HIV pre-exposure prophylaxis

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INTRODUCTION

Over one million new human immunodeficiency virus (HIV) infections occur yearly worldwide, with more than 30,000 annually in the United States. As there are no effective vaccines to prevent HIV transmission, behavioral and biomedical HIV prevention strategies are needed to reduce HIV acquisition.

The use of pre-exposure prophylaxis (PrEP) with antiretroviral therapy (ART) for those without HIV has proven to be an effective HIV prevention strategy. Among persons who are adherent to treatment, PrEP can reduce the risk of HIV transmission by greater than 99 percent [1], although rare infections may still occur [2-4]. However, less than one-third of people who meet PrEP indications have ever been prescribed PrEP. Uptake has been particularly limited in certain populations who are at greatest risk for HIV infection (eg, at-risk African Americans, Hispanic/Latin Americans, adolescents, and transgender individuals) [5-7].

This topic will review the approach to using PrEP in persons who are at risk for acquiring HIV. Other strategies to prevent HIV infection (eg, ART for patients with HIV, post-exposure prophylaxis [PEP], and voluntary male circumcision) are discussed elsewhere. (See "HIV

infection: Risk factors and prevention strategies" and "Management of nonoccupational exposures to HIV and hepatitis B and C in adults" and "Management of health care personnel exposed to HIV".)

DETERMINING ELIGIBILITY FOR PREP

Assessing risk of acquiring HIV — All sexually active patients should be informed about HIV PrEP. .

Clinicians should obtain a detailed sexual and drug use history from all patients to determine if the patient is at high risk of acquiring HIV (table 1 and table 2). (See 'Indications based upon risk' below.)

A more detailed discussion of risk factors for HIV infection is found elsewhere. (See "HIV infection: Risk factors and prevention strategies", section on 'Risk factors for infection'.)

Indications based upon risk — The decision to initiate PrEP depends primarily on the person's risk for acquiring HIV. (See 'Assessing risk of acquiring HIV' above.)

PrEP has been associated with a reduction in HIV transmission in several populations, including [8]:

- Men who have sex with men (MSM) and transgender women who report sexual behaviors associated with HIV infection (eg, condomless anal sex)
- Heterosexually active persons who have sex with partners who are at high risk of HIV infection (eg, partners from high HIV prevalence areas and partners who inject drugs)
- Persons who inject drugs

In a systematic review of randomized trials and observational studies with over 18,000 participants, oral PrEP was associated with a reduced risk of HIV infection compared with placebo or no PrEP (relative risk 0.46 [95% CI, 0.33-0.66]; absolute risk reduction, −2.0 percent [95 % CI,−2.8 to −1.2] after four months to four years) [9]. In six trials where adherence to PrEP was ≥70 percent, the benefit was more pronounced (1 versus 4.1 percent [RR 0.27, 95% CI 0.19-0.39]).

By contrast, the benefit of PrEP in those with lower risk (eg, heterosexual men who engaged in condomless sex with partners from areas of low general HIV prevalence) is less certain.

Sexual risk — We recommend PrEP for the following patient groups:

- Persons who have a sexual partner with HIV if the partner has a detectable viral load or if the partner's recent virological status is unknown.

  Although PrEP can be considered for all individuals without HIV who have a serodiscordant partner, in clinical trials, transmission to an uninfected partner has not been reported if the partner with HIV is confirmed to have a stably suppressed plasma HIV RNA and is adherent to their antiretroviral therapy (ART) regimen. In a prospective observational study of serodiscordant couples (ie, one partner has HIV and the other does not) there were no documented intracouple transmission events after more than 1200 couple-years of follow-up when the partner with HIV had a viral load <200 copies/mL [10]. (See "HIV infection: Risk factors and prevention strategies", section on 'Treatment as prevention'.)

  Similarly, if the patient's partner with HIV recently initiated ART, PrEP does not need to be continued indefinitely. PrEP should be continued until the partner with HIV has achieved a stably suppressed viral load (eg, typically by six months after initiating ART) [11,12]. However, PrEP should be continued if there was concern about sustained adherence to antiretroviral medication by the partner living with HIV.

  More detailed information on discontinuing PrEP is discussed below. (See 'Discontinuing PrEP' below.)

- MSM and transgender women who have sex with men if, within the last six months:

  - They have engaged in condomless anal sex (insertive or receptive) with multiple or anonymous sex partners (or a main partner with HIV risk factors).

  - Had a documented bacterial sexually transmitted infection (STI) [13] or were diagnosed with another infection associated with sexual activity (eg, mpox). (See "Screening for sexually transmitted infections" and "Epidemiology, clinical manifestations, and diagnosis of mpox (formerly monkeypox)".)

There have been a number of large trials demonstrating the efficacy of PrEP in reducing HIV transmission in MSM and transgender women who are at high risk for HIV transmission [14-16]. In the multinational iPrEx trial, 2470 HIV-seronegative men and 29 transgender women were randomly assigned to either tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) or placebo once daily [15]. Participants were followed for a median of 1.2 years, during which time 100 patients acquired HIV (36 in the intervention arm and 64 in the placebo group); this was consistent with a 44 percent reduction in the incidence of HIV with TDF-FTC (95% CI 15-63). The protective efficacy of TDF-FTC increased to ≥96 percent for those with drug levels that were consistent with taking at least four doses per week [1,17].

Although some studies in transgender women have found the efficacy of PrEP to be variable [18,19], the differences appear to be due to the level of adherence. In a study that included 24 transgender men and 24 transgender women on stable sex hormone therapy, TDF-FTC did not affect serum levels of gender-affirming hormones, and all persons achieved protective levels of tenofovir diphosphate [20].

- Heterosexually active men from regions with generalized HIV epidemics who have condomless sex with female partners. This includes those who have condomless sex with one or more female partners with known HIV infection or multiple female partners of unknown HIV status.

  According to the World Health Organization (WHO), this refers to geographic regions or populations where the prevalence of HIV is ≥3 percent (eg, several countries in sub-Saharan Africa), though the WHO recommends that individual characteristics and behaviors are also important when considering who might benefit from PrEP use [21]. However, other guideline panels have suggested a lower prevalence threshold of ≥2 percent [22].

  In Africa, two large trials demonstrated that TDF-FTC reduced the risk of HIV acquisition in heterosexual men and women by approximately 80 percent compared with placebo [23,24].

We also suggest PrEP for certain other populations. These include:

- Heterosexual cisgender women who have, in the last six months, engaged in condomless sex with male partners who are at high risk of HIV infection (eg, persons who inject drugs, bisexual male partners, partners from areas where there is a high HIV

prevalence).

PrEP should also be offered to those diagnosed with bacterial STIs associated with increased risk for HIV, such as syphilis or gonorrhea. Although PrEP should be discussed with cisgender women diagnosed with chlamydia, we do not routinely offer PrEP to such patients and individualize consideration of PrEP since the co-occurrence of this STI with HIV is less common than for other bacterial STIs.

In resource-limited settings, trials of oral and topical PrEP to prevent HIV acquisition in at-risk cisgender heterosexual women have yielded variable results. In some trials, oral TDF-FTC was found to have no effect on reducing transmission in females, whereas in others, transmission was reduced by approximately 70 percent overall and by more than 90 percent in those who had drug levels consistent with daily use [23,25-28]. These differences in PrEP efficacy estimates appear to be primarily due to the variable levels of adherence in the different studies.

- Heterosexual men who have, in the last six months, been diagnosed with a bacterial STI or have engaged in condomless sex with partners from areas of low general HIV prevalence but who are at high risk of HIV infection (eg, sex workers, persons who inject drugs). However, there are limited data in these populations, due in part to limited participation in clinical trials and uptake of PrEP [29].

For transgender and nonbinary individuals, the decision to offer PrEP should be determined based on their sexual risk, as described for the populations above, since some groups (eg, transgender women who engage in sex work) are at increased risk for HIV while others are not.

Injection drug use — We suggest PrEP for people who inject drugs if, within the last six months, they report sharing needles/equipment, even if they have initiated substance use treatment. In a double-blind trial in Thailand, 2413 HIV-seronegative males and females with a history of injection drug use during the previous year were randomly assigned to once-daily therapy with tenofovir or placebo [30]. Fifty patients became infected during follow-up (17 in the intervention arm and 33 in the placebo group), which is consistent with a 49 percent reduction in the incidence of HIV with tenofovir (95% CI 9.6-72.2). However, the findings from this study were insufficient to reliably determine the degree of protection from PrEP in persons who inject drugs since the trial only used TDF

(rather than TDF-FTC, which is used for PrEP); in addition, the trial was unable to determine the degree of protection from sexual versus needle risk.

Unclear risk — PrEP is generally not needed for persons who consistently engage in low-risk behaviors (eg, consistent condom use when engaging in anal or vaginal intercourse, no mucosal exposure to genital secretions) and those who are in mutually monogamous relationships. However, on occasion, a patient may not endorse high-risk behaviors but still request PrEP.

In these circumstances, clinicians should try to better understand the person's reasons for wanting to use PrEP. We typically provide PrEP if we feel the potential risks and benefits of treatment are fully understood, and there are no underlying behavioral health issues that would impact their decision. Some individuals who engage in behaviors that put them at increased risk for HIV acquisition may not be comfortable disclosing information related to their sexual practices or substance use.

DETERMINING PREFERENCE FOR ORAL VERSUS INJECTABLE THERAPY

Oral and injectable PrEP are both effective in reducing HIV transmission. The decision to use one strategy over the other depends upon availability and patient preference.

When both options are available, we review the pros and cons of the different regimens to determine which modality will optimize adherence, as this equates to effectiveness (table 3).

For most patients, we suggest oral therapy with tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) pending additional real-world experience with long-acting cabotegravir (cabotegravir LA). Reasons include:

- TDF-FTC is the most studied regimen and is well tolerated. It can also be administered as event-driven therapy for persons who engage only in anal sex (unless they have concurrent chronic hepatitis B virus [HBV] infection).
- TDF-FTC is well suited for patients who want to start PrEP on the same day as their initial visit. Cabotegravir LA must be administered in the clinic, and this may require additional resources.

- Patients who acquire HIV while taking cabotegravir LA are at risk for developing resistance to integrase strand transfer inhibitors (INSTIs), which can limit HIV treatment options. By contrast, if a patient develops drug resistance while taking TDF-FTC, many of the preferred treatment options can still be used.

- Patients who take cabotegravir LA may still need to take an oral regimen (eg, TDF-FTC or tenofovir alafenamide-emtricitabine [TAF-FTC]) for a period of time after discontinuing injectable therapy to reduce the risk of developing INSTI resistance. Cabotegravir LA has a long half-life, and low levels can be detected for at least a year after it is discontinued. Without oral therapy, those who continue to engage in high-risk behaviors would be at increased risk for developing drug-resistant HIV when levels of cabotegravir are suboptimal. (See 'Persons with a positive HIV test' below.)

- Cabotegravir LA has not been fully evaluated in persons who inject drugs. In addition, there are only limited data in persons who are pregnant or who desire pregnancy. Although there was no increase in the incidence of adverse birth outcomes among those who became pregnant in the randomized trial that evaluated cabotegravir LA in cisgender women, the number of pregnancies was small [31].

By contrast, injectable therapy:

- Is preferable for those who do not like or may forget to take pills or are unable to store medications (eg, those with housing instability).

- May be reasonable for certain persons at risk for renal or bone disease since TDF-FTC should be avoided and TAF-FTC has not yet been fully studied in all populations (eg, cisgender women). However, clinicians must first assess if the patient is able to take TDF-FTC or TAF-FTC, use condoms consistently, or engage in abstinence for a finite period if cabotegravir LA is discontinued (ie, to provide protection while cabotegravir levels are waning). (See 'Discontinuing PrEP' below.)

The efficacy of cabotegravir LA administered every eight weeks was compared to TDF-FTC in two large, randomized trials [14,31]. Although the findings from these trials suggest that cabotegravir LA is superior to TDF-FTC, this may be due in large part to superior adherence. The trial that compared these agents in 4570 men who have sex with men (MSM) and transgender women was stopped early after a median follow-up of 1.4 years because there were fewer new infections in those who received cabotegravir LA (13 versus 39,

respectively; hazard ratio 34 95% CI 0.18 to 0.62) [14]. However, in this trial only two of the incident infections that occurred in persons taking oral therapy had appropriate TDF-FTC levels [32].

Similarly, in the study of 3224 cisgender women in sub-Saharan Africa, there were fewer infections in those who received cabotegravir LA compared with TDF-FTC (4 versus 36) [31]. In this trial, poor adherence to TDF-FTC (<2 doses per week) was observed in all but one of the incident infections that occurred in those taking oral therapy.

PRETREATMENT EVALUATION

Prior to initiating PrEP, it is important to confirm that the individual does not already have HIV. For those choosing an oral therapy regimen, the pretreatment evaluation includes an assessment of renal function, hepatitis B virus (HBV) status, and evidence of bone disease, as these factors can impact regimen selection [13].

Evaluation for all patients

HIV testing — All patients should have plasma HIV testing prior to receiving PrEP to be certain that they do not have undiagnosed HIV infection (algorithm 1) [13,33]. Although PrEP regimens contain antiretroviral agents, they are not sufficient for treatment, and unless additional agents are added, a person with HIV is at risk for developing drug-resistant virus. In the iPrEX trial, most cases of HIV drug resistance occurred in patients with undiagnosed acute HIV at baseline [15].

HIV testing should be obtained within the week before initiating PrEP [13]. The choice of test (antibody/antigen versus testing for HIV RNA) depends on whether the person is planning to initiate oral versus injectable therapy and if they are initiating PrEP for the first time. In both settings, rapid tests that use oral fluid should not be used because of lower sensitivity to detect early HIV infection.

- **Treatment-naïve initiating oral PrEP** – In treatment-naïve persons initiating oral PrEP, we typically use a laboratory-based fourth-generation antigen/antibody assay, although a point-of-care antigen/antibody test using a finger stick can also be used. A third-generation assay is acceptable if an antigen/antibody test is not available but only if the clinical history clearly suggests that acute HIV infection is unlikely. (See 'Symptoms of acute HIV' below.)

Most patients with a negative antigen/antibody test can initiate oral PrEP. However, additional HIV RNA testing should be performed prior to initiating PrEP in the following groups of patients (regardless of which HIV antibody screening test is used):

- Those who describe signs or symptoms suggestive of acute HIV infection within the previous four weeks. Patients with acute HIV infection may present with a viral syndrome (eg, lymphadenopathy, fever, malaise, and/or a maculopapular eruption) and have a detectable HIV RNA in the absence of an HIV antibody and antigen in early cases. In the iPrEx trial, 10 of the 110 participants who seroconverted during the study had a negative antibody test at baseline but were found to have a positive HIV RNA when testing was done on stored samples from enrollment [15]. Five of these patients had symptoms consistent with acute infection, underscoring the significance of eliciting a full history to determine the need for additional testing. (See "Acute and early HIV infection: Clinical manifestations and diagnosis".)

- Patients with an indeterminate antigen/antibody test. (See "Screening and diagnostic testing for HIV infection in adults", section on 'Management of indeterminate test results'.)

- Patients who report a known HIV exposure (eg, recent sexual exposure to a partner with documented untreated HIV infection) within four weeks of starting PrEP, regardless of symptoms.

In settings where access to prompt HIV RNA testing is not feasible, a fourth-generation HIV antigen/antibody test can be repeated.

- **Treatment-naïve initiating injectable therapy** – For treatment-naïve patients initiating injectable therapy, an antigen/antibody test can be used to determine eligibility for cabotegravir LA as long as the patient has no signs or symptoms of acute HIV or no known exposure to a person with uncontrolled HIV in the last four weeks.

  For those with a negative antigen/antibody test, a baseline HIV RNA should also be obtained. Although cabotegravir LA does not need to be withheld pending the results, it is important to use the most sensitive test possible in those initiating cabotegravir LA because of the long duration of drug exposure following injection. In the efficacy trials of cabotegravir LA, several patients were not diagnosed with acute HIV when they initiated PrEP, and there was a several-month delay in diagnosing their infection because of viral suppression from the medication [14]. In one of these patients, the prolonged exposure to monotherapy led to the selection of integrase strand transfer inhibitor (INSTI) resistance, constraining future treatment options.

- **Treatment-experienced** – For patients reinitiating PrEP, antigen/antibody and HIV RNA testing should be performed if the patient received oral PrEP within the last three months or long-acting injectable PrEP within the prior 12 months. In such patients, the sensitivity of antigen/antibody testing may be reduced. Additional considerations for patients receiving post-exposure prophylaxis (PEP) are discussed below. (See 'Persons receiving post-exposure prophylaxis' below and 'Discontinuing PrEP' below.)

Assessing barriers to PrEP adherence — Potential challenges to PrEP adherence (eg, depression, active substance use, stigma) should be identified and addressed in those initiating therapy [34]. There is a clear association between the efficacy of PrEP in decreasing HIV transmission and adherence [1,15,17,23,24,26,35-37]. In the 72-week open-label extension of the iPrEx trial that evaluated the efficacy of tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) for PrEP, there were 4.7 infections per 100 person-years if levels indicated that no drug was taken, 2.3 infections per 100 person-years if drug concentrations suggested less than two tablets were taken per week, and 0.6 infections per 100 person-years if levels indicated that two to three tablets were taken each week [17]. No infections occurred among those who were likely taking four or more tablets each week.

Adolescents appear to have particular challenges adhering to PrEP. The Adolescent Trials Network studied daily TDF-FTC PrEP in 78 patients 15 to 17 years of age [38]. TDF-FTC was well tolerated among those who took their medication; however, adherence was suboptimal for many of the youth (protective levels of tenofovir were found in approximately 50 percent at 12 weeks when they were being seen every four weeks but only in 22 percent at 48 weeks when visits were quarterly).

The relationship between adherence and PrEP efficacy has been found in all populations (eg, men who have sex with men [MSM], transgender and cisgender women, and heterosexual men). However, patients exclusively engaging in receptive anal sex may be able to miss an occasional dose and still be protected. Data suggest that men who engage in anal sex and take about four doses of TDF-FTC per week continue to have a high level of protection [17,39]. By contrast, data suggest that six or seven doses per week may be needed to protect patients who are exposed to HIV through vaginal intercourse [40,41]. These differences may be due to the high concentration of tenofovir achieved in rectal tissues, which is greater than that seen in cervicovaginal tissues [42,43].

STI testing — Patients who are being considered for PrEP should be screened for common bacterial sexually transmitted infections (STIs) (table 4). STI testing should be performed even in the absence of symptoms. (See "Screening for sexually transmitted infections".)

Screening for bacterial vaginosis and trichomonas is not routinely performed as part of the work-up before initiating PrEP since these infections have not had as strong an association with HIV. However, their presence suggests that recent condomless sex has occurred, and this should lead the clinician to ask about recent sexual behaviors and potential risks of partners.

Additional considerations

Persons considering oral therapy — Patients considering oral PrEP should be evaluated for conditions that could increase their risk of developing adverse outcomes (eg, reduced kidney function and osteoporosis with TDF-FTC, weight gain and dyslipidemia with tenofovir alafenamide-emtricitabine [TAF-FTC]) (table 5). (See 'Available oral agents' below.)

- **Renal function** – Serum creatinine should generally be measured prior to or at the time of initiating PrEP (table 5). Individuals with an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 are not candidates for TDF-FTC; those with an eGFR <30 mL/min/1.73 m^2 should not receive TDF-FTC or TAF-FTC. By contrast, cabotegravir LA can be used regardless of renal function and is the only option for patients with an eGFR <30 mL/min/1.73 m^2. (See 'Injectable therapy (cabotegravir LA)' below.)

  For patients with an eGFR ≥60 mL/min/1.73 m^2 but with risk factors for renal disease (eg, diabetes, hypertension, older age [eg, >40 years], nephrotoxic medications), it is reasonable to obtain a baseline urinalysis in those planning to initiate oral PrEP to assess for proteinuria and glycosuria. We find this information useful when monitoring such patients (table 6).

  In patients receiving TDF-FTC for PrEP, there is a low but increased risk of kidney injury. In a meta-analysis of 12 trials, oral PrEP with TDF-FTC or TDF alone was associated with an increased risk of kidney adverse events (relative risk, 1.43 [95% CI 1.18-1.75]; absolute risk difference, 0.56 percent [95% CI 0.09-1.04]); however, most were mild creatinine level elevations that did not require treatment discontinuation [9].

  Renal effects appear to be less frequent with TAF-FTC. In a randomized study of 5387 MSM or transgender women (the DISCOVER study), use of TAF-FTC as PrEP was associated with small but statistically significant differences in eGFR at 96 weeks when compared with TDF-FTC PrEP [16]. However, adverse clinical events were rare with both, with only 13 patients discontinuing treatment due to renal adverse events (5 TAF-FTC and 8 TDF-FTC); in addition, there were no differences in significant renal adverse outcomes

between the groups. More detailed information on the renal effects of the different agents is discussed below. (See 'Available oral agents' below.)

- **Hepatitis B infection** – Patients who are considering oral PrEP should be evaluated for the presence of hepatitis B virus (HBV) infection prior to initiating treatment. Tenofovir and emtricitabine are also used to treat chronic HBV, and such patients may experience clinically significant hepatitis flares if tenofovir is discontinued [13,33]. Although data from the iPrEx trial did not demonstrate a flare in the six hepatitis B surface antigen (HBsAg)-positive patients who discontinued TDF-FTC [44], additional data are needed to determine the exact risk.

  Testing for HBV infection should include HBsAg, hepatitis B core antibody (anti-HBc), and hepatitis B surface antibody (anti-HBs). (See "Hepatitis B virus: Screening and diagnosis in adults".)

  - **No evidence of immunity** – Patients without evidence of immunity (ie, anti-HBs-, anti-HBc-, HBsAg-negative) should be vaccinated against HBV since individuals who engage in high-risk sexual and drug use behaviors are at increased risk for acquiring hepatitis B. (See "Hepatitis B virus immunization in adults" and "Epidemiology, transmission, and prevention of hepatitis B virus infection", section on 'Transmission of HBV'.)

  - **Resolved HBV** – Patients with resolved HBV (anti-HBs- and anti-HBc-positive) do not require vaccination, and no additional monitoring is needed if oral PrEP is initiated.

  - **Chronic HBV** – For patients with evidence of chronic HBV infection (ie, HBsAg-positive), a tenofovir-containing PrEP regimen is well suited for those who require treatment of their HBV. Indications for treatment of chronic HBV are presented elsewhere. (See "Hepatitis B virus: Overview of management".)

    However, some persons with chronic HBV do not require treatment. For such patients, injectable therapy with cabotegravir LA may be preferred since cabotegravir is not active against HBV, and it can be safely discontinued if the patient no longer desires PrEP (ie, the patient would not be at risk for HBV flare). However, when cabotegravir LA is discontinued, patients must use condoms consistently or engage in abstinence for a finite period of time during the period when cabotegravir levels are waning. (See 'Discontinuing PrEP' below.)

- **Isolated core antibody** – Some patients may only be positive for anti-HBc. This could mean the patient has resolved (or is resolving) infection or low-level chronic infection; it could also be a false positive. In this setting, the approach to PrEP must be determined on a case-by-case basis. Additional information on the evaluation of patients with isolated anti-HBc is found elsewhere. (See "Hepatitis B virus: Screening and diagnosis in adults", section on 'Isolated anti-HBc'.)

- **Hepatitis C infection** – Persons who inject drugs and MSM who engage in condomless anal sex with multiple partners are at risk for hepatitis C virus (HCV) infection. Thus, such patients should be tested for HCV as part of the initial laboratory assessment. Patients who test positive should be referred for treatment. More detailed information on screening, including routine screening, is presented in a separate topic review. (See "Screening and diagnosis of chronic hepatitis C virus infection".)

  It is important to note that certain agents used for the treatment of HCV (ledipasvir-sofosbuvir) may increase the level of TDF, and patients who are taking these agents should be monitored for TDF toxicity [13].

- **Osteoporosis** – Information should be obtained regarding a history of (or risk factors for) osteoporosis, since TDF has been associated with reductions in bone density. Bone loss appears to be greatest during the first six months and then stabilizes after that [24,45]. By contrast, TAF-FTC was not associated with loss of bone mineral density when used as PrEP in a large clinical trial [46]. A more detailed discussion of regimen selection in patients with osteoporosis is found below. (See 'Regimen selection' below.)

  For patients considering oral PrEP with TDF-FTC, the need for routine bone density screening prior to initiating treatment is unclear. We typically obtain a dual-energy x-ray absorptiometry (DXA) scan only in patients who have a history of osteoporosis if testing within the prior two years is not available as well as in those who are at high risk for osteoporosis. For those with or at high risk for osteoporosis, we obtain a repeat DXA scan after one to two years of PrEP use with TDF-FTC. (See "Evaluation and treatment of premenopausal osteoporosis", section on 'Screening' and "Clinical manifestations, diagnosis, and evaluation of osteoporosis in men", section on 'Patient selection for BMD measurement'.)

  More detailed information on the risk of osteoporosis in patients receiving tenofovir is found below. (See 'Available oral agents' below.)

- **Lipid testing** – If TAF-FTC is being considered for PrEP, patients should have a baseline cholesterol panel performed. In clinical trials, higher rates of triglyceride elevation and weight gain were seen among men taking TAF-FTC compared with those taking TDF-FTC, although these increases were only modest [13]. In one study, there was a median of 0.05 mmol/L increase in triglycerides at 48 weeks in those who received TAF-FTC compared with no change from baseline in the TDF-FTC arm [16]. In addition, for weight, there was a 1.1 kg increase from baseline in the TAF-FTC arm versus 0.1 kg loss from baseline in the TDF-FTC arm.

Persons of child bearing potential — Persons of childbearing potential should have a pregnancy test prior to initiating PrEP. For those who are pregnant, the risk of acquiring HIV must be weighed against the risk of using antiviral medications during pregnancy and the limited data on the efficacy of PrEP during pregnancy.

Although the oral agents used for PrEP (TDF, TAF, and emtricitabine) are felt to be safe for use in pregnancy, only TDF-FTC is recommended [47]. Oral TAF-FTC has not yet been demonstrated to be effective for HIV prevention in people whose risk factor is receptive vaginal exposure. (See 'Persons who engage in vaginal sex' below.)

However, there are some concerns about fetal bone development associated with the use of TDF. In a post-hoc analysis of 288 pregnancies among African women enrolled in a PrEP efficacy trial, there were similar rates of pregnancy loss in those assigned TDF (with or without emtricitabine) and placebo (34 versus 32 percent) [48]. Although rates of preterm birth, congenital anomalies, and postnatal growth throughout the first year were also similar, PrEP was discontinued when pregnancy was detected; therefore, the effect of taking TDF with or without emtricitabine during the later stages of pregnancy was not assessed.

The decision to use cabotegravir must be determined on a case-by-case basis given current limited safety data. Studies are underway to determine the safety profile of injectable cabotegravir during pregnancy.

A more detailed discussion of the risks of these agents during pregnancy is found elsewhere. (See "Safety and dosing of antiretroviral medications in pregnancy", section on 'Tenofovir' and "Safety and dosing of antiretroviral medications in pregnancy", section on 'Cabotegravir'.)

Persons receiving post-exposure prophylaxis — Some patients will receive a three-drug antiretroviral regimen after a potential sexual or percutaneous exposure to HIV to reduce the risk of HIV transmission. This is referred to as post-exposure prophylaxis (PEP). (See

"Management of nonoccupational exposures to HIV and hepatitis B and C in adults", section on 'HIV post-exposure management'.)

Patients who receive PEP and are at risk for repeat exposure should be offered PrEP when they complete their PEP regimen. For those who decide to transition from PEP to PrEP, a repeat HIV test (antigen/antibody test) and HIV RNA test should be performed at the end of the 28-day course.

- The patient can transition from their PEP regimen to PrEP without interruption if the HIV antigen/antibody and HIV RNA tests are negative and there is no concern for acute HIV. (See 'Pretreatment evaluation' above.)
- By contrast, PEP should be continued pending further evaluation (eg, repeat plasma RNA screening) if there is still any suspicion for acute HIV infection (eg, discordant HIV test results, symptoms of acute infection). (See "Acute and early HIV infection: Clinical manifestations and diagnosis".)

The approach to regimen selection in these patients is the same as for others. (See 'Determining preference for oral versus injectable therapy' above and 'Regimen selection' below.)

ORAL THERAPY REGIMENS

Both oral and injectable regimens are available for PrEP. Factors influencing the decision to use oral versus injectable therapy are summarized in the table (table 3) and discussed in detail above. (See 'Determining preference for oral versus injectable therapy' above.)

Available oral agents — The combination of tenofovir-based antiretrovirals with emtricitabine has proven to be effective in reducing new HIV infections when used for PrEP. There are two formulations of tenofovir, tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF), and each is available as a single coformulated tablet with emtricitabine. In 2022, long-acting cabotegravir (cabotegravir LA), an injectable agent, was also approved for use as PrEP. (See 'Injectable therapy (cabotegravir LA)' below.)

- Tenofovir disoproxil fumarate-emtricitabine **(TDF-FTC)** – For PrEP, once-daily TDF-FTC (tenofovir disoproxil fumarate 300 mg-emtricitabine 200 mg) is the most widely studied regimen among various populations, and if taken as prescribed, can reduce the

risk of sexual HIV transmission by nearly 100 percent [17,49-51]. TDF-FTC has been studied in many different populations, as described above. (See 'Indications based upon risk' above.)

Clinical trials have described only mild adverse effects (eg, nausea or diarrhea in a minority of patients) compared with placebo [15], and these usually resolve during the first few weeks.

However, there is potential for mild to moderate renal and bone toxicity with long-term use.

- **Reduced kidney function** – Although TDF-FTC has been associated with renal toxicity, the risk of kidney injury is low in patients without HIV [15,23-25,52-54]. In a meta-analysis that included data from 10 randomized trials, there was an increased risk of creatinine elevations in patients who received TDF-based PrEP compared with placebo (odds ratio 1.36, 95% CI 1.09-1.71) [55]. However, of the 352 patients who experienced creatinine elevations, only 23 had increases that were greater than 1.3 times the upper limit of normal. In a separate meta-analysis that included data from 13 randomized trials, there was no difference in serious, grade 3 creatinine elevations (>1.8 to <3.5 times the upper limit of normal or an increase to 1.5 to <2.0 times the participant's baseline) among participants receiving TDF-based PrEP versus placebo or no treatment (difference 0 percent, 95% CI 0-0) [56]. However, in one report, a patient who received TDF-FTC developed Fanconi syndrome while taking concurrent nephrotoxic medications [57]. (See "Etiology and diagnosis of distal (type 1) and proximal (type 2) renal tubular acidosis".)

  Certain risk factors have been associated with declines in renal function, such as baseline estimated glomerular filtration rate (eGFR) <90 mL/min/1.73 m^2 and age greater than 40 [58]. Higher tenofovir concentrations have also been associated with reductions in kidney function; however, there is insufficient evidence to incorporate therapeutic drug level monitoring into routine care.

- **Bone loss** – In clinical trials, adults without HIV who were assigned to TDF-FTC had greater declines in z-scores at the hip, lumbar spine, and forearm compared with those taking placebo [24,45,59]. In an analysis of seven trials, there was a trend towards an increase in the rate of fractures, although the difference was not statistically different (relative rate, 1.23; 95% CI, 0.97 to 1.56) [59].

Bone loss appears to be greatest when therapy is started. In the iPrEx trial, 247 patients who received TDF-FTC and 251 who received placebo were evaluated with dual-energy x-ray absorptiometry (DXA) scans every six months [45]. After 24 weeks, modest but significant declines in bone mineral density were seen in those who received TDF-FTC (spine: net difference -0.91 percent [95% CI -1.44 to -0.38]; hip: -0.61 percent [95% CI, -0.96 to -0.27]); however, there were only small further decreases in bone mineral density to week 96. A subsequent study found that bone loss normalized in most patients approximately six months after PrEP was discontinued [60].

In adolescent men who have sex with men (MSM), the bone loss seen with TDF may pose additional risks that are not seen in adults [38,61-64]. In adolescents, bone loss seems to occur before peak bone mass is attained, and the full recovery of age-adjusted bone mineral density that is seen in adult MSM who discontinue PrEP may not occur in young MSM. In one study that included 200 MSM ages 18 to 22 years old, modest decreases in hip, spine, and whole body bone mineral density z-scores occurred after 24 weeks of TDF-FTC, with further decreases only in hip bone mineral density z-scores after 48 weeks [64]. In a pooled analyses of 91 MSM who had DXA scans performed 48 weeks after discontinuing TDF-FTC, spine and whole body bone mineral density z-scores remained below baseline, with larger declines among participants 15 to 19 years of age [63].

There are no proven strategies to attenuate bone loss in patients taking TDF-FTC. Vitamin D3 plus calcium supplementation was found to mitigate bone loss in patients with HIV taking a TDF-based antiretroviral therapy (ART) regimen [65]. Although there are no data on the use of vitamin D to attenuate PrEP-related bone loss, measures to maintain adequate vitamin D levels could theoretically be helpful [66] and are being evaluated. (See "Overview of vitamin D".)

- Tenofovir alafenamide-emtricitabine **(TAF-FTC)** – TAF has less potential bone and renal toxicity compared with TDF and, in the United States, TAF-FTC is approved for PrEP (tenofovir alafenamide 25 mg-emtricitabine 200 mg) [67]. However, TAF-FTC should generally be avoided in those whose main risk for HIV is receptive vaginal sex or injection drug use since efficacy data are not yet available in these populations.

  In a multinational efficacy study comparing once-daily TAF-FTC with TDF-FTC in 5387 at-risk MSM and transgender women, TAF-FTC was equivalent to TDF-FTC in preventing HIV infection (HIV incidence of 0.16 per 100 person-years versus 0.34 per 100 person-years, respectively) [16]. TAF-FTC had better bone and renal biomarker safety outcomes but was associated with mild weight gain and dyslipidemia, although the magnitude of the differences was small for all of these outcomes. In an open-label extension of this

study, 2080 MSM who continued TAF-FTC and 2128 MSM who were switched from TDF-FTC to TAF-FTC were followed for an additional 48 weeks; switching to TAF-FTC was associated with small increases in renal function and bone mineral density but also modest increases in weight and lipid parameters [68].

Regimen selection — The choice of regimen and frequency of administration depends in part upon the specific population.

Men who have sex with men

Preferred regimen — For most MSM initiating oral PrEP, we suggest once daily TDF-FTC since there is extensive experience with this agent, it is effective, and it is well tolerated (table 3). This includes transgender men who exclusively engage in anal sex. (See 'Sexual risk' above and 'Available oral agents' above.)

However, TDF-FTC should generally be avoided in those with or at risk for bone or kidney disease. The approach to regimen selection in these patients is discussed below. (See 'Patients with/at risk for kidney or bone disease' below.)

When initiating therapy in those who engage in anal sex, we encourage patients to use condoms for seven days to allow for drug concentrations that protect against HIV; this recommendation is based upon pharmacokinetic data with TDF-FTC [42,43,69]. Some experts believe that administering a double dose of TDF-FTC when starting PrEP may accelerate the time to protective drug levels [70]. While we generally agree with this approach, the decision to use a double dose should be determined on a case-by-case basis since the double dose may be associated with an increase in initial side effects.

If possible, we administer oral PrEP the same day as the initial visit. Studies have found that same-day PrEP can improve early retention in PrEP care [71,72]. Testing for HIV and hepatitis B virus (HBV) should ideally be performed prior to the visit. However, if that is not possible, testing can be done that day since the harms of short-term PrEP are likely to be minimal, even if someone has undiagnosed renal disease, HBV, or HIV. (See 'Pretreatment evaluation' above.)

When prescribing PrEP, we typically dispense as a 90-day supply, renewable only after HIV testing [13]. Prescribing a limited quantity of medication increases the likelihood that a patient will follow up for ongoing safety monitoring and adherence counseling. However, when a patient cannot come in for an office visit, but the provider has reason to anticipate stable medication adherence, prescribing

extra medication without a recent HIV antibody test may be preferable to reduce the likelihood of a lapse in PrEP. (See 'Patient monitoring' below.)

Alternative regimens — Alternative oral options include once daily TAF-FTC and event-driven/on-demand TDF-FTC (table 3).

- **TAF-FTC** – Once daily TAF-FTC is a reasonable alternative for cisgender MSM who are at risk for kidney or bone disease and those who desire a smaller pill size. However, it is also associated with mild but greater weight gain and slight changes in lipid parameters that are less favorable than TDF-FTC [16,68]. (See 'Available oral agents' above and 'Patients with/at risk for kidney or bone disease' below.)

  There is no formal guidance regarding timing of protection with TAF-FTC, so we encourage patients to use condoms for seven days to allow for drug concentrations that protect against HIV, similar to TDF-FTC, as discussed above.

  Guidelines do not specifically address the use of TAF-FTC in transgender MSM [13,29,73]. However, TAF-FTC has not been studied in this population.

- **Event-driven TDF-FTC** – Some patients prefer event-driven (also referred to as on-demand) dosing rather than daily therapy. Event-driven therapy is reasonable for cisgender MSM who are taking TDF-FTC and can reliably predict when they will have condomless sex. In addition, it is also reasonable for certain transgender persons who engage exclusively in anal sex. (See 'Transgender persons' below.)

  We do not use event-driven PrEP in patients with chronic HBV infection since discontinuing TDF-FTC may be associated with a flare of their hepatitis. This approach is consistent with recommendations from the United States Centers for Disease Control and Prevention (CDC); however other guidelines differ [74]. There are no data evaluating event-driven dosing in those taking TAF-FTC.

  For those who are eligible for on-demand PrEP, "2-1-1" dosing is as follows:

  - A loading dose of TDF-FTC (two tablets) is taken 2 to 24 hours prior to sexual activity (closer to 24 hours is preferred). For patients who initiate on-demand/event-driven therapy more than once within a week, the second loading dose should be reduced to one tablet instead of two [75].

- One tablet is then taken 24 hours after the loading dose. Once daily TDF-FTC should be continued if the patient continues to be sexually active.

- The patient should continue taking PrEP for two more days after sexual activity has stopped.

As an example, if a patient wants to use event-driven PrEP for a single event, the person should take two pills 2 to 24 hours prior to sex, one pill 24 hours after sex, and a third pill 48 hours after sex.

The use of event-driven dosing was evaluated in a randomized trial of MSM who engage in condomless anal sex (IPERGAY) [75,76]. Among the 400 men who were enrolled, 16 new infections occurred, 14 in those taking placebo, and 2 in those receiving on-demand TDF-FTC, consistent with an 86 percent reduction in HIV transmission (95% CI 40-98). In a post-hoc analysis, event-driven PrEP remained effective among the 269 patients who took ≤15 pills/month (median of 9.5) [76]. In an observational study in France, largely comprised of MSM, only three HIV infections were reported among approximately 1500 study participants taking event-driven PrEP, and all had discontinued PrEP several weeks prior to infection [77-79].

Although this dosing strategy is not approved for use by the US Food and Drug Administration (FDA; which has only approved oral PrEP for daily use), the International Antiviral Society USA and the World Health Organization (WHO) have endorsed 2-1-1 PrEP [70,74,80], and the CDC has stated that event-driven PrEP can be considered as an alternative to daily use [13].

Patients with/at risk for kidney or bone disease

- **Patients with or at risk for kidney disease** – For patients with reduced kidney function and an eGFR <30 mL/min/1.73 m^2 neither TDF-FTC nor TAF-FTC should be used. For such patients, injectable therapy can be used; however, patients should be informed that they will need to use condoms consistently or engage in abstinence for a finite period if cabotegravir LA is discontinued, and tenofovir should still be avoided. (See 'Injectable therapy (cabotegravir LA)' below.)

  TAF-FTC can be used for those with moderately reduced kidney function (eGFR between 30 and 60 mL/min/1.73 m^2 (calculator 1)) since it has been safely administered to those with an eGFR >30 mL/min/1.73 m^2. By contrast, TDF has been associated with acute and chronic kidney disease in patients with HIV, and the safety of this agent has not been examined in patients without HIV who have an eGFR <60 mL/min/1.73 m^2.

For patients with an eGFR >60 mL/min/1.73 m^2 but with risk factors for renal disease, we try to balance the different risks of TDF and TAF. As an example, in patients who also have pre-existing obesity or dyslipidemia, we favor a trial of TDF-FTC with close monitoring for decreased renal function since TAF-FTC has been associated with mild but greater weight gain and slight changes in lipid parameters compared with TDF [16,68].

- **Patients with or at risk for bone disease** – TAF-FTC is preferred for those with reduced bone density. In the DISCOVER trial, a large trial comparing TAF-FTC with TDF-FTC for PrEP, TDF-FTC but not TAF-FTC was associated with bone loss [16]. (See 'Available oral agents' above.)

  For this reason, some providers may prefer to administer TAF-FTC to certain patients without bone disease, particularly to adolescents, since such patients appear to be at higher risk for loss of bone mineral density during the growth phase of bone development. However, we prefer TDF-FTC for most adolescents, since TAF-FTC has not been studied in patients <18 years of age.

Consideration for other populations

Transgender persons — The approach to regimen selection in transgender persons depends upon the type of sexual risk (eg, anal versus vaginal sex). As an example, preferred regimens for transgender women are similar to cisgender MSM since transgender women have been included in clinical trials evaluating once daily TDF-FTC and TAF-FTC. (See 'Preferred regimen' above.)

However, we do not routinely offer event-driven dosing since the data on event-driven PrEP in transgender persons are limited. For those who desire event-driven dosing, we discuss the risks and benefits and determine the best approach on a case-by-case basis. In general, we avoid event-driven dosing for those using exogenous estrogens because the drug interactions have not been fully studied and some data suggest that estrogens can lower tenofovir levels [81]. By contrast, for those who are not taking gender-affirming hormones, we feel event-driven dosing is reasonable for those who engage in receptive anal intercourse or insertive intercourse (penile-anal or penile-vaginal) since the trials in MSM can likely be extrapolated to this population. However, there are no data yet about the efficacy of on-demand PrEP for individuals exposed vaginally to HIV. More detailed information on event-driven dosing is found above. (See 'Alternative regimens' above.)

Persons who inject drugs — For persons whose main risk for HIV transmission is injection drug use, we suggest once daily TDF-FTC, as this is the only regimen that has been studied in the population. (See 'Injection drug use' above.)

There are no data on time to protection in persons who inject drugs. As such, we counsel patients to use additional HIV prevention strategies for several weeks after staring PrEP, if possible.

For persons with kidney or bone disease, our approach depends upon the presence of other risk factors for HIV acquisition, since there are no studies evaluating the use of TAF-FTC for PrEP in patients whose sole risk factor is injection drug use.

As an example, in patients with moderately reduced kidney function, we would administer TAF-FTC to MSM and transgender women who endorse sexual risk in addition to injection risk. However, for those who endorse vaginal sex as a risk factor for HIV acquisition in addition to injection risk, the decision must be individualized since the efficacy of TAF-FTC for PrEP has not yet been fully evaluated in injection drug users or those who engage primarily in vaginal sex.

In patients who only have injection drug use as their risk factor for HIV transmission, we think TAF-FTC is a reasonable alternative to TDF-FTC for those with an eGFR between 30 and 60 mL/min/1.73 m^2 (calculator 1) and those with osteoporosis. TAF achieves higher peripheral blood mononuclear cell concentrations than TDF and therefore is likely to be as effective for PrEP in the setting of injection drug use. For those with osteoporosis, we base the decision to use TAF versus TDF on the severity of bone disease, weighing the risk of potential bone loss with the uncertain efficacy of TAF-FTC.

All persons who inject drugs should receive information on other risk reduction strategies in addition to PrEP.

Persons who engage in vaginal sex

- **General approach** – For persons whose main risk for HIV transmission is vaginal sex (also referred to as frontal sex), we suggest once daily TDF-FTC, as this is the only oral regimen that has been studied in this population. Clinical trials of cisgender women receiving PrEP are described above. (See 'Sexual risk' above.)

  For such persons, it is unclear when protective levels of tenofovir are achieved, and there are differences in guideline recommendations based on the interpretation of the pharmacology. The WHO suggests that protective levels are achieved after

one week of daily dosing [41,82], while the CDC indicates that is prudent to wait 21 days to ensure adequate tissue concentrations [13]. While we generally adhere to CDC guidelines, we are aware that some patients may not be willing to wait three weeks, and those patients should be counseled about the importance of medication adherence and careful monitoring.

Unlike other patient groups, TAF-FTC should generally be avoided because efficacy studies have not yet been completed in this population. We feel the results from studies of MSM and transgender women cannot be generalized to those who engage in vaginal sex given the uncertainty of the clinical significance of mucosal concentrations of TAF in vaginal fluids. Clinical trials evaluating the efficacy of TAF-FTC PrEP for cisgender women are underway [83,84].

Similarly, there are insufficient data to recommend event-driven/on-demand dosing in those who engage in vaginal sex, since pharmacologic studies support the need for routine daily adherence in this patient group [81,85].

- **Considerations for those with bone or kidney disease** – If a person who engages in vaginal sex has bone or kidney disease, our approach to using oral PrEP depends on the person's risk for HIV and why TDF should be avoided. As examples:

  - For those who have risk factors for renal disease but still have an eGFR ≥60 mL/min/1.73 m^2, we suggest a trial of TDF-FTC with follow-up monitoring of renal function.

  - For those with or at risk of osteoporosis, we determine whether to initiate PrEP with TDF-FTC by weighing the risk of HIV with the potential risk of exacerbating bone disease. Cabotegravir LA can also be considered. (See 'Determining preference for oral versus injectable therapy' above.)

  - For persons who have renal impairment (eGFR is <60 mL/min/1.73 m^2), injectable therapy with cabotegravir LA may be the best option since TDF-FTC should not be used and TAF-FTC should generally be avoided as it has not been fully studied in this population.

  If TDF-FTC should be avoided and cabotegravir is not available, clinicians can discuss the risks and benefits of using TAF-FTC given the limited safety and efficacy data with the risks of acquiring HIV with no PrEP. However, even TAF-FTC should be avoided in those with severely reduced kidney function (eGFR is <30 mL/min/1.73 m^2).

If cabotegravir is used for patients who cannot take oral PrEP, patients must use condoms consistently or engage in abstinence for a finite period if cabotegravir LA is discontinued. (See 'Injectable therapy (cabotegravir LA)' below and 'Discontinuing PrEP' below.)

INJECTABLE THERAPY (CABOTEGRAVIR LA)

Long-acting cabotegravir (cabotegravir LA), an injectable integrase inhibitor that is administered every eight weeks, was approved for use as PrEP in 2022. This agent is approved for use in adults and adolescents weighing at least 35 kg.

Cabotegravir LA is administered as 600 mg (3 mL) injected into the gluteal muscle monthly for two months and then every two months thereafter. For those who are concerned about side effects of long-acting injectable cabotegravir, oral cabotegravir (30 mg once daily) can be administered for a four-week lead-in period prior to initiating injections.

When administering cabotegravir LA, a 2-inch needle should be used for those with a body-mass index (BMI) of ≥30; for those with a BMI <30, a 1.5-inch needle can be used.

For the first two to three injections, patients may choose to take an agent such as acetaminophen or ibuprofen a couple of hours before or soon after the injection. This can be continued for one to two days if they continue to have discomfort at the injection site. Patients can also apply a warm compress or heating pad to the injection site for 15 to 20 minutes after the injection.

It is unclear when patients are maximally protected after initiating cabotegravir (oral or injectable formulations). We advise patients to avoid behaviors that would put them at increased risk for HIV for at least a week, but this can be extended up to one month in those who want to take a more conservative approach pending additional data.

Patients should be educated about the long half-life when discontinuing cabotegravir LA and the need to receive an oral agent (tenofovir disoproxil fumarate-emtricitabine [TDF-FTC] or tenofovir alafenamide-emtricitabine [TAF-FTC]) for a period of time after stopping treatment to reduce the risk of developing a drug-resistant strain if HIV infection is acquired during that time. Those who cannot take tenofovir should use condoms consistently or engage in abstinence during this period. The approach to discontinuing treatment is discussed below. (See 'Discontinuing PrEP' below.)

In the clinical trial that compared cabotegravir LA with TDF-FTC, the safety of the two agents was similar, except for injection site reactions leading to discontinuation (2.4 percent versus none) [14,86].

More detailed information on efficacy of cabotegravir LA in men who have sex with men (MSM), transgender women, and cisgender heterosexual women is described above. (See 'Determining preference for oral versus injectable therapy' above.)

The use of cabotegravir LA in adolescent MSM in the United States and cisgender adolescent girls in Africa is being evaluated [87].

PATIENT COUNSELING

Medication adherence — Patients should be counseled regarding the importance of taking the medication as prescribed in order to achieve adequate drug concentrations. There is a clear association between adherence to the drug regimen and the efficacy of PrEP in decreasing HIV transmission [1,15,17,23,24,26,35-37]. (See 'Assessing barriers to PrEP adherence' above.)

In addition to educating patients about the importance of adherence, adherence counseling includes reviewing their medication dose and schedule and identifying reminders and devices (eg, alarms, calendars) to help minimize structural barriers.

Some patients may discontinue PrEP temporarily. It is important that clinicians educate patients about the risks of stopping therapy, such as the risk of new HIV infection and the risk of developing drug resistance [88,89]. (See 'Persons with a positive HIV test' below.)

Reducing risk of other infections — Risk reduction counseling involves providing patients with information on the benefits of condom use and/or reducing substance use in addition to using PrEP. Clinicians should also help patients identify feasible steps towards risk reduction.

- **Condom use** – Patients should be counseled to use condoms whenever possible (in addition to using PrEP) to reduce the risk of acquiring other sexually transmitted infections (STIs) and hepatitis B and C virus [90-92]. In addition, rare cases of HIV transmission have occurred, even in the setting of appropriate PrEP medication adherence [3,4,93]. (See 'Persons with a positive HIV test' below.)

However, patients often engage in condomless sex because of difficulty adhering to condom use (eg, due to substance use or depression) or in negotiating condom use with partners or because of their desire for improved sexual pleasure and intimacy. In clinical trials and observational studies of men who have sex with men (MSM), approximately 30 to 50 percent of the men who received PrEP were diagnosed with a bacterial STI [15,49,50,94-97]. Although some providers may be concerned that the use of PrEP is associated with high rates of STIs, we continue PrEP in such patients since the risk of HIV transmission remains low despite the large number of STIs [49,50,94,98]. As an example, in one study that followed 657 men receiving PrEP, no new HIV infections occurred over approximately seven months of follow-up, even though approximately 30 percent were diagnosed with at least one STI [49].

- **Safe injection practices** – Patients who inject drugs should be educated about safe injection practices and should also be given a referral to treatment for substance use disorders. Such patients remain at risk for acquiring other viral and bacterial infections (eg, hepatitis C virus [HCV] [90,91] and *Staphylococcus aureus*) that can be transmitted through unsafe injection practices. Those without evidence of immunity to hepatitis B virus (HBV) should be immunized. (See "Hepatitis B virus immunization in adults".)

  It is also important to educate patients about pharmacologic and behavioral treatments to reduce both injection and noninjection drug use. (See "Opioid use disorder: Pharmacologic management" and "Opioid use disorder: Psychosocial management".)

Symptoms of acute HIV — Patients should be educated about the signs and symptoms of acute HIV infection (eg, lymphadenopathy, fever, malaise, and/or a maculopapular eruption). They should seek medical attention if such symptoms develop so they can be tested for HIV and initiate appropriate therapy if seroconversion occurred. (See "Acute and early HIV infection: Clinical manifestations and diagnosis".)

MANAGEMENT ON THERAPY

Patient monitoring — Patients receiving PrEP should have regular follow-up with a medical provider. Patients receiving PrEP should be monitored on a regular basis for evidence of acute HIV, sexually transmitted infections (STIs), and toxicity to the regimen. Providers should also monitor adherence. In one study, there was a notable drop in adherence over three years, with the estimated adherence of daily PrEP dropping from approximately 96 to 74 percent [14].

- **Patients receiving oral PrEP** – We typically see patients receiving oral PrEP one month and three months after starting treatment and then follow them every three months thereafter. Quarterly screening for bacterial STIs is an important part of routine monitoring. The approach to monitoring is described in the table (table 6).

- **Patients receiving** cabotegravir **LA** – Patients receiving cabotegravir LA are followed every month for two months and every other month thereafter.

  HIV testing should be performed at these visits. The United States Centers for Disease Control and Prevention (CDC) recommends that HIV RNA testing be performed in addition to an antigen/antibody test to monitor for HIV [13]. However, this may not always be feasible (eg, due to cost or availability). In these settings, we feel an antigen/antibody test alone is reasonable for those who have not missed doses and are without evidence of acute HIV infection.

  In addition to HIV testing, for those receiving cabotegravir LA, routine STI testing should be performed in men who have sex with men (MSM) and transgender women every four months and heterosexually active men and women every six months.

The management of patients with a positive HIV test is discussed separately. (See 'Persons with a positive HIV test' below.)

Additional follow-up is also necessary for patients who have been exposed to and/or have symptoms of an STI (table 4) as well as those with evidence of possible adverse reactions to treatment (eg, reduced kidney function in patients receiving tenofovir disoproxil fumarate-emtricitabine [TDF-FTC]). (See 'Patients who develop renal abnormalities' below.)

Clinicians should evaluate the need to continue PrEP (ie, ongoing risk behaviors) at least annually. The approach to discontinuing treatment is discussed below. (See 'Discontinuing PrEP' below.)

Patients who develop renal abnormalities — The approach to patients who develop evidence of renal abnormalities on oral PrEP depends upon the specific laboratory findings (eg, elevated creatinine, new proteinuria or glycosuria).

For patients using TDF-FTC, we discontinue TDF-FTC if:

- The estimated glomerular filtration rate (eGFR) falls below 60 mL/min/1.73 m^2 (calculator 1). Most creatinine elevations resolve with treatment discontinuation [15,99,100].

For many patients with an eGFR >30 mL/min/1.73 m^2, it is reasonable to replace TDF-FTC with tenofovir alafenamide-emtricitabine (TAF-FTC), which has been associated with fewer renal abnormalities when used as PrEP and has been approved for this indication [16]. Alternatively, cabotegravir LA can be used. (See 'Injectable therapy (cabotegravir LA)' above.)

- There is evidence of moderate or severe proximal tubular dysfunction or Fanconi syndrome (eg, hypophosphatemia due to hyperphosphaturia, renal glycosuria, hypouricemia, and/or aminoaciduria). (See "Etiology and diagnosis of distal (type 1) and proximal (type 2) renal tubular acidosis", section on 'Proximal (type 2) RTA'.)

  In such patients, TAF-FTC shou**ld not** be used, and cabotegravir LA is the only option for PrEP. However, patients must use condoms consistently or engage in abstinence for a finite period if cabotegravir LA is discontinued. (See 'Injectable therapy (cabotegravir LA)' above.)

For patients whose eGFR declines significantly on TDF-FTC (eg, a 20 percent decrease) but remains above 60 mL/min/1.73 m^2 and for those who develop new mild proteinuria without additional evidence of proximal tube dysfunction, switching to an alternative agent should be considered. These patients should also be evaluated for other causes of renal disease, in consultation with a specialist if possible. (See "Diagnostic approach to adult patients with subacute kidney injury in an outpatient setting" and "Urinalysis in the diagnosis of kidney disease".)

Persons who become pregnant — For persons who become pregnant, the risk of acquiring HIV must be weighed against the risk of using antiviral medications during pregnancy and the limited, albeit increasing, data on the efficacy of PrEP during pregnancy. As an example, the CDC states that cabotegravir LA for PrEP may be continued in people who become pregnant while receiving injections, although TDF-FTC is preferred given the more robust safety and efficacy data [47].

More detailed discussions of the use of antiretroviral agents in pregnancy are found elsewhere. (See "Safety and dosing of antiretroviral medications in pregnancy".)

Persons exposed to multidrug-resistant HIV — If a patient has a known exposure to multidrug-resistant HIV, tenofovir-emtricitabine, and potentially cabotegravir LA, may not be effective. In this setting, a post-exposure prophylaxis (PEP) regimen should be initiated that

contains antiretrovirals active against the resistant virus. Such patients should be managed in consultation with an HIV specialist. (See "Management of nonoccupational exposures to HIV and hepatitis B and C in adults".)

Persons with a positive HIV test — Patients should be routinely monitored for new HIV infection while receiving PrEP. The approach to HIV monitoring depends upon the regimen, as described in the table (table 6).

- **Patients on oral PrEP** – For patients receiving oral PrEP, an HIV viral load test and genotype test should be obtained if an antigen/antibody is positive, even if the reflex differentiation assay is negative or indeterminate. Pending these results, our approach to treatment depends upon the likelihood that the patient has acquired HIV.

  If new infection seems unlikely (eg, no recent exposures, optimal adherence), it is reasonable to continue the PrEP regimen while awaiting the results of the viral load testing.

  By contrast, if new infection seems likely (patient with poor adherence or evidence of acute HIV), we continue TDF-FTC or TAF-FTC **and** add a third agent with a high barrier to resistance such as dolutegravir, bictegravir, or boosted darunavir while awaiting viral load testing [101]. We **do not** use a non-nucleoside reverse transcriptase inhibitor as the third agent since transmitted drug resistance is more common with this class. (See "Selecting antiretroviral regimens for treatment-naïve persons with HIV-1: General approach", section on 'Patients with transmitted drug resistance'.)

  The subsequent approach to treatment then depends upon the results of the viral load testing:

  - If testing is consistent with acute HIV infection (positive antigen/antibody test and high viral load), we continue the HIV treatment regimen or add an integrase inhibitor with a high barrier to resistance, if not started already. Most patients will suppress their HIV viral load on the expanded regimen, even if there is resistance to tenofovir or emtricitabine (specifically, the M184V mutation).

    However, if the patient is found to have multidrug resistance (eg, K65R) on genotype testing, the regimen may need to be modified. Such patients should be managed with a provider experienced in managing drug-resistant virus. (See "Selecting an antiretroviral regimen for treatment-experienced patients with HIV who are failing therapy".)

- On rare occasion, the testing results may be discordant (positive antigen/antibody test with a negative or very low HIV viral load [eg, <100 copies/mL]). In this setting, the treatment approach is less clear, and such patients should be managed in consultation with an HIV specialist.

  Obtaining a thorough history of recent risk behaviors and medication adherence patterns will help to inform the approach to clinical management. One option is to continue HIV treatment for four weeks (similar to PEP) and then discontinue treatment with all antiretroviral agents and repeat HIV testing in four weeks (or sooner if the patient reports acute retroviral symptoms). However, if the index of suspicion for acute infection is high, an alternative approach would be to continue treatment but to do more sensitive testing for occult HIV (eg, HIV Proviral DNA, or ultrasensitive HIV RNA NAAT screening).

Among patients who acquire HIV while receiving oral PrEP, most are unlikely to have drug-resistant virus [15,23-25]. In a meta-analysis that evaluated drug resistance in six clinical trials, drug resistance was identified in 6 of the 533 patients who acquired HIV after enrollment [8].

However, in some patients, drug resistance occurs because they were infected with a drug-resistant strain. In two case reports, a patient became infected with HIV that contained drug resistance mutations for several classes of antiretroviral agents, including tenofovir and emtricitabine [2,3]. Transmission occurred despite tenofovir levels that were consistent with recent administration of the drug and long-term adherence. (See 'Persons exposed to multidrug-resistant HIV' above.)

In other patients, exposure to tenofovir was believed to cause drug resistance. This was felt to be the cause of drug resistance in 4 of the 33 women in the Fem-PrEP trial and in 2 of the 51 patients in the Partners PrEP study [25,102]. In such patients, the M184V and the less common M184I mutations are most likely to emerge since the genetic barrier to resistance for emtricitabine is low. By contrast, the genetic barrier to resistance for tenofovir is high, and, therefore, resistance to tenofovir (eg, K65R mutation) is less likely to occur. In an observational study of 204 seroconversions on PrEP in sub-Saharan Africa, 21 percent of patients had M184V/I mutations and 3 percent had K65R mutations [103]. A more detailed discussion of HIV drug resistance mutations is found elsewhere. (See "Interpretation of HIV-1 drug resistance testing".)

- **Patients receiving injectable therapy** – If an HIV antigen/antibody test or HIV RNA test is positive in a person receiving cabotegravir LA, we do not administer a new injection until the patient's HIV status has been determined. Instead, patients should

be started on a regimen of boosted darunavir with either TAF-FTC or TDF-FTC pending the evaluation. (See "Acute and early HIV infection: Treatment".)

If an antigen/antibody testing is suggestive of new infection, an HIV RNA should be obtained (if not done so already). In addition, a genotype should be obtained for routine and integrase testing in all patients suspected of acquiring HIV on cabotegravir LA. (See "Overview of HIV-1 drug resistance testing assays", section on 'Genotypic resistance assays'.)

In the trial evaluating the efficacy of cabotegravir LA, 12 patients developed new infection, and resistance testing was able to be performed in nine patients [14,32]. Five incident infections occurred in individuals with no recent exposure to cabotegravir LA (ie, no injections or last injection ≥6 months before their first HIV-positive visit). In these patients there were low or unquantifiable concentrations of cabotegravir, and no resistance was identified. Three infections occurred during the oral lead-in period, and resistance developed in two of these patients. Resistance also developed in two patients who received appropriately timed cabotegravir LA doses and were thought to have plasma cabotegravir concentrations that would provide protection against HIV; in these patients, resistance may have resulted from delays in detecting HIV infection.

DISCONTINUING PREP

Patients should continue PrEP as long as the risk of infection with their main or nonmain partners persists. (See 'Indications based upon risk' above.)

For persons who initiate PrEP because their partner has HIV, PrEP should be continued until their partner has achieved a stably suppressed viral load (eg, <200 copies/mL), which typically occurs by six months after initiating antiretroviral therapy (ART). Although the duration of ART required to suppress HIV in semen and cervical secretions is unclear, in a clinical trial of patients with HIV initiated on ART, there were no reports of HIV transmission when the person with HIV was on ART and achieved suppression of their plasma viral load. However, PrEP should be continued in individuals who are having condomless sex with other partners or if there is concern that the partner with HIV is not taking their ART regimen as prescribed (and therefore is at risk for virologic failure).

When a person decides to discontinue PrEP, treatment should be continued for a period of time after their last sexual encounter. In addition, HIV testing should be performed at the time they discontinue PrEP.

- **Persons receiving oral PrEP** – It is unclear how long patients should continue oral PrEP after their last sexual exposure. For cisgender men who have sex with men (MSM), we typically continue PrEP for two days after their last sexual exposure based on the efficacy of the 2-1-1 event-driven PrEP regimen. (See 'Alternative regimens' above.)

  By contrast, for other populations, we continue PrEP for one month after the last high-risk exposure based upon experiences using post-exposure prophylaxis (PEP) [42]. (See "Management of nonoccupational exposures to HIV and hepatitis B and C in adults".)

  For patients with chronic hepatitis B virus (HBV) infection, the decision to switch to an alternative agent for treatment of HBV after PrEP is discontinued or to monitor for HBV flare should be discussed with a provider experienced in the management of HBV. This is particularly important for patients with cirrhosis. (See "Hepatitis B virus: Overview of management".)

- **Persons receiving** cabotegravir **LA** – Patients who discontinue injectable PrEP but continue to engage in high-risk sexual behaviors or sharing of injection equipment should receive oral PrEP with tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) or tenofovir alafenamide-emtricitabine (TAF-FTC) for at least 12 months to cover the period when levels of cabotegravir are detectable but not protective. This will reduce the risk of developing drug-resistant HIV should transmission occur. They should be encouraged to continue PrEP thereafter if they continue to engage in high-risk behaviors.

NOVEL APPROACHES TO TREATMENT

- **Dapivirine ring** – A vaginal ring containing dapivirine, a non-nucleoside reverse transcriptase inhibitor, has been approved by the World Health Organization (WHO) as an HIV prevention modality [104] and is available in some European and African countries. The dapivirine ring is not approved by the US Food and Drug Administration (FDA).

  In a randomized trial of 2629 cisgender African women who received a monthly vaginal ring containing dapivirine or placebo, the incidence of HIV infection was reduced by 27 percent (71 versus 97 infections; 95% CI 1-46) in those assigned to dapivirine [105]. When data from sites with reduced retention and adherence were excluded, the incidence of HIV infection was reduced by 37

percent (95% CI 12-56). Findings from a separate study reported similar results [106]. However, data from subsequent analyses suggest that women who are highly adherent to the product have much greater levels of protection (eg, >70 percent) [107,108].

The dapivirine ring has also been evaluated in two open-label studies to assess real-world effectiveness, and data support a modest but important degree of efficacy [109,110]. In one open-labeled trial of 1456 women who had access to the dapivirine vaginal ring, acceptance rates were high, and HIV incidence was 2.7 per 100 person-years compared with an expected incidence of 4.4 per 100 person-years.

- **Investigational approaches**

  - **Long-acting agents** – Lenacapavir, an HIV-1 capsid inhibitor, is a long-acting agent that is administered subcutaneously every six months. Although lenacapavir is not yet approved for use as PrEP, emerging data has found that it is effective in reducing HIV transmission in several populations, including men who have sex with men (MSM), transgender and nonbinary people who have sex with men, and cisgender women [111,112].

    In a randomized trial of PrEP in 3265 men and gender-diverse patients, twice-yearly subcutaneous lenacapavir reduced the incidence of new HIV infections by 96 percent compared with background HIV incidence (incidence rate ratio 0.04, 95% CI 0.01 to 0.18) [112]. In addition, lenacapavir was more effective than daily oral tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) in preventing new HIV infections (2 of 2179 participants in the lenacapavir group versus 9 of 1086 participants in the TDF-FTC group; incidence rate ratio 0.11, 95% CI 0.02 to 0.51). All nine participants who were diagnosed with HIV in the oral therapy group had low or no adherence to their regimen before diagnosis. Adverse events were similar between both groups.

    Lenacapavir has demonstrated similar efficacy in cisgender women. In a double-blind trial of 5338 adolescent girls and young women in South Africa and Uganda that compared lenacapavir with daily oral emtricitabine-tenofovir alafenamide and daily oral emtricitabine-tenofovir disoproxil fumarate, none of the 2134 patients who received lenacapavir acquired HIV, whereas 55 incident HIV infections were observed in the 3204 participants who received tenofovir alafenamide-emtricitabine (TAF-FTC) or TDF-FTC (39 and 16, respectively) [111]. Adherence to oral therapy was low, and there was no meaningful difference in HIV incidence between TAF-FTC and TDF-FTC (incidence rate ratio, 1.20, 95% CI, 0.67 to 2.14). In general, all of the therapies were well tolerated; however, four participants in the lenacapavir group discontinued the trial regimen because of injection site reactions.

- **Alternative delivery systems** – Topical formulations (eg, gels) are not commercially available for PrEP. Although topical administration remains an attractive intervention because early studies suggested that it is safe and can achieve high drug concentrations in the genital mucosa [69], the results of randomized trials evaluating the efficacy of tenofovir vaginal gel have been conflicting [26,36,37,113]. However, studies of rectal microbicides and douches are underway, given the frequent use of topical lubricants by individuals who engage in receptive anal intercourse.

- **Neutralizing antibodies** – Two randomized trials of the broadly neutralizing antibody VRC01 given as infusions every eight weeks to women or cisgender men and transgender women did not show efficacy in preventing HIV infections [114]. However, among participants who became HIV infected, having an isolate that was readily neutralized in vitro was associated with significant protection. This finding has led to optimism that new antibodies that are more potent and/or broadly neutralizing and/or using combinations of antibodies might result in effective protection against HIV. Clinical trials are being conducted globally to examine combinations of neutralizing antibodies for safety and tolerability, and some combinations will ultimately be evaluated in efficacy trials [14,115,116].

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: HIV prevention".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topics (see "Patient education: Taking medicines to prevent HIV before exposure (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Candidates for PrEP** – Pre-exposure prophylaxis (PrEP) with antiretroviral therapy (ART) is associated with marked reductions in HIV transmission in several populations. (See 'Determining eligibility for prep' above.)

  For the following persons who engage in sexual behaviors associated with HIV transmission, we recommend PrEP (**Grade 1A**). (See 'Sexual risk' above.)

  - Any person who has a sexual partner with HIV and a detectable viral load.
  - Cisgender men who have sex with men (MSM) and transgender women who, in the last six months, have engaged in condomless anal sex (insertive or receptive) with multiple or anonymous sex partners (or a main partner with HIV risk factors) and/or had a documented sexually transmitted infection (STI; eg, syphilis, gonorrhea, chlamydia).
  - Heterosexually active men who have condomless sex with female partners from regions with generalized HIV epidemics. This includes those who have condomless sex with one or more female partners with known HIV infection or multiple female partners of unknown HIV status.

  We also suggest PrEP for:

  - Heterosexual cisgender women, transgender men, and nonbinary people who, in the last six months, have engaged in condomless receptive vaginal or anal sex with male partners who are at high risk of HIV infection (eg, persons who inject drugs, bisexual male partners, partners from areas where there is a high HIV prevalence) or have been diagnosed with a bacterial STI, such as syphilis or gonorrhea (**Grade 2B**). (See 'Sexual risk' above.)

- People who inject drugs and report sharing needles/equipment in the last six months (**Grade 2B**). PrEP should be initiated even if they are receiving treatment for their substance use. (See 'Injection drug use' above.)

- Heterosexual men who have, in the last six months, been diagnosed with a bacterial STI or have engaged in condomless sex with partners from areas of low general HIV prevalence but who are at high risk of HIV infection (eg, sex workers, persons who inject drugs). However, there are limited data in these populations. (See 'Sexual risk' above.)

PrEP is generally not needed for persons who consistently engage in low-risk behaviors (eg, consistent condom use) and those who are in mutually monogamous relationships. (See 'Unclear risk' above.)

- **Available regimens** – There are two single tablet oral agents for PrEP, both contain tenofovir, but one uses tenofovir disoproxil fumarate (TDF) while the other uses tenofovir alafenamide (TAF). These are usually prescribed as a once daily regimen; event-driven dosing of tenofovir disoproxil fumarate-emtricitabine (TDF-FTC) can be used for specific patient groups. Another option is injectable therapy with long-acting cabotegravir (cabotegravir LA), which is administered intragluteally every month for two months and then every two months thereafter. (See 'Available oral agents' above and 'Injectable therapy (cabotegravir LA)' above.)

- **Evaluation prior to initiating treatment** – HIV testing should be performed in all persons prior to initiating PrEP to confirm that the person does not have pre-existing infection (algorithm 1). For those receiving an oral regimen, additional evaluation includes an assessment of renal function, hepatitis B virus (HBV) status, history of bone disease, and lipids (table 5). (See 'Pretreatment evaluation' above.)

- **Choice of agent** – For persons initiating PrEP, we discuss the use of oral versus long-acting injectable therapy (table 3). (See 'Determining preference for oral versus injectable therapy' above.)

  For most patients, we suggest once-daily TDF-FTC (**Grade 2C**). This is the most widely studied regimen and has been evaluated in all patient populations. If taken as prescribed, TDF-FTC can reduce the risk of sexual HIV transmission by nearly 100 percent. However, TDF should be avoided in persons with reduced kidney function or osteoporosis. (See 'Regimen selection' above.)

  Once daily tenofovir alafenamide-emtricitabine (TAF-FTC) and event-driven dosing of TDF-FTC may be appropriate alternatives for persons who engage exclusively in anal sex (table 3). (See 'Alternative regimens' above.)

Cabotegravir is a reasonable alternative for individuals who prefer injectable therapy. (See 'Injectable therapy (cabotegravir LA)' above.)

The best choice of regimen for any given patient is the one to which they can best adhere.

- **Patient counseling** – When initiating PrEP, persons who engage in anal sex should use condoms for seven days so that protective drug concentrations can be achieved. For those who engage in vaginal sex, we endorse condom use for 21 days after initiating PrEP. These recommendations are based on pharmacokinetic data. (See 'Men who have sex with men' above and 'Persons who engage in vaginal sex' above.)

  Patients should be counseled about the importance of taking PrEP as prescribed. There is a clear association between adherence to the drug regimen and the efficacy of PrEP in decreasing HIV transmission. (See 'Medication adherence' above.)

  Patients should also be educated about the signs and symptoms of acute HIV infection (eg, lymphadenopathy, fever, maculopapular eruption) and the importance of seeking medical attention if symptoms develop. (See 'Symptoms of acute HIV' above.)

- **Management on PrEP** – Patients receiving PrEP should have regular follow-up with a medical provider and should be monitored regularly for evidence of acute HIV, STIs, and toxicity to the regimen (table 6). (See 'Management on therapy' above.)

- **Discontinuing PrEP** – Patients should continue PrEP as long as the risk of infection with their main or nonmain partners exists. For those who want to discontinue PrEP, treatment should be continued for a period of time after their last sexual or drug-using encounter. The duration depends upon the specific agent. (See 'Discontinuing PrEP' above.)

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Topic 113426 Version 23.0

GRAPHICS

Estimated per-act risk for acquisition of HIV, by exposure route

Exposure route		Risk per 10,000 exposures to an infected source (risk
Blood-borne exposure	Blood transfusion	9000 (9/10)
	Needle-sharing injection drug use	67 (1/150)
	Percutaneous needle stick	23 (1/435)
	Mucous membrane exposure to blood (eg, splash to eye)	10 (1/1000)
Sexual exposure	Receptive anal intercourse	138 (1/72)
	Insertive anal intercourse	11 (1/900)
	Receptive penile-vaginal intercourse	8 (1/1250)
	Insertive penile-vaginal intercourse	4 (1/2500)
	Receptive or insertive penile-oral intercourse	0-4
Other	Biting, spitting, throwing body fluids (including semen and saliva), sharing sex toys	Negligible

There are scant empiric data on per contact risk of exposure. This table lists the estimated risk by exposure type in the absence of antiretroviral treatment of the HIV-infected source and in the absence of amplifying factors. Most of these estimates are derived through modeling studies of different cohorts. Clinicians need to be aware that estimates of sexual risk are often based on studies of monogamous couples among whom amplifying factors have been treated and repeated exposure may offer as yet unexplained protection from infection. Using a single value for assessing risk of HIV transmission based on route of sexual exposure fails to reflect the variation associated with important cofactors. A variety of amplifying factors and conditions have been identified, and these factors can be expected to increase transmission probability.

Data from:

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Graphic 60145 Version 6.0

Evaluation for PrEP: Assessing risk for acquiring HIV

Sexual risk behaviors*

To determine if a patient is at risk of acquiring HIV through sexual transmission, clinicians should assess sexual risk behaviors over the last 6 months.

Providers should assess the following:

- The HIV status and risk behaviors of the patient's sex partners, if available.
- If the patient is in a monogamous relationship with someone living with HIV, the viral suppression status of the partner.
- If the patient has had condomless penile-anal or penile-vaginal sex with partners other than their main partner.
- The number of sexual partners.
- If the patient has a history of any bacterial STIs.

Sexually transmitted infections

STI testing should be performed in patients who are considering PrEP, even in the absence of symptoms.¶

Providers should test for the following:

- Serologic testing for syphilis, including confirmation of seroreactive results.
- Nucleic acid amplification testing for gonorrhea and chlamydia at relevant mucosal sites (based on sexual history).Δ
- Assessment of hepatitis B serostatus (HBsAg, anti-HBc, anti-HBs) and hepatitis C serostatus.

Drug-using behaviors

To assess a patient's risk for HIV acquisition through parenteral and other drug use, clinicians should ask about their drug use history over the last 6 months.

This includes:

- Injecting heroin, fentanyl, cocaine, and/or methamphetamine.
- Sharing needles or equipment.
- Using nonparenteral drugs during sex (particularly methamphetamine).◇

Clinicians should discuss PrEP with all sexually active adolescents and adults. This table should be used to assess the risk of HIV acquisition to help inform suitability for PrEP.

PrEP: pre-exposure prophylaxis; STI: sexually transmitted infection; HBsAg: hepatitis B surface antigen; anti-HBc: hepatitis B core antibody; anti-HBs: hepatitis B surface antibody.

* It is important that the clinician ask about the patient's sexual behaviors with both main and casual partners. Although some studies have reported a higher number of transmissions from casual partners, some HIV transmissions among men who have sex with men (MSM) have been from a main partner. It is also important to understand the context of different social and situational factors (eg, does the patient have discussions about HIV status with their partners or does the patient have anonymous partners of unknown HIV status). Several online resources (eg, the Fenway National Center for LGBTQIA+, the Ready, Set, Go guidelines, the CDC website) are available to help guide providers in obtaining an HIV risk assessment.

¶ Relying on self-reported risk alone may not be sufficient to make an informed decision about PrEP initiation; the presence of certain STIs (eg, syphilis, anogenital gonorrhea, rectal chlamydia) have been highly associated with HIV acquisition and are indications for PrEP.

Δ Screening for bacterial vaginosis, *Mycoplasma genitalium*, and trichomonas is not routinely performed as part of the work-up before initiating PrEP since these infections have not had as strong an association with HIV. However, their presence suggests that recent condomless sex has occurred and should lead the clinician to ask about number of partners and potential risks of partners and discuss PrEP.

◇ Certain nonparenteral drugs, such as methamphetamines, can decrease the likelihood of using condoms and increase the number of sexual partners.

Graphic 140043 Version 1.0

Factors to consider when choosing a PrEP regimen

	Benefits	Risks	Additional considerations
TDF-FTC	▪ Well tolerated. ▪ Most studied regimen and can be used in all populations. ▪ Can be administered as event-driven therapy for persons who engage only in anal sex (unless they have concurrent chronic HBV infection).	▪ Can result in reduced kidney function. ▪ Can result in bone loss. ▪ For patients with chronic HBV, they are at risk for flare of their liver disease if therapy is discontinued.	▪ TDF should not be used in persons with an eGFR <60. ▪ Patients require monitoring of creatinine on therapy.
TAF-FTC	▪ Well tolerated. ▪ Less bone and renal toxicity compared with TDF.	▪ Should only be administered as daily therapy. ▪ Higher rates of mild triglyceride elevations and weight gain compared with TDF-FTC. ▪ Should not be used in those whose main risk for HIV is vaginal (frontal) sex or who inject drugs. ▪ Less experience compared with TDF, particularly in certain populations (eg, adolescents). ▪ For patients with chronic HBV, they are at risk for flare of their liver disease if therapy is discontinued.	▪ Has not been well studied for PrEP in persons who engage in vaginal (frontal) sex, pregnant persons, or those who inject drugs. ▪ There are no data evaluating event-driven dosing in those taking TAF-FTC.
Cabotegravir LA	▪ Well tolerated. ▪ Administered every other month. ▪ Clinical trials suggest efficacy greater than TDF-FTC (possibly related to improved adherence).	▪ Cabotegravir LA has a long half-life (drug may be detectable in blood for more than a year). An oral agent (TDF-FTC or TAF-FTC) is required for a period of time when discontinuing cabotegravir LA injections to reduce	▪ For those who are concerned about side effects of cabotegravir LA, oral cabotegravir (30 mg once daily) can be administered for a 4-week lead-in period prior to initiating injections.

	■ Can be considered for patients with conditions that are associated with an increased risk of adverse events with TDF-FTC or TAF-FTC (eg, those with reduced kidney function, bone disease)*.	the risk of developing an integrase inhibitor-resistant strain if HIV infection is acquired when cabotegravir levels are suboptimal*. ■ Future HIV treatment options (ie, use of an integrase strand transfer inhibitor) may be limited if HIV infection occurs and resistance to cabotegravir develops. ■ Need to be near a center that administers cabotegravir LA so doses are not missed. ■ Injection site reactions (generally mild).	■ There are only limited data in person who are pregnant or who desire pregnancy. ■ Cabotegravir LA has not yet been studied in persons who inject drugs.

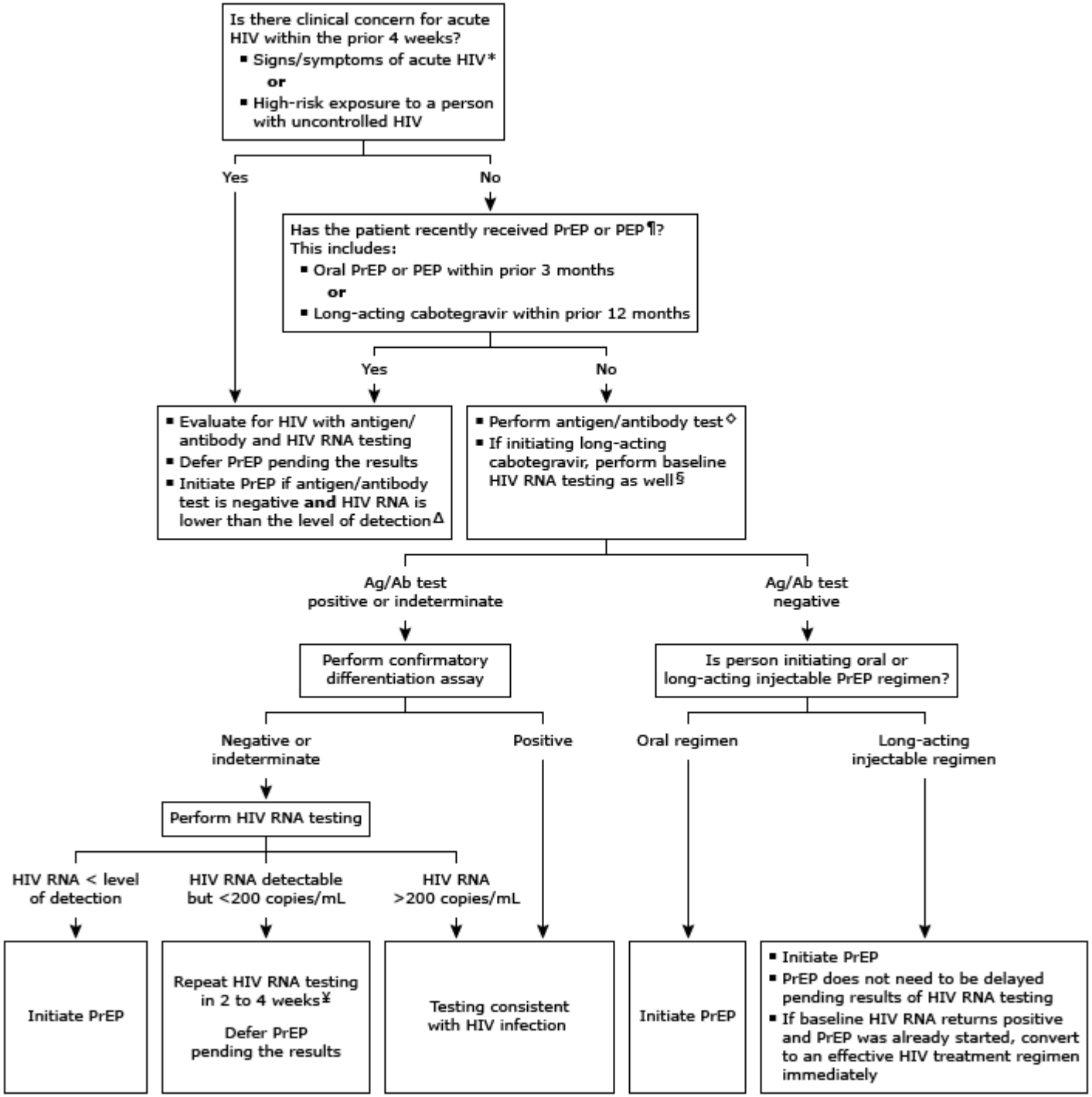
This table should be used in conjunction with UpToDate content on pre-exposure prophylaxis.

PrEP: pre-exposure prophylaxis; TDF-FTC: tenofovir disoproxil fumarate-emtricitabine; HBV: hepatis B virus; TAF-FTC: tenofovir alafenamide-emtricitabine; LA: long-acting injectable formulation.

* For patients with an absolute contraindication to TDF-FTC or TAF-FTC, consistent condom use or abstinence is required for a period of time if cabotegravir LA is discontinued.

Graphic 140045 Version 2.0

HIV testing prior to initiating PrEP


Is there clinical concern for acute HIV within the prior 4 weeks?
Signs/symptoms of acute HIV*
or
High-risk exposure to a person with uncontrolled HIV
Yes
No
Has the patient recently received PrEP or PEP¶?
This includes:
Oral PrEP or PEP within prior 3 months
or
Long-acting cabotegravir within prior 12 months
Yes
No
Evaluate for HIV with antigen/antibody and HIV RNA testing
Defer PrEP pending the results
Initiate PrEP if antigen/antibody test is negative and HIV RNA is lower than the level of detection△
Perform antigen/antibody test◇
If initiating long-acting cabotegravir, perform baseline HIV RNA testing as well§
Ag/Ab test positive or indeterminate
Ag/Ab test negative
Perform confirmatory differentiation assay
Is person initiating oral or long-acting injectable PrEP regimen?
Negative or indeterminate
Positive
Oral regimen
Long-acting injectable regimen
Perform HIV RNA testing
HIV RNA < level of detection
HIV RNA detectable but <200 copies/mL
HIV RNA >200 copies/mL
Initiate PrEP
Repeat HIV RNA testing in 2 to 4 weeks¥
Defer PrEP pending the results
Testing consistent with HIV infection
Initiate PrEP
Initiate PrEP
PrEP does not need to be delayed pending results of HIV RNA testing
If baseline HIV RNA returns positive and PrEP was already started, convert to an effective HIV treatment regimen immediately

This algorithm discusses the approach to HIV testing in persons who plan to initiate PrEP. Testing should be performed within one week of initiating therapy. The choice of agent (tenofovir disoproxil fumarate-emtricitabine, tenofovir alafenamide-emtricitabine, long-acting cabotegravir) depends upon availability, patient preference, and the presence of certain comorbid conditions. Refer to UpToDate content on pre-exposure prophylaxis for a discussion of regimen selection as well as the approach to HIV testing for monitoring people receiving PrEP. Patients who test positive for HIV should be referred for appropriate HIV care as soon as possible so they can be started on an effective antiretroviral therapy regimen.

PrEP: pre-exposure prophylaxis; PEP: post-exposure prophylaxis; Ag: antigen; Ab: antibody.

* Signs and symptoms of acute HIV may include fevers, chills, rash, and/or pharyngitis. Refer to topics on Acute HIV for additional information.

¶ Additional testing with HIV RNA is warranted in persons who have recently received PrEP or PEP since the sensitivity of the antigen/antibody test may be reduced.

Δ If antigen/antibody test is positive or HIV RNA is detected at any level, PrEP should not be initiated. Such patients should be managed in consultation with a specialist in HIV care.

◇ If a rapid antigen/antibody test was performed, a laboratory-based test should be sent as well. However, PrEP does not need to be delayed pending the result of the laboratory-based test.

§ An HIV RNA test should be performed in addition to an antigen/antibody test to minimize the risk of unrecognized HIV infection, which may result in cabotegravir resistance and limit HIV treatment options.

¥ In persons with a low HIV RNA, a false positive result is possible.

Preexposure Prophylaxis for the Prevention of HIV Infection in the United States (2021 Update) – Clinical Practice Guideline. United States Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf. (Accessed on August 26, 2022).

Graphic 140264 Version 1.0

Sexually transmitted infection screening recommendations by sex assigned at birth and population

Sex assigned at birth	Population	Routine screening recommendation	Screening frequency	Additional screening recommendations and comments
Cisgender females	Age <25 years and sexually active	Genital chlamydia*	Annually	If at increased risk¶, additionally screen for: ▪ Syphilis ▪ Trichomoniasis
		Genital gonorrhea*	Annually	
		HIV	At least once	
		HBV	At least once (if age ≥18 years and immunity not already documented)Δ	
		HCV	At least once (if age ≥18 years)◇	
	Age ≥25 years	HIV	At least once	If at increased risk¶, additionally screen for: ▪ Genital chlamydia and gonorrhea* ▪ Syphilis ▪ Trichomoniasis
		HBV	At least once (if immunity not already documented)Δ	
		HCV	At least once◇	
	Pregnant	Genital chlamydia*	First trimester (if <25 years or at increased risk¶)	Repeat screening for these infections in third trimester if a increased risk. Additional screening at first prenatal visit: ▪ HCV for those at risk (or if ≥18 years with no prior screening)◇ ▪ Trichomoniasis for those with HIV
		Genital gonorrhea*	First trimester (if <25 years or at increased risk¶)	

		Syphilis	First trimester	
		HIV	First trimester	
		HBV	First trimester	
	With HIV infection	Genital chlamydia*	Annually	
		Genital gonorrhea*	Annually	
		Genital trichomoniasis	Annually	
		Syphilis	Annually	
		HBV	At least once (eg, at first visit)	
		HCV	At least once (eg, at first visit)◇	
	WSW and WSWM	WSW and WSWM should not be assumed to be at lower risk for STIs on the basis of their sexual orientation. Screening for cervical cancer and STIs should be conducted according to guidelines for women, based on an open discussion of sexual and behavioral risk factors.		

Cisgender males	MSW only without HIV infection	HIV	At least once	If at increased risk[§], additionally screen for: ▪ Genital chlamydia and gonorrhea ▪ Syphilis Targeted screening venues for chlamydia include adolescent clinics, STI clinics, and correctional facilities.
		HBV	At least once (if age ≥18 years and immunity not already documented)[Δ]	
		HCV	At least once (if age ≥18 years)[◇]	
	MSM without HIV infection	Genital chlamydia	At least annually	More frequent screening (every 3 months) for chlamydia, gonorrhea, and syphilis is recommended in those with risk factors. More frequent screening for HIV, HBV, and HCV may also be warranted.[¥]
		Rectal chlamydia (if exposed)	At least annually	
		Genital gonorrhea	At least annually	
		Rectal gonorrhea (if exposed)	At least annually	
		Pharyngeal gonorrhea (if exposed)	At least annually	
		Syphilis	At least annually	
		HIV	At least annually	
		HAV	At least once	
		HBV	At least once	
		HCV	At least once[◇]	
	MSW only with HIV infection	Genital chlamydia	Annually	
		Genital gonorrhea	Annually	
		Syphilis	Annually	

		HBV	At least once (eg, at first visit)	
		HCV	At least once (eg, at first visit)◇	
	MSM with HIV infection	Genital chlamydia	At least annually	More frequent screening (every 3 months) for chlamydia, gonorrhea, and syphilis is recommended in those with risk factors. More frequent screening for HBV and HCV may also be warranted.¥
		Rectal chlamydia (if exposed)	At least annually	
		Genital gonorrhea	At least annually	
		Rectal gonorrhea (if exposed)	At least annually	
		Pharyngeal gonorrhea (if exposed)	At least annually	
		Syphilis	At least annually	
		HAV	At least once (eg, at first visit)	
		HBV	At least once (eg, at first visit)	
		HCV	At least annually◇	
Transgender and gender-diverse individuals	Screening for STIs should be based on an individual's anatomy: ▪ Transgender men and gender-diverse individuals with a cervix should be screened for genital gonorrhea, chlamydia, and cervical cancer according to recommendations for cisgender women. ▪ Transgender women and gender-diverse individuals assigned male at birth should be screened for genital gonorrhea and chlamydia according to recommendations for cisgender men. Screening for other STIs should be based on sexual practice, risk factors, and exposures.			

HAV: hepatitis A virus; HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus; MSM: men who have sex with men; MSW: men who have sex only with women; STI: sexually transmitted infection; WSW: women who have sex with women; WSWM: women who have sex with

women and men.

* Screening for nongenital infections in females (eg, rectal chlamydial infection, pharyngeal and rectal gonococcal infection) can be considered based on reported sexual behaviors and exposure, via shared clinical decision-making between the patient and the provider.

¶ Factors conferring increased risk for gonorrhea, chlamydia, and trichomoniasis in females include transactional sex, new sex partner, multiple sex partners, a sex partner with concurrent partners, or a sex partner with an STI. Risk factors for syphilis include residence in high-prevalence areas, history of incarceration, or transactional sex work. STI screening may also be considered in high-prevalence settings (eg, STI clinic or correctional facility).

Δ For all adults 18 years of age or older, regardless of risk factors, at least 1-time screening for HBV infection is recommended, unless they have documented vaccine receipt and serologic evidence of vaccine response. Those who are susceptible should be vaccinated. For those who have risk factors for HBV exposure, ongoing screening is warranted if they are unvaccinated or have nonresponse to vaccination. Refer to other UpToDate content on STIs for details.

◇ All adults 18 years of age or older should be screened for HCV at least once, except in settings where the HCV positivity is <0.1%. Repeated screening is warranted for those with ongoing risk factors (eg, injection drug use). Increased risk factors for hepatitis C infection among MSM include HIV infection, high community HCV prevalence and incidence, high-risk sexual behaviors, and concomitant ulcerative STIs or STI-related proctitis. Refer to other UpToDate content on hepatitis C screening for details.

§ Factors conferring increased risk for gonorrhea and chlamydia in MSW include an infection in the preceding 24 months. Screening for chlamydia in young males can be considered in high-prevalence clinical settings (adolescent clinics, correctional facilities, STI/sexual health clinic). Increased risk factors for syphilis may be based on geography, race/ethnicity, history of incarceration, transactional sex work, or age <29 years.

¥ Increased risk factors for gonorrhea, chlamydia, syphilis, and HIV among MSM include multiple or anonymous partners; intravenous drug use; sex in conjunction with illicit drug use, including methamphetamines; and sex partners who engage in these activities. MSM who have not been vaccinated for HBV or have had nonresponse to vaccination remain at risk for HBV infection.

References:

1. *California sexually transmitted infections (STI) screening recommendations, 2021. California Department of Public Health. https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/California-STI-Screening-Recommendations.aspx (Accessed on January 24, 2023).*
2. *Workowski KA, Bachmann LH, Chan PA, et al. sexually transmitted infections treatment guidelines, 2021. MMWR Recomm Rep 2021; 70:1.*
3. *Conners EE, Panagiotakopoulos L, Hofmeister MG, et al. Screening and testing for hepatitis B virus infection: CDC recommendations – United States, 2023. MMWR Recomm Rep 2023; 72:1.*

Graphic 103391 Version 14.0

Evaluation of patients prior to initiation of oral pre-exposure prophylaxis (PrEP) against HIV[1-3]

Before initiating PrEP

Determine eligibility*

- Document negative HIV test(s) (typically antigen/antibody test) within one week of starting PrEP medication
- Test for acute HIV infection with HIV RNA if patient has symptoms consistent with acute HIV infection or has had a known exposure to HIV in the last 4 weeks
- Confirm that patient is at ongoing, high risk for acquiring HIV infection based upon detailed sexual and drug use history and results of STI testing*
- Confirm that calculated estimated glomerular filtration rate is ≥30 mL/min/1.73 m^2 ¶Δ

Other tests to determine risks of PrEP

- Screen for HBV◇ and HCV§
- Obtain urinalysis in patients with risk factors for renal disease¥
- Perform DXA scan in patients with, or at high risk for, osteoporosis‡
- Obtain baseline lipid panel and weight if TAF-FTC is being considered for PrEP†
- Perform pregnancy testing for patients who could become pregnant

Beginning PrEP medication regimen

- Prescribe 1 tablet of TDF-FTC or TAF-FTC daily Δ
- In general, prescribe no more than a 90-day supply, renewable only after HIV testing confirms that patient remains HIV uninfected
- Provide counseling on condoms,** risk reduction for sexual and drug-using behaviors, and PrEP medication adherence

This table addresses the evaluation of patients prior to initiating oral PrEP with a tenofovir-containing regimen and should be used in conjunction with UpToDate content on PrEP.

DXA: dual-energy x-ray absorptiometry; FTC: emtricitabine; HBV: hepatitis B virus; HCV: hepatitis C virus; HIV: human immunodeficiency virus; PrEP: pre-exposure prophylaxis; STI: sexually transmitted infection.

* Some patients may request PrEP but not endorse specific risk factors for HIV acquisition. In this setting we typically administer PrEP, assuming there are no other contraindications, since some people may not feel comfortable disclosing HIV risk behaviors.

¶ Individuals with an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 are not candidates for PrEP with TDF-FTC. Individuals with an eGFR <30 ml/min/1.73 m^2 are not candidates for PrEP with either TDF-FTC or TAF-FTC. For such persons, injectable therapy with long-acting cabotegravir can be considered.

Δ Daily TDF-FTC is our preferred oral regimen for most patients. For men who have sex with men (MSM) without chronic HBV infection, on-demand/event driven PrEP with TDF-FTC (referred to as 2-1-1) is an alternative to daily PrEP. In addition, TAF-FTC is an alternative regimen for MSM and transgender women with renal and bone issues. Refer to the UpToDate topic on PrEP for additional information on regimen selection.

◇ Vaccinate against hepatitis B if susceptible. If chronic HBV is diagnosed, patients with chronic HBV should also be managed in conjunction with a specialist in the management of HBV. Although TDF-FTC or TAF-FTC can be used for both treatment of chronic HBV and HIV prevention, there is a theoretical risk that discontinuing therapy may result in a flare of HBV.

§ Persons who inject drugs and MSM who engage in high-risk sexual behaviors are at risk for HCV infection. Patients who test positive should be referred for treatment.

¥ It is reasonable to obtain a baseline urinalysis when starting TDF-FTC in patients with risk factors for renal disease, such as hypertension, diabetes, proteinuria, and prior history of renal insufficiency. This may help inform the choice of agent (TDF-FTC versus TAF-FTC) and be used for comparison when monitoring.

‡ Refer to the topic within UpToDate that discusses risk factors for osteoporosis.

† Although lipid testing and weight are not specifically recommended by guideline panels, in clinical trials, higher rates of triglyceride elevation and weight gain were seen among men taking TAF-FTC compared with those taking TDF-FTC.

** In addition to preventing sexually transmitted infections, condoms should be encouraged until adequate levels of tenofovir are achieved in the rectal and cervicovaginal tissues (eg, 7 days in patients engaging in anal sex and 21 days for women engaging in receptive vaginal sex).

References:

1. *Interim guidance: preexposure prophylaxis for the prevention of HIV infection in men who have sex with men. MMWR 2011; 60:65.*
2. *Interim Guidance for Clinicians Considering the Use of Preexposure Prophylaxis for the Prevention of HIV Infection in Heterosexually Active Adults. MMWR 2012; 61:586.*
3. *Preexposure Prophylaxis for the Prevention of HIV Infection in the United States (2021 Update) – Clinical Practice Guideline. United States Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf (Accessed on August 26, 2022).*

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Routine monitoring for patients on a stable PrEP regimen*

What to monitor	Frequency for patients receiving TDF-FTC or TAF-FTC	Frequency for patients receiving cabotegravir LA
▪ Perform an HIV test¶	Every 3 months	Every 2 months
▪ Evaluate and support PrEP medication adherence	Every 3 months	Every 2 months
▪ Assess for side effects	Every 3 months	Every 2 months
▪ Assess risk behaviors and provide risk-reduction counseling and condoms	Every 3 months	Every 2 months
▪ Assess pregnancy status for patients who could become pregnant△	Every 3 months	Every 2 months
▪ Test for STIs among individuals with high-risk sexual behaviors, even if patient is asymptomatic◇	MSM and transgender women: Every 3 months All others: Every 6 months	MSM and transgender women: Every 4 months All others: Every 6 months
▪ Serum creatinine	Persons at risk for renal disease§¥: Every 6 months All others: Every 12 months	Routine monitoring not needed
▪ HCV testing	MSM, transgender women, persons who inject drugs: Every 12 months	MSM, transgender women, persons who inject drugs: Every 12 months
▪ Lipids and weight	Persons on TAF-FTC: Every 12 months	Routine monitoring not needed

This table addresses routine monitoring in patients on a stable PrEP regimen. Additional information on monitoring (eg, the first month after antiviral therapy is started, when therapy is discontinued) and management of adverse outcomes are discussed in the UpToDate topic review on PrEP.

FTC: emtricitabine; HCV: hepatitis C virus; HIV: human immunodeficiency virus; MSM: men who have sex with men; PrEP: pre-exposure prophylaxis; STI: sexually transmitted infection; TAF: tenofovir alafenamide; TDF: tenofovir disoproxil fumarate.

* For persons who are asymptomatic, routine monitoring can occur in conjunction with scheduled follow-up visits. Additional monitoring should be performed if there are specific concerns (eg, inconsistent adherence is identified, person has signs or symptoms of an STI or acute HIV infection).

¶ Patients receiving oral PrEP should have plasma HIV testing with a fourth-generation antigen/antibody test. We obtain RNA testing if the patient has signs or symptoms suggestive of acute HIV infection or has an indeterminate antigen/antibody test, although some experts recommend HIV RNA testing for monitoring all patients on oral PrEP.

For patients receiving cabotegravir LA, our approach is generally consistent with the United States Centers for Disease Control and Prevention (CDC), which recommends that HIV RNA testing be performed in addition to an antigen/antibody test to monitor for HIV. However, this many not always be feasible (eg, due to cost or availability). In these settings, an antigen/antibody test alone is reasonable for those who have not missed doses and are without evidence of acute HIV infection. If testing is consistent with new HIV infection, clinicians should order and document results of resistance testing and establish immediate linkage to HIV care. PrEP regimens are not sufficient for treatment of HIV.

Δ Oral PrEP can be used in pregnancy after an informed decision is made. Refer to the UpToDate topic that discusses PrEP for information on regimen selection.

◇ STI screening should include serum testing for syphilis and screening for gonorrhea and chlamydia at mucosal sites with potential exposures (eg, throat, rectum, urogenital). Refer to the topic that discusses screening for STIs within UpToDate.

§ Discontinue oral PrEP if there is evidence of moderate or severe proximal tubular dysfunction or Fanconi syndrome. In other settings the approach must be individualized. As an example, TDF-FTC should be discontinued in persons whose estimated glomerular filtration rate falls below 60 mL/minute/1.73 m^2 but switching to TAF-FTC or cabotegravir LA may be reasonable.

¥ The United States CDC states risk factors for renal disease include age 50 and older and/or having an estimated creatinine clearance <90 mL/minute. We also consider hypertension, diabetes, proteinuria, and prior history of renal insufficiency as risk factors for renal disease. For such patients, we obtain a urinalysis every six months in addition to monitoring the creatinine. More frequent monitoring may be required for those who develop abnormal findings.

Reference:

1. *Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2021 Update: A Clinical Practice Guideline. Centers for Disease Control and Prevention. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf (Accessed on August 26, 2022).*
2. *Gandhi RT, Bedimo R, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2022 recommendations of the International Antiviral Society-USA Panel. JAMA 2023; 329:63.*

3. *Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring: Recommendations for a Public Health Approach. World Health Organization 2021. https://www.who.int/publications/i/item/9789240031593 (Accessed on May 24, 2022).*

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Conflict of interest policy

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