PrEP using daily oral TDF/FTC or TDF in Women (and Men)[1]: What the science tells us in March 2012

Oral PrEP is an HIV prevention strategy that doesn't need to be used at the time of sex. This offers women (and men) an HIV risk reduction option that could be used without negotiating with their partners. The data to-date come from trials in which participants were counseled to take either one tablet of oral TDF/FTC (brand name Truvada) or oral TDF (brand name Viread) every day. Other forms of ARV-based prevention, including 1% tenofovir gel, ARV-containing vaginal rings and long-acting injectable ARVs are also being evaluated. Daily oral PrEP using oral TDF/FTC for women and men is now being considered by the US Food and Drug Administration for a formal label indication for HIV prevention and is being implemented in demonstration projects in several countries. Other resources on PrEP and ARV-based prevention can be found at www.avac.org.

PrEP using a daily oral TDF or TDF/FTC tablet reduces risk of HIV in women *and* men. In the past there has been confusion about whether there are clear data on the efficacy of TDF or TDF/FTC as PrEP in heterosexual women. Recently, the picture has become clearer as trials have examined their data more closely. Today, the message is: daily oral PrEP using TDF/FTC or TDF reduces HIV risk in women and men who take it correctly and consistently. The estimates of effectiveness vary in each trial. In each trial, when adherence was low, there was low or no protection. This is true for both women and men.

The Partners PrEP trial studied daily PrEP using TDF/FTC or TDF in HIV-negative women and men with HIV-positive partners or spouses (serodiscordant couples) in East Africa. The trial found very high rates of adherence and high rates of protection for both TDF and TDF/FTC for both HIV-negative women and men. The CDC-sponsored TDF2 trial in Botswana also found that daily oral TDF/FTC reduced risk of HIV infection in female and male participants.

The FEM-PrEP trial found no effect of daily oral TDF/FTC among African women. Further analysis of the FEM-PrEP data showed that the participants didn't adhere well to the daily PrEP regimen. In fact, adherence was too low for the trial to ultimately determine whether the intervention provided any protection. The ongoing VOICE trial found no effect of either oral TDF or tenofovir gel in women, but the oral TDF/FTC arm is ongoing. We don't yet know why the oral TDF and gel arms did not show benefit in VOICE—those data are not expected before 2013.

Putting it altogether, right now the science says that there is a biological basis for using oral TDF or TDF/FTC for HIV prevention in women, as shown in the Partners PrEP and TDF2 studies—but this PrEP strategy requires sufficient adherence to reduce the risk of HIV infection. We also know that in FEM-PrEP, women didn't have high levels of adherence. It will be valuable to learn more about why and to build these lessons into future research and programs.

PrEP doesn't work if you don't take it. The trials tell us: there is no protection without drug detectable in the blood. Regular pill-taking is required to reduce HIV risk via oral TDF or TDF/FTC as PrEP. The FEM-PrEP trial tells us that, in at least one setting, women weren't able to adhere to the regimen as prescribed.

Risk perception matters—a lot. The trials so far suggest that an individual's perception of HIV risk might affect adherence to PrEP. FEM-PrEP researchers report that participants' risk perception was quite low at the start of the trial. In Partners PrEP, the women and men were in stable serodiscordant relationships. They may have had a strong sense of their individual risk and thus a high motivation to adhere—but it's too soon to draw firm conclusions. What we can say is that it is also premature to draw the conclusion that "single women won't take PrEP." We need more nuanced answers.

Testing is key. The majority of documented cases of resistance in PrEP trial participants have been in individuals who were in the window period before seroconversion at the time that they started taking study drug (either TDF or TDF/FTC). Participants in the trials were tested on a monthly basis. For anyone using PrEP, it will be essential to be tested for HIV on a regular basis.

More data are needed in pregnant women, adolescents and other groups of women—and men. These can be gathered through open-label demonstration projects (structured programs with monitoring of key populations and outcomes) and other ongoing trials.

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[1] Oral PrEP using TDF/FTC or TDF has been evaluated and showed benefit in heterosexual men (in Partners PrEP and TDF2 trials) and in gay men and other men who have sex with men and transgender women (in the iPrEx trial).