



PRE-EXPOSURE PROPHYLAXIS (PrEP) FOR HIV PREVENTION

Planning for Potential Implementation in the U.S.

The Promise of PrEP

Almost 30 years into the epidemic, HIV remains a major health crisis. Worldwide, 2.7 million new infections are estimated to occur each year¹— including more than 56,000 in the United States.² Safe and effective new approaches to prevent HIV are urgently needed to reduce the toll of the disease.

One promising approach being explored is pre-exposure prophylaxis (PrEP) — the use of HIV treatment medications to protect uninfected individuals from HIV infection. The Centers for Disease Control and Prevention (CDC), the National Institutes of Health, and other researchers³ are conducting clinical trials around the world to test the effectiveness of the use of once-daily PrEP pills among populations at high risk for infection, including men who have sex with men in the U.S., Latin America, Asia, and Africa; heterosexual men, women, and couples in Africa; and injection drug users in Asia. The first trial results may be reported this year.

If effective, PrEP could play an important role in slowing the spread of HIV around the world by providing a much-needed option for women who are at high risk and unable to negotiate condom use, and could serve as an additional safety net for others at high risk of HIV infection. Additionally, PrEP could provide some protection for discordant couples (i.e., in which one partner is infected and the other is not) who are trying to conceive.

Key Implementation Issues in the United States

Because PrEP is unlikely to be 100 percent effective, it will need to be used in combination with other proven HIV prevention approaches, and with critical supportive services, such as HIV testing, prevention counseling, and clinical monitoring.

CDC is currently working with public health partners and the HIV community to begin to assess several complex issues related to potential use of PrEP in the United States and future PrEP research. Some of the most significant include:

- ▶ **Identifying the most effective mix of interventions:** As the range of prevention options grows, it will be critical to determine the combination of specific interventions that can most effectively reduce HIV infections in the United States. As data on PrEP efficacy emerge from the trials in various high-risk populations, the potential impact of PrEP, as well as its cost-effectiveness, must be evaluated and compared to other proven prevention interventions to determine the role of PrEP in publicly funded HIV prevention programs for each population.
- ▶ **Avoiding increases in risk behaviors:** If PrEP or other partially effective interventions are identified, it will be critical to ensure that individuals do not use these prevention approaches as a substitute for other, more effective prevention tools, or increase their risk behavior under the false assumption that PrEP is fully protective. Careful implementation and communications planning will be essential to minimize the potential for these unintended consequences.



- ▶ **Cost:** Published studies^{4,5} estimate that the costs of PrEP implementation in the U.S.⁶ — even if only used in the highest-risk populations — could be substantial. These studies suggest that if PrEP were targeted to 100,000 people at highest risk, the costs would exceed \$1 billion annually, a figure significantly more than the current CDC budget for HIV prevention programs in the United States. Given the critical need to maintain existing prevention programs in combination with PrEP, significant additional funding would be required to implement PrEP as part of a comprehensive HIV prevention approach.
- ▶ **Access to PrEP:** Because many of those at greatest risk for HIV infection are uninsured or will not initially have insurance coverage for PrEP, financial barriers will have to be addressed to ensure access when PrEP use is indicated.
- ▶ **Continuation of PrEP research:** No single trial will give us the answers to whether PrEP works for all populations. The drugs may not work the same way for all types of exposures (injection, vaginal sex, anal sex) since different factors influence transmission through each route. For example, results from the trial in injection drug users will not tell us whether PrEP works for men who have sex with men. As results emerge from each trial, public health officials and key stakeholders will have to assess the results and determine whether additional research is required to recommend PrEP use for each population. In addition, if one or more of these trials demonstrate that daily PrEP is effective, additional research may be needed to consider other PrEP regimens, such as PrEP delivered intermittently (e.g., weekly or close to the time of sex), which could be more cost-effective.

CDC Planning for Potential PrEP Implementation

As CDC prepares for potential implementation of PrEP in the United States, our planning efforts are focused on two priority areas: developing clinical guidelines for PrEP use and assessing the potential role of PrEP in publicly funded HIV prevention programs.

Clinical Guidelines for PrEP Use

If PrEP is proven effective, there will likely be interest in immediately using PrEP in the U.S., given widespread availability of the FDA-approved medications (tenofovir and tenofovir- emtricitabine pills) being evaluated in the trials. Therefore, CDC’s highest PrEP implementation planning priority is preparing for the development of guidelines on the proper clinical use of PrEP in the United States.

CDC will be the lead federal agency in developing clinical guidelines, in collaboration with other federal health agencies. Clinical guidelines will depend first and foremost on the results of the clinical trials. However, given the complexity of PrEP and the importance of rapid guidance to ensure proper use, CDC has already convened workgroups to begin exploring those elements that can be developed in advance of trial outcomes. The workgroups include health experts, researchers, advocates, and representatives of affected communities.

If PrEP proves effective in reducing HIV transmission, it will likely be recommended only for individuals at very high risk in the populations for whom it has proven effective. Additionally, given that PrEP is unlikely to be 100 percent effective, it would be recommended in conjunction with other proven interventions and HIV testing.

Topics to be addressed in PrEP guidelines would include:

- Populations for which PrEP is recommended, based on data from clinical trials
- Procedures for assessing the appropriateness of PrEP for individual patients, including initial screening for risk, existing HIV infection, and other health conditions



- Specific drugs and dosing for PrEP
- Necessary support services to help ensure adherence to PrEP
- Needed risk-reduction counseling to be delivered in conjunction with PrEP, as well as referrals and/or transition to other interventions
- Monitoring for side effects, HIV infection, and possible drug resistance among those who become infected

Potential Role of PrEP in Publicly Funded HIV Prevention Programs

CDC is examining the potential role of PrEP in publicly funded HIV prevention programs. The agency has consulted with public health partners, the HIV community and potential PrEP providers and users since 2007 to understand how and under what circumstances PrEP could be effectively delivered to populations at highest risk for HIV infection as part of a comprehensive national HIV prevention strategy.

CDC efforts underway or planned include:

- Assessing awareness, understanding, and acceptability of PrEP among both potential users and health-care providers
- Gathering information on the potential staffing, training, and programmatic needs at sites that could deliver PrEP to high-risk populations, such as STD clinics, community health centers, and substance abuse treatment sites
- Conducting research to determine how to most effectively communicate the limitations of PrEP and the continued need for other prevention measures
- Developing training materials for health-care providers
- Conducting economic evaluations to define program costs and potential cost-effectiveness of PrEP compared to other interventions
- Planning for demonstration projects that could be implemented soon after trial results are available to assess real-world feasibility

While there is no way to predict the outcomes of clinical trials, these efforts will help the nation prepare for a more effective and rapid response, should PrEP prove effective. Ultimately, the impact of PrEP will be determined not only by efficacy results, but also by careful implementation planning to ensure that the approach is used effectively.

References

- 1 2008 Report on the global AIDS epidemic. Geneva: UNAIDS, 2008.
- 2 Hall HI, Song R, Rhodes P, Prejean J, An Q, Lee LM, Karon J, Brookmeyer R, Kaplan EH, McKenna MT, Janssen RS for the HIV Incidence Surveillance Group. Estimation of HIV Incidence in the United States. *JAMA* 2008;300(5):520-529.
- 3 A full list of organizations and funding agencies involved in PrEP research can be found at http://www.prepwatch.org/pdf/Trials/PrEP_trials_table.pdf.
- 4 Desai K, Sansom SL, Ackers ML, Stewart SR, Hall HI, Hu DJ, Sanders R, Scotton CR, Soorapanth S, Boily MC, Garnett GP, McElroy PD. Modeling the impact of HIV chemoprophylaxis strategies among men who have sex with men in the United States: HIV infections prevented and cost-effectiveness. *AIDS*. 2008 Sep 12; 22(14): 1829-39.
- 5 Paltiel AD, Freedberg KA, Scott CA, Schackman BR, Losina E, Wang B, Seage GR 3rd, Sloan CE, Sax PE, Walensky RP. HIV preexposure prophylaxis in the United States: impact on lifetime infection risk, clinical outcomes, and cost-effectiveness. *Clin Infect Dis*. 2009 Mar 15;48(6):806-15.
- 6 Cost estimates for PrEP include the price of drugs and distribution systems; HIV testing services; monitoring for side-effects, adherence, and drug resistance; risk-reduction counseling to ensure that individuals using PrEP do not increase risk behaviors; and linking high-risk individuals to additional prevention services. Researchers are working to develop more precise costs estimates, as well as examining factors influencing the cost-effectiveness of PrEP use.