



About FEM-PrEP

What is the FEM-PrEP clinical trial?

FEM-PrEP is a Phase III randomized, placebo-controlled, clinical trial designed to assess the safety and effectiveness of a daily oral dose of an antiretroviral drug (ARV) called Truvada for HIV prevention among women. FEM-PrEP is testing an approach known as pre-exposure prophylaxis (PrEP).

FEM-PrEP is also studying various behaviors, clinical measures, and health outcomes among the trial's participants. The trial is:

- Assessing several clinical measures—HIV-1 viral load, viral set point, and CD4+ T cell counts—among HIV-infected participants assigned to Truvada compared to HIV-infected participants assigned to the placebo pill during the trial.
- Assessing the frequency of resistance to emtricitabine (FTC) and tenofovir (TDF)—the two ARV components of Truvada—among participants who took Truvada compared to participants who took the placebo pill.
- Evaluating the effects of administering Truvada or placebo among women who became pregnant after the study began.¹
- Assessing participant adherence to once-daily pill-taking.
- Assessing whether participants changed their sexual behavior because they took the study pill.
- Comparing sexual behaviors of participants who became HIV positive to participants who remained HIV negative during the study.

What is pre-exposure prophylaxis (PrEP) for HIV?

Pre-exposure prophylaxis (PrEP) for HIV refers to a potential HIV-prevention strategy in which HIV-negative people would take a drug on a regular basis to reduce the chance that they will get HIV. (People would also need to use other strategies, such as condom use, along with the drug, to reduce their risk of getting HIV.) PrEP for HIV is based on the concept that drugs can be used by healthy people

¹ Pregnant women are not enrolled in the trial because Truvada's effects on a fetus are unknown. To enroll in FEM-PrEP, participants must have no desire to become pregnant during the course of the study and are required to use an effective study-approved contraceptive method at enrollment -- a standard practice among microbicides trials and PrEP trials with female participants. If a woman becomes pregnant during the trial, she is immediately taken off the study pill.

to prevent certain infections. For example, travelers use prophylactic drugs to avoid malaria. Another example is that an ARV (nevirapine) is given to HIV-positive mothers in labor and to their infants (within 72 hours of birth) to help prevent the transmission of HIV from mother to child.

Why do women need HIV prevention methods?

Women make up nearly 52 percent of the 33.3 million people living with HIV/AIDS worldwide.² And, in sub-Saharan Africa, women constitute 60 percent of the adults living with HIV.³ In several southern African countries, young women (ages 15 to 24) are at least three times more likely than their male peers to be infected with HIV.⁴

Why is research on PrEP for HIV needed?

More than 7,000 people around the world become infected with HIV every day.⁵ Current prevention options—such as condoms, abstinence and male circumcision—are not always practical. For example, women often have difficulty getting their male partners to use condoms, so women need a new method that they can use. The development of an effective PrEP drug would provide an important new way to reduce HIV infection.

What is Truvada?

Truvada combines two ARVs—tenofovir disoproxil fumarate (TDF 300 mg) and emtricitabine (FTC 200 mg)—into one pill that is taken once daily.

Why was Truvada chosen for FEM-PrEP?

Truvada has already been proven safe and effective as a treatment for HIV-positive people. It is licensed for this use by drug regulatory agencies in a number of countries, including Kenya, Tanzania, South Africa, Zimbabwe, and the United States. Truvada has a number of positive qualities: it needs to be taken only once a day, it can be taken with or without food, and it has few side effects among HIV-positive people. Moreover, many scientists believe there is little chance that people who acquire HIV while taking Truvada for prevention will develop resistance to the drug because Truvada includes two antiretroviral drugs—and research shows that HIV-positive people who take more than one ARV are less likely to develop a resistant version of HIV.

Who were the participants in FEM-PrEP?

HIV-negative women between the ages of 18 and 35 who were at higher risk of HIV exposure volunteered to take part in FEM-PrEP.

² UNAIDS Report on the Global AIDS Epidemic 2010.

³ Adults are defined as people age 15 years or older. UNAIDS Report on the Global AIDS Epidemic 2010.

⁴ Gouws E., et al. (2008). The epidemiology of HIV infection among young people aged 15–24 years in southern Africa. *AIDS*, 22 (Supp. 4):S5–S16.

⁵ UNAIDS Report on the Global AIDS Epidemic 2010.

Which countries were involved in FEM-PrEP?

FEM-PrEP was conducted at four sites in three countries:

- Impact Research and Development Organization (Bondo, Kenya)
- Setshaba Research Centre (Pretoria, South Africa)
- Josha Research (Bloemfontein, South Africa)
- Kilimanjaro Christian Medical Center (Arusha, Tanzania)

A site in Harare, Zimbabwe, in collaboration with the University of Zimbabwe, was scheduled to begin FEM-PrEP in mid-2011 but the site was never initiated due to the premature closure of FEM-PrEP. No participants were enrolled.

Who are the FEM-PrEP investigators?

- Dr. Lut Van Damme (Clinical Principal Investigator, FHI)
- Dr. Amy Corneli (Behavioral Principal Investigator, FHI)
- Dr. Kawango Agot, Impact Research and Development Organization (Bondo)
- Dr. Khatija Ahmed, Setshaba Research Center (Pretoria)
- Dr. Johan Lombaard, Josha Research (Bloemfontein)
- Dr. Rachel Manogni, Kilimanjaro Christian Medical Center (Arusha)
- Dr. James Hakim, University of Zimbabwe (Harare)

What is FHI?

FHI is a global health and development organization dedicated to bringing lasting change to the world's most vulnerable people. FEM-PrEP is a partnership between FHI and local scientists and project staff at each site. Members of the FHI project team oversee the scientific clinical and behavioral activities, provide overall management of the trial, support community activities, provide technical assistance in communications, and monitor the clinical trial and the socio-behavioral and community research.

How were the study sites selected?

Study sites were selected based on several criteria, such as prior experience conducting clinical trials, government support for HIV prevention research, strong commitment to community involvement and behavioral research, and being located in areas where women are at particularly high risk for HIV infection.

Who funded this clinical trial?

The United States Agency for International Development (USAID) funds FEM-PrEP. The Bill & Melinda Gates Foundation provided additional funding during the early phase of FEM-PrEP.

What is Gilead Sciences?

Gilead Sciences, which makes Truvada, provided the active drug and the placebo free of charge for FEM-PrEP. Gilead is not involved in the development or implementation of the study or the analysis of the study's data.

What ethical oversight is in place for FEM-PrEP?

FEM-PrEP received initial and yearly renewal from the Protection of Human Subjects Committee at FHI and the Ethics Committee(s) at each of the study sites. The following agencies and organizations also reviewed and approved the research: the U.S. Food and Drug Administration, the South Africa Medicines Control Council, the Pharmacy and Poisons Board in Kenya, the Tanzania Food and Drugs Authority, and the Medicines Control Authority of Zimbabwe. FEM-PrEP is being conducted under U.S. FDA Investigational New Drug (IND) #101,767.

Was the FEM-PrEP study independently reviewed during the course of the trial?

Yes, an independent data and safety monitoring board (otherwise known as an independent data monitoring committee) regularly reviewed FEM-PrEP data. The board included an international group (from Africa, Europe, and the United States) of clinical trial experts, scientists, biostatisticians, and an HIV advocate.

How long did participants take part in FEM-PrEP?

Participants first went through a screening process, and if they were eligible, they were enrolled within 4 weeks of the screening. Enrolled participants took the drug for approximately 12 months and attended monthly clinic visits for approximately 14 months. Participants who became HIV positive during the clinical trial stopped taking the study pill. They were asked to stay in the trial and to continue to come to the clinic for another 12 months.

What were the benefits of participating in this clinical trial?

During the trial, participants received free of charge:

- physical exams
- counseling and testing for HIV and other sexually transmitted infections (STIs)
- treatment for curable STIs
- a regular supply of male and female condoms (where available)
- contraception

The general community benefited from the trial by having access to HIV information and improved clinical facilities.

Why couldn't HIV-positive women enroll in the FEM-PrEP clinical trial?

FEM-PrEP was not investigating the *treatment* of HIV infections; it was investigating how to *prevent* HIV infections. Thus, the clinical trial could only enroll HIV-negative participants. Participants who tested positive for HIV during the screening visit were referred to HIV care and treatment services.

What resources were offered to participants who became HIV positive during the clinical trial?

Participants who became HIV positive during the clinical trial received counseling and were referred to medical and social services available in the community. Each study site has strong linkages and formal referral agreements with local organizations that provided these services. Women who became HIV positive continued their study visits, if they were willing, for 12 months after they became infected. During this time, they are monitored for disease progression and resistance to Truvada. These participants continue to receive individual risk-reduction counseling to limit the transmission of the virus to others. Some sites offer support groups for participants who become HIV positive.

Why was the informed consent process such an important component of FEM-PrEP?

Participation in research is voluntary. As in all research, before a potential participant can provide informed consent to participate, she must understand the purpose of the trial and the potential implications of her participation. It is the responsibility of the researchers to ensure that adequate information is provided to potential participants to allow them to make decisions about their participation and to put procedures into place to ensure comprehension of that information.

Participants express their willingness to voluntarily participate in research by signing an informed consent form, which documents that the participant 1) has been fully informed about the research, 2) understands the research, 3) willingly agrees to take part in the research, and 4) understands that she can withdraw at any time. No participant was screened or enrolled into FEM-PrEP unless she had willingly given her consent.

As part of the FEM-PrEP informed consent process, the potential participant received clear information about the purpose of the clinical trial and the study procedures, as well as its possible benefits and risks. Information used to describe the study during the informed consent process was enhanced using data acquired during the site-preparedness phase, which identified areas that might be difficult for some participants to understand.

During the screening and enrollment process—after the potential participant received information about the clinical trial and all her questions were fully answered—study staff members formally assessed the potential participant’s understanding with the aid of a quiz. If the potential participant was able to correctly answer all questions asked at enrollment, and she was willing to participate, then she was asked to sign or mark the informed consent form. There was a similar process for illiterate participants, except that staff members read the informed consent forms to these participants in the presence of an impartial witness.

Each participant’s knowledge of the study was also formally assessed every quarter. Participants were not excluded if they were unable to answer all questions correctly. Instead, FEM-PrEP staff members helped to explain the correct answers to all participants who responded incorrectly to a question.

The informed consent form was available in the most common local language(s) at each site.

How is the confidentiality of the participants protected?

The confidentiality of all the participants in the trial is protected to the fullest extent possible. The study staff was trained on the best ways to protect the confidentiality of the participants.

Are the participants compensated for being in this clinical trial?

Compensation is provided for time and travel expenses. The appropriate level of compensation was decided locally and approved by ethics committees.

Why was a placebo used?

The effectiveness of Truvada for HIV prevention in women was not known when the trial began. Drug studies typically compare one group of participants that receives the drug being tested to another group that does not. The group that does not receive the drug being tested is called the “control group.” The goal is to determine whether the group that receives the drug being tested does better than the control group. There is no other scientifically valid way to test a drug.

Ethically, placebos alone may only be used by a control group when there is no intervention that is known to work. FEM-PrEP provided *all* participants with individual risk-reduction counselling, STI screening and treatment for curable infections, and free condoms. So this clinical trial compares a group that receives standard prevention services plus Truvada to a group that receives standard prevention services plus a placebo.

How is the community involved?

Community involvement is extremely important to FHI and FEM-PrEP investigators. Extensive socio-behavioral and community activities were carried out before, during, and after the clinical trial. See *FEM-PrEP Fact Sheets on the Socio-Behavioral Aspects of FEM-PrEP and Community Engagement* for details.

We are proud to work with so many excellent partners—including the local communities, universities, and expert researchers in Africa—to undertake this important research. Advances in our understanding of ways to prevent HIV can only come from this kind of close collaboration between scientists and communities, and the individuals who participate in clinical trials.

How can I learn more about the FEM-PrEP clinical trial?

Please contact Beth Robinson, Associate Director, Project Communications. E-mail: brobinson@fhi.org