



# 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?

PrEP is an experimental approach that would use antiretroviral medications (ARVs) to reduce the risk of HIV infection in HIV-negative people. ARVs are used to treat people living with HIV. In this intervention, HIV-negative people would take a single drug or a combination of drugs with the hope that it would lower their risk of infection if exposed to HIV. PrEP trials are ongoing around the world.

There are two ARVs currently being tested in PrEP safety and efficacy trials: tenofovir disoproxyl fumarate (TDF), marketed as Viread, and a combination of TDF and emtricitabine (FTC) marketed as Truvada. Scientists have focused on these drugs because they are taken once a day, 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 current large-scale trials are testing once-daily PrEP and there is expanding research around the concept of intermittent PrEP (for more see [www.avac.org/prep](http://www.avac.org/prep)).

## Why are we looking at 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. Although prophylaxis works for other diseases, like malaria, it is important to remember that PrEP is not a proven strategy for HIV.

The scientific basis for testing PrEP in humans comes from laboratory studies and other fields of HIV prevention. Studies of PrEP strategies in monkeys 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). There are also relevant data 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 will we know if PrEP works?

Every HIV biomedical prevention candidate goes through an extensive series of evaluations, first in laboratory and animal studies and then in humans. The animal studies provide preliminary information about the safety and efficacy of the candidate. Only those candidates that appear safe in animals are considered for human testing. Efficacy data from animals can also be used to inform decisions about whether to test a candidate in humans. However, studies in animals cannot give a clear answer about whether a strategy will reduce HIV risk in humans. In PrEP trials, scientists control exactly when the drug is taken and when the animal is challenged with the infectious virus. Trials in humans provide information about how the strategy works in situations where drug usage may not be 100 percent consistent and the timing of potential exposure to HIV is frequently not known. The drugs in today's PrEP trials have been approved and used safely and effectively in HIV-positive people for many years. Prior to starting large-scale efficacy trials, smaller safety studies have been launched or completed in HIV-negative people. No major safety issues have been identified to date and PrEP efficacy trials have moved ahead in several countries.

PrEP is being tested in large-scale efficacy or effectiveness trials. There are technical reasons why some trial designs are called efficacy and others are called effectiveness studies. Both terms refer to trials that look at whether a candidate reduces the risk of HIV infection. For simplicity, the term efficacy is used below.

The details of these large-scale efficacy studies vary, but the design of PrEP efficacy trials is similar to that of most HIV prevention trials. These trials enroll healthy, HIV-negative people, most commonly in communities where researchers have conducted preparatory work to learn about the rates of risk behaviors and incidence. Each participant receives a basic prevention package including treatment for sexually transmitted infections, condoms, and behavior change counseling. [Unfortunately, needle exchange is not provided in all of the efficacy trials involving injection drug users and this area is receiving continued attention from advocates and activists.] Some of the participants are randomly assigned to receive PrEP drugs, while the other participants receive a placebo—a pill that has no effect on the body. No participant knows whether he or she is receiving PrEP drugs or a placebo. All participants are counseled at every study visit that they can't assume they will be protected by PrEP and that they cannot know whether they have received PrEP or the placebo pill.

Over the course of the trial period, some participants get infected even though they are being counseled and receiving prevention services. This is consistent with what we know about the AIDS epidemic: even with information and services, not everyone can protect himself or herself all the time. At the end of the trial, researchers compare the rates of new infections in the participants who received PrEP drugs and in those who received a placebo. If there are significantly fewer new infections in the PrEP group—that is, if the difference is greater than can be reasonably explained by chance—this suggests that PrEP is beneficial.

#### **Where are PrEP trials taking place?**

PrEP trials are taking place in Botswana, Brazil, Ecuador, Kenya, Malawi, Peru, South Africa, Tanzania, Thailand, Uganda, the United States and Zimbabwe. Visit [www.avac.org/globalmap](http://www.avac.org/globalmap) for a map of ongoing 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 nearly 20,000 people participating in PrEP trials.

#### **When are results from PrEP trials expected?**

Some safety data have come from a PrEP trial that enrolled women in Cameroon, Ghana and Nigeria. These data indicate that once-daily TDF was safe and well-tolerated by participants over the course of their study participation.

Additional PrEP safety data is expected in the third quarter of 2010 from an extended safety trial in gay men and other men who have sex with men (MSM). This trial, which took place in the US, will provide information about the safety of once-daily TDF in HIV-negative MSM. It will also gather data on how participation in a PrEP study affects HIV risk behaviors. Every PrEP study also gathers information about volunteers' adherence to the medication. In cases where participants become infected, additional data are gathered to learn more about drug resistance, should it emerge.

Initial effectiveness data on whether PrEP works to reduce the risk of HIV infection should be available from a number of trials in late 2010/early 2011. For a detailed timeline of PrEP trials and expected results, visit [www.avac.org/trials](http://www.avac.org/trials).

*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](http://www.avac.org).*