Pre-exposure Prophylaxis (PrEP) to Prevent HIV During Periconception, Antepartum, and Postpartum Periods

(Last updated December 30, 2021; last reviewed December 30, 2021)

Panel's Recommendations
• Health care providers should offer and promote daily oral combination tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) pre-exposure prophylaxis (PrEP), when indicated, for uninfected individuals who are trying to conceive or are pregnant, postpartum, or breastfeeding to prevent HIV acquisition **(AII)**. Indications for PrEP include risk factors for acquiring HIV, such as condomless sex with a partner with HIV whose HIV-RNA level is detectable or unknown, recent sexually transmitted infection (STI), or injection drug use. Because risk factors may be underreported, health care providers should discuss PrEP with those with behaviors or experiences that can be associated with HIV, such as intimate partner violence, repeated post-exposure prophylaxis courses, or reporting feeling at risk for HIV acquisition.
• People who become pregnant while using TDF/FTC as PrEP can continue PrEP throughout their pregnancy. Risk for HIV acquisition should be reassessed, and people should be counseled regarding benefits and risks of PrEP use in pregnancy **(AII)**.
• Providers should counsel patients about the benefits of PrEP to prevent HIV acquisition and perinatal transmission **(AI)** and about potential risks of PrEP during periconception, pregnancy, postpartum, and breastfeeding periods **(AII)**.
• In cases when the individual's risk factor is one identified partner with HIV and that partner is on antiretroviral therapy (ART) with sustained viral suppression, condomless sexual intercourse is associated with effectively no risk of sexual HIV transmission when HIV viral load is suppressed **(AI)** (see [Reproductive Options for Couples When One or Both Partners Have HIV](#)).
• Providers should counsel patients about the importance of daily adherence to oral TDF/FTC PrEP to prevent HIV acquisition **(AI)**. Patients should be counseled to continue additional protection for the first 20 days after initiating PrEP and for 28 days after last potential vaginal exposure **(BII)**. No available data support on-demand PrEP use for people exposed to HIV through vaginal exposure.
• Providers should offer routine PrEP follow-up, including testing for HIV every 3 months and counseling on signs and symptoms of acute retroviral syndrome **(AI)** (see the Centers for Disease Prevention and Control [Guidelines for HIV Pre-Exposure Prophylaxis](#) and [Maternal HIV Testing and Identification of Perinatal HIV Exposure](#)). More frequent testing may be appropriate when clinically indicated (e.g., adherence challenges, nonstandard visit schedule).
Dapivirine vaginal ring and injectable cabotegravir have been shown to reduce the risk of HIV acquisition via receptive vaginal exposure, and cabotegravir has been approved by the U.S. Food and Drug Administration (FDA) for use as PrEP in people with exposure to HIV. However, safety data are limited for their use during conception, pregnancy, or breastfeeding. Oral tenofovir alafenamide (TAF)/FTC has not been demonstrated to be effective for HIV prevention in people with receptive vaginal exposure.
Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

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HIV pre-exposure prophylaxis (PrEP) is the use of specific antiretroviral (ARV) drugs to prevent HIV acquisition. The use of combination tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as daily oral PrEP to reduce HIV acquisition was approved by the U.S. Food and Drug Administration (FDA) in 2012. When taken as prescribed, TDF/FTC provides greater than 90 percent protection against acquiring HIV. Susceptibility to HIV acquisition is greater during the periconception period, throughout pregnancy, and through 6 months postpartum. Acute or recent HIV infection during pregnancy or breastfeeding is associated with an increased risk of perinatal HIV transmission (see Acute HIV Infection).[1,2] The Panel on Treatment of HIV Infection During Pregnancy and Prevention of Perinatal Transmission (the Panel) recommends that people without HIV who are planning to have a child or who are pregnant or breastfeeding should be offered TDF/FTC as PrEP or referred for PrEP care services when indicated to prevent HIV acquisition and potential perinatal HIV transmission.[3] Although injectable cabotegravir was recently approved by the FDA for use as PrEP in adolescents and adults, it is not recommended for use in pregnancy or breastfeeding.

The guidance in this section focuses on the use of TDF/FTC as PrEP during periconception, antepartum, and postpartum periods (through 6 months postpartum and/or throughout breastfeeding). Most research on PrEP cited in this section was conducted with participants who self-identified as women (presumed to be predominantly cisgender women). However, patients with an intact uterus and ovaries who do not identify as women (i.e., transgender men, genderqueer, or nonbinary individuals) can become pregnant, give birth, and breastfeed or chestfeed. PrEP should be offered and promoted for all individuals with an indication for PrEP using a gender-affirming approach to care (see Transgender People with HIV in the Adult and Adolescent Antiretroviral Guidelines).

Clinical Management of PrEP Use During Periconception, Antepartum, and Postpartum Periods

Initiating and Stopping PrEP

The Centers for Disease Control and Prevention (CDC) has issued guidelines about the use of TDF/FTC PrEP for people at risk of HIV through vaginal exposure.[3] Data suggest that these guidelines miss some people who are at risk.[4] Therefore, the Panel recommends that PrEP for HIV prevention should be discussed with individuals who—

- Have a history of bacterial sexually transmitted infection (STI);[5,6]

- Have infrequent condom use with one or more partners of unknown HIV status, especially within a high-prevalence sexual network;

- Are taking non-occupational post-exposure prophylaxis (nPEP) and anticipate ongoing risk or have used multiple courses of nPEP;[7]

- Engage in transactional sex;

- Have substance use disorder and/or substance use associated with sex;

- Have a partner with HIV without consistent virologic suppression;

- Have a history of experiencing intimate partner violence;[8] or

- Have a partner with any of the factors listed above.

Given possible stigma associated with reporting several of these elements, the Panel also

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recommends offering PrEP to those who feel at risk for HIV exposure or ask for PrEP.

When prescribing PrEP, clinicians should provide the following appropriate information and counseling:

- TDF/FTC is FDA approved for those weighing at least 35 kg.

- Counsel patients about potential risks and benefits of PrEP and all available strategies for reducing HIV acquisition risks during periconception, antepartum, and postpartum periods, including the use of PrEP for safer conception (see Reproductive Options for Couples When One or Both Partners Have HIV). People who become pregnant while using PrEP can continue PrEP throughout their pregnancy.

- Explain that condomless sex with a partner who has sustained viral suppression is associated with effectively no risk of HIV sexual transmission.[9-12]

- Although it is unknown how long PrEP needs to be taken before a person can be considered protected from vaginal HIV exposure, or how long it needs to be continued after last exposure, conservative guidance is to take daily oral TDF plus FTC for 20 days before considering an individual fully protected and to continue it for 28 days after last exposure.[3]

- Prescribe TDF/FTC as a once-daily, fixed-dose combination tablet, whenever possible. Provide counseling about the importance of adherence and suggest adherence supports, such as use of a pillbox (see Adherence Support below).

- Counsel that episodic or on-demand PrEP has not been shown to be effective for vaginal exposure.

- Counsel individuals who are taking PrEP about the symptoms associated with acute HIV infection and instruct them to contact their provider immediately for HIV testing and further evaluation if symptoms occur (see Acute HIV Infection). Patients experiencing symptoms of acute HIV infection should be instructed to use a condom during sex, stop attempts at conception, and stop breastfeeding.

- PrEP does not protect against other STIs. Condom use is important for reducing risks of STI acquisition.

- Regularly assess and discuss ongoing needs for PrEP.

Indications for PrEP use may change across the course of periconception, antepartum, and postpartum periods. Even after the postpartum period, HIV vulnerability may remain. In addition, people may have repeat pregnancies and, therefore, ongoing discussion regarding the possibility of pregnancy (planned or unplanned) and the need for PrEP should continue.

Of note, dapivirine vaginal ring and injectable cabotegravir reduce the risk of HIV acquisition via vaginal exposure, and cabotegravir has been approved by the FDA for use as PrEP in people with vaginal exposure to HIV.[13-15] However, safety and pharmacokinetic data are limited for their use during conception, pregnancy, or breastfeeding. Oral tenofovir alafenamide (TAF)/FTC has not been tested to prevent HIV infection in people with vaginal exposure to HIV.

Laboratory Testing

Recommended laboratory testing for individuals receiving PrEP includes—

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- HIV diagnostic testing with an antigen/antibody combination immunoassay at baseline and then every 3 months, or more frequently if indicated based on clinical symptoms.

- HIV testing for individuals taking PrEP during pregnancy should include HIV testing at entry into antenatal care, with re-testing in the second and third trimester. More frequent testing may be appropriate when clinically indicated (e.g., known adherence challenges) (see Maternal HIV Testing and Identification of Perinatal HIV Exposure).

- If HIV is documented in people receiving PrEP, they should be referred immediately to an HIV specialist, started on ART, and receive appropriate care to prevent perinatal transmission if pregnancy has occurred.

- Renal function testing is recommended at baseline and then every 6 months. TDF/FTC as PrEP should not be initiated in patients with a confirmed calculated creatinine clearance (CrCl) <60 mL/min. Clinicians should discontinue daily TDF/FTC as PrEP if a patient develops a confirmed calculated CrCl <50 mL/min.

- Testing for hepatitis B virus (HBV) infection should be performed before initiating PrEP. Individuals with no prior HBV infection who lack HBV immunity should be vaccinated if they have not received HBV vaccination or consider reimmunization if they have been vaccinated but still lack immunity. Individuals with chronic HBV should be monitored for possible hepatitis flares when PrEP is stopped.[16]

- Pregnancy testing should be completed at baseline and then every 3 months for those who can become pregnant.

- Testing for STIs (gonorrhea, chlamydia, syphilis) is recommended at baseline and then every 3 months.

Additional information and details about recommended laboratory testing is available in the CDC HIV pre-exposure prophylaxis guidelines. Clinicians are encouraged strongly to register people who become pregnant while receiving PrEP with the Antiretroviral Pregnancy Registry.

Adherence Support

Adherence is particularly important to achieve effective drug concentrations in vaginal and cervical tissues and may be even more important in the second and third trimesters of pregnancy, when drug levels drop because of expanding volume of distribution and increased renal clearance. Studies in nonpregnant women demonstrate that it may take up to 20 days to reach maximum intracellular concentrations of tenofovir and/or FTC in cervicovaginal tissue, compared to only 7 days in anal tissues.[17-19] Although pharmacokinetic data are limited in pregnant women, data suggest that pregnant women taking daily PrEP experience lower tenofovir drug levels; it remains unknown what drug level or number of pills per week correlates with protection for this population.[20,21] The available data are limited and the CDC guidelines suggest 20 days are needed to achieve protective levels in cervicovaginal tissues, whereas World Health Organization (WHO) guidelines suggest that 7 days of oral PrEP use are needed to achieve systemic protection from vaginal receptive exposure to HIV.[3,22]

Given the increased volume of distribution and concomitant lower levels of TDF/FTC in plasma, the Panel recommends continued use of other prevention strategies until PrEP has been taken for at least 20 days and protection against transmission can be assumed in pregnant or postpartum PrEP users. Six to seven doses a week (or daily dosing) are needed to maintain drug levels in cervicovaginal

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tissue in nonpregnant women. When people initiate PrEP and have not yet reached protective drug levels or struggle with daily adherence, other strategies should be used to prevent HIV.

Before initiating PrEP, providers should assess barriers to PrEP adherence and address concerns regarding PrEP use during the periconception, antepartum, and postpartum periods. The decision to initiate PrEP should be reached using a shared decision-making process, and barriers to PrEP adherence should be addressed at each visit. Data suggest that some adherence challenges stem from adherence fatigue, low personal perceptions of risk, stigma, cost, misinformation about PrEP, peer perspectives, mental health challenges, and intimate partner violence.[23-25] Based on barriers, providers can discuss strategies tailored to each patient's needs to promote adherence and maximize benefits. Approaches include providing accurate information about the risks and benefits of PrEP, developing reminder strategies, and identifying supportive individuals as part of the health care team or the patient's social network who can provide social support toward PrEP adherence. Just like HIV care, PrEP ideally should be delivered in a comprehensive manner and address social determinants of health—including how clients will make sure that PrEP and related services are affordable—and address housing instability, access to health insurance, and transportation because these factors have been shown to interfere with adherence. CDC provides PrEP resources for providers and consumers and a compendium of evidence-based PrEP support interventions.

Contraception

Contraception is an important component of reproductive health care for people receiving PrEP who do not want to become pregnant.[9] No known significant drug–drug interactions exist between TDF and different modes of hormonal contraception used during periconception and the postpartum period.[26-28] For additional information, refer to CDC's U.S. Medical Eligibility Criteria for Contraceptive Use, 2016 and the most recent update regarding use of contraception by women at high risk of HIV infection.

Background on Use of PrEP During Periconception, Antepartum, and Postpartum Periods

Women account for nearly 20 percent of new HIV diagnoses in the United States, most via heterosexual transmission.[29,30] PrEP is recommended for all people who are vulnerable to HIV acquisition.[3,31] Although data about the use of PrEP among periconception, pregnant, and postpartum people are less robust than for nonpregnant people, PrEP is highly efficacious for women, and a large body of data from pregnant women using TDF/FTC as treatment for HIV and HBV suggests these agents are safe for pregnant and breastfeeding women and their infants.[32-35]

Susceptibility to HIV acquisition is greater during periconception, antepartum, and early postpartum periods through 6 months. Data suggest that people trying to conceive are at higher risk for HIV acquisition, likely due to increased condomless sex.[36,37] The increase in HIV acquisition risk continues in pregnancy and is likely due to a combination of behavioral factors—such as no longer needing to use condoms for contraception—and biological factors that include increased innate and suppressed adaptive immunity, increased genital tract inflammation, alterations in the vaginal microbiome, decreased integrity of the vaginal epithelium, and both gross trauma and microtrauma to the genital tract during delivery.[38-40] HIV incidence among women during pregnancy and postpartum is two to six times greater than outside of pregnancy.[40-44] Two large HIV prevention studies conducted in Africa demonstrated that the probability of HIV acquisition per condomless sex act increases beginning in early pregnancy and peaks in the early postpartum period (in data analyzed

from birth through 24 weeks postpartum in most studies). After adjustment for age, use of PrEP, and male partner HIV viral load, the probability of HIV acquisition was significantly higher throughout pregnancy and the postpartum period (adjusted relative risk 2.76; 95% CI, 1.58–4.81).[45] In addition, people who acquire HIV while pregnant or breastfeeding are more likely to transmit HIV to their infant.[46-48]

Despite the risks of HIV acquisition and known efficacy of PrEP,[33-35] PrEP remains vastly underutilized among women,[49,50] especially during pregnancy and breastfeeding. The American College of Obstetricians and Gynecologists[31] and the WHO[22] agree that all HIV prevention options, including PrEP, should be encouraged for people with HIV vulnerability, especially during pregnancy and breastfeeding, given the increased risk of HIV acquisition during pregnancy and the potential for perinatal transmission with seroconversion during pregnancy. For people with a sexual partner who is taking ART and virally suppressed, the risk of HIV acquisition is effectively zero.[9-11] However, because viral suppression can be variable and not all people with HIV remain in care or maintain effective adherence, some partners of people with HIV may choose to use PrEP.[51] People who inject drugs during pregnancy and postpartum also should be offered PrEP for prevention.[3,31,52]

Efficacy of TDF/FTC as PrEP During Periconception, Pregnancy, and Postpartum Periods

Data from two randomized controlled trials that enrolled heterosexual-identifying men and women demonstrated the efficacy of TDF/FTC as PrEP to be 63 percent to 75 percent. In women with detectable drug levels (or taking PrEP), PrEP protected against 90 percent of incident transmissions.[53] In a meta-analysis of all available clinical trial data, modeling suggested that if women adhere to at least 75 percent of doses, PrEP decreases HIV acquisition by 61 percent (relative risk 0.39; 95% CI, 0.25–0.60).[54]

Although people planning for pregnancy were not enrolled in these clinical trials, subsequent data from demonstration projects suggest that PrEP uptake and adherence are high during periconception periods. In Kenya, 74 HIV-serodifferent couples—including 40 women without HIV—enrolled into a safer conception study. In the month preceding pregnancy confirmation, 81 percent of partners who were HIV negative were highly adherent to PrEP.[55] In South Africa, 526 individuals (334 women and 192 men) from 334 partnerships were enrolled into a study to promote safer conception care. PrEP was initiated as part of safer conception care by 51 percent (n=22) of women without HIV in this study. No sexual or perinatal HIV transmission events were observed.[56] In a small cohort of U.S. women using PrEP to prevent HIV infection during the periconception period, adherence was excellent, with 87% having intracellular tenofovir levels consistent with protection.[57]

Pregnant people are interested in PrEP. In a survey of 200 pregnant women in Washington, D.C., 11 percent reported the intention to initiate PrEP during pregnancy, despite relatively low awareness of PrEP. Pregnant women identified PrEP safety, efficacy, and social network and medical provider support as key factors in PrEP intention.[58] In Kenya, 9,736 pregnant and postpartum women were assessed for behavioral risk factors and willingness to initiate PrEP. Overall, 2,030 women (22%) initiated PrEP.[59] In South Africa, an ongoing observational study of PrEP use in pregnancy observed that 414 (91%) of 455 enrolled women opted to start PrEP at their first antenatal visit.[60]

Safety of TDF/FTC as PrEP for Women, Including Those Who Are Pregnant or

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Breastfeeding

Efficacy trials of TDF/FTC as PrEP excluded women who reported plans to become pregnant and/or were pregnant, but abundant data are available from (a) PrEP use during early pregnancy among women who are HIV negative, due to inadvertent exposure in clinical trials (e.g., pregnancy occurred and the study drug was discontinued once pregnancy was detected); (b) PrEP use during periconception, pregnancy, and breastfeeding from demonstration projects that included pregnant women and those planning for pregnancy; (c) tenofovir use during late pregnancy for HBV treatment in women who are HIV negative; and (d) use of tenofovir and FTC as ART by pregnant women with HIV. These data all indicate that TDF/FTC PrEP is safe for use during pregnancy.

A 2017 systematic review of 26 studies involving TDF and FTC exposure during pregnancy did not identify safety concerns that would limit the use of PrEP in pregnant or lactating women or require discontinuation of PrEP in women who become pregnant while still at continuing risk of HIV acquisition.[32] In 2020, an additional systematic review examined five completed studies that included 1,042 PrEP-exposed pregnancies.[61] Four of the five studies did not observe differences in pregnancy or perinatal outcomes associated with PrEP exposure. One study did find that PrEP-exposed infants had a lower z-score for length at 1 month of age; however, no difference was observed at 1 year. These studies all come from subanalyses of clinical trials. Because pregnant women were excluded from these trials, most of the data regarding PrEP exposure reflect early first-trimester exposures. The authors also noted that at least nine ongoing studies, to be completed by 2022, will provide data on more than 6,200 additional PrEP-exposed pregnancies and will assess perinatal, infant growth, and bone health outcomes. Currently available data suggest that the benefits of TDF/FTC as PrEP to prevent HIV outweigh any potential toxicities. PrEP should be promoted as an HIV prevention strategy during periconception, pregnancy, and postpartum periods.

Additional data and primary sources describing what is known about TDF and FTC on birth outcomes, renal and bone effects for women, and renal and bone effects for infants exposed to TDF/FTC *in utero* or while breastfeeding are available in the Tenofovir Disoproxil Fumarate and Emtricitabine sections of this guideline.

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