PrEP

Pre-exposure Prophylaxis for HIV

You can help end the HIV epidemic with pre-exposure prophylaxis (PrEP).

PrEP prevents HIV. It is a component of the **Prevent** pillar of the United States government's Ending the HIV Epidemic initiative and is recommended by the United States Preventive Services Task Force (USPSTF) [1,2]. The Centers for Disease Control and Prevention (CDC) recommend that all sexually active people be informed about PrEP [3].

This **PrEP Action Kit** is an educational tool about PrEP for clinicians; it is not intended to serve as clinical advice. For detailed information about managing PrEP, please refer to CDC's 2021 PrEP Guidelines [3].

Prescribing PrEP

Three medications are available for PrEP.

- Oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC, Truvada)
- Oral tenofovir alafenamide/ emtricitabine (TAF/FTC, Descovy)
- Long-acting intramuscular cabotegravir (CAB, Apretude)

PrEP is highly effective when taken as prescribed.

- Daily TDF/FTC lowers the risk of HIV by more than 90% [4]. Protection from HIV diminishes with lower adherence.
- Efficacy of TAF/FTC is similar to that of TDF/FTC for PrEP among men who have sex with men (MSM) and transgender women [5]. TAF/FTC is not currently recommended for PrEP among cisgender women and other people who have receptive vaginal sex, pending the results of ongoing studies.
- CAB is superior to TDF/ FTC for PrEP among MSM, transgender women, and cisgender women [6,7].

PrEP is indicated for people with an increased likelihood for HIV through sex or injection drug use.

More than a million people in the United States may benefit from taking PrEP [8]. People who may benefit from PrEP include [3]:

- Those who have had anal or vaginal sex in the past 6 months who:
  - Have a sex partner with HIV who has an unknown or detectable HIV viral load
  - Have one or more sex partners of unknown HIV status with whom they do not always use condoms
  - Have had a bacterial sexually transmitted infection (STI) within the past 6 months. STIs that indicate increased risk for HIV include:
    - Gonorrhea, chlamydia, and syphilis for MSM
    - Gonorrhea or syphilis for others
- Those who have injected drugs in the past 6 months and share injection equipment

PrEP is also indicated for people who request it, even if they do not report the behaviors listed above. They may have exposures to HIV that clinicians did not elicit or that they did not want to disclose, or they may simply want to protect themselves in advance of a future exposure.

All forms of PrEP are generally well-tolerated.

- Side effects of TDF/FTC include nausea that tends to improve with continued adherence to the medication, a small decrease in bone mineral density without an associated increase in fractures, and, rarely, renal dysfunction that resolves with cessation of the medication.
- In a clinical trial, TAF/FTC impacted biomarkers of bone and renal integrity less than TDF/FTC [5]. TAF/FTC or CAB should be considered for PrEP for people who are at risk for bone or renal disease.
- Most people who receive CAB have pain or swelling at the site of injection, but these reactions tend to be mild and rarely caused discontinuation of the drug in a clinical trial [6]. Antiretroviral resistance from PrEP is rare.
- Some PrEP users may decrease condom use and/or increase their number of sexual partners [9]. These changes do not negate the HIV-protective benefit of PrEP, though they do increase the likelihood of acquiring sexually transmitted infections (STIs) such as chlamydia, gonorrhea, and syphilis [10]. Clinicians should recommend that patients taking PrEP consider using condoms to protect against non-HIV STIs. However, condom use is not a pre-requisite for PrEP.

Managing PrEP consists of three steps [3].

Providing PrEP involves selecting a medication, performing a baseline evaluation, and monitoring.

Selecting a PrEP medication:
The choice of medication depends on patient preference, the source of HIV risk (sexual behavior and/or injection drug use), comorbidities, and potentially cost.

Medication	Advantages	Disadvantages
Oral TDF/FTC	• Prevents HIV acquisition through sex and injection drug use • Effective when used in an on-demand fashion among MSM • Available as a generic	• Should not be used when estimated creatinine clearance is < 60 mL/min • Risks of renal adverse events and decreased bone mineral density
Oral TAF/FTC	• Prevents HIV acquisition through sex • Less likely than TDF/FTC to adversely affect kidneys or bone • Can be used if the estimated creatinine clearance is ≥ 30 mL/min	• Use in an on-demand fashion or among cisgender women has not been studied • Risk of weight gain and adverse metabolic effects
Intramuscular CAB	• Superior to TDF/FTC for PrEP among MSM, transgender women, and cisgender women • Every-two-month injections obviate the need for taking a pill daily	• Requires more frequent clinic visits than oral PrEP • Injection site reactions are common but tend to be mild • Limited data about safety in pregnancy

Baseline and ongoing laboratory monitoring for PrEP:

The baseline evaluation varies by PrEP medication, but a crucial step for all PrEP candidates is to exclude baseline HIV infection. Baseline testing for oral PrEP should also include assessment of renal function and testing for chronic hepatitis B. The information below is adapted from CDC's PrEP guidance [3]; please refer to that document for additional information.

For TDF/FTC and TAF/FTC:

- **Baseline:**
  - *Confirm that the patient does not have HIV*: Perform an HIV antibody/antigen test.
  - *Estimate the creatinine clearance by obtaining a serum creatinine*
  - *Assess hepatitis B status by obtaining a hepatitis B surface antibody, hepatitis B core antibody, and hepatitis B surface antigen.* People without evidence of chronic infection with, or immunity to, hepatitis B should be vaccinated. Both tenofovir and emtricitabine are active against hepatitis B infection. Pre-existing hepatitis B is not a contraindication to PrEP with TDF/FTC or TAF/FTC but may necessitate continuation of the medication even when it is no longer needed for HIV prevention.
  - *Assess hepatitis C status by obtaining a hepatitis C antibody* for MSM, transgender women, and people who inject drugs.
  - *Check for STIs at baseline*. Screening includes a syphilis serology and gonorrhea and chlamydia nucleic acid amplification tests (NAAT) at all potential sites of exposure.
  - *Obtain a lipid panel for those starting TAF/FTC.*

- **Monitoring while on PrEP:**
  - *Test for HIV with an HIV antibody/antigen assay and HIV RNA assay every 3 months.* The rationale for performing an HIV RNA assay is that, in rare cases of HIV acquisition despite PrEP, HIV antibody/antigen seroconversion may be delayed.
  - *Check the estimated creatinine clearance.* For those who are ≥ 50 years old or whose baseline estimated creatinine clearance is < 90 mL/min, check renal function every 6 months. Otherwise, check every 12 months.
  - *Screen for STIs* every 3 months for MSM and transgender women; otherwise, screen every 6 months.
  - *Screen for hepatitis C* every 12 months for MSM and transgender women.
  - *Check a lipid panel* every 12 months in people taking TAF/FT

For CAB:

- **Baseline:**
  - *Confirm that the patient does not have HIV:* Perform an HIV antibody/antigen test and an HIV RNA assay.
  - *Check for STIs at baseline.* Screening includes a syphilis serology and gonorrhea and chlamydia nucleic acid amplification tests (NAAT) at all potential sites of exposure.
- **Monitoring while on PrEP:**
  - *Test for HIV with an HIV antibody/antigen assay and HIV RNA assay after 1 month (when the patient returns for the second dose of CAB) and every 2 months thereafter.* The rationale for performing an HIV RNA assay is that, in rare cases of HIV acquisition despite PrEP, HIV antibody/antigen seroconversion may be delayed.
  - *Screen* for STIs every 4 months for MSM and transgender women; otherwise, screen every 6 months.

Stopping PrEP

At follow-up visits, re-assess HIV risk. If HIV risk diminishes, PrEP may no longer be indicated. Counsel patients about the implications of stopping PrEP if exposures to HIV continues or recurs. This is particularly important for patients who receive cabotegravir, because drug concentrations will dwindle over months after the last injection. If HIV is acquired during this "tail" phase, the virus may develop resistance to CAB. Patients who stop CAB and yet have ongoing exposures to HIV should be provided with oral PrEP and continue laboratory monitoring for HIV.

Common Clinical Questions

Is PrEP worthwhile for the seronegative partner in a serodifferent relationship?

A serodifferent relationship is a sexual relationship in which one partner has HIV and one does not. Whether PrEP is beneficial in this setting depends upon the treatment status of the partner with HIV and the potential for other HIV exposures on the part of the seronegative partner.

- Virologic suppression with antiretroviral therapy prevents sexual transmission of HIV [11,12]; thus, if the partner with HIV is durably virologically suppressed on treatment and the seronegative partner is not otherwise at risk for HIV (i.e., no other sexual partners or injection drug use), PrEP for the seronegative partner would not be beneficial.
- If the partner with HIV is not durably virologically suppressed on treatment, the virologic suppression status is unknown or not confirmed, or if the seronegative partner has sexual contacts outside the relationship and/or shares injection drug use equipment, PrEP may be beneficial.

U = U: Undetectable = Untransmissible

- In a large randomized trial of serodifferent heterosexual couples, no within-couple HIV transmissions occurred when the partner living with HIV was virologically suppressed on antiretroviral therapy [11].
- Likewise, in a large observational study of serodifferent male couples in which the partner living with HIV was taking suppressive antiretroviral therapy, there were no within-couple HIV transmissions [12].
- In other words, people living with HIV who have undetectable HIV viral loads on treatment are not sexually infectious: **U = U**.

Can PrEP be prescribed to adolescents who are at risk for HIV?

Yes. All currently available PrEP medications are approved for adolescents who weigh more than 35 kilograms and otherwise meet the clinical indications for PrEP. Local laws may dictate whether parental/guardian consent is required for PrEP. When parental/guardian consent is not legally required and the adolescent does not wish to share their PrEP use with parents/guardians, care must be taken to ensure that PrEP prescribing is not inadvertently disclosed with health insurance or clinical billing information.

Can I prescribe oral PrEP in an on-demand fashion?

Yes, in certain circumstances. On-demand dosing – also called event-driven, episodic, or 2-1-1 PrEP – refers to the use of TDF/FTC only in conjunction with sex. On-demand PrEP, in which people take two doses of TDF/FTC within two to twenty-four hours before sex and one dose daily for two days afterwards, is highly effective among MSM and is considered an alternative dosing strategy by the International Antiviral Society-USA Panel and CDC [3,13,14]. However, on-demand PrEP is not currently approved by the FDA, and it has not been studied in cisgender women, adolescents, transgender people, or people who inject drugs. On-demand dosing would not be appropriate for people with chronic hepatitis B, because it would provide only intermittent treatment of that infection. On demand use of TAF/FTC has not been studied. If on-demand dosing is prescribed, CDC recommends providing no more than 30 tablets at a time, renewing the prescription only after follow-up HIV testing [3].

Implementing PrEP

How PrEP is implemented varies based on the clinical setting (community health center, STI clinic, pharmacy, etc.), the population of interest (e.g., MSM, transgender women, people who inject drugs, cisgender women, etc.), and the local health insurance environment and availability of drug assistance programs. Regardless of the model of care, successful PrEP programs address three core tasks:

1. Identifying and engaging PrEP candidates
2. Completing the initial and follow-up medical evaluations
3. Employing health insurance and drug assistance programs to overcome financial barriers

For each of these tasks, multiple strategies can, and have, been employed successfully [15]:

Identifying and engaging PrEP candidates

Health centers offering PrEP should list themselves on CDC's online PrEP Locator. Self-referral for PrEP, however, has not been sufficient to engage people in PrEP care, particularly those who face the highest likelihood of HIV infection. Below are additional strategies to recruit and engage PrEP candidates.

- Advertising PrEP services to key populations (e.g., to MSM on gay dating apps)
- Incorporating PrEP into substance use disorder treatment programs or STI testing and treatment services
- Utilizing STI Partner Notification Services to refer PrEP candidates to care
- Offering PrEP initiation at mobile clinics in conjunction with community events
- Identifying and linking PrEP candidates to care through collaborations between community- and faith-based organizations and health centers
- Using clinical decision support to identify PrEP candidates for clinicians [16,17].

Regardless of the strategies employed, because most people with indications for PrEP in the United States are thought to be sexual and gender minority people, clinical settings where PrEP is provided should be welcoming to gay, bisexual, transgender, gender diverse, and queer people.

Completion of initial and follow-up medical evaluations

- Any clinician who can prescribe medication can prescribe PrEP. Thus, across contexts where PrEP is available, physicians, nurse practitioners, and physician assistants may all provide PrEP.
- Nurses may help identify PrEP candidates, support medication adherence, triage concerns about side effects, and perform routine follow-up visits.
- Community health workers/PrEP navigators can also support medication and follow-up visit adherence.
- Some pharmacists prescribe PrEP through collaborative drug therapy agreements with physicians [18]. Potential advantages of this approach include the widespread availability of pharmacies and the possibility of care on evenings and weekends. Laws regarding collaborative drug therapy agreements between clinicians and pharmacists vary by state.
- Some programs have developed telehealth models of PrEP care. Telehealth may be particularly helpful for patients in rural areas who live far from health centers, for those for whom transportation to the health center is difficult, and/or for those who would like to maintain additional privacy around PrEP care by not visiting a clinic in person.
- Same-day prescribing of PrEP may increase uptake of the medication among people at risk for HIV (see box).

Same-Day PrEP Prescribing

PrEP can safely be prescribed based on a negative HIV test and a clinical evaluation which does not reveal other contraindications, before the results of other baseline tests are available. In one study, this approach led to higher uptake of the medication among eligible adult men, without a clinically significant increase in adverse events [19]. It is crucial to ensure that patients can be contacted promptly if pending laboratory results reveal a concern that would warrant stopping PrEP.

Employing health insurance and drug assistance programs to overcome financial barriers.

Without financial assistance for the costs of medication, clinical visits, and laboratory tests, PrEP would be prohibitively expensive for many patients. Many health centers which prescribe PrEP frequently employ staff members to help PrEP candidates navigate insurance and benefits program enrollment as well assist with identification of PrEP candidates and adherence to clinical follow-up (see PrEP navigators).

PrEP has a grade A recommendation from the USPSTF and should thus be covered without cost-sharing under the Affordable Care Act.

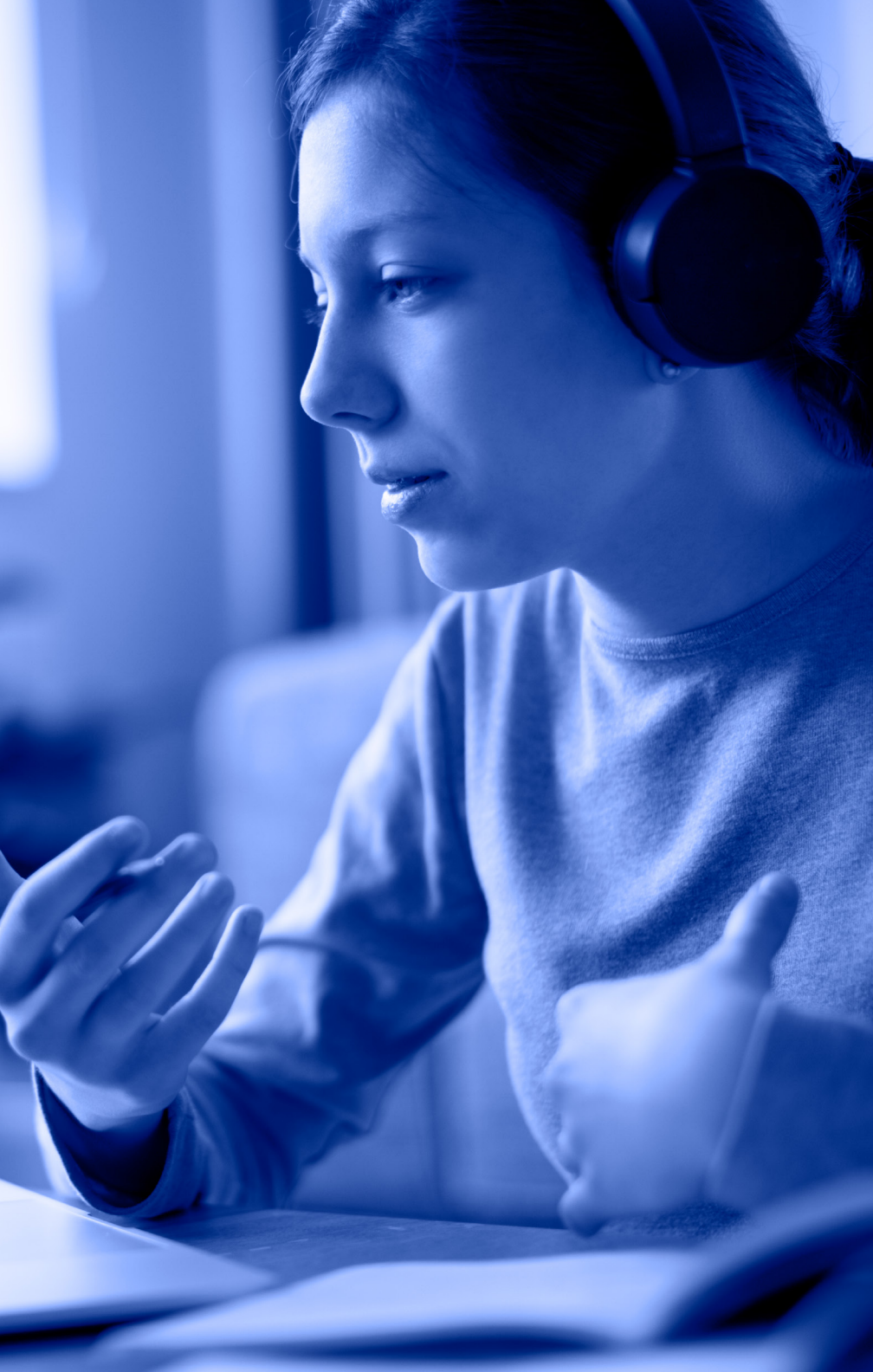
For uninsured patients, key resources for PrEP include:

- The federal Ready, Set, PrEP program, which provides PrEP medication for people without prescription drug coverage who live in the United States.
- Local and state PrEP drug assistance programs. Check with your local Department of Health to learn about resources in your area.

Some PrEP candidates may be eligible for but unenrolled in governmental health insurance programs such as Medicaid and Medicare. Clinical benefits managers and/or PrEP navigators can assist with insurance enrollment.

PrEP Navigators

- Many health centers hire PrEP navigators to facilitate PrEP uptake and persistence.
- Depending on the health centers' needs, these individuals may perform outreach and collaborate with community- and faith-based organizations to identify and engage PrEP candidates, assist patients in enrolling in health insurance and/or drug assistance programs for PrEP medication, and support medication and clinical follow-up adherence.
- PrEP navigators are often community health workers who are members of the populations needing PrEP in the local community.



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