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## Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults:

### 2018 Recommendations of the International Antiviral Society–USA Panel

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## Abstract

**IMPORTANCE**—Antiretroviral therapy (ART) is the cornerstone of prevention and management of HIV infection.

**OBJECTIVE**—To evaluate new data and treatments and incorporate this information into updated recommendations for initiating therapy, monitoring individuals starting therapy, changing regimens, and preventing HIV infection for individuals at risk.

**EVIDENCE REVIEW**—New evidence collected since the International Antiviral Society–USA 2016 recommendations via monthly PubMed and EMBASE literature searches up to April 2018;

data presented at peer-reviewed scientific conferences. A volunteer panel of experts in HIV research and patient care considered these data and updated previous recommendations.

**FINDINGS**—ART is recommended for virtually all HIV-infected individuals, as soon as possible after HIV diagnosis. Immediate initiation (eg, rapid start), if clinically appropriate, requires adequate staffing, specialized services, and careful selection of medical therapy. An integrase strand transfer inhibitor (InSTI) plus 2 nucleoside reverse transcriptase inhibitors (NRTIs) is generally recommended for initial therapy, with unique patient circumstances (eg, concomitant diseases and conditions, potential for pregnancy, cost) guiding the treatment choice. CD4 cell count, HIV RNA level, genotype, and other laboratory tests for general health and co-infections are recommended at specified points before and during ART. If a regimen switch is indicated, treatment history, tolerability, adherence, and drug resistance history should first be assessed; 2 or 3 active drugs are recommended for a new regimen. HIV testing is recommended at least once for anyone who has ever been sexually active and more often for individuals at ongoing risk for infection. Preexposure prophylaxis with tenofovir disoproxil fumarate/emtricitabine and appropriate monitoring is recommended for individuals at risk for HIV.

**CONCLUSIONS AND RELEVANCE**—Advances in HIV prevention and treatment with antiretroviral drugs continue to improve clinical management and outcomes for individuals at risk for and living with HIV.

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New drugs and new approaches to prevent and manage HIV infection necessitate an update to the International Antiviral (formerly AIDS) Society–USA (IAS-USA) recommendations, last published in 2016.<sup>1</sup> This report incorporates current data on new regimens and new approaches into recommendations for the treatment and prevention of HIV.

## Methods

Recommendations were developed by an international panel of 16 volunteer experts in HIV research and care. Members were screened for expertise, involvement in research and care, financial relationships, and ability to work toward consensus (ie, ability to consider all available data, evidence, and group discussions or opinions to reach agreement on recommendations). The panel convened in person (N = 2) and by conference calls (N = 10 full-panel and multiple subgroup calls) from September 2017 to June 2018. Teams for each section evaluated relevant evidence and drafted recommendations for full-panel review.

New evidence used was published in the literature, presented at major conferences, or released as safety reports.<sup>1</sup> Monthly literature searches were conducted in PubMed and EMBASE between July 2016 and April 2018. Approximately 237 relevant citations were identified from more than 4490 reports. Abstracts presented at scientific conferences since July 2016 were identified. Relevant scientific publications or abstracts presented at peer-reviewed conferences were requested from drug manufacturers.

These updated recommendations focus on adults (> 18 years) with or at risk for HIV infection in settings in which most antiretroviral drugs are available or in late-stage development (new drug application filed). Recommendations were made by consensus and rated according to strength of the recommendation and quality of the evidence (Table 1). For

recommendations that have not changed substantially or for which few new data have become available since 2016, the prior report should be reviewed.<sup>1</sup> Details about the development process, panel, evidence collection and literature searches, and sponsor (IAS-USA) and its policies are reported in the Supplement.

## When to Start

Recommendations for initiating antiretroviral therapy (ART) are summarized in Box 1. In patients with established HIV, ART should be initiated as soon as possible after diagnosis.<sup>1</sup> The question of when to start ART is focused now on whether immediate ART (same day to 14 days after diagnosis) is preferred. The World Health Organization endorsed ART initiation within 7 days of new diagnosis (including same day), citing improved viral suppression.<sup>4</sup> Rapid initiation of ART requires improving linkage to care and addressing structural barriers (eg, staffing and services availability) within clinics and ART distribution systems.

## Rapid ART Start

Randomized trials in Lesotho, Haiti, and South Africa showed significant improvements in viral load suppression at 10 or 12 months and retention in care with rapid initiation of therapy.<sup>5-7</sup> In 1 study, individuals were randomized to early ART with simplified counseling and point-of-care CD4 cell assays or to standard care. In the intervention group, 80% began ART within 14 days and 71% started ART the same day of eligibility, compared with 38% and 18%, respectively, in the control group. Virologic suppression at 1 year was improved in the intervention group (85% vs 75%).<sup>8</sup>

Several cohorts examined the feasibility, outcomes, and challenges of rapid ART start.<sup>9</sup> Meta-analyses of 8 cohorts showed an improvement in the proportion of patients starting ART within 3 months but no benefit on retention in care.<sup>10</sup> A statistically non-significant trend toward worse viral suppression was observed for those who started ART rapidly in 1 cohort.<sup>10</sup> San Francisco implemented a citywide rapid ART program in which newly diagnosed persons were linked to care within 5 days from diagnosis and offered treatment on the day of their clinic visit. Of 265 newly diagnosed persons, 97% were linked to care (30% within 5 days) and 81% started ART; time from diagnosis to HIV RNA level below 200 copies/mL decreased by more than 50% and time from first care visit to ART decreased from 27 days to 1 day.<sup>11,12</sup> A large HIV clinic in Atlanta implemented rapid access to ART on the day of the initial visit. Median time from initial diagnosis to HIV-1 RNA level below 200 copies/mL decreased from 67 to 41 days; however, the program was not sustainable because of increased patient load and inadequate funding for staffing.<sup>13</sup>

Despite the success of rapid ART initiation in some settings, starting ART on the day of diagnosis requires coordination between testing and treatment settings and access to resources that may limit treatment uptake. All elements of conventional treatment initiation must be in place at the treatment site but provided in a way that ensures immediate access.<sup>12</sup>

ART initiation, including rapid start, is recommended for all infected ambulatory patients committed to starting ART (unless the patient has symptoms that suggest an opportunistic

infection for which immediate ART is contraindicated) or for those with unclear HIV diagnosis (eg, discordant serologic or rapid test results) (evidence rating AIII). Because of concerns about transmitted drug resistance (eg, K103N mutation), immediate ART should not be nonnucleoside reverse transcriptase inhibitor (NNRTI)-based (evidence rating AIII). Dolutegravir/tenofovir alafenamide (TAF) (or tenofovir disoproxil fumarate [TDF])/emtricitabine (or lamivudine) or bictegravir/TAF/emtricitabine or boosted darunavir TAF (or TDF)/emtricitabine (or lamivudine) are recommended for rapid initiation (AIII). Patients requiring abacavir should not begin until the result of testing for the HLA-B\*5701 allele is available (evidence rating AIa).

### When to Start ART in the Setting of Active Opportunistic Infections and Malignancies

Recommendations for initiating ART in the setting of active opportunistic infections (OIs) remain unchanged.<sup>1</sup> ART should be started within the first 2 weeks after diagnosis for most OIs (evidence rating AIa). Data further support the recommendation to start ART within the first 2 weeks of initiation of tuberculosis treatment for patients with CD4 cell counts below 50/ $\mu$ L and within the first 2 to 8 weeks for those with CD4 cell counts of 50/ $\mu$ L and above (evidence rating AIa). For patients with cryptococcal meningitis in high-resourced settings with access to optimal antifungal therapy, frequent monitoring, and aggressive management of intracranial pressure, ART should begin within 2 weeks of diagnosis.<sup>14,15</sup> Careful monitoring for immune reconstitution inflammatory syndrome is essential. For individuals diagnosed with HIV and a malignancy concurrently, ART should be initiated immediately.<sup>3</sup> Early adverse effects of ART can be monitored and managed while cancer staging and molecular testing are performed.

### Primary OI Prophylaxis

With ART universally recommended, the incidence of *Pneumocystis* pneumonia and major AIDS-associated OIs has declined to less than 1.45 and 0.4 per 100 person-years, respectively, in the United States.<sup>16</sup> For individuals with viral suppression while taking ART, the incidence and overall mortality of *Mycobacterium avium* complex disease is sufficiently low<sup>17,18</sup> that primary *Mycobacterium avium* complex prophylaxis is no longer recommended (evidence rating AIIa). Primary prophylaxis for *Pneumocystis* pneumonia is still recommended for patients meeting CD4 criteria (evidence rating AIa).<sup>17,19</sup> Primary prophylaxis for cryptococcal disease is not recommended in settings where incidence is low (evidence rating AIII).

### Recommended Initial Regimens

Recommendations for initial ART are summarized in Box 2. Regimens that do not require boosting with ritonavir or cobicistat are favored. Choosing a combination with a high barrier to resistance is important, particularly for individuals with inconsistent adherence. As more generic ART medications become available, cost and access to medications are likely to be of increasing importance (see below). Regimens are also listed for patients who cannot take the generally recommended initial regimens owing to anticipated problems with adherence, drug interactions, patient preference, financial considerations, or lack of availability of recommended options.

Recommended initial ART for most patients is listed in alphabetic order by integrase strand transfer inhibitor (InSTI) component (see also Table 2 for medications and their associated advantages and disadvantages). Bictegravir and dolutegravir do not require pharmacologic boosting, have a high barrier to resistance, and are part of regimens with low pill burden and toxicity. Studies of these drugs in initial regimens have shown comparable efficacy and no emergence of resistant virus.<sup>20,21</sup> There are substantially more data and longer-term experience with dolutegravir (approved in the United States in 2013) than with bictegravir (approved in 2018). Preliminary data have raised concerns regarding use of dolutegravir (and potentially other InSTIs) for individuals capable of becoming pregnant (see below). Raltegravir is well tolerated and has fewer drug interactions than other InSTIs but has a lower barrier to resistance and a higher pill burden. Elvitegravir regimens also have a lower barrier to resistance and include a pharmacologic booster (cobicistat) that results in more drug interactions.

In combination with 2 nucleoside reverse transcriptase inhibitors (NRTIs), the NNRTIs efavirenz and rilpivirine each demonstrate high rates of virologic suppression as initial therapy. Efavirenz-based treatment was standard initial therapy for many years, but studies have demonstrated higher rates of adverse effects (rash and central nervous system adverse effects) than InSTI-based therapy. Rilpivirine has a lower rate of central nervous system adverse effects and rash than efavirenz and is coformulated with TAF/emtricitabine into the smallest single tablet for initial therapy. However, rilpivirine must be taken with food, requires stomach acidity for adequate absorption, and is recommended only for patients with baseline HIV RNA level below 100 000 copies/mL and CD4 cell count above 200/ $\mu$ L.

The NNRTI doravirine is currently under investigation for initial therapy. In phase 3 trials, doravirine was noninferior to efavirenz and to ritonavir-boosted darunavir in achieving virologic suppression and had fewer central nervous system adverse events than efavirenz and a better lipid profile than either efavirenz or ritonavir-boosted darunavir.<sup>22,23</sup> Thus, doravirine may be preferable to existing NNRTIs, but no prospective studies compare it with InSTI-based regimens. Non-InSTI initial regimens are summarized in Table 3.

Abacavir is a component of the recommended regimen dolutegravir/abacavir/lamivudine. Individuals who test positive for the HLA-B\*5701 allele are at risk of a potentially life-threatening hypersensitivity reaction to abacavir.<sup>1</sup> Results of HLA-B\*5701 testing must be available before use (evidence rating A1a); patients who test positive should not be given abacavir (evidence rating A1a), and this information should be documented in the medical record.

Although some prior comparisons of abacavir/lamivudine and TDF/emtricitabine demonstrated an efficacy advantage of TDF/emtricitabine in patients with high HIV-1 RNA levels,<sup>1</sup> the differences have not been observed in studies that use InSTIs.<sup>20</sup> Abacavir has no activity against hepatitis B virus (HBV) and should not be used in patients with HIV and HBV.

TAF- and TDF-containing regimens are similar virologically. Compared with TDF, TAF results in a lower plasma level of tenofovir and higher intracellular concentration of the



active antiviral component tenofovir diphosphate. This results in fewer tenofovir-associated renal and bone toxic effects.<sup>25</sup> These differences between TAF and TDF are accentuated when TDF is used with ritonavir or cobicistat, which increase tenofovir plasma levels.<sup>26</sup>

### Two-Drug Initial Therapy

Initial 2-drug regimens are under investigation. This strategy may offer cost or toxicity advantages over standard 3-drug regimens, but efficacy needs to be confirmed.<sup>27</sup> Darunavir/ritonavir plus raltegravir was noninferior to darunavir/ritonavir plus 2 NRTIs, but the 2-drug regimen had higher rates of treatment failure in patients with a CD4 cell count below 200/ $\mu$ L or an HIV RNA level above 100 000 copies/mL.<sup>28</sup>

Dolutegravir plus lamivudine and darunavir/ritonavir plus lamivudine are being studied.<sup>29,30</sup> Until further data are available, initial 2-drug regimens are reserved for the rare situation when individuals cannot take abacavir, TAF, or TDF. In this situation, darunavir/ritonavir plus raltegravir (if <100 000 HIV RNA copies/mL and CD4 cell count >200/ $\mu$ L) or darunavir/ritonavir plus lamivudine may be used (if there is no lamivudine resistance) (evidence rating BIIa). Short-term data from comparative trials may provide support for dolutegravir plus lamivudine as initial 2-drug therapy (NCT02831764). Dolutegravir plus rilpivirine has not yet been assessed for initial therapy.<sup>31</sup>

### Unique Considerations

**Pregnancy**—Individuals who are pregnant should initiate ART as soon as possible for their own health and to reduce transmission to the infant (evidence rating AIIa).<sup>1</sup> The NRTI options include abacavir/lamivudine (or emtricitabine) if patient tests negative for HLA-B\*5701 or TDF/emtricitabine (or lamivudine). Insufficient safety data for TAF preclude use of this drug during pregnancy.

A preliminary report revealed neural tube defects among infants born to women taking a dolutegravir-containing regimen at conception, suggesting, for now, that dolutegravir should be avoided in individuals of childbearing age who wish to become pregnant, are trying to get pregnant, or are sexually active and not reliably using contraception.<sup>32</sup> All individuals of childbearing age should have documentation of a negative pregnancy test result before starting dolutegravir and should be counseled regarding this potential risk. More data are expected; it is not yet clear whether other InSTIs pose a similar risk of neural tube defects.

Raltegravir is the recommended InSTI for individuals who are already pregnant. Elvitegravir/cobicistat should not be used during pregnancy (evidence rating AIIa). Pregnant women already taking elvitegravir/cobicistat should be switched to a recommended regimen.<sup>33</sup> Bictegravir should not be used during pregnancy because available safety data are insufficient.

Recommended protease inhibitors (PIs) include atazanavir/ritonavir (once daily) or darunavir/ritonavir (twice daily). Drugs boosted with cobicistat (eg, darunavir/cobicistat and atazanavir/cobicistat) are not recommended for use during pregnancy because of pharmacokinetic concerns or insufficient data (evidence rating AIIb).<sup>32</sup> Efavirenz and rilpivirine are alternatives in pregnancy. There were initial concerns regarding potential

neural tube defects with efavirenz, but accumulated data now support the safety of efavirenz during pregnancy.

**HBV and Hepatitis C Virus Co-infection**—HIV-infected patients with HBV co-infection should initiate an ART regimen that contains TDF or TAF (evidence rating A1a), lamivudine or emtricitabine, and a third component.<sup>34–36</sup> Patients with HIV co-infected with hepatitis C virus (HCV) are candidates for HCV treatment and therefore should start an ART regimen with drugs that have minimal drug interactions with HCV therapies (evidence rating A1a), such as dolutegravir/abacavir/lamivudine, dolutegravir/TAF/emtricitabine, bictegravir/TAF/emtricitabine, or raltegravir plus TAF/emtricitabine. Clinicians should consult current HCV treatment guidelines (<https://www.hcvguidelines.org>).

**Bone, Kidney, and Cardiovascular Disease**—HIV is associated with osteoporosis and fractures.<sup>37</sup> Baseline bone mineral density testing is recommended in postmenopausal women and in anyone older than 50 years (evidence rating B111). During the first 1 to 2 years after ART initiation, patients may lose 2% to 6% of bone mineral density at the hip and spine. Patients taking TDF-containing regimens have a greater initial decline in bone mineral density than those who take a TAF- or abacavir-containing regimen.<sup>1,20,38</sup> Accordingly, TDF is not recommended for patients with osteopenia or osteoporosis (evidence rating B111). Abacavir does not require dose adjustment based on renal function. TAF can be used if creatinine clearance is above 30 mL/min/1.73 m<sup>2</sup> (evidence rating A1a).<sup>1</sup> Dose reduction of lamivudine is recommended for patients with creatinine clearance below 50mL/min/1.73m<sup>2</sup>. There are data supporting use of elvitegravir/cobicistat/TAF/emtricitabine once daily in patients with end-stage renal disease (estimated glomerular filtration rate <15 mL/min) receiving long-term hemodialysis.<sup>39</sup> HIV-infected patients with end-stage renal disease should be evaluated for kidney transplantation (evidence rating A1a).

The association between abacavir use and increased risk of myocardial infarction remains controversial.<sup>1,40</sup> Given the uncertainty, abacavir should be used with caution or avoided in patients who have or are at high risk for cardiovascular disease.

### Recommended Initial ART in the Setting of OIs and Malignancies

Choice of ART regimen in the setting of OIs and malignancies is guided by drug-drug interactions with the antimicrobial or chemotherapy regimen. Unboosted INSTI-based regimens are recommended. In the setting of malignancy, OI prophylaxis should be instituted, regardless of CD4 cell count, according to specific chemotherapy regimens used.

The recommended regimens for initial ART in the setting of rifamycin-based antituberculosis therapy are 2 NRTIs (excluding TAF) plus efavirenz (600 mg daily), raltegravir (800 mg twice daily), or dolutegravir (50 mg twice daily) (evidence rating A1a).<sup>1,41</sup> Coadministration of bictegravir (along with TAF/emtricitabine) twice daily with rifampin for 28 days is not recommended, owing to significantly decreased area under the curve (AUC) and peak serum concentration after administration ( $C_{max}$ ) for bictegravir (evidence rating A1a).<sup>42</sup> When TAF is administered with rifampin, plasma TAF  $C_{max}$  and AUC as well as intracellular tenofovir diphosphate levels were decreased; however, intracellular tenofovir diphosphate concentrations were higher than those achieved with



standard-dose TDF. Further evaluation of TAF in tuberculosis co-infection is under way.<sup>43</sup> Boosted PIs should be used only if an efavirenz- or InSTI-based regimen is not an option, and rifabutin (150 mg daily) should be substituted for rifampin in the antituberculosis regimen (evidence rating AIIa).<sup>1</sup>

For latent tuberculosis, a 1-month course of daily rifapentine plus isoniazid was equivalent to 9 months of isoniazid in persons with HIV.<sup>44</sup> Daily rifapentine can be safely administered with efavirenz-based ART. Once-weekly rifapentine/isoniazid is also safe, well-tolerated, and has an acceptable pharmacokinetic profile when used with raltegravir. Dolutegravir-based regimens should not be used with rifapentine/isoniazid for treatment or prevention of tuberculosis, pending further evaluation.<sup>45</sup>

## When and How to Switch

Recommendations for when and how to switch ART regimens are summarized in Box 3. The most common reasons for switching therapy are regimen simplification, newly diagnosed comorbidities (or to prevent comorbid conditions), and management of interactions with drugs or supplements. In addition to these reasons, a regimen switch may be required to minimize the patient's insurance co-payments or to satisfy payer formulary requirements.

Switching from older antiretroviral regimens should be considered when there is evidence of or potential for chronic toxicity, drug-drug interactions, or emergent adverse effects with current regimens.<sup>1,31,46</sup> Proactive switching from TDF- to TAF-containing regimens to minimize renal or bone adverse effects may be beneficial.<sup>47</sup> Care should be taken when switching from regimens boosted with ritonavir to ones boosted with cobicistat because of different drug-drug interactions.<sup>48</sup> In patients without a history of treatment failure, data support switching from regimens containing TDF to single-tablet regimens including dolutegravir/abacavir/lamivudine,<sup>46,49</sup> dolutegravir/rilpivirine,<sup>31</sup> elvitegravir/cobicistat/emtricitabine/TAF,<sup>1</sup> rilpivirine/emtricitabine/TAF,<sup>50</sup> darunavir/cobicistat/emtricitabine /TAF,<sup>51</sup> and bicitegravir/emtricitabine/TAF.<sup>20</sup> The switch to TAF-containing regimens is effective in maintaining HIV and HBV suppression in HIV/HBV co-infection.<sup>52</sup>

Simplification from a boosted PI<sup>53</sup> or from emtricitabine/TAF plus dolutegravir<sup>54</sup> to a single-tablet bicitegravir/emtricitabine/TAF regimen maintained viral suppression above 90%. Switching to 2 antiretroviral drugs has been used to reduce NRTI-related bone, kidney, and cardiovascular complications and cost. Dolutegravir/rilpivirine maintained virologic suppression in patients with no previous virologic failure or evidence of resistance who switched from a 3-drug ART regimen.<sup>31</sup> Dual-therapy regimens that include a boosted PI (lopinavir, atazanavir, or darunavir) and lamivudine were noninferior to 3-drug regimens in maintenance of virologic suppression up to 2 years.<sup>55–57</sup> Dolutegravir and lamivudine maintained virologic suppression to 48 weeks among patients with no prior virologic failure or transmitted NRTI resistance.<sup>58,59</sup>

Fewer options exist for regimen simplification in virologically suppressed individuals in whom several previous regimens have failed over time. Preexistent NRTI and NNRTI

mutations were associated with viral rebound after switching to rilpivirine/emtricitabine/TDF.<sup>60</sup> Darunavir/cobicistat/emtricitabine/TAF maintained virologic suppression in patients switching from a boosted PI plus emtricitabine/TDF, even if there was previous virologic failure, provided there was no history of darunavir failure or darunavir-resistance mutations.<sup>51</sup> Elvitegravir/cobicistat/emtricitabine/TAF combined with darunavir taken once daily effectively maintained virologic suppression in patients with 2-class drug resistance (up to 3 thymidine analogue-associated mutations but no multi-NRTI or darunavir mutations) while taking multidrug regimens.<sup>61</sup>

Monotherapy with PIs or InSTIs as a maintenance strategy is not recommended because of higher rates of virologic rebound,<sup>1,62–65</sup> often with resistant virus (evidence rating AIIb).<sup>62,63</sup>

### Virologic Failure

Virologic failure is increasingly uncommon with currently recommended ART regimens. Exploration for reasons of inconsistent adherence, drug-drug interactions, and collation of all resistance mutations identified by genotype, along with the ART history, are required to select a new treatment regimen.

For failure of an initial NNRTI-based regimen, dolutegravir plus NRTIs was superior to lopinavir plus NRTIs when the next regimen included at least 1 active NRTI.<sup>66</sup> For failure of initial PI-based or InSTI-based therapy (without resistance), boosted PI-or dolutegravir-based therapy with 1 or 2 fully active NRTIs should be effective.

For virologic failure after initial raltegravir- or elvitegravir-based regimens with the presence of integrase mutations, dolutegravir (50 mg twice daily) with at least 1 other active drug may be effective, but clinical data are lacking.<sup>1</sup> For virologic failure with more complex treatment history, therapy with at least 2 fully active drugs from different antiretroviral classes, perhaps including maraviroc in the setting of CC chemokine receptor 5 (CCR5)-tropic virus, is recommended.

Ibalizumab, an anti-CD4 monoclonal antibody that inhibits HIV cell entry via CD4 binding, is active against CCR5-and C-X-C chemokine receptor 4 (CXCR4)-tropic HIV isolates and may be useful as a fully active agent for patients with multiclass-resistant virus (evidence rating BII). Almost 50% of adults with virologic failure from multidrug-resistant HIV achieved undetectable HIV RNA levels at 24 weeks after receipt of biweekly intravenous ibalizumab (800 mg) with at least 1 other active drug.<sup>67,68</sup>

### Laboratory Monitoring

Recommendations for laboratory monitoring are summarized in Table 4 and Box 4. All individuals who have ever been sexually active should be tested for HIV at least once in their lives (evidence rating AIII). Risk for HIV often changes over a person's lifetime; risk evaluation is recommended at each routine clinical visit (evidence rating AIII). For men who have sex with men (MSM), transgender women, people who inject drugs, and others with increased risk, testing is recommended at least annually and perhaps as frequently as every 3

months (evidence rating BIII).<sup>69</sup> Diagnosis of sexually transmitted infections (STIs) and HCV can help identify individuals who should be tested more regularly for HIV and who might benefit from preexposure prophylaxis (PrEP) (evidence rating BIII).<sup>70-72</sup> Testing performed with assays that measure HIV antibody and antigen is recommended because it can take 3 weeks or longer for HIV antibodies to be detected after initial infection. In contrast, HIV RNA or combination antibody with p24 antigen tests that can detect HIV within 10 to 14 days after infection are recommended (evidence rating AIIa).<sup>73</sup> Relying on symptoms of the acute retroviral syndrome to trigger testing will miss infections because acute infection may be asymptomatic.<sup>1,74,75</sup> Available home-based HIV tests do not detect acute HIV infection but can be useful for people without access to testing otherwise.<sup>76</sup> All available tests can have false-positive results, so confirmatory measurement of HIV RNA level is recommended before ART initiation, although treatment can be initiated before results are available (evidence rating AIa).

Before starting ART, recommended laboratory monitoring includes HIV RNA level, CD4 cell count, and reverse transcriptase and protease genotype (InSTI genotyping generally is not recommended because it is not cost-effective)<sup>77</sup>; general health (testing for kidney/liver function, lipid levels, complete blood cell count, glucose level, and pregnancy status); and co-infections (hepatitis A, B, and C, tuberculosis, and STIs) (evidence rating AIa). Unless preexisting kidney or liver damage or high likelihood of transmitted drug resistance exists, the results of these tests should not delay start of ART (evidence rating BIII).<sup>78-81</sup> Testing for CCR5 tropism is recommended each time when considering maraviroc, and HLA-B\*5701 testing (only needed once) is recommended before starting abacavir (evidence rating AIa).

### Monitoring During ART

Within 6 weeks of starting ART, adherence and tolerability of therapy should be assessed, along with HIV RNA level. HIV RNA suppression may take up to 24 weeks, or faster with INSTI-based regimens.<sup>1,82</sup> Once the HIV RNA level is below 50 copies/mL, monitoring is recommended every 3 months until suppressed for at least 1 year. After that year, monitoring can be performed every 6 months if the patient maintains consistent medication adherence (evidence rating AIII). Of note, when monitoring intervals are extended and therapy fails, resistance has more time to emerge.<sup>80</sup>

Once viral suppression occurs with ART, CD4 cell counts usually increase.<sup>1,83</sup> CD4 measurements are recommended every 6 months until above 250/ $\mu$ L for at least 1 year with concomitant viral suppression (evidence rating BIII).<sup>1,84</sup> Afterward, CD4 cell counts need not be measured unless ART fails (defined below) or the patient has an immunosuppressive condition or treatment, such as steroid treatments or chemotherapy (evidence rating AIII).<sup>85</sup> Patients taking ART should have regular clinical and laboratory evaluations, including age- and risk-appropriate screening.

HIV RNA testing is used to detect if ART is failing. When HIV RNA level is above 50 copies/mL, repeating measurement of HIV RNA level within 4 weeks and reassessing for medication adherence and tolerability is recommended (evidence rating AIIb). Virologic failure is defined as HIV RNA level above 200 copies/mL on at least 2 consecutive

measurements. Once virologic failure is diagnosed, an HIV genotype should be obtained while the patient is taking the failing regimen.<sup>1</sup> If HIV genotyping is unsuccessful (eg, HIV RNA level is <1000 copies/mL), a proviral DNA analysis using deep sequencing methods may be used.<sup>86</sup> For virologic failure of InSTI containing ART, integrase resistance testing is recommended (evidence rating AIII).<sup>1,87–89</sup> Once a new regimen is started, HIV RNA level should be checked 4 to 6 weeks after initiation, following the same schedule as for monitoring of initial therapy (evidence rating AIII).<sup>1</sup>

Optimal care for patients with persistent viremia between 50 and 200 copies/mL is unclear. The ART regimen should be continued, with assessment of medication adherence (evidence rating BIII). There is no indication to intensify the regimen with additional antiretrovirals.<sup>90</sup>

## Engagement in Care and ART Adherence

Recommendations for engagement in care and ART adherence are summarized in Box 5. The HIV care continuum provides a framework to enhance individual health outcomes and maximize the benefits afforded by treatment as prevention. In the setting of sustained viral suppression, individuals with HIV do not transmit HIV to sexual partners (described as “undetectable = untransmissible” [U = U]).<sup>91,92</sup> In the United States, 22% of initial HIV diagnoses occur within 3 months of an AIDS diagnosis, indicating that persons are entering HIV care late.<sup>93</sup> Clinicians not offering HIV testing in emergency departments and acute medical care settings appears to be a major limitation in early diagnosis of HIV.<sup>94</sup>

Monitoring successive steps on the HIV care continuum helps address barriers that impede initial linkage, subsequent retention, and successful reengagement of patients lost to care.<sup>1</sup> Missed medical care visits can be assessed in real time and are consistently associated with poor HIV outcomes.<sup>95</sup> Assessment of missed visits in the prior year predicts future risk for missing future appointments, allowing for clinic-level intervention.<sup>96</sup> Coordination of appointment data with public health surveillance systems (eg, “Data to Care”) enhances linkage to, and retention and reengagement in, care.<sup>97,98</sup>

Resource-intensive interventions among vulnerable individuals (eg, those hospitalized or with substance use disorders) have yielded modest short-term improvements in care engagement and viral suppression.<sup>99,100</sup> Cash incentives to encourage adherence with treatment and follow-up do not work consistently and generally are not recommended (evidence rating AIa).<sup>99,101</sup> However, noncash incentives as part of combination strategies are effective.<sup>102,103</sup> Tiered strategies using risk stratification to identify high-acuity patients are recommended (evidence rating CIIB), as is providing low-threshold medical care, such as open access (ie, “walk in”) clinics, integrated with high-intensity outreach implemented in conjunction with public health agencies, jails, housing, and mental health case management (evidence rating CIII).<sup>104</sup>

Guidelines exist for ART adherence monitoring and interventions.<sup>105</sup> Systematic screening for ART medication adherence via patient self-report using validated instruments or using pharmacy refill measures, and not relying solely on plasma viral load, is recommended.<sup>1</sup> Individuals with suboptimal adherence should be assessed for inadequate housing,<sup>106–108</sup>

food insecurity,<sup>109–111</sup> active substance use,<sup>110</sup> psychiatric disorders, medication adverse effects, and pill burden.

Internalized stigma, defined as a patient's negative feelings or thoughts related to their HIV status, and depression are associated with poor medication adherence, visit retention, and clinical outcomes.<sup>112–114</sup> Chronic depression increases the risk for missed clinic visits, virologic failure, and a 2-fold increase in mortality risk.<sup>115</sup> Treatment with antidepressants can improve virologic suppression, CD4 cell counts, and remission from clinical symptoms.<sup>116</sup>

## Cost

From the patient perspective, the most relevant cost is the out-of-pocket expense of accessing treatment. The payer perspective is to use the lowest-cost medications to avoid the most expensive and severe HIV outcomes (eg, hospitalizations). The latter perspective often places greater value on immediate costly outcomes rather than prevention of events occurring remotely in time (eg, renal or cardiovascular toxicity). For example, a patient and clinician might value the renal and bone safety of TAF over that of TDF, but the payer might determine that the similar virologic efficacy does not justify the higher cost of TAF.<sup>117</sup>

The societal perspective considers the cost and outcomes for all parties involved. Since this perspective does not favor one group over another, it is adopted by most cost-effectiveness analyses for which therapies are considered in relation to each other, with the one providing the greatest return on investment being preferred. For example, despite its high cost, the benefits of ART are so large it is considered cost-effective.<sup>118–120</sup>

The availability of more generic antiretrovirals and the use of 2-drug regimens could reduce the costs of treatment substantially. Generic antiretrovirals have already reduced the cost of HIV treatment globally, allowing millions of patients to be treated in resource limited settings. In developed countries, many antiretroviral agents and coformulations are available as lower-cost generics. Limitations include a forced switch from branded coformulated regimens to separate pills<sup>121,122</sup>; more pharmacy co-pays for separate prescriptions; use of older agents that are not part of current recommended regimens; and high costs if an insufficient number of generic manufacturers enter the market. However, a modeling study found that use of a partially generic regimen including multiple pills would be highly cost-effective.<sup>123</sup>

Ultimately, the first priority for clinicians and patients is to find the most effective and safest treatment. If multiple options exist with similar outcomes, choosing the lowest-cost options makes intuitive sense, provided there are no additional patient cost barriers.

## Prevention

Recommendations for the prevention of HIV infection are summarized in Box 6. Use of antiretrovirals for HIV prevention spans 3 domains: treatment as prevention, prophylaxis for currently uninfected individuals (PrEP and postexposure prophylaxis [PEP]), and prevention of mother-to-child transmission.

As noted, maintaining U = U status requires continued viral suppression. There are 2 caveats to consider when counseling patients about U = U: The only transmissions that occurred in studies happened early after starting treatment and 3 to 6 months of viral suppression may therefore be required; and durable viral suppression cannot be assessed based on a single measurement.<sup>124</sup> Importantly, transmission can occur when an HIV-seronegative partner in a serodiscordant relationship has partners outside of that relationship.

Guidelines exist for occupational (needle stick and fluid splash to mucous membranes)<sup>125</sup> and nonoccupational (sexual-and injection–drug related) PEP.<sup>126</sup> PEP should be started as soon as possible after a potential exposure to maximize effectiveness.<sup>125</sup> Abacavir-based PEP is not recommended unless the exposed patient is known to be HLA-B\*5701 negative (evidence rating AIII). Available data are insufficient to recommend TAF-based regimens for PEP.

PrEP with TDF/emtricitabine is highly effective in preventing HIV acquisition from sexual exposures.<sup>1</sup> TDF alone prevented infection in people who inject drugs, but TDF/emtricitabine is recommended for these persons. Substance use and medical histories (particularly renal and bone disease) are important in deciding whether to provide PrEP to best balance potential risks and benefits. PrEP is recommended for populations with an HIV incidence above 2% per year (evidence rating AIII) and for HIV-seronegative partners of HIV-infected persons who are not consistently virally suppressed.<sup>127,128</sup> Unlike condoms, PrEP does not prevent other STIs. For people who inject drugs, clean injection equipment and access to substance use treatment should be available.

Daily TDF/emtricitabine is recommended for persons at risk of HIV through sexual exposure (evidence rating AIa) and for people who inject drugs (evidence rating BIa).<sup>1</sup> Daily dosing is required for optimal protection.<sup>129</sup> This is especially important for women, given that tenofovir concentrates at 10-fold lower levels in vaginal tissue than in rectal tissue and clearance is faster.<sup>130</sup>

### **On-Demand or Event-Driven PrEP (“2–1–1”)**

Pericoital TDF/emtricitabine, known as on-demand or event-driven PrEP, is effective for HIV prevention among MSM and an alternative to daily PrEP for MSM with infrequent sexual exposures (evidence rating AIa). The IPERGAY (Intervention Préventive de l’Exposition aux Risques avec et pour les Gays) study assessed on-demand PrEP with TDF/emtricitabine given as 2 doses with food 2 to 24 hours before sex, 1 dose 24 hours after the first (double) dose, and 1 dose 24 hours later (“2–1–1” dosing). For consecutive sexual contacts, men were instructed to take 1 pill per day until 2 days after the last sexual encounter. With each new sexual encounter, PrEP was to be initiated with a double dose, unless the last PrEP dose had occurred within 7 days, in which case only 1 preexposure dose was recommended. The IPERGAY and PROUD (Pre-exposure Option for Reducing HIV in the UK: Immediate or Deferred) trials (using daily TDF/emtricitabine) reduced risk by 86%.<sup>131,132</sup> An analysis of MSM having infrequent sexual intercourse in the IPERGAY study and subsequent open-label extension studies found high levels of efficacy, including in a subgroup who took an average of 2 or 3 doses of TDF/emtricitabine per week.<sup>133,134</sup> Clinical experience with on-demand PrEP confirmed efficacy of this dosing among MSM.



<sup>135,136</sup> The 2–1–1 regimen achieved target exposures of tenofovir diphosphate and emtricitabine triphosphate in colorectal tissue at the time of coitus in 81% and 98% of the population when administered 2 and 24 hours before coitus, respectively; target exposure was sustained for the next 10 days.<sup>130,137–139</sup> If intercourse is planned, the first (double) dose of TDF/emtricitabine should be taken closer to the 24-hour pre-coital time than the 2-hour time (evidence rating CIII).

Lack of data among heterosexual men and women, transgender men and women, and people who inject drugs precludes recommendation of the 2–1–1 regimen in these populations (evidence rating AIII). The 2–1–1 regimen also is not recommended for patients with active HBV, because of risks of HBV reactivation and HBV resistance (evidence rating BIIa).

### Regimen Choice and Laboratory Monitoring

TDF/emtricitabine is the recommended PrEP agent (evidence rating BIII); TDF/lamivudine, TAF/emtricitabine, or TDF alone are not recommended for PrEP at this time (evidence rating BIII). TDF-based PrEP is not recommended for persons with creatinine clearance below 60 mL/min/1.73 m<sup>2</sup> (evidence rating AIIa). Glomerular dysfunction may occur with therapy, particularly in individuals older than 50 years. The dysfunction is usually reversible, and rechallenge with PrEP is often possible.<sup>140</sup> Such patients should have more frequent creatinine clearance monitoring (evidence rating BIIa).

A combination HIV antigen-antibody assay should be performed within 7 days before initiation of TDF/emtricitabine PrEP to exclude HIV infection (evidence rating AIII). An HIV RNA assay may be needed to exclude acute HIV infection in high-risk populations. A 1-month follow-up visit is recommended to assess adherence and tolerability and to ensure the absence of primary HIV infection (evidence rating BIII).<sup>141</sup> Subsequent follow-up is recommended every 3 months to allow for STI screening (urine, throat, anal, and vaginal tests) (evidence rating AIIa) and HIV testing (evidence rating AIII). HCV serologic testing should be performed at least annually and more frequently in high-risk individuals (eg, people who inject drugs) or those with elevated transaminase levels (evidence rating BIIa). PrEP prescription should not exceed 90 days without interval testing for HIV infection (evidence rating AIII).

### Seroconversion in the Setting of PrEP

Diagnosing HIV infection in individuals taking PrEP can be challenging because PrEP can alter and delay antibody responses and decrease plasma HIV RNA levels.<sup>142,143</sup> Any positive HIV screening test result in this setting should prompt immediate confirmatory testing with HIV RNA and genotype testing if confirmed. For suspected HIV infection or equivocal screening test results, PrEP should be stopped and other prevention methods used until HIV infection is confirmed or excluded. If HIV infection is confirmed or strongly suspected, fully suppressive ART should be administered as quickly as possible with a recommended regimen; resistance testing should be performed and treatment altered, as needed (evidence rating AIII). Resistance (typically with an M184V/I mutation) has been observed rarely, usually when PrEP with TDF/emtricitabine is initiated during undiagnosed acute HIV infection.

## Additional Considerations

For high-risk individuals (including those who do not use safer sex or injection practices), the office visit to discuss PrEP is an opportunity to reduce risk. Same-day PrEP initiation is reasonable in some clinical scenarios. Asymptomatic individuals who are HIV-seronegative by rapid assay could initiate daily oral TDF/emtricitabine without awaiting results of the concomitant baseline testing of creatinine level, hepatitis B surface antigen level, STIs, and HIV by fourth-generation assay. Condom use should be encouraged for all genital contact to prevent STIs (evidence rating AIIa). TDF/emtricitabine PrEP is not fail-safe, and seroconversion despite excellent adherence has been reported in cases of high inoculum or viral resistance.<sup>142,144,145</sup>

Unanticipated interruptions in PrEP delivery (eg, insurance coverage lapse, incarceration, and relocation) have been associated with seroconversions and should be avoided.<sup>146</sup> For individuals being treated with a course of 3-drug PEP for a recent exposure, who are likely to be at risk of ongoing exposure, a seamless transition from PEP to PrEP is recommended (evidence rating CIII). Given a negative result for a fourth-generation instrumented test (eg, combination HIV antigen-antibody test) at the conclusion of a 28-day PEP course, PrEP with daily TDF/emtricitabine may be initiated or resumed.<sup>147</sup>

## Future Directions

New treatments continue to be developed, most notably long-acting formulations of antiretrovirals for treatment and prevention. Injectable rilpivirine combined with cabotegravir was successful in phase 2 studies<sup>148</sup> and is being evaluated in phase 3 clinical trials (NCT03299049). Also in development are implantable sustained release platforms, nanoparticles, viral vector delivery, monoclonal antibodies, and other long-acting oral agents.<sup>1</sup>

Injectable and other long-acting preparations for PrEP, such as injectable cabotegravir<sup>149</sup> and the dapivirine vaginal ring, are in clinical trials (NCT01617096). Open-label trials of the dapivirine vaginal ring demonstrated higher uptake and adherence than in the blinded trials, as well as HIV-1 incidence that was half the expected rate.<sup>150,151</sup>

Broadly neutralizing antibodies (bNAbs) targeting conserved antigenic sites on the HIV-1 envelope trimer are being evaluated for therapy and prevention.<sup>152–154</sup> Newer approaches to increase the potency, breadth,<sup>155</sup> and half-life<sup>156,157</sup> of bNAbs, evaluate different methods of bNAb administration,<sup>158</sup> and assess the efficacy of combinations of bNAbs are being investigated.<sup>159,160</sup>

HIV cure efforts focus on inducing HIV expression from latently infected cells, augmenting the immune system to clear infected cells (eg, with therapeutic vaccines, checkpoint inhibitors, chimeric antigen receptor T cells), and using gene therapy to modify host CD4 cells to make them resistant to HIV. Using ART with a toll-like receptor 7 agonist (an innate immune stimulant) plus a bNAb during acute infection in monkeys suppressed viral rebound after stopping ART in a substantial number of animals.<sup>161</sup> These interventions are moving forward in clinical trials.

Clinicians who care for patients with HIV have a major role in advocating for programs and their patients at the local, national, and international levels. Advocacy should go beyond access to ART and include access to mental health and substance abuse services as well as efforts to end policies such as HIV criminalization that impede the ability to provide evidence-based care and prevention services.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## REFERENCES

1. Günthard HF, Saag MS, Benson CA, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2016 recommendations of the International Antiviral Society—USA panel. *JAMA*. 2016;316(2):191–210. doi:10.1001/jama.2016.8900 [PubMed: 27404187]
2. Canadian Task Force on the Periodic Health Examination. The periodic health examination. *Can Med Assoc J*. 1979;121(9):1193–1254. [PubMed: 115569]
3. Gopal S, Patel MR, Yanik EL, et al. Association of early HIV viremia with mortality after HIV-associated lymphoma. *AIDS*. 2013;27(15):2365–2373. doi:10.1097/QAD.0b013e3283635232 [PubMed: 23736149]
4. World Health Organization (WHO). Guidelines for Managing Advanced HIV Disease and Rapid Initiation of Antiretroviral Therapy. WHO website. <http://www.who.int/hiv/pub/guidelines/advanced-HIV-disease/en/>. Published 2017.
5. Rosen S, Maskew M, Fox MP, et al. Initiating antiretroviral therapy for HIV at a patient's first clinic visit: the RapIT randomized controlled trial. *PLoS Med*. 2016;13(5):e1002015. doi:10.1371/journal.pmed.1002015 [PubMed: 27163694]
6. Koenig SP, Dorvil N, Dévieux JG, et al. Same-day HIV testing with initiation of antiretroviral therapy versus standard care for persons living with HIV: a randomized unblinded trial. *PLoS Med*. 2017;14(7):e1002357. doi:10.1371/journal.pmed.1002357 [PubMed: 28742880]
7. Labhardt ND, Ringera I, Lejone TI, et al. Effect of offering same-day ART vs usual health facility referral during home-based HIV testing on linkage to care and viral suppression among adults with HIV in Lesotho: the CASCADE randomized clinical trial. *JAMA*. 2018;319(11):1103–1112. doi:10.1001/jama.2018.1818 [PubMed: 29509839]
8. Amanyire G, Semitala FC, Namusobya J, et al. Effects of a multicomponent intervention to streamline initiation of antiretroviral therapy in Africa: a stepped-wedge cluster-randomised trial. *Lancet HIV*. 2016;3(11):e539–e548. doi:10.1016/S2352-3018(16)30090-X [PubMed: 27658873]
9. Hoenigl M, Chaillon A, Mehta SR, Smith DM, Graff-Zivin J, Little SJ. Screening for acute HIV infection in community-based settings: cost-effectiveness and impact on transmissions. *J Infect*. 2016;73(5):476–484. doi:10.1016/j.jinf.2016.07.019 [PubMed: 27521468]
10. Ford N, Migone C, Calmy A, et al. Benefits and risks of rapid initiation of antiretroviral therapy. *AIDS*. 2018;32(1):17–23. doi:10.1097/QAD.0000000000001671 [PubMed: 29112073]

11. Bacon O, Chin JC, Hsu L, et al. The Rapid ART Program Initiative for HIV Diagnoses (RAPID) in San Francisco. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
12. Pilcher CD, Ospina-Norvell C, Dasgupta A, et al. The effect of same-day observed initiation of antiretroviral therapy on HIV viral load and treatment outcomes in a US public health setting. *J Acquir Immune Defic Syndr*. 2017;74(1):44–51. doi:10.1097/QAI.0000000000001134 [PubMed: 27434707]
13. Colasanti J, Sumitani J, Mehta C, et al. Implementation of a rapid entry program decreases time to viral suppression among vulnerable persons living with HIV in the Southern United States. *Open Forum Infect Dis*. 2018;5(6):1–8.
14. Perfect JR, Dismukes WE, Dromer F, et al. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2010;50(3):291–322. doi:10.1086/649858 [PubMed: 20047480]
15. Ingle SM, Miro JM, Furrer H, et al. Impact of ART on mortality in cryptococcal meningitis patients: high-income settings. Presented at: 22nd Conference on Retroviruses and Opportunistic Infections (CROI); February 23–26, 2015; Seattle, WA.
16. Buchacz K, Lau B, Jing Y, et al.; North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of IeDEA. Incidence of AIDS-defining opportunistic infections in a multicohort analysis of HIV-infected persons in the United States and Canada, 2000–2010. *J Infect Dis*. 2016;214(6):862–872. doi:10.1093/infdis/jiw085 [PubMed: 27559122]
17. Djawe K, Buchacz K, Hsu L, et al. Mortality risk after AIDS-defining opportunistic illness among HIV-infected persons—San Francisco, 1981–2012. *J Infect Dis*. 2015;212(9):1366–1375. doi:10.1093/infdis/jiv235 [PubMed: 26044289]
18. Yangco BG, Buchacz K, Baker R, Palella FJ, Armon C, Brooks JT; HIV Outpatient Study Investigators. Is primary *Mycobacterium avium* complex prophylaxis necessary in patients with CD4 <50 cells/μL who are virologically suppressed on cART? *AIDS Patient Care STDS*. 2014;28(6):280–283. doi:10.1089/apc.2013.0270 [PubMed: 24833016]
19. Mocroft A, Reiss P, Kirk O, et al.; Opportunistic Infections Project Team of the Collaboration of Observational HIV Epidemiological Research in Europe (COHERE). Is it safe to discontinue primary *Pneumocystis jirovecii* pneumonia prophylaxis in patients with virologically suppressed HIV infection and a CD4 cell count <200 cells/microL? *Clin Infect Dis*. 2010;51(5):611–619. doi:10.1086/655761 [PubMed: 20645862]
20. Gallant J, Lazzarin A, Mills A, et al. Bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir, abacavir, and lamivudine for initial treatment of HIV-1 infection (GS-US-380-1489): a double-blind, multicentre, phase 3, randomised controlled non-inferiority trial. *Lancet*. 2017;390(10107):2063–2072. doi:10.1016/S0140-6736(17)32299-7 [PubMed: 28867497]
21. Sax PE, Pozniak A, Montes ML, et al. Coformulated bictegravir, emtricitabine, and tenofovir alafenamide versus dolutegravir with emtricitabine and tenofovir alafenamide, for initial treatment of HIV-1 infection (GS-US-380-1490): a randomised, double-blind, multicentre, phase 3, non-inferiority trial. *Lancet*. 2017;390(10107):2073–2082. doi:10.1016/S0140-6736(17)32340-1 [PubMed: 28867499]
22. Squires KE, Molina J-M, Sax PE, et al. Fixed dose combination of doravirine/lamivudine/TDF is non-inferior to efavirenz/emtricitabine/TDF in treatment-naïve adults with HIV-1 infection: week 48 results of the phase 3 DRIVE-AHEAD study. Presented at: 9th International AIDS Society Conference on HIV Science; July 23–26, 2017; Paris, France.
23. Molina JM, Squires K, Sax PE, et al. Doravirine versus ritonavir-boosted darunavir in antiretroviral-naïve 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. [PubMed: 29592840]
24. Eron J, Orkin C, Gallant J, et al.; AMBER Study Group. Week 48 results of AMBER: a phase 3, randomised, double-blind trial in antiretroviral treatment-naïve HIV-1-infected adults to evaluate the efficacy and safety of the once-daily, single-tablet regimen of darunavir/cobicistat/emtricitabine/tenofovir alafenamide (D/C/F/TAF) versus darunavir/cobicistat plus emtricitabine/tenofovir disoproxil fumarate. Presented at: 16th European AIDS Conference (EACS); October 25–27, 2017; Milan, Italy.

25. Arribas JR, Thompson M, Sax PE, et al. Briefreport: randomized, double-blind comparison of tenofovir alafenamide (TAF) vs tenofovir disoproxil fumarate (TDF), each coformulated with elvitegravir, cobicistat, and emtricitabine (E/C/F) for initial HIV-1 treatment: week 144 results. *J Acquir Immune Defic Syndr*. 2017;75(2):211–218. doi:10.1097/QAI.0000000000001350 [PubMed: 28282300]
26. Hill A, Hughes SL, Gotham D, Pozniak AL. Tenofovir alafenamide versus tenofovir disoproxil fumarate: is there a true difference in efficacy and safety? *J Virus Erad*. 2018;4(2):72–79. [PubMed: 29682298]
27. Girouard MP, Sax PE, Parker RA, et al. The cost-effectiveness and budget impact of 2-drug dolutegravir-lamivudine regimens for the treatment of HIV infection in the United States. *Clin Infect Dis*. 2016;62(6):784–791. doi:10.1093/cid/civ981 [PubMed: 26658053]
28. Lambert-Niclot S, George EC, Pozniak A, et al.; NEAT 001/ANRS 143 Study Group. Antiretroviral resistance at virological failure in the NEAT 001/ANRS 143 trial: raltegravir plus darunavir/ritonavir or tenofovir/emtricitabine plus darunavir/ritonavir as first-line ART. *J Antimicrob Chemother*. 2016;71(4):1056–1062. doi:10.1093/jac/dkv427 [PubMed: 26702926]
29. Taiwo BO, Zheng L, Stefanescu A, et al. ACTGA5353: a pilot study of dolutegravir plus lamivudine for initial treatment of human immunodeficiency virus-1 (HIV-1)-infected participants with HIV-1 RNA <500 000 copies/mL. *Clin Infect Dis*. 2017;66(11):1689–1697. doi:10.1093/cid/cix1083
30. Figueroa MI, Sued OG, Gun AM, et al. DRV/r/3TC FDC for HIV-1 treatment naive patients: week 48 results of the ANDES study. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
31. Llibre JM, Hung CC, Brinson C, et al. Efficacy, safety, and tolerability of dolutegravir-rilpivirine for the maintenance of virological suppression in adults with HIV-1: phase 3, randomised, non-inferiority SWORD-1 and SWORD-2 studies. *Lancet*. 2018;391(10123):839–849. doi:10.1016/S0140-6736(17)33095-7 [PubMed: 29310899]
32. World Health Organization (WHO). Potential safety issue affecting women living with HIV using dolutegravir at the time of conception. WHO website. [http://www.who.int/medicines/publications/drugalerts/Statement\\_on\\_DTG\\_18May\\_2018final.pdf](http://www.who.int/medicines/publications/drugalerts/Statement_on_DTG_18May_2018final.pdf). 5 18, 2018.
33. Best B, Capparelli E, Stek A, et al. Elvitegravir/cobicistat pharmacokinetics in pregnancy and postpartum. Presented at: 24th Conference on Retroviruses and Opportunistic Infections (CROI); February 16, 2017; Seattle, WA.
34. Gallant JE, Daar ES, Raffi F, et al. Efficacy and safety of tenofovir alafenamide versus tenofovir disoproxil fumarate given as fixed-dose combinations containing emtricitabine as backbones for treatment of HIV-1 infection in virologically suppressed adults: a randomised, double-blind, active-controlled phase 3 trial. *Lancet HIV*. 2016;3(4):e158–e165. doi:10.1016/S2352-3018(16)00024-2 [PubMed: 27036991]
35. Chan HL, Fung S, Seto WK, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of HBeAg-positive chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial. *Lancet Gastroenterol Hepatol*. 2016;1(3):185–195. doi:10.1016/S2468-1253(16)30024-3 [PubMed: 28404091]
36. Buti M, Gane E, Seto WK, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of patients with HBeAg-negative chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial. *Lancet Gastroenterol Hepatol*. 2016;1(3):196–206. doi:10.1016/S2468-1253(16)30107-8 [PubMed: 28404092]
37. Borges AH, Hoy J, Florence E, et al. Antiretrovirals, fractures, and osteonecrosis in a large European HIV cohort [abstract 46]. Presented at: 23rd Conference on Retroviruses and Opportunistic Infections (CROI); February 22–25, 2016; Boston, MA.
38. Molina JM, Ward D, Brar I, et al. Switching to fixed-dose bicitgravir, emtricitabine, and tenofovir alafenamide from dolutegravir plus abacavir and lamivudine in virologically suppressed adults with HIV-1: 48 week results of a randomised, double-blind, multicentre, active-controlled, phase 3, non-inferiority trial [published online June 18, 2018]. *Lancet HIV*. doi:10.1016/S2352-3018(18)30092-4

39. Eron JJ, Lelievre JD, Kalayjian R, et al. Safety and efficacy of E/C/F/TAF in HIV-infected adults on chronic hemodialysis. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
40. Elion RA, Althoff KN, Zhang J, et al.: North American AIDS Cohort Collaboration on Research and Design of IeDEA. Recent abacavir use increases risk of type 1 and type 2 myocardial infarctions among adults with HIV. *J Acquir Immune Defic Syndr*. 2018;78(1):62–72. doi:10.1097/QAI.0000000000001642 [PubMed: 29419568]
41. Dooley K, Kaplan R, Mwelase N, et al. Safety and efficacy of dolutegravir-based ART in TB/HIV coinfecting adults at week 24. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
42. Custodio JM, West SK, Collins S, et al. Pharmacokinetics of bicitegravir administered twice daily in combination with raltegravir. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
43. Cerrone M, Alfarisi O, Neary M, et al. Rifampin effect on tenofovir alafenamide (TAF) plasma/ intracellular pharmacokinetics. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
44. Swindells S, Ramchandani R, Gupta A, et al. One month of rifapentine/isoniazid to prevent TB in people with HIV: Brief TB/A5279 [abstract 37LB]. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
45. Brooks KM, George JM, Pau AK, et al. Cytokine-mediated systemic adverse drug reactions in a drug-drug interaction study of dolutegravir with once-weekly isoniazid and rifapentine [published online February 23, 2018]. *Clin Infect Dis*. 2018. doi:10.1093/cid/ciy082
46. Trottier B, Lake JE, Logue K, et al. Dolutegravir/abacavir/lamivudine versus current ART in virally suppressed patients (STRIVING): a 48-week, randomized, non-inferiority, open-label, phase IIIb study. *Antivir Ther*. 2017;22(4):295–305. doi:10.3851/IMP3166 [PubMed: 28401876]
47. Post FA, Yazdanpanah Y, Schembri G, et al. Efficacy and safety of emtricitabine/tenofovir alafenamide (FTC/TAF) vs. emtricitabine/tenofovir disoproxil fumarate (FTC/TDF) as a backbone for treatment of HIV-1 infection in virologically suppressed adults: subgroup analysis by third agent of a randomized, double-blind, active-controlled phase 3 trial. *HIV Clin Trials*. 2017;18(3): 135–140. doi:10.1080/15284336.2017.1291867 [PubMed: 28303753]
48. Marzolini C, Gibbons S, Khoo S, Back D. Cobicistat versus ritonavir boosting and differences in the drug-drug interaction profiles with co-medications. *J Antimicrob Chemother*. 2016;71 (7): 1755–1758. doi:10.1093/jac/dkw032 [PubMed: 26945713]
49. Negredo E, Estrada V, Domingo P, et al. Switching from a ritonavir-boosted PI to dolutegravir as an alternative strategy in virologically suppressed HIV-infected individuals. *J Antimicrob Chemother*. 2017;72(3):844–849. [PubMed: 27999056]
50. Orkin C, DeJesus E, Ramgopal M, et al. Switching from tenofovir disoproxil fumarate to tenofovir alafenamide coformulated with rilpivirine and emtricitabine in virally suppressed adults with HIV-1 infection: a randomised, double-blind, multicentre, phase 3b, non-inferiority study. *Lancet HIV*. 2017;4(5):e195–e204. doi:10.1016/S2352-3018(17)30031-0 [PubMed: 28259777]
51. Orkin C, Molina JM, Negredo E, et al.; EMERALD Study Group. Efficacy and safety of switching from boosted protease inhibitors plus emtricitabine and tenofovir disoproxil fumarate regimens to single-tablet darunavir, cobicistat, emtricitabine, and tenofovir alafenamide at 48 weeks in adults with virologically suppressed HIV-1 (EMERALD): a phase 3, randomised, non-inferiority trial. *Lancet HIV*. 2018;5(1):e23–e34. doi:10.1016/S2352-3018(17)30179-0 [PubMed: 28993180]
52. Daar ES, DeJesus E, Ruane P, et al. Efficacy and safety of switching to fixed-dose bicitegravir, emtricitabine, and tenofovir alafenamide from boosted protease inhibitor-based regimens in virologically suppressed adults with HIV-1: 48 week results of a randomised, open-label, multicentre, phase 3, non-inferiority trial [published online June 15, 2018]. *Lancet HIV*. doi: 10.1016/S2352-3018(18)30091-2
53. Gallant J, Brunetta J, Crofoot G, et al.; GS-US-292–1249 Study Investigators. Brief report: efficacy and safety of switching to a single-tablet regimen of elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide in HIV-1/hepatitis B-coinfecting adults. *J Acquir Immune Defic Syndr*. 2016;73(3): 294–298. doi:10.1097/QAI.0000000000001069 [PubMed: 27171740]



54. Sax PE, DeJesus E, Crofoot G, et al. A randomized trial of bicitegravir or dolutegravir with emtricitabine and tenofovir alafenamide (F/TAF) followed by open label switch to bicitegravir/F/TAF fixed dose combination. Presented at: IDWeek; October 4–8, 2017; San Diego, CA.
55. Di Giambenedetto S, Fabbiani M, Quiros Roldan E, et al.; Atlas-M Study Group. Treatment simplification to atazanavir/ritonavir + lamivudine versus maintenance of atazanavir/ritonavir + two NRTIs in virologically suppressed HIV-1-infected patients: 48 week results from a randomized trial (ATLAS-M). *J Antimicrob Chemother.* 2017;72(4):1163–1171. [PubMed: 28093483]
56. Perez-Molina JA, Rubio R, Rivero A, et al.; GeSIDA 7011 Study Group. Simplification to dual therapy (atazanavir/ritonavir+lamivudine) versus standard triple therapy [atazanavir/ritonavir+two nucleos(t)ides] in virologically stable patients on antiretroviral therapy: 96 week results from an open-label, non-inferiority, randomized clinical trial (SALT study). *J Antimicrob Chemother.* 2017;72(1): 246–253. doi:10.1093/jac/dkw379 [PubMed: 27629070]
57. Pulido F, Ribera E, Lagarde M, et al.; DUAL-GESIDA-8014-RIS-EST45 Study Group. Dual therapy with darunavir and ritonavir plus lamivudine vs triple therapy with darunavir and ritonavir plus tenofovir disoproxil fumarate and emtricitabine or abacavir and lamivudine for maintenance of human immunodeficiency virus type 1 viral suppression: randomized, open-label, noninferiority DUAL-GESIDA 8014-RIS-EST45 trial. *Clin Infect Dis.* 2017;65(12):2112–2118. doi:10.1093/cid/cix734 [PubMed: 29020293]
58. Joly V, Burdet C, Landman R, et al. Promising results of dolutegravir + lamivudine maintenance in ANRS 167 LAMIDOL trial [abstract 458]. Presented at: 24th Conference on Retroviruses and Opportunistic Infections (CROI); February 13–16, 2017; Seattle, WA
59. Taiwo BO, Marconi VC, Berzins B, et al. Dolutegravir plus lamivudine maintains human immunodeficiency virus-1 suppression through week 48 in a pilot randomized trial. *Clin Infect Dis.* 2018;66(11):1794–1797. doi:10.1093/cid/cix1131 [PubMed: 29293895]
60. Armenia D, Di Carlo D, Calcagno A, et al. Pre-existent NRTI and NNRTI resistance impacts on maintenance of virological suppression in HIV-1-infected patients who switch to a tenofovir/emtricitabine/rilpivirine single-tablet regimen. *J Antimicrob Chemother.* 2017;72(3):855–865. [PubMed: 27999048]
61. Huhn GD, Tebas P, Gallant J, et al. A randomized, open-label trial to evaluate switching to elvitegravir/cobicistat/emtricitabine/tenofovir alafenamide plus darunavir in treatment-experienced HIV-1-infected adults. *J Acquir Immune Defic Syndr.* 2017;74(2):193–200. doi:10.1097/QAI.0000000000001193 [PubMed: 27753684]
62. Brenner BG, Thomas R, Blanco JL, et al. Development of a G118R mutation in HIV-1 integrase following a switch to dolutegravir monotherapy leading to cross-resistance to integrase inhibitors. *J Antimicrob Chemother.* 2016;71(7):1948–1953. doi:10.1093/jac/dkw071 [PubMed: 27029845]
63. Wijting I, Rokx C, Boucher C, et al. Dolutegravir as maintenance monotherapy for HIV (DOMONO): a phase 2, randomised non-inferiority trial. *Lancet HIV.* 2017;4(12):e547–e554. doi:10.1016/S2352-3018(17)30152-2 [PubMed: 29107562]
64. Galli L, Spagnuolo V, Bigoloni A, et al.; MODAt Study Group. Atazanavir/ritonavir monotherapy: 96 week efficacy, safety and bone mineral density from the MODAt randomized trial. *J Antimicrob Chemother.* 2016;71(6):1637–1642. doi:10.1093/jac/dkw031 [PubMed: 26945711]
65. Girard PM, Antinori A, Arribas JR, et al. Week 96 efficacy and safety of darunavir/ritonavir monotherapy vs. darunavir/ritonavir with two nucleoside reverse transcriptase inhibitors in the PROTEA trial. *HIV Med.* 2017;18(1):5–12. doi:10.1111/hiv.12386 [PubMed: 27279571]
66. Aboud M, Kaplan R, Lombaard J, et al. Superior efficacy of dolutegravir (DTG) plus 2 nucleoside reverse transcriptase inhibitors (NRTIs) compared with lopinavir/ritonavir (LPV/RTV) plus 2 NRTIs in second-line treatment: interim data from the DAWNING study. Presented at: 9th International AIDS Society Conference on HIV Science; July 23–27, 2017; Paris, France.
67. Lewis S, Fessel J, Emu B, et al. Long-acting ibalizumab 17 in patients with multi-drug resistant HIV-1: a 24-week 18 study. *Top Antivir Med.* 2017;25 (suppl 1):185s.
68. Emu B, Fessel WJ, Schrader S, et al. 48-Week safety and efficacy on-treatment analysis of ibalizumab in patients with multi-drug resistant HIV-1. Presented at: IDWeek; October 6, 2017; San Diego, CA.

69. DiNunno EA, Prejean J, Irwin K, et al. Recommendations for HIV screening of gay, bisexual, and other men who have sex with men—United States, 2017. *MMWR Morb Mortal Wkly Rep*. 2017;66(31):830–832. doi:10.15585/mmwr.mm6631a3 [PubMed: 28796758]
70. Hooenenborg E, Achterbergh RCA, Schim van der Loeff MF, et al.; Amsterdam PrEP Project team in the HIV Transmission Elimination Amsterdam Initiative, MOSAIC Study Group. MSM starting preexposure prophylaxis are at risk of hepatitis C virus infection. *AIDS*. 2017;31(11):1603–1610. doi:10.1097/QAD.0000000000001522 [PubMed: 28657964]
71. Girometti N, Gutierrez A, Nwokolo N, McOwan A, Whitlock G. High HIV incidence in men who have sex with men following an early syphilis diagnosis: is there room for pre-exposure prophylaxis as a prevention strategy? *Sex Transm Infect*. 2017;93(5):320–322. doi:10.1136/sextrans-2016-052865 [PubMed: 28729516]
72. Katz DA, Dombrowski JC, Bell TR, Kerani RP, Golden MR. HIV incidence among men who have sex with men after diagnosis with sexually transmitted infections. *Sex Transm Dis*. 2016;43(4):249–254. doi:10.1097/OLQ.0000000000000423 [PubMed: 26967302]
73. Branson BM. The future of HIV testing. *J Acquir Immune Defic Syndr*. 2010;55(suppl 2):S102–S105. doi:10.1097/QAI.0b013e3181fbca44 [PubMed: 21406978]
74. Braun DL, Kouyos RD, Balmer B, Grube C, Weber R, Günthard HF. Frequency and spectrum of unexpected clinical manifestations of primary HIV-1 infection. *Clin Infect Dis*. 2015;61(6):1013–1021. doi:10.1093/cid/civ398 [PubMed: 25991469]
75. Crowell TA, Colby DJ, Pinyakorn S, et al.; RV254/SEARCH010 Study Group. Acute retroviral syndrome is associated with high viral burden, CD4 depletion, and immune activation in systemic and tissue compartments. *Clin Infect Dis*. 2018;66(10):1540–1549. doi:10.1093/cid/cix1063 [PubMed: 29228130]
76. LeGrand S, Muessig KE, Horvath KJ, Rosengren AL, Hightow-Weidman LB. Using technology to support HIV self-testing among MSM. *Curr Opin HIV AIDS*. 2017;12(5):425–431. doi:10.1097/COH.0000000000000400 [PubMed: 28617712]
77. 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 [PubMed: 28605418]
78. Stekler JD, McKernan J, Milne R, et al. Lack of resistance to integrase inhibitors among antiretroviral-naïve subjects with primary HIV-1 infection, 2007–2013. *Antivir Ther*. 2015;20(1):77–80. doi:10.3851/IMP2780 [PubMed: 24831260]
79. Ambrosioni J, Nicolás D, Manzardo C, et al. Integrase strand-transfer inhibitor polymorphic and accessory resistance substitutions in patients with acute/recent HIV infection. *J Antimicrob Chemother*. 2017;72(1):205–209. doi:10.1093/jac/dkw376 [PubMed: 27624569]
80. Scherrer AU, Yang WL, Kouyos RD, et al.; SwissHIV Cohort Study. Successful prevention of transmission of integrase resistance in the Swiss HIV Cohort Study. *J Infect Dis*. 2016;214(3):399–402. doi:10.1093/infdis/jiw165 [PubMed: 27130429]
81. Tostevin A, White E, Dunn D, et al.; UK HIV Drug Resistance Database. Recent trends and patterns in HIV-1 transmitted drug resistance in the United Kingdom. *HIV Med*. 2017;18(3):204–213. doi:10.1111/hiv.12414 [PubMed: 27476929]
82. Sax PE, DeJesus E, Mills A, et al.; GS-US-236–0102 Study Team. Co-formulated elvitegravir, cobicistat, emtricitabine, and tenofovir versus co-formulated efavirenz, emtricitabine, and tenofovir for initial treatment of HIV-1 infection: a randomised, double-blind, phase 3 trial, analysis of results after 48 weeks. *Lancet*. 2012;379(9835):2439–2448. doi:10.1016/S0140-6736(12)60917-9 [PubMed: 22748591]
83. Hunt PW, Deeks SG, Rodriguez B, et al. Continued CD4 cell count increases in HIV-infected adults experiencing 4 years of viral suppression on antiretroviral therapy. *AIDS*. 2003;17(13):1907–1915. doi:10.1097/00002030-200309050-00009 [PubMed: 12960823]
84. Ford N, Meintjes G, Pozniak A, et al. The future role of CD4 cell count for monitoring antiretroviral therapy. *Lancet Infect Dis*. 2015;15(2):241–247. doi:10.1016/S1473-3099(14)70896-5 [PubMed: 25467647]

85. Sauter R, Huang R, Ledergerber B, et al.; Swiss HIV Cohort Study. CD4/CD8 ratio and CD8 counts predict CD4 response in HIV-1-infected drug naive and in patients on cART. *Medicine* (Baltimore). 2016;95(42):e5094. doi:10.1097/MD.0000000000005094 [PubMed: 27759638]
86. Zaccarelli M, Santoro MM, Armenia D, et al. Genotypic resistance test in proviral DNA can identify resistance mutations never detected in historical genotypic test in patients with low level or undetectable HIV-RNA. *J Clin Virol*. 2016;82:94–100. doi:10.1016/j.jcv.2016.07.007 [PubMed: 27472519]
87. Doyle T, Dunn DT, Ceccherini-Silberstein F, et al.; CORONET Study Group. Integrase inhibitor (INI) genotypic resistance in treatment-naive and raltegravir-experienced patients infected with diverse HIV-1 clades. *J Antimicrob Chemother*. 2015; 70(11):3080–3086. doi:10.1093/jac/dkv243 [PubMed: 26311843]
88. Hurt CB, Sebastian J, Hicks CB, Eron JJ. Resistance to HIV integrase strand transfer inhibitors among clinical specimens in the United States, 2009–2012. *Clin Infect Dis*. 2014;58(3):423–431. doi:10.1093/cid/cit697 [PubMed: 24145878]
89. Gunthard HF, Calvez V, Paredes R, et al. HIV drug resistance: 2018 review and recommendations of the International Antiviral Society–USA 1440 Panel [published online July 20, 2018]. *Clin Infect Dis*. doi:10.1093/cid/ciy463
90. Gandhi RT, Zheng L, Bosch RJ, et al.; AIDS Clinical Trials Group A5244 Team. The effect of raltegravir intensification on low-level residual viremia in HIV-infected patients on antiretroviral therapy: a randomized controlled trial. *PLoS Med*. 2010;7(8):e1000321. doi:10.1371/journal.pmed.1000321 [PubMed: 20711481]
91. U=U taking off in 2017. *Lancet HIV*. 2017;4(11): e475. doi:10.1016/S2352-3018(17)30183-2 [PubMed: 29096785]
92. Rodger AJ, Cambiano V, Bruun T, et al.;PARTNER Study Group. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA*. 2016;316(2):171–181. doi:10.1001/jama.2016.5148 [PubMed: 27404185]
93. Dailey AF, Hoots BE, Hall HI, et al. Vital signs: human immunodeficiency virus testing and diagnosis delays—United States. *MMWR Morb Mortal Wkly Rep*. 2017;66(47):1300–1306. doi: 10.15585/mmwr.mm6647e1 [PubMed: 29190267]
94. Elgalib A, Fidler S, Sabapathy K. Hospital-based routine HIV testing in high-income countries: a systematic literature review. *HIV Med*. 2018;19(3): 195–205. doi:10.1111/hiv.12568 [PubMed: 29168319]
95. Mugavero MJ, Westfall AO, Cole SR, et al.; Centers for AIDS Research Network of Integrated Clinical Systems (CNICS). Beyond core indicators of retention in HIV care: missed clinic visits are independently associated with all-cause mortality. *Clin Infect Dis*. 2014;59(10):1471–1479. doi:10.1093/cid/ciu603 [PubMed: 25091306]
96. Pence B, Mugavero M, Boswell S, et al. Who will show? predicting missed visits in the CFAR Network of Integrated Systems (CNICS) cohort of patients in HIV care in the United States. Presented at: 11th International Conference on HIV Treatment and Prevention Adherence; May 9–11, 2016; Fort Lauderdale, FL.
97. Hart-Malloy R, Brown S, Bogucki K, Tesoriero J. Implementing data-to-care initiatives for HIV in New York state: assessing the value of community health centers identifying persons out of care for health department follow-up. *AIDS Care*. 2018;30 (3):391–396. doi: 10.1080/09540121.2017.1363851 [PubMed: 28791877]
98. Magnus M, Herwehe J, Gruber D, et al. Improved HIV-related outcomes associated with implementation of a novel public health information exchange. *Int J Med Inform*. 2012;81 (10):e30–e38. doi:10.1016/j.ijmedinf.2012.06.005 [PubMed: 22883431]
99. Metsch LR, Feaster DJ, Gooden L, et al. Effect of patient navigation with or without financial incentives on viral suppression among hospitalized patients with HIV infection and substance use: a randomized clinical trial. *JAMA*. 2016;316(2):156–170. doi:10.1001/jama.2016.8914 [PubMed: 27404184]
100. Giordano TP, Cully J, Amico KR, et al. A randomized trial to test a peer mentor intervention to improve outcomes in persons hospitalized with HIV infection. *Clin Infect Dis*. 2016;63(5):678–686. doi:10.1093/cid/ciw322 [PubMed: 27217266]

101. El-Sadr WM, Donnell D, Beauchamp G, et al.; HPTN 065 Study Team. Financial incentives for linkage to care and viral suppression among HIV-positive patients: a randomized clinical trial (HPTN 065). *JAMA Intern Med.* 2017;177(8):1083–1092. doi:10.1001/jamainternmed.2017.2158 [PubMed: 28628702]
102. McNairy ML, Lamb MR, Gachuhi AB, et al. Effectiveness of a combination strategy for linkage and retention in adult HIV care in Swaziland: the Link4Health cluster randomized trial. *PLoS Med.* 2017;14(11):e1002420. doi:10.1371/journal.pmed.1002420 [PubMed: 29112963]
103. Elul B, Lamb MR, Lahuerta M, et al. A combination intervention strategy to improve linkage to and retention in HIV care following diagnosis in Mozambique: a cluster-randomized study. *PLoS Med.* 2017;14(11):e1002433. doi:10.1371/journal.pmed.1002433 [PubMed: 29136001]
104. Dombrowski JC, Galagan S, Ramchandani M, Dhanireddy S, Harrington RD, Golden MR. Improved outcomes with maximum assistance, low-threshold HIV care (the “MAX CLINIC”). Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
105. Thompson MA, Mugavero MJ, Amico KR, et al. Guidelines for improving entry into and retention in care and antiretroviral adherence for persons with HIV: evidence-based recommendations from an International Association of Physicians in AIDS Care panel. *Ann Intern Med.* 2012;156(11):817–833. doi:10.7326/0003-4819-156-11-201206050-00419 [PubMed: 22393036]
106. Aidala AA, Wilson MG, Shubert V, et al. Housing status, medical care, and health outcomes among people living with HIV/AIDS: a systematic review. *Am J Public Health.* 2016;106(1):e1–e23. doi:10.2105/AJPH.2015.302905
107. Clemenzi-Allen AA, Geng E, Christopoulos KA, et al. Degree of housing instability shows independent “dose-response” with HIV suppression. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
108. Bowen EA, Canfield J, Moore S, Hines M, Hartke B, Rademacher C. Predictors of CD4 health and viral suppression outcomes for formerly homeless people living with HIV/AIDS in scattered site supportive housing. *AIDS Care.* 2017;29(11): 1458–1462. doi:10.1080/09540121.2017.1307920 [PubMed: 28335616]
109. Spinelli MA, Frongillo EA, Sheira LA, et al. Food insecurity is associated with poor HIV outcomes among women in the United States. *AIDS Behav.* 2017;21(12):3473–3477. doi:10.1007/s10461-017-1968-2 [PubMed: 29119474]
110. Palar K, Napoles T, Hufstедler LL, et al. Comprehensive and medically appropriate food support is associated with improved HIV and diabetes health. *J Urban Health.* 2017;94(1):87–99. doi:10.1007/s11524-016-0129-7 [PubMed: 28097614]
111. Martinez H, Palar K, Linnemayr S, et al. Tailored nutrition education and food assistance improve adherence to HIV antiretroviral therapy: evidence from Honduras. *AIDS Behav.* 2014;18(suppl 5):S566–S577. doi:10.1007/s10461-014-0786-z [PubMed: 24788781]
112. Turan B, Rogers AJ, Rice WS, et al. Association between perceived discrimination in healthcare settings and HIV medication adherence: mediating psychosocial mechanisms. *AIDS Behav.* 2017;21(12):3431–3439. doi:10.1007/s10461-017-1957-5 [PubMed: 29081045]
113. Rice WS, Crockett KB, Mugavero MJ, Raper JL, Atkins GC, Turan B. Association between internalized HIV-related stigma and HIV care visit adherence. *J Acquir Immune Defic Syndr.* 2017;76 (5):482–487. doi:10.1097/QAI.0000000000001543 [PubMed: 28885270]
114. Corless IB, Hoyt AJ, Tyer-Viola L, et al. 90–90–90-Plus: maintaining adherence to antiretroviral therapies. *AIDS Patient Care STDS.* 2017;31(5):227–236. doi:10.1089/apc.2017.0009 [PubMed: 28514193]
115. Pence BW, Mills JC, Bengtson AM, et al. Association of increased chronicity of depression with HIV appointment attendance, treatment failure, and mortality among HIV-infected adults in the United States [published online February 21, 2018]. *JAMA Psychiatry.* 2018. doi:10.1001/jamapsychiatry.2017.4726
116. Mills JC, Harman JS, Cook RL, et al. Comparative effectiveness of dual vs. single-action antidepressants on HIV clinical outcomes in HIV-infected people with depression. *AIDS.* 2017;31(18):2515–2524. doi:10.1097/QAD.0000000000001618 [PubMed: 28832409]

117. Walensky RP, Horn TH, Paltiel AD. The Epi-TAF for tenofovir disoproxil fumarate? *Clin Infect Dis*. 2016;62(7):915–918. doi:10.1093/cid/civ1000 [PubMed: 26658300]
118. Freedberg KA, Losina E, Weinstein MC, et al. The cost effectiveness of combination antiretroviral therapy for HIV disease. *N Engl J Med*. 2001;344 (11):824–831. doi:10.1056/NEJM200103153441108 [PubMed: 11248160]
119. Goldie SJ, Yazdanpanah Y, Losina E, et al. Cost-effectiveness of HIV treatment in resource-poor settings—the case of Côte d’Ivoire. *N Engl J Med*. 2006;355(11):1141–1153. doi:10.1056/NEJMs060247 [PubMed: 16971720]
120. Bayoumi AM, Barnett PG, Joyce VR, et al. Cost-effectiveness of newer antiretroviral drugs in treatment-experienced patients with multidrug-resistant HIV disease. *J Acquir Immune Defic Syndr*. 2013;64(4):382–391. doi:10.1097/QAI.0000000000000002 [PubMed: 24129369]
121. Sutton SS, Magagnoli J, Hardin JW. Odds of viral suppression by single-tablet regimens, multiple-tablet regimens, and adherence level in HIV/AIDS patients receiving antiretroviral therapy. *Pharmacotherapy*. 2017;37(2):204–213. doi:10.1002/phar.1889 [PubMed: 28028855]
122. Clay PG, Nag S, Graham CM, Narayanan S. Meta-analysis of studies comparing single and multi-tablet fixed dose combination HIV treatment regimens. *Medicine (Baltimore)*. 2015;94(42):e1677. doi:10.1097/MD.0000000000001677 [PubMed: 26496277]
123. Walensky RP, Sax PE, Nakamura YM, et al. Economic savings versus health losses: the cost-effectiveness of generic antiretroviral therapy in the United States. *Ann Intern Med*. 2013; 158(2):84–92. doi:10.7326/0003-4819-158-2-201301150-00002 [PubMed: 23318310]
124. Crepaz N, Tang T, Marks G, Mugavero MJ, Espinoza L, Hall HI. Durable viral suppression and transmission risk potential among persons with diagnosed HIV infection: United States, 2012–2013. *Clin Infect Dis*. 2016;63(7):976–983. doi:10.1093/cid/ciw418 [PubMed: 27358354]
125. Kuhar DT, Henderson DK, Struble KA, et al.; US Public Health Service Working Group. Updated US Public Health Service guidelines for the management of occupational exposures to human immunodeficiency virus and recommendations for postexposure prophylaxis [published correction appears in *Infect Control Hosp Epidemiol*. 2013;34(11):1238]. *Infect Control Hosp Epidemiol*. 2013;34(9):875–892. doi:10.1086/672271 [PubMed: 23917901]
126. Centers for Disease Control and Prevention(CDC). Updated guidelines for antiretroviral postexposure prophylaxis after sexual, injection drug use, or other nonoccupational exposure to HIV—United States, 2016. CDC website. <https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf>. Published 2016.
127. Lancki N, Almirol E, Alon L, McNulty M, Schneider JA. Preexposure prophylaxis guidelines have low sensitivity for identifying seroconverters in a sample of young black MSM in Chicago. *AIDS*. 2018;32(3):383–392. [PubMed: 29194116]
128. Gilead Sciences. TRUVADA (emtricitabine and tenofovir disoproxil fumarate) [package insert]. Foster City, CA: Gilead Sciences Inc; 2014.
129. Anderson PL, Glidden DV, Liu A, et al.; iPrEx Study Team. Emtricitabine-tenofovir concentrations and pre-exposure prophylaxis efficacy in men who have sex with men. *Sci Transl Med*. 2012;4(151):151ra125. doi:10.1126/scitranslmed.3004006
130. Cottrell ML, Yang KH, Prince HM, et al. A translational pharmacology approach to predicting outcomes of HIV preexposure prophylaxis against HIV in men and women using tenofovir disoproxil fumarate with or without emtricitabine. *J Infect Dis*. 2016;214(1):55–64. doi:10.1093/infdis/jiw077 [PubMed: 26917574]
131. Molina JM, Capitant C, Spire B, et al.; ANRSIPERGAY Study Group. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. *N Engl J Med*. 2015;373(23):2237–2246. doi:10.1056/NEJMoa1506273 [PubMed: 26624850]
132. McCormack S, Dunn DT, Desai M, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet*. 2016;387(10013):53–60. doi:10.1016/S0140-6736(15)00056-2 [PubMed: 26364263]
133. Antoni G, Tremblay C, Charreau I, et al. On-demand PrEP with TDF/FTC remains highly effective among MSM with infrequent sexual intercourse: a sub-study of ANRS iPERGAY trial. Presented at: IAS Conference on HIV Science; July 23–27, 2017; Paris, France.



134. Molina JM, Charreau I, Spire B, et al. Efficacy, safety, and effect on sexual behaviour of on-demand pre-exposure prophylaxis for HIV in men who have sex with men: an observational cohort study. *Lancet HIV*. 2017;4(9):e402–e410. doi:10.1016/S2352-3018(17)30089-9 [PubMed: 28747274]
135. Molina JM, Pialoux G, Ohayon M, et al. One-year experience with pre-exposure prophylaxis (PrEP) implementation in France with TDF/FTC. Presented at: 9th International AIDS Society Conference on HIV Science; July 23–27, 2017; Paris, France.
136. Balavoine S, Noret M, Loze B, et al. PrEP uptake, safety and efficacy in a hospital-based clinic in Paris. Presented at: 9th International AIDS Society Conference on HIV Science; July 23–26, 2017; Paris, France.
137. European AIDS Clinical Society (EACS). EACS Guidelines Version 8.2 EACS website. [http://www.eacsociety.org/files/guidelines\\_8.2-english.pdf](http://www.eacsociety.org/files/guidelines_8.2-english.pdf). Published 2017.
138. British HIV Association (BHIVA). Consultation version of the BHIVA/BASHH guidelines on the use of HIV pre-exposure prophylaxis (PrEP) 2017. BHIVA website. <http://www.bhiva.org/PrEP-guidelines-consultation.aspx>. Published 2017.
139. Tan DHS, Hull MW, Yoong D, et al.; Biomedical HIV Prevention Working Group of the CIHR Canadian HIV Trials Network. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. *CMAJ*. 2017;189(47): E1448–E1458. doi:10.1503/cmaj.170494 [PubMed: 29180384]
140. Mugwanya KK, Wyatt C, Celum C, et al.; Partners PrEP Study Team. Reversibility of glomerular renal function decline in HIV-uninfected men and women discontinuing emtricitabine-tenofovir disoproxil fumarate pre-exposure prophylaxis. *J Acquir Immune Defic Syndr*. 2016;71(4):374–380. doi:10.1097/QAI.0000000000000868 [PubMed: 26914909]
141. Delaugerre C, Antoni G, Mahjoub N, et al.; IPERGAY Study Group. Assessment of HIV screening tests for use in preexposure prophylaxis programs. *J Infect Dis*. 2017;216(3):382–386. [PubMed: 28666370]
142. Hoorneborg E, Prins M, Achterbergh RCA, et al.; Amsterdam PrEP Project Team in the HIV Transmission Elimination Amsterdam Consortium (H-TEAM). Acquisition of wild-type HIV-1 infection in a patient on pre-exposure prophylaxis with high intracellular concentrations of tenofovir diphosphate: a case report. *Lancet HIV*. 2017;4(11):e522–e528. doi:10.1016/S2352-3018(17)30132-7 [PubMed: 28919303]
143. Donnell D, Ramos E, Celum C, et al.; Partners PrEP Study Team. The effect of oral preexposure prophylaxis on the progression of HIV-1 seroconversion. *AIDS*. 2017;31(14):2007–2016. doi:10.1097/QAD.0000000000001577 [PubMed: 28692542]
144. Knox DC, Anderson PL, Harrigan PR, Tan DH. Multidrug-resistant HIV-1 infection despite preexposure prophylaxis. *N Engl J Med*. 2017;376(5):501–502. doi:10.1056/NEJMc1611639
145. Markowitz M, Grossman H, Anderson PL, et al. Newly acquired infection with multidrug-resistant HIV-1 in a patient adherent to preexposure prophylaxis. *J Acquir Immune Defic Syndr*. 2017;76(4):e104–e106. doi:10.1097/QAI.0000000000001534 [PubMed: 29076941]
146. Krakower P, Maloney KM, Levine K. Unplanned discontinuation of HIV pre-exposure prophylaxis during clinical care. Presented at: 2nd HIV Research for Prevention Conference (HIVR4P); October 17–21, 2016; Chicago, IL.
147. Jain S, Krakower DS, Mayer KH. The transition from postexposure prophylaxis to preexposure prophylaxis: an emerging opportunity for biobehavioral HIV prevention. *Clin Infect Dis*. 2015; 60(suppl 3):S200–S204. doi:10.1093/cid/civ094 [PubMed: 25972505]
148. Margolis DA, Gonzalez-Garcia J, Stellbrink HJ, et al. Long-acting intramuscular cabotegravir and rilpivirine in adults with HIV-1 infection (LATTE-2): 96-week results of a randomised, open-label, phase 2b, non-inferiority trial. *Lancet*. 2017;390(10101): 1499–1510. doi:10.1016/S0140-6736(17)31917-7 [PubMed: 28750935]
149. Markowitz M, Frank I, Grant R, et al. ÉCLAIR: phase 2A safety and PK study of cabotegravir LA in HIV-uninfected men [abstract 106]. Presented at: 23rd Conference on Retroviruses and Opportunistic Infections (CROI); February 22–25, 2016; Boston, MA.



150. Baeten J, Palanee-Phillips T, Mgodhi N, et al. High uptake and reduced HIV-1 incidence in an open-label trial of the dapivirine ring. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
151. Nel A, van Niekerk N, Van Baelen B, Rosenberg Z. HIV incidence and adherence in DREAM: an open-label trial of dapivirine vaginal ring. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.
152. McCoy LE, Burton DR. Identification and specificity of broadly neutralizing antibodies against HIV. *Immunol Rev.* 2017;275(1):11–20. doi:10.1111/imr.12484 [PubMed: 28133814]
153. Caskey M, Klein F, Lorenzi JC, et al. Viraemia suppressed in HIV-1-infected humans by broadly neutralizing antibody 3BNC117. *Nature.* 2015;522 (7557):487–491. doi:10.1038/nature14411 [PubMed: 25855300]
154. Caskey M, Schoofs T, Gruell H, et al. Antibody10–1074 suppresses viremia in HIV-1-infected individuals. *Nat Med.* 2017;23(2):185–191. doi:10.1038/nm.4268 [PubMed: 28092665]
155. Huang J, Kang BH, Ishida E, et al. Identification of a CD4-binding-site antibody to HIV that evolved near-pan neutralization breadth. *Immunity.* 2016; 45(5):1108–1121. doi:10.1016/j.immuni.2016.10.027 [PubMed: 27851912]
156. Gaudinski MR, Coates EE, Houser KV, et al.; VRC 606 Study Team. Safety and pharmacokinetics of the Fc-modified HIV-1 human monoclonal antibody VRC01LS: a phase 1 open-label clinical trial in healthy adults. *PLoS Med.* 2018;15(1):e1002493. doi:10.1371/journal.pmed.1002493 [PubMed: 29364886]
157. Boesch AW, Alter G, Ackerman ME. Prospects for engineering HIV-specific antibodies for enhanced effector function and half-life. *Curr Opin HIV AIDS.* 2015;10(3):160–169. doi: 10.1097/COH.000000000000149 [PubMed: 25700208]
158. Fuchs SP, Desrosiers RC. Promise and problems associated with the use of recombinant AAV for the delivery of anti-HIV antibodies. *Mol Ther Methods Clin Dev.* 2016;3:16068. doi:10.1038/mtm.2016.68 [PubMed: 28197421]
159. Hua CK, Ackerman ME. Increasing the clinical potential and applications of anti-HIV antibodies. *Front Immunol.* 2017;8:1655. doi:10.3389/fimmu.2017.01655 [PubMed: 29234320]
160. Kong R, Louder MK, Wagh K, et al. Improving neutralization potency and breadth by combining broadly reactive HIV-1 antibodies targeting major neutralization epitopes. *J Virol.* 2015;89(5): 2659–2671. doi:10.1128/JVI.03136-14 [PubMed: 25520506]
161. Borducchi E, Abbink P, Nkolola J, Lewis MG, Geleziunas R, Barouch D. PGT121 combined with GS-9620 delays viral rebound in SHIV-infected rhesus monkeys. Presented at: 25th Conference on Retroviruses and Opportunistic Infections (CROI); March 4–7, 2018; Boston, MA.

**Box 1.****Selected Recommendations for When to Start ART**

ART should be initiated as soon as possible after diagnosis, including immediately after diagnosis, unless patient is not ready to commit to starting therapy (evidence rating AIa).

Structural barriers that delay receipt of ART should be removed to allow newly diagnosed persons to receive ART at the first clinic visit after diagnosis, if they and their clinician determine that this approach is appropriate (evidence rating AIa).

Samples for HIV-1 RNA level; CD4 cell count; HIV genotype for NRTI, NNRTI, and PI; laboratory tests to exclude active viral hepatitis; and chemistries should be drawn before beginning ART, but treatment may be started before results are available. Result of testing for HLA-B\*5701 allele should be available if an abacavir-containing regimen is anticipated (evidence rating AIa).

NNRTIs and abacavir should not be used for rapid ART start (evidence rating AIII).

ART should be started as soon as possible but within the first 2 weeks after diagnosis for most OIs (evidence rating AIa).

Primary MAC prophylaxis is no longer recommended if effective ART is initiated (evidence rating AIIa).

Primary prophylaxis for *Pneumocystis* pneumonia should be initiated for patients with CD4 cell counts below 200/ $\mu$ L (evidence rating AIa).

Prophylaxis for cryptococcal disease is not recommended in highly resourced settings with low prevalence of disease (evidence rating AIII).

ART should be implemented immediately in the setting of newly diagnosed malignancy, with attention to drug-drug interactions (evidence rating BIIa).<sup>3</sup>

Abbreviations: ART, antiretroviral therapy; MAC, *Mycobacterium avium* complex; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; OI, opportunistic infection; PI, protease inhibitor

**Box 2.****Selected Recommendations for Initial ART Regimens<sup>a</sup>**

Generally Recommended Initial Regimens (Listed in Alphabetic Order by InSTI Component)

- Bictegravir/TAF/emtricitabine (evidence rating AIa)<sup>b</sup>
- Dolutegravir/abacavir/lamivudine (evidence rating AIa)<sup>c,d</sup>
- Dolutegravir plus TAF/emtricitabine (evidence rating AIa)<sup>c,e</sup>

Recommended Initial Regimens for Individuals for Whom Generally Recommended Regimens Are Not Available or Not an Option (Listed in Alphabetic Order by First Component)

- Darunavir/cobicistat plus TAF (or TDF)/emtricitabine (evidence rating AIa)<sup>e</sup>
- Darunavir boosted with ritonavir plus TAF (or TDF)/emtricitabine (evidence rating AIa)<sup>e</sup>
- Efavirenz/TDF/emtricitabine (evidence rating AIa)
- Elvitegravir/cobicistat/TAF (or TDF)/emtricitabine (evidence rating AIa)<sup>e</sup>
- Raltegravir plus TAF (or TDF)/emtricitabine (evidence rating AIa for TDF)<sup>e</sup>
- Rilpivirine/TAF (or TDF)/emtricitabine (if pretreatment HIV RNA level is <100 000 copies/mL and CD4 cell count is >200/μL) (evidence rating AIa)<sup>e</sup>

TDF is not recommended for individuals with or at risk for kidney or bone disease (osteopenia or osteoporosis) (evidence rating BIII).

Initial 2-drug regimens are only recommended in the rare situations in which a patient cannot take abacavir, TAF, or TDF (evidence rating BIa).

Pregnant individuals with HIV infection should initiate ART for their own health and to reduce the likelihood of HIV transmission to the infant (evidence rating AIa).

Abbreviations: ART, antiretroviral therapy; InSTI, integrase strand transfer inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

<sup>a</sup> Components separated with a slash (/) indicate that they are available as coformulations.

<sup>b</sup> There are fewer long-term safety and efficacy data with bictegravir than with dolutegravir.

<sup>c</sup> There are important considerations related to interim reports of potential teratogenicity of dolutegravir when initiated before conception. See text for details.

<sup>d</sup> Testing for HLA-B\*5701 allele should be performed before abacavir use (evidence rating AIa); patients who test positive should not be given abacavir (evidence rating AIa). Because it typically takes several days or longer to obtain results for HLA-B\*5701 testing, tenofovir-containing regimens should be used when starting ART on the same day as HIV diagnosis or until HLA-B\*5701 testing results are available. In patients with

or at high risk for cardiovascular disease, a tenofovir-containing regimen, rather than an abacavir-containing regimen, should be used if possible.

<sup>e</sup> In settings in which TAF/emtricitabine is not available or if there is a substantial cost difference, TDF (with emtricitabine or lamivudine) is effective and generally well tolerated, particularly if the patient does not have, or is not at high risk for, kidney or bone disease.

**Box 3.****Selected Recommendations for When and How to Switch ART Regimens**

- Review of the ART treatment history, regimen tolerability, comedications, and results of prior resistance tests is recommended before any treatment switches are made (evidence rating AIa).
- In patients with NRTI mutations, switching from a boosted PI to a regimen containing a drug with a low genetic barrier to resistance (eg, NNRTI or raltegravir) is not recommended (evidence rating AIa).
- HIV viral load should be checked 1 month after switching regimens to ensure virologic suppression has been maintained (evidence rating BIII).

**Switching When Virologically Suppressed**

- Patients taking older ART drugs with known toxicity should be questioned carefully to identify subtle adverse effects of which they may be unaware or that they may not attribute to the drug. The presence of these toxicities should prompt a change in regimen (evidence rating BIII).
- In general, if the older regimen is well tolerated without evidence of toxicity, there is little reason to switch to a newer regimen (evidence rating BIII).
- Proactive switching from TDF to TAF is recommended for patients at high risk of renal or bone toxicity (evidence rating BIa). Review of comedications is essential to ensure no change in dosing is required with the use of TAF.
- Switching from 3-drug regimens to certain 2-drug regimens in the setting of viral suppression, using dolutegravir/rilpivirine (evidence rating AIa), a boosted PI with lamivudine (evidence rating AIIa), or dolutegravir with lamivudine (evidence rating AIIa) can be used in patients with no prior virologic failure or transmitted drug resistance. (Longer-term follow-up is needed to confirm the durability of these strategies).
- Patients who are co-infected with HIV and HBV should receive a regimen that contains 2 drugs active against HBV, usually TAF or TDF plus lamivudine or emtricitabine, in addition to a third ART drug (evidence rating AIIa). Such patients should generally not be switched to 2-drug ART.
- Monotherapy with boosted PIs or dolutegravir is not recommended (evidence rating AIIa).

**Switching for Virologic Failure**

- Resistance testing is recommended while taking the failing ART regimen or within 4 weeks of stopping (evidence rating AIIa).
- Virologic failure should be confirmed and, if resistance is identified, a prompt switch to another active regimen using results of current and past resistance

testing to prevent accumulation of additional resistance mutations is recommended (evidence rating BIIa).

- Dolutegravir, plus 2 NRTIs (with at least 1 active by genotype) is recommended after initial treatment failure with an NNRTI (evidence rating AIa).
- A boosted PI plus 2 NRTIs (with at least 1 active NRTI) are recommended for initial treatment failure of an InSTI-containing regimen (evidence rating AIII).
- Dolutegravir plus at least 1 fully active other agent may be effective in the setting of raltegravir or elvitegravir resistance. Dolutegravir should be dosed twice daily in this setting (evidence rating BIII).
- A single active agent added to a failing regimen is not recommended (evidence rating AIa).
- For multiclass resistance, the next regimen should be constructed using drugs from new classes if available (evidence rating BIII).

Abbreviations: ART, antiretroviral therapy; HBV, hepatitis B virus; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; PI, protease inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.



**Box 4.****Selected Recommendations for Laboratory Monitoring**

All persons who have ever been sexually active should be tested for HIV at least once in their lives (evidence rating AIII).

Risk for HIV often changes over a person's lifetime; risk evaluation is recommended at each routine clinical visit (evidence rating AIII).

For sexually active men who have sex with men and for transgender women, people who inject drugs, and others at increased risk, testing is recommended at least annually and as frequently as every 3 months (evidence rating BIII).

Diagnosis of sexually transmitted infections and hepatitis C virus can help identify persons who should be tested more regularly for HIV and who might benefit from preexposure prophylaxis (evidence rating BIII).

HIV screening with assays that can detect recent HIV infection, either an instrument-based combination antigen/antibody assay or a combination of a stand-alone antibody assay and nucleic acid testing, is recommended (evidence rating AIIa).

Persons with ongoing condomless sexual exposures or sharing of needles or works need to be tested with assays that can detect HIV RNA or with combination antibody + p24 antigen tests (evidence rating AIIa). Individuals with signs or symptoms of acute or primary HIV infection should be tested with HIV RNA assays.

All available tests can have false-positive results, so additional testing with an HIV viral load is recommended before ART initiation, although treatment may be started before results are available (evidence rating AIa).

HIV genotype to assess transmitted NRTI and NNRTI resistance should be performed; InSTI genotyping at baseline is not recommended unless exposure to a partner with InSTI resistance is suspected (evidence rating BIII).

CCR5 tropism testing is recommended each time when considering maraviroc and HLA-B\*5701 testing (only needed once) before use of abacavir (evidence rating AIa).

Once HIV RNA level is below 50 copies/mL, monitoring is recommended every 3 months until virus is suppressed for at least a year. After 1 year of viral suppression, monitoring can be reduced to every 6 months if the patient maintains consistent medication adherence (evidence rating AIII).

Measurement of CD4 cell counts is recommended every 6 months until cell counts are above 250/ $\mu$ L for at least 1 year with concomitant viral suppression (evidence rating BIII).

Age- and risk-appropriate screening for STIs at various anatomical sites, anal or cervical dysplasia, tuberculosis, general health, and medication toxicity is recommended (evidence rating AIII).

Once a viral load above 50 copies/mL is detected, measurement should be repeated within 4 weeks, and reassessing for medication adherence and tolerability is recommended (evidence rating AIII).

Measurement of viral load at 4 to 6 weeks after starting a new ART regimen is recommended (evidence rating AIII).

If the viral load has not declined, adherence and toxicity should be discussed with the patient. If adherence appears to be sufficient, a genotype assay is recommended (evidence rating AIII).

Abbreviations: ART, antiretroviral therapy; CCR5, CC chemokine receptor 5; InSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; STI, sexually transmitted infection.

**Box 5.****Selected Recommendations for Engagement in Care and ART Adherence**

Routine, opt-out HIV screening is recommended in primary medical care settings, emergency departments, and for all pregnant women (evidence rating AIIa).

Routine screening and treatment for depression is recommended (evidence rating AIIa).

Systematic monitoring of time to care linkage after initial HIV diagnosis, retention in care, reengagement in care, ART adherence, and rates of viral suppression is recommended in all care settings and at a population level (evidence rating AIIa).

Brief, strengths-based case management is recommended after HIV diagnosis to facilitate linkage to care (evidence rating AIa).

Systematic monitoring of missed clinic visits and rapid intervention after a missed visit is recommended (evidence rating AIIa).

Personal telephone and interactive text reminders in advance of scheduled appointments and shortly after missed appointments (eg, 24–48 hours) are recommended (evidence rating AIa).

Adherence monitoring using patients' self-report obtained by validated adherence instruments and pharmacy refill data is recommended (evidence rating AIIa).

Integration of directly observed ART in methadone maintenance programs (evidence rating BIa) and as a treatment strategy among persons with substance use disorders (evidence rating BIa) and those who are incarcerated or released to the community (evidence rating CIII) is recommended to enhance adherence and viral suppression.

Opioid substitution therapy for opioid-dependent patients is recommended (evidence rating AIa).

Rapid HIV test algorithms may be used to confirm a preliminary positive rapid test result, allowing for same-day referral to treatment from nonclinical settings (evidence rating AIa).

Use of public health surveillance in conjunction with clinic-level data to guide individual-level linkage and reengagement in care activities is recommended (evidence rating BIIa).

Cash financial incentives for clinic appointment attendance and achievement of viral suppression are generally not recommended as a retention-in-care strategy (evidence rating AIa).

Data-driven risk stratification to identify high-acuity, high-need patients for combination intervention strategies to improve care engagement and viral suppression is recommended (evidence rating CIIb).

Screening for and addressing housing instability, food insecurity, ongoing substance use, psychiatric disorders, medication adverse effects, and pill burden is recommended (evidence rating BIIa).

Abbreviation: ART, antiretroviral therapy.

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**Box 6.****Selected Recommendations for Prevention of HIV Infection**

HIV-seropositive and -negative individuals should be reminded that condoms are required to prevent acquisition of non-HIV STIs (evidence rating AIIa).

Quarterly screening for asymptomatic STIs is recommended for all populations with high rates of bacterial STIs and incomplete condom use (evidence rating AIIa).

Abacavir-based PEP is not recommended unless the exposed patient is known to be negative for the HLA-B\*5701 allele (evidence rating AIII).

PrEP is recommended for populations whose annual HIV incidence is at least 2% (evidence rating AIII).

Daily TDF/emtricitabine is the recommended regimen for men and women (evidence rating AIa) and transgender individuals (evidence rating AIIa) at risk of sexual exposure (evidence rating AIa) and people who inject drugs (evidence rating BIa).

A 1-week lead-in time is recommended with daily dosing for rectal, penile, and vaginal exposures with daily TDF/emtricitabine to ensure adequate tissue levels are achieved (evidence rating CIII).

At PrEP discontinuation, TDF/emtricitabine should continue for 1 week after the last sexual exposure (evidence rating CIII).

For individuals with active HBV infection (detectable HBsAg), discontinuation of TDF/emtricitabine PrEP could lead to acute HBV flares or hepatic decompensation, particularly for patients with hepatic cirrhosis; careful monitoring of HBV infection and liver function is recommended after discontinuation of TDF/emtricitabine (evidence rating AIIa).

Pericoital TDF/emtricitabine PrEP, also known as on-demand, event-driven, or “2–1–1” dosing may be considered as an alternative to daily PrEP for MSM with infrequent sexual exposures (evidence rating AIa). This regimen is not recommended in other risk groups or in patients with active HBV infection because of the risk of hepatitis flare and hepatic decompensation (evidence rating BIIa).

If intercourse is planned in the context of 2–1–1 PrEP regimen, the first (double) dose of TDF/emtricitabine should be taken closer to the 24-hour precoital time than the 2-hour time (evidence rating CIII).

TDF/lamivudine, TAF/emtricitabine, and TDF alone are *not* recommended for PrEP (evidence rating BIII).

TDF-based PrEP is not recommended in persons with creatinine clearance below 60 mL/min/1.73m<sup>2</sup> (evidence rating AIIa)

HIV testing, preferably with a combination antigen-antibody assay (evidence rating AIII), to confirm HIV-seronegative status is mandatory at time of initiation of TDF/emtricitabine PrEP; HIV RNA testing should be obtained if acute HIV is suspected.

Measurement of serum creatinine level, determination of estimated glomerular filtration rate, and HBsAg testing are recommended before initiation of PrEP but need not impede PrEP initiation (evidence rating BIII).

During PrEP, intervals of follow-up every 3 months are recommended to allow for HIV testing (evidence rating AIII) and STI screening (evidence rating AIIa).

HCV serologic testing should be performed at least annually and more frequently in the case of elevated transaminase levels or in high-risk individuals (eg, people who inject drugs) (evidence rating BIIa).

PrEP prescription should not exceed 90 days without interval testing for HIV infection (evidence rating AIII); a visit 30 days after PrEP start is recommended for follow-up HIV testing, to assess adverse effects and support adherence (evidence rating BIII).

Measurement of creatinine level should be performed at least every 6 months (evidence rating AIII) and more frequently for some patients (eg, those >50 years, taking hypertension or diabetes medications, or with glomerular filtration rates <90 mL/min) (evidence rating BIIa).

Each PrEP visit should be used to assess and troubleshoot barriers to adherence to PrEP (evidence rating BIII).

For confirmed HIV infection in the setting of PrEP use, a recommended initial antiretroviral regimen should be started, pending results of resistance testing (evidence rating AIII).

For individuals being treated with a course of 3-drug PEP for a recent exposure who are likely to be at risk of ongoing exposure, a seamless transition from PEP to PrEP is recommended (evidence rating CIII).

If during PrEP treatment, exposure to HIV is known to occur, intensification of treatment with additional agent(s) is not recommended (evidence rating BIII).

Abbreviations: HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; MSM, men who have sex with men; PEP, postexposure prophylaxis; PrEP, preexposure prophylaxis; STI, sexually transmitted infection; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.



**Table 1.**Strength of Recommendation and Quality of Evidence Rating Scale<sup>a</sup>

Category, Rating	Definition
Strength of Recommendation	
A	Strong support for the recommendation
B	Moderate support for the recommendation
C	Limited support for the recommendation
Quality of Evidence	
Ia	Evidence from 1 randomized clinical trials published in the peer-reviewed literature
Ib	Evidence from 1 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

<sup>a</sup>Adapted in part from Canadian Task Force on Periodic Health Examination.<sup>2</sup>

**Table 2.** Advantages and Disadvantages of Currently Available Integrase Strand Transfer Inhibitors

Drug <sup>a</sup>	Year of FDA Approval	Advantages	Disadvantages
Bictegravir	2018	<ul style="list-style-type: none"> <li>Coformulated with TAF/emtricitabine as part of a complete initial regimen</li> <li>Noninferior to dolutegravir in comparative trials</li> <li>Once-daily dosing</li> <li>Low risk of resistance with virologic failure</li> <li>Relatively few drug interactions</li> <li>Can be taken with or without food</li> <li>Can be started without HLA-B*5701 testing</li> </ul>	<ul style="list-style-type: none"> <li>Coformulation precludes combination with other antiretrovirals</li> <li>Cannot be used with rifampin</li> <li>Less long-term experience and data than with other INSTIs</li> <li>Raises serum creatinine levels (<math>\approx 0.1</math> mg/dL) through inhibition of tubular secretion of creatinine</li> <li>Insufficient data in pregnant women</li> <li>Concerns regarding neural tube defects in infants born to women who conceived while taking dolutegravir; unknown whether this is a class effect (see text)</li> </ul>
Dolutegravir	2013	<ul style="list-style-type: none"> <li>Noninferior to bictegravir in 2 comparative trials and superior to darunavir and efavirenz in comparative trials</li> <li>Once-daily dosing</li> <li>Available as a single agent, allowing it to be used in other combinations</li> <li>Low risk of resistance with virologic failure</li> <li>Relatively few drug interactions</li> <li>Can be taken with or without food</li> <li>Superior to raltegravir in treatment-experienced patients</li> </ul>	<ul style="list-style-type: none"> <li>Raises serum creatinine levels (0.1–0.15 mg/dL) through inhibition of tubular secretion of creatinine</li> <li>Higher rates of insomnia and headache than with comparators in some studies</li> <li>Coformulated with abacavir/lamivudine, is the largest tablet among coformulated single-pill regimens; abacavir requires HLA-B*5701 testing</li> <li>Concerns regarding neural tube defects in infants born to women who conceived while taking dolutegravir; unknown whether this is a class effect (see text)</li> </ul>
Elvitegravir	2012	<ul style="list-style-type: none"> <li>Once-daily dosing</li> <li>Coformulated with TDF/emtricitabine or TAF/emtricitabine as a complete regimen</li> </ul>	<ul style="list-style-type: none"> <li>Requires pharmacokinetic boosting with cobicistat for once-daily dosing</li> <li>Lower barrier to resistance than bictegravir and dolutegravir</li> <li>Frequent drug interactions attributable to cobicistat boosting</li> <li>Cobicistat raises serum creatinine levels (0.1–0.15 mg/dL) through inhibition of tubular secretion of creatinine</li> <li>Should be taken with food</li> <li>Should be avoided in pregnant women because of inadequate plasma levels</li> <li>Concerns regarding neural tube defects in infants born to women who conceived while taking dolutegravir; unknown whether this is a class effect (see text)</li> </ul>
Raltegravir	2007	<ul style="list-style-type: none"> <li>Superior to ritonavir-boosted atazanavir and ritonavir-boosted darunavir in a comparative clinical trial</li> <li>Longest safety record</li> <li>Fewest drug interactions</li> <li>Can be taken with or without food</li> </ul>	<ul style="list-style-type: none"> <li>Not coformulated as part of a complete regimen</li> <li>Lower barrier to resistance than bictegravir or dolutegravir</li> <li>Higher pill burden than with other INSTIs</li> <li>Concerns regarding neural tube defects in infants born to women who conceived while taking dolutegravir; unknown whether this is a class effect (see text)</li> </ul>

Abbreviations: FDA, US Food and Drug Administration; INSTI, integrase strand transfer inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

SI conversion factor: To convert creatinine values to  $\mu\text{mol/L}$ , multiply by 88.4

<sup>a</sup>In alphabetic order. The use of abacavir and TAF or TDF is described in the text

Table 3.

Initial Non-InSTI Antiretroviral Treatment<sup>a,b,c</sup>

Regimen	Advantages	Disadvantages
Darunavir (boosted with cobicistat or ritonavir) plus TAF/emtricitabine or TDF/emtricitabine	Low risk of resistance with virologic failure, even with intermittent adherence Available as a single tablet regimen in Europe and perhaps soon in the United States (darunavir/cobicistat/TAF/emtricitabine) <sup>24</sup> Can be started without results of HLA-B*57:01, hepatitis B, and resistance testing	Requires pharmacokinetic boosting; many drug interactions Ritonavir-boosted darunavir inferior to raltegravir and dolutegravir in comparative clinical trials, largely because of lower tolerability Cobicistat should not be given in pregnancy because of inadequate plasma levels
Efavirenz/TDF/emtricitabine	High efficacy in patients with baseline HIV RNA levels >100000 copies/mL Extensive experience in patients with concomitant tuberculosis Widely available globally Available as a generic coformulation at 600 or 400 mg with TDF/lamivudine	Relatively high rate of rash No single-tablet form available with TAF Efavirenz may cause neuropsychiatric adverse effects Increased risk of suicidality; avoid in patients with a history of depression
Rilpivirine/TAF (or TDF)/emtricitabine	Lowest risk of rash among NNRTI-based therapies Low risk of metabolic adverse effects	Not recommended for patients with HIV RNA levels >100000 copies/mL or CD4 cell count <200/μL because of increased risk of virologic failure Must be taken with a meal (at least 390 calories) to optimize absorption Should not be administered with proton-pump inhibitors; stagger dosing if given with an H <sub>2</sub> blocker

Abbreviations: InSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate.

<sup>a</sup>In alphabetic order by first component. Initial NNRTI-based regimens should not be used without baseline resistance data because of the possible presence of transmitted NNRTI-resistant virus. In the rare circumstance in which maraviroc might be included in initial therapy, initiation should not occur before confirmation of CC chemokine receptor 5 tropism.

<sup>b</sup>Of note, doravirine, an investigational NNRTI, is currently under regulatory review. If approved, doravirine/lamivudine/TDF would likely be an effective initial regimen in patients for whom use of an InSTI-containing regimen is not possible.

<sup>c</sup>See text with regard to interchanging TDF for TAF and interchanging emtricitabine for lamivudine and vice versa.

**Table 4.**

**Recommended Laboratory Assessments and Monitoring Across the HIV Care Continuum**

Test	At HIV Diagnosis	During ART	At Virologic Failure
HIV RNA level	✓	Within the first 6 weeks of starting ART or a new ART regimen, then every 3 mo until <50 copies/mL for 1 y, then every 6 mo	✓
CD4 cell count	✓	Every 6 mo until >2,500 $\mu$ L for 1 y then stop as long as virus is suppressed	✓
HIV RT-pro genotype	✓		✓
HIV integrase genotype			If failing ART regimen included an INSTI
Viral tropism			Each time before the start of ART that includes maraviroc
HLA-B*5701	✓ (before initiating abacavir; just once)	✓ (if considering abacavir and not determined previously)	✓
Safety testing	✓	✓	✓
Co-infection (STIs, tuberculosis, hepatitis, Pap test)	✓	✓	
Health maintenance	✓	✓	

Abbreviations: ART, antiretroviral therapy; INSTI, integrase strand transfer inhibitor; Pap, Papanicolaou; RT-pro, reverse transcriptase and protease; STI, sexually transmitted infection.