Reproductive Options for Couples in Which One or Both Partners are Living with HIV  

Panel’s Recommendations

For Couples Who Want to Conceive When One or Both Partners are Living with HIV:

- Expert consultation is recommended to tailor guidance to couples’ specific needs (AIII).
- Partners should be screened and treated for genital tract infections before attempting to conceive (AII).
- Partners living with HIV should attain maximum viral suppression before attempting conception to prevent HIV sexual transmission (AI) and, for women living with HIV, to minimize the risk of HIV transmission to the infant (AII).
- For couples with differing HIV statuses, when the partner living with HIV is on ART and has achieved sustained viral suppression, sexual intercourse without a condom limited to the 2 to 3 days before and the day of ovulation (peak fertility) is an approach to conception with effectively no risk of sexual HIV transmission to the partner without HIV (BII).
- Partners living with HIV should attain maximum viral suppression before attempting conception to prevent HIV sexual transmission (AI) and, for women living with HIV, to minimize the risk of HIV transmission to the infant (AII). Couples should still be counseled to limit sex (without condoms) to the period of peak fertility (AII).
- When the woman is living with HIV, assisted insemination at home or in a provider’s office with semen from a partner without HIV during the periovulatory period is an option for conception that eliminates the risk of HIV transmission to the partner without HIV (AIII).
- When the man is living with HIV, the use of donor sperm from a man without HIV is an option for conception that eliminates the risk of HIV transmission to the partner without HIV (BIII).
- For couples with differing HIV statuses who attempt conception (sexual intercourse without a condom limited to peak fertility) when the partner living with HIV has achieved viral suppression, it is unclear whether administering PrEP to the partner without HIV further reduces the risk of sexual transmission (CIII).

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

The objective of this section is to provide guidance for safe conception and pregnancy while maximizing efforts to prevent HIV transmission to partners and infants. For couples who want to conceive while one or both partners are living with HIV, expert consultation is recommended so that approaches can be tailored to their specific needs.

For couples in which one or both partners are living with HIV, couples should be counseled to only attempt conception after the partners living with HIV have initiated antiretroviral therapy (ART) and have achieved sustained suppression of plasma viral load below the limits of detection.

Before attempting to conceive, both partners should be screened for genital tract infections. Treatment of such infections is important, because genital tract inflammation is associated with genital tract shedding of HIV.1-6

Couples with Differing HIV Statuses

Before attempting conception, the partner living with HIV should be on ART and have achieved sustained suppression of plasma viral load below the limits of detection. HPTN 052 was a randomized clinical trial designed to evaluate whether immediate initiation of ART in people with CD4 T lymphocyte (CD4) cell counts of 350 to 550 cells/mm3 could prevent sexual transmission of HIV among couples with differing HIV statuses more effectively than delaying ART. Most of the participants were from Africa (54%), with 30% from Asia and 16% from North and South America. This study showed that earlier initiation of ART led to a 93% reduction in sexual transmission of HIV to the partner. Of 46 cases of HIV infection documented to be genetically linked to the partner living with HIV, 43 cases occurred among the 877 couples in which the partner living with HIV delayed initiation of ART until the CD4 cell count fell below 250 cells/mm3, and three cases of HIV infection occurred among the 886 couples in which a partner living with HIV began
immediate ART. Thus, this randomized trial clearly demonstrated that provision of treatment to persons living with HIV can reduce the risk of transmission of HIV to their sexual partners. In addition, the PARTNERS trial—which studied 1,166 couples of differing HIV statuses (both heterosexual couples and men who have sex with men) where the partner with HIV was on suppressive ART and had sex without using a condom—had no cases of transmission after 1.3 years.

Among 161 couples with differing HIV statuses (133 couples included a male partner living with HIV) where the partner living with HIV received suppressive ART and the couple opted for natural conception, a total of 144 natural pregnancies occurred and 107 babies were born. No cases of sexual (to partner) or vertical (to infant) transmission occurred.

It is important to recognize that no single method (including treatment of the partner living with HIV) is fully protective against transmission of HIV, though the risk appears to approach zero when the partner living with HIV maintains a consistently undetectable plasma viral load on ART. Effective ART that decreases plasma viral load to undetectable levels is also associated with decreased concentration of virus in genital secretions. However, discordance between plasma and genital viral loads has been reported, and individuals with an undetectable plasma viral load may have detectable genital tract virus. In addition, antiretroviral (ARV) drugs vary in their ability to penetrate the genital tract. In a prospective study of 2,521 African couples with differing HIV statuses, higher genital HIV RNA concentrations were associated with greater risk of heterosexual HIV-1 transmission, and this effect was independent of plasma HIV concentrations. Each log₁₀ increase in genital HIV-1 RNA levels increased the risk of female-to-male or male-to-female HIV transmission by 1.7-fold. However, there were no cases of transmission in the context of undetectable plasma viral load but detectable genital tract HIV.

In addition to reducing the risk of HIV transmission between partners, starting ART before conception in women living with HIV may also further reduce the risk of perinatal transmission. Evidence suggests that early and sustained control of HIV may decrease the risk of perinatal transmission, but it does not completely eliminate the risk of perinatal transmission. In addition, reports are mixed on the possible effects of ART on prematurity and low birthweight, with some, but not all, data suggesting that such outcomes may be more frequent in women on ART at conception.

The implications of initiating therapy before conception and the need for strict adherence to achieve plasma viral load below the limits of detection should be discussed with the couple. Consultation with an expert in HIV care is strongly recommended.

**Options for Safer Conception**

When a woman living with HIV is in a serodiscordant relationship, assisted insemination during the periovulatory period at home or in a provider’s office with semen from a partner without HIV infection is an option for conception that eliminates the risk of HIV transmission to her partner.

When a man living with HIV is in a serodiscordant relationship, the use of donor sperm from a man without HIV is an option for conception that eliminates the risk of HIV transmission to the partner without HIV.

However, as described above, studies have shown that the risk of HIV infection to the partner without HIV is very low when the partner living with HIV is on ART and has demonstrated sustained plasma viral load below the limits of detection. For couples with differing HIV statuses, where the partner living with HIV is on ART and has achieved sustained viral suppression, sexual intercourse without a condom that occurs only during the 2 to 3 days before ovulation and on the day of ovulation (peak fertility) is an approach to conception with effectively no risk of sexual HIV transmission to the partner without HIV. The use of an ovulation kit is the optimal method for identifying the most fertile time of the cycle.

When a man living with HIV is in a serodiscordant relationship, the use of sperm preparation techniques coupled with either intrauterine insemination or in vitro fertilization with intracytoplasmic sperm injection has been reported. However, the appropriate role of semen preparation techniques in the current context is
unclear, particularly given their expense and technical requirements. These sperm preparation techniques were largely developed before studies had demonstrated the efficacy of ART and pre-exposure prophylaxis (PrEP) in decreasing transmission to sexual partners without HIV. Sperm preparation techniques may be useful in cases of male infertility.

**Pre-Exposure Prophylaxis Provision and Monitoring in Couples with Differing HIV Statuses**

For serodiscordant couples who attempt conception via sexual intercourse without a condom (despite counseling) when the partner living with HIV has not been able to achieve viral suppression or when viral suppression status is not known, administration of antiretroviral PrEP to the partner without HIV is recommended to reduce the risk of sexual transmission of HIV. PrEP is the use of ARV medications by an individual who is HIV negative to maintain blood and genital drug levels sufficient to prevent acquisition of HIV. Only daily dosing of a combination of tenofovir disoproxil fumarate (TDF) and emtricitabine is currently Food and Drug Administration-approved for use as PrEP. **Adherence is critical.** Couples should still be counseled to limit sex without a condom to the period of peak fertility. If conception does not occur 6 months providers should pursue a workup for infertility, including a semen analysis. HIV, and possibly ART, may be associated with a higher prevalence of sperm abnormalities, such as low sperm count, low motility, a higher rate of abnormal forms, and low semen volume. Early evaluation is indicated to limit periods of unprotected sex in the context of infertility.  

Sun et al. reported on 91 serodiscordant couples (43 with men living with HIV and 48 with women living with HIV) in which the partner with HIV was on effective ART, the partner without HIV received PrEP (or post-exposure prophylaxis), and intercourse was timed to maximally reduce the risk of HIV transmission. There were 196 acts of intercourse without a condom, 100 natural conceptions, and 97 live births. There were no cases of HIV seroconversion in the sexual partner without HIV.  

One study followed 1,013 Kenyan and Ugandan serodiscordant couples (67% of couples involved women living with HIV) who had a high risk of sexual transmission. After an integrated ART and PrEP strategy for HIV prevention was implemented, there were no HIV transmissions to male partners among these couples. Only two incident infections were observed in the women (HIV incidence of 0.2 per 100 person years). These two infections occurred in the absence of ART or PrEP.  

Many studies have demonstrated that PrEP reduces the risk of HIV acquisition in both men and women, with minimal risk of incident ARV resistance. Other trials failed to demonstrate PrEP efficacy, likely because of suboptimal levels of adherence.  

Table 4 summarizes clinical trials of PrEP.
Table 4. Clinical Trials of Pre-Exposure Prophylaxis

<table>
<thead>
<tr>
<th>Trial</th>
<th>Study Population</th>
<th>Location</th>
<th>Intervention</th>
<th>Outcome</th>
<th>Comments</th>
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<tbody>
<tr>
<td>TDF2</td>
<td>1,219 sexually active adults; 55% male, 45% female; 94% unmarried; approximately 90% aged 21–29 years</td>
<td>Botswana</td>
<td>Daily oral TDF/FTC</td>
<td>63% protection</td>
<td>&gt;30% did not complete study; cannot draw definitive conclusions for women and men separately.</td>
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<tr>
<td>PIP</td>
<td>4,758 serodiscordant heterosexual couples; 38% HIV-negative female partner, 62% HIV-negative male partner, 98% married; median age 33 years</td>
<td>Botswana, Kenya, Rwanda, South Africa, Tanzania, Uganda, Zambia</td>
<td>Daily oral TDF or TDF/FTC</td>
<td>67% protection with TDF alone; 75% protection with TDF/FTC</td>
<td>Serodiscordant couples may be a distinct, unique population.</td>
</tr>
<tr>
<td>FEM-PrEP</td>
<td>1,951 heterosexual women aged 18–35 years and at high risk of infection</td>
<td>Kenya, South Africa, Tanzania</td>
<td>Daily oral TDF/FTC</td>
<td>Trial discontinued for futility in April 2011</td>
<td>Adherence assessment with monthly clinical samples to measure drug concentration is pending.</td>
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<tr>
<td>VOICE</td>
<td>5,029 heterosexual women aged 18–45 years in areas with a high prevalence of HIV</td>
<td>Uganda, South Africa, Zimbabwe</td>
<td>Daily oral TDF or daily oral TDF/FTC or daily topical TFV gel</td>
<td>No study drug significantly reduced the risk of HIV acquisition. Estimates of effectiveness were &lt;0 for TDF and TDF/FTC daily oral dosing (negative 48.8% and negative 4.2% TDF/FTC, respectively), and reduced risk of HIV infection of 14.7% for TFV gel.</td>
<td>Adherence to study drugs was low; TFV was detected in 30% of the oral TDF arm, 29% in the oral TDF/FTC arm, and 25% in the TFV gel arm.</td>
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**Key to Acronyms:** FTC = emtricitabine; TDF = tenofovir disoproxil fumarate; TFV = tenofovir

Pregnancy and breastfeeding are not contraindications to PrEP. There is no evidence of an increase in congenital anomalies among children born to women exposed to TDF or emtricitabine during the first trimester. Data from studies of infants born to mothers living with HIV and exposed to TDF through breast milk suggest limited drug exposure. Condom use should be encouraged during pregnancy, because several studies have reported increased incidence of HIV acquisition during pregnancy, which may also lead to increased perinatal transmission.

For couples with differing HIV status who attempt conception (sexual intercourse without a condom limited to periods of peak fertility) when the partner living with HIV has achieved viral suppression, it is unclear if PrEP for the partner without HIV further reduces the risk of sexual transmission. A modeling study analyzed the utility of PrEP under different conditions. In an analysis by Hoffman et al., PrEP provided little added benefit when the male partner was on ART, had a suppressed viral load, limited sex without a condom to the ovulation window, and optimized other modifiable transmission risks.

If clinicians elect to prescribe PrEP in couples with differing HIV status, couples should be educated about the potential risks and benefits and all available alternatives for safer conception. The Centers for Disease Control and Prevention (CDC) has issued guidelines for the use of PrEP in sexually active heterosexual adults. The CDC recommends that an individual who does not have HIV and is planning a pregnancy with a partner who does have HIV start daily oral TDF plus emtricitabine beginning 1 month before conception is attempted and continuing for 1 month after conception is attempted. Recommended laboratory testing should include...
HIV diagnostic testing at baseline and then every 3 months, renal function testing at baseline and then every 6 months, and pregnancy testing at baseline and then every 3 months. Testing for hepatitis B virus (HBV) infection should be performed before initiating PrEP. Individuals without HBV infection should be vaccinated if they have not received HBV vaccination or they lack immunity to HBV. Individuals receiving PrEP should be educated about symptoms associated with acute HIV infection and advised to contact their providers immediately for further evaluation if symptoms occur. Partners who are HIV negative should undergo frequent HIV testing to detect HIV infection quickly. If HIV infection is documented, the PrEP ARV agents should be discontinued to minimize selection of drug-resistant virus, measures should be instituted to prevent perinatal transmission if pregnancy has occurred and attempts at conception should be stopped if pregnancy has not occurred, and the patient should be referred to an HIV specialist immediately. Individuals with chronic HBV should be monitored for possible hepatitis flares when PrEP is stopped. Clinicians are strongly encouraged to register women who become pregnant while receiving PrEP with the Antiretroviral Pregnancy Registry.

Couples Where Both Partners are Living with HIV

Both partners should be on ART with maximum viral suppression before attempting conception. Periovulatory unprotected intercourse (with use of condoms at all other times) is a reasonable option for monogamous couples. The risk of HIV superinfection or infection with a resistant virus is negligible when both partners are on ART and have fully suppressed plasma viral loads.

Monitoring of Pregnant Women Without HIV who have Partners with HIV

Women without HIV who present during pregnancy and indicate that their partners are living with HIV should, like all pregnant women, be notified that HIV screening is recommended and that they will receive an HIV test as part of the routine panel of prenatal tests unless they decline (i.e., “op-out strategy”). Pregnant women without HIV should also be counseled to always use condoms to reduce the risk of HIV acquisition and informed that their partners with HIV should have attained virologic suppression on ART. These women should be tested for HIV at least once per trimester, or more often if the partner’s viral load is not known. Acute HIV infection during pregnancy increases the risk of transmitting HIV to the fetus (see Acute Infection). A woman who presents in labor with suspicion of acute seroconversion should be screened with an expedited HIV test and offered zidovudine during labor. If results are not received until after delivery, the infant can also start ARV drug(s) until a negative test is obtained. If at any time during pregnancy a clinician suspects that a pregnant woman may be in the “window” period of seroconversion (i.e., she has signs or symptoms consistent with acute HIV infection), then a plasma HIV RNA test should be used in conjunction with an HIV antigen/antibody fourth-generation test. If the plasma HIV RNA is negative, it should be repeated in 2 weeks. Pregnant women who do not have HIV but who have partners who are living with HIV should be counseled on methods to prevent acquisition of HIV, including suppressive ART for her partner, PrEP, and condom use. Women should be counseled regarding the symptoms of acute retroviral syndrome (i.e., fever, pharyngitis, rash, myalgia, arthralgia, diarrhea, and headache) and the importance of seeking medical care and testing if they experience such symptoms.

Women who test HIV seropositive on either conventional or rapid HIV tests should receive appropriate evaluation and interventions to reduce perinatal transmission of HIV, including immediate initiation of appropriate ART and consideration of elective cesarean delivery according to established guidelines (see Transmission and Mode of Delivery). In cases where confirmatory test results are not readily available, such as with rapid testing during labor, it is still appropriate to initiate interventions to reduce perinatal transmission (see Infant Antiretroviral Therapy/Prophylaxis).

Women who test HIV seronegative and have partners who are living with HIV should continue to be regularly counseled regarding consistent condom use to decrease their risk of sexual transmission of HIV. They should also be counseled on the importance of their partners’ adherence to ART and the need for achievement of sustained virologic suppression to reduce the risk of sexual transmission of HIV. Women with primary HIV infection during pregnancy or lactation are at high risk of transmitting HIV to their infants.
Coordination of care across multiple disciplines, including HIV primary care, Ob/Gyn, family planning, case management, and peer support, is advised. Integration of reproductive health counseling, including pregnancy desires and/or prevention, is recommended.

**Monitoring of Men Without HIV Who Have Female Partners with HIV**

Men who are HIV seronegative and are attempting pregnancy with women partners who are living with HIV should continue to be regularly counseled regarding consistent condom use to decrease the risk of sexual transmission of HIV. They should also be counseled on the importance of their partners’ adherence to ART and the need to achieve sustained virologic suppression to reduce the risk of sexual transmission of HIV. They should be tested for HIV every 3 months while attempting conception without condoms.

The National Perinatal HIV Hotline (1-888-448-8765) is a resource for a list of institutions offering reproductive services for HIV concordant/serodiscordant couples.

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