Frequently Asked Questions

Q. What is the FEM-PrEP Clinical Trial?

A. FEM-PrEP is a randomized, placebo-controlled, clinical trial of the effectiveness of daily, oral Truvada for HIV prevention among HIV-uninfected women in Kenya, South Africa and Tanzania. Truvada combines two antiretroviral drugs—emtricitabine (FTC) and tenofovir disoproxil fumarate (TDF) —in a single pill. Truvada has been proven safe and effective as a treatment for HIV-positive people. FEM-PrEP has a strong socio-behavioral and community engagement component. The study is funded by the U.S. Agency for International Development (USAID), and received early support from the Bill & Melinda Gates Foundation.

Q. What was the outcome of the FEM-PrEP study?

A. The interim FEM-PrEP study results are inconclusive. As determined by a preliminary data review, the study would not be able to demonstrate whether or not Truvada is effective in preventing HIV in women in this study, even if it were continued. FHI has decided to close the trial; however, it important to note that there is still work to be done. Data collection will continue over the next few months. A final analysis will be conducted and shared in approximately six to nine months.

Q. Does the result of 28 HIV-infection endpoints in each arm mean that Truvada is not effective in preventing HIV in women?

A. No. The trial was designed to close at 72 HIV-infection endpoints. According to the trial protocol, the Independent Data Monitoring Committee (IDMC) was scheduled to review the data at certain milestones during the trial. In the latest IDMC review, there were 56 endpoints, with 28 endpoints in each of the two arms, leaving 16 endpoints until the trial was complete. If the trial continued, it would be very unlikely that FEM-PrEP would be able to prove statistically that Truvada is effective in preventing HIV in this population of women.

Q. Does Truvada work for the prevention of HIV among women?

A. Truvada is an approved, widely-used *treatment* for HIV infection that has been proven safe and effective. Based on the FEM-PrEP trial results, it cannot be determined whether or not Truvada is effective in the *prevention* of HIV infection in women.

Q. What are next steps in the orderly closure of the trial?

A. Participants have been notified of the decision to begin the orderly closure of the FEM-PrEP study and are being asked to come to the study clinics for a series of three final visits. At their first visit they will be taken off the study drug. They will each then have two additional follow-up visits after stopping the study drug. FHI and its partners are especially grateful to the women whose willingness to participate and commitment to the study were essential. Study participants who became infected with HIV during the study are being followed by the study team for an additional year and are referred for appropriate medical care and treatment in their community. After final data are collected, FHI will conduct further data analyses and will share additional findings in the coming months.

Q. When will the final results of the study be available?

A. Participants have just been notified of the decision to close the trial and are being asked to come to the study clinics for final visits. Data collection will continue over the next few months. Final analysis will be conducted and shared in approximately six to nine months.

Q. What additional analyses will take place?

A. The study team will assess whether adherence to the study drug was sufficient to measure an effect of Truvada. We measure adherence to study product in three ways: 1) participant self-report, on which we have already shared preliminary data, 2) pill counts, and 3) the presence of tenofovir and emtricitabine in blood samples. If adherence was low, then the study team will need to understand why women chose not to take their study pills, especially given the focus on participant-centered and goal-oriented adherence counseling. The sexual behaviors among trial participants will also be analyzed to determine if study participation resulted in risk compensation. Risk compensation occurs when a participant increases risky behaviors because she feels the study pill will protect her from HIV.

Q. Were trial participants at risk of developing drug resistance?

A. The best way to prevent resistance is to prevent the infection, which is the research team's goal in this study of pre-exposure prophylaxis (PrEP). Every four weeks, each participant was tested for HIV, received risk reduction counseling, and was provided with a supply of condoms. Women who became HIV positive were immediately taken off the study drug and referred for appropriate medical care and treatment in the community. They will be followed by the study team for an additional year. Women who refused HIV testing during their monthly visit were not given a new bottle of study product in an effort to limit potential exposure to Truvada in case of HIV infection. Through the informed consent process, women participating in the trial were informed of all of the risks, which included the possibility of developing drug resistance.

Q. What was the adherence rate and how was it measured?

A. Based on preliminary data of self-reported pill-taking, adherence to study product was approximately 95 percent among women who had gone to the clinic for their monthly study appointment to receive the next month's supply. Questions about pill adherence were not asked if a woman missed her previous clinic visit and therefore had not collected study pills. Study pills were available to women at every appointment. Due to additional factors that will be considered in the final analyses, such as time off study product due to pregnancy and missed visits, the final adherence rate will be lower.

Q. What were the demographics of the study participants?

A. The FEM-PrEP study enrolled HIV-negative women between the ages of 18 and 35 who were at higher risk for HIV infection and volunteered to take part in FEM-PrEP. Higher risk was defined as: 1) has had at least one vaginal sex act in the last two weeks, OR 2) has had more than one sexual partner in the last month. Only women who did not anticipate or desire pregnancy during the time of study participation and who used effective study-approved contraception at enrollment could participate. The study was conducted at four sites in three countries heavily affected by the HIV epidemic: Bondo, Kenya; Bloemfontein and Pretoria, South Africa; and Arusha, Tanzania.

Q. What was the pregnancy rate of participants?

A. All women in FEM-PrEP were using an effective method of contraception. At enrollment, 66 percent were using injectables and 30 percent were using oral contraceptive pills. The overall pregnancy rate was 9 percent per year.

Q. Were women taken off the study drug when they became pregnant? What will be done for the women who became pregnant during the trial?

A. Yes. If a participant became pregnant during the trial, she was immediately taken off of the study pill. The FEM-PrEP trial was designed to reduce a participant's exposure to Truvada, if she became pregnant, by testing the participants for pregnancy every four weeks. Pregnant women were counseled and offered referral to antenatal clinics and were encouraged to continue to come for follow-up visits at the study clinic. If the pregnant participant agreed, the study's staff members remained in contact with the participant until the outcome of the pregnancy was known. The infant was/will be examined by a pediatrician.

Q. Was there an interaction between Truvada and contraceptives that increased the rate of pregnancy in that arm of the trial?

A. Pregnancy rates were higher in women taking hormonal contraceptives and Truvada compared with those taking hormonal contraceptives and the placebo. At this time, we cannot explain this observation. These data are unexpected and inconsistent with known drug interactions involving tenofovir (TDF) and contraceptive hormones, and with known metabolic effects of emtricitabine (FTC). Possible explanations include differential pill adherence by group, previously undefined drug-drug interactions, chance, or a combination of factors (including yet unknown factors). FHI will conduct further analyses of these data.

Q. What additional analyses will be conducted on the pregnancy data?

A. FHI will be reviewing all the data for women who became pregnant during the study, examining factors such as type of contraceptive method and whether women were actually using the method, study site, randomization to Truvada or placebo, and other factors. Findings will be shared in the coming months.

Q. What does this mean for other PrEP trials?

A. It would be premature to modify other PrEP trials, which are using different designs in different study populations, based on the preliminary data from FEM-PrEP.