

## Pre-exposure Prophylaxis (PrEP) to Reduce the Risk of Acquiring HIV During Periconception, Antepartum, and Postpartum Periods

(Last updated December 29, 2020; last reviewed December 29, 2020)

### Panel's Recommendations

- Health care providers should offer and promote oral combination tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) pre-exposure prophylaxis (PrEP) to individuals who are at risk for HIV and are trying to conceive or are pregnant, postpartum, or breastfeeding (**All**). Indications for PrEP include any 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, those who report feeling at risk for HIV acquisition should be counseled on the benefits and risks of and be offered PrEP.
- 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 (**All**).
- Providers should counsel patients about the benefits of PrEP to reduce the risk of maternal HIV acquisition and perinatal HIV transmission (**AI**) and about potential risks of PrEP to mother and fetus or infant during periconception, pregnancy, postpartum, and breastfeeding periods (**All**).
- 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, PrEP may be optional because 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 PrEP in preventing HIV acquisition (**AI**). Women should be counseled to take a once-daily pill of coformulated TDF/FTC PrEP for 20 days prior to being protected from HIV and therefore should use back-up protection in the interim (**BII**). No 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).

*Other novel PrEP agents including oral tenofovir alafenamide (TAF)/FTC and injectable agents are not yet recommended for people exposed to HIV through receptive vaginal sex.*

**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

### Rationale for Use of PrEP During Periconception, Antepartum and Postpartum Periods

HIV pre-exposure prophylaxis (PrEP) is the use of specific antiretroviral (ARV) drugs to prevent HIV acquisition among persons at risk for acquiring HIV. The use of combination tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) as daily oral PrEP to reduce HIV acquisition among individuals exposed to HIV was approved by the U.S. Food and Drug Administration (FDA) in 2012. When taken as prescribed, TDF/FTC can confer greater than 90 percent protection against acquiring HIV. PrEP is recommended for all people who have condomless sex with a partner with HIV who has not achieved HIV RNA suppression or whose viral suppression status is unknown, and for people with other risks, such as recent sexually transmitted infection (STI), injection drug use, or reporting that one feels at risk for HIV.<sup>1,2</sup> Women account for nearly 20 percent of new HIV diagnoses in the United States, most via heterosexual transmission.<sup>3,4</sup> Although data about the use of PrEP among periconception, pregnant, and postpartum women are less robust than for non-pregnant women,

PrEP is highly efficacious for women, and a large body of data from pregnant women using TDF/FTC as treatment for HIV and hepatitis B virus (HBV) suggests these agents are safe for pregnant and breastfeeding women and their infants.<sup>5-8</sup> Of note, other novel PrEP agents, including oral tenofovir alafenamide (TAF)/FTC and injectable cabotegravir, are not yet approved for people with vaginal exposure to HIV, and only limited safety data are available for their use during pregnancy.

Partners of people with HIV who do not have HIV themselves and are planning to have a child or who are pregnant or breastfeeding should be offered PrEP or referred for PrEP care services when indicated to reduce the risk of HIV acquisition and potential perinatal HIV transmission.<sup>1</sup>

The guidance in this section focuses on the use of PrEP during periconception, antepartum, and postpartum periods (through 6 months postpartum and throughout breastfeeding). Most research on PrEP cited here was conducted with cisgender women, but there are patients who are assigned female at birth, do not identify as female (i.e., transgender men, genderqueer, or non-binary individuals), and become pregnant and give birth. 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.

**Susceptibility to HIV acquisition is greater during periconception, antepartum, and early postpartum periods through 6 months.** Data suggest that women trying to conceive are at higher risk for HIV acquisition, likely due to increased condomless sex.<sup>9,10</sup> 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 and micro-trauma to the genital tract during delivery.<sup>11-13</sup> HIV incidence among women during pregnancy and postpartum is two to six times greater than outside of pregnancy.<sup>13-17</sup> Two large HIV prevention studies conducted in Africa demonstrated 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).<sup>18</sup> In addition, women who acquire HIV while pregnant or breastfeeding are more likely to transmit HIV to their infant. The risk of perinatal transmission is 9 to 15 times higher in women diagnosed with HIV during pregnancy compared to those diagnosed prior to pregnancy.<sup>19-21</sup>

Despite the risks of HIV acquisition and known efficacy of PrEP,<sup>6-8</sup> PrEP remains underutilized among women<sup>22,23</sup>, especially during pregnancy and breastfeeding. The American College of Obstetricians and Gynecologists<sup>2</sup> and the World Health Organization (WHO)<sup>24</sup> agree that all viable HIV prevention options, including PrEP, should be encouraged for women at risk for HIV, especially during pregnancy and breastfeeding, given the increased risk of HIV acquisition during pregnancy and the potential for perinatal transmission with maternal seroconversion during pregnancy. Of note, although the bulk of the data on HIV acquisition risk comes from populations exposed to HIV in the context of sexual exposure, women who inject drugs during pregnancy and postpartum also face substantial risks and should be offered PrEP for prevention.<sup>1,2,25</sup>

## **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 to 75 percent. In women with detectable drug levels (or taking PrEP), PrEP protected against 90 percent of incident transmissions.<sup>26</sup> In a meta-analysis of all available

clinical trial data, a mixed-effects model suggested that if women adhere to at least 75 percent of doses, PrEP decreases HIV acquisition risk by 61 percent (relative risk 0.39, 95% CI, 0.25– 0.60).<sup>27</sup> Although pregnant women were not enrolled in these clinical trials, subsequent data from demonstration projects suggest that PrEP uptake and adherence are high during periconception and pregnancy and can reduce HIV acquisition risks. 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.<sup>28</sup> 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.<sup>29</sup>

In terms of demand for PrEP, pregnant and postpartum women (n=9,736) in the PrEP Implementation in Young Women and Adolescents (PrIYA) program in Kenya were assessed for behavioral risk factors and willingness to initiate PrEP. Overall, 2,030 women (22%) initiated PrEP.<sup>30</sup> 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.<sup>31</sup>

### ***Adherence and Timing Considerations for PrEP Use***

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 non-pregnant 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.<sup>32-34</sup> Although pharmacokinetic data are limited in pregnant women, data suggest that pregnant women taking daily PrEP experience lower drug levels.<sup>35,36</sup> The available data are limited and the Centers for Disease Control and Prevention (CDC) guidelines suggest 20 days are needed to achieve protective levels in cervicovaginal tissues, whereas WHO guidelines suggest that 7 days of oral PrEP use are needed to achieve systemic protection from vaginal receptive exposure to HIV.<sup>1,24</sup> Given the increased volume of distribution and concomitant lower levels of TDF/FTC in plasma, the Panel recommends continued use of other prevention strategies (e.g., condoms) 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 levels in cervicovaginal tissue in non-pregnant women. When women initiate PrEP and have not yet reached protective drug levels or struggle with daily adherence, other strategies should be used to prevent HIV in the presence of ongoing risk factors for acquiring HIV.

### ***Safety of TDF/FTC as PrEP for Women, Including Those Who Are Pregnant or 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, including 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 antiretroviral therapy (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.<sup>5</sup> In 2020, an additional systematic review examined five completed studies that included 1,042 PrEP-exposed pregnancies.<sup>37</sup> 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 sub-analyses 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 for women who are at risk of HIV acquisition during periconception, pregnancy, and postpartum periods.

### ***TDF/FTC and Birth Outcomes***

Data on birth outcomes, including congenital abnormalities, among women who used PrEP during pregnancy are commensurate with the general population.<sup>38-41</sup> In women with HIV who take TDF/FTC as treatment during pregnancy, similarly, no evidence exists of increased aneuploidy, congenital anomalies, or adverse maternal or neonatal pregnancy outcomes, such as low birth weight.<sup>5,42-48</sup> Conflicting data exist regarding a possible association between TDF-containing ART regimens and possible preterm birth, but the evidence is mixed, and benefits of HIV prevention outweigh this possible risk.<sup>49</sup>

### ***Renal and Bone Effects of TDF/FTC as PrEP for Women***

The main toxicities of concern for women taking TDF as PrEP or ART involve the renal and bone systems, based on animal data. Data from humans suggest minimal and reversible impacts to maternal renal systems.<sup>50,51</sup> Reversible bone density changes have been observed in adults taking TDF/FTC as PrEP.<sup>52,53</sup> These data are more limited for exposure during pregnancy or breastfeeding, when bone turnover is high. In a substudy of a randomized controlled trial of TDF to prevent perinatal transmission of HBV, no significant effects of maternal TDF use (from 28 weeks gestation to 2 months postpartum) on maternal bone density were observed at 1 year.<sup>54</sup>

### ***Renal and Bone Effects of TDF/FTC as PrEP for Infants Exposed to PrEP in Utero or During Breastfeeding***

No evidence suggests renal pathophysiology in infants exposed to TDF/FTC in utero. The only signal of bone impact on infants, to date, was in the Partners PrEP clinical trial, in which PrEP-exposed infants had a lower z-score for length at 1 month of age; however, no difference between PrEP-exposed infants and those not exposed was observed at 1 year.<sup>38</sup> In a substudy of a randomized controlled trial of TDF to prevent perinatal transmission of HBV, no significant effects of maternal TDF use (from 28 weeks gestation to 2 months postpartum) on infant or maternal bone density were observed at 1 year.<sup>54</sup>

### ***Impacts of TDF/FTC on Breastfeeding Infants***

TDF/FTC impacts on breastfeeding infants appear to be minimal given that (a) very little drug is contained in breastmilk and (b) the drug in breastmilk is tenofovir (not TDF), which has limited bioavailability.<sup>55</sup> In a short-term study of oral TDF/FTC as PrEP in women without HIV who were breastfeeding, the estimated infant doses from breast milk and plasma concentrations were 12,500-fold (tenofovir) and >200-fold (FTC) lower, respectively, than proposed therapeutic doses for infants. Tenofovir was not detected in 94 percent of plasma samples from infants, suggesting minimal infant exposure.<sup>56</sup> Additional studies confirm minimal systemic exposure to tenofovir and FTC via breastmilk.<sup>55</sup> For women who are at risk for acquiring HIV, the benefits of PrEP appear to outweigh the risks, and the Panel recommends that TDF/FTC as PrEP be offered to people exposed to HIV while breastfeeding.

See the [Tenofovir Disoproxil Fumarate](#) and [Emtricitabine](#) sections for additional data about TDF and FTC during pregnancy and breastfeeding.

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

### *Initiating and Stopping PrEP*

Clinicians who prescribe PrEP should counsel patients about potential risks and benefits and all available strategies for reducing HIV acquisition risks during periconception, antepartum, and postpartum periods. People who become pregnant while using PrEP can continue PrEP throughout their pregnancy and should be counseled regarding risks and benefits as outlined above. CDC has issued guidelines for the use of PrEP for people exposed to HIV through vaginal exposure.<sup>1</sup> It is recommended that an individual who does not have HIV and may be at risk for acquiring HIV through vaginal exposure start daily oral TDF plus FTC beginning 20 days before condomless sex exposure and continuing for 28 days after such exposures.<sup>1</sup> Adherence is easiest with one daily pill, and TDF/FTC is available as a fixed-dose combination tablet. Of note, for people using PrEP for periconception, antepartum, and postpartum periods, indications for PrEP use may change during the course of their reproductive journey; for example, indications for PrEP may resolve if a partner is found not to have HIV or to have HIV-RNA suppression. As the increased risks for HIV acquisition associated with pregnancy and postpartum status resolve, women may have ongoing risks of HIV acquisition, regardless of pregnancy status. In addition, women may have repeat pregnancies and, therefore, ongoing discussion regarding the possibility of pregnancy (planned or unplanned) and the need for PrEP should continue. Because PrEP does not protect against other STIs, condom use remains an important strategy for reducing risks of STI acquisition.

Episodic or on-demand PrEP has not been shown to be effective for vaginal exposure and is not expected to be effective given that six to seven doses per week are required to achieve protective levels in cervicovaginal compartments.

Patients should be counseled that, once their HIV risk is reduced (i.e., a partner with HIV has initiated ART and maintained reliable HIV viral suppression), PrEP should be continued for an additional month to minimize risks of seroconversion. Condomless sex with a partner who has sustained viral suppression is associated with effectively no risk of HIV sexual transmission.<sup>57-60</sup> For additional information, see [Reproductive Options for Couples When One or Both Partners Have HIV](#).

### *Adherence Support*

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.<sup>61-63</sup> Based on barriers, providers can discuss strategies tailored to each woman'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 woman's social network who can provide social support toward PrEP adherence. Just like HIV care, PrEP should ideally 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, since 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](#).

### *Laboratory Testing*

Recommended laboratory testing for individuals receiving PrEP should include 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 pregnant women taking PrEP should include HIV testing

at entry into antenatal care, with re-testing in the second and third trimester. More frequent testing may be appropriate for women when clinically indicated (e.g., adherence challenges, non-standard visit schedule). See [Maternal HIV Testing and Identification of Perinatal HIV Exposure](#).

Renal function testing is recommended at baseline and then every 6 months, and pregnancy testing should be done at baseline and then every 3 months for those who can become pregnant. Testing for 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.<sup>64</sup> 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 strongly encouraged to register women who become pregnant while receiving PrEP with the [Antiretroviral Pregnancy Registry](#).

Individuals who are taking PrEP should be educated about the symptoms that are associated with acute HIV infection and advised to contact their providers immediately for HIV testing and further evaluation if symptoms occur (see [Acute HIV Infection](#)). Patients experiencing symptoms of acute retroviral syndrome should be instructed to use a condom during sex, stop attempts at conception, and stop breastfeeding. If HIV is documented, they should be immediately referred to an HIV specialist, started on ART, and receive appropriate care to prevent perinatal transmission if pregnancy has occurred.

### ***Contraception***

Contraception is an important component of reproductive health care for women receiving PrEP who do not want to become pregnant.<sup>57</sup> No known significant drug-drug interactions exist between TDF and different modes of hormonal contraception used during periconception and the postpartum period, although interactions with FTC have not been studied.<sup>65,66</sup> However, TDF/FTC PrEP does not seem to alter significantly the effectiveness of contraception for pregnancy prevention.<sup>67</sup> For additional information, refer to CDC's [U.S. Medical Eligibility Criteria for Contraceptive Use, 2016](#), a subsequent update addressing hormonal contraception among women at high risk of HIV infection, and the [most recent update](#) regarding use of contraception by women at [high risk of HIV infection](#).

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