART for their own health and to prevent transmission of HIV to the fetus.[1] Those diagnosed with HIV during pregnancy should begin ART immediately with a recommended 3-drug regimen (evidence rating: AIa). Cobicistat should not be used during pregnancy owing to low drug levels that can impair efficacy (evidence rating: AIIb). At present, there are insufficient data to recommend initiation with bictegravir, doravirine, cabotegravir, and DTG/3TC during pregnancy (evidence rating: AIII). Although bictegravir, doravirine, DTG/3TC, or DTG/RPV should not be initiated during pregnancy, if patients are already stable with these regimens and choose to continue after being informed about the insufficient data, they should be followed up with more frequent HIV RNA monitoring (evidence rating: CIII).[23]

Although preliminary data from the Tsepamo study initially suggested an association between neural tube defects and dolutegravir exposure at the time of conception, updated results now show no statistically significant difference in the incidence of neural tube defects between regimens with and without dolutegravir when taken at the time of conception.[24] Dolutegravir, therefore, is a recommended agent for most people with HIV, including during pregnancy. The IMPAACT 2010 trial found dolutegravir regimens to be virologically superior to efavirenz (EFV)/TDF/FTC and demonstrated that dolutegravir plus TAF/FTC was associated with lower rates of adverse events and improved infant outcomes. Therefore, the recommended regimen for pregnancy is

TAF/XTC plus dolutegravir (evidence rating: AIa), with TDF/XTC plus dolutegravir a suitable alternative if tenofovir alafenamide is not available (evidence rating: AIa). In the same study, efavirenz was associated with higher levels of infant growth stunting than dolutegravir.[25,26] An analysis from the Pediatric HIV/AIDS Cohort and the Swiss Mother and Child HIV Cohort also supports the use of dolutegravir in pregnancy, finding that rates of viral suppression with ritonavir-boosted atazanavir or raltegravir were lower than with dolutegravir.[27]

Initiating ART in the Setting of Active Opportunistic Infections and Cancer

For persons with a concurrent opportunistic infection, initiation of ART within 2 weeks of initiation of treatment for the opportunistic infection is recommended, except where evidence supports delaying ART because of increased risk of morbidity or mortality from immune reconstitution inflammatory syndrome. With the availability of InSTIs and the use of adjunctive corticosteroid therapy, earlier recommendations for delaying *Mycobacterium tuberculosis* treatment have been reconsidered. For persons with active tuberculosis, ART should be initiated within 2 weeks after starting treatment for tuberculosis, particularly if the CD4 cell count is less than 50/μL (evidence rating: AIa). For those with tuberculous meningitis, high-dose steroids along with tuberculosis treatment is recommended, with ART initiation within 2 weeks thereafter (evidence rating: BIa).[28]

For persons with cryptococcal meningitis and with access to close monitoring and supportive care for adverse events, ART should be initiated 2 to 4 weeks after starting antifungal therapy (evidence rating: BIIb). The data supporting a delay in ART initiation for persons with cryptococcal meningitis were largely generated in resource-constrained settings where access to close monitoring and supportive care may not be as readily available and in persons who were not being treated with InSTI-based ART. A cohort study that did not show an increase in adverse outcomes with earlier initiation of ART[29] coupled with the availability of ART regimens with lower rates of adverse effects and drug interactions support earlier ART initiation. ART-naive individuals who have asymptomatic cryptococcal antigenemia and a negative lumbar puncture result should start ART immediately[30] (evidence rating: BIII), as should patients with cancer and untreated HIV (evidence rating: BIIa).

Drug-drug interactions must be considered for all patients, but particularly for those with a diagnosis of HIV and tuberculosis. The only regimens that may be safely used with rifampin include dolutegravir (50 mg twice daily[31]) (evidence rating: BIa), efavirenz (600 mg once daily) (evidence rating: AIa), or raltegravir (800 mg twice daily) (evidence rating: BIa) (but not raltegravir [400 mg twice daily[32]] [evidence rating: AIa]), each given with TXF/XTC.[31-33] (There is a pharmacokinetic interaction between rifampin and tenofovir alafenamide; clinical data with coadministration are limited.) There are inadequate data to support use of DTG/3TC in this setting (evidence rating: BIII). Poorer adherence with twice-daily raltegravir contributed to increased virologic failure in 1 study, underscoring the need for adherence support when twice-daily regimens are used.[34] If none of these regimens can be used, ritonavir-boosted atazanavir or lopinavir with TXF/XTC may be used with rifabutin (150 mg daily).

Table 2. Other Recommended Initial Antiretroviral Therapy (ART) Regimens

Regimen[a,b]	Potential uses and cautions
DRV/COBI/TAF/FTC[c]	Preferred for patients with prior cabotegravir PrEP exposure when an InSTI genotype is not available
Darunavir plus cobicistat or ritonavir plus TXF/XTC	Potential use for known or suspected pretherapy multidrug resistance or InSTI resistance or in people with HIV at high risk of poor adherence
DOR/TDF/3TC[c] or doravirine plus TXF/XTC	May be useful in people with HIV who have intolerance to InSTIs
EFV (600 or 400 mg)/TDF/FTC or 3TC[c]	Potential use for treatment of HIV/tuberculosis coinfection; pregnancy or pregnancy intention
Raltegravir plus TXF/XTC	Potential use for treatment of HIV/tuberculosis; pregnancy or pregnancy intention; when there is high risk of drug-drug interactions
RPV/TAF/FTC[c]	Small pill size; use only if pretreatment HIV RNA level is <100 000 copies/mL and CD4 cell count is >200/μL
Rilpivirine plus TDF/3TC[d]	Use only if pretreatment HIV RNA level is <100 000 copies/mL and CD4 cell count is >200/μL

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

[a] The recommended initial ART regimens are reported in Box 2.

[b] Regimens are listed in alphabetical order. Drug components separated with a virgule (/) indicate that these are available as coformulations.

[c] Available as a single-tablet coformulation.

[d] Available in generic formulations in many countries.

Other Recommended Regimens

Other recommended regimens appear in **Table 2**. Although InSTI-based regimens are recommended for most persons, there are special circumstances in which other regimens may be considered as initial ART. A boosted darunavir regimen may be used when InSTI or multidrug resistance is a consideration, including when there has been prior exposure to cabotegravir as PrEP (evidence rating: AIIb).

When and How to Switch ART Regimens

Regimen switches can be broadly categorized into those for patients with and for patients without viral suppression. Both indications for switching treatment require careful review of a patient's ART regimen history, medication tolerability, concomitant medications, food requirements, reproductive plans, potential issues with insurance and coverage, and results from all prior resistance testing before switching (evidence rating: AIII).

Regimen changes should also prompt more frequent clinical and laboratory follow-up until it is established that the regimen is well tolerated, not associated with toxicity, and is effective (evidence rating: AIII), with the first assessment of HIV RNA and safety laboratory assays at approximately 1 month after changing therapy. For patients who switched owing to virologic failure, the viral load test should be repeated monthly until suppression to undetectable is documented and then every 6 months thereafter (evidence rating: AIa).

Switching in the Setting of Viral Suppression

Persons with suppressed virus and no history of transmitted or acquired HIV drug resistance can generally switch therapy to any of the recommended initial regimens and maintain viral suppression. Recently, there has been increased interest in 2-drug strategies as a way of reducing drug exposure. Most data supporting this strategy come from prospective randomized trials of persons with no history of treatment failure switching to DTG/3TC[35,36] or DTG/RPV.[37] These studies demonstrated ongoing viral suppression comparable to continued 3-drug treatment, without evidence of loss of virologic control.[38] In addition, InSTI resistance was not observed in these studies, although NNRTI resistance occurred in 1% of participants receiving DTG/RPV. Furthermore, retrospective studies of baseline samples in the trials of DTG/3TC showed no adverse effect from archived resistance mutations, including M184V.[39,40] Thus, unless there is documented or suspected history of treatment failure, proviral resistance testing is not required prior to switching to 2-drug therapy, even if there is no available pretreatment resistance test result (evidence rating: BII).

An important limitation of both 2-drug regimens is that they provide insufficient treatment for people with concomitant chronic hepatitis B who should, therefore, continue 3-drug regimens that include TXF/XTC. Furthermore, all people with HIV who lack immunity to hepatitis B should undergo immunization. Recent data show that hepatitis B CpG oligodeoxynucleotide vaccine (which is being investigated and compared with other vaccines in an ongoing clinical trial) is highly immunogenic in people with HIV who have high CD4 cell counts and suppressed virus while receiving ART.[41] Documenting a seropositive response to the vaccine is recommended prior to switching from a TXF-based 3-drug regimen to a 2-drug regimen that does not include TXF.

Recent clinical trials in persons with viral suppression have demonstrated the safety of switching to dolutegravir plus 2 nRTIs or BIC/FTC/TAF, even in the setting of likely or proven nRTI resistance. In the 2SD study conducted in Kenya, participants receiving second-line regimens consisting of a boosted PI plus nRTIs were randomly assigned to continue their current treatment or switch to dolutegravir plus 2 nRTIs.[42] At 48 weeks, dolutegravir plus 2 nRTIs was noninferior to the continued therapy. Although no prior resistance assessments were performed in that trial, other studies of second-line boosted PI regimens in Africa have shown extensive nRTI resistance, including high rates of M184V and K65R mutations, and such resistance would be expected in the population enrolled in the 2SD trial.

Similar results have been seen with switches to BIC/FTC/TAF in people with resistant virus.[43,44] Preexisting M184V/I mutations had no effect on efficacy in this setting.[45] In addition, prospective studies of people with treatment failure show high rates of viral suppression with dolutegravir plus 2 nRTIs,[46,47] implying that this regimen would maintain suppression regardless of nRTI resistance. By contrast, switches to first-generation InSTIs (raltegravir or elvitegravir) or NNRTIs from high resistance–barrier regimens containing a boosted PI are not recommended (evidence rating: AIa). The use of dolutegravir plus TXF/XTC or BIC/FTC/TAF in patients with current viral suppression and a documented history of M184V and K65R mutations is supported by the existing data from switch and failure studies. Situations where such regimens might be chosen include limited other treatment options, to avoid drug interactions or to maximize treatment simplicity to enhance adherence.

Switches to Long-acting Cabotegravir and Rilpivirine

In persons with no history of treatment failure and no known or suspected resistance to either drug, injectable cabotegravir and rilpivirine, given either every 1 or 2 months, was noninferior to continued oral ART.[48,49] Those interested in non-oral options for ART because of privacy, stigma, or convenience reasons will usually have greater satisfaction with cabotegravir and rilpivirine than continued oral ART.[50] One recent report described use of this regimen in 15 people with viremia not receiving oral ART.[19] Despite the short-term success of this approach in this study, cabotegravir plus rilpivirine is not recommended in the setting of viremia outside of a research setting and should be started only after viral suppression has been achieved with oral ART.

Cabotegravir plus rilpivirine injections can be started after an oral lead-in to ensure tolerability or, alternatively, without an oral cabotegravir plus rilpivirine lead-in based on patient preference.[51] Since the regimen is administered by clinic staff, cabotegravir plus rilpivirine requires more clinical resources than oral ART. Staff must be trained in proper administration techniques; in addition, the prescribing clinician will need to ensure that pharmacy, insurance, and scheduling logistics are in place prior to offering this therapy. Moreover, patients need to travel to and from sites of administration, which may pose a barrier for some individuals.

Even among patients who receive all of the scheduled injections in a timely fashion, there is a risk of treatment failure with emergent resistance, including both InSTI and NNRTI mutations in some. Although this risk is small (approximately 1%-2% in clinical trials), it is higher than for continued oral ART with dolutegravir- or bictegravir-based regimens, and patients should be informed of this risk prior to switching to long-acting injectable ART. The risk appears to be higher when giving cabotegravir plus rilpivirine every 8 weeks than every 4 weeks. Treatment options for those who experience treatment failure with long-acting cabotegravir plus rilpivirine and develop resistance will be limited, because neither NNRTI-based nor InSTI-based regimens are optimal choices.

If scheduled doses of cabotegravir plus rilpivirine are missed, resumption of therapy should follow redosing guidance as outlined in the product prescribing information. For patients who have maintained viral suppression, switching from long-acting injectable cabotegravir plus rilpivirine back to daily oral therapy can be done without the need for proviral DNA resistance testing (evidence rating: BIII).

Switching for Virologic Failure

Virologic failure (defined as HIV RNA level >200 copies/mL) should be confirmed by repeating a viral load measurement as soon as possible. If virologic failure is confirmed, genotype resistance testing should be performed, preferably while patients are taking the failing therapy. Resistance testing is still recommended even if a regimen has been discontinued or a person acknowledges poor medication adherence (evidence rating: AIII).

Proviral DNA resistance testing can identify resistance even if HIV RNA level is less than 500 copies/mL (including undetectable levels), but results of such testing do not correlate reliably with

Table 3. Recommendations for Laboratory Monitoring for Persons With HIV

Description of monitoring	At HIV diagnosis and start of ART	During ART	At virologic failure
HIV RNA level	Yes (evidence rating: AIII)	Every 3 mo until suppressed and then every 6 mo (evidence rating: AIa)	Yes (evidence rating: AIa)
CD4 cell count	Yes (evidence rating: AIII)	Every 6 mo until >250 cells/uL for 1 y, then stop provided viral suppression is maintained (evidence rating: BIII)	Yes (evidence rating: AIII)
HIV RT-pro genotype test	Yes (evidence rating: AIII)	If switching to injectable ART when patient has viral suppression, proviral RT-pro genotype can be collected for those who do not have a documented pre-ART RT-pro genotype (evidence rating: BIII)	Yes (evidence rating: AIa)
HIV integrase genotype test	If a patient's partner is known to have a failing ART regimen that includes an InSTI or individual has received cabotegravir for PrEP (evidence rating: BIII)		If failing ART regimen included an InSTI (evidence rating: AIII)
Viral tropism test			Before start of maraviroc (evidence rating: AIa)
HLA B*5701 test	Before start of abacavir (evidence rating: AIa)		
Cryptococcal antigen test if CD4 cell count <100 cells/μL	Yes (evidence rating: AIa)		
Safety laboratory and coinfection screening (eg, STIs, viral hepatitis)	Yes (evidence rating: AIa)	Yes (evidence rating: AIII)	Yes (evidence rating: AIII)

Abbreviations: ART, antiretroviral therapy; InSTI, integrase strand transfer inhibitor; PrEP, preexposure prophylaxis; RT-pro, reverse transcriptase–protease; STI, sexually transmitted infection.

standard genotypes and may miss important mutations, so results should be interpreted with caution.[52]

The most common reason for virologic failure is poor medication adherence. Additional potential causes such as food effects, drug interactions, and pharmacy dispensing errors should be investigated. If no resistance mutations are found, clinicians should offer tools to improve adherence and regimen change to improve simplicity or tolerability, if indicated. Based on the results of prospective clinical trials, dolutegravir plus 2 nRTIs (with at least 1 active nRTI as determined by genotypic testing) is recommended after treatment failure with an NNRTI plus 2 nRTIs (evidence rating: AIa).[1] Although not studied in virologic failure, BIC/FTC/TAF should have similar activity to dolutegravir plus TXF/XTC. If no active nRTIs are present after virologic failure and a boosted PI and an InSTI remain fully active, then treatment choices include boosted darunavir plus TXF/XTC (evidence rating: AIa) or dolutegravir plus a boosted PI with or without additional agent(s) (evidence rating: BIII). Dolutegravir plus TXF/XTC (evidence rating: AIa) is an alternative option to avoid drug interactions and maximize treatment simplicity, although this regimen has an approximate 4% risk of emergence of dolutegravir resistance.[47]

Management of InSTI resistance can be difficult. Owing to the rarity of such resistance, the common presence of extensive resistance to other drug classes, and relative paucity of prospective studies evaluating treatment outcomes in this population, guidance from an expert in HIV drug resistance is recommended for selection of an optimal regimen (evidence rating: AIII).

If InSTI resistance is relatively limited (as commonly occurs after treatment failure with raltegravir or elvitegravir) and a new ART regimen is to include an InSTI, dolutegravir should be administered twice daily.[53] This regimen should also include at least 1 and preferably 2 other fully active drugs, optimally from drug classes not previously used. These might include fostemsavir (except for treatment of HIV subtype CRF01_AE, because available data suggest that this subtype has naturally occurring resistance to fostemsavir),[54] lenacapavir (currently approved in the European Union and under US Food and Drug Administration [FDA] review), maraviroc (if the patient's virus is documented to be R5 tropic when tested), ibalizumab, or enfuvirtide. Recycling of nRTIs with partial antiretroviral activity may also be warranted.

If there is both high-level InSTI resistance and decreased PI susceptibility, then a multidrug regimen with at least 2 fully active agents from these novel drug classes should be used, along with recycled nRTIs because of their ongoing partial antiviral activity (evidence rating: AIII).

Laboratory Monitoring in Individuals With Established HIV at HIV Diagnosis and Starting ART

Recommendations are summarized in **Table 3**. Recommended laboratory monitoring before ART is started (evidence rating: AIII) should characterize (1) HIV stage (HIV RNA level, CD4 cell count), (2) general health (kidney and liver function, lipid levels, complete blood cell count, glucose level, and pregnancy), (3) ART resistance (reverse transcriptase–protease [RT-pro] genotype), and (4) presence of coinfections (viral hepatitis A, B, and C; tuberculosis; and sexually transmitted infections [STIs]). Unless there is a history of preexisting kidney or liver injury or a high likelihood of transmitted drug resistance, the results of these laboratory tests should not delay starting ART (evidence rating: BIII), but follow-up of these results should occur quickly to maximize safety. Given the low prevalence of transmitted InSTI resistance,[55] InSTI genotyping prior to ART initiation is not recommended unless there is suspicion that infection was transmitted from a partner with InSTI failure or if the patient previously received PrEP with cabotegravir (evidence rating: BIII).[1,56] An assessment for latent tuberculosis (initially, after immune reconstitution, and then if there is exposure) and, if the

Box 3. Weight Gain and Metabolic Complications While Receiving Antiretroviral Therapy (ART)

- Documentation of weight and BMI at baseline and every 6 months is recommended for people with HIV initiating or switching regimens to identify those with excessive weight gain (evidence rating: AIIa)
- Counseling regarding possibility of weight gain and potential cardiometabolic complications is recommended for people with HIV initiating or switching ART (evidence rating: AIII)
- Yearly diabetes screening and assessment of cardiovascular risk score of patients receiving InSTI-based ART is recommended (evidence rating: BIII)
- Lifestyle changes (exercise and diet) are recommended to support people with HIV who gain greater than 5% body weight (evidence rating: AIII)

Abbreviations: BMI, body mass index; InSTI, integrase strand transfer inhibitor.

CD4 cell count is less than 100 cells/μL, cryptococcal antigen testing at presentation should be performed.

During ART

Within 6 weeks of starting ART, assessment of treatment adherence and tolerability is recommended, along with the measurement of HIV RNA level (evidence rating: BIII). Although suppression of HIV RNA levels to undetectable may occur faster with InSTI-based regimens, it may take up to 24 weeks of continuous therapy.[57,58] If the HIV RNA level has not declined by 2 $\log_{10}$ copies/mL within 12 weeks of therapy and adherence appears to be sufficient, then a genotype based on the patient's regimen is recommended (evidence rating: AIII).[1]

If the patient remains virally suppressed, clinically stable, and adherent to medications, then HIV RNA levels should be monitored every 3 months until virally suppressed for at least 1 year. Afterward, the frequency of viral monitoring can be changed to every 6 months (evidence rating: AIII).

Before starting an injectable ART regimen for a patient with viral suppression, proviral RT-pro genotype should be collected for those who do not have a documented pre-ART RT-pro genotype (evidence rating: BIII). Of note, NNRTI resistance may not always be detected by a proviral genotype, and proviral genotyping has not yet been validated as a method to decide whether it is safe to switch to injectable cabotegravir plus rilpivirine. If a patient has rilpivirine-associated mutations on genotypic testing or a history of virologic failure while receiving an NNRTI, injectable cabotegravir plus rilpivirine should be avoided (evidence rating: BIa).[48,59]

Once viral suppression occurs with ART, CD4 cell counts should be measured every 6 months until they are greater than 250 cells/μL for at least 1 year (evidence rating: AIII).[1] Afterward, CD4 cell counts do not need to be measured unless ART failure is identified or the patient experiences an immunosuppressive condition (evidence rating: AIII). Patients receiving tenofovir disoproxil fumarate should also have urinary glucose and protein monitoring when starting tenofovir disoproxil fumarate and at least every year thereafter (evidence rating: BIII).[60-64]

Patients should have regular age- and risk-appropriate screening for coinfections such as STIs (at all exposed mucosal sites), tuberculosis, and viral hepatitis; cancer screening (including for cervical and anal cancer); general health maintenance assessments; vaccinations; and evaluation for medication toxicity at each visit.[65]

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

If an HIV RNA level greater than 20 to 50 copies/mL is detected during ART after previous viral suppression, then an early repeat HIV RNA level and assessment of medication adherence, drug-drug interactions, and tolerability is recommended (evidence rating: AIa).[1] If HIV RNA level is greater than 200 copies/mL on 2 consecutive measurements, then HIV RT-pro genotype and InSTI genotype (if the patient was receiving an InSTI) testing are recommended (evidence rating: AIII).[1] For patients with intermittent or persistent low-level viremia between 50 and 200 copies/mL, assessments for ART adherence, tolerability, and toxic effects are recommended (evidence rating: CI), but changing ART regimens is not recommended unless ART toxicity or intolerability are identified (evidence rating: AIII). Of note, a common cause of low-level viremia in patients receiving an InSTI are interactions with multivalent cations (Ca^{2+}, Fe^{3+}, Mg^{2+}, Al^{3+}, Zn^{2+}), such as those in mineral supplements and antacids.[1] Before starting maraviroc, testing for viral CCR5 tropism is recommended each time (unless X4 virus was previously detected), in which case maraviroc should not be used (evidence rating: AIa).

Weight Gain and Metabolic Complications With ART

Recommendations are summarized in **Box 3**. Weight gain is generally observed within the first year following initiation of most ART regimens, but treatment with InSTI- and tenofovir alafenamide–based regimens is associated with greater weight gain than regimens containing tenofovir disoproxil fumarate, efavirenz, or a boosted PI. Weight gain can occur with (1) initiation of InSTI- or tenofovir alafenamide–containing ART in previously ART-naive individuals[66]; (2) switch to InSTI- or tenofovir alafenamide–containing ART in individuals with viral suppression[67]; or (3) initiation of tenofovir alafenamide or InSTI for PrEP.[68] This weight gain with ART is more likely to occur in women and Black and Hispanic individuals and appears to occur mostly within the first year of ART initiation[69] or switch.[70] In the ADVANCE trial, most of the weight gain in dolutegravir groups was fat gain in trunk and limbs, and it was higher with concomitant tenofovir alafenamide use.[71]

Exposure to efavirenz or tenofovir disoproxil fumarate for ART or PrEP is associated with weight suppression, compared with other antiretroviral drugs or no ART exposure.[72] This might complicate assessment of weight gain after switching from tenofovir disoproxil fumarate to tenofovir alafenamide or after changing efavirenz to an InSTI.

Weight gain while receiving an InSTI is likely mediated by adipocyte dysfunction, inducing adipogenesis, lipogenesis, oxidative stress, fibrosis, and insulin resistance.[73,74] CYP2B6 genotypes have been associated with greater weight gain after switch from efavirenz to InSTI-based ART.[75] Mechanism(s) of tenofovir alafenamide–associated weight gain remain incompletely elucidated. A switch from tenofovir disoproxil fumarate to tenofovir

alafenamide is associated with increases in lipid levels and cardiovascular risk score, perhaps because tenofovir disoproxil fumarate lowers lipid levels.[76]

Although decreased in the general population, the risk of cardiovascular disease has not declined among people with HIV.[77] In addition to traditional risk factors and the chronic inflammation associated with HIV itself, some ART regimens may contribute to this risk, but more research is needed. Recent cohort studies suggest that InSTI-based ART may be associated with an increased risk of incident cardiovascular disease, new-onset diabetes, hyperglycemia,[78-80] elevated blood pressure,[80] and de novo hepatic steatosis. These cardiometabolic effects were not observed in other studies, and it remains unclear whether they are transient or sustained or whether InSTI exposure is causative. The retrospective nature and lack of availability of weight measurements in most data make it difficult to ascertain whether this risk (if confirmed) is a direct InSTI toxic effect or the result of InSTI-related weight gain. In one study, the InSTI-diabetes association was attenuated when accounting for 12-month weight change.[81] Nonetheless, data suggest that diabetes risk with weight gain at ART initiation is significant.[82] Further research is needed to evaluate the role of appetite, caloric intake, and energy expenditure in InSTI- and tenofovir alafenamide–related weight gain.

Whether weight gain is reversible with switch to non-InSTI or non–tenofovir alafenamide regimens is unclear and under investigation (ClinicalTrials.gov Identifier: NCT04636437). Data from the SALSA[83] and TANGO[39] studies suggest that switching off of tenofovir alafenamide does not lead to weight loss. Until there are data proving benefit, switching regimens because of weight gain is not recommended (evidence rating: BIIa); instead, lifestyle modifications, like exercise and diet intervention, are recommended (evidence rating: AIII). Semaglutide and other glucagon-like peptide 1 analogues that decrease weight in people without HIV are being studied in people with HIV.[84,85]

HIV and Aging

Recommendations for older people with established HIV are summarized in **Box 4**. Not only is the prevalence of HIV and diagnoses of new infections in people older than 50 years increasing, but more than half of older people with HIV are diagnosed at a late stage of disease (ie, CD4 cell count <350/μL).[86,87] Delayed diagnosis is a lost opportunity to initiate ART early for maximal health benefits and for prevention of transmission.

Early diagnosis and initiation of ART is particularly important in older persons because they are more likely to have a blunted immune response following ART initiation[88] and have a higher risk of serious non-AIDS complications. Choice of initial ART requires consideration of the background risk and burden of non-AIDS comorbidity, drug-drug interactions, and polypharmacy to manage multimorbidity in older people with HIV (evidence rating: BIII). Recommended initial ART includes InSTI-based regimens with TAF/FTC or DTG/3TC (see Initiation of ART section). Caution should be exercised in the use of tenofovir disoproxil fumarate because of its associated kidney and bone toxicity.[89] Studies of pharmacokinetics of ART are limited in older people with HIV. Whether clinically relevant pharmacokinetic changes and potential increased toxicity associated with aging require dose adjustment in older people with HIV remains unclear and is currently not warranted (evidence rating: AIII).[90]

Box 4. Recommendations for Older People With HIV

- Screening for HIV is recommended in older individuals to prevent late diagnosis with advanced disease (evidence rating: AIIa)
- Initiation of ART is recommended as soon as possible after diagnosis, either the same day of diagnosis, first clinic visit, or within 7 days. Assessment of comorbidities, kidney function, and medications will influence the choice of ART (evidence rating: AIa)
- Assessment of polypharmacy and simplification of complex regimens, both ART and comorbidity treatments, is recommended to improve adherence, prevent adverse drug-drug interactions, reduce falls risk, and reduce costs (evidence rating: AIIb)
- Screening for comorbidities, impaired cognitive and function, poor mobility, frailty, and falls risk is recommended for older people with HIV, using validated tools. The frequency of assessment is determined by the baseline assessment (evidence rating: BIII)[1]
- Consideration of integrated care models and Antiretroviral Stewardship models is recommended to improve outcomes and quality of life for people aging with HIV (evidence rating: BIII)

Abbreviation: ART, antiretroviral therapy.

Polypharmacy occurs more frequently in older people with HIV and is associated with increased risk of adverse health outcomes such as falls, frailty, hospitalization and mortality, and drug-drug interactions.[91] Management of polypharmacy includes (1) optimization of ART, including simplification of ART when possible (see When and How to Switch ART Regimens section), and (2) regular medication review with "pruning" of nonessential medications.[92,93] Antiretroviral stewardship programs effectively reduce medication errors, dose antiretroviral drugs appropriately for kidney and liver dysfunction, manage drug-drug interactions, and offer an opportunity to assess and deprescribe potentially inappropriate medication.[94]

There is an ongoing growing burden of neurocognitive dysfunction and frailty in people aging with HIV, which results in decreased quality of life, greater health care utilization, and higher mortality.[95,96] Recommendations for screening and management of comorbidities in older people with HIV, assessment of functional impairment and frailty, and evaluation of neurocognitive impairment are unchanged since the previous report.[1] Recent studies have shown that accumulation of comorbidities had greater negative effect on neurocognitive performance than did HIV disease parameters.[97,98] Intensification of ART with either dolutegravir or maraviroc did not improve cognitive impairment, despite lower cerebrospinal fluid HIV viral loads in the intensified group.[99] Aggressive management of comorbidities, rather than ART modification, may be the most beneficial strategy for improving neurocognitive function.

By the end of this decade, the proportion of people with HIV who will be older than 65 years is projected to be almost 25%.[100] The aging of people with HIV has highlighted the need for integrated care

models, including multidisciplinary teams of geriatricians, HIV specialists, pharmacists, and allied health practitioners (such as physiotherapists) offering holistic patient-centered care.[101-103]

Prevention of HIV Infection

Recommendations for HIV prevention are summarized in **Table 4**. Tools to prevent the acquisition of HIV infection are highly effective and continue to increase in breadth. Strategies to test, identify, link to care, and quickly treat and virally suppress individuals with HIV are crucial to prevention efforts (evidence rating: AIa); such efforts have health benefit for the individual and eliminate sexual transmission of HIV. Use of condoms continues to be recommended as the cornerstone of STI prevention efforts for all penetrative sex acts (evidence rating: AIIa). Medical circumcision for heterosexual males and harm reduction interventions (including but not limited to medication treatment for opioid use disorder and syringe access) are effective prevention strategies for applicable populations.

PrEP should be discussed with all sexually active adolescents and adults and anyone who injects nonprescription drugs (eg, opioids, methamphetamine) or who has a substance use disorder, without specific criteria for risk behaviors or screening tools (evidence rating: AIII).[105] Populations with disproportionately high HIV incidence rates should be particularly encouraged to consider PrEP as part of their HIV prevention plans; these include cisgender men and transgender individuals who have sex with men; young adults and adolescents; people whose sexual partners are from regions of generalized HIV epidemic; persons who use nonprescription drugs and alcohol; individuals who exchange sex for money, goods, or services; partners of incarcerated individuals; and anyone with a recent bacterial STI. Prescription of PrEP for adolescents should be done with specific attention to their additional support and adherence needs (evidence rating: AIa) and with care around potential disclosure of sexual behaviors and gender identity to parents or guardians (evidence rating: AIII).

Choosing the PrEP Regimen

The optimal PrEP regimen for a given person is the one most acceptable to that person and congruent with their sexual behavior, ability to take medications reliably, likelihood of anticipating sexual activity, and adverse effect profile. The choice of PrEP regimen made initially may need to be reconsidered over time. For example, someone challenged by taking daily oral tablets is likely to have better prevention effectiveness from an injectable regimen; for someone who prefers to take an oral medication, that preference should be respected.

Oral PrEP Regimens

Daily oral TDF/FTC (including generic tenofovir formulations) remains a recommended PrEP regimen for all populations at risk (evidence rating: AIa). For cisgender males, oral dosing should be initiated with a double dose of TDF/FTC for the first day, followed by daily single tablets, and should not be discontinued until at least 2 doses after last sexual activity[1]; this approach is anticipated to provide protection within 24 hours of initial dosing. For non–cisgender male populations, 7 days of daily dosing is likely required to reach maximal protection and is recommended for at least 7 days after last risk activity.[1] This daily regimen is also recommended for people who are pregnant or breastfeeding (evidence rating: AIIa).

On-demand (2-1-1) oral dosing is recommended for cisgender men of any sexual orientation, but there are insufficient data to support its use to prevent HIV acquisition via receptive vaginal sex (including neovaginal sex) or injection drug use. TDF/FTC 2-1-1 dosing is initiated with a double dose 2 to 24 hours before planned sexual activity and single additional doses 24 and 48 hours subsequent to the first dose; if additional sexual activity occurs within 7 days of the initial planned activity, daily single dosing should be continued until 2 doses after the last planned activity. The 2-1-1 regimen should be used with caution in transgender women receiving gender-affirming hormone therapy, particularly with first use, or reinitiation of TDF/FTC after prolonged hiatus, because rectal tissue concentrations may be somewhat lower early after starting 2-1-1 regimens and may have reduced efficacy.[106,107]

Daily oral TAF/FTC is preferred over TDF/FTC for individuals with creatinine clearance between 30 and 60 mL/min or when there is known osteopenia or osteoporosis. (Bone density scans are not necessary before starting TDF/FTC.) Further, TAF/FTC use should be limited to cisgender men of any sexual orientation and anyone whose risks do not include receptive vaginal sex (including neovaginal sex) or those whose risk is exclusively posed by injection drug use. Data on efficacy of TAF/FTC for preventing HIV acquisition through receptive vaginal sex are not available.

Prescribing for all oral PrEP regimens (including the 2-1-1 regimen) should be for no more than 1 month initially and 3 months thereafter to ensure appropriate HIV testing intervals. Tenofovir-based oral PrEP regimens have extremely low failure rates when taken as prescribed.

Same-Day or Rapid PrEP Start

Delaying PrEP is not recommended for individuals at risk. If HIV test results are available from samples drawn within 7 days of initiation or if the result of a rapid (point-of-care) HIV antibody test is negative, then PrEP should be initiated while awaiting the results of HIV, hepatitis B, and kidney function testing, as long as the patient is willing to take such an approach. Clinicians should follow up on test results and make adjustments as needed. If a high-risk encounter occurred within the past 72 hours, then a 3-drug postexposure prophylaxis (PEP) regimen is recommended (evidence rating: AIa) (see below), which can be changed to PrEP on PEP completion.

Injectable PrEP Regimen

Long-acting injectable cabotegravir was approved by the FDA for the prevention of sexual acquisition of HIV infection in December 2021 and is recommended for prevention of sexual transmission of HIV across populations (evidence rating: AIa).[20,108] There are insufficient data to recommend its use for injection drug exposures, but if a person who injects drugs is also at risk for acquiring HIV through sex, cabotegravir is a recommended option (evidence rating: AIII). An oral lead-in of cabotegravir of approximately 1 month duration should be limited to those with severe atopic histories or concerns, because potential nonadherence to oral dosing may create a period

Table 4. Recommendations for Biomedical HIV Prevention by Population and Transmission Risk Behavior[a]

	TDF/FTC (evidence rating)[b]		Daily oral TAF/FTC (evidence rating)	Intramuscular cabotegravir (evidence rating)
	Daily oral	On-demand oral		
Cisgender men/women				
Insertive sex (vaginal/anal)	Yes (AIa)	Yes (BIa)	Yes (AIa)	Yes (AIa)
Receptive vaginal sex	Yes (AIa)	Insufficient data	Insufficient data	Yes (AIa)
Receptive anal sex	Yes (AIa)	Yes (AIa)	Yes (AIa)	Yes (AIa)
Injection drug use (if sexual risk as well, apply appropriate category above)[c]	Yes (AIa)	Insufficient data	Insufficient data	Insufficient data
Transgender women				
Insertive sex (vaginal/anal)	Yes (AIa)	Yes (AIII/CIII)[d]	Yes (AIa)	Yes (AIa)
Receptive (neo) vaginal sex	Yes (BIII)	Insufficient data	Insufficient data	Yes (BIII)
Receptive anal sex	Yes (AIa)	Yes (AIII/CIII)[d]	Yes (BIa)	Yes (AIa)
Injection drug use (if sexual risk as well, apply appropriate category above)[c]	Yes (AIa)	Insufficient data	Insufficient data	Insufficient data
Transgender men				
Receptive vaginal ("front-hole") sex	Yes (AIII)	Insufficient data	Insufficient data	Yes (AIII)
Receptive anal sex	Yes (AIII)	Yes (AIII)	Yes (AIII)	Yes (AIII)
Injection drug use (if sexual risk as well, apply appropriate category above)[c]	Yes (AIII)	Insufficient data	Insufficient data	Insufficient data
Prerequisites and safety considerations				
Creatinine clearance, mL/min	>60	>60	>30	No restrictions; caution with end-stage kidney disease not yet receiving dialysis
Drug-drug interactions	NA	NA	NA	Do not use with certain anticonvulsants and antimycobacterials[e] Adjust dosing if using with rifabutin[f]
Other	Avoid use if individual has known osteopenia or osteoporosis	Avoid use if individual has known osteopenia or osteoporosis; caution during first use for transgender woman who uses exogenous estrogens or androgen blockers	Not applicable	Use caution if gluteal fillers or implants are present or if patient is using anticoagulants or has bleeding diathesis or thrombocytopenia
Prescribing				
Initial	30-d supply	30-d supply	30-d supply	30 d of oral (optional) First and second injections separated by 4 wk
Follow-up	90-d supply	90-d supply	90-d supply	One injection every 8 wk[g]
Dosing	TDF (300 mg)/FTC (200 mg)	TDF (300 mg)/FTC (200 mg)	TAF (25 mg)/FTC (200 mg)	Oral: 30 mg
				Injection: 600 mg (3 mL)
Laboratory tests				
Initiation[h]	HIV Ag/Ab[i] HIV RNA[j] Creatinine HAV IgG[k] HBsAg HBsAb HCV IgG Gonorrhea/chlamydia NAAT[l] Syphilis test Pregnancy test[m]	HIV Ag/Ab[i] HIV RNA[j] Creatinine HAV IgG[k] HBsAg HBsAb HCV IgG Gonorrhea/chlamydia NAAT[l] Syphilis test Pregnancy test[m]	HIV Ag/Ab[i] HIV RNA[j] Creatinine HAV IgG[k] HBsAg HBsAb HCV IgG Gonorrhea/chlamydia NAAT[l] Syphilis test Pregnancy test[m]	HIV Ag/Ab[i] HIV RNA[j] HAV IgG[k] HBsAg HBsAb HCV IgG Gonorrhea/chlamydia NAAT[l] Syphilis test Pregnancy test[m]
After 1 mo	HIV Ag/Ab	HIV Ag/Ab	HIV Ag/Ab	HIV Ag/Ab HIV RNA[j,n]
Every 2 mo				HIV Ag/Ab HIV RNA

(continued)

Table 4. Recommendations for Biomedical HIV Prevention by Population and Transmission Risk Behavior[a] (continued)

	TDF/FTC (evidence rating)[b]		Daily oral TAF/FTC (evidence rating)	Intramuscular cabotegravir (evidence rating)
	Daily oral	On-demand oral		
Every 3-4 mo[o]	HIV Ag/Ab Creatinine[p] Gonorrhea/chlamydia NAAT[l] Syphilis[q] Pregnancy test[m]	HIV Ag/Ab Creatinine[p] Gonorrhea/chlamydia NAAT[l] Syphilis[q] Pregnancy test[m]	HIV Ag/Ab Creatinine[p] Gonorrhea/chlamydia NAAT[l] Syphilis[q] Pregnancy test[m]	HIV Ag/Ab HIV RNA Gonorrhea/chlamydia NAAT[1] Syphilis[q] Pregnancy test[m]
Annually	Creatinine HCV IgG[r]	Creatinine HCV IgG[r]	Creatinine HCV IgG[r]	HCV IgG[r]
HIV testing considerations	If discordant or difficult-to-interpret HIV test results, call CDC (800-232-4636) for additional guidance	If discordant or difficult-to-interpret HIV test results, call CDC (800-232-4636) for additional guidance	If discordant or difficult-to-interpret HIV test results, call CDC (800-232-4636) for additional guidance	Results of HIV Ag/Ab test and HIV RNA are not needed before administering follow-up injections If discordant or difficult-to-interpret HIV test results, call CDC (800-232-4636) for additional guidance
Other considerations				
Late or missed doses	When starting or after 7 or more consecutive missed doses, restart with double dose of TDF/FTC and resume 1 tablet daily	NA	Resume with single-tablet daily dosing	If any injection is more than 7 d late, consider oral "bridging" with daily oral TDF/FTC or TAF/FTC as appropriate for sexual risk factors until injections can be resumed If any injection is ≥8 wk late, reload with 4-wk interval before resuming with 8-wk interval injections
ART regimen in the event of HIV acquisition	Bictegravir or dolutegravir + TXF/XTC	Bictegravir or dolutegravir + TXF/XTC	Bictegravir or dolutegravir + TXF/XTC	TXF/XTC/RTV/DRV (or COBI/DRV) unless a genotype exonerates NNRTI resistance, in which case TXF/XTC/EFV, rilpivirine, or doravirine can be considered

Abbreviations: Ab, antibody; Ag, antigen; ART, antiretroviral therapy; BIC, bictegravir; CDC, Centers for Disease Control and Prevention; COBI, cobicistat; DRV, darunavir; EFV, efavirenz; FTC, emtricitabine; HAV, hepatitis A virus; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; NA, not applicable; NAAT, nucleic acid amplification testing; NNRTI, nonnucleoside reverse transcriptase inhibitor; RTV, ritonavir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; 3TC, lamivudine; TXF, tenofovir alafenamide or tenofovir disoproxil fumarate; XTC, emtricitabine or lamivudine.

[a] Recommendations in this table are based on currently available data.

[b] This applies equally to generic tenofovir disoproxil formulations.

[c] Consider individual balance of risk behaviors—persons who inject drugs are frequently also sexually active within the same networks; therefore, the absence of data for an agent's protective efficacy in the setting of parenteral exposures should not preclude the agent's use if demonstrated to have efficacy for that individual's predominant route of sexual exposure. In such cases, refer to the relevant sexual risk category

[d] Evidence rating AIII if patient is using no gender-affirming hormone therapy, CIII if using therapy.

[e] Carbamazepine, oxcarbazepine, phenobarbital, phenytoin, rifampin, rifapentine, and St. John's Wort.

[f] When rifabutin is started before or concomitantly with the first initiation injection, the recommended dosing is one 600-mg (3-mL) injection, followed 2 weeks later by a second 600-mg (3-mL) initiation injection and monthly thereafter while receiving rifabutin. When rifabutin is started at the time of the second initiation injection or later, the recommended dosing schedule is 600 mg (3 mL) monthly while receiving rifabutin.

[g] The first 2 injections on injection initiation are separated by 4 weeks.

[h] If results for the following tests have not been received, preexposure prophylaxis initiation should not be delayed: creatinine, HAV IgG, HBsAg, HBsAb, HCV IgG, GC/CT NAAT, and syphilis.

[i] Within 7 days of preexposure prophylaxis initiation or if not available, rapid test on site and blood drawn for a fourth-generation assay the same day.

[j] When initiating oral preexposure prophylaxis regimens, HIV RNA testing is recommended if high-risk exposure in last 4 weeks or signs and symptoms of HIV infection. When initiating cabotegravir, HIV RNA testing is recommended in all cases. If HIV RNA not available, use the most sensitive assay that is implementable and feasible.

[k] For men who have sex with men and persons who inject drugs (if not known to be immune).

[l] Test all sites used for sexual activity (vaginal, rectal, urethral (via urine testing), and pharyngeal).

[m] For individuals of childbearing potential.

[n] After 1 month of oral (if oral lead-in is used, before first injection) and 4 weeks after first injection.

[o] Laboratory testing conducted every 3 months for oral tenofovir disoproxil fumarate–based preexposure prophylaxis and every 4 months for injectable cabotegravir.

[p] Estimated creatinine clearance rate at first quarterly visit and annually thereafter; every 3 to 6 months for patients with or at risk for kidney injury (>50 y and/or estimated glomerular filtration rate <90 mL/min/1.73 m^2).

[q] Syphilis screening per CDC guidelines with consideration of both conventional and "reverse" screening algorithms.[104]

[r] Every 3 to 6 months for men who have sex with men and persons who inject drugs who use recreational drugs and alcohol at the time of sex or if liver function test results are incidentally found to be abnormal (assays are not part of routine monitoring).

of vulnerability to HIV acquisition (evidence rating: AIII). Injections should be administered gluteally at a dose of 600 mg (3 mL). The first 2 injections should be separated by 4 weeks, and subsequent injections by 8 weeks. Because the timing of onset of protection is unknown but is likely to be approximately 7 days after first injection, barrier protection is recommended in the first week of the first injection cycle. If an individual is more than 7 days late for any injection, it is recommended to "bridge" the period from that 7-day delay until the next injection can be given with an oral PrEP regimen (see Oral PrEP Regimens section above) (evidence rating: BIII). If a resumed injection schedule is 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), a "reloading" dose should be given with a 4-week interval between the 2 injections after the hiatus, before returning to every-8-weeks dosing (evidence rating: AIa). The recommended HIV testing algorithm at dispensation of oral bridging and at the time of injection resumption includes both antigen/antibody and HIV RNA testing (evidence rating: AIII).

Because of the prolonged pharmacologic "tail" phase after discontinuation of cabotegravir injections (median 43.7 weeks for males, 67.3 weeks for females),[109] there has been concern for InSTI resistance should infection occur during this period. Individuals who are stopping injectable cabotegravir but who remain at risk for HIV acquisition should be transitioned to an oral PrEP regimen (see Oral PrEP Regimens section above), and that regimen should be continued during the period of ongoing risk (evidence rating: AIa). Injectable cabotegravir should be dose-adjusted for coadministration with rifabutin and should not be used with potent inducers of UDP-glucuronosyltransferase 1A1. It should be used with particular caution in individuals with gluteal implants or fillers. Strategies to optimize on-time injections should be implemented and may include reminder communications, clinic transportation support, or home visiting nursing services (evidence rating: AIII).

Laboratory Testing in People Receiving PrEP

Recommendations on frequency and type of laboratory testing are reported in Table 4. In patients initiating an oral TXF-based regimen, recommended HIV screening includes a fourth- or fifth-generation laboratory-based, antigen-antibody assay. For cabotegravir-based regimens, HIV testing at initiation and at all visits should ideally include an HIV RNA test with a lower limit of quantification of 50 copies/mL or lower AND a laboratory-based antigen-antibody test (evidence rating: AIa). If RNA testing is not available, cabotegravir PrEP can still be considered using antigen/antibody screening only (evidence rating: BIa). Results of such testing do not need to be available to provide injections. Injectable cabotegravir may "mask" or delay the reactivity/positivity of conventional HIV testing owing to its high potency and prolonged pharmacokinetics, making breakthrough infections (ie, PrEP failures) challenging to identify. Such failures are often asymptomatic and characterized by inconsistent HIV assay results with very low levels of HIV RNA.[110] A high degree of suspicion for HIV infection should be maintained for any reactive/detectable HIV testing results in the setting of a recent HIV exposure or when there are delays in dosing.

Discordant or difficult-to-interpret combinations of HIV test results should be discussed with experts, including the PrEP Warmline at the National Clinician Consultation Center, available at (855) HIV-PrEP.[111]

Adherence to PrEP and Persistence/Retention

Individuals most at risk for acquiring HIV are often challenged by adhering to and persisting with oral PrEP medication and services, with high rates of loss to follow-up.[112,113] Numerous structural barriers contribute to this and are also likely to be applicable to long-acting cabotegravir PrEP.[22] Strategies to enhance adherence and persistence include PrEP navigators, telehealth or telephone check-ins, smartphone reminders, mobile service delivery, and pillboxes.

ART Choice for PrEP Breakthrough Infections

In instances of breakthrough infections, which can occur rarely with oral or injectable PrEP, see the Initiation of ART in the Setting of PrEP Failure section above.

Postexposure Prophylaxis for HIV and Bacterial STIs

A 3-drug fully suppressive ART regimen for 28 days is recommended to be administered as rapidly as possible but within 72 hours of a percutaneous, mucous membrane, or sexual exposure to known or suspected HIV-positive blood, genital secretions, or visibly bloody secretions. The recommended regimen is TXF/XTC plus dolutegravir or bictegravir (evidence rating: AIII). PEP should be initiated even if awaiting results of HIV testing on the source person (evidence rating: BIII). If there is concern for drug-resistant HIV or in the setting of pregnancy or breastfeeding, expert consultation is advised (evidence rating: AIII) (for example, through the National Clinician Consultation Center).[111]

Randomized studies suggest benefit of postexposure doxycycline (200 mg once after condomless intercourse) to prevent acquisition of gonorrhea, chlamydia, and syphilis in men who have sex with men (MSM) and in transgender women.[114,115] Importantly, data on its use for cisgender women and its effects on antimicrobial resistance and the microbiome are still pending. Until more information is available, this strategy should be considered only on a case-by-case basis for individuals at high risk for acquiring syphilis, chlamydia, or gonorrhea.

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 substance use disorders (SUDs) are summarized in **Box 5**. Substance use (eg, opioids, stimulants, alcohol) and SUD can interfere with all stages of the HIV prevention and treatment care continuum.[116] Substance use increases the risk of acquiring HIV through sharing injection drug use equipment and condomless sexual intercourse and may adversely affect HIV outcomes by interfering with ART adherence and the ability to achieve or maintain HIV suppression.[117-119]

Substance use and SUDs are more common among people with HIV than among the general population. Despite the high prevalence of SUDs, only a small number of people with HIV are linked to or initiate treatment for SUD. To increase diagnosis and treatment

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

- Provide screening and treatment for substance use disorders to all persons at risk for and living with HIV (evidence rating: AIa)
- Substance use treatment should be integrated into HIV prevention and treatment services (evidence rating: AIa)
- Persons with substance use disorders and HIV infection or risk for HIV should receive integrated addiction treatment with:
  - Pharmacotherapy for opioid and alcohol use disorders (evidence rating: AIa)
  - Contingency management for stimulant use disorders (evidence rating: AIII)
- Persons with opioid use and alcohol use disorders should be offered timely initiation of medications for substance use disorder regardless of HIV and HCV treatment plans (evidence rating: AIa)
- Peer/patient support staff, telehealth, extended hours, mobile clinics, and walk-in clinic options should be available to persons with substance use disorders who are receiving HIV treatment or prevention (evidence rating: AIIb)
- Peer/patient support staff, mobile health units, and pharmacy delivery services should be available to persons with substance use disorders who are receiving HIV treatment or prevention (evidence rating: AIIb)

Abbreviation: HCV, hepatitis C virus.

of SUDs, screening for and linkage to SUD treatment should be integrated into HIV prevention and treatment services (evidence rating: AIa) (eTable 4 in the Supplement).[120,121] Reducing substance use (even if abstinence is not achieved) is associated with improved HIV outcomes.[122] Therefore, offering addiction treatment, including pharmacotherapy and behavioral-based therapies, is recommended for all people with HIV with SUDs (evidence rating: AIa).[118]

Medication treatments for opioid use disorder (OUD), including buprenorphine, methadone, and extended-release naltrexone, reduce nonmedical opioid use and reduce risk for HIV and hepatitis C virus (eTable 5 in the Supplement).[123-125] For persons with alcohol use disorder (AUD), medications (extended-release naltrexone, oral naltrexone) reduce alcohol use, thereby reducing HIV risk (eTable 6 in the Supplement).[126] For those with HIV, medication treatment of OUD and AUD improves ART adherence and viral suppression and thus is recommended with ART (eFigure in the Supplement) (evidence rating: AIa).[127-130] Clinically significant drug-drug interactions between ART or hepatitis C virus direct-acting antiviral medications and medications used to treat SUDs are infrequent[131,132]; neither ART nor medication treatments for SUDs should be withheld (evidence rating: AIII). Although there are as yet no FDA-approved medications to treat stimulant use disorders (eg, methamphetamine, cocaine), there are data supporting the use of contingency management to promote reduced stimulant use.[133-136]

Interventions that reduce substance use, including medication treatments for OUD and AUD, may also improve PrEP outcomes for HIV prevention. Although oral PrEP is approved for reducing HIV transmission via injection drug use, TAF/FTC and injectable cabotegravir have not yet been evaluated for injection drug use–related risk among persons who inject drugs.[137] However, persons who use drugs may acquire HIV via condomless sexual intercourse; therefore, if they are at sexual risk of HIV acquisition, they should be offered PrEP (evidence rating: AIa).[138-140]

Among persons engaged in HIV prevention or treatment services, SUD can create an additional hurdle for retention in care. Structural barriers to retention, including lack of transportation, insurance, and housing, as well as criminal legal barriers, poverty, mental illness, racism, and stigma should be evaluated and addressed.[141] Innovative service delivery options, including telehealth, extended hours, mobile clinics, walk-in clinics, and staff who are peers or near-peers with lived experience with addiction, are recommended as ways to improve access for patients (evidence rating: AIIb).[9,142,143] Rapid HIV testing combined with rapid ART or PrEP provision among persons at risk should be available to persons who use substances and who have SUDs (see above).

COVID-19 and HIV

Recommendations are summarized in **Box 6**. The COVID-19 pandemic disrupted access to and delivery of HIV care and services.[144-147] An extended review is beyond the scope of this document, but several key points should be considered.[148,149] Recent studies indicate that people with HIV are not at increased risk of acquisition of SARS-CoV-2 compared with people without HIV after controlling for underlying immunosuppression, viral suppression while receiving ART, and comorbidities.[149,150] Data are conflicting and influenced by regional heterogeneity about the independent contribution of HIV to higher risk of severe disease and mortality due to COVID-19.[151] The preponderance of data suggests that people with HIV who are receiving effective ART, virally suppressed with a CD4 cell count greater than 200/μL (or in some studies >350 cells/μL), and without key comorbidities do not appear to be at substantially increased risk for severe disease or death compared with people without HIV.[152] There are 3 potential explanations for some of the contradictory findings. First, published reports did not control for (or may have been confounded by) higher prevalence among people with HIV of underlying comorbidities such as cardiovascular disease, diabetes, chronic kidney disease, chronic pulmonary disease, and obesity, all of which are associated with increased risk of severe COVID-19 and mortality.[153-155] Second, published reports had not accounted for HIV RNA, residual HIV-associated inflammation, or incomplete CD4 cell reconstitution in some people with HIV despite receiving ART. Third, social determinants of poor COVID-19 outcomes also intersect with higher prevalence of HIV among racial and ethnic minority populations.

Primary COVID-19 vaccination and vaccine boosting is recommended for all people with HIV (evidence rating: AIa). For those who have untreated HIV infection or a CD4 cell count less than 200/μL, the primary vaccination series should include at least 3 primary vaccine doses, and vaccine booster doses are recommended regardless of age (evidence rating: AIIa). For persons with HIV with viral suppression while receiving ART and with CD4 cell counts greater than 350/μL, antibody responses to SARS-CoV-2 infection or vaccines are not substantially different than among those without HIV. People with HIV also do not have higher rates of adverse events related to SARS-CoV-2 vaccines.[156-158] However, some studies suggest that vaccine efficacy, as measured by reduction in hospitalizations and mortality, and antibody response rates are lower for people with HIV with advanced immunosuppression, especially those with CD4 cell counts less than 200/μL or without viral suppression, than those without HIV.[159-162] Many of the large phase 3 vaccine trials excluded people with HIV or enrolled numbers too small to draw firm

conclusions. Again, some published data on vaccine immunogenicity in people with HIV are conflicting, possibly owing to small numbers, insufficient controls for underlying age, comorbidities, HIV RNA levels, or other factors that may affect antibody responses.[163,164] People with HIV who have CD4 cell counts less than 200/μL or untreated HIV may benefit from PrEP with tixagevimab plus cilgavimab, but only if the circulating SARS-CoV-2 variants are susceptible (evidence rating: BIII). People with HIV, particularly those with CD4 cell counts less than 200/μL, do appear to be at increased risk of vaccine breakthrough infections.[165] This risk was lower for those with CD4 cell counts greater than 500/μL.

Current COVID-19 treatment guidelines do not recommend that treatment be intensified, withheld, or altered based on HIV-related immunosuppression or ART.[166-168] One emerging issue is whether postacute sequelae of COVID-19 ("long COVID") is more prevalent among people with HIV. Risk factors for postacute sequelae in people with HIV appear to be the same as for people without HIV.[169] The degree to which underlying immunosuppression, viral suppression while receiving ART, or other factors affect the risk of postacute sequealae remains to be determined.

Monkeypox Virus Infection

A global surge in monkeypox virus infections, primarily among MSM and with up to 50% occurring among people with HIV, was first identified in 2022. Most cases are related to skin-to-skin transmission during sexual encounters. Although the infection can be asymptomatic,[170] the predominant symptoms are skin lesions that progress from papules to pustules and ulcers, often associated with fever, lymphadenopathy, myalgias, headache, or fatigue.[171,172] Skin lesions are typically painful and can coalesce. Patients also often have anogenital or oral lesions, although lesions may exist without any symptoms. People with HIV and low CD4 cell counts or with no viral suppression may experience more severe disease.[173] Coinfection with other STIs is frequent and should be screened for when monkeypox is first recognized or suspected (evidence rating: AIII).

Diagnosis of monkeypox currently requires nucleic acid amplification testing of lesions. Treatment recommendations are evolving, but those patients who are immunosuppressed or otherwise at high risk for progression or those with severe disease should receive oral or intravenous tecovirimat (evidence rating: BIII), an investigational agent with activity against smallpox and monkeypox viruses. Oral dosing is every 8 or 12 hours (depending on weight) for 14 days, administered within 30 minutes of a full fatty meal. Potential drug interactions exist between tecovirimat and rilpivirine, doravirine, and maraviroc, but dose adjustment is not required.[174]

The incubation time for monkeypox virus is approximately 12 days. For individuals with a known exposure, the JYNNEOS vaccine (smallpox and monkeypox vaccine, live, nonreplicating [Bavarian Nordic]) should be administered to asymptomatic contacts ideally within 4 days but up to 14 days (evidence rating: AIII). Primary JYNNEOS vaccination with 2 doses given at least 28 days apart is recommended for individuals at high risk (evidence rating: AIII) (eg, MSM with multiple sexual partners). It is crucial that health messaging center on an equity approach to ensure that education and services reach the most affected populations while simultaneously fighting the stigma increasingly directed toward these communities.

Box 6. Recommendations for COVID-19 and People With HIV

- Primary COVID-19 vaccination and vaccine boosting is recommended for all people with HIV (evidence rating: AIa). For those who have untreated HIV infection or a CD4 cell count less than 200/μL, the primary vaccination series should include at least 3 vaccine doses, and vaccine booster doses are recommended regardless of age (evidence rating: AIIa)
- If circulating SARS-CoV-2 variants anticipated to be susceptible, preexposure prophylaxis for susceptible subvariants with tixagevimab (300 mg) plus cilgavimab (300 mg) to prevent COVID-19 is recommended for adults and adolescents (aged ≥12 years and weighing ≥40 kg) with HIV who have untreated HIV infection or a CD4 cell count less than 200/μL or those not able to be fully vaccinated owing to a history of severe adverse reactions to a COVID-19 vaccine or its components (evidence rating: BIII)
- Postexposure prophylaxis is not recommended for people with HIV (evidence rating: AIII). Currently available monoclonal antibody agents have not been shown to be sufficiently effective against the predominant circulating Omicron variants and subvariants
- People with HIV who develop COVID-19 should be treated according to current guidelines for management of COVID-19, regardless of CD4 cell count or viral suppression (evidence rating: AIa)
- People with HIV with CD4 cell counts less than 200/μL or without viral suppression who develop mild-moderate COVID-19 infection should be treated with ritonavir-boosted nirmatrelvir (evidence rating: AIIa). With the exception of maraviroc, ART can be co-administered with ritonavir-boosted nirmatrelvir without dose adjustment (except as needed for estimated glomerular filtration rate <60 mL/min), but people with HIV should be monitored closely for adverse effects while receiving this treatment. Drug-drug interactions may still limit the use of this treatment if medications used for underlying comorbidities or opportunistic infections are contraindicated with ritonavir-boosted nirmatrelvir
- People with HIV who recover from severe COVID-19 should be monitored for postacute sequelae of SARS-CoV-2 (long COVID) and HIV treatment should be optimized to the extent possible to further reduce inflammatory responses to COVID-19 and HIV (evidence rating: AIII)

Abbreviation: ART, antiretroviral therapy.

Promoting Equity in HIV Treatment and Prevention

Despite advances in HIV treatment and prevention, large disparities exist in the global HIV epidemic. The 2021 Global AIDS Update titled "Confronting Inequalities" describes the inequity that continues to drive the HIV epidemic in all regions of the world, with a focus on low- and middle-income countries.[175] However, HIV epidemics in high-income countries also are characterized by ongoing disparities. The US epidemic is a prime example: HIV disproportionately affects people who are Black or Hispanic, those who live in the US South, MSM, transgender individuals, and people who use drugs, compared with the general population.[176] In 2020, HIV testing and services were disrupted by the COVID-19 pandemic in the US, particularly among priority populations including men who have sex with men, transgender persons, and Black or African American and Hispanic persons.[177] In addition, Black/African American people were furthest from the

Ending the HIV Epidemic Initiative targets for linkage to care (80%), viral suppression (60%), and PrEP coverage (9%).[178] Among Black people with HIV in the US, 52% reside in geographic areas with high social vulnerability index scores.[179] The greatest burden of HIV in the US is in the South, driven by structural factors including long-standing inequitable policies based in racism, and resulting in high levels of poverty, failure to expand health care access through Medicaid expansion, low educational attainment, intersectional stigma and discrimination, and clinician shortages that result in inequitable access to HIV prevention and treatment services. Striking disparities also exist across other high-income settings. For example, in the European Union and European Economic Area, 44% of new diagnoses in 2019 were among the migrant populations.[180]

Global disparities in PrEP utilization limit its ability to reduce HIV transmission,[181,182] and there is serious concern that, although long-acting cabotegravir for PrEP has the potential for considerable benefit,[183] its cost and implementation complexity will only widen disparities.

The United Nations General Assembly Political Declaration on HIV and AIDS, titled "Ending Inequalities and Getting on Track to End AIDS by 2030," offers roadmaps to address global health disparities, including those associated with HIV status, sex, gender, race, ethnicity, disability, age, income level, education, occupation, geographic disparities, migratory status, and incarceration.[184] Ending the HIV epidemic will require an equity approach that focuses resources on addressing societal disparities (for example, tackling poverty as an HIV prevention strategy), addressing stigma as a root cause of HIV risk, eliminating laws that target people with HIV, and ensuring access to care for all.

Limitations

First, this article is meant to provide general recommendations and is not designed as mandates or to replace clinical judgment. Second, the recommendations are based on the body of evidence that was available at the time of preparation and may change as new data become available. Third, the recommendations were developed for high- and medium-income settings, for which most of the drugs and tools are available. The specific recommendations may not be applicable in all resource-limited settings.

Conclusions

Advances in treatment and prevention of HIV continue to improve outcomes, but challenges and opportunities remain.

ARTICLE INFORMATION

Accepted for Publication: November 13, 2022.

Published Online: December 1, 2022. doi:10.1001/jama.2022.22246

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

Author Contributions: Dr Gandhi had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Gandhi, Bedimo, Hoy, Landovitz, Eaton, Lehmann, Sax, Thompson, Benson, Buchbinder, del Rio, Eron, Günthard, Jacobsen, Saag.
Acquisition, analysis, or interpretation of data: Gandhi, Bedimo, Hoy, Landovitz, Smith, Eaton, Lehmann, Springer, Thompson, Benson, Buchbinder, del Rio, Eron, Günthard, Molina, Saag.
Drafting of the manuscript: Gandhi, Bedimo, Hoy, Landovitz, Smith, Eaton, Lehmann, Springer, Sax, Thompson, Benson, del Rio, Jacobsen, Saag.
Critical revision of the manuscript for important intellectual content: Gandhi, Bedimo, Hoy, Landovitz, Smith, Eaton, Lehmann, Springer, Thompson, Benson, Buchbinder, del Rio, Eron, Günthard, Molina, Saag.
Obtained funding: Jacobsen.
Administrative, technical, or material support: Landovitz, Smith, Eaton, Lehmann, Jacobsen, Saag.
Supervision: Gandhi, Sax, Benson, Jacobsen, Saag.

Conflict of Interest Disclosures: Dr Gandhi reported receiving grants from the National Institutes of Health (NIH). Dr Bedimo reported receiving grants from Merck and ViiV Healthcare and serving on the scientific advisory board of Merck, ViiV Healthcare, Gilead Sciences, Theratechnologies, and Janssen Scientific. Dr Hoy reported serving on the advisory board of ViiV Healthcare and Gilead Sciences. Dr Landovitz reported serving on the scientific advisory board of Gilead Sciences and Merck; receiving consulting fees from Cepheid; and receiving grants from the NIH and ViiV Healthcare. Dr Smith reported receiving grants from the NIH San Diego Center for AIDS Research and receiving personal fees from Linear Therapies, Model Medicines, Pharma Holdings, Bayer Pharmaceuticals, and Evidera. Dr Eaton reported receiving grants paid to her institution from NIH and Bristol Myers Squibb and receiving consulting fees from Gilead Sciences. Dr Lehmann reported receiving personal fees from VIIV Healthcare, Gilead, Pfizer, Janssen, Novartis, BioNTech, and Merck Sharp & Dohme and receiving grants from the German Center of Infection Research and the German Ministry of Research. Dr Springer reported receiving grants from the National Institute on Drug Abuse, National Center for Advancing Translational Science, and Veterans Affairs Cooperative Studies Program; receiving consulting fees from Alkermes Inc; and receiving in-kind drug donation from Alkermes Inc (Vivitrol) and Indivior (Sublocade) for NIH-sponsored research. Dr Sax reported receiving grants from Gilead and ViiV and receiving personal fees from Gilead, Janssen, Merck, and ViiV. Dr Thompson reported receiving research funding to the AIDS Research Consortium of Atlanta from Bristol Myers Squibb, Cepheid Inc, Cytodyne Inc, Frontier Biotechnologies, Gilead Sciences, GlaxoSmithKline, Merck Sharp & Dohme, and ViiV and serving as chair of an independent data monitoring committee for Excision Biotherapeutics. Dr Benson reported receiving grants from NIH/National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Mental Health; receiving grants to her institution from Fogarty, Gilead, and DNAe; receiving lecture/symposia honoraria from International Antiviral Society–USA; serving as deputy editor of *Clinical Infectious Diseases*; and receiving consulting fees from NDA Partners. Dr Buchbinder reported receiving grants from Gilead Sciences and ViiV Healthcare. Dr del Rio reported receiving grants from the NIH/NIAID Emory Center for AIDS Research and receiving consulting fees from Resverlogix. Dr Eron reported receiving personal fees from Merck, ViiV Healthcare, and Gilead Sciences and receiving grants from ViiV Healthcare, Gilead Sciences, and Janssen. Dr Günthard reported receiving grants from the Swiss National Science Foundation, NIH, Yvonne Jacob Foundation, Gilead, the Swiss HIV Cohort Study, and advisory board, consulting, and data and safety monitoring board fees from Merck, Gilead Sciences, ViiV Healthcare, GlaxoSmithKline, Janssen, Johnson & Johnson, and Novartis. Dr Molina reported receiving grants from Gilead and serving on the advisory board for Gilead, Merck, and ViiV. Dr Saag reported receiving grants

to his institution from ViiV Healthcare and Gilead Sciences and receiving consulting fees from TFF Pharmaceuticals and American Gene Technologies. No other disclosures were reported.

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

Role of the Funder/Sponsor: The IAS-USA determined the need to update recommendations, vetted and selected the panel members, and provided administrative support and oversight. The panel had a role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: We thank Paul A. Volberding, MD, who initiated the volunteer panel in 1995 and helped guide the committee for 25 years. We also thank Michelle Valderama, BS, production and web manager from the IAS-USA, for assistance in managing the manuscript versions; Sherry Wu, BS, for administrative support; and Kimberly R. Powell, MIS, a research impact informationist from Emory University for conducting the PubMed and Embase literature searches. Dr Volberding and Ms Powell received no financial compensation from the sponsor for this article. Ms Valderama and Ms Wu are salaried employees of the sponsor of this article.

Additional Information: This article is dedicated to the memory of Scott M. Hammer, MD, founding member of the panel and former panel chair.

REFERENCES

1. Saag MS, Gandhi RT, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2020 recommendations of the International Antiviral Society-USA Panel. *JAMA*. 2020;324(16):1651-1669. doi:10.1001/jama.2020.17025

2. Canadian Task Force on the Periodic Health Examination. The periodic health examination. *Can Med Assoc J*. 1979;121(9):1193-1254.

3. Pathela P, Jamison K, Braunstein SL, et al. Initiating antiretroviral treatment for newly diagnosed HIV patients in sexual health clinics greatly improves timeliness of viral suppression. *AIDS*. 2021;35(11):1805-1812. doi:10.1097/QAD.0000000000002937

4. Michienzi SM, Barrios M, Badowski ME. Evidence regarding rapid initiation of antiretroviral therapy in patients living with HIV. *Curr Infect Dis Rep*. 2021;23(5):7. doi:10.1007/s11908-021-00750-5

5. Huhn GD, Crofoot G, Ramgopal M, et al. Darunavir/cobicistat/emtricitabine/tenofovir alafenamide in a rapid-initiation model of care for human immunodeficiency virus type 1 infection: primary analysis of the DIAMOND study. *Clin Infect Dis*. 2020;71(12):3110-3117. doi:10.1093/cid/ciz1213

6. Baisley K, Orne-Gliemann J, Larmarange J, et al. Early HIV treatment and survival over six years of observation in the ANRS 12249 treatment as prevention trial. *HIV Med*. 2022;23(8):922-928. doi:10.1111/hiv.13263

7. Stanic A, Rybin D, Cannata F, et al. The impact of the housing status on clinical outcomes and health care utilization among individuals living with HIV. *AIDS Care*. 2021;33(1):1-9. doi:10.1080/09540121.2019.1695728

8. Maragh-Bass AC, Gamble T, El-Sadr WM, Hanscom B, Tolley EE. Exploring individual-level barriers to HIV medication adherence among men who have sex with men in the HIV Prevention Trials Network (HPTN 065) study. *AIDS Care*. 2021;33(11):1404-1413. doi:10.1080/09540121.2020.1828799

9. Higa DH, Crepaz N, Mullins MM, et al. Strategies to improve HIV care outcomes for people with HIV who are out of care. *AIDS*. 2022;36(6):853-862. doi:10.1097/QAD.0000000000003172

10. National Academies of Sciences Engineering and Medicine. *Opportunities to Improve Opioid Use Disorder and Infectious Disease Services*. National Academies Press; 2020.

11. Martin TCS, Abrams M, Anderson C, Little SJ. Rapid antiretroviral therapy among individuals with acute and early HIV. *Clin Infect Dis*. 2021;73(1):130-133. doi:10.1093/cid/ciaa1174

12. Chéret A, Bauer R, Meiffrédy V, et al. Once-daily dolutegravir versus darunavir plus cobicistat in adults at the time of primary HIV-1 infection: the OPTIPRIM2-ANRS 169 randomized, open-label, phase 3 trial. *J Antimicrob Chemother*. 2022;77(9):2506-2515. doi:10.1093/jac/dkac207

13. Rasmussen TA, Ahuja SK, Kuwanda L, et al. Antiretroviral initiation at ≥800 CD4+ cells/mm3 associated with lower human immunodeficiency virus reservoir size. *Clin Infect Dis*. 2022;75(10):1781-1791. doi:10.1093/cid/ciac249

14. Hunt PW, Brenchley J, Sinclair E, et al. Relationship between T cell activation and CD4+ T cell count in HIV-seropositive individuals with undetectable plasma HIV RNA levels in the absence of therapy. *J Infect Dis*. 2008;197:126-133. doi:10.1086/524143

15. Li JZ, Segal FP, Bosch RJ, et al; AIDS Clinical Trials Group Study A5308 Team. Antiretroviral therapy reduces T-cell activation and immune exhaustion markers in human immunodeficiency virus controllers. *Clin Infect Dis*. 2020;70(8):1636-1642. doi:10.1093/cid/ciz442

16. Plaçais L, Boufassa F, Lécuroux C, et al; ANRS CO21 Study Group. Antiretroviral therapy for HIV controllers: reasons for initiation and outcomes in the French ANRS-CO21 CODEX cohort. *EClinicalMedicine*. 2021;37:100963. doi:10.1016/j.eclinm.2021.100963

17. Girometti N, Lander F, McOwan A, Nwokolo N, Boffito M, Whitlock G; Dean Street Collaborative Group. Rapid ART start in early HIV infection: time to viral load suppression and retention in care in a London cohort. *HIV Med*. 2020;21(9):613-615. doi:10.1111/hiv.12900

18. Jaschinski N, Greenberg L, Neesgaard B, et al; RESPOND Study Group. Recent abacavir use and incident cardiovascular disease in contemporary treated people living with HIV. *AIDS*. Published online August 24, 2022. doi:10.1097/QAD.0000000000003373

19. Christopoulos KA, Grochowski J, Mayorga-Munoz F, et al. First demonstration project of long-acting injectable antiretroviral therapy for persons with and without detectable HIV viremia in an urban HIV clinic. *Clin Infect Dis*. Published online August 1, 2022. doi:10.1093/cid/ciac631

20. Landovitz RJ, Donnell D, Clement ME, et al; HPTN 083 Study Team. Cabotegravir for HIV prevention in cisgender men and transgender women. *N Engl J Med*. 2021;385(7):595-608. doi:10.1056/NEJMoa2101016

21. Eshleman SH, Fogel JM, Piwowar-Manning E, et al. Characterization of human immunodeficiency virus (HIV) infections in women who received injectable cabotegravir or tenofovir disoproxil fumarate/emtricitabine for HIV prevention: HPTN 084. *J Infect Dis*. 2022;225(10):1741-1749. doi:10.1093/infdis/jiab576

22. 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] in special issue: Abstracts From the 2022 Conference on Retroviruses and Opportunistic Infections. *Top Antiv Med*. 2022;30(1 suppl):37.

23. Department of Health and Human Services. Recommendations for the use of antiretroviral drugs during pregnancy and interventions to reduce perinatal HIV transmission in the United States. ClinicalInfo. Updated March 17, 2022. Accessed November 9, 2022. https://clinicalinfo.hiv.gov/en/guidelines/perinatal/whats-new-guidelines?view=full

24. Zash R, Holmes LB, Diseko M, et al. Update on neural tube defects with antiretroviral exposure in the Tsepamo study, Botswana. Poster presented at: 11th IAS Conference on HIV Science; July 18-21, 2022.

25. 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

26. Stranix-Chibanda L, Ziemba L, Brummer S, et al. Growth of infants with perinatal exposure to maternal DTG vs EFV and TDF vs TAF [Abstract 30] in special issue: Abstracts From the 2022 Conference on Retroviruses and Opportunistic Infections. *Top Antiv Med*. 2022;30(1 suppl):10-11.

27. 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

28. Burke RM, Rickman HM, Singh V, et al. What is the optimum time to start antiretroviral therapy in people with HIV and tuberculosis coinfection? a systematic review and meta-analysis. *J Int AIDS Soc*. 2021;24(7):e25772. doi:10.1002/jia2.25772

29. Ingle SM, Miro JM, Furrer H, et al. Impact of ART on mortality in cryptococcal meningitis patients: high-income settings. Poster presented at: 22nd Conference on Retroviruses and Opportunistic Infections; February 23-26, 2015; Seattle, Washington.

30. 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 https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection

31. Dooley KE, Kaplan R, Mwelase N, et al; International Study of Patients With HIV on Rifampicin ING Study Group. Dolutegravir-based antiretroviral therapy for patients coinfected with tuberculosis and human immunodeficiency virus: a multicenter, noncomparative, open-label, randomized trial. *Clin Infect Dis*. 2020;70(4):549-556.

32. De Castro N, Marcy O, Chazallon C, et al; ANRS 12300 Reflate TB2 Study Group. Standard dose raltegravir or efavirenz-based antiretroviral treatment for patients co-infected with HIV and tuberculosis (ANRS 12 300 Reflate TB 2): an open-label, non-inferiority, randomised, phase 3 trial. *Lancet Infect Dis*. 2021;21(6):813-822. doi:10.1016/S1473-3099(20)30869-0

33. Grinsztejn B, Hosseinipour MC, Ribaudo HJ, et al; HPTN 052-ACTG Study Team. Effects of early versus delayed initiation of antiretroviral treatment on clinical outcomes of HIV-1 infection: results from the phase 3 HPTN 052 randomised controlled trial. *Lancet Infect Dis*. 2014;14(4):281-290. doi:10.1016/S1473-3099(13)70692-3

34. Marcy O, De Castro N, Chazallon C, et al. Adherence and factors associated with virologic success in HIV-1 infected adults witH tuberculosis receiving raltegravir or efavirenz in the ANRS 12300 Reflate TB2 trial. Poster presented at: International AIDS Conference; 2020.

35. Osiyemi O, De Wit S, Ajana F, et al. Efficacy and safety of switching to dolutegravir/lamivudine (DTG/3TC) versus continuing a tenofovir alafenamide-based 3- or 4-drug regimen for maintenance of virologic suppression in adults living with HIV-1: results through week 144 from the phase 3, non-inferiority TANGO randomized trial. *Clin Infect Dis*. 2022;75(6):975-986. doi:10.1093/cid/ciac036

36. Llibre JM, Brites C, Cheng CY, et al. Efficacy and safety of switching to the 2-drug regimen dolutegravir/lamivudine versus continuing a 3- or 4-drug regimen for maintaining virologic suppression in adults living with HIV-1: week 48 results from the phase 3, non-inferiority SALSA randomized trial. *Clin Infect Dis*. Published online March 2, 2022. doi:10.1093/cid/ciac130

37. van Wyk J, Orkin C, Rubio R, et al. Brief report: durable suppression and low rate of virologic failure 3 years after switch to dolutegravir + rilpivirine 2-drug regimen: 148-week results from the SWORD-1 and SWORD-2 randomized clinical trials. *J Acquir Immune Defic Syndr*. 2020;85(3):325-330. doi:10.1097/QAI.0000000000002449

38. Greenberg L, Ryom L, Neesgaard B, et al; RESPOND (International Cohort Consortium of Infectious Diseases) Study Group. Clinical outcomes of 2-drug regimens vs 3-drug regimens in antiretroviral treatment-experienced people living with human immunodeficiency virus. *Clin Infect Dis*. 2021;73(7):e2323-e2333. doi:10.1093/cid/ciaa1878

39. van Wyk J, Ajana F, Bisshop F, et al. Efficacy and safety of switching to dolutegravir/lamivudine fixed-dose 2-drug regimen vs continuing a tenofovir alafenamide-based 3- or 4-drug regimen for maintenance of virologic suppression in adults living with human immunodeficiency virus type 1: phase 3, randomized, noninferiority TANGO study. *Clin Infect Dis*. 2020;71(8):1920-1929. doi:10.1093/cid/ciz1243

40. Underwood M, Osiyemi O, Rubio R, et al. Archived resistance and response to <40 c/mL & TND–DTG/3TC FDC at week 48 in SALSA [Abstract 481] in special issue: Abstracts From the 2022 Conference on Retroviruses and Opportunistic Infections. *Top Antiv Med*. 2022;30(1 suppl):184.

41. Marks K, Kang M, Umbleja T, et al. High HBsAb seroprotection achieved 4 weeks after 3 doses of HepB-CpG vaccine in people living with HIV (PLWH) without Prior HBV vaccination (ACTG A5379 Group B Preliminary Results). Poster presented at: ID Week; October 11-15, 2022; Washington, DC.

42. Ombajo LA, Penner J, Nkuranga J, et al. A randomized trial of switching treatment-experienced adults from PI/r to DTG [Abstract 136] in special issue: Abstracts From the 2022 Conference on Retroviruses and Opportunistic Infections. *Top Antiv Med*. 2022;30(1 suppl):52.

43. Sax PE, Rockstroh JK, Luetkemeyer AF, et al; GS-US-380–4030 Investigators. Switching to bictegravir, emtricitabine, and tenofovir alafenamide in virologically suppressed adults with human immunodeficiency virus. *Clin Infect Dis*. 2021;73(2):e485-e493. doi:10.1093/cid/ciaa988

44. Hagins D, Kumar P, Saag M, et al; BRAAVE2020 Investigators. Switching to bictegravir/emtricitabine/tenofovir alafenamide in Black Americans with HIV-1: a randomized phase 3b, multicenter, open-label study. *J Acquir Immune Defic Syndr*. 2021;88(1):86-95. doi:10.1097/QAI.0000000000002731

45. Sax PE, Andreatta K, Molina JM, et al. High efficacy of switching to bictegravir/emtricitabine/tenofovir alafenamide in people with suppressed HIV and preexisting M184V/I. *AIDS*. 2022;36(11):1511-1520. doi:10.1097/QAD.0000000000003244

46. Aboud M, Kaplan R, Lombaard J, et al. Dolutegravir versus ritonavir-boosted lopinavir both with dual nucleoside reverse transcriptase inhibitor therapy in adults with HIV-1 infection in whom first-line therapy has failed (DAWNING): an open-label, non-inferiority, phase 3b trial. *Lancet Infect Dis*. 2019;19(3):253-264. doi:10.1016/S1473-3099(19)30036-2

47. 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

48. Rizzardini G, Overton ET, Orkin C, et al. Long-acting injectable cabotegravir + rilpivirine for HIV maintenance therapy: week 48 pooled analysis of phase 3 ATLAS and FLAIR trials. *J Acquir Immune Defic Syndr*. 2020;85(4):498-506. doi:10.1097/QAI.0000000000002466

49. Overton ET, Richmond G, Rizzardini G, et al. Long-acting cabotegravir and rilpivirine dosed every 2 months in adults with HIV-1 infection (ATLAS-2M), 48-week results: a randomised, multicentre, open-label, phase 3b, non-inferiority study. *Lancet*. 2021;396(10267):1994-2005. doi:10.1016/S0140-6736(20)32666-0

50. Murray M, Antela A, Mills A, et al. Patient-reported outcomes in ATLAS and FLAIR participants on long-acting regimens of cabotegravir and rilpivirine over 48 weeks. *AIDS Behav*. 2020;24(12):3533-3544. doi:10.1007/s10461-020-02929-8

51. Orkin C, Bernal Morell E, Tan DHS, et al. Initiation of long-acting cabotegravir plus rilpivirine as direct-to-injection or with an oral lead-in in adults with HIV-1 infection: week 124 results of the open-label phase 3 FLAIR study. *Lancet HIV*. 2021;8(11):e668-e678. doi:10.1016/S2352-3018(21)00184-3

52. Ellis KE, Nawas GT, Chan C, et al. Clinical outcomes following the use of archived proviral HIV-1 DNA genotype to guide antiretroviral therapy adjustment. *Open Forum Infect Dis*. 2019;7(1):ofz533. doi:10.1093/ofid/ofz533

53. Castagna A, Maggiolo F, Penco G, et al; VIKING-3 Study Group. Dolutegravir in antiretroviral-experienced patients with raltegravir- and/or elvitegravir-resistant HIV-1: 24-week results of the phase III VIKING-3 study. *J Infect Dis*. 2014;210(3):354-362. doi:10.1093/infdis/jiu051

54. Fostemsavir [prescribing information]. ViiV Healthcare; 2020.

55. Kamelian K, Lepik KJ, Chau W, et al. Prevalence of human immunodeficiency virus-1 integrase strand transfer inhibitor resistance in British Columbia, Canada between 2009 and 2016: a longitudinal analysis. *Open Forum Infect Dis*. 2019;6(3):ofz060. doi:10.1093/ofid/ofz060

56. Koullias Y, Sax PE, Fields NF, Walensky RP, Hyle EP. Should we be testing for baseline integrase resistance in patients newly diagnosed with human immunodeficiency virus? *Clin Infect Dis*. 2017;65(8):1274-1281. doi:10.1093/cid/cix542

57. Zhu J, Rozada I, David J, et al. The potential impact of initiating antiretroviral therapy with integrase inhibitors on HIV transmission risk in British Columbia, Canada. *EClinicalMedicine*. 2019;13:101-111. doi:10.1016/j.eclinm.2019.07.001

58. Berenguer J, Parrondo J, Landovitz RJ. Mathematical modeling of HIV-1 transmission risk from condomless anal intercourse in HIV-infected MSM by the type of initial ART. *PLoS One*. 2019;14(7):e0219802. doi:10.1371/journal.pone.0219802

59. Charpentier C, Storto A, Soulié C, et al. Prevalence of genotypic baseline risk factors for cabotegravir +rilpivirine failure among ARV-naive patients. *J Antimicrob Chemother*. 2021;76(11):2983-2987. doi:10.1093/jac/dkab161

60. Sise ME, Hirsch JS, Canetta PA, Herlitz L, Mohan S. Nonalbumin proteinuria predominates in biopsy-proven tenofovir nephrotoxicity. *AIDS*. 2015;29(8):941-946. doi:10.1097/QAD.0000000000000628

61. Samarawickrama A, Cai M, Smith ER, et al. Simultaneous measurement of urinary albumin and total protein may facilitate decision-making in HIV-infected patients with proteinuria. *HIV Med*. 2012;13(9):526-532. doi:10.1111/j.1468-1293.2012.01003.x

62. Joshi K, Boettiger D, Kerr S, et al. Changes in renal function with long-term exposure to antiretroviral therapy in HIV-infected adults in Asia.

Pharmacoepidemiol Drug Saf. 2018;27(11):1209-1216. doi:10.1002/pds.4657

63. Kaboré NF, Poda A, Zoungrana J, et al. Chronic kidney disease and HIV in the era of antiretroviral treatment: findings from a 10-year cohort study in a west African setting. *BMC Nephrol*. 2019;20(1):155. doi:10.1186/s12882-019-1335-9

64. Jotwani V, Scherzer R, Estrella MM, et al. HIV infection, tenofovir, and urine α1-microglobulin: a cross-sectional analysis in the Multicenter AIDS Cohort Study. *Am J Kidney Dis*. 2016;68(4):571-581. doi:10.1053/j.ajkd.2016.03.430

65. Thompson MA, Horberg MA, Agwu AL, et al. Primary care guidance for persons with human immunodeficiency virus: 2020 update by the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2021;73(11): e3572-e3605. doi:10.1093/cid/ciaa1391

66. 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

67. Surial B, Mugglin C, Calmy A, et al; Swiss HIV Cohort Study. Weight and metabolic changes after switching from tenofovir disoproxil fumarate to tenofovir alafenamide in people living with HIV: a cohort study. *Ann Intern Med*. 2021;174(6):758-767. doi:10.7326/M20-4853

68. Ogbuagu O, Ruane PJ, Podzamczer D, et al; DISCOVER Study Team. Long-term safety and efficacy of emtricitabine and tenofovir alafenamide vs emtricitabine and tenofovir disoproxil fumarate for HIV-1 pre-exposure prophylaxis: week 96 results from a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet HIV*. 2021;8(7):e397-e407. doi:10.1016/S2352-3018(21)00071-0

69. Bourgi K, Jenkins CA, Rebeiro PF, et al; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Weight gain among treatment-naïve persons with HIV starting integrase inhibitors compared to non-nucleoside reverse transcriptase inhibitors or protease inhibitors in a large observational cohort in the United States and Canada. *J Int AIDS Soc*. 2020;23 (4):e25484. doi:10.1002/jia2.25484

70. Mallon PW, Brunet L, Hsu RK, et al. Weight gain before and after switch from TDF to TAF in a U.S. cohort study. *J Int AIDS Soc*. 2021;24(4):e25702. doi:10.1002/jia2.25702

71. Venter WDF, Sokhela S, Simmons B, et al. Dolutegravir with emtricitabine and tenofovir alafenamide or tenofovir disoproxil fumarate versus efavirenz, emtricitabine, and tenofovir disoproxil fumarate for initial treatment of HIV-1 infection (ADVANCE): week 96 results from a randomised, phase 3, non-inferiority trial. *Lancet HIV*. 2020;7(10):e666-e676. doi:10.1016/S2352-3018(20)30241-1

72. Bischoff J, Gu W, Schwarze-Zander C, et al. Stratifying the risk of NAFLD in patients with HIV under combination antiretroviral therapy (cART). *EClinicalMedicine*. 2021;40:101116. doi:10.1016/j.eclinm.2021.101116

73. Gorwood J, Bourgeois C, Pourcher V, et al. The integrase inhibitors dolutegravir and raltegravir exert proadipogenic and profibrotic effects and induce insulin resistance in human/simian adipose tissue and human adipocytes. *Clin Infect Dis*. 2020; 71(10):e549-e560. doi:10.1093/cid/ciaa259

74. González-Cordón A, Assoumou L, Moyle G, et al; NEAT022 Study Group. Switching from boosted PIs to dolutegravir decreases soluble CD14 and adiponectin in high cardiovascular risk people living with HIV. *J Antimicrob Chemother*. 2021;76 (9):2380-2393. doi:10.1093/jac/dkab158

75. Leonard MA, Cindi Z, Bradford Y, et al. Efavirenz pharmacogenetics and weight gain following switch to integrase inhibitor-containing regimens. *Clin Infect Dis*. 2021;73(7):e2153-e2163. doi:10.1093/cid/ciaa1219

76. Plum PE, Maes N, Sauvage AS, et al. Impact of switch from tenofovir disoproxil fumarate-based regimens to tenofovir alafenamide-based regimens on lipid profile, weight gain and cardiovascular risk score in people living with HIV. *BMC Infect Dis*. 2021;21(1):910. doi:10.1186/s12879-021-06479-9

77. Silverberg MJ, Lyass A, Hurley L, et al. Trends in myocardial infarction risk by HIV status in 2 US healthcare systems [Abstract 39] in special issue: Abstracts From the 2022 Conference on Retroviruses and Opportunistic Infections. *Top Antiv Med*. 2022;30(1 suppl):15.

78. Nolan NS, Adamson S, Reeds D, O'Halloran JA. Bictegravir-based antiretroviral therapy-associated accelerated hyperglycemia and diabetes mellitus. *Open Forum Infect Dis*. 2021;8(5):ofab077. doi:10.1093/ofid/ofab077

79. O'Halloran JA, Sahrmann J, Parra-Rodriguez L, et al. Integrase strand transfer inhibitors are associated with incident diabetes mellitus in people with HIV. *Clin Infect Dis*. Published online May 6, 2022. doi:10.1093/cid/ciac355

80. Summers NA, Lahiri CD, Angert CD, et al. Metabolic changes associated with the use of integrase strand transfer inhibitors among virally controlled women. *J Acquir Immune Defic Syndr*. 2020;85(3):355-362. doi:10.1097/QAI.0000000000002447

81. Rebeiro PF, Jenkins CA, Bian A, et al. Risk of incident diabetes mellitus, weight gain, and their relationships with integrase inhibitor-based initial antiretroviral therapy among persons with human immunodeficiency virus in the United States and Canada. *Clin Infect Dis*. 2021;73(7):e2234-e2242. doi:10.1093/cid/ciaa1403

82. Petoumenos K, Kuwanda L, Ryom L, et al; D:A:D Study Group. Effect of changes in body mass index on the risk of cardiovascular disease and diabetes mellitus in HIV-positive individuals: results from the D:A:D study. *J Acquir Immune Defic Syndr*. 2021;86(5):579-586. doi:10.1097/QAI.0000000000002603

83. Hagins D, Mussini C, Zhang F, et al. Week-48 metabolic health after switch to DTG/3TC vs CAR by baseline regimen: SALSA [Abstract 603] in special issue: Abstracts From the 2022 Conference on Retroviruses and Opportunistic Infections. *Top Antiv Med*. 2022;30(1 suppl):236.

84. Wilding JPH, Batterham RL, Calanna S, et al; STEP 1 Study Group. Once-weekly semaglutide in adults with overweight or obesity. *N Engl J Med*. 2021;384(11):989-1002. doi:10.1056/NEJMoa2032183

85. Semaglutide's efficacy in achieving weight loss for those with HIV (SWIFT) [NCT04174755]. ClinicalTrials.gov. Accessed November 9, 2022. https://clinicaltrials.gov/ct2/show/NCT04174755

86. Justice AC, Goetz MB, Stewart CN, et al. Delayed presentation of HIV among older individuals: a growing problem. *Lancet HIV*. 2022;9(4):e269-e280. doi:10.1016/S2352-3018(22)00003-0

87. Lee JS, Humes E, Hogan BC, et al; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Observed CD4 counts at entry into HIV care and at antiretroviral therapy prescription by age in the USA, 2004-18: a cohort study. *Lancet HIV*. 2022;9(suppl 1):S2. doi:10.1016/S2352-3018(22)00067-4

88. Zhabokritsky A, Szadkowski L, Burchell AN, et al; Canadian Observational Cohort (CANOC) Collaboration. Immunological and virological response to initial antiretroviral therapy among older people living with HIV in the Canadian Observational Cohort (CANOC). *HIV Med*. 2021;22 (8):759-769. doi:10.1111/hiv.13125

89. Richterman A, Sax PE. Antiretroviral therapy in older people with HIV. *Curr Opin HIV AIDS*. 2020;15 (2):118-125. doi:10.1097/COH.0000000000000614

90. Courlet P, Stader F, Guidi M, et al; Swiss HIV Cohort Study. Pharmacokinetic profiles of boosted darunavir, dolutegravir and lamivudine in aging people living with HIV. *AIDS*. 2020;34(1):103-108. doi:10.1097/QAD.0000000000002372

91. Smith L, Letendre S, Erlandson KM, Ma Q, Ellis RJ, Farhadian SF. Polypharmacy in older adults with HIV infection: effects on the brain. *J Am Geriatr Soc*. 2022;70(3):924-927. doi:10.1111/jgs.17569

92. Blanco JR, Morillo R, Abril V, et al; Gesida and SEFH. Deprescribing of non-antiretroviral therapy in HIV-infected patients. *Eur J Clin Pharmacol*. 2020;76(3):305-318. doi:10.1007/s00228-019-02785-z

93. López-Centeno B, Badenes-Olmedo C, Mataix-Sanjuan A, et al. Potentially inappropriate medications in older adults living with HIV. *HIV Med*. 2020;21(8):541-546. doi:10.1111/hiv.12883

94. Koren DE, Scarsi KK, Farmer EK, et al. A call to action: the role of antiretroviral stewardship in inpatient practice, a joint policy paper of the Infectious Diseases Society of America, HIV Medicine Association, and American Academy of HIV Medicine. *Clin Infect Dis*. 2020;70(11):2241-2246. doi:10.1093/cid/ciz792

95. Greene M, Shi Y, Boscardin J, Sudore R, Gandhi M, Covinsky K. Geriatric conditions and healthcare utilisation in older adults living with HIV. *Age Ageing*. 2022;51(5):afac093. doi:10.1093/ageing/afac093

96. Liu S, Yan Q, Jiang Y, et al. The impact of frailty on all-cause mortality in patients with HIV infection: a systematic review and meta-analysis. *AIDS Res Hum Retroviruses*. 2022;38(9):692-699. doi:10.1089/aid.2021.0155

97. Ellis RJ, Paolillo E, Saloner R, Heaton RK. Higher comorbidity burden predicts worsening neurocognitive trajectories in people with human immunodeficiency virus. *Clin Infect Dis*. 2022;74(8): 1323-1328. doi:10.1093/cid/ciab655

98. Aung HL, Gates TM, Mao L, Brew BJ, Rourke SB, Cysique LA. Abnormal cognitive aging in people with HIV: evidence from data integration between two countries' cohort studies. *AIDS*. 2022;36(8): 1171-1179. doi:10.1097/QAD.0000000000003230

99. Letendre SL, Roa J, Chen H, et al. ACTG A5324: a randomized trial of ART intensification for cognitive impairment in PWH [Abstract 133] in special issue: Abstracts From the 2022 Conference

on Retroviruses and Opportunistic Infections. *Top Antiv Med*. 2022;30(1 suppl):50-51.

100. 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

101. Davis AJ, Greene M, Siegler E, et al. Strengths and challenges of various models of geriatric consultation for older adults living with human immunodeficiency virus. *Clin Infect Dis*. 2022;74(6):1101-1106. doi:10.1093/cid/ciab682

102. Kiplagat J, Tran DN, Barber T, et al. How health systems can adapt to a population ageing with HIV and comorbid disease. *Lancet HIV*. 2022;9(4):e281-e292. doi:10.1016/S2352-3018(22)00009-1

103. Lazarus JV, Safreed-Harmon K, Kamarulzaman A, et al. Consensus statement on the role of health systems in advancing the long-term well-being of people living with HIV. *Nat Commun*. 2021;12(1):4450. doi:10.1038/s41467-021-24673-w

104. Syphilis. Centers for Disease Control and Prevention. Updated March 24, 2022. Accessed November 9, 2022. https://www.cdc.gov/std/treatment-guidelines/syphilis.htm

105. US Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States–2021 Update: A Clinical Practice Guideline. Centers for Disease Control and Prevention. Published 2021. Accessed July 28, 2022. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

106. Shieh E, Marzinke MA, Fuchs EJ, et al. Transgender women on oral HIV pre-exposure prophylaxis have significantly lower tenofovir and emtricitabine concentrations when also taking oestrogen when compared to cisgender men. *J Int AIDS Soc*. 2019;22(11):e25405. doi:10.1002/jia2.25405

107. Yager JL, Anderson PL. Pharmacology and drug interactions with HIV PrEP in transgender persons receiving gender affirming hormone therapy. *Expert Opin Drug Metab Toxicol*. 2020;16(6):463-474. doi:10.1080/17425255.2020.1752662

108. Delany-Moretlwe S, Hughes JP, Bock P, et al; HPTN 084 Study Group. 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

109. Landovitz RJ, Li S, Eron JJ Jr, et al. Tail-phase safety, tolerability, and pharmacokinetics of long-acting injectable cabotegravir in HIV-uninfected adults: a secondary analysis of the HPTN 077 trial. *Lancet HIV*. 2020;7(7):e472-e481. doi:10.1016/S2352-3018(20)30106-5

110. Eshleman S, Fogel JM, Halvas EK, et al. CA-LA PrEP: early detection of HIV infection may reduce InSTI resistance risk [Abstract LB95] in special issue: Abstracts From the 2022 Conference on Retroviruses and Opportunistic Infections. *Top Antiv Med*. 2022;30(1 suppl):36-37.

111. National Clinician Consultation Center website. Accessed November 9, 2022. https://aidsetc.org/aetc-program/national-clinician-consulation-center

112. Krakower D, Maloney KM, Powell VE, et al. Patterns and clinical consequences of discontinuing HIV preexposure prophylaxis during primary care. *J Int AIDS Soc*. 2019;22(2):e25250. doi:10.1002/jia2.25250

113. Marcus JL, Hurley LB, Dentoni-Lasofsky D, et al. Barriers to preexposure prophylaxis use among individuals with recently acquired HIV infection in Northern California. *AIDS Care*. 2019;31(5):536-544. doi:10.1080/09540121.2018.1533238

114. Molina JM, Squires K, Sax PE, et al; DRIVE-FORWARD Study Group. Doravirine versus ritonavir-boosted darunavir in antiretroviral-naive adults with HIV-1 (DRIVE-FORWARD): 48-week results of a randomised, double-blind, phase 3, non-inferiority trial. *Lancet HIV*. 2018;5(5):e211-e220. doi:10.1016/S2352-3018(18)30021-3

115. Luetkemeyer A, Dombroski J, Cohen S. Doxycycline post-exposure prophylaxis for STI prevention among MSM and transgender women on HIV PrEP or living with HIV: high efficacy to reduce incident STIs in a randomised trial [Abstract OALBX0103]. Poster presented at: 24th International AIDS Conference; 2022; Montreal, Quebec, Canada.

116. Wagman JA, Wynn A, Matsuzaki M, et al. Hazardous alcohol use, antiretroviral therapy receipt, and viral suppression in people living with HIV who inject drugs in the United States, India, Russia, and Vietnam. *AIDS*. 2020;34(15):2285-2294. doi:10.1097/QAD.0000000000002716

117. Springer SA, Larney S, Alam-Mehrjerdi Z, Altice FL, Metzger D, Shoptaw S. Drug treatment as HIV prevention among women and girls who inject drugs from a global perspective: progress, gaps, and future directions. *J Acquir Immune Defic Syndr*. 2015;69(suppl 2):S155-S161. doi:10.1097/QAI.0000000000000637

118. Feelemyer J, Arasteh K, Huong DT, et al; DRIVE Study Team. Associations between methamphetamine use and lack of viral suppression among a cohort of HIV-positive persons who inject drugs in Hai Phong, Vietnam. *AIDS*. 2020;34(13):1875-1882. doi:10.1097/QAD.0000000000002680

119. Satre DD, Sarovar V, Leyden W, et al. Changes in days of unhealthy alcohol use and antiretroviral therapy adherence, HIV RNA levels, and condomless sex: a secondary analysis of clinical trial data. *AIDS Behav*. 2020;24(6):1784-1792. doi:10.1007/s10461-019-02742-y

120. Springer SA, Merluzzi AP, Del Rio C. Integrating responses to the opioid use disorder and infectious disease epidemics: a report from the National Academies of Sciences, Engineering, and Medicine. *JAMA*. 2020;324(1):37-38. doi:10.1001/jama.2020.2559

121. Springer SA, Barocas JA, Wurcel A, et al. Federal and state action needed to end the infectious complications of illicit drug use in the United States: IDSA and HIVMA's advocacy agenda. *J Infect Dis*. 2020;222(suppl 5):S230-S238. doi:10.1093/infdis/jiz673

122. Nance RM, Trejo MEP, Whitney BM, et al. Impact of abstinence and of reducing illicit drug use without abstinence on human immunodeficiency virus viral load. *Clin Infect Dis*. 2020;70(5):867-874. doi:10.1093/cid/ciz299

123. Hoffman KA, Baker R, Fanucchi LC, et al. Perspectives on extended-release naltrexone induction among patients living with HIV and opioid use disorder: a qualitative analysis. *Addict Sci Clin Pract*. 2021;16(1):67. doi:10.1186/s13722-021-00277-z

124. 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

125. 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

126. Puryear SB, Balzer LB, Ayieko J, et al. Associations between alcohol use and HIV care cascade outcomes among adults undergoing population-based HIV testing in East Africa. *AIDS*. 2020;34(3):405-413. doi:10.1097/QAD.0000000000002427

127. McNamara KF, Biondi BE, Hernández-Ramírez RU, Taweh N, Grimshaw AA, Springer SA. A systematic review and meta-analysis of studies evaluating the effect of medication treatment for opioid use disorder on infectious disease outcomes. *Open Forum Infect Dis*. 2021;8(8):ofab289. doi:10.1093/ofid/ofab289

128. Springer SA, Qiu J, Saber-Tehrani AS, Altice FL. Retention on buprenorphine is associated with high levels of maximal viral suppression among HIV-infected opioid dependent released prisoners. *PLoS One*. 2012;7(5):e38335. doi:10.1371/journal.pone.0038335

129. Springer SA, Di Paola A, Azar MM, et al. Extended-release naltrexone improves viral suppression among incarcerated persons living with HIV with opioid use disorders transitioning to the community: results of a double-blind, placebo-controlled randomized trial. *J Acquir Immune Defic Syndr*. 2018;78(1):43-53. doi:10.1097/QAI.0000000000001634

130. Springer SA, Di Paola A, Barbour R, Azar MM, Altice FL. Extended-release naltrexone improves viral suppression among incarcerated persons living with HIV and alcohol use disorders transitioning to the community: results from a double-blind, placebo-controlled trial. *J Acquir Immune Defic Syndr*. 2018;79(1):92-100. doi:10.1097/QAI.0000000000001759

131. Fanucchi L, Springer SA, Korthuis PT. Medications for treatment of opioid use disorder among persons living with HIV. *Curr HIV/AIDS Rep*. 2019;16(1):1-6. doi:10.1007/s11904-019-00436-7

132. Seval N, Eaton E, Springer SA. Beyond antibiotics: a practical guide for the infectious disease physician to treat opioid use disorder in the setting of associated infectious diseases. *Open Forum Infect Dis*. 2019;7(1):ofz539. doi:10.1093/ofid/ofz539

133. Silverman K, Holtyn AF, Rodewald AM, et al. Incentives for viral suppression in people living with HIV: a randomized clinical trial. *AIDS Behav*. 2019;23(9):2337-2346. doi:10.1007/s10461-019-02592-8

134. Prendergast M, Podus D, Finney J, Greenwell L, Roll J. Contingency management for treatment of substance use disorders: a meta-analysis. *Addiction*. 2006;101(11):1546-1560. doi:10.1111/j.1360-0443.2006.01581.x

135. Menza TW, Jameson DR, Hughes JP, Colfax GN, Shoptaw S, Golden MR. Contingency management to reduce methamphetamine use and sexual risk among men who have sex with men: a randomized controlled trial. *BMC Public Health*. 2010;10:774. doi:10.1186/1471-2458-10-774

136. Landovitz RJ, Fletcher JB, Shoptaw S, Reback CJ. Contingency management facilitates the use of postexposure prophylaxis among stimulant-using men who have sex with men. *Open Forum Infect Dis*. 2015;2(1):ofu114. doi:10.1093/ofid/ofu114

137. Mistler CB, Copenhaver MM, Shrestha R. The pre-exposure prophylaxis (PrEP) care cascade in people who inject drugs: a systematic review. *AIDS Behav*. 2021;25(5):1490-1506. doi:10.1007/s10461-020-02988-x

138. Assoumou SA, Paniagua SM, Gonzalez P, et al. HIV pre-exposure prophylaxis and buprenorphine at a drug detoxification center during the opioid epidemic: opportunities and challenges. *AIDS Behav*. 2021;25(8):2591-2598. doi:10.1007/s10461-021-03220-0

139. 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

140. Belludi A, McFall AM, Solomon SS, et al. Awareness of and willingness to use pre-exposure prophylaxis (PrEP) among people who inject drugs and men who have sex with men in India: results from a multi-city cross-sectional survey. *PLoS One*. 2021;16(2):e0247352. doi:10.1371/journal.pone.0247352

141. Broz D, Zibbell J, Foote C, et al. Multiple injections per injection episode: high-risk injection practice among people who injected pills during the 2015 HIV outbreak in Indiana. *Int J Drug Policy*. 2018;52:97-101. doi:10.1016/j.drugpo.2017.12.003

142. 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

143. Taweh N, Schlossberg E, Frank C, et al. Linking criminal justice-involved individuals to HIV, hepatitis C, and opioid use disorder prevention and treatment services upon release to the community: progress, gaps, and future directions. *Int J Drug Policy*. 2021;96:103283. doi:10.1016/j.drugpo.2021.103283

144. Jiang T, Liu C, Zhang J, Huang X, Xu J. Impact of the COVID-19 pandemic on the UNAIDS six 95% HIV control targets. *Front Med (Lausanne)*. 2022;9:818054. doi:10.3389/fmed.2022.818054

145. Santos GM, Hong C, Wilson N, et al. Persistent disparities in COVID-19-associated impacts on HIV prevention and care among a global sample of sexual and gender minority individuals. *Glob Public Health*. 2022;17(6):827-842. doi:10.1080/17441692.2022.2063362

146. Dear N, Duff E, Esber A, et al; AFRICOS Study Group. Transient reductions in human immunodeficiency virus (HIV) clinic attendance and food security during the coronavirus disease 2019 (COVID-19) pandemic for people living with HIV in 4 African countries. *Clin Infect Dis*. 2021;73(10):1901-1905. doi:10.1093/cid/ciab379

147. Jewell BL, Mudimu E, Stover J, et al; HIV Modelling Consortium. Potential effects of disruption to HIV programmes in sub-Saharan Africa caused by COVID-19: results from multiple mathematical models. *Lancet HIV*. 2020;7(9):e629-e640. doi:10.1016/S2352-3018(20)30211-3

148. Ambrosioni J, Blanco JL, Reyes-Urueña JM, et al; COVID-19 in HIV Investigators. Overview of SARS-CoV-2 infection in adults living with HIV. *Lancet HIV*. 2021;8(5):e294-e305. doi:10.1016/S2352-3018(21)00070-9

149. Brown LB, Spinelli MA, Gandhi M. The interplay between HIV and COVID-19: summary of the data and responses to date. *Curr Opin HIV AIDS*. 2021;16(1):63-73. doi:10.1097/COH.0000000000000659

150. Park LS, McGinnis KA, Gordon KS, et al; CIVET Collaboration of the NA-ACCORD of IeDEA. SARS-CoV-2 testing and positivity among persons with and without HIV in 6 US cohorts. *J Acquir Immune Defic Syndr*. 2022;90(3):249-255. doi:10.1097/QAI.0000000000002943

151. Treskova-Schwarzbach M, Haas L, Reda S, et al. Pre-existing health conditions and severe COVID-19 outcomes: an umbrella review approach and meta-analysis of global evidence. *BMC Med*. 2021;19(1):212. doi:10.1186/s12916-021-02058-6

152. Nomah DK, Reyes-Urueña J, Díaz Y, et al; PISCIS Study Group. Sociodemographic, clinical, and immunological factors associated with SARS-CoV-2 diagnosis and severe COVID-19 outcomes in people living with HIV: a retrospective cohort study. *Lancet HIV*. 2021;8(11):e701-e710. doi:10.1016/S2352-3018(21)00240-X

153. Shapiro AE, Bender Ignacio RA, Whitney BM, et al; CFAR Network of Integrated Clinical Systems. Factors associated with severity of COVID-19 disease in a multicenter cohort of people with HIV in the United States, March-December 2020. *J Acquir Immune Defic Syndr*. 2022;90(4):369-376. doi:10.1097/QAI.0000000000002989

154. Braunstein SL, Lazar R, Wahnich A, Daskalakis DC, Blackstock OJ. Coronavirus disease 2019 (COVID-19) infection among people with human immunodeficiency virus in New York City: a population-level analysis of linked surveillance data. *Clin Infect Dis*. 2021;72(12):e1021-e1029. doi:10.1093/cid/ciaa1793

155. Dandachi D, Geiger G, Montgomery MW, et al. Characteristics, comorbidities, and outcomes in a multicenter registry of patients with human immunodeficiency virus and coronavirus disease 2019. *Clin Infect Dis*. 2021;73(7):e1964-e1972. doi:10.1093/cid/ciaa1339

156. Woldemeskel BA, Karaba AH, Garliss CC, et al. The BNT162b2 mRNA vaccine elicits robust humoral and cellular immune responses in people living with human immunodeficiency virus (HIV). *Clin Infect Dis*. 2022;74(7):1268-1270. doi:10.1093/cid/ciab648

157. González de Aledo M, Cañizares A, Vázquez-Rodríguez P, et al. Safety and Immunogenicity of SARS-CoV-2 vaccines in people with HIV. *AIDS*. 2022;36(5):691-695. doi:10.1097/QAD.0000000000003161

158. Lee ARYB, Wong SY, Chai LYA, et al. Efficacy of covid-19 vaccines in immunocompromised patients: systematic review and meta-analysis. *BMJ*. 2022;376:e068632. doi:10.1136/bmj-2021-068632

159. Hassold N, Brichler S, Ouedraogo E, et al. Impaired antibody response to COVID-19 vaccination in advanced HIV infection. *AIDS*. 2022;36(4):F1-F5. doi:10.1097/QAD.0000000000003166

160. Xu X, Vesterbacka J, Aleman S, Nowak P; COVAXID Study Group. High seroconversion rate after vaccination with mRNA BNT162b2 vaccine against SARS-CoV-2 among people with HIV—but HIV viremia matters? *AIDS*. 2022;36(3):479-481. doi:10.1097/QAD.0000000000003135

161. Haidar G, Agha M, Bilderback A, et al. Prospective evaluation of coronavirus disease 2019 (COVID-19) vaccine responses across a broad spectrum of immunocompromising conditions: the COVID-19 Vaccination in the Immunocompromised Study (COVICS) study. *Clin Infect Dis*. 2022;75(1):e630-e644. doi:10.1093/cid/ciac103

162. Nault L, Marchitto L, Goyette G, et al. Covid-19 vaccine immunogenicity in people living with HIV-1. *Vaccine*. 2022;40(26):3633-3637. doi:10.1016/j.vaccine.2022.04.090

163. Schmidt KG, Harrer EG, Tascilar K, et al. Characterization of serum and mucosal SARS-CoV-2-antibodies in HIV-1-infected subjects after BNT162b2 mRNA vaccination or SARS-CoV-2 infection. *Viruses*. 2022;14(3):651. doi:10.3390/v14030651

164. Madhi SA, Moodley D, Hanley S, et al; 2019nCoV-501 Study Group. Immunogenicity and safety of a SARS-CoV-2 recombinant spike protein nanoparticle vaccine in people living with and without HIV-1 infection: a randomised, controlled, phase 2A/2B trial. *Lancet HIV*. 2022;9(5):e309-e322. doi:10.1016/S2352-3018(22)00041-8

165. Coburn SB, Humes E, Lang R, et al; Corona-Infectious-Virus Epidemiology Team (CIVETs) of the NA-ACCORD of IeDEA. Analysis of postvaccination breakthrough COVID-19 infections among adults with HIV in the United States. *JAMA Netw Open*. 2022;5(6):e2215934. doi:10.1001/jamanetworkopen.2022.15934

166. Guidance for COVID-19 and People with HIV. Guidelines Working Groups of the NIH Office of AIDS Research Advisory Council and US Department of Health and Human Services (HHS). Updated February 22, 2022. Accessed July 28, 2022. https://clinicalinfo.hiv.gov/en/guidelines/guidance-covid-19-and-people-hiv/whats-new-covid-19-and-hiv-guidance

167. National Institutes of Health. COVID-19 treatment guidelines. Accessed November 9, 2022. https://www.covid19treatmentguidelines.nih.gov/

168. Bhimraj A, Morgan RL, Shumaker AH, et al. Infectious Diseases Society of America guidelines on the treatment and management of patients with COVID-19. *Clin Infect Dis*. Published online April 27, 2020.

169. Mazzitelli M, Trunfio M, Sasset L, et al. Factors associated with severe COVID-19 and post-acute COVID-19 syndrome in a cohort of people living with HIV on antiretroviral treatment and with undetectable HIV RNA. *Viruses*. 2022;14(3):493. doi:10.3390/v14030493

170. Ferré VM, Bachelard A, Zaidi M, et al. Detection of monkeypox virus in anorectal swabs from asymptomatic men who have sex with men in a sexually transmitted infection screening program in Paris, France. *Ann Intern Med*. 2022;175(10):1491-1492. doi:10.7326/M22-2183

171. Loncharich MF, Anderson CW. Interferon inhibition for lupus with anifrolumab: critical appraisal of the evidence leading to FDA approval. *ACR Open Rheumatol*. 2022;4(6):486-491. doi:10.1002/acr2.11414

172. Thornhill JP, Barkati S, Walmsley S, et al; SHARE-net Clinical Group. Monkeypox virus infection in humans across 16 countries—April-June 2022. *N Engl J Med*. 2022;387(8):679-691. doi:10.1056/NEJMoa2207323

173. Health Alert Network (HAN). Severe manifestations of monkeypox among people who are immunocompromised due to HIV or other conditions. Published September 29, 2022. Accessed November 1, 2022. https://emergency.cdc.gov/han/2022/han00475.asp

174. Clinical Info HIV. Guidelines for the use of antretroviral agents in adults and adolescents with HIV. Updated September 1, 2022. Accessed November 9, 2022. https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/overview?view=full

175. UNAIDS. 2021 UNAIDS Global AIDS Update: Confronting Inequalities—Lessons for Pandemic Responses From 40 Years of AIDS. Published July 14, 2021. Accessed November 9, 2022. https://www.unaids.org/en/resources/documents/2021/2021-global-aids-update

176. 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

177. DiNenno EA, Delaney KP, Pitasi MA, et al. HIV testing before and during the COVID-19 pandemic—United States, 2019-2020. *MMWR Morb Mortal Wkly Rep*. 2022;71(25):820-824. doi:10.15585/mmwr.mm7125a2

178. Centers for Disease Control and Prevention (CDC). Diagnoses of HIV infection in the United States and dependent areas 2020. Accessed November 9, 2022. https://www.cdc.gov/hiv/library/reports/hiv-surveillance/vol-33/index.html

179. Dailey AF, Gant Z, Hu X, Johnson Lyons S, Okello A, Satcher Johnson A. Association between social vulnerability and rates of HIV diagnoses among black adults, by selected characteristics and region of residence—United States, 2018. *MMWR Morb Mortal Wkly Rep*. 2022;71(5):167-170. doi:10.15585/mmwr.mm7105a2

180. HIV/AIDS Surveillance in Europe 2021: 2020 data. European Centre for Disease Prevention and Control. Published 2021. Accessed November 9, 2022. https://www.ecdc.europa.eu/sites/default/files/documents/2021-Annual_HIV_Report_0.pdf

181. Schaefer R, Schmidt HA, Ravasi G, et al. Adoption of guidelines on and use of oral pre-exposure prophylaxis: a global summary and forecasting study. *Lancet HIV*. 2021;8(8):e502-e510. doi:10.1016/S2352-3018(21)00127-2

182. Keen P, Bavinton BR. Could disparities in PrEP uptake limit the public health benefit? *Lancet Public Health*. 2020;5(9):e467-e468. doi:10.1016/S2468-2667(20)30183-3

183. Smith JA, Garnett GP, Hallett TB. The potential impact of long-acting cabotegravir for HIV prevention in South Africa: a mathematical modeling study. *J Infect Dis*. 2021;224(7):1179-1186. doi:10.1093/infdis/jiaa296

184. Political Declaration on HIV and AIDS: Ending Inequalities and Getting on Track to End AIDS by 2030. UNAIDS. Published June 9, 2021. Accessed July 28, 2022. https://www.unaids.org/sites/default/files/media_asset/2021_political-declaration-on-hiv-and-aids_en.pdf