



## Backgrounder

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HIV discordant couples, where one partner has HIV and the other does not have HIV infection, are in urgent need of prevention strategies. Stable, heterosexual, HIV discordant couples are an important risk group for HIV infection in Africa, accounting for up to half or more of new infections. Many of these couples are in committed relationships and desire children; thus, abstinence and condoms are not often sufficient to prevent HIV transmission.

HIV discordance in couples is very common. Studies in Africa have found that the partner of an HIV infected person has about a 50% chance of being HIV uninfected, even if the couple has been together for several years. The factors that lead some couples to be HIV discordant are not well understood. Many couples have been in relationships for years and may not know each other's HIV status. In spite of this, however, the HIV uninfected partner in a discordant couple can become infected at any time. Thus, HIV uninfected individuals within HIV discordant couples are at considerable risk for getting HIV.

Antiretroviral medication taken as daily preventive treatment is known as pre-exposure prophylaxis, or PrEP. PrEP is based on the scientific principle that, if medication is in the bloodstream when someone is exposed to HIV, then the virus will not be able to establish itself in the uninfected person, and prevents them from becoming HIV infected. For PrEP, the person without HIV takes an antiretroviral medication (ARV) daily to prevent infection. Two antiretroviral medications – tenofovir (tenofovir disoproxil fumarate, also known by its brand name, Viread) and a combination of tenofovir plus emtricitabine (brand name, Truvada) – are safe and effective as *treatment* of HIV. However, we need to know whether tenofovir alone or tenofovir in combination with emtricitabine will be effective in *preventing* HIV infection for different groups of people at risk of HIV infection. Two medications might be better than one, or tenofovir alone might be just as good as the emtricitabine/tenofovir combination for preventing HIV. At the same time, two medications might cause more side effects than one. Since we don't know the answers to these questions, it is essential to evaluate both of these promising strategies.

The idea of providing a medication to prevent an infection is not new. One example is that of mothers who are infected with HIV, who take medications during pregnancy to prevent passing HIV to their babies at birth. Another example is that of travelers who take medication to prevent from getting malaria. Key to both of these examples is that the medication is in the bloodstream before exposure to the infection, so it prevents the infection from happening.

### **Purpose of the Study**

The Partners PrEP Study is designed to determine whether the once daily use of PrEP medication (tenofovir or combination emtricitabine/tenofovir) by an HIV uninfected person can reduce their risk of acquiring HIV from their HIV infected partner. The study will also assess the safety of daily PrEP by comparing rates of adverse events among the HIV uninfected partners randomized to PrEP medication compared to those on placebo.

Currently, there are four additional PrEP studies being conducted to determine whether PrEP prevents HIV among various populations including heterosexual women and injection drug users. The Partners PrEP Study is the only study focusing on HIV discordant couples and the only one including heterosexual men.

### **Study Design**

The Partners PrEP Study enrolled 4,758 HIV discordant couples who volunteered to participate. Enrollment began in July 2008 and finished in November 2010. Each couple will be in the study for 24-36 months. Couples are enrolled at clinical sites in Kenya (Eldoret, Kisumu, Nairobi, and Thika) and Uganda (Jinja, Kabwohe, Kampala, Mbale, and Tororo).

The study is a randomized, double-blind, placebo-controlled clinical trial. For each couple, the partner who is HIV uninfected will be randomly divided into one of three groups: tenofovir, combination emtricitabine/tenofovir, or placebo. This is a “double-blind” study, meaning that neither the researchers, health care providers nor the participants know to which group the participants are assigned. This blinding ensures that provider’s counseling and participants’ behavior (i.e. drug adherence, sexual behavior, etc.) is not affected by knowledge of whether the person is taking PrEP or placebo.

All participants receive a package of HIV prevention services, including risk-reduction, counseling at every visit (individual and couple), free condoms, screening and treatment for sexually transmitted infections, access to free contraception and contraception counseling, and referral or provision on-site of antiretroviral therapy (for HIV infected participants) and male circumcision (for HIV uninfected men).

HIV uninfected partners are seen monthly to receive counseling, health checks, and supplies. Counselors talk with the partner about family planning, adherence to the study drug and risk reduction practices. Health checks include physical examinations, blood samples (including HIV tests), pregnancy testing for women, and treatment for medical problems. Condoms and study drug tablets are also provided. If women become pregnant, their study drug is stopped during the pregnancy.

HIV infected partners are seen every three months to receive counseling about risk reduction and condom use, a physical exam, treatment for sexually transmitted diseases, and have their CD4 T cell count measured. If anti-retroviral therapy is needed it will be provided based on national guidelines.

The study is led by scientists at the University of Washington in Seattle, USA. The clinic sites are overseen by researchers affiliated with 12 collaborating partners, including: Indiana University, Infectious Disease Institute of Makerere University, Kabwohe Clinical Research Center, Kenya Medical Research Institute, Kenyatta National Hospital, Moi University, The AIDS Support Organization (TASO), CDC-Uganda, University of California San Francisco, and University of Washington. The study is funded by the Bill & Melinda Gates Foundation.

### **Participant Safety**

The Partners PrEP Study is designed to protect the safety of all participants. All participants are provided standard HIV prevention services including condoms, referrals for adult male circumcision and treatment for curable sexually transmitted infections. A unique feature of this study is that couples were already engaged in long-term relationships when they enrolled in the study, and most had only recently learned that they were in an HIV discordant partnership. Thus, all couples receive specialized couples counseling to help them address the challenges of being in an HIV discordant relationship, and to reduce their risks of transmitting HIV.

This study is overseen by multiple institutional review boards which review and approve the research study to assure the safety of the participants. A data and safety monitoring board (DSMB) meets every six months during the course of the study to monitor the safety of participants and review the progress of the study.

Participants who become HIV infected during the study will receive counseling, supportive services, CD4 T cell counts, clinical evaluation, and referrals to necessary health services, including antiretroviral therapy based on national guidelines.

### **Why this Study is Important**

If this study is successful, PrEP could be an additional tool in the fight against HIV for discordant couples. A phase III efficacy trial of PrEP for the prevention of HIV infection in men who have sex with men found that oral combination emtricitabine/tenofovir was effective when used with other risk reduction measures<sup>1</sup>. PrEP will need to be used as part of a combination HIV prevention strategies including existing behavioral interventions, male and female condoms, and male circumcision.

If the Partners PrEP Study demonstrates that PrEP is an effective HIV prevention method, countries and international donors could expand access to PrEP and save lives by providing another tool to prevent HIV.

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<sup>1</sup> Grant RM et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010 Nov 23; [e-pub ahead of print]. (<http://dx.doi.org/10.1056/NEJMoa1011205>)