

# Clinical Practice Guidelines for Providing PrEP for Pregnant and Breastfeeding Populations



## Table of Contents

Background .....	5
WORLD HEALTH ORGANIZATION Guidelines .....	6
Summary of evidence for PrEP safety during pregnancy and breastfeeding .....	7
Medications prescribed in pregnancy and postpartum periods .....	9
Before starting PrEP .....	10
Identifying pregnant and breastfeeding clients for PrEP use .....	10
Contraindications for PrEP use .....	11
Bringing up the topic of PrEP for pregnant and breastfeeding women.....	11
PrEP use counseling.....	12
Ruling out current HIV infection before starting PrEP .....	14
Laboratory testing before starting PrEP USE .....	14
Documentation in the client's clinical record.....	15
Scheduling follow-up contacts and promoting PrEP continuation .....	15
Client-centered care after starting PrEP .....	16
Integration of PrEP into care for pregnant and breastfeeding clients.....	16
Family planning settings providing PrEP for breastfeeding clients.....	16
Managing PrEP side effects during pregnancy and postnatal period.....	17
Laboratory data: monitoring kidney function during pregnancy.....	19
Monitoring kidney function during the postnatal period.....	20
Deciding whether to pause or stop PrEP use for pregnant and breastfeeding women .	21
Stopping PrEP use due to HIV seroconversion .....	22
Evaluating potential problems in breastfeeding infants.....	23
Transitioning between clinical contexts or service delivery settings.....	23

PrEP use in special situations .....	24
PrEP use in women with hypertensive disorders of pregnancy .....	24
Hepatitis B infection during pregnancy.....	27
Other important services at settings providing PrEP for pregnant and breastfeeding women.....	27
Other HIV prevention and family planning/reproductive health services .....	27
Screening for intimate partner violence .....	28
Appendix 1. Sample Checklist for PrEP Start-up for Pregnant and Breastfeeding Clients ...	31

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## Background

The antenatal and postnatal periods may include complex health care decisions, including identifying best strategies for helping clients to avoid acquiring HIV. Health care providers and their clients need to understand available options and the evidence on potential benefits and harms. Consideration of a client's age, gender, comorbidities, contextual risks, preferences, and a range of practical constraints such as cost supports a comprehensive approach to making these decisions.

Pre-exposure prophylaxis (PrEP) has been shown to prevent HIV infection in different HIV-negative populations throughout the world. In most settings, PrEP regimens use co-formulated TDF/emtricitabine (TDF/FTC) to prevent HIV acquisition. World Health Organization (WHO) guidelines state that oral PrEP (containing TDF) should be offered as an additional prevention choice for people at substantial risk of acquiring HIV as part of combination prevention approaches,<sup>1</sup> and in some settings, this has included co-formulated TDF/lamivudine (TDF/3TC).

Evidence has shown that women are at increased risk of HIV acquisition during pregnancy and breastfeeding.<sup>2,3,4</sup> This increased risk is due to a combination of biological, social, and behavioral factors. Women who become infected with HIV during pregnancy and breastfeeding have a higher risk of transmitting HIV to their infants, compared to women who became infected with HIV before becoming pregnant. Given evidence that PrEP is a safe and appropriate strategy for pregnant and breastfeeding women, increased vulnerability during these periods, and implications for potential transmission to infants, it is important to include and prioritize these populations in PrEP screening, delivery, and management.

**This document is intended to build on and be complementary to the comprehensive existing WHO guidelines and the WHO *Implementation tool for pre-exposure prophylaxis of HIV infection*.**<sup>5</sup> The guidance herein also assumes that clients are receiving appropriate antenatal care (ANC) during pregnancy, facility-based delivery with a skilled birth attendant, and recommended postnatal care (PNC) in accordance with national guidelines.

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<sup>1</sup> WHO. 2015. Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV. [https://apps.who.int/iris/bitstream/handle/10665/186275/9789241509565\\_eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/186275/9789241509565_eng.pdf).

<sup>2</sup> Drake et al. Incident HIV during pregnancy and postpartum and risk of mother-to-child HIV transmission: a systematic review and meta-analysis. *PLOS Medicine*. 2014;11(2):e1001608.

<sup>3</sup> Gray et al. Increased risk of incident HIV during pregnancy in Rakai, Uganda: a prospective study. *Lancet*. 2005;366(9492):1182–8.

<sup>4</sup> Mugo et al. Increased risk of HIV-1 transmission in pregnancy: a prospective study among African HIV-1-serodiscordant couples. *AIDS*. 2011;25(15):1887–95.

<sup>5</sup> At: <https://www.who.int/hiv/pub/prep/prep-implementation-tool/en/>.

## WORLD HEALTH ORGANIZATION GUIDELINES

WHO guidance supports provision of PrEP to pregnant and breastfeeding women who are at continuing substantial risk of HIV infection [Box 1].

### Box 1. 2015 WHO RECOMMENDATION ON PREP

Oral PrEP (containing TDF) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches.

*High-quality evidence, strong recommendation*

This recommendation is also included in the following WHO guidelines, recommendations, and technical briefing papers:

- *Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection: recommendations for a public health approach – 2nd edition.*<sup>6</sup>
- The 2016 *WHO recommendations on ANC for a positive pregnancy experience.*<sup>7</sup> The text of the recommendation is below [Box 2].
- *WHO Technical Brief: Preventing HIV during pregnancy and breastfeeding in the context of PrEP.*<sup>8</sup>

### Box 2. 2016 WHO RECOMMENDATION ON PREP USE IN PREGNANCY

Oral pre-exposure prophylaxis (PrEP) containing tenofovir disoproxil fumarate (TDF) should be offered as an additional prevention choice for pregnant women at substantial risk of HIV infection as part of combination prevention approaches.<sup>2</sup>

This recommendation from the WHO publication *Guideline on when to start antiretroviral therapy and on pre-exposure prophylaxis for HIV* was integrated into the 2016 *WHO recommendations on antenatal care for a positive pregnancy experience*. Substantial risk of HIV infection is defined by an incidence of HIV infection in the absence of PrEP that is sufficiently high (>3% incidence) to make offering PrEP potentially cost-saving (or cost-effective). Offering PrEP to people at substantial risk of HIV infection maximizes the benefits relative to the risks and costs.

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<sup>6</sup> At: <https://www.who.int/hiv/pub/arv/arv-2016/en/>.

<sup>7</sup> At: [https://www.who.int/reproductivehealth/publications/maternal\\_perinatal\\_health/anc-positive-pregnancy-experience/en/](https://www.who.int/reproductivehealth/publications/maternal_perinatal_health/anc-positive-pregnancy-experience/en/).

<sup>8</sup> At: <https://www.who.int/hiv/pub/toolkits/prep-preventing-hiv-during-pregnancy/en/>.

Further guidance on identifying clients at substantial risk for acquiring HIV is included in this document in the section, IDENTIFYING PREGNANT AND BREASTFEEDING CLIENTS FOR PREP USE.

### **SUMMARY OF EVIDENCE FOR PREP SAFETY DURING PREGNANCY AND BREASTFEEDING**

PrEP use has been shown to be generally safe across a range of different countries and populations, based on data that have been gathered so far. Most PrEP clients do not experience significant side effects. Based on data gathered from non-pregnant PrEP users, it is estimated that about one in 10 people who take PrEP may have mild side effects. These side effects may include mild kidney problems that are only detected by laboratory tests, inability to sleep, decreased energy or tiredness, headache, upset stomach, passing gas, vomiting, soft or liquid stools, and dizziness. For most users, gastrointestinal symptoms typically resolve within the first few weeks of use, often sooner. Some side effects of PrEP may be confused with symptoms of early pregnancy (e.g., nausea, vomiting, and fatigue) (further detailed in Table 3, later in this document). People with hepatitis B infection who suddenly stop taking PrEP may have a worsening of hepatitis symptoms (see the section, HEPATITIS B INFECTION DURING PREGNANCY.

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*About one in 10 PrEP users may have side-effects such as nausea, abdominal cramps, or headache. These are usually mild and resolve in the first few weeks of taking PrEP. About one in 200 may have creatinine elevation (typically reversible if the client stops PrEP). PrEP users may experience about 1% average loss of bone mineral density (also recovers after stopping PrEP).*

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Studies have shown that exposure to TDF and FTC as treatment during pregnancy among women living with HIV is safe and well tolerated. Limited studies of PrEP among pregnant women not living with HIV are also reassuring.<sup>9</sup> A recent systematic review identified 14 studies (five completed; nine planned) that evaluated or will evaluate maternal and/or infant outcomes following PrEP exposure during pregnancy or breastfeeding.<sup>10</sup> None of the completed studies found differences in pregnancy or perinatal outcomes associated with PrEP exposure.

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<sup>9</sup> Mofenson et al. Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding. *AIDS*. 2017;31(2):213–32.

<sup>10</sup> Davey et al. Emerging evidence from a systematic review of safety of pre-exposure prophylaxis for pregnant and postpartum women: where are we now and where are we heading? *J Int AIDS Soc*. 2020 Jan;23(1): e25426.

In general, oral PrEP has been well tolerated by breastfeeding mothers and infants. In previous research, symptoms were generally mild and resolved quickly. Some mothers had mild abdominal pain, diarrhea, and nausea, and a few infants had diarrhea. However, for both mothers and infants, the symptoms resolved in 2–3 days. The amount of PrEP drug that passes into milk has been shown to be very low.<sup>11, 12</sup>

Lamivudine (3TC) is a medication (nucleoside analog) used for HIV treatment, in combination with other antiretroviral drugs. Research has also shown a reassuring safety profile for lamivudine, in both non-pregnant and pregnant populations. As noted previously, some countries—including Pakistan, South Sudan, Namibia, Kenya, Zambia, and Zimbabwe—have PrEP recommendations that allow use of a regimen containing lamivudine for PrEP (TDF/3TC) in addition to TDF/FTC. Lesotho’s guidelines currently recommend exclusively TDF/3TC for PrEP; in Lesotho, TDF/3TC has been part of the nucleoside reverse transcriptase inhibitor backbone since the onset of HIV treatment services, including for pregnant women.

Data from the Antiretroviral Pregnancy Registry (a collection of data from different studies of antiretroviral medicines used during pregnancy) showed fewer spontaneous abortions and preterm births with use of lamivudine-containing regimens compared to use of antiretroviral regimens that did not include lamivudine, in the context of HIV treatment.<sup>13</sup> In a large U.S. study of infants without HIV born to women living with HIV, lamivudine exposure during pregnancy was not associated with increased risk of adverse infant outcomes in growth, hearing, language, neurodevelopment, metabolic, hematologic/clinical chemistry, or blood lactate outcomes.<sup>14</sup> Based on reports of over 11,000 exposures to lamivudine during pregnancy resulting in live births (including over 4,500 exposed during the first trimester), there was no difference between the overall risk of birth defects for lamivudine compared to the background birth defect rate of 2.7% in the U.S. reference population used for the registry.<sup>15</sup>

A note of caution when using regimens containing 3TC in patients living with hepatitis B virus (HBV) infection: It is possible that HBV flare may occur if lamivudine is stopped in a person

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<sup>11</sup> U.S. National Library of Medicine. 2006. Tenofovir. At: [https://www.ncbi.nlm.nih.gov/books/NBK501549/pdf/Bookshelf\\_NBK501549.pdf](https://www.ncbi.nlm.nih.gov/books/NBK501549/pdf/Bookshelf_NBK501549.pdf). Accessed 29 July 2020.

<sup>12</sup> WHO. 2017. Technical brief: Preventing HIV during pregnancy and breastfeeding in the context of pre-exposure prophylaxis (PrEP).

<sup>13</sup> Vannappagari et al. Abacavir and Lamivudine Exposures During Pregnancy and Non-defect Adverse Pregnancy Outcomes. *JAIDS*. 2015;68(3):359–364.

<sup>14</sup> Williams et al. Antiretroviral Exposure During Pregnancy and Adverse Outcomes in HIV-exposed Uninfected Infants and Children Using a Trigger-based Design: The SMARTT Study. *AIDS*. 2016;30(1):133–144.

<sup>15</sup> Antiretroviral Pregnancy Registry Steering Committee. 2019. Antiretroviral Pregnancy Registry Interim Report for 1 January 1989 through 31 July 2019.



who has HBV. Additional guidance is available in the section, HEPATITIS B INFECTION DURING PREGNANCY.

### **MEDICATIONS PRESCRIBED IN PREGNANCY AND POSTPARTUM PERIODS**

Part of understanding medication safety is understanding potential drug interactions. The medications used in PrEP have no known interactions with the medications most commonly prescribed in pregnancy, including but not limited to the following:

- Iron and folic acid tablets, multiple micronutrient supplements, or prenatal vitamins
- Penicillin injection for treatment of syphilis or other antibiotics used for treatment of sexually transmitted infections
- Antibiotics for asymptomatic bacteriuria or urinary tract infection
- Tetanus toxoid or pertussis vaccines
- Intermittent prophylactic treatment of malaria in pregnancy with sulfadoxine-pyrimethamine (where this is used)
- Preventive chemotherapy (deworming), using single-dose albendazole (400 mg) or mebendazole (500 mg)
- Multiple micronutrient supplements, balanced energy and protein supplements, calcium supplements, or vitamin A
- Stool softeners such as docusate sodium
- Medications and supplements recommended in the 2016 WHO ANC guidelines for treatment of common physiologic symptoms of pregnancy, such as the following:
  - Ginger, chamomile, and vitamin B6 for nausea and vomiting
  - Antacid preparations for women with troublesome symptoms of heartburn that are not relieved by lifestyle modification
  - Wheat bran or other fiber supplements to relieve constipation in pregnancy if the condition fails to respond to dietary modification

The medications used in PrEP have no known interactions with the medications most commonly prescribed to women in the postnatal period, including but not limited to the following:

- Family planning methods such as oral contraceptive pills, injectable progestin methods, sub-dermal implants, intrauterine devices, and barrier methods
- Medications commonly used for fever and pain (e.g., paracetamol)
- Antibiotics

- Malaria treatment medications
- Anti-diarrheal medications
- Rubella vaccine

## Before starting PrEP

### IDENTIFYING PREGNANT AND BREASTFEEDING CLIENTS FOR PREP USE

**In settings of high HIV incidence, all HIV-negative pregnant and breastfeeding women should be considered candidates for PrEP, unless individual clinical contraindications exist.**<sup>16</sup> Even ANC and PNC clients who are presumably in a monogamous relationship with a confirmed HIV-negative partner are at risk for acquiring HIV during pregnancy and breastfeeding, due to a range of factors, including the possibility of their own or their partners' undisclosed additional partners, changes in condom use patterns, sexual violence, and transactional sex.

Comprehensive application of this recommendation includes all of the following types of clients:

- Routine ANC and PNC clients;
- Clients who are taking PrEP and then subsequently become pregnant;
- Clients seeking pregnancy, currently pregnant, or currently breastfeeding, with partner(s) who may:
  - Have unknown HIV status;
  - Be living with HIV, but not on HIV treatment;
  - Be living with HIV, but on treatment less than 6 months, not virally suppressed, or viral suppression status unknown;
- Clients who may access PrEP through facility- or community-based PrEP delivery programs, including adolescent girls and young women.

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<sup>16</sup> Machezano et al. HIV incidence among pregnant and postpartum women in a high prevalence setting. PLOS ONE. 2018;13(12): e0209782.

## CONTRAINDICATIONS FOR PREP USE

Contraindications for PrEP use in pregnancy and breastfeeding include the same contraindications used for non-pregnant, non-breastfeeding clients:

- HIV;
- Signs/symptoms of acute HIV infection (see Box 3);
- Probable recent exposure to HIV;
- Estimated creatinine clearance of less than 60 ml/min (if known);
- Allergy or contraindication to any medicine in the PrEP regimen; and
- Unable to commit to adhere to PrEP and attend scheduled visits.

### Box 3. SIGNS AND SYMPTOMS OF ACUTE HIV INFECTION

Acute HIV infection may include signs and symptoms of fever, sore throat, aches and pains, lymphadenopathy (swollen glands), mouth sores, headache, or rash. If the client has any of these signs or symptoms, the health provider should consider the possibility that acute HIV is present. In such circumstances, consider deferring PrEP start for 4 weeks and having the person tested for HIV again, which will allow time for possible HIV seroconversion to be detected.

In addition to the contraindications listed above, it is prudent to avoid starting PrEP on clients with suspected or confirmed diagnosis of a condition that may impair the function of their liver or kidneys, such as pre-eclampsia. In the case of pre-eclampsia, it is generally safe to start or restart PrEP after delivery, provided that the client has normal laboratory tests for kidney function (e.g., serum creatinine), as most cases of pre-eclampsia resolve shortly after birth. A sample eligibility checklist is provided in the Appendix.

Further guidance is available in the WHO *Implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection (Module 1: Clinical)*, including comprehensive guidance on eligibility for PrEP, practical screening questions, a sample record form for PrEP and HIV post-exposure prophylaxis (PEP) screening, and general contraindications to PrEP.

## BRINGING UP THE TOPIC OF PREP FOR PREGNANT AND BREASTFEEDING WOMEN

The topic of PrEP for pregnant and breastfeeding women (PBFW) may be introduced in a variety of different community- and facility-based contexts. At any entry point to care, discuss the option of PrEP for PBFW (Figure 1).





 <p>In group counseling sessions for ANC or PNC clients and/or their partners</p>	 <p>During individual ANC contacts at community or facility level</p>	 <p>During individual PNC and family planning contacts at community or facility level</p>	 <p>In other community-based settings</p>
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Figure 1. Bring up PrEP for PBFW at a variety of settings

If introducing the topic at an individual ANC or PNC contact, it may be helpful to bring up PrEP whenever discussing other preventive interventions that protect the mother and baby, such as taking daily iron and folic acid tablets. This helps to normalize PrEP as care available to every pregnant woman. One option is to start by asking the client if they have heard about PrEP before, and then counsel the client on what PrEP is, its safety during pregnancy and breastfeeding, and how they start PrEP in that setting, as well as other key PrEP counseling messages outlined in the section below on PrEP use counseling, and as prompted by the client’s individual questions. If clients decline PrEP, providers may remind patients that if their situation or preferences change, PrEP is always an option available to them. Inviting PBFW to ask questions about PrEP and other aspects of ANC and PNC builds trust and increases the value of the visit to the client, which also encourages them to engage with the health system and continue their PrEP regimen. In the context of serodifferent relationships, it is especially critical that ANC clients feel safe to ask questions about PrEP. Due to potential stigma, many clients in this situation may plan conception and become pregnant without consulting health care providers.<sup>17, 18</sup>

### PREP USE COUNSELING

Shared decision-making between the client and PrEP provider is one approach that may be helpful when counseling pregnant and breastfeeding clients regarding PrEP.<sup>19</sup> In this approach, the client reviews their potential vulnerabilities to HIV. The PrEP provider shares

<sup>17</sup> Breitnauer et al. Community perceptions of childbearing and use of safer conception strategies among HIV-discordant couples in Kisumu, Kenya. *J Int AIDS Soc.* 2015;18:19972.

<sup>18</sup> West et al. “I don’t know if this is right but this is what I’m offering”: healthcare provider knowledge, practice, and attitudes towards safer conception for HIV-affected couples in the context of Southern African guidelines. *AIDS Care.* 2016;28 (3):390–6.

<sup>19</sup> Seidman et al. Offering pre-exposure prophylaxis for HIV prevention to pregnant and postpartum women: a clinical approach. *J Int AIDS Soc.* 2017;20(Suppl 1):21295.

evidence-based information about the client's options for HIV prevention and invites the client to share their experiences, values, and preferences about HIV prevention options and taking a daily medicine. The PrEP provider can help the client to weigh their competing priorities before making their choice.

In addition to routine counseling messages for all PrEP users included in the WHO *Implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection*, providers should integrate the following counseling messages into other routine counseling messages for PBFW, as appropriate:

- In general, women are at higher risk for acquiring HIV when they are pregnant or breastfeeding compared to times when they are not.
- For most healthy women who live in areas where HIV is common, the potential benefits of PrEP use to mothers and infants outweigh potential risks. Acquiring HIV is a greater risk to the woman and her baby's health, compared to PrEP.
- There is no evidence that PrEP increases the chance of birth defects, miscarriage, or other complications during pregnancy, birth, or after the birth.
- PrEP does not have any known negative interactions with the medications and supplements most commonly prescribed for women in pregnancy and during breastfeeding.
- The amount of PrEP drug that may pass to the baby during pregnancy and breastfeeding is very small, and has not been shown to cause any serious health problems for babies.
- PrEP use during pregnancy and breastfeeding has not been shown to cause the baby to be too big or too small.
- PrEP has not been shown to have any impact on the woman's ability to become pregnant in the future.
- Some people taking PrEP experience side effects, but they are generally mild, not dangerous, and resolve quickly.
- The woman should be careful to keep her PrEP supply in a safe place where children cannot reach it.
- Exclusive breastfeeding for the first 6 months of life is the recommended way of feeding infants, followed by continued breastfeeding with appropriate complementary foods for up to 2 years or beyond.
- PrEP has not been shown to affect a mother's milk production or the taste or quality of breast milk.
- The health care provider should explore whether the woman is experiencing violence in her life, and if so, discuss ways they can help her and her baby stay safe.

If a client declines PrEP, the provider should counsel on other safe and effective approaches for HIV prevention, the availability of PEP, and the option to change her mind in the future. Those providers offering ANC, PNC, and PrEP services for PBFW must be familiar with and comfortable providing PEP, due to the time-sensitive nature of eligibility (i.e., within 72 hours of exposure). Clients who decline PrEP still need to know about their options for testing of partner(s), treatment of partner(s) living with HIV as prevention, condom use, use of safer sexual practices, and sexually transmitted infection (STI) testing and treatment.<sup>20</sup>

### **RULING OUT CURRENT HIV INFECTION BEFORE STARTING PREP**

As with clients who are not pregnant or breastfeeding, HIV should be ruled out by testing before initiation of PrEP. HIV testing should be performed the same day that PrEP is started, using a point-of-care rapid HIV test, following the national HIV testing algorithm. The first test in the testing strategy should be the most sensitive test available.

Clients with possible HIV exposure in the previous 72 hours should not be offered PrEP but instead be offered PEP. Then, retest the client for HIV after 28 days. PrEP may be offered to clients who test negative at this point. However, PrEP does not need to be held while waiting for the 28-day test; there should be no gap in medication provision as individuals transition from PEP to PrEP.

If the client has signs or symptoms of an acute viral syndrome, such as flu-like illness, the health care provider should consider the possibility that acute HIV is present. In such circumstances, consider deferring PrEP start for 4 weeks and having the person tested for HIV again, which will allow time for possible HIV seroconversion to be detected.

### **LABORATORY TESTING BEFORE STARTING PREP USE**

Before prescribing PrEP, the following tests should be done for both pregnant and breastfeeding women:

- HIV test (this test will be **repeated every 3 months**)
- Serum creatinine, where capacity allows, to monitor kidney function (this test will be **repeated every 3 months**)
- Hepatitis B surface antigen
- STIs such as syphilis, gonorrhea, and chlamydia

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<sup>20</sup> Ibid.

**Laboratory evidence of hepatitis B, syphilis, gonorrhea, or chlamydia should prompt evaluation for complications of these conditions, as well as appropriate treatment according to local standard of care. Results from these tests do not inform the decision to start PrEP. Clients can start PrEP while waiting for results. Additional guidance related to hepatitis B is included in this document in the section, HEPATITIS B INFECTION DURING PREGNANCY.**

*Table 1. Integrative PrEP-related laboratory testing into routine testing at first ANC contact*

	Part of routine ANC	Before starting PrEP
Anemia	X	
Tuberculosis	X*	
Asymptomatic bacteriuria	X	
HIV	X	X
Syphilis	X	X
<b>Serum creatinine</b>		Where capacity allows
<b>Hepatitis B surface antigen</b>		Where capacity allows
<b>Gonorrhea and chlamydia</b>		Where capacity allows

*\* In settings where TB prevalence in general population is 100/100 000 population or higher*

## **DOCUMENTATION IN THE CLIENT'S CLINICAL RECORD**

Normally, all prescriptions would be documented on the client's handheld ANC record (if this is used) as well as any relevant ANC, PNC, family planning, or PrEP-specific facility-based client records and registers. All clinical care related to PrEP use should be documented in facility-based records. However, providers should consult with the client before documenting PrEP use on handheld records. Providers may wish to use more discreet strategies for documentation related to PrEP on handheld records carried by clients, so as to avoid unintentional disclosure to partners, family, or other household members, given the real potential for stigmatization of PrEP use and related social harm.

## **SCHEDULING FOLLOW-UP CONTACTS AND PROMOTING PREP CONTINUATION**

If the client is receiving PrEP services through an ANC, PNC, or family planning service delivery site, try to align her visits to minimize trips to the clinic, as frequent visits may discourage some clients from continuing PrEP. Follow national guidance on the timing of ANC contacts.

To optimize her chances for PrEP continuation, try to do the following:

- Understand her motivations for taking PrEP

- Provide her with a supply of PrEP that will last beyond the time of her next recommended visit or community-based contact
- Ask her about potential barriers that she may face in returning to the clinic and continuing PrEP, as well as ways that she might overcome these barriers
- Ask about partner reactions and strategies to communicate about PrEP with partners who are not supportive
- Provide anticipatory counseling to help her manage any PrEP side effects, as these have been shown to impact motivation to continue to PrEP (if PrEP is started in the first trimester, remind her that nausea and vomiting of pregnancy may be confused with PrEP side effects, and she may benefit from anti-emetic medications, especially if she is already experiencing nausea/vomiting of pregnancy prior to PrEP initiation)
- Help her identify an existing habit with which to “couple” taking the PrEP tablet
- Help her to identify a trigger to remind her to take her tablet (e.g., a specific radio show, children leaving for school)
- Assist her to set up a reminder on her phone, if she has one, with a message she finds personally motivating (e.g., My baby is healthy and so am I!)

## Client-centered care after starting PrEP

### INTEGRATION OF PREP INTO CARE FOR PREGNANT AND BREASTFEEDING CLIENTS

After the pregnant or breastfeeding client starts PrEP, the health provider has several important roles:

- If PrEP provision is in the context of ANC or PNC, continue providing high-quality ANC or PNC (including family planning services) to the client to address her needs, and integrate PrEP care into the client’s routine ANC or PNC services
- Monitor how the client is doing on PrEP
- Help her to be an active partner in her care, whether that means support for safe continuation of PrEP or transitioning to other strategies for protection of her health and the health of her baby

At each follow-up visit, the health provider needs to integrate information from history-taking, targeted physical examination, and any laboratory data to help the client reach her goals for a healthy pregnancy or postnatal experience and protection from HIV.

### FAMILY PLANNING SETTINGS PROVIDING PREP FOR BREASTFEEDING CLIENTS

In general, clinical guidance is the same for breastfeeding clients receiving PrEP services in PNC and family planning settings. As mentioned previously, PrEP drugs have no known adverse interaction with family planning methods. Clinical priorities include the following:



- Providing counseling that assists clients to meet their personal family planning and HIV prevention goals.
- Providing comprehensive clinical assessment to support safe continuation of family planning and HIV prevention methods.

Additional recommendations for improved integration of HIV prevention and family planning services are available in a WHO technical brief (*Actions for improved clinical and prevention services and choices: preventing HIV and other sexually transmitted infections among women and girls using contraceptive services in contexts with high HIV incidence*).<sup>21</sup>

### **MANAGING PREP SIDE EFFECTS DURING PREGNANCY AND POSTNATAL PERIOD**

PrEP use is generally well tolerated outside of and during pregnancy and the postnatal periods. Some side effects are possible, although they are typically mild. To provide high-quality care, PrEP providers should address client concerns with a thoughtful and systematic approach that includes history-taking, targeted physical examination, diagnosis, suggested measures to alleviate side effects, appropriate counseling, and a plan for future evaluation.

Separating PrEP side effects from common pregnancy complaints and effects from other causes may be challenging. Most PrEP side effects are mild, temporary, and resolve without serious safety concerns. Table 3 provides more details on specific symptoms and potential causes. Any provider decision to discontinue PrEP based on side effects should be discussed with the client, including careful consideration of potential risks (including risk of acquiring HIV in the absence of PrEP), benefits, and alternatives.

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<sup>21</sup> At: <https://www.who.int/publications/i/item/actions-for-improved-clinical-and-prevention-services-and-choices-preventing-hiv-and-other-stis-among-women-and-girls-using-contraceptive-services>.

Table 2. Evaluation of possible PrEP side effects during pregnancy and breastfeeding

Sign or symptom	Possible expected finding in pregnancy	Possible expected finding in postnatal period	Expected with some (not all) family planning methods	May be related to PrEP	May be related to another condition
<b>Back pain</b>	X	X			Yes, like back injury
<b>Constipation</b>	X				Yes, like iron pills
<b>Nausea or vomiting</b>	X		X	X	Yes, like foodborne illness
<b>Diarrhea</b>				X	Yes, like foodborne illness
<b>Mild abdominal pain or cramping</b>	X (especially round ligament pain or heartburn)	X (uterine involution or post-cesarean pain)	X	X	Yes, like preterm contractions, foodborne illness
<b>Vaginal discharge</b>	X	X (if consistent with normal lochia)	X		Yes, like vaginitis or sexually transmitted infection
<b>Frequent urination</b>	X				Yes, like urinary tract infection
<b>Dizziness</b>	X		X	X	Yes, like anemia, dehydration
<b>Headache</b>	X		X	X	Yes, like pre-eclampsia (serious complication of blood pressure)
<b>Fatigue</b>	X	X	X	X	Yes, like anemia or depression, other possibilities
<b>Sleep issues</b>	X	X		X	Yes, like anxiety or depression
<b>Abnormal kidney function tests (e.g., serum creatinine)</b>				X	Yes, like pre-eclampsia
<b>Abnormal liver function tests (e.g., AST, ALT)</b>				X	Yes, like HELLP syndrome (serious complication of pre-eclampsia) or hepatitis (liver infection)

\*Additional guidance on recognizing and managing side effects that may be associated with some family planning methods is available in WHO's *Family Planning: A Global Handbook for Providers*.<sup>22</sup> Most PrEP-related side effects are mild, temporary, and resolve without any serious safety concerns.

## LABORATORY DATA: MONITORING KIDNEY FUNCTION DURING PREGNANCY

**Where capacity allows, serum creatinine is recommended to monitor kidney function for PrEP users who are pregnant, with a repeat test performed every 3 months.**

Pregnancy can change how medications affect the body, and how the body may process a medication. Because of normal, physiologic changes in pregnancy—including increased blood volume and kidney function—normal values of serum creatinine are typically lower in pregnant compared to non-pregnant women. At baseline (before PrEP use starts), if the serum creatinine is greater than 0.9 mg/dl in pregnancy at baseline (before onset of PrEP use), the health provider should evaluate the client for possible acute kidney injury or undiagnosed prior chronic kidney disease. Consultation with an obstetrician and/or kidney specialist, if available, should be sought.

If a pregnant client with normal serum creatinine levels before PrEP use develops elevated levels outside the reference range for normal after starting PrEP, the provider should pause PrEP provision, due to the possibility of abnormal kidney function, and consult with an obstetrician and/or kidney specialist, if available.

The Cockcroft-Gault equation may also be used to estimate kidney function, based on serum creatinine level. This equation uses measured serum creatinine, sex at birth, age, and estimated lean body mass to estimate creatinine clearance, but it does not incorporate normal pregnancy changes into the calculation. Thus, the Cockcroft-Gault equation provides a general estimate for the pregnant woman's kidney function, but may not provide an optimal measure of kidney function for healthy pregnant clients taking PrEP. More information on Cockcroft-Gault is included in the WHO *Implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection*. WHO and Jhpiego have developed an app to access the WHO *Implementation tool for pre-exposure prophylaxis of HIV infection*,<sup>23</sup> and a free creatinine clearance calculator is available within this app.

Increased protein detected in urine is one potential sign of renal dysfunction.<sup>24</sup> Urine dipstick is a method of point-of-care semi-quantitative testing for proteinuria. Because vaginal secretions or amniotic fluid may contaminate a urine specimen, only clean-catch midstream

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<sup>22</sup> At: <https://www.who.int/reproductivehealth/publications/fp-global-handbook/en/>.

<sup>23</sup> At: <https://www.who.int/hiv/mediacentre/news/oral-prep-app/en/>.

<sup>24</sup> Côté AM et al. (2008) The 24-hour urine collection: gold standard or historical practice? *Am J Obstet Gynecol* 199: 625.

specimens should be used.<sup>25</sup> The threshold of 1+ urine protein is known to have poor predictive value for significant proteinuria in pregnancy. While the 2+ level may be a reasonable cut-off for suspicion of clinically significant proteinuria, it should be acknowledged that dipstick urinalysis has not been studied as a strategy for monitoring renal function in PBFW taking PrEP. Clients with 2+ proteinuria on urine dipstick should be referred for serum creatinine testing. It is important to rule out pre-eclampsia before assigning another etiology for the presence of proteinuria in a pregnant woman with elevated blood pressure.<sup>26</sup>

Given current WHO recommendations, challenges with accessing laboratory services in many regions where PrEP is implemented, the relatively strong safety record to date for tenofovir-based regimens in pregnancy (including PrEP), and the known protective benefit of PrEP against HIV infection, either of the strategies listed in Table 2 may be reasonable approaches to monitoring kidney function during PrEP use for pregnant clients.

*Table 3. Approaches to monitoring kidney function for PrEP users who are pregnant*

Approach	Advise client to pause PrEP use if follow-up laboratory test shows this result
1. Monitor serum creatinine every 3 months	Serum creatinine level greater than 0.9 mg/dL or 79.6 µmol/L
2. Monitor creatinine clearance every 3 months	Creatinine clearance less than 60 ml/min
Pregnant client may resume PrEP use if there is resolution of laboratory test abnormalities, provided no other contraindications are present.	

## MONITORING KIDNEY FUNCTION DURING THE POSTNATAL PERIOD

For most women, kidney function rapidly returns to pre-pregnant levels soon after delivery. For PrEP clients who are breastfeeding, monitor serum creatinine every 3 months after the start of PrEP. More frequent creatinine monitoring may be warranted if there are co-morbid conditions that can affect renal function, such as diabetes mellitus and hypertension. The laboratory should calculate estimated creatinine clearance and report this with the creatinine result.

<sup>25</sup> At: [https://www.who.int/maternal\\_child\\_adolescent/documents/managing-complications-pregnancy-childbirth/en/](https://www.who.int/maternal_child_adolescent/documents/managing-complications-pregnancy-childbirth/en/).

<sup>26</sup> At: [https://www.who.int/maternal\\_child\\_adolescent/documents/managing-complications-pregnancy-childbirth/en/](https://www.who.int/maternal_child_adolescent/documents/managing-complications-pregnancy-childbirth/en/).

## DECIDING WHETHER TO PAUSE OR STOP PREP USE FOR PREGNANT AND BREASTFEEDING WOMEN

When a client presents with a sign or symptom that they associate with PrEP use, it is helpful to get more information to determine if it may be caused by PrEP. Before deciding to pause or stop PrEP use, it is important to consider whether or not there is reasonable suspicion that a complaint was caused by PrEP use. To help determine this, clinicians can consider the following guiding questions:

- Sign/symptom: What is the sign or symptom noted by the client? Ask about the onset, location, duration, characteristics, aggravating and relieving factors, and any treatment.
- Timing: Did the problem begin soon after the start of PrEP use?
- Association with PrEP: If the client has already stopped PrEP use, has there been any improvement after stopping? Did the issue come back if the participant stopped and restarted PrEP? Is the problem something that has been seen before in other people using PrEP?
- Logic: Is it plausible (does it make sense) that PrEP could have caused the problem?
- Other causes: Is there any other explanation?

These questions, as well as an understanding of the severity of any side effects, will help providers make good clinical judgments about continuing, pausing, or discontinuing PrEP use.

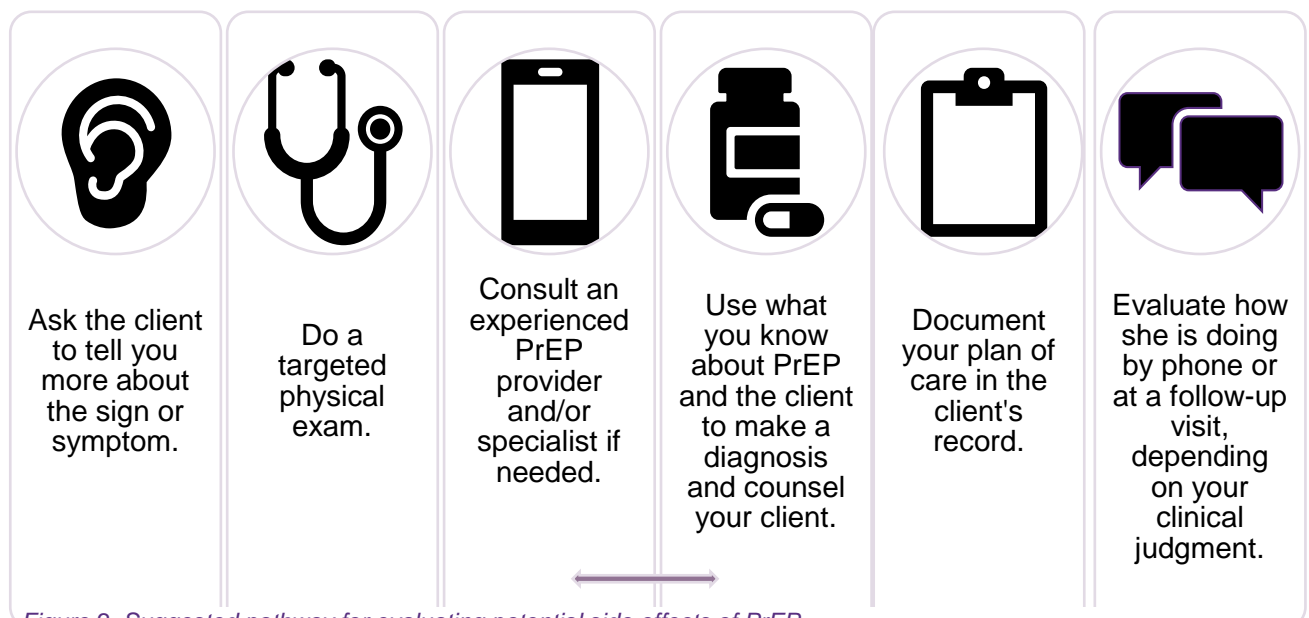


Figure 2. Suggested pathway for evaluating potential side effects of PrEP

If the health care provider and client decide that she may safely continue PrEP use (e.g., because symptoms are mild and expected), the provider should offer reassurance and

suggest strategies that may help to alleviate her symptoms. The provider should also create a plan with her to re-evaluate her symptoms on a specified date, either by phone or in person. Showing the client that they care about the acceptability and safety of her PrEP experience is an important way to build her trust and provide her with client-centered care.

As noted in *the WHO Implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection*,<sup>27</sup> PrEP can also be stopped 28 days after the last possible exposure to HIV. People can consider stopping PrEP if they are no longer at substantial risk of acquiring HIV. However, pregnancy and breastfeeding place women at significant risk for acquiring HIV, even in the absence of other known risks. Ways to lower risk include:

- Adopting safer sexual practices, such as not having vaginal or anal intercourse, or using condoms for all vaginal and anal intercourse.
- Changing circumstances, such as leaving sex work or stopping injecting drug use; or, moving to a place that has a low prevalence of HIV.
- For people in a serodifferent relationship, HIV transmission risk is very low when the HIV-positive partner is virally suppressed on antiretroviral therapy.

### **STOPPING PREP USE DUE TO HIV SEROCONVERSION**

Consistent PrEP use reduces the risk of becoming infected with HIV. However, it is possible that a pregnant or breastfeeding client who has been prescribed PrEP will experience HIV seroconversion. In the event that this occurs, it is important for the health provider to take several actions:

- Counsel the client on key post-test counseling topics:
  - Coping with the diagnosis;
  - Learning the actions to take to keep her and her baby healthier and prevent mother-to-child transmission, including antiretroviral drugs and infant feeding;
  - Deciding whether to share her test results with others, especially her partner, so he can also get tested.
- Start the client on recommended antiretroviral therapy as soon as possible after a confirmed positive HIV test result (seroconversion). PrEP providers who do not feel comfortable treating HIV in the context of pregnancy or breastfeeding should receive additional training or identify HIV treatment sites for referrals.

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<sup>27</sup> At: <https://apps.who.int/iris/bitstream/handle/10665/255889/WHO-HIV-2017.17-eng.pdf>.

- Confirm the client’s reactive rapid test result by retesting a second sample (according to the national testing algorithm). When confirmation of a positive test result is delayed more than a few hours, transition to fully suppressive therapy can be considered while confirmatory testing is underway.

Additional information regarding appropriate counseling and treatment strategies for PBFW living with HIV can be found in national guidelines for prevention of mother-to-child transmission of HIV.

## EVALUATING POTENTIAL PROBLEMS IN BREASTFEEDING INFANTS

PrEP use in breastfeeding mothers has not been associated with significant safety concerns. Severe abnormal signs or symptoms in an infant are unlikely to be related to maternal PrEP use, but should be evaluated promptly according to the WHO *Paediatric emergency triage, assessment and treatment: care of critically-ill children*<sup>28</sup> or other national guidance, as appropriate.

When assessing whether a finding might be related to the mother’s PrEP use, providers can consider the guiding questions noted above in the section, *DECIDING WHETHER TO PAUSE OR STOP PREP USE FOR PREGNANT AND BREASTFEEDING WOMEN*.

Any provider decision to discontinue PrEP based on side effects in a breastfeeding infant should be discussed with the client, including careful consideration of potential risks (including risk of mother and infant acquiring HIV in the absence of PrEP), benefits, and alternatives.

## TRANSITIONING BETWEEN CLINICAL CONTEXTS OR SERVICE DELIVERY SETTINGS

There is no single best place to manage PrEP use for PBFW who are transitioning from one care setting to another, or who may be eligible to receive services from multiple settings at once (e.g., key population program and ANC). Determining the best (or multiple locations) for clients to receive services should consider the following:

- Client needs and preferences
- Capacity of each service delivery setting to meet the individual needs of the client (as related to both PrEP and maternal newborn health care)

Thus, clients should be supported to continue PrEP as they transition between different clinical contexts and service delivery settings. Examples of such transitions may include the following:

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<sup>28</sup> At: [https://apps.who.int/iris/bitstream/handle/10665/204463/9789241510219\\_eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/204463/9789241510219_eng.pdf).

- From safer conception to ANC
- From programs for key populations or adolescent girls and young women to ANC
- From family planning to ANC
- From ANC to PNC
- From ANC to family planning services, following delivery, if client does not access PNC
- From PNC to family planning or other facility- or community-based PrEP provider, if client wishes to continue PrEP due to ongoing behavioral, social, and/or structural risk

**In the absence of any contraindications, clients do not need a “break” from PrEP use, which may only serve to increase their risk for acquiring HIV.** WHO guidance does not specify that pregnant PrEP users need to pause their PrEP during the intrapartum and early postnatal periods. While some women may wish to pause PrEP use during the first 6 weeks following delivery, especially if following traditional or clinical guidance for abstinence during this period, the risk of unplanned exposure to HIV via sexual intercourse should be considered and discussed with the client. If the client wishes to pause her PrEP use, refer to PrEP eligibility guidelines when restarting PrEP in the postnatal period, and provide information on where to access the appropriate services.

Try to ensure continuity of PrEP supply. When possible, facilitate a “warm hand off” (e.g., personal introduction to next PrEP provider) when client is switching from one PrEP delivery setting to another.

## PrEP use in special situations

### PREP USE IN WOMEN WITH HYPERTENSIVE DISORDERS OF PREGNANCY

Pregnant clients are at risk of developing hypertensive disorders of pregnancy and should be monitored at each ANC and PNC contact for clinical criteria and symptoms for the disease. The *WHO Managing Complications in Pregnancy and Childbirth (MCPC): A Guide for Midwives and Doctors (2<sup>nd</sup> Edition)*<sup>29</sup> provides guidance on symptoms, clinical criteria for diagnosis, and management of hypertensive disorders of pregnancy.

Specific WHO guidance has not been issued to guide clinical management of PrEP use in clients with hypertensive disorders of pregnancy. **However, it is prudent to avoid starting PrEP in clients with evidence of impaired renal function or conditions that may impair**

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<sup>29</sup> At: [https://www.who.int/maternal\\_child\\_adolescent/documents/managing-complications-pregnancy-childbirth/en/](https://www.who.int/maternal_child_adolescent/documents/managing-complications-pregnancy-childbirth/en/).



**renal function, such as pre-eclampsia. Such clients require prompt assessment and management of those conditions to avoid life-threatening complications.** Refer to the WHO MCPC (2<sup>nd</sup> edition) for guidance on monitoring and timing of childbirth for mild and severe pre-eclampsia.

PrEP may be used safely in clients with hypertension (or diabetes) prior to pregnancy, provided normal kidney function is established prior to PrEP start, and in the setting of individualized clinical management.

WHO’s Classification framework for hypertensive disorders of pregnancy is as follows:

- Chronic hypertension (elevation of blood pressure noted before 20 weeks of gestation or persisting more than 12 weeks postpartum)
- Gestational hypertension
- Mild pre-eclampsia
- Severe pre-eclampsia
- Eclampsia
- Chronic hypertension with superimposed pre-eclampsia

*Table 4. Managing PrEP use in the context of hypertensive disorders of pregnancy*

Category	WHO Diagnostic Criteria	Suggested Management
<b>Chronic hypertension</b>	Elevation of blood pressure noted before 20 weeks of gestation or persisting more than 12 weeks postpartum	Initiate PrEP only after laboratory assessment of kidney function, in consultation with an experienced obstetrician or high-risk pregnancy specialist, and follow an individualized, comprehensive plan for monitoring of blood pressure, medication use, and kidney function.
<b>Mild pre-eclampsia</b>	New onset hypertension and proteinuria after 20 weeks of gestation: <ul style="list-style-type: none"> <li>• Systolic blood pressure (SBP) &gt;140 and/or diastolic blood pressure (DBP) &gt;90 after 20 weeks of gestation</li> <li>• Proteinuria 2+ on dipstick</li> <li>• No severe features of PE/E present</li> </ul>	Do not initiate or continue PrEP use in clients with suspected or confirmed diagnosis of mild pre-eclampsia. These clients should have management consistent with recommendations in the WHO MCPC manual.  For clients who are initially suspected to have pre-eclampsia, but are subsequently ruled out for this diagnosis, consider starting or restarting PrEP use, with careful monitoring for recurrence of signs or symptoms of pre-eclampsia.

		Clients with pre-eclampsia may begin PrEP after birth if kidney function remains normal, or when kidney impairment resolves.
<b>Severe pre-eclampsia</b>	<p>New onset hypertension and proteinuria after 20 weeks of gestation:</p> <ul style="list-style-type: none"> <li>• SBP &gt;160 and/or DBP &gt;110 after 20 weeks of gestation</li> <li>• Proteinuria 2+ on dipstick</li> </ul> <p>Pre-eclampsia with <b>any of the following</b> present is severe pre-eclampsia:</p> <ul style="list-style-type: none"> <li>• <b>Neurologic:</b> headache, vision changes, hyperreflexia, or clonus</li> <li>• <b>Pulmonary:</b> difficulty breathing (rales on auscultation due to fluid in lungs)</li> <li>• <b>Hepatic:</b> upper abdominal pain, nausea/vomiting or liver enzymes elevated (&gt;2 times the baseline)</li> <li>• <b>Renal:</b> serum creatinine &gt;1.1mg/dL or doubling of baseline, oliguria (&lt;40 cc urine in 24 hours)</li> <li>• <b>Hematologic:</b> platelets &lt;100,000 cells/mcL</li> </ul>	<p>Do not initiate or continue PrEP use in clients with suspected or confirmed diagnosis of severe pre-eclampsia. These clients should have management consistent with recommendations in the WHO MCPC manual.</p> <p>For clients who are initially suspected to have pre-eclampsia, but are subsequently ruled out for this diagnosis, consider starting or restarting PrEP use, with careful monitoring for recurrence of signs or symptoms of pre-eclampsia.</p> <p>Clients with pre-eclampsia may begin PrEP after birth if kidney function remains normal, or when kidney impairment resolves.</p>

For some PrEP clients who have signs and/or symptoms of pre-eclampsia, estimating creatinine clearance from a combination of blood and urine testing may be of value, if adequate laboratory capacity is present. If the woman's kidneys are damaged by pre-eclampsia, the creatinine clearance value will decrease because the kidneys are filtering less creatinine from the blood. Evaluating creatinine clearance during pregnancy requires a blood sample and a sample of all the urine collected for 24 hours (24-hour urine sample). Feasibility of this test will vary by client and setting. Suspected pre-eclampsia should trigger discontinuation of PrEP, and eventually counseling on alternative strategies for HIV prevention, once evaluation and management of pre-eclampsia have been completed. However, as kidney impairment related to pre-eclampsia generally resolves at birth or shortly after birth, PrEP may be initiated in the early postpartum period.

## HEPATITIS B INFECTION DURING PREGNANCY

People who are sexually active and those who inject drugs (and their sexual and injection partners) are at risk of acquiring HBV. Clients should be tested for HBV before they are prescribed PrEP, where capacity allows.

Pregnant women who test positive for hepatitis B surface antigen should be referred to specialist care and be tested for hepatitis B virus deoxyribonucleic acid (HBV DNA), which can help to guide the use of antiviral medication to prevent perinatal transmission of HBV. While HBV is not an absolute contraindication to PrEP use, pregnant clients with HBV who wish to use PrEP should receive their care from an experienced HBV care provider.

Patients with HBV who are taking PrEP and then stop PrEP must have close follow-up of liver function tests. Reactivation of HBV replication can result in liver damage after PrEP is stopped.

Health providers caring for clients with HBV during pregnancy should also follow local guidance on case management to ensure timely HBV prophylaxis and follow-up for the infant. When a pregnant mother is infected with HBV, hepatitis B immune globulin and hepatitis B vaccine should be provided to the infant at birth.

Clients living with hepatitis C can safely receive PrEP, as there are no known interactions with hepatitis C. However, those clients with a new diagnosis of hepatitis C should have the opportunity to be seen by a hepatitis specialist, where available.

## Other important services at settings providing PrEP for pregnant and breastfeeding women

### OTHER HIV PREVENTION AND FAMILY PLANNING/REPRODUCTIVE HEALTH SERVICES

Within ANC and PNC settings, a range of HIV prevention services should be provided, in addition to PrEP:

- Provide HIV testing services to identify those who can benefit from HIV prevention services (repeat testing every 3 months during pregnancy and breastfeeding).
- Offer HIV testing services to women's sexual partners and drug injecting partners, and refer those partners testing positive for immediate antiretroviral treatment services.
- Refer male sexual partners to voluntary medical male circumcision.
- Screen for and treat STIs according to local guidance, and offer the same to sexual partners.
- Offer male and female condoms and counsel on correct and consistent use (male and female condoms provide dual protection against unintended pregnancies and against STIs including HIV).

- Provide HIV risk reduction counseling.

Treatment of STIs in pregnancy and the postnatal period is important, as STIs can cause a range of adverse outcomes in mothers, as well as harm to the fetus. STIs in pregnant women can infect the baby before or during birth and cause complications in infants, such as blindness, deafness, severe anemia, and death. Having an STI during pregnancy can cause different kinds of problems:

- Premature labor (labor before 37 weeks of pregnancy). Early (preterm) birth is the number one cause of infant death and can lead to long-term developmental and health problems in children;
- Infection in the newborn (e.g., syphilis, herpes simplex virus); and
- Infection in the uterus (womb) after birth.

Family planning allows families to decide the number and spacing of their children. Family planning counseling should be offered to all pregnant and breastfeeding clients, with appropriate method provision also offered to those who are breastfeeding. Where possible, family planning services should be accessible within the same service delivery setting for all clients, including those who are using PrEP.

## SCREENING FOR INTIMATE PARTNER VIOLENCE

Women may experience new, continued, or increased intimate partner violence (IPV) during pregnancy and the postnatal period. Providers should also be aware that IPV has been associated with increased vulnerability to HIV.<sup>30</sup> IPV puts the mental, sexual, and physical health of women at severe risk, and is also associated with lower PrEP uptake,<sup>31</sup> increased PrEP interruption,<sup>32</sup> and lower adherence to PrEP.<sup>33</sup> Research has also shown that IPV can lead to stress and forgetting to take pills, leaving home without pills, and partners throwing pills away.

In PEPFAR-funded programs, all PrEP sites must conduct routine enquiry for IPV (sometimes referred to as gender-based violence screening) with all clients.<sup>34</sup> Routine

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<sup>30</sup> Stockman et al. Forced sexual initiation, sexual intimate partner violence and HIV risk in women: A global review of the literature. *AIDS Behav.* 2013 Mar;17(3): 832–847.

<sup>31</sup> Lanham et al. Sexual Violence Research Initiative Forum. Oct 2019.

<sup>32</sup> Cabral et al. Intimate Partner Violence and Self-Reported Pre-exposure Prophylaxis Interruptions Among HIV-Negative Partners in HIV Serodiscordant Couples in Kenya and Uganda. *J Acquir Immune Defic Syndr.* 2018; 77(2): 154–59.

<sup>33</sup> Roberts et al. Intimate Partner Violence and Adherence to HIV Pre-exposure Prophylaxis (PrEP) in African Women in HIV Serodiscordant Relationships: A Prospective Cohort Study. *J Acquir Immune Defic Syndr.* 2016; 73(3): 313–22.

<sup>34</sup> A Peltz. 2019. Gender Equality and Gender-Based Violence Priorities for USAID’s PEPFAR Programs.

enquiry does not meet the public health criteria of a complete screening program where all clients are asked about IPV (i.e., universal screening); but denotes a low threshold for women being routinely asked about abuse in a health care setting. Routine enquiry is used in settings where clinical enquiry (identifying individuals experiencing violence through the use of questions based on presenting conditions, history, and where appropriate, physical examination by a trained health provider) cannot be conducted but where violence is a known risk factor for HIV. After conducting routine enquiry for IPV, sites must offer appropriate first-line support based on the WHO LIVES approach (see Box 4) and make referrals to IPV response services, as needed. First-line support is immediate care given to an IPV survivor upon first contact with the health care system.<sup>35, 36</sup> Routine enquiry for IPV can also be used in non-PEPFAR-funded programs.

There are six minimum requirements for conducting routine enquiry:

1. A protocol or standing operating procedure exists for conducting routine enquiry
2. A questionnaire, with standard questions where providers can document responses, exists
3. Providers offer first-line support (WHO LIVES approach)
4. Providers have received training on how to ask about IPV or sexual violence
5. Private setting and confidentiality are ensured
6. A system for referrals or linkages to other services is in place

All community- and facility-based programs delivering HIV or IPV prevention activities must ensure that facilitators are trained in providing

#### **Box 4. THE WHO LIVES APPROACH**

**Listen** – listen closely with empathy, not judging

**Inquire** about the client’s needs and concerns – assess and respond to the survivor’s needs and concerns (emotional, physical, social, practical)

**Validate** – show that you believe and understand the survivor

**Enhance safety** – conduct a safety assessment and safety planning to reduce the risk of further harm

**Support** – help the survivor connect to services and social support

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<sup>35</sup> Pan American Health Organization. 2017. Clinical Handbook: Health care for women subjected to intimate partner violence or sexual violence. <https://www.paho.org/en/documents/clinical-handbook-health-care-women-subjected-intimate-partner-violence-or-sexual>.

<sup>36</sup> WHO. 2019. Caring for women subjected to violence: A WHO curriculum for training health-care providers. <https://www.who.int/reproductivehealth/publications/caring-for-women-subject-to-violence/en/>

first-line support so they can respond appropriately to someone who discloses violence. Facilitators should have referral cards and information available to help survivors to access IPV response services. For survivors who test negative at dedicated IPV sites (e.g., one-stop center), ensure linkage to HIV and IPV prevention programs. <sup>3738</sup>When providers help clients deal with practical needs, it helps with their emotional needs. Helping with her emotional needs strengthens her ability to deal with practical needs.

## Appendix 1. Sample Checklist for PrEP Start-up for Pregnant and Breastfeeding Clients

Instructions: Complete checklist and file in individual's clinical record.

Screening Checklist Questions	Yes	No
1. Does client have a positive HIV test immediately prior to initiating PrEP?		
2. Does client have any signs or symptoms of acute HIV infection?  Acute HIV infection may include signs and symptoms of fever, sore throat, aches and pains, lymphadenopathy (swollen glands), mouth sores, headache, or rash. If the client has any of these signs or symptoms, the health provider should consider the possibility that acute HIV is present. In such circumstances, consider deferring PrEP start for 4 weeks and having the person tested for HIV again, which will allow time for possible HIV seroconversion to be detected.		
3. Does client have any probable recent exposure to HIV?  Clients with possible HIV exposure in the previous 72 hours should not be offered PrEP but instead be offered PEP. Then, retest the client for HIV after 28 days. PrEP may be offered to clients who test negative at this point. However, PrEP does not need to be held while waiting for the 28-day test; there should be no gap in medication provision as individuals transition from PEP to PrEP.		
4. Does client have a confirmed allergy or contraindication to any medicine in the PrEP regimen?		
5. Does client have an estimated creatinine clearance of less than 60 ml/min (or a serum creatinine level of greater than 0.9 mg/dL, if pregnant) (where screening is feasible)?		
6. Does client have a current diagnosis of impaired liver dysfunction, kidney dysfunction, or pre-eclampsia?  In the case of pre-eclampsia, it is generally safe to start or restart PrEP after delivery, provided the client has normal laboratory tests for kidney function (e.g., serum creatinine), as most cases of pre-eclampsia resolve shortly after birth.		
7. Does client have a positive test for hepatitis B virus (where screening is feasible)?		

If the answer to any of the above questions is “Yes”, do not start PrEP. Clients whose exclusionary conditions have resolved may be able to start PrEP at a later date (see Clinical Practice Guidelines for additional guidance). The list above is specific to PrEP start-up and is not exhaustive of all appropriate assessment that clients may require. Other recommended assessments (e.g., in the context of antenatal care, postnatal care, and routine enquiry for intimate partner violence, etc.) should also occur.