CDC FACT SHEET

# PrEP: A New Tool for HIV Prevention

Pre-exposure prophylaxis, or PrEP, is a new HIV prevention method in which people who do not have HIV infection take a pill daily to reduce their risk of becoming infected. The pill contains medicines that prevent HIV from making new virus as it enters the body. In this way PrEP medicines can help keep the virus from establishing a permanent infection.

Providing a preventive medication before exposure to a germ or virus is not a new practice and has been used to prevent other diseases. For example, when individuals travel to an area where malaria is common, they are advised to take malaria medication before and during travel to prevent getting infected if bitten by a mosquito carrying the malaria parasite. However, the use of medication to prevent HIV infection has only recently been evaluated. When used consistently, PrEP has been shown to reduce the risk of HIV infection among adults at very high risk for HIV infection through sex, including men who have sex with men and heterosexually-active men and women. CDC is also evaluating PrEP's effectiveness in preventing HIV infection among individuals exposed to HIV through injecting drugs, but those results are not yet available.

For some individuals at very high risk for sexual exposure to HIV, PrEP may represent a much-needed additional prevention method — but it will not be right for everyone. PrEP is an intensive approach that requires strict adherence to daily medication and regular HIV testing. It is not intended to be used in isolation, but rather in combination with other HIV prevention methods. If it is used effectively and by persons at very high risk, PrEP may play a role in helping to reduce the number of new HIV infections in the United States.

### PrEP Medications

Most PrEP efficacy trials have tested a combination of the antiretroviral drugs tenofovir disoproxil fumarate (also called TDF, or tenofovir) and emtricitabine (also called FTC), taken in a single pill daily for HIV prevention. This combination pill (brand name Truvada®) was approved by the U.S. Food and Drug Administration (FDA) for use as an HIV treatment in 2004, and was approved as PrEP in July 2012. Some clinical studies have also evaluated the use of tenofovir on its own as a preventive drug, but this drug alone is not FDA-approved as PrEP.

## PrEP Proven Safe and Effective in Preventing Sexual HIV Acquisition

Strong research evidence indicates that PrEP, when used consistently, is safe and effective for reducing the risk of acquiring HIV sexually.

### Research among Men Who Have Sex with Men

In November 2010, the multinational iPrEx study showed that a once-daily pill containing tenofovir plus emtricitabine was safe and provided an average of 44 percent additional protection against HIV infection among men who have sex with men (MSM) who were also provided with a comprehensive package of prevention services. These services included provision of condoms, monthly HIV testing, counseling to reduce risk behavior and encourage adherence to the daily pill regimen, and management of other sexually transmitted infections.

The level of protection varied widely depending on how consistently participants used PrEP, with significantly greater levels of protection among those who adhered well to the daily dosing regimen. Among MSM with detectable levels of the medication in their blood, the risk of HIV acquisition was reduced by more than 90 percent.

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

AUGUST 2012

The iPrEx study followed an earlier study by CDC that examined safety and adherence among MSM in the United States who were using daily tenofovir alone. The study found that the regimen was safe and did not lead to increases in risk behavior.

### Research among Heterosexually-active Men and Women

In July 2011, researchers announced the results of two PrEP studies finding strong evidence that PrEP is effective and safe among heterosexually-active men and women.

- The TDF2 study found that a once-daily tablet containing tenofovir plus emtricitabine reduced the risk of acquiring HIV infection by roughly 62 percent overall in the study population of uninfected heterosexually-active men and women.
- The Partners PrEP study found that that daily doses of tenofovir plus emtricitabine or daily doses of tenofovir alone reduced HIV transmission among heterosexual serodiscordant couples (in which one partner is infected with HIV and the other is not) by 75 percent and 67 percent, respectively. The trial found that PrEP was equally effective among men and women, and that there was no statistically significant difference in efficacy between the two medication regimens.

As with the iPrEx study, both TDF2 and Partners PrEP showed that the level of protection offered by PrEP is strongly related to the level of adherence to the daily medication doses.

- In Partners PrEP, participants in the tenofovir-plus-emtricitabine group with detectable levels of the medication experienced a 90 percent reduction in risk for HIV infection; in the tenofovir- only group, the presence of medication in the blood was associated with an 86 percent reduction in risk.
- In TDF2, only half of the participants in the tenofovir-plus-emtricitabine group who became infected with HIV had any detectable medication in their blood, and even those participants had very low levels of medication present. This suggests that they had not taken PrEP consistently. In contrast, over 80 percent of matched participants who remained uninfected had detectable medication in their blood and the average medication level was substantially higher.

Two other research studies also reported results in 2011: a study called FEM-PrEP examining PrEP with tenofovir plus emtricitabine and a single group of participants in the VOICE trial examining PrEP with oral tenofovir alone did not show a protective effect among heterosexually-active women. Further sub-analysis of a sample of women in the FEM-PrEP trial showed that fewer than half of women assigned to take tenofovir plus emtricitabine were actually taking the drug, indicating that lack of adherence was likely a major factor contributing to the lack of efficacy in that trial.

Other than low adherence, no factors have yet been identified that appear to influence the efficacy of PrEP in reducing sexual transmission of HIV. The VOICE trial, which is still evaluating daily oral tenofovir plus emtricitabine in women, remains underway and may provide additional insight once those results are available.

## CDC Interim Guidance on PrEP Use

**MSM:** Following the publication of the iPrEx trial results, CDC published interim clinical guidance for physicians electing to provide PrEP for HIV prevention among MSM in January 2011. CDC guidance stressed the importance of targeting PrEP to MSM at very high risk for HIV acquisition; delivering PrEP as part of a comprehensive set of prevention services; providing counseling regarding risk reduction and the importance of PrEP medication adherence; ensuring MSM who are prescribed PrEP are confirmed to be HIV negative prior to use; and providing regular monitoring of HIV status, side effects, adherence, and risk behaviors.

**Heterosexuals:** Following the publication of final results from the TDF2 and Partners PrEP trials, in August 2012 CDC published interim guidance to help clinicians safely and effectively provide PrEP for heterosexually-active adults. This guidance included recommendations similar to those for MSM, as well as new recommendations relevant to women who may become pregnant while taking PrEP and to couples in which one partner is HIV-positive and the other is HIV-negative.

CDC is also leading the development of comprehensive U.S. Public Health Service (PHS) guidelines on the use of PrEP for the prevention of sexually-acquired HIV infection. These guidelines will include more detailed recommendations for PrEP use with adults at very high risk for HIV infection, including MSM as well as heterosexually-active men and women. They are being developed in partnership with other PHS agencies and will incorporate input from providers, HIV prevention partners, and affected communities. The guidelines will be updated as information from additional trials and studies about factors affecting efficacy and safety for all transmission risk groups becomes available.

# CDC Interim Guidance on HIV Pre-Exposure Prophylaxis

## Before initiating PrEP

**Determine eligibility:**

- Document negative HIV antibody test immediately before starting PrEP medication.
- Test for acute HIV infection if patient has symptoms consistent with acute HIV infection or reports unprotected sex with an HIV-positive person in the preceding month.
- Determine if women are planning to become pregnant, are currently pregnant, or are breastfeeding.
- Confirm that patient is at ongoing, very high risk for acquiring HIV infection.
- If any sexual partner is known to be HIV-infected, determine whether receiving antiretroviral therapy; assist with linkage to care if not in care or not receiving antiretroviral therapy.
- Confirm that calculated creatinine clearance is ≥60 mL per minute (Cockcroft-Gault formula).

**Other recommended actions:**

- Screen for hepatitis B infection; vaccinate against hepatitis B if susceptible, or treat if active infection exists, regardless of decision regarding prescribing PrEP.
- Screen and treat as needed for sexually transmitted infections (STIs).
- Disclose to women that safety for infants exposed during pregnancy is not fully assessed but no harm has been reported.
- Do not prescribe PrEP to women who are breastfeeding.

## Beginning PrEP medication regimen:

- Prescribe tenofovir disoproxil fumarate 300 mg (TDF) plus emtricitabine 200 mg (FTC) (i.e., one Truvada [Gilead Sciences] tablet) daily.
- In general, prescribe no more than a 90-day supply, renewable only after HIV testing confirms that patient remains HIV-uninfected. For women, ensure that pregnancy test is negative or, if pregnant, that the patient has been informed about use during pregnancy.
- If active hepatitis B infection is diagnosed, consider using TDF/FTC, which may serve as both treatment of active hepatitis B infection and HIV prevention.
- Provide risk-reduction and PrEP medication-adherence counseling and condoms.

## Follow-up while PrEP medication is being taken:

- Every 2–3 months, perform an HIV antibody test (or fourth generation antibody/antigen test) and document negative result.
- At each follow-up visit for women, conduct a pregnancy test and document results; if pregnant, discuss continued use of PrEP with patient and prenatal-care provider.
- Evaluate and support PrEP medication adherence at each follow-up visit, more often if inconsistent adherence is identified.
- Every 2–3 months, assess risk behaviors and provide risk-reduction counseling and condoms. Assess STI symptoms and, if present, test and treat for STIs as needed.
- Every 6 months, test for bacterial STIs even if asymptomatic, and treat as needed.
- Three months after initiation, then every six months while on PrEP medication, check serum creatinine and calculate creatinine clearance.

## On discontinuing PrEP (at patient request, for safety concerns, or if HIV infection is acquired):

- Perform HIV test(s) to confirm whether HIV infection has occurred.
- If HIV positive, order and document results of resistance testing, establish linkage to HIV care.
- If HIV negative, establish linkage to risk reduction support services as indicated.
- If active hepatitis B is diagnosed at initiation of PrEP, consider appropriate medication for continued treatment of hepatitis B infection.
- If pregnant, inform prenatal-care provider of TDF/FTC use in early pregnancy and coordinate care to maintain HIV prevention during pregnancy and breastfeeding.

Recommendations in black apply to both adult MSM and heterosexually-active men and women; items in blue are specific to heterosexual women.

# Ongoing and Planned PrEP Trials

## Injection Drug Users

CDC is sponsoring the only clinical trial of PrEP among injection drug users (IDUs), the Bangkok Tenofovir Study. The study, being conducted in Thailand, is assessing the efficacy of PrEP with daily oral tenofovir alone to prevent HIV infection among 2,400 male and female IDUs. Like other PrEP trials, this study is also examining the effects of taking a daily pill on HIV risk behaviors, adherence to and acceptability of the regimen, and in cases where participants become HIV-infected, the resistance characteristics of the acquired virus. Results are anticipated in late 2012.

## Other PrEP Studies

Other trials are underway or planned to examine the safety, adherence, acceptability, and feasibility of other PrEP regimens and dosing strategies. For detailed information on the full range of PrEP trials, visit **www.avac.org**.

# Next Steps in Assessing and Maximizing the Benefits of PrEP

PrEP offers a new tool to help combat the HIV epidemic among the hardest-hit populations in the United States and around the world, but its overall impact on the epidemic will depend on many things that at this point remain unknown, including access and acceptability among the populations at highest risk. Impact will also depend upon whether programs implemented in community settings can achieve the key requirements for success, including ensuring regular HIV testing, maintaining high levels of medication adherence, and preventing increases in risk behavior.

CDC and its partners are working to assess many of these key questions to determine how PrEP can most effectively be used in the United States.

- "Open-label extension" studies of the iPrEx, Partners PrEP, and TDF2 trials — in which all participants in those trials are provided PrEP knowing that they are taking medication with proven efficacy — are planned or underway, and will provide additional valuable information in research settings about acceptability, adherence to PrEP, and risk behavior.
- Demonstration research projects to evaluate PrEP use among MSM are planned in several California cities and Miami to provide similar information in "open-label" studies conducted with new research participants.
- CDC is working with federal, state, local, and private partners to identify additional ways to evaluate key PrEP implementation questions at community sites providing PrEP as a clinical HIV prevention service.

With limited resources available to combat the HIV epidemic, we will have to carefully consider how to most effectively use this tool in combination with other proven approaches to have the greatest possible impact on the HIV epidemic. Other key strategies such as HIV testing and treatment of individuals with HIV infection are critical, and will need to be expanded to reach the substantial number of Americans who are either unaware of their HIV status or not being effectively treated. CDC estimates indicate that only one-quarter of Americans with HIV currently have their virus suppressed to the levels needed to maintain their own health and prevent transmission to others.

Nevertheless, while expanded HIV treatment for those with HIV infection is essential, it will not be sufficient to end the epidemic. Even if we can improve treatment outcomes for all of those diagnosed with HIV, individuals who do not know they are infected are likely to continue to unknowingly transmit HIV infection to others.

With 2.7 million people becoming infected annually worldwide, including approximately 50,000 in the United States, we must capitalize on every available prevention tool. While the most appropriate uses of PrEP as part of these efforts is yet to be determined, available data suggest that this prevention method, if used strategically and effectively, could be cost-effective and may help reduce the continuing toll of HIV infection in this nation.