Data are lacking for quantifying HIV transmission risk in the presence of effective antiretroviral therapy

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The current era of HIV/AIDS epidemics is one in which highly effective combination antiretroviral therapy (ART) is being used to treat a high proportion of HIV-infected individuals who are diagnosed with their infection in the developed world, and universal treatment access is becoming closer to reality for treatment-eligible individuals in the developing world. Therefore, it is of greater importance to understand the magnitude of HIV transmission risk in the presence of ART. In this issue of AIDS, Attia et al. [1] report results from a systematic review of the literature and meta-analysis of the risk of HIV through unprotected sexual intercourse according to viral load, with or without the presence of ART. A review of this kind is timely, particularly as the role of ART in prevention is currently a hotly debated topic [2–5]. Several longitudinal and cross-sectional studies of HIV discordant couples have reported on transmission risk against viral load, with or without the presence of ART. Until now, however, no study had carried out a transparent and comprehensive review and analysis of the body of evidence available.

Attia et al. [1] established that very few studies, with relatively small numbers of person-years of follow-up, have reported HIV transmission in discordant partnerships in which viral load was reported in the presence of ART. The overall HIV transmission rate in the presence of ART, irrespective of viral load, was calculated to be approximately 0.5 per 100 person-years. Considerably more studies with substantially longer follow-up times have been published on transmission rates according to viral load in the absence of ART; Fig. 1 demonstrates the findings of Attia et al. [1] regarding transmission risk versus viral load. There is a predictable relationship between HIV viremia and transmission rates for viral levels above approximately 400 copies per ml (Fig. 1). However, in the range of viral levels relevant to suppressive therapy, there is large uncertainty in the transmission rate. There may well be a sharp threshold level below which transmission becomes highly improbable. But it seems more apparent that studies conducted to date have been insufficiently powered to measure transmission rates for lower viral loads, and there is likely to be a continuous association between viremia and transmission risk. Available data on transmission events for viral load less than 400 copies/ml led to a transmission rate estimate of 0.16 [0.02–1.13, 95% confidence interval (CI)] per 100 person-years. Mathematical curve fits of the data diverge at low viral levels, due to insufficient data, and extrapolation of standard regression models (linear relationships on the log-log scale) is inappropriate for estimating transmission risk for low viral loads. In summary, as highlighted by Attia et al. [1], data are currently lacking for quantifying transmission risk for low HIV levels or in the presence of suppressive ART. Evidence is also currently not available for distinguishing transmission rates under ART according to condom use, presence or absence of other sexually transmitted infections, or direction and mode of sexual intercourse (insertive or receptive vaginal or anal sex).

Although there is large uncertainty in transmission risk in the presence of effective ART, greater precision can be...
obtained. Results from the prospective cohort study led by Cohen [6] are eagerly anticipated to fill the knowledge gap. Accumulating case reports of transmission events from HIV-infected partners with low viral loads may also assist in determining a transmission threshold, if it exists. Transmission rates (and threshold levels) could also be expected to depend not only on viral load but also on whether or not ART is present and which combination antiretroviral regimen is used. ART regimens penetrate genital fluids to differing degrees; the correlation between plasma viral load and viral load in semen, cervicovaginal, or rectal fluids is not perfect and differs by drug class and regimen [7–9].

ART does decrease HIV-RNA levels in blood and semen [7–9], strongly suggesting that effective treatment will also lower the risk of transmission from a person infected with HIV [10]. But the magnitude of reduction is still not well known. Mathematical models have been used to predict the effect of ART on epidemics. Modeling is a useful tool for linking individual-level parameters with population-level outcomes if appropriate assumptions are made. Models have made assumptions of ART reducing transmission ranging from two to 100 times [3,4,11,12]. Attia et al. [1] calculated that ART reduces transmission rates by approximately 30-fold (5.71 per 100 person-years to 0.19 per 100 person-years), irrespective of viral load. The use of mathematical models in the future to forecast HIV epidemics under conditions of high ART coverage will depend on the accuracy of estimates of transmission risk in the presence of ART. Paradoxically, in an era of increasing rates of successful treatment that achieves viral suppression and lowers infectiousness, many settings are experiencing increases in HIV notifications, particularly in the developed world [13–17]. It is of high importance and relevance to counseling in clinical practice as well as modeling and public health evaluation that the international HIV research community works toward elucidating the actual risk of transmission under effective ART.

References


