

# What is pre-exposure prophylaxis (PrEP) and is it effective in preventing HIV?

UCSF

Center for AIDS  
Prevention Studies (CAPS)  
Technology and Information  
Exchange (TIE) Core

Prepared by Stephanie Cohen MD MPH and AI Liu MD, SF DPH | Gabriel R. Galindo DrPH; CAPS

Fact Sheet: 19 October 2012

## What is PrEP?

PrEP stands for pre-exposure prophylaxis and it is a promising biomedical HIV intervention. It is an approach to prevention where HIV-negative people take HIV drugs in order to prevent HIV infection. PrEP is started **before** possible exposure to HIV, and is taken on an ongoing basis. PrEP is not a vaccine and it is different from post-exposure prophylaxis (PEP), where the medication is started soon after exposure to HIV and continued for 28 days only. Taking a medication before exposure has been shown to be effective in preventing other infectious diseases. Likewise, providing antiretroviral therapy to pregnant women and their infants has been used effectively for many years to prevent mother-to-child transmission of HIV [1]. PrEP can be in the form of a pill taken by mouth, known as “oral PrEP”. [2,3,4 ] In clinical trials PrEP has been provided in combination with other HIV prevention interventions, such as condom distribution, behavioral counseling, HIV testing, and screening of other sexually transmitted infections (STIs).

were transgender women) participants from 6 countries, and included two cities in the US. All participants received frequent HIV testing, risk reduction counseling, condoms and lubricants, and screening and treatment for STIs. Half of the participants were randomly assigned to receive Truvada®, and the other half a placebo. The participants who received Truvada® had 44% fewer HIV infections than the participants who received the placebo. This means that PrEP prevented almost half of the infections that would have occurred if the medication was not provided. The protective effect of PrEP was even higher for those who were able to take the drug more consistently, including those who had evidence of Truvada® in their blood.

The effectiveness of PrEP in other populations, such as heterosexual men and women, and

injection drug users, is currently unknown as clinical trials have had mixed results. Still, there are several ongoing studies happening around the world in these populations, and those results will further enhance our understanding of PrEP’s efficacy [9,10]. For detailed information on PrEP trials occurring globally, click **here** for a table of ongoing and planned studies [11], and **here** for a PrEP trials timeline [12].

## Why is PrEP important?

Globally there are 2.6 million new HIV infections each year, and in the US, there are an estimated 56,000 new HIV infections annually.[5] While risk reduction counseling, condoms, male circumcision and other methods have been shown to reduce HIV infections, by themselves they are not enough and new approaches to HIV prevention are urgently needed – especially for men who have sex with men (MSM) and transgender women, the groups who disproportionately bear the greatest HIV burden in the US [6].

## Is PrEP safe?

The iPrEx trial found that Truvada® was safe and generally well-tolerated by participants in the study. There were a few mild side effects related to Truvada®, such as nausea, which were infrequent and decreased with time. While a small amount of bone loss was seen in men receiving PrEP, a finding commonly seen in HIV-positive individuals starting similar antiretroviral treatment regimens, these changes had no apparent negative health impact. Drug resistance was not seen among those who became HIV-infected during the iPrEx study,. Still, HIV testing and medical evaluation before starting, and while using, PrEP are important to prevent resistance and to monitor side effects on an individual level.

Like the iPrEx study, there were also no significant safety concerns raised in the trials of PrEP that have been conducted among heterosexual men and women. However, it is important to note that the follow-up in these studies was relatively short. Therefore, evaluating the longer-term safety of oral PrEP is important and will require further investigation in ongoing studies. Additional research is also needed to determine how frequently people taking PrEP will need to be seen by a health care provider and how often they will need to have laboratory monitoring, including HIV testing and monitoring of kidney function.

## What drugs are currently being tested for PrEP?

Recently completed and ongoing studies of **oral PrEP** have tested the HIV drug tenofovir (also known as Viread®) alone or in combination with emtricitabine. The combination of tenofovir and emtricitabine is known as Truvada®. These medications were chosen because they only have to be taken once daily, they have few side effects, they don’t interact with most other medications, and they have been shown to be safe and effective in animal studies of PrEP. Different topical formulations are currently being studied in clinical trials, and other forms of **topical PrEP**, including a vaginal ring and a gel formulated for rectal use, are also under development.[7]

## How effective is PrEP in preventing HIV infection?

For MSM and transgender women, the iPrEx study results, released in November 2010, demonstrated for the first time that daily oral Truvada® is effective for HIV prevention.[2] The iPrEx study enrolled nearly 2500 MSM (1.2% of participants

## What are current recommendations for PrEP?

In January 2011, the Centers for Disease Control and Prevention (CDC) issued interim guidance on the use of PrEP for HIV prevention in MSM.[13] The CDC emphasizes that:

- PrEP should only be considered for MSM at high risk for HIV infection (and not other populations until additional data are available).
- PrEP should only be used in individuals with negative HIV antibody test(s) confirmed immediately prior to starting PrEP. If symptoms of recent HIV infection are present, PrEP should be deferred and testing for acute HIV infection should be performed.
- PrEP should never be seen as the first line of defense against HIV. PrEP should be delivered as a part of a comprehensive prevention package that includes risk-reduction and adherence counseling, encouragement of condom use, and diagnosis and treatment of STIs.
- PrEP should be taken daily. Only the regimen tested in iPrEx (daily Truvada®) should be used, and not other antiretroviral medications or other dosing regimens (such as intermittent or occasional use).
- PrEP should be obtained and used in close collaboration with healthcare providers to monitor side effects, adherence, safety, and risk behaviors at regular intervals.

Individuals taking PrEP should undergo regular HIV testing and should stop taking PrEP if they test HIV-positive. Those interested in PrEP should discuss this with their physicians and should not use PrEP on their own. Comprehensive guidelines for PrEP use will be developed by the United States Public Health Service through expert consultation and community input.

## What are the next steps for PrEP?

In July 2012 the U.S. Food and Drug Administration approved Truvada® to reduce the risk of HIV infection in uninfected individuals who are at high risk and who may engage in sexual activity with HIV-infected partners. Recognizing that no infectious disease has ever been eliminated through medications alone, we need to carefully consider how to best use this tool in combination with other prevention strategies to make the largest impact on HIV/AIDS in the US and worldwide. In the iPrEx, Partners PrEP and TDF-2 studies, PrEP was shown to be partially effective when used in combination with regular HIV testing, condoms, and other proven prevention methods, like individual risk reduction counseling. Combination prevention approaches that integrate biomedical, behavioral, and structural components are necessary to optimize HIV prevention efforts.[14] As such, the effectiveness of PrEP depends not just on the effectiveness and safety of the drugs, but also on several other implementation factors, including good adherence to the drug, maintaining safer sex behaviors, and access to clinical and social support services. Interventions and programs that help HIV-negative individuals access PrEP, take the pills on a regular schedule, manage potential side effects, undergo regular HIV testing, and maintain safer sex and drug-using practices are key to maximizing PrEP's effectiveness and acceptance.[15,16] Additional studies, community-wide discussions, and advocacy work are underway to try to address and assess many of these important considerations.

## Says who?

1. WHO. Guidance on global scale-up of the prevention of mother-to-child-transmission of HIV: Towards universal access for women, infants and young children and eliminating HIV and AIDS among children. The Interagency Task Team on Prevention of HIV Infection in Pregnant Women, Mothers and Their Children, 2007.
2. Grant RM, Lama JR, Anderson PL, et al. Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men. *NEJM* 2010;363(27):2587-99. Epub 2010 Nov 23.
3. Abdool Karim Q, Abdool Karim SS, Frohlich JA, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science* 2010;329:1168-74.
4. Centers for Disease Control and Prevention. CDC Trials: Pre-Exposure Prophylaxis for HIV Prevention. February 2011. [http://www.cdc.gov/hiv/prep/pdf/PrEP\\_TrialsFactSheet.pdf](http://www.cdc.gov/hiv/prep/pdf/PrEP_TrialsFactSheet.pdf)
5. Hall HI, Song R, Rhodes P, et al. Estimation of HIV incidence in the United States. *JAMA* 2008;300(5):520-9
6. Centers for Disease Control and Prevention. Estimates of new HIV infections in the United States.

CDC Fact Sheet, 2008. Available at: <http://www.cdc.gov/nchhstp/newsroom/docs/Fact-Sheet-on-HIV-Estimates.pdf>.

7. Stone A, Harrison PF. Microbicides – Ways Forward. Alliance for Microbicide Development: Silver Spring, MD, USA. 2010.
8. Buchbinder SP, Liu A. Pre-exposure prophylaxis and the promise of combination prevention approaches. *AIDS and Behavior*. 2011;15,S1:72-79.
9. Peterson L, Taylor D, Roddy R, et al. Tenofovir disoproxil fumarate for prevention of HIV infection in women: a phase 2, double-blind, randomized, placebo-controlled trial. *PLoS Clin Trials* 2007;2:e27.
10. Grohskopf L, Gvetadze R, Pathak S, et al. Preliminary analysis of biomedical data from the phase II clinical safety trial of tenofovir disoproxil fumarate (TDF) for HIV-1 pre-exposure prophylaxis (PrEP) among U.S. men who have sex with men (MSM). Abstract no. FRLBC102, International AIDS Society 2010, Vienna.
11. AIDS Vaccine Advocacy Coalition. (2012, April). Ongoing and planned pre-exposure prophylaxis (PrEP) trials. Retrieved from <http://www.avac.org/ht/a/GetDocumentAction/i/3113>

12. AIDS Vaccine Advocacy Coalition. (2011, May). Oral and topical PrEP trials timeline. Retrieved from <http://www.avac.org/ht/d/sp/a/GetDocumentAction/i/3618>

13. Smith DK, Grant RM, Weidle PJ, et al. Interim guidance: preexposure prophylaxis for the prevention of HIV infection in men who have sex with men. *Morbidity and Mortality Weekly Report*. 2011;60:65-68.

14. Centers for Disease Control and Prevention. Pre-exposure prophylaxis (PrEP) for HIV prevention: Promoting safe and effective use in the United States. February 2011. <http://www.cdc.gov/hiv/prep/pdf/PrEPfactsheet.pdf>

15. Underhill K, Operario D, Skeer MR, et al. Packaging PrEP to prevent HIV: An integrated framework to plan for pre-exposure prophylaxis implementation in clinical practice. *JAIDS*.2010;55:8-13.

16. Underhill K, Operario D, Mimiaga MJ, Skeer MR, Mayer KH. Implementation Science of Pre-exposure Prophylaxis: Preparing for Public Use. *Curr HIV/AIDS Rep* 2010;7:210-9.

Special thanks to the following reviewers of this Fact Sheet: David Abbott, Tom Aloisi, Susan Buchbinder, Katerina Christopoulos, Chris Collins, Jen Hect, Quarrasha Abdool Karim, Delia Molloy, Stephen Morin, Don Operario, Kristen Underhill and Dana Van Gorder. Reproduction of this text is encouraged; however, copies may not be sold, and the University of California San Francisco should be cited as the source. Fact Sheets are also available in Spanish. ©2012, University of CA. CAPS.Web@ucsf.edu.