

Antiretroviral Therapy to Prevent HIV Acquisition: Limits of Estimation From a Population Cohort

TO THE EDITOR—We [1, 2] and others [3] have studied human immunodeficiency virus (HIV)–discordant couples to assess the ability of antiretroviral treatment (ART) to prevent sexual transmission of HIV. In these studies, HIV transmission was not observed when viral replication was suppressed.

Oldenburg et al [4] evaluated data from a longitudinal survey of households in KwaZulu-Natal, South Africa, to assess the ability of ART to prevent HIV transmission in the “real world” (outside of a clinical trial or observational study). The authors noted a 77% reduction in HIV transmission in HIV-discordant couples that they ascribed to ART provided to the HIV-infected partner. However, we believe the results likely underestimate the effectiveness of ART for prevention.

Proof of HIV transmission within a couple requires viral linkage studies to document that the HIV-infected person and the partner share the same HIV variant(s) [5]. The study by Oldenburg et al did not include viral linkage analysis; therefore, it is not possible to determine which or how many incident infections resulted from index-to-partner transmission. In 2 large studies of HIV-discordant couples that included viral linkage analysis, 25%–30% of the incident infections observed were unlinked, indicating that the infections were most likely acquired outside of the primary partnership [1, 2, 6]. Therefore, it seems likely that some portion of the incident infections interpreted by Oldenburg et al as “real world” failures of ART in HIV prevention were actually infections acquired from other individuals.

Effective use of ART for HIV prevention requires rapid and sustained viral suppression. Oldenburg et al analyzed data collected from 2005 to 2013; in that period, ART regimens and access to ART and adherence support were still evolving. More rapid and durable viral suppression on ART is likely to have improved over time, increasing the effectiveness of ART for HIV prevention.

Finally, while the study by Oldenburg includes a large cohort (17 016 persons) and extensive follow-up (60 349 person-years), the number of person-years accrued for serodiscordant couples was limited. The authors observed 4 HIV acquisition events over 294 person-years when HIV-infected partners were receiving ART, and 23 events over 413 person-years when HIV-infected partners were not receiving ART. While straightforward calculation yields a point estimate of the rate ratio of 0.24 with a 76% risk reduction for HIV acquisition, the 95% confidence intervals for the rate ratio and risk reduction are very wide (.06–.72 for rate ratio; 28%–94% for risk reduction).

In conclusion, clinical trials and observational studies demonstrate that HIV transmission in serodiscordant couples is extremely rare when HIV in the treated person is stably suppressed by ART [2, 3]. In the study by Oldenburg et al, the source of HIV infection in household partners is not known, which makes it difficult to assess the impact of ART on HIV transmission. Immediate initiation of the best available ART regimen for all HIV-infected people, effective counseling of couples to reduce risk of both linked and unlinked HIV acquisition, careful monitoring of viral load on ART, and rapid modification of ART in those who

fail treatment will maximize the benefits of “treatment as prevention.”

Note

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