Early treatment reduces HIV transmission in heterosexual serodiscordant couples

17 May 2011

The early results of a clinical trial, called HPTN 052, show that starting treatment early can significantly reduce the transmission of HIV in heterosexual serodiscordant couples.

Treatment as prevention

The use of antiretroviral treatment by HIV-positive individuals to reduce their risk of transmitting HIV to their sexual partners is commonly referred to as “treatment as prevention.” Antiretroviral treatment can reduce the amount of HIV in bodily fluids (such as rectal fluid, semen and vaginal fluid) of someone living with HIV and may therefore make them less likely to transmit HIV to others during unprotected sex. The possibility of reducing the risk of HIV transmission is one argument made to support early initiation of HIV treatment.

Until now, the strongest evidence for “treatment as prevention” came from observational studies. These studies have involved heterosexual, serodiscordant couples (where one partner is HIV-positive and one partner is HIV-negative). By systematically combining the results from multiple observational studies, researchers recently found that the overall rate of HIV transmission among serodiscordant couples on treatment was lower than the rate of transmission among couples who were not on treatment. Transmission rates were reduced by 66% to 84%, depending on which studies the authors included in their analysis.

Unfortunately, with observational “treatment as prevention” studies, it is difficult to conclude that HIV transmission was reduced as a result of the HIV-positive partner being on treatment and not due to other factors that researchers may not have taken into account (also known as biases). For example, people on treatment may be more likely to use condoms regularly, which would explain how they have prevented transmitting HIV to their partners. Also the studies provide little information about the relative importance of the time of initiation of HIV treatment on potential risk reduction.

The first “treatment as prevention” trial

Last week, preliminary results from the first randomized controlled trial studying “treatment as prevention”, known as HPTN 052, were released. Randomized controlled trials are generally considered the “gold standard” of evidence because they minimize—but do not eliminate—the influence of possible biases. This type of study can more confidently attribute the reduced risk of HIV transmission to the antiretroviral treatment.

Study design and enrolment

The HPTN 052 trial studied the effect of “treatment as prevention” among 1,763 serodiscordant couples. Specifically, the trial was designed to determine if starting HIV treatment very early would reduce the risk of HIV transmission between partners in a stable, serodiscordant relationship. The vast majority of the couples (97%) were heterosexual. All of the couples enrolled had been in a stable relationship for at least three months prior to enrolment (most of the couples were married). The trial took place in several countries, including Botswana, Brazil, India, Kenya, Malawi, South Africa, Thailand, Zimbabwe and the United States. Due to difficulties enrolling participants in the United States, only one US couple participated in the trial.

To be eligible for the trial, the HIV-positive partner had to meet the following criteria at the time of enrolment:
• test positive for HIV within 60 days of entering the study
• not be on treatment for HIV
• have a CD4 cell count between 350 and 550 cells/mm$^3$
• be willing to start treatment earlier than suggested by the treatment guidelines in their country

The HIV-negative partner had to have tested negative for HIV within 14 days of entering the study.

A total of 890 HIV-positive men and their partners, and 873 HIV-positive women and their partners participated in the study. Half of the HIV-positive men and women started treatment immediately upon enrolment (early treatment). The other half did not start treatment until their CD4 count dropped to between 200 and 250 cells/mm$^3$ or they developed an AIDS-related illness (delayed treatment).

All couples received regular adherence counselling, HIV risk-reduction counselling, free condoms, HIV testing, and screening for and treatment of other sexually transmitted infections (STIs).

**Preliminary results**

Although the clinical trial is scheduled to be completed in 2015, preliminary results have been released early as a result of an interim review by an independent data and safety monitoring board (DSMB). Based on the study data, the DSMB concluded that earlier initiation of HIV treatment by people living with HIV substantially protects their HIV-uninfected heterosexual partners from acquiring HIV.

Overall, 39 HIV-negative partners became infected during the study. In each case, researchers used genetic matching to determine the source of the HIV infection. In 28 cases, the HIV-positive partner in the study was the source of HIV transmission. In 7 cases, the HIV-positive partner in the study was not the source. In the remaining four cases, the sources are still undetermined.

Researchers then looked at the 28 cases where genetic matching confirmed that HIV was transmitted from one partner to the other within the serodiscordant relationship. Of these 28 transmissions, 27 were among couples where the HIV-positive partner delayed treatment and only 1 was in a couple where the HIV-positive partner started treatment immediately. Therefore, the study showed that earlier initiation of treatment by the HIV-positive partner reduced the risk of transmission to the HIV-negative partner by 96%.

The study also found that starting treatment earlier provided additional health benefits for the HIV-positive partner. Whereas 17 cases of extrapulmonary tuberculosis (tuberculosis that occurs outside of the lungs) were reported among the HIV-positive people who delayed their treatment, there were only 3 cases among the HIV-positive people who started treatment immediately.

**Limitations of the study**

The vast majority of the couples enrolled in the HPTN 052 study were heterosexual and at risk of transmission primarily through vaginal sex. Therefore, the results may not apply to other populations—such as men who have sex with men and injecting drug users, who are at risk of HIV infection through other routes, including anal sex and sharing needles.

The study also does not tell us about the effectiveness of earlier treatment at reducing the risk of heterosexual transmission in a “real-world” setting. The participants in this trial were provided with a comprehensive package of prevention services, including HIV risk-reduction counselling, adherence counselling, and screening for and treatment of STIs. It is possible that HIV treatment may be less effective at reducing transmission in the absence of these services. For example, “treatment as prevention” may be less effective if the HIV-positive partner does not adhere to their medications, if either partner has other sexually transmitted infections, or if a couple engages in more risky behaviours because they feel that the treatment protects them fully from transmission.

Finally, the trial involved people who had recently received an HIV-positive test result and who had relatively high CD4 counts. This suggests that the HIV-positive people in this study are more likely to be recently infected with HIV. Therefore, it is hard to tell from the data that is currently available if the reduction in HIV transmission as a result of early treatment seen in this trial would apply to other stages of HIV infection.
Additional results and analysis are expected from the study at the International AIDS Society 2011 Conference in July. These results will include further information on risk behaviour, viral load, sexually transmitted infections and pregnancies.

**For more information**


[Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples (review)]. Cochrane Database of Systematic Reviews, 2011 May 11.

[Treatment as Prevention: We've all heard about it but what does it really mean?](https://www.preventioninfocus.org), Prevention in Focus, 2010 Spring.
Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

CATIE provides information resources to help people living with HIV and/or hepatitis C who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

CATIE endeavours to provide the most up-to-date and accurate information at the time of publication. However, information changes and users are encouraged to ensure they have the most current information. Users relying solely on this information do so entirely at their own risk. Neither CATIE nor any of its partners or funders, nor any of their employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. Any opinions expressed herein or in any article or publication accessed or published or provided by CATIE may not reflect the policies or opinions of CATIE or any partners or funders.

Information on safer drug use is presented as a public health service to help people make healthier choices to reduce the spread of HIV, viral hepatitis and other infections. It is not intended to encourage or promote the use or possession of illegal drugs.

Permission to Reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: This information was provided by CATIE (the Canadian AIDS Treatment Information Exchange). For more information, contact CATIE at 1.800.263.1638.

© CATIE

Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.

Available online at: