



Pre-Exposure Prophylaxis (PrEP)

This fact sheet provides basic information on pre-exposure prophylaxis (PrEP), one of the options being tested now as part of the effort to identify additional tools to reduce the risk of HIV transmission.

What is PrEP? • What drugs are currently being tested for PrEP? • Why study PrEP for HIV prevention? • How might PrEP reduce risk of HIV infection? • How will we determine if PrEP should be added to HIV prevention programs? • Where are PrEP trials taking place? • Who is involved in PrEP research? • When are results from PrEP trials expected?

What is PrEP?

PrEP is an experimental approach that would use antiretroviral medications (ARVs) to reduce the risk of HIV infection in HIV-negative people. In the recent iPrEx effectiveness trial among men who have sex with men, PrEP using daily dosing of a pill containing tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) had reduced risk of HIV by 44 percent compared to participants receiving the placebo. iPrEx provided initial evidence that PrEP using daily oral TDF/FTC can work in gay men and other MSM. Additional research is needed and more information will come from trials in other populations and other parts of the world. PrEP is not a strategy that any individual should try on his or her own.

What drugs are currently being tested for PrEP?

All of the current effectiveness trials are testing TDF/FTC (sold under the brand name *Truvada*) or TDF (sold under the brand name *Viread*). Scientists have focused on these drugs because they are taken once a day for treatment, have relatively low rates of side effects, and because there is significant data on their long-term safety and resistance profiles in HIV-positive people. The effectiveness trials are all evaluating daily dosing. There are trials planned to explore effectiveness in the context of other *intermittent* dosing strategies. Other drugs are also being considered as PrEP agents.

Why study PrEP for HIV prevention?

The science of PrEP builds on the concept that medications can be used by healthy people to prevent infection by some diseases. This concept is known as *prophylaxis*. iPrEx provided the first evidence that this concept can be applied to sexual HIV exposure in gay men and other men who have sex with men. The scientific basis for testing PrEP in iPrEx and other trials came from animal studies in which PrEP strategies have shown that dosing with ARVs prior to exposure reduces risk of infection among animals challenged with strains of SHIV (an HIV-like virus that can cause disease in monkeys).

Other relevant data come from humans: ARVs are given to HIV-negative infants born to HIV-positive pregnant women as part of effective strategies to reduce the risk of vertical transmission. The ARVs taken by the HIV-negative infants may contribute to their reduced risk HIV infection. ARVs are also used for *post-exposure* prophylaxis (PEP). In PEP, someone who's recently been exposed to HIV (through a needle stick or an unprotected sex act, for example) takes ARVs for several weeks to reduce the risk of acquiring HIV. PEP differs from PrEP in that, with PEP, people start taking the drugs after they think they may have been exposed. Most PrEP strategies being tested ask people to take the medications on an ongoing basis that is not tied to specific behavior or possible exposure.

How might PrEP reduce risk of HIV infection?

Antiretrovirals block HIV as it infects cells or copies itself once inside a cell. TDF and TDF/FTC are reverse-transcriptase inhibitors, drugs that are absorbed into cells and help block a critical step in viral replication (the process of the virus copying itself). In HIV-positive people, this action helps control viral replication and reduce viral load. (In HIV-positive people multiple drugs, targeting different stages of the viral lifecycle must be used to achieve viral suppression.) In HIV-negative people, the drug appears to provide protection by stopping HIV from successfully copying itself. Once in the cell, HIV fails to replicate, and infection does not proceed. It is important to note that the iPrEx trial found that people who were in the TDF/FTC arm of the trial and who had detectable levels of drug in their blood had the lowest risk of HIV infection. People who were in the TDF/FTC arm and had no detectable drug in their blood were at higher risk. Presence of drug in the blood correlated with protection from HIV.

How will we determine if PrEP should be added to HIV prevention programs?

iPrEx suggests that daily oral TDF/FTC can reduce risk in gay men and other men who have sex with men. Other ongoing trials will provide information about PrEP in the context of penile-vaginal sex and injection drug use. These trials will shed more light on whether PrEP is safe and effective in other populations. Each of these trials provides intensive counseling, monthly HIV testing, condoms and a range of prevention messages and services to all participants. In the real world, it is not feasible to provide such a package to every person who might consider using PrEP. iPrEx has therefore prompted a range of follow-up activities, including an open-label extension study open to all iPrEx participants that offers PrEP in the context of less rigorous monitoring. There are also calls for demonstration projects, which would pilot and evaluate various strategies for providing PrEP in ways that optimize its benefit and minimize risks for individuals. These projects would guide provision of PrEP to targeted groups of gay men and other men who have sex with men. They must be considered as a next step in other populations where PrEP shows effectiveness.

Given that iPrEx tested an already licensed drug, there is the potential for immediate, off-label use. In the US, the Centers for Disease Control and Prevention issued interim guidance on PrEP as an HIV prevention strategy for MSM (www.cdc.gov/mmwr/pdf/wk/mm6003.pdf). It addresses key considerations for health care providers in the US considering daily oral TDF/FTC as PrEP for their MSM clients. Other national and international agencies have yet to provide any formal guidance.

Where are PrEP trials taking place?

PrEP trials are currently ongoing in Botswana, Brazil, Ecuador, Kenya, Peru, South Africa, Tanzania, Thailand, Uganda, the United Kingdom, the United States and Zimbabwe. Visit www.avac.org/prep for a map of past and present PrEP trials.

Who is involved in PrEP research?

Like other HIV prevention strategies, PrEP is being tested among different populations including gay men and other men who have sex with men, injecting drug users, sex workers and heterosexual men and women in sub-Saharan Africa. These trials are designed to answer how PrEP might work in the context of different routes of exposure. There are over 20,000 people participating in PrEP trials.

When are results from PrEP trials expected?

The iPrEx data were released in November 2010. The next effectiveness trial data are expected in 2012 and 2013. Other completed studies include expanded safety evaluations among heterosexual women (Cameroon, Ghana and Nigeria), and gay men and other men who have sex with men (United States.) Both studies found no serious adverse events or safety concerns. For details on these results visit www.avac.org/trials/prep.

Initial data from a small study of intermittent PrEP use (twice-weekly and after sex) in Uganda and Kenya has also been released, providing some information about the potential challenges and feasibility of alternative dosing strategies. More information will be needed on such strategies, should PrEP show effectiveness.

For additional details on PrEP, a timeline of expected results and related issues visit www.avac.org/prep. For details on the research process visit www.avac.org/researchprocess.

Founded in 1995, AVAC is an international, non-profit organization that uses education, policy analysis, advocacy and community mobilization to accelerate the ethical development and eventual global delivery of AIDS vaccines and other new HIV prevention options as part of a comprehensive response to the pandemic. For more information, visit www.avac.org.