



Pre-Exposure Prophylaxis (PrEP) Health Department Issues for Consideration November 23, 2010

The [National HIV/AIDS Strategy \(NHAS\)](#) highlights that current approaches to preventing HIV must be coupled with research on new and innovative prevention methods that can have a long-term impact. Such strategies include pre-exposure prophylaxis (PrEP), the use of antiretroviral (ARV) therapy by high-risk, uninfected populations, including HIV-negative gay and bisexual men and other men who have sex with men (MSM).

Initial data from the Global iPrEx study indicates that there is some proven effectiveness in a PrEP regimen (see NASTAD [Global iPrEx MSM Efficacy Study fact sheet](#)). [Other studies](#) are currently underway to test the further feasibility of PrEP for MSM as well as in other populations. Even if these other studies prove effective, additional research will be needed to assess the cost effectiveness of these approaches and their adaptability outside of carefully controlled research studies. There will also be a need to couple these approaches with behavioral interventions to ensure that any positive outcomes from PrEP or other innovative interventions are not erased by changes in risk behaviors.

Despite the potential for PrEP to be an effective intervention to prevent HIV infection, several significant concerns are likely to remain even after the recent completion of the Global iPrEx trial and as other trials currently underway are completed. This document highlights issues for consideration for health departments in the discussion of PrEP as an HIV prevention strategy.

Who are potential users of PrEP?

- HIV uninfected persons
 - with a sexual partner known to be HIV+
 - with frequent partner change or concurrency
 - with partner(s) at high risk of HIV infection (e.g. injection drug users, non-monogamous individuals)
 - with other evidence of risk (e.g., frequent STDs or unintended pregnancies)
 - unable to (consistently) use other prevention modalities

Who are the potential PrEP providers?

- Primary care clinicians
 - Routine, clinical HIV test providers
 - STD, family planning, and Ob-Gyn clinics
 - Community and rural health centers

- Providers serving MSM and IDU
 - Many others (e.g., historically black college and university clinics)
- Ryan White and other HIV care providers
- HIV testing programs
- Allied CBOs/ASOs, pharmacies, syringe exchange programs

Issues for Consideration

- **Cost:** Cost will be a major factor in the broad use of PrEP. Cost effectiveness data is not currently available in the primary efficacy and safety analysis conducted as part of Global iPrEx. Daily doses of TDF alone for HIV treatment can cost as much as \$7,100 per year (varies depending upon the payer source). In addition to the drug itself, an effective PrEP program, as demonstrated in the iPrEx study, will likely require regular HIV testing and counseling, so the overall cost of PrEP will be even higher than drug costs alone. Some of these costs are already incurred by HIV-negative people who test regularly, off-setting the total cost of PrEP. Some prevention advocates are concerned that only people who can afford the drugs and/or with access to health care will have access to PrEP. In any case, at the current price, PrEP may be hard to justify.
- **Effectiveness:** Willingness to invest in daily oral PrEP as a prevention strategy (by patients, public and private insurers, and public health providers) will be directly related to the degree of protection that PrEP indicates in trials. Data from the Global iPrEx study indicate PrEP reduces the chance of infection by approximately 44 percent. A PrEP regimen may be too costly compared to other prevention methods, except possibly in the highest risk individuals. It also may not be appealing to most potential users.

Data from clinical trials will have to be evaluated in terms of clinical efficacy in relation to the entire cost of PrEP delivery to determine the feasibility and cost-effectiveness of PrEP in various communities and settings. In addition, exact drug levels in blood necessary for protection are still unanswered, however Global iPrEx data indicate detectable drug in blood is strongly correlated with its prophylactic effect.

- **Financing:** Gilead Sciences, Inc., has approached the FDA about expedited review and will submit the use of PrEP for HIV prevention implication. There are anecdotal reports that some private insurance companies are currently paying for drugs used for daily oral PrEP (for both short-term and long-term use) in the small number of instances where clinicians are prescribing it off-label. Insurance companies do not necessarily require a diagnosis or indication with prescriptions. If the drugs are on their formulary, insurance companies may sometimes cover their cost for HIV-negative individuals. Even if private insurance were to cover the cost of PrEP medication, insured individuals may be afraid to receive it through their own physicians and insurance companies out of fear of judgment about their behaviors. As is frequently the case with HIV testing, some privately insured individuals may be more likely to use PrEP if it is made available through community-based, publicly

funded sources. Building and financing a new program of this kind will be difficult, particularly in the short term with budget cuts for many programs and with growing waiting lists for ADAP. Advocacy to build a distinct funding stream to pay for PrEP for those individuals who will not be insured as a result of health care reform or who will not rely on their private insurance may be necessary.

- **Safety:** Global iPrEx further highlights data from trial of the biological and behavioral safety of daily oral TDF use for HIV prevention in gay and bisexual men in three U.S. cities which were released in July 2010 and suggested no significant safety issues on the part of participants. An earlier study among young women in Ghana, Nigeria, and Cameroon also provided data showing daily oral PrEP with TDF to be both safe and acceptable for use by African women. Neither study included long-term safety data nor did either assess potential effectiveness of the PrEP regimens.
- **“Behavioral disinhibition” or “risk compensation:”** There have also been concerns raised, although no specific data is currently available, that taking ARVs might lead some individuals using PrEP to think that they do not also have to continue to practice safer sex or syringe use, which could lead to increased risk of HIV exposure. The CDC safety study among gay and bisexual men in the U.S. mentioned above reported that “behavioral disinhibition” or “risk compensation” did not occur in this group. However, it is important to note that study participants received significant behavioral counseling and reinforcement for safer sex behaviors; more perhaps than will generally be available if PrEP is widely implemented.
- **Behavioral effects:** Although it is clear that future PrEP programs will need to include a counseling component that reinforces the importance of continued condom use and/or use of sterile syringes for injection drug use, there could be some for whom counseling is insufficient to reduce and maintain low levels of risk behaviors. These factors could vary for and even within different groups, such as the broad population of gay and bisexual men compared to serodiscordant couples. Therefore, more research is needed about potential behavioral effects of PrEP among at-risk groups.
- **Resistance:** Much is unknown (and will remain so until PrEP has been used for some time) about the possible development of drug resistance from its use. If, over time, PrEP users nonetheless, due to multiple potential factors, become HIV-infected, they may already have developed drug resistance, making ARV treatment for their HIV disease less effective. Experts currently disagree about the potential for drug resistance to develop as a result of PrEP use. Thus far, resistance has not been observed in seroconverters in the completed safety trials of PrEP.
- **Adherence:** There is also concern about some individuals’ ability to adhere to the daily oral PrEP regimen. Global iPrEx data indicate that half of the seronegative participants had no drug level in their blood and therefore did not adhere consistently to their prescribed regimen. For some individuals, life situations such as concurrent drug use may interfere with adherence to PrEP

regimens. Missed doses might affect the regimen's effectiveness and may contribute to drug resistance if the virus establishes an infection and continues to replicate while the individual is on a regimen that is suboptimal for treatment. In ongoing PrEP clinical trials, participants generally have much more adherence counseling support than may be available in real-life situations where PrEP may be implemented. On the other hand, trial participants are told that they may be getting placebo or active agent, and even with the active agent, efficacy is unknown, so adherence could actually be higher when people taking PrEP in real world situations know that it has been demonstrated to be effective enough to prescribe. Additional studies are necessary to determine strategies for adopting a PrEP regimen into real-life situations.

More information about key issues in the iPrEx study and the future of PrEP are available by visiting the AIDS Vaccine Advocacy Coalition (AVAC) website at www.avac.org/iprex or the iPrEx Study website at www.globaliprex.net/

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