

HPTN 067/ADAPT Study

Results Brief on Daily vs. Non-daily PrEP Dosing Regimens for South African Women

Summary

HPTN 067, also known as the ADAPT Study, evaluated the feasibility of non-daily oral pre-exposure prophylaxis (PrEP) using emtricitabine/tenofovir disoproxil fumarate (Truvada®). The study of more than 500 participants was conducted among women who have sex with men in Cape Town, South Africa, and among men who have sex with men and transgender women in Bangkok, Thailand and New York, United States.

This brief focuses exclusively on results from women participants in Cape Town, South Africa which ended follow up in June 2013. Data from the Bangkok and New York sites which ended follow up more recently are currently being analyzed.

Among Cape Town participants, the HPTN 067 study found that women assigned to a daily dosing regimen led to better adherence of PrEP and coverage of sexual acts, when compared to those assigned to non-daily dosing regimens. Researchers found fewer women on non-daily dosing regimens took their pills as prescribed, and post-sex doses appeared to have the lowest adherence. Daily dosing appeared to foster better adherence, better coverage of potential sexual exposure, and more sustained use of PrEP. These findings support current recommendations for daily use of oral PrEP in women.

Study Overview

HPTN 067 aimed to evaluate whether non-daily dosing would result in better adherence and coverage of sex events with pre-and post-sex PrEP dosing compared to a daily PrEP dosing regimen.

After a four-week period of once-a-week directly observed dosing, participants were randomly assigned to one of three PrEP dosing regimens for 24 weeks: a) daily, b) time-driven: twice weekly with a post-sex dose, or c) event-driven: before and after sex. Study participants were given a Wisepill device that tracks each time a participant opens the container to take a pill. These data were then used by a study team member to conduct weekly phone or in-person interviews to ask participants if the date and time recorded by the Wisepill device did indeed involve taking a dose. Dates and times of sex events over the past week were also collected in these interviews. The interviews were for data collection only, so interviewers remained neutral and no messaging on adherence or non-adherence was provided, nor were data shared with study adherence counselors.

Blood samples were collected and analyzed for tenofovir (FTC/TDF) and their active metabolites at 10 and 30 weeks on study. In addition to overall adherence, the study evaluated PrEP coverage for each sex event, defined as taking at least one pill in the four days before the sex event and at least

one pill within 24 hours after sexual intercourse. The regimens used in this trial and the definition of PrEP coverage was based on information that was available when the trial was designed in 2010. More current information suggests that higher concentrations of PrEP medications are required for protection from vaginal exposure to HIV, as would be afforded by daily oral dosing or any topical dosing.

In addition to the quantitative analysis, the study team also conducted six focus groups and 18 in-depth interviews among participants in the study to better understand their experiences with the three PrEP dosing regimens. Results of this work are in preparation.

Results

- The median age of 179 women who were randomized to the three PrEP regimens was 26 years (range 18-52), 80% were unmarried and 83% unemployed.
- When sex was reported in the prior week, tenofovir was detected in plasma in more women on the daily dosing regimen at weeks 10 and 30, when compared with the non-daily dosing regimens. See the data in the table below. For “as expected” drug detection, regardless of report of recent sex for the two arms with scheduled dose times, drug detection was still high at week 10 (93% for daily arm and 84% for time-driven) and lower at week 30 (68% for daily arm and 56% for time-driven).

By the Numbers:

Dosing Regimen	Drug in Plasma at Week 10	Drug in Plasma at Week 30
Daily	93%	79%
Time-driven	87%	63%
Event-driven	78%	53%

- PrEP coverage of sexual activity differed by arm: 75% coverage for daily dosing participants; 56% coverage for time-driven dosing participants; and 52% coverage for event-driven dosing participants.
- Side effects were uncommon in daily dosing participants, and less frequent in time- and event-driven dosing participants.
- There was no significant difference in the number of women who became HIV-positive between the three dosing arms, with two identified HIV infections during the directly observed therapy (DOT) phase and five HIV infections after randomization into the three dosing arms.

HPTN 067: The Way Forward

Uptake of and adherence to oral FTC/TDF PrEP among African women has been highly variable between studies. HPTN 067/ADAPT provides information about experiences of women receiving open-label PrEP after the HIV prevention method was proven effective.

Study findings support current recommendations for daily use of oral FTC/TDF PrEP in women. The majority of women in the HPTN 067 study took oral PrEP when made available in an open-label study. Daily dosing resulted in better coverage of sex acts and adherence, and higher drug levels.

Meanwhile, post-sex dosing appeared to have the lowest adherence, suggesting potential unique difficulties with post-sex dosing. Nuanced exploration of the factors influencing women's use of each regimen is the focus of qualitative work in progress in Cape Town.

Additional Background

HPTN 067 was conducted by the HIV Prevention Trials Network (HPTN) and was funded by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Mental Health (NIMH), which are part of the U.S. National Institutes of Health (NIH). The study's full title is: *HPTN 067: A Phase II randomized open-label clinical trial of oral Truvada® [tenofovir disoproxil fumarate (TDF) plus emtricitabine (FTC)] PrEP among HIV-uninfected MSM/TGW and WSM, at high risk of acquiring HIV infection.*

For more information about HPTN 067, visit: http://www.hptn.org/research_studies/hptn067.asp