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**CDC Trial and Another Major Study Find PrEP Can
Reduce Risk of HIV Infection among Heterosexuals**

CDC Assessing Data from All Heterosexual Trials to Develop Interim Guidance for Use

A new CDC study called the TDF2 study, along with a separate trial released today, provide the first evidence that a daily oral dose of antiretroviral drugs used to treat HIV infection can reduce HIV acquisition among uninfected individuals exposed to the virus through heterosexual sex.

The CDC TDF2 study, conducted in partnership with the Botswana Ministry of Health, found that a once-daily tablet containing tenofovir disoproxil fumarate and emtricitabine (TDF/FTC, known by the brand name Truvada) reduced the risk of acquiring HIV infection by roughly 63 percent overall in the study population of uninfected heterosexual men and women. The strategy of providing daily oral antiretroviral drugs to uninfected individuals prior to HIV exposure is called pre-exposure prophylaxis, or PrEP.

In a separate announcement, the University of Washington (UW) released preliminary results of the Partners PrEP study, which also found that daily PrEP reduced HIV transmission among heterosexual couples in Kenya and Uganda. CDC co-managed two of the nine sites for this study. The Partners PrEP study found that two separate antiretroviral regimens – tenofovir (known by the brand name Viread) and TDF/FTC – significantly reduced HIV transmission among serodiscordant couples, in which one partner is infected with HIV and the other is not. The findings were released after the trial's independent data safety monitoring board conducted an interim review of the trial data and recommended that the study be stopped early due to strong evidence of effectiveness so that all participants could be offered PrEP. For more information on this study, visit <http://www.uwicrc.org>.

The CDC study findings were scheduled to be released next week at the International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention (www.ias2011.org) in Rome by the CDC principal investigator Michael C. Thigpen, M.D. However, due to the unexpected release of the Partners PrEP data today, CDC is releasing the TDF2 results now, to ensure that all emerging trial data are concurrently available to fully inform public health and policy discussions moving forward. The results will still be presented and discussed at the IAS 2011 conference on Wednesday, July 20.

“These are exciting results for global HIV prevention. We now have findings from two studies showing that PrEP can work for heterosexuals, the population hardest hit by HIV worldwide,”

said Kevin Fenton, M.D., director of CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. "Taken together, these studies provide strong evidence of the power of this prevention strategy."

A previous study (iPrEx) had already shown PrEP reduced HIV transmission among men who have sex with men (MSM) last fall, but it was not previously known if the strategy could prevent HIV infection among heterosexuals.

The CDC and UW study results follow preliminary findings from another PrEP study earlier this year, the FEM-PrEP trial, which did not demonstrate a protective effect of PrEP among heterosexual women. Researchers from that study are conducting additional analyses, including a close examination of adherence among women in the trial, to better understand the potential reasons for the interim outcome of that study.

More Information on CDC TDF2 Study and Results

In addition to finding PrEP reduced the risk of HIV infection by roughly 63 percent in the study population overall, researchers from CDC's TDF2 study also conducted a separate analysis to better understand the level of effectiveness among trial participants believed to be taking study medications. This analysis excludes any HIV infections that occurred more than 30 days after a participant's last reported drug dose, because those individuals could not have been taking study pills at the time of infection. These results indicate that TDF/FTC reduced the risk of HIV infection by 78 percent.

Overall, a total of 1,219 HIV-uninfected heterosexual male and female participants (aged 18-39) in Botswana were enrolled in the TDF2 trial and randomly assigned to take a daily TDF/FTC pill or a placebo pill. All participants in the study were provided comprehensive HIV prevention services, including male and female condoms, intensive risk-reduction behavioral counseling, and testing and treatment for sexually transmitted infections. Three participants were determined to be HIV-infected at the time of enrollment, and 16 of the participants randomized never began study medication. Those individuals were excluded from these analyses, which include data on the remaining 1,200 participants who were HIV-negative at the time of enrollment and began study medication (54.7 percent male, 45.3 percent female).

In the primary analysis, among the 601 participants who received TDF/FTC, there were nine who became infected with HIV during the study. Among the 599 individuals who received a placebo, 24 became infected with HIV during the study. This translates into a statistically significant overall reduction in risk of 62.6 percent.

Among participants known to have a supply of study drugs (the separate analysis described above), protection was even greater, with a statistically significant risk reduction of 77.9 percent (95% CI 41.2 to 93.6, $p=.0053$). Additional analyses of the level of effectiveness based on the level of adherence to the study regimen, as well as an examination of the level of protection provided by detectable drugs in the blood, are under way but are not yet complete.

Consistent with other PrEP studies, preliminary analyses did not identify any significant safety concerns associated with daily use of TDF/FTC. Participants assigned to receive the study drug

were more likely than those assigned to the placebo arm to report nausea, vomiting, and dizziness.

All participants infected during the study were immediately referred to medical care. All uninfected participants will be offered the study drug for a year as part of a CDC follow-up study.

CDC officials note that the trial would not have been possible without the dedication of the more than 1,200 participants and the strong collaboration between the Botswana Ministry of Health and CDC. Additional study funding was also provided by the National Institutes of Health, and Gilead Sciences, based in Foster City, Calif., donated the study drug.

“Given the severity of the HIV epidemic among heterosexual men and women globally – and the critical need for female-controlled prevention methods – this study provides exciting and welcome news,” said Jonathan Mermin, M.D., director of CDC’s Division of HIV/AIDS Prevention. “The next important step is to fully review the data and assess when and how PrEP should best be used for HIV prevention among heterosexuals.”

TDF/FTC is FDA-approved and marketed for use in the United States under the name Truvada, for use in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients 12 years of age and older. It is not FDA-approved for PrEP.

Next steps

In the wake of today’s announcements, CDC will fully review the data from all of the heterosexual trials and will begin working with a range of stakeholders and with established guidelines development working groups to develop guidance specific to the use of PrEP among heterosexual men and women in the United States.

CDC urges heterosexual men and women and their health care providers in the United States to await that guidance before considering PrEP. However, if providers have patients for whom they believe the initiation of PrEP is urgent, CDC recommends following the cautions and procedures previously published for PrEP use in MSM (http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6003a1.htm?s_cid=mm6003a1_w). The Partners PrEP finding that TDF alone was as effective as TDF/FTC in studies for prevention of heterosexual transmission suggests that providers may consider daily doses of either regimen in this population. However, for MSM, the interim guidance remains that only TDF/FTC should be prescribed, because there are no data on effectiveness for TDF alone to prevent HIV acquisition by MSM.

It will also be critical for providers to consider factors unique to heterosexuals, including concerns related to the use of PrEP among women who may become pregnant.

Importantly, anyone considering using PrEP should know:

- PrEP should only be used among individuals who have been confirmed to be HIV-negative. Initial and regular HIV testing is critical for anyone considering using PrEP. All

individuals considering PrEP must also be evaluated for other health conditions that may impact PrEP use.

- PrEP should never be seen as the first line of defense against HIV. It was only shown to be effective in clinical trials when provided in combination with regular HIV testing, condoms, and other proven prevention methods.
- Taking PrEP daily is critical. No other dosing regimen was evaluated in these studies.
- PrEP must be obtained and used in close collaboration with health care providers to ensure regular HIV testing, risk reduction and adherence counseling, and careful safety monitoring. Anyone considering using PrEP should speak with his or her doctor.
- PrEP has only been shown in clinical trials to reduce HIV infection among heterosexual men and women and among men who have sex with men. At this time, there are no data on its benefits or risks among injection drug users.
- Because pregnant and breastfeeding women were excluded from participation in PrEP trials, further evaluation of available data will be needed before any recommendations can be made regarding the use of PrEP for women during conception, pregnancy, or breastfeeding.

For more information on efforts to evaluate and plan for PrEP implementation in the United States, visit www.cdc.gov/hiv/prep.

For a complete list of PrEP trials being conducted, see <http://www.avac.org/ht/a/GetDocumentAction/i/3113>.

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