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ISSUE BRIEF: PrEP

Why PrEP?

Despite over a decade of global investment in fighting the HIV epidemic and an overall decrease in HIV transmission, HIV continues to be transmitted to millions of people every year, with 1.8 million new infections in 2016 alone.[1] HIV researchers are determined to develop a vaccine that can protect patients exposed to HIV from acquiring HIV and/or a cure to eliminate HIV from patients already infected with the virus – but those breakthroughs are still years, if not decades, away from use in patients. Until such time, identifying new and improved ways to prevent the spread of HIV and scaling-up evidence-based HIV prevention efforts is growing in importance as part of global and national endeavors.

One area showing significant promise in the field of HIV prevention is using antiretroviral (ARV) drugs to prevent HIV transmission. Studies have shown that not only can adherence to antiretroviral treatment (ART) by HIV-positive individuals reduce the risk of further transmission to HIV-negative individuals, but daily use of oral ARVs by HIV-negative individuals — pre-exposure prophylaxis (PrEP) — can significantly reduce their own risk of HIV acquisition.

Other means of HIV prevention do exist, such as male and female condoms and voluntary medical male circumcision. However, oral PrEP offers the unique advantages of being effective and having the ability to be used independently without requiring partner consent. These are desirable attributes for prevention services, particularly for those individuals at significant risk of acquiring HIV and who may not be able to negotiate safe sex practices, such as key-populations (i.e. men who have sex with men (MSM) and sex workers), men and women in sero-discordant relationships, and adolescent girls and young women.

What is PrEP?

PrEP is the use of ARVs to prevent the acquisition of HIV. Various forms of PrEP have been studied over the years, including microbicides, such as vaginal gels and rings, and daily oral pills. Those that have shown positive results in trials include single drug daily oral pills of tenofovir disoproxil fumarate (TDF) and combination daily oral pills of TDF and emtricitabine (FTC). As described below, PrEP studies illustrate that measurable levels of TDF and TDF/FTC in an HIV-negative person's system can provide significant protection against HIV-acquisition, reducing the risk of transmission.

What does the research tell us?

Since 2005, clinical trials have demonstrated the efficacy of PrEP in specific populations at significant risk of HIV. The iPrEx trial, which was the first trial of combination daily oral PrEP, showed a 44% reduction of HIV acquisition among MSM and transgender women who have sex with men. The effectiveness of oral

PrEP in the iPrEx study reached as high as 90% in reducing HIV acquisition for those who had better adherence to treatment, as demonstrated by adequate drug levels in their system. The TDF2 trial looked at combination oral PrEP in heterosexual men and women, showing a 63% reduction in risk of HIV acquisition. Finally, the Partners PrEP study among sero-discordant couples in Kenya and Uganda showed results of 67% effectiveness with single drug daily oral pills (TDF) and 75% with combination drug daily oral pills (TDF/FTC). As with the previous studies, this trial also demonstrated increased effectiveness with increased adherence to the daily regimen, 86% for TDF and 90% for TDF/FTC.[2]

What are the current guidelines for PrEP?

Based on the research demonstrating the protection provided by PrEP against HIV acquisition in at-risk populations, the World Health Organization (WHO) published updated guidelines in 2015 for the use of PrEP. This update expanded the use of PrEP to include all people at "substantial risk of HIV," recommending that PrEP be offered as a "priority for populations with an HIV incidence of about 3 per 100 person-years or higher."[3] PrEP should not be offered as a stand-alone intervention but rather be included as part of a combination of prevention services, such as condoms and voluntary medical male circumcision.

The U.S. President's Plan for Emergency AIDS Relief (PEPFAR) also updated its guidelines to include the use of PrEP within its programs. As noted in the 2018 Country Operating Plan guidance, "PEPFAR supports WHO guidelines on the use of PrEP as part of a package of comprehensive prevention services…"[4] Specifically, PEPFAR recommends prioritizing PrEP in areas with high HIV prevalence and incidence and targeting at-risk populations. These populations include: sex workers of all genders; MSM; people who inject drugs; older adolescent girls and young women (AGYW); and in sero-discordant couples as an interim protective measure until the partner living with HIV has initiated and adhered to ART and viral suppression is achieved.

Since PrEP is a relatively new intervention, PEPFAR also supports activities to help countries establish an enabling environment to support future implementation of PrEP, including the development of national policies and guidelines, aiding in the registration of PrEP drugs in country, and building awareness and support for the implementation of PrEP within health facilities and throughout the community.

What are the concerns and challenges with implementing PrEP in low-resource settings?

While research demonstrates overwhelmingly the benefits of PrEP, the results seen in a controlled study are not always easily replicable through wide-scale implementation in low-resource settings. Several factors need to be considered and evaluated to ensure successful implementation of PrEP. These factors include drug resistance, adherence, policy barriers, health workforce training, misconceptions and stigma reduction, adequate supply, and funding.

Drug resistance – Research in PrEP indicates a low risk for drug resistance. However, the reported cases of drug resistance (approximately 1 in 1,000 PrEP users) are among


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those who initiate PrEP shortly after acquiring HIV or those who become HIV-positive while receiving PrEP. An important measure to take when implementing PrEP to mitigate this risk is to ensure that all potential users are tested for HIV prior to initiation and that there is regular HIV testing for those on PrEP.

Adherence – Adherence to PrEP is critical for its success in protecting individuals from HIV. Adherence is particularly important for women because research has shown that women require greater adherence to oral PrEP because penetration of the drug in the genital tissues is lower in women then in men. Ensuring adequate wrap-around services to support adherence – such as peer support groups and counseling services – are imperative when implementing PrEP so that patients are educated on the importance of adherence and receive adherence support.

Policy barriers – There remain some policy challenges that could limit AGYW's access to PrEP. For instance, age of consent laws for access to HIV testing and sexual and reproductive health services may prohibit adolescent girls from having access to this preventive intervention. In addition, TDF-FTC is not registered for use as PrEP in some countries. Before implementing PrEP in specific countries, the policy landscape should be evaluated to understand potential barriers to services and take steps to improve access for those populations at substantial risk of HIV who would benefit from PrEP.

Health workforce training – Healthcare workers must be adequately trained in how to counsel, administer, and monitor PrEP. Since PrEP is a newer intervention, it is important that healthcare workers and patients are appropriately informed on what PrEP is and is not, how it works, and why it is important. This will assist with not only uptake of PrEP by those at high risk of HIV, but increased adherence due to an understanding of the protection provided. In addition, it is important that healthcare workers are appropriately trained to provide non-judgmental counseling to patients and provide PrEP as a component of a more comprehensive HIV prevention package. Once PrEP is prescribed, healthcare workers must appropriately monitor adherence and conduct regular HIV testing.

Misconceptions and stigma – Misconceptions and stigma by both individuals and healthcare providers pose significant barriers to treatment access. For instance, in many places

it is not common for patients to take preventative treatment – one only takes medicine if he or she is sick. This makes it challenging to get patients to come to the clinic for prevention services. In addition, some are afraid of their PrEP treatment being mistaken for HIV treatment and the stigma associated with it. There is also a fear of being stigmatized and treated poorly by healthcare workers who may not be educated or adequately trained on how to engage with patients who are receiving HIV treatment or seeking prevention services. Measures should be taken to educate the community, patients, and healthcare workers on PrEP to clarify any misconceptions, raise awareness about PrEP, and provide accurate and adequate information in order to reduce stigma and increase acceptance of this lifesaving intervention.

Adequate supply – In order to avoid stock-outs and stock shortages, it is important to support accurate quantification and strong supply chain management systems from the port of entry to the facility level. During the introduction of a new drug, demand may be rapidly changing and thus, careful stock monitoring and forecasting is important.

Funding – National health system funding constraints may limit patient access to PrEP. Many countries are still working to reach all HIV-positive patients with ART, and shifting limited resources to reach HIV-negative patients with ART could be perceived as a drain on the healthcare system. Implementation of PrEP should not pull funding away from access to ART for those living with HIV. It will be important to continue to demonstrate the benefits of offering PrEP as part of a comprehensive HIV prevention package in order to stem the tide of new infections and prevent individuals from a lifetime of ART treatment.

What is EGPAF's position on PrEP?

EGPAF supports the use of PrEP where included in national guidelines and as part of comprehensive HIV prevention strategies. Currently EGPAF is directly supporting the introduction of PrEP in Kenya, Lesotho, and Uganda. All three of these countries have PrEP indicated in their national guidelines. In addition, EGPAF is engaging with stakeholders in other countries where we work and that have ongoing implementation programs for PrEP, including Cote d'Ivoire, Democratic Republic of the Congo, Malawi, Mozambique, eSwatini, Tanzania, Zambia, and Zimbabwe.[6]

There is significant overlap between the populations that have been identified as priority for PrEP by both WHO and PEPFAR and the populations served by EGPAF programs. While EGPAF supports the implementation and use of PrEP per national guidelines more broadly, there is unique interest for EGPAF to focus its programmatic efforts around PrEP on pregnant and breastfeeding women in sero-discordant relationships and AGYW.

As noted in the studies above, the risk of HIV-acquisition in sero-discordant couples is significantly reduced when the HIV-negative partner adheres to daily oral PrEP. In addition, given the increased risk of HIV transmission from mother to baby for pregnant women who acquire HIV during pregnancy, it is recommended that HIV-negative women consider continuing PrEP until the end of the breastfeeding period to ensure their babies are born and remain HIV-negative.[5] Taking into consideration the significant protection offered by PrEP, the PEPFAR DREAMS program also includes PrEP as part of its core package of services to help empower AGYW to take control of their own health. In many areas in which EGPAF works, pregnant and breastfeeding women and AGYW fall within the high-risk categories outlined by WHO. This aligns with EGPAF's core mission to ultimately end AIDS in children – by preventing new infections in pregnant and breastfeeding women and AGYW, as well as helping others to remain HIV free, EGPAF is helping to prevent new infections in children.

EGPAF is aware that additional implementation and operations research is needed to successfully roll-out PrEP in the countries where we work. EGPAF supports building evidence for feasibility and acceptability of PrEP in country, developing programmatic tools to aid in implementation of PrEP, and assisting health authorities and health systems in prioritizing human and financial capacity for this intervention, among other activities. PrEP should continue to remain part of a broader and more comprehensive prevention package and should not take away from other key HIV services such as ART coverage.

How to improve PrEP access in country?

Assessment of country need – Before advocating for PrEP in country, there needs to be a clear understanding of the populations at substantial risk for HIV that fall within the existing WHO and PEPFAR guidelines. If these populations are in need of and not currently able to receive PrEP in country, then additional action should be taken to improve access.

National guidelines and supportive policy frameworks – It is important to identify existing guidelines for PrEP and HIV prevention more broadly in country. If there are no guidelines or there is no mention of oral PrEP, advocacy for the creation or inclusion of PrEP in national guidelines is warranted, specifically identifying the populations at substantial risk for HIV as discovered during the assessment. In addition, when rolling out oral PrEP in country, it is important that there are strong policies in place to support implementation, including specifics around who is eligible for PrEP, details for what is included in the package of services, and appropriate age of consent laws. If these do not exist, advocacy should be undertaken to call for their development to help create an enabling environment for PrEP to flourish.

Drug registration and national budgets – It is important that oral PrEP ARVs be registered in country in order to ensure it is a possible prevention option. Sometimes ARVs are registered in country for HIV treatment but additional registration is required in order for those same ARVs to be offered as PrEP. In addition, there needs to be funding to purchase oral PrEP. Advocacy for the quick registration of oral PrEP, as well as the inclusion of PrEP in national HIV budgets, will help to ensure that oral PrEP is included as part of a comprehensive prevention package for those at substantial risk of HIV.

Demand creation – In order for PrEP to be successful, people need to understand what it is and is not, how it works, the benefits provided, and the importance of adherence. Public awareness campaigns are an important component of

rolling out any PrEP program in country in order to mobilize communities to take up services. In addition, efforts to reduce stigma associated with the populations at substantial risk of HIV will help lead to increased clinic visits and PrEP uptake by those who would benefit most from PrEP.

Conclusion

As efforts to end the HIV epidemic move forward, it is imperative that PrEP be included as an integral part of a comprehensive prevention package for those at risk of acquiring HIV. Studies continue to demonstrate its effectiveness in preventing new infections – now is the time to implement PrEP in real world settings. Oral PrEP will remain a promising intervention to lead to an HIV-free generation until the time when a cure or a vaccine is available.

Sources:

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4. PEPFAR. 2018 Country Operational Plan Guidance for Standard Process Countries. https://www.pepfar.gov/documents/organization/276459.pdf. Accessed April 19, 2018. p. 249.

5. CDC. Provider Information Sheet – PrEP During Conception, Pregnancy and Breastfeeding. https://www.cdc.gov/hiv/pdf/prep_gl_clinician_factsheet_pregnancy_english.pdf. Accessed May 10, 2018.

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