Pre-exposure prophylaxis (PrEP) is a novel biomedical strategy being investigated for HIV prevention among diverse high-risk populations worldwide. Two completed clinical trials have demonstrated partial efficacy of PrEP in decreasing HIV acquisition risk by 39% and 44% respectively in heterosexual women and men who have sex with men (Abdool Karim et al 2010, Grant et al 2010). If safe and efficacious in ongoing trials, PrEP will likely be targeted to high-risk subpopulations. However, several questions remain regarding the most effective dosages; length and time of use; topical versus oral; patient adherence, and whether inadvertent PrEP use by HIV-infected individuals could lead to drug resistance. Additionally, the global health community will have to figure out how PrEP can fit within the larger package of sexual health promotion and HIV prevention strategies.

This discussion emanated from a GHDonline Expert Panel Discussion organized in collaboration with the HOPE Conference at Massachusetts General Hospital. Members discussed issues related to adherence and tactics being tested to promote good adherence; risks and benefits of implementing PrEP depending on patients’ risk profiles; acceptability among clinicians and patients; and topic areas for future research, including cost effectiveness, long-term safety and efficacy, different formulations and varying delivery strategies.

Key Points

Adherence

- Results from the CAPRISA and iPrEx studies suggest that adherence levels are likely to correlate strongly with prophylactic effect for PrEP. In these studies, adherence levels were suboptimal in substantial numbers of participants.
- Maintaining long-term medication adherence in healthy asymptomatic individuals in real-world settings may be challenging. Using pillboxes, diaries or cell phone alarms and involving a spouse or family members are useful adherence strategies.

Implementation

- Innovative use of existing public health infrastructure and online media tools could facilitate dissemination of information on PrEP in some settings.
- Risk and benefit assessments must accompany PrEP implementation. Identifying individuals who are most likely to benefit from PrEP will entail patient-provider communication around high-risk behaviors. Efforts to reduce stigma associated with high-risk behaviors could enhance this important communication.
- Guidelines could facilitate prescribing. The CDC has developed interim guidelines for oral PrEP for men who have sex with men. (MMWR Jan 2011)
- Acceptability among clinicians must be addressed. Clinicians may worry, and appropriately so, that the use of PrEP will cause individuals to increase their risk-taking behaviors, thereby causing a net increase in the risk of HIV acquisition when using a partially effective PrEP agent. Studies need to monitor for this phenomenon called "risk compensation" or "behavioral disinhibition." Data published so far do not support these concerns. In the CAPRISA 004 microbicide gel trial, participants reported a decrease in the number of sex partners and stable, high-levels of condom use. In oral PrEP trials, no evidence of risk compensation has been published to date.
- Serodiscordant couples could also be considered a high-risk subpopulation that could benefit from PrEP. HIV serodiscordant couples wanting to have children face the difficult choice between wanting to conceive and risking transmission of HIV. In resource-limited settings, where assisted reproduction techniques are not available or feasible, PrEP, in conjunction with behavioral risk-reduction strategies (e.g., timing condomless intercourse to coincide with peak fertility), may provide ways to reduce the risk of transmission in this context.

Future Research Needs

- Evaluation of long-term safety and efficacy in special populations of HIV-uninfected individuals, including those with chronic active hepatitis B infection or renal dysfunction, adolescents, and pregnant and breastfeeding women.
• Determining optimal delivery methods, such as oral versus topical, varying dosages and delivery strategies for these subpopulations.
• Monitoring rates of drug resistance and their impact on future treatment options.
• Cost-effectiveness of PrEP.
• Understanding ways to engage and train primary care providers to perform HIV risk assessments with patients to identify potential PrEP consumers and provide PrEP when appropriate.

**Key References**


**Enrich the GHDonline Knowledge Base**

*Please consider replying to this discussion with the following information*

- If you have experience prescribing PrEP or have patients requesting it.
- If you have worked on developing or implementing PrEP guidelines.
- If you have recommendations for future research into this area.