# Study Confirms Viral Load Most Important Predictor of HIV Transmission

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A new African study of heterosexual HIV-serodiscordant couples—in which one partner is positive and the other is negative—confirms that viral load is the most important factor influencing the risk of transmitting the virus, according to data published in the February 1 issue of The Journal of Infectious Diseases. The findings also stress the importance of other transmission variables, including condom use, age, male circumcision status and the presence of other sexually transmitted infections (STIs).

The primary goal of the study was to calculate the risk of HIV transmission per act of sexual intercourse with an HIV-positive partner in the absence of antiretroviral treatment, notably among heterosexuals in sub-Saharan Africa, who make up roughly two thirds of the world's population of people living with HIV. According to study authors James Hughes, PhD, of the University of Washington and his colleagues, the average rate of infection was found to be 1 per 900 coital acts.

Though estimates of the probability of HIV infection per act of sexual intercourse can be confusing on a level of personal decision making—it only takes one unsafe sexual encounter to become infected with the virus—these estimates are of importance to experts in the field of HIV epidemiology and prevention. According to an editorial accompanying Hughes and his team's paper, Ronald Gray, PhD, and Maria Wawer, MD, of Johns Hopkins University point out that these estimates are needed "for modeling the epidemic and for projecting the effects of preventive interventions." Indeed, they add, these estimates "[have] been the holy grail of HIV epidemiology for [more than] two decades."

Estimates, however, haven't been consistent, given variations in the populations included in studies, including those residing in low- and high-income countries, male-to-female versus female-to-male transmission, stage of HIV infection in the positive partner, the effects of demographic and behavioral characteristics and STI cofactors.

In an effort to provide more consistent results, Hughes and his colleagues—including researchers in eastern and southern African—analyzed data from a study that included 3,297 HIV-discordant couples in South Africa, Kenya, Rwanda and Zambia who received either acyclovir or placebo to determine the effects of suppressing genital herpes, or herpes simplex virus-2 (HSV-2)

infection, on HIV transmission rates. The couples had frequent follow-up to measure viral loads in the positive partner; this included genetic testing to link the transmitted virus to the HIV-positive partner in order to prevent including infections acquired from other possible partners.

Though the study did not find an association between acyclovir use and HIV transmission, it provided the researchers with the opportunity to estimate per coital HIV transmission, considering that antiretroviral therapy was only offered once the positive partner's CD4 cell count fell below 250.

Overall, there were one to two incidents of HIV transmission per 1,000 acts of sexual intercourse—a rate similar to those found in other low-income countries, but higher than estimates from many industrialized countries.

The viral load in the original infected partner was the main driver of transmission, with the risk increasing 2.9 times for every log increase in viral load (for example, an increase from 10,000 copies to 100,000 copies). This finding was somewhat higher than previous estimates of transmission risk associated with viral load, possibly because the short follow-up intervals and frequent viral load measurements in the study allowed more precise estimates of the association between HIV levels and infectivity.

The study also confirmed that condoms are highly protective, reducing the risk of HIV transmission by 78 percent when volunteers self-reported condom use. "[This] suggests a very high rate of consistent use, which is atypical for married couples in sub-Saharan Africa," Gray and Wawer note.

Older age was also associated with reduced transmission per sex act, as has been previously reported, and male circumcision reduced female-to-male transmission by about 47 percent, an effect compatible with the efficacy reported in three randomized trials of circumcision for HIV prevention.

HSV-2 infection and genital ulceration increased transmission between 2 and 2.7 times, another confirmation of previous research findings.

The findings also showed that the risk of an HIV-positive man transmitting the virus to a negative woman was about twice the risk of an HIV-positive woman transmitting it to an HIV-negative man. However, this difference can be attributed to the difference in viral loads between men and women, the authors noted. After adjusting the data for viral load differences—the men in the study tended to have higher levels, on average—the male-to-female and female-to-male transmission rates per act of sexual intercourse were found to be similar. This finding differs from those in high-income countries, where the transmission risk from men to women is significantly higher, even after adjusting for viral load differences.

Differences in age and HSV-2 infection in the HIV-negative partners also help account for the gender disparity—the HIV-negative female partners were, on average, younger and had higher rates of genital herpes than their male counterparts.

"Our results underscore the importance of antiretroviral therapy"—findings underscored by the encouraging results of the HPTN 052 study—"and, possibly, treatment of coinfections, to reduce plasma HIV-1 viral load in HIV-1 infected partners, and condom promotion, male circumcision, and

treatment of symptomatic sexually transmitted infections for HIV-1 uninfected partners as potential interventions to reduce HIV-1 transmission," Hughes and his colleagues conclude.

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