Key Considerations for Integration of PrEP for Pregnant and Breastfeeding People into National Prevention of Vertical Transmission Polices

MOSAIC POLICY BRIEF
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This brief outlines key recommendations for integration of HIV pre-exposure prophylaxis (PrEP) for pregnant and breastfeeding people (PBFP) in national prevention of vertical transmission policies. Countries aiming to update their policies can refer to these considerations to help advance integration of WHO-recommended actions into their nationally endorsed prevention of vertical transmission strategies.

Introduction

This brief follows and is informed by a landscape analysis which summarized the status of PrEP inclusion for PBFP in national prevention of vertical transmission policies (previously referred to as prevention of mother to child transmission (PMTCT) or elimination of mother to child transmission (eMTCT) policies) across eight countries participating in Maximizing Options to Advance Informed Choice for HIV Prevention (MOSAIC). MOSAIC is a five-year global project funded by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) through the U.S. Agency for International Development (USAID) to help adolescent girls and young women and other women[1] prevent HIV by accelerating introduction and scale-up of new and emerging biomedical prevention products.

Among the countries included in the landscape analysis, the amount and nature of PrEP guidance for PBFP included in prevention of vertical transmission policies varied widely, and gaps in national policies regarding provision of PrEP for PBFP were noted. Many countries included in this analysis currently house guidance related to prevention of vertical transmission in consolidated country policies for treatment and prevention of HIV, and in these cases prevention of vertical transmission policies are a chapter within a larger policy. Several countries also have stand-alone PrEP policies or PrEP implementation guides, referenced by other HIV consolidated policies or vertical transmission policies. In countries where guidance for PrEP for PBFP is included in these various policies (vertical transmission policies, consolidated HIV guidelines, and/or PrEP stand-alone guidance), it is important that language/guidance is aligned among the policy documents. When updates are made around guidance for PrEP for PBFP to one policy – they should be quickly revised and reflected in the other policies. Inconsistent language across policies may lead to misunderstanding and errors

[1] MOSAIC end users include cisgender women, transgender women, and nonbinary people and transgender men assigned female at birth; in addition, specific underrepresented groups within these end user populations include very young adolescents, sex workers, pregnant and breastfeeding individuals, those engaged in transactional sex, and individuals who use drugs.

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by providers and implementers.

This brief is the next step in the process to recommend the most essential information on PrEP for PBFP that should be included in prevention of vertical transmission policies to assist country planners to strengthen the quality of national guidance. Evidence has shown that people have an increased need for HIV prevention during pregnancy and the postnatal period, and that people who become infected with HIV during pregnancy or the postnatal period have a higher chance of transmitting HIV to their infants as compared to people who became infected with HIV before becoming pregnant (World Health Organization [WHO], 2017). Inclusion of clear guidance around providing PrEP to PBFP within prevention of vertical transmission policies is essential not only to reduce HIV incidence in such individuals, but also to address remaining gaps in vertical transmission and by extension pediatric HIV.

What is meant by vertical transmission of HIV?

Vertical transmission of HIV, previously referred to as mother to child transmission, is the transmission of HIV from a mother to a child during gestation, delivery, or the period of breastfeeding. Prevention of vertical transmission policies are also commonly referred to as prevention of mother to child transmission (PMTCT) policies or elimination of mother to child transmission (eMTCT) policies.

What is meant by PrEP for PBFP?

Pre-exposure prophylaxis, or PrEP, is the use of antiretroviral drugs by people without HIV before a potential exposure to prevent HIV. It is one of several HIV prevention strategies and, where possible, should be used in combination with condoms and condom-compatible lubricants and other HIV prevention strategies. PrEP should only be delivered after HIV testing has been confirmed as negative.

Guidance from the WHO supports provision of PrEP to PBFP who are at substantial risk of HIV infection. Given evidence that PrEP is a safe and appropriate strategy for PBFP, increased vulnerability during these periods, and implications for potential transmission to infants, it is important to include and prioritize these populations in PrEP counseling, assessment, delivery, and management (WHO, 2021; Bunge et al., 2022; Owor et al., 2023).

Other key resources for policy guidance for PrEP and PrEP for PBFP:

- For further resources including clinical guidelines and training packages on PrEP for PBFP: PrEP for Pregnant and Breastfeeding People – Clinical Guidelines and Training Package
- PrEP Guideline Template to support development and adoption of national guidelines around PrEP recommendations and guidance. This document is broader than the guidance outlined in this brief, as it focuses on PrEP for all individuals at substantial risk of HIV, and not specifically on PrEP for PBFP for prevention of vertical transmission policies as this document does.

Currently three HIV PrEP methods exist: pills that are taken by mouth (oral PrEP), a ring that is inserted into the vagina (PrEP ring), and an injection given in the buttocks muscle (CAB PrEP). Although targeted WHO guidelines on PrEP ring and CAB PrEP use in PBFP are yet to be released, emerging data suggest that both PrEP ring and CAB PrEP may be safe for use by PBFP (HPTN 084, n.d.; MTN-042-Deliver, n.d.; MTN-043-B-Protected, n.d.; Bunge et al., 2022). However, safety research is still ongoing and countries should defer to

their national guidelines for the use of new PrEP products among PBFP.

Why should countries consider integration of key information on PrEP for PBFP into prevention of vertical transmission policies?

The potential role of PrEP in reducing vertical transmission of HIV cannot be understated, yet because the practice of PrEP use for PBFP is relatively new and emerging, inclusion of PrEP for PBFP in national policies, including prevention/elimination of vertical transmission policies is lacking. A substantial proportion of vertical transmission is driven by incidental HIV infection during pregnancy and breastfeeding. According to epidemiologic estimates by UNAIDS for the year 2020, the cause of 35,000 (23%) new vertical HIV transmissions was due to a person acquiring HIV during pregnancy or breastfeeding (UNAIDS, 2022). It will be impossible to eliminate vertical transmission of HIV without expanding access to HIV prevention strategies, such as PrEP, for PBFP.

A recent review of national HIV guidelines for PEPFAR-supported countries found only 36% of national guidelines included PBFP as a specific priority population for PrEP (Abadan et al., 2022). The earlier referenced landscape analysis showed that the amount and nature of PrEP guidance for PBFP included in prevention of vertical transmission policies varies widely and highlights the importance of including key information for these populations in prevention of vertical transmission policies.

Key language to integrate PrEP for PBFP into prevention of vertical transmission policies

The following topics, supported by WHO guidance, are suggested as key language to include specifics around PrEP for PBFP in prevention of vertical transmission policies. Countries can use the following points as an adaptable template to frame out the essential information as they update prevention of vertical transmission policies.

1) Rationale for integrating PrEP for PBFP as part of prevention of vertical transmission policies

Prevention of vertical transmission policy language should include clear and comprehensive rationale for and guidance on the provision of PrEP for PBFP, and why integrating this into programming is essential.

Key messages

- The likelihood of acquiring HIV is higher during pregnancy and the postnatal period (WHO, 2021). According to epidemiologic estimates by UNAIDS for the year 2020, the cause of 35,000 (23%) of new vertical HIV transmissions was due to a person acquiring HIV during pregnancy or breastfeeding (Joint United Nations Programme on HIV/AIDS (UNAIDS), 2022).

- The WHO recommends that PrEP should be used for PBFP as part of a combination prevention package, including condoms, sexually transmitted infection prevention, and regular HIV testing

(WHO, 2017). Many countries are also implementing triple elimination plans, including hepatitis, syphilis and HIV, so it is critical to align and integrate with those plans as well.

- The proportion of P/BF clients initiating PrEP ranges from 10-22%, on average (Nelson et al., 2023; Scott et al., 2022; Kinuthia et al. 2020; Joseph Davey et al., 2022). Studies suggest that when PrEP is offered to ANC/PNC clients, rates of PrEP initiation are relatively high. Thus, integrating PrEP at a P/BF client's every interaction with the health system, when possible, can be an effective strategy to prevent vertical transmission.

2) Describe the approved PrEP methods for PBFP which should be integrated into prevention of vertical transmission services

All HIV prevention methods available to PBFP in the country should be reviewed with clients.

Key messages

- Oral PrEP for PBFP: Given evidence that oral PrEP is a safe and appropriate strategy for PBFP throughout pregnancy and breastfeeding, increased vulnerability during these periods, and implications for potential transmission to infants, it is important to include and prioritize these populations in PrEP counseling, screening, delivery, and management as part of prevention of vertical transmission services (WHO, 2021).

- PrEP ring or CAB PrEP for PBFP: Although targeted WHO guidelines on PrEP ring and CAB PrEP use in PBFP are yet to be released, emerging data suggest that both PrEP ring and CAB PrEP may be safe for use by PBFP (WHO, 2022; MTN-042-Deliver, n.d.; HPTN 084, n.d.). However, safety research is still ongoing and countries should defer to their national guidelines for the use of new PrEP products among PBFP. Given the limited data, any method specific guidance below in this brief will be focused on oral PrEP.

3) Clearly define the criteria to be used in prevention of vertical transmission policies to specify provision of PrEP for PBFP, with a recommendation to offer PrEP to every PBFP at every interaction with the health system when possible

For most healthy pregnant people who live in areas where HIV is common, the potential benefits of PrEP use to mothers and infants outweigh potential risks. It is critical that all PBFP receive counseling at every visit for preventing HIV with PrEP. Given that the likelihood of acquiring HIV is higher during pregnancy and the postnatal period, most pregnant and breastfeeding individuals living in countries where HIV is common are at substantial risk by virtue of simply being pregnant or breastfeeding.

Specific subpopulations of PBFP may be at an even higher risk of acquiring HIV. These may include HIV seronegative partners who are part of a serodifferent couple, sex workers, adolescent girls, young women, and transgender people. Prevention of vertical transmission policies should, however, avoid ambiguous language when it comes to referencing such populations as “at risk” people, as this may leave providers with the misconception that only pregnant or breastfeeding clients who fall into these categories should be

eligible for PrEP, which may incorrectly exclude all other PBFP broadly who would benefit from PrEP. Research has shown that similar numbers of PBFP initiate PrEP, regardless of whether a risk-based approach or opt-out approach are used (Kinuthia et al., 2023). A risk-based approach would be an approach whereby PrEP is offered to the specific subpopulations of PBFP who are at higher risk of acquiring HIV, whereas an opt-out approach is an approach whereby every PBFP is offered PrEP at every visit and given the opportunity to individually 'opt out' after a complete discussion regarding PrEP benefits. The opt-out approach has the advantage of catching people the health worker may neglect to understand are at higher risk and also may serve to simplify and avoid confusion in counseling messages.

Key messages

- When clients live in settings where HIV is common, all HIV-negative pregnant and breastfeeding persons should be considered candidates for PrEP, unless individual clinical contraindications exist, using the 'OPT OUT' approach.

- With the OPT OUT approach, every pregnant person and lactating person is offered PrEP at every visit and given the opportunity to individually 'opt out' after a complete discussion regarding PrEP benefits. If a pregnant or breastfeeding person deems themself low risk after complete discussion regarding PrEP benefits, clearly document refusal and offer PrEP again at the next visit.

- ANC and postnatal care (PNC) clients are at increased risk for acquiring HIV during pregnancy and breastfeeding, due to a range of factors, including biologic factors, the possibility of their own or their partners' undisclosed multiple partners, changes in condom use patterns, sexual violence, and transactional sex.

- Contraindications for oral PrEP use in pregnancy and breastfeeding clients:[2]

  1) Most contraindications are the same in PBFP as for non-pregnant, non-breastfeeding individuals:

  - An HIV-positive test result according to the national HIV testing algorithm
  - Known recent exposure to HIV (because such clients may derive more benefit from post exposure prophylaxis (PEP) if the potential for HIV exposure was high)
  - Signs/symptoms of acute HIV infection (AHI) and potential exposure within the past 14 days
  - Inability to commit to using PrEP effectively and attend scheduled follow-up visits
  - Allergy or contraindication to any medicine in the PrEP regimen

[2] For further guidance, see the PrEP Clinical Practice Guidelines for PBFP, as well as 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 postexposure prophylaxis (PEP) screening, and general contraindications to PrEP.

- Estimated creatinine clearance of less than 60 ml/min (if known)

- 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.

2) A note about PrEP ring and CAB PrEP: being pregnant and/or breastfeeding may be contraindications to use of the PrEP ring or CAB PrEP in certain countries, if specified as such by the regulatory authority or policies. In countries where PrEP ring use or CAB PrEP are not contraindicated for PBFP, there are different contraindications during pregnancy and the postnatal period. These are outlined in the PrEP Clinical Practice Guidelines for PBFP.

4) Prevention of vertical transmission guidelines should include concrete guidance around when, by whom, and where to provide PrEP to PBFP

Key messages

- Prevention of vertical transmission interventions, including PrEP, should be integrated into maternal, newborn, child, and adolescent health (MNCAH) services, which include but are not limited to services for STIs and sexual and reproductive health, antenatal and postnatal care, adolescent clinics, sick child visits, primary health care visits, and in a range of settings, including clinics, pharmacies and the community.

- PrEP should be offered for women of reproductive age and pregnant and breastfeeding people in service delivery entry points, when trained nurses are available and where appropriate supplies, re-testing for HIV, and psychosocial support can be guaranteed.

- If the client is receiving PrEP services at ANC or PNC service delivery site, align visits to standard ANC/PNC visits to minimize trips to the clinic, as frequent visits may discourage some clients from continuing PrEP.

- As with clients who are not pregnant or breastfeeding, HIV should be ruled out by testing before initiation of any form of PrEP. HIV testing should be performed the same day that PrEP is started, using a point-of care rapid HIV test, with additional testing according to the national HIV testing algorithm. (Please see PrEP for Pregnant and Breastfeeding People – Clinical Guidelines and Training Package - PrEPWatch for more information). Testing should be followed by an assessment for HIV exposure in the prior 72 hours, in case post-exposure prophylaxis is warranted, and then an assessment for suspicion of acute HIV infection based upon signs and symptoms and HIV risk in the prior two weeks.

- Prevention of vertical transmission guidelines should also advise when PBFP should be retested after initiation of PrEP, following national protocols. Further re-testing of HIV negative pregnant persons and PrEP refill schedules should optimally align with the ANC and the mother-baby pair (MBP) visits.

- 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: from FP to ANC, from ANC to PNC, from PNC to FP or other facility- or community-based PrEP provider.

Key messages around possible side effects with PrEP use for PBFP

At this time, few studies have assessed specific side effects experienced by PBFP using PrEP. There are, however, studies that show that experiencing side effects while using PrEP during pregnancy or postpartum periods are associated with lower rates of PrEP continuation. Support and counseling for PBFP using PrEP is therefore critical.

Information on the side effects among those who are not pregnant and not breastfeeding have been documented. Oral PrEP use has generally been shown to be safe across a range of different countries and populations, based on data gathered so far. One in ten PrEP users may have mild side effects and most side effects resolve within one month. Side effects from oral PrEP may include: gastrointestinal symptoms (diarrhea and nausea, decreased appetite, abdominal cramping, and flatulence), dizziness, headaches, decreased kidney function, though rare, is another potential side effect. The possible side effects of the ring are typically mild and include urinary tract infections (experienced by about 15% of users), vaginal discharge (experienced by about 7% of users), vulvar itching (experienced by about 6% of users), and pelvic and lower abdominal pain (experienced by about 6% of users) (WHO 2021).

To help determine whether a symptom is a side effect or a discomfort related to pregnancy, clinicians can consider the guiding questions included in the PrEP Clinical Practice Guidelines (https://www.prepwatch.org/resources/prep-for-pregnant-and-breastfeeding-people/). If the health care provider and client decide that it is safe to continue PrEP use (because symptoms are mild and expected), the provider should offer reassurance and suggest strategies that may help to alleviate or improve coping with symptoms. The provider should also create a plan with the client to re-evaluate symptoms on a specified date, either by phone or in person. Showing the client that the health care provider cares about the acceptability and safety of oral PrEP and the ring experience is an important way to build trust and provide client-centered care.

Key messages for screening for intimate partner violence (IPV) in prevention of vertical transmission and PrEP settings for PBFP

Women may experience new, continued, or increased intimate partner violence (IPV) during pregnancy and the postnatal period. Intimate partner violence puts the mental and physical health of women at severe risk, and is also associated with lower PrEP uptake, increased PrEP interruption, and lower adherence to PrEP. Prevention of vertical transmission services should include routine enquiry for IPV (sometimes referred to as gender-based violence [GBV] screening) with all clients. After conducting routine enquiry for IPV, sites should offer appropriate first-line support based on **L**isten, **I**nquire, **V**alidate, **E**nhance safety and **S**upport (LIVES) approach and referrals to GBV response services. For more information: PrEP for Pregnant and Breastfeeding People – Clinical Guidelines and Training Package - PrEPWatch

Conclusion

Elimination of vertical transmission of HIV will require expanded access to HIV prevention strategies, including a strong emphasis on provision of PrEP, for pregnant and breastfeeding people. Inclusion of PrEP for PBFP in national prevention of vertical transmission policies is a critical step for ensuring countries have a comprehensive roadmap for reducing HIV acquisition among pregnant and breastfeeding people and onward transmission to their infants. Doing so could bring elimination of vertical transmission a step closer to reality, as well as help close persistent HIV incidence reduction gaps in the context of 95-95-95 achievements.

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