



# PRE-EXPOSURE PROPHYLAXIS (PrEP) FOR HIV PREVENTION

## Promoting Safe and Effective Use in the United States

### New Tool to Reduce the Risk of HIV Infection among Gay and Bisexual Men

In November 2010, the National Institutes of Health (NIH) announced the results of the iPrEx trial, a large research study examining whether a pill containing drugs used to treat HIV can also help prevent HIV infection — an approach called pre-exposure prophylaxis, or PrEP. These findings represent a major advance in HIV prevention research, providing the first evidence that PrEP, when combined with other prevention strategies, can reduce HIV risk among men who have sex with men (MSM) (see Key Findings box).

The iPrEx results have immediate implications for the U.S., because tenofovir-emtricitabine pills are already FDA-approved and available with a prescription for the treatment of HIV infection. As the agency responsible for protecting public health, CDC is taking steps to promote the safe and effective use of PrEP in the United States.

**HIV among MSM in the U.S.:** The HIV epidemic among MSM in the U.S. is severe, and additional risk reduction strategies for this population are urgently needed. MSM represent more than half of new HIV infections and nearly half of all people living with HIV in the U.S., and the rate of new HIV diagnoses among MSM is more than 44 times that of other men. Moreover, data suggest that HIV infections have been steadily increasing in this group since the mid-1990s.

**Implications of findings for other PrEP trials:** While we don't yet know if PrEP will work for preventing HIV transmission in other populations, these findings among MSM give us hope that this approach might also prove effective among heterosexuals at high-risk for HIV and injection drug users. CDC, NIH, and other institutions are conducting trials around the world to determine the safety and effectiveness of PrEP for these populations; those results are expected within the next few years. The iPrEx results may also be the first step toward other effective and potentially more feasible options for PrEP, as other regimens and dosing strategies are also being evaluated.

**CDC next steps:** CDC is pursuing two primary goals in the wake of the iPrEx trial findings: developing guidance on the safe and effective use of PrEP and determining how to most effectively use PrEP in combination with other prevention strategies to reduce new infections in the U.S. The following pages describe these goals in greater detail, and discuss key remaining questions about PrEP as an HIV prevention tool.

### iPrEx Trial: Key Findings

**Efficacy:** The trial found that a once-daily pill containing tenofovir plus emtricitabine (brand name Truvada®) provided an average of 44 percent protection to men who have sex with men and transgender women who have sex with men who also received comprehensive prevention services which included monthly HIV testing, condom provision, counseling, and management of other sexually transmitted infections.

**Consistent use of PrEP:** The level of protection varied widely depending on how consistently participants used PrEP. Among those whose data (based on self-reports, bottles dispensed, and pill counts) indicates use on 90 percent or more days, HIV risk was reduced by 73 percent, while among those whose adherence by the same measure was less than 90 percent, HIV risk was reduced by only 21 percent.

**Risk behavior:** Risk behavior among participants declined overall during the trial both in terms of decreases in the number of sexual partners and increases in condom use, likely as a result of the intensive risk reduction counseling provided as part of the trial.



# Working Toward Safe and Effective Use in the U.S.

CDC is currently leading national efforts to develop formal U.S. Public Health Service guidelines on PrEP among MSM. However, given the commercial availability of Truvada® and the possibility of immediate interest in PrEP among some high risk gay and bisexual men and their physicians, CDC has already provided initial cautions on PrEP use (see below), as well as interim guidance for physicians electing to provide PrEP for HIV prevention among high risk MSM (see box on page 3).

## Initial Cautions for Gay and Bisexual Men

For MSM at high risk for HIV infection, PrEP may represent a much-needed additional prevention tool. However, PrEP should be used only in combination with other HIV prevention strategies, requires strict adherence, and is an intensive approach that won't be right for everyone.

Anyone considering using PrEP should know:

- To date, PrEP has only been shown to reduce HIV infection among gay and bisexual men and transgendered women who have sex with men, and there are no data regarding its benefit among heterosexuals or injection drug users.
- PrEP should only be used among individuals who have been confirmed to be HIV-negative. Initial and regular HIV testing is critical for anyone considering using PrEP. All individuals considering PrEP must also be evaluated for other health conditions that may impact PrEP use.
- PrEP should never be seen as the first line of defense against HIV. It was only shown to be partially effective when used in combination with regular HIV testing, condoms, and other proven prevention methods. Men who have sex with men should still:
  - Use condoms correctly and consistently
  - Get tested to know their status and that of their partner(s) for certain
  - Get tested — and treated if needed — for other sexually transmitted infections that can facilitate HIV transmission, such as syphilis and gonorrhea
  - Get information and support to reduce drug use and sexual risk behavior
  - Reduce their number of sexual partners
- Taking PrEP daily is critical. This study found that PrEP provided a high level of protection only to those who took the pills regularly; protection was very low among those who did not adhere to the daily regimen well.
- PrEP must be obtained and used in close collaboration with healthcare providers to ensure regular HIV testing, risk reduction and adherence counseling, and careful safety monitoring. Anyone considering using PrEP should speak with their doctor.



## Interim Guidance for Physicians

CDC recently published interim guidance for physicians to help inform clinical practice as formal U.S. Public Health Service guidelines are being developed.

### CDC Interim Guidance on HIV Pre-Exposure Prophylaxis for Men Who Have Sex with Men

#### Before initiating PrEP

##### Determine eligibility

- ▶ Document negative HIV antibody test(s) immediately before starting PrEP medication.
- ▶ Test for acute HIV infection if patient has symptoms consistent with acute HIV infection.
- ▶ Confirm that patient is at substantial, ongoing, high risk for acquiring HIV infection.
- ▶ Confirm that calculated creatinine clearance is  $\geq 60$  mL per minute (via 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 about prescribing PrEP.
- ▶ Screen and treat as needed for STIs.

##### Beginning PrEP medication regimen

- ▶ Prescribe 1 tablet of Truvada\* (TDF [300 mg] plus FTC [200 mg]) daily.
- ▶ In general, prescribe no more than a 90-day supply, renewable only after HIV testing confirms that patient remains HIV-uninfected.
- ▶ If active hepatitis B infection is diagnosed, consider using TDF/FTC for 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; document negative result.
- ▶ 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 STI as needed.
- ▶ Every 6 months, test for STI even if patient is asymptomatic, and treat as needed.
- ▶ 3 months after initiation, then yearly while on PrEP medication, check blood urea nitrogen and serum creatinine.

#### 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 and 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.

Abbreviations: STI = sexually transmitted infection; TDF = tenofovir disoproxil fumarate; FTC = emtricitabine

\* These recommendations do not reflect current Food and Drug Administration-approved labeling for TDF/FTC.

Source: "Interim Guidance: Pre-exposure prophylaxis for the prevention of HIV infection in men who have sex with men," CDC *Morbidity and Mortality Weekly Report*, January 28, 2011.

## Developing Formal U.S. Public Health Service Guidelines on PrEP Use

CDC is the lead federal agency in developing U.S. Public Health Service guidelines, in collaboration with other federal health agencies. The guidelines will be based on a full review of trial data and other research, and will incorporate input from providers, HIV prevention partners, and affected communities. The guidelines will help ensure both physicians and MSM have accurate information to guide decisions about the use of PrEP.

Topics to be addressed in the guidelines will include:

- Guidance on how to assess which populations of MSM may benefit most from PrEP
- Procedures for health care providers to assess whether PrEP is appropriate for individual patients (e.g., methods for evaluating patients' risk behavior)
- Recommended support services to help ensure adherence to the daily PrEP regimen
- Recommended risk reduction counseling to prevent inadvertent increases in risk behavior (known as "risk compensation" or "disinhibition"), as well as to provide referrals to — and/or transition individuals to — other, more effective prevention interventions
- Procedures for initial HIV testing and health screening, as well as ongoing monitoring for side effects, clinical toxicities, HIV infection, and possible drug resistance among those who become infected despite taking PrEP



# Maximizing the Potential Benefits of PrEP in the U.S.

The iPrEx trial findings offer a new tool to help combat HIV among MSM, one of the hardest hit populations in the U.S. and many areas of the world.

We will have to carefully consider how to most effectively use this tool in combination with other prevention strategies to reduce the continuing toll of HIV and AIDS. There are a significant number of HIV-positive individuals in the U.S. and around the world who do not have access to antiretroviral drugs to treat their infection, and we know that treatment not only benefits infected individuals, but can also reduce transmission of HIV to others. But, we also know that treatment alone will not end the epidemic. With 2.7 million people becoming infected annually worldwide, including approximately 56,000 in the U.S., we must capitalize on every available prevention tool.

Ultimately, the impact of PrEP on the U.S. HIV epidemic will depend on difficult decisions and many things that remain unknown, including the feasibility, cost, and impact of this strategy in real-world settings.

Available data suggest that PrEP, used strategically and effectively among MSM, could have a positive impact on the U.S. epidemic and be cost-effective, but only if certain conditions are met, including:

- Reaching the MSM at highest risk for HIV infection
- Effectively delivering PrEP in tandem with effective risk reduction counseling, condoms, and other prevention tools as were delivered in the trial setting. This will be critical to prevent increases in risk behavior that could offset the benefits of PrEP
- Identifying ways to achieve the high levels of adherence needed for maximum protection

## CDC's Next Steps

CDC will be implementing a range of activities to promote the effective and strategic use of PrEP in the U.S. In addition to developing public health guidelines, CDC will:

- Develop updated risk reduction messages for MSM that address PrEP and other proven HIV prevention strategies
- Adapt national HIV surveillance and program monitoring systems to help evaluate the use and impact of PrEP in the U.S.
- Examine potential program costs, impact, and cost-effectiveness compared to other interventions
- Communicate guidance to providers and MSM through multiple information channels

CDC has also identified other activities that could help address remaining research questions and is currently exploring all avenues to identify resources to support them. Key among these is the need for demonstration projects in clinics serving MSM to assess feasibility, acceptability, and the impact of PrEP in real-world settings. It will also be critical for public and private sector partners to begin to collectively address the significant financial barriers that may place PrEP out of reach for many MSM at highest risk for HIV infection.

Given the urgency of addressing the HIV epidemic among gay and bisexual men in this nation, CDC is working to maximize the impact of this important new intervention in combination with all available HIV prevention strategies.

For more information on PrEP and HIV prevention, please visit [www.cdc.gov/hiv/prep](http://www.cdc.gov/hiv/prep).