

## **4/20 HIV PJA Strategy Webinar Recap: FEM-PrEP Trial Closure, U.S. Pricing & Access Issues after iPrex, & UN Update**

HIV PJA convened a full slate of policy and research experts for our April 20<sup>th</sup> strategy call to explore current issues relating to PrEP research and rollout in the United States. Check back soon for a video recording; you can also view the presentation slides on this website.

Keith Green, Director of Federal Affairs at the AIDS Foundation of Chicago, opened the discussion by framing the evidence coming out of pre-exposure prophylaxis (PrEP) trials in terms of ultimate implications for a U.S. rollout. A key question is *who is PrEP for?* Risk relates to identity, community, and behavior; and multiple populations are categorized as high-risk for HIV: gay men and other men who have sex with men (MSM), HIV negative partners, African Americans, sex workers, injection drug users. Will PrEP be another means of division between groups affected by HIV or is there a way it can pull us all together? He also recognized that PrEP is a controversial topic that can bring up strong feelings, and urged us to hear each other out, and to base our discussions in facts whenever possible.

### **FEM-PrEP Trial Closure – Dr. Tim Mastro, Senior Director of Research, Family Health International**

Dr. Tim Mastro joined the call to discuss the FEM-PrEP clinical trial, sponsored by Family Health International (FHI). Last week many were surprised and disappointed to learn that FEM-PrEP will be closed in response to preliminary results that show an equal rate of HIV infection in the treatment and control groups. HIV PJA appreciated the opportunity to hear from one of the trial sponsors at this early stage and looks forward to engaging with other voices, including women involved in the study, over time and as more FEM-PrEP data becomes available.

FEM-PrEP enrolled 1,951 women in Kenya, South Africa, and Tanzania in order to study if a daily oral dose of the antiretroviral combined drug Truvada could be safely used by women to prevent HIV. Like the iPrex study, FEM-PrEP is a randomized treatment-control trial in which all participants received either daily Truvada or a placebo along with a comprehensive package of prevention services including counseling, male and female condoms, HIV and STI screening (and treatment if applicable), and physical exams. Participants in FEM-PrEP were also required to be using an effective form of contraception at the time of enrollment.

The study participants represented a fairly high-risk sample of women (21% of the 3,700 applicants screened were turned away due to testing positive for HIV at enrollment). During the trial itself, there was a 5% per year new infection rate. In both the Truvada and placebo groups, 28 new HIV infections occurred. Having reached 56 HIV infection endpoints in a study designed for a capacity of 72 infections, the investigators concluded that continuation of the study was highly unlikely to be able to prove Truvada's effectiveness in the sample.

**Dr. Mastro cautioned that it is too early to explain the results or lack thereof of the FEM-PrEP trial: the study is ongoing at this time, and final analysis of the data (including sexual behavior reports and blood tests for drug resistance in the virus) may not be available for six months or more.** One major question to be answered is the level of treatment adherence by the women who seroconverted (got

HIV) while taking Truvada. During the study, adherence was self-reported and measured by counting returned pills at monthly visits, but the investigators also collected blood specimens that will reveal the level of the drug in participants' blood (which is a much more accurate way to assess adherence than self-report). Interestingly, the treatment group saw a higher rate of pregnancy than the control group, but it is too early to tell if this is due to imperfect contraceptive adherence or to an unidentified drug interaction between Truvada and birth control. There is a possibility of a biological basis for the failure to observe a protective effect. The antiretrovirals in oral Truvada may distribute to rectal and vaginal tissues differentially; since the primary mode of HIV transmission among women is vaginal intercourse, Truvada may be less effective in this context than it is for populations whose primary mode of HIV transmission is receptive anal intercourse (such as gay men, other men who have sex with men and transgender women who have sex with men, the iPrex study populations). Topical application of tenofovir (a component of Truvada), as in the CAPRISA study, may result in a different effect than oral ingestion. **Importantly, all hypotheses are speculative at this point; no conclusions can be reached until the FEM-PrEP data is fully analyzed and other clinical trials are completed.**

Much more information on FEM-PrEP can be found at FHI's website [link].

#### **PrEP in the U.S.: Pricing & Access Issues – Kevin Fisher, AVAC Policy Director**

Currently Gilead Sciences, maker of Truvada, charges “full value” for the medication in countries that are not considered low-income and/or experiencing an unusually high HIV burden. Thus, while Truvada is provided in parts of the developing world for \$140/year, the U.S. price ranges from \$10,000 - \$14,000/year. (The ADAP negotiated price, which is safeguarded against price increases beyond the inflation rate, is about half or \$5,000-\$7,000.) Pricing options to ensure equitable access in the U.S. market include:

- *Lowering the Price Directly* – via negotiation with Gilead, reducing the required dosage for PrEP, waiting for a generic version of Truvada (the patents for each ARV expire in 2017, though the patent on the combination may last longer), or pursuit of a dual pricing scheme that differentiates treatment and prevention uses (which has been largely rejected as impractical). *A key issue here is getting Gilead to agree for Truvada to become generic for both treatment and prevention at the same time – while it is not totally clear when it would become generic for treatment, it may be as soon as 2017.*
- *Demonstrate Cost-Effectiveness* – PrEP may be able to significantly reduce the cost and increase the sustainability of treatment programs by reducing community HIV incidence and demand for treatment. The more its effectiveness can be demonstrated, the more likely insurance companies will be to cover it.
- *Third-Party Payment* – There seems to be openness among private insurers, but self-insured plans likely won't cover PrEP anytime soon. Even under insurance coverage, with a tiered system patients could still be liable for up to 30% in co-pays. By 2014, Medicare will be expanded to cover all non-elderly individuals up to 133% of the poverty level, which would help expand access.

- *CDC & State Health Departments* – There is likely little room for funding from current health departments, and the cost of covering everyone indicated for PrEP exceeds the entirety of the CDC's prevention funds.

The best way forward is likely a multi-pronged approach: negotiate ADAP-level pricing with Gilead, target interventions to demonstrate PrEP's cost-effectiveness, and develop a patchwork coverage system through Medicare and private insurance for the most high-risk populations. A caller asked what prevents an individual from using PEP (*post-exposure prophylaxis*, which should be available at emergency rooms, and is more widely available in a few cities through specific programs) as PrEP—while this is probably feasible, it would not be a reliable method of obtaining the drugs. Typically PEP is dispensed in a one-month supply.

### **FDA Oral PrEP Review – Robert Reinhard, Public & Global Health Consultant**

A critical decision regarding U.S. rollout of Truvada as PrEP lies with the FDA. In the best-case scenario, the FDA process can be used to address the concerns that surround PrEP: how it can/should be used, adherence in the real world, safety, efficacy, equity in availability, and the possibility for risk compensation (i.e. would people have more risky and/or condom-free sex if they have access to PrEP?). Although Truvada is approved for treatment use in the U.S., it requires a separate approval by the FDA to be used for *prevention*, which is currently an off-label use open to physician discretion. FDA approval could define the prevention use broadly or narrowly. It may best be reviewed and possibly approved sequentially to apply it when justified to the vulnerable populations for which the balance of efficacy and safety show desirable benefits starting with men in response to the iPrEX findings and perhaps later to other vulnerable populations such as serodiscordant married couples, or women.

If approved for prevention, PrEP would be more easily reimbursed by insurance, and physicians might be more likely to prescribe it, lacking current liability concerns. However, there is little to no precedent for approval of this type of prevention drug, so any FDA approval process will be highly case-specific. There are efforts in the works to identify alternatives to Truvada as PrEP, including a search for a prevention drug not used in treatment regimens (though currently most of the candidates have less favorable resistance profiles). As with Truvada, affordability, ease of use, and safety considerations are paramount.

Any process for PrEP approval is likely to be politically fraught. A transparent, equitable route through the FDA requires input from experts in the field, a commitment not to politicize or stigmatize the issues, and a fulfillment of the FDA's mandate to protect and advance public health relying on accurate and up-to-date medical science.

### **UN High-Level Meeting on AIDS – Matt Kavanagh, Director of U.S. Advocacy, Health GAP**

The 2011 UN General Assembly High Level Meeting on AIDS will convene in New York from June 8-11. Given advances in the last 10 years (since the landmark UN General Assembly Special Session on HIV/AIDS) including expanded access to ARVs in the global South, acceptance of harm reduction techniques, and a greater focus on the drivers of the pandemic, it's an exciting time – but also a time of

crisis, as the epidemic continues and the global economic situation puts key funding, programs, and lives at risk. At the meeting in June, member countries will report on their progress towards the 2001 targets and will sign on to a new declaration. A “zero draft” of the declaration will be released next week.

Health GAP is planning a midday demonstration on June 8<sup>th</sup>, and welcomes other voices in shaping the demonstration and the demands that will be presented. How can we make use of this meeting? How can we ensure President Obama attends and brings bold targets to the table? What do we want to see the U.S. and world leaders doing in the fight to end AIDS in the next year? What is the plan for the roll-out of new prevention technologies and harm reduction practices? How can we ensure universal access to treatment, prevention, and care? How can we better employ treatment as prevention? These questions and others will shape our mobilization efforts for the UN meeting *and* the International AIDS Conference (AIDS 2012) in Washington D.C. – a gathering that will be held on U.S. soil for the first time in 19 years, in a U.S. election year.

Get in touch with Matt Kavanagh to engage! [matthew@healthgap.org](mailto:matthew@healthgap.org).

Thanks to presenters Tim Mastro, Kevin Fisher, Robert Reinhard and Matt Kavanagh as well as moderator Keith Green, for such an in-depth look at the problems and promise of PrEP as well as the UN mobilization. If you have questions for any of the presenters or related to any of these topics, feel free to email [jmerrell@aidschicago.org](mailto:jmerrell@aidschicago.org). Hope to see you at next month’s strategy call!