



Systemic (Oral) Pre-Exposure Prophylaxis (PrEP)

What is systemic pre-exposure prophylaxis (PrEP)?

Systemic pre-exposure prophylaxis (PrEP), otherwise known as oral PrEP, is a prevention method whereby an HIV-negative person ingests antiretroviral medications (ARVs) regularly in order to reduce the risk of contracting HIV.¹ In July 2012, the US Food and Drug Administration approved Truvada, a tenofovir-based drug manufactured by Gilead Sciences, to be used as PrEP. This marked the first time an ARV has been approved for prevention of HIV acquisition among HIV-negative adults.¹⁻²

How does PrEP work?

The daily use of tenofovir-based ARVs is believed to stop HIV replication following exposure to the virus.³

What is the evidence supporting PrEP?

In recent clinical trials, PrEP demonstrated effectiveness at preventing HIV acquisition among both men who have sex with men (MSM) and heterosexual couples.⁴ In 2010, the multi-country iPrEx study showed that PrEP was 44% protective against HIV infection among MSM when used in combination with other HIV prevention methods (eg, testing, counseling, and condom promotion).⁵

Two studies targeting heterosexual men and women demonstrated even stronger results than iPrEx—reporting reductions in HIV acquisition ranging from 62% to 75%.⁶⁻⁷ Conversely, 2 other studies involving heterosexual women showed that PrEP did not protect against HIV.⁸ However, significant numbers of

participants in these 2 studies did not adequately adhere to the PrEP regimen. This suggests that in order for PrEP to work, the medication must be taken consistently on a daily basis.³

What are the recommendations regarding systemic PrEP and MSM?

In January 2011, the US Centers for Disease Control and Prevention released technical guidance for the use of PrEP among MSM. Summary points are as follows:

- PrEP should be delivered as part of a comprehensive package of HIV prevention approaches, including testing and counseling, condom promotion and access, and management of other sexually transmitted infections.⁹
- PrEP should target individuals at highest risk for HIV acquisition, such as those in sero-discordant sexual relationships.
- Adherence is paramount: Those taking PrEP must take the medication consistently, given that protection from HIV is closely linked to adherence.

What are the considerations and limitations of systemic PrEP as an HIV prevention strategy for MSM?

PrEP has the potential to be an important resource in the HIV prevention toolbox. For those who lack access to condoms, those who cannot use them due to severe stigma or safety concerns, or those who refuse for reasons related to pleasure

or personal preference, systemic PrEP may offer a viable option to prevent the acquisition and transmission of HIV.

The implementation of PrEP is both complicated and costly. Some possible challenges and limitations of PrEP implementation targeting MSM are as follows:

- **Adherence and health behavior:** Even under ideal study conditions, where research and clinical staff are usually well trained to provide education and support to PrEP participants, adherence to PrEP regimens remained difficult. Hence, in the “real world” (ie, outside of a controlled study), ensuring adherence will likely be an implementation challenge that may seriously jeopardize the potential effectiveness of this intervention

Moreover, providing PrEP will likely require healthy, HIV-negative, sexually active adults to see a provider at least 3–4 times a year for monitoring. This demographic may be unaccustomed to seeing providers this often, which may further impede PrEP uptake, adherence and retention.¹⁷

Additionally, public health systems globally most often see clients on a drop-in basis. Current common models of care are not designed and/or ready for the rollout of PrEP, which will require consistent and continuous monitoring of patients. This may be especially true in resource-constrained settings where health infrastructure is weak.¹⁰

- **Costs, financing, and equity:** PrEP is expensive. In the United States, the current cost of PrEP is estimated at over \$1000 per month (\$12 000–\$14 000 per year).¹¹ Thus, in order to save health system costs, PrEP implementation will likely target the highest-risk populations (eg, low-income MSM). However, these populations are also the least likely to have health insurance coverage and/or the financial means to pay for medications. This raises implications for country-level and multinational donors who will need to ensure PrEP access for low-resource, vulnerable populations.¹²
- **Adverse events, side effects, and widespread drug resistance:** Although patients who participated in PrEP clinical trials reported mild side effects and little risk compensation (for example, few patients stopped using condoms in response to a perception of decreased risk) and study findings revealed few to no adverse events and little to no drug resistance, it is important that future studies and implementation continue to monitor these potential issues over the long term in various populations.¹³

- **Resource shortage and ethical implications:** Globally, there are millions of people living with HIV/AIDS (PLHIV) who are not on treatment, some of whom are on waiting lists to gain access to medication. Some advocates have raised important questions about whether it is ethical to provide PrEP when there are so many PLHIV in need of life-saving treatment.¹⁴
- **Community engagement and identification of community needs:** Local communities must be fully engaged in PrEP implementation, taking a lead role. Ensuring ethical and successful implementation of PrEP will require community mobilization, raising awareness through education, and rigorous social research to determine community needs and barriers.

What does recent research tell us about overall knowledge of PrEP among MSM?

From June through August 2010, the Global Forum on MSM and HIV (MSMGF) conducted a global study on access to and knowledge of HIV prevention strategies—including PrEP¹—among more than 5000 gay men and other MSM worldwide.¹⁵ The study generated several key findings regarding knowledge of and attitudes regarding PrEP.

Knowledge and understanding of PrEP

- Only 31% of the entire sample reported being “very knowledgeable” or “somewhat knowledgeable” about PrEP as a method of HIV prevention among gay men and other MSM.
- Respondents in the Global South (Asia, Middle East, Africa, Latin America) were significantly less knowledgeable about PrEP than respondents from the Global North (Europe, North America, Australia/New Zealand) (25% vs 57% reported being “very knowledgeable” or “somewhat knowledgeable” respectively, $p < .001$).
- Only 28% of all respondents correctly answered the true/false question, “PrEP should only be used by HIV-negative persons.” Moreover, only 39% responded correctly to the following true/false question: “PrEP is different from post-exposure prophylaxis (PEP) in that it is taken BEFORE exposure to HIV” (3% responded incorrectly and 58% answered “I don’t know”).

¹Survey asked about PrEP in general and did not specify “topical” or “systemic” PrEP.

- Overall, participants expressed a strong desire to learn more about PrEP. Approximately 93.4% “strongly agreed” or “somewhat agreed” with the statement, “I would like to learn more about Pre-Exposure Prophylaxis (PrEP) to prevent transmission of HIV among gay men/MSM.”

Perceptions and attitudes regarding PrEP

- In total, only 35% of respondents “strongly agreed” or “somewhat agreed” with the statement, “I believe that PrEP should be used by gay men/MSM to prevent HIV infection.”
- About a quarter of respondents indicated that they “would be comfortable with the idea of taking antiretroviral medications every day in order to prevent HIV,” signaling skepticism about PrEP and potentially low demand for the intervention in the future.

Conclusion

PrEP offers the opportunity to add another important HIV prevention strategy to the spectrum of interventions targeting gay men and other MSM. However, PrEP is not a “silver bullet,” and it must be utilized as part of a comprehensive HIV prevention package that includes behavioral and structural interventions as well (eg, community-based outreach; condom and condom-compatible lubricant promotion; HIV counseling and testing; campaigns and policies that reduce HIV stigma and homophobia; and STI prevention, screening, and treatment).¹⁶

Going forward, research must be conducted to assess long-term side effects and drug resistance, as well as the possibility of intermittent PrEP (before and after a sexual act instead of

once daily). Furthermore, future operations and social science research will be needed to better understand adherence rates in “real world settings” as opposed to clinical trial conditions, as well as the threat of risk compensation among MSM (eg, PrEP leading to decreased condom use).¹⁷

In order for PrEP implementation to be successful among MSM, several necessary conditions must be met. First, communities of MSM must organize to determine their sexual health needs. Efforts addressing these needs must be adequately resourced in a sustained manner, and they must include competent and accessible health care services, HIV testing and treatment opportunities, and mental health services.

Second, considerable efforts should be made to improve overall understanding, awareness, and knowledge of PrEP within MSM communities. Lack of correct information within MSM communities will impede access and uptake and may stymie the impact potential of PrEP to avert future HIV infections.¹⁸

Additionally, PrEP is only likely to be successful when delivered to MSM in a safe and culturally competent manner, buttressed by organized and well-informed communities with access to effective health systems. Health systems and providers must understand the unique needs of the populations they serve.¹⁹

Last, MSM need to feel safe attending clinics and accessing prevention and care services. This need for safety underscores the importance of an enabling sociopolitical environment that mitigates HIV stigma and homophobia. Country-level and multi-lateral support of policies and legislation that decriminalize homosexuality, mitigate HIV stigma, and address homophobia are all essential to ensuring the successful implementation of systemic PrEP.

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