

CORRESPONDENCE



Prevention of HIV-1 Infection with Antiretroviral Therapy

TO THE EDITOR: To recommend antiretroviral therapy (ART) as a policy to prevent transmission of the human immunodeficiency virus type 1 (HIV-1), it is critical to understand the risk of transmission through sex without condom use when the plasma viral load in patients receiving ART is fully suppressed. In addition to data reported by Cohen et al. (Aug. 11 issue),¹ a 2009 meta-analysis² showed no transmissions in 291 person-years, and the Partners in Prevention Study (ClinicalTrials.gov number, NCT00194519)³ showed one transmission in 273 person-years, but some couples used condoms. Accounting for the proportions of couples having sex without the use of condoms (approximately 4%,¹ 75%,² and 4%³ in these three studies, respectively), only approximately 292 person-years of sex without the use of condoms with viral-load suppression have been observed over all studies combined. Even with no transmissions, these findings are associated with an upper 95% confidence limit

for the transmission rate of 1.3 per 100 person-years. We think this is too high a rate on which to base a public health prevention policy. Further, there remain no data on men who have sex with men, among whom transmission rates for anal sex are likely to be different than rates for vaginal sex.

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THIS WEEK'S LETTERS

- 1934 Prevention of HIV-1 Infection with Antiretroviral Therapy
- 1936 Tissue Plasminogen Activator and DNase in Empyema
- 1937 Chimeric Antigen Receptor–Modified T Cells in CLL
- 1939 Malpractice Risk According to Physician Specialty
- 1940 HRAS Mutation Mosaicism Causing Urothelial Cancer and Epidermal Nevus
- 1942 Nitric Oxide during Altitude Acclimatization

TO THE EDITOR: Cohen et al. compared the effects of early and delayed therapy for HIV-1–infected subjects among serodiscordant couples and found that the first regimen more significantly reduced the rates of sexual transmission and the incidence of clinical events of HIV-1. However, a comprehensive survey should be performed to assess the changes in sexual behavior among the subjects in response to ART. During the study, although interviews regarding sexual behavior were conducted at each visit, the changes in sexual behavior before and after ART were not compared. Reynolds et al.¹ found that HIV-1 transmission was reduced among HIV-1–discor-

dant couples after initiation of ART because of the reduced HIV-1 viral load and the increased consistency of condom use. Nonetheless, the data indicate that ART increases risk-taking sexual behavior.² Furthermore, the high prevalence of HIV-1 drug resistance in persons who did not receive ART in other studies^{3,4} suggests that drug-resistance testing is necessary for the selection of the initial ART regimen and helpful in discussing the possible reasons for HIV-1 transmission among serodiscordant couples.

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THE AUTHORS REPLY: Rodger and colleagues rightly note that we do not know the benefits of ART in persons who have unprotected sex (sex without the use of condoms). We recommended condoms to all couples at every visit in the HIV Prevention Trials Network (HPTN) 052 clinical trial (NCT00074581), and subjects in the early-therapy and delayed-therapy groups of the trial reported similar condom usage, both at baseline and during follow-up. Subjects who reported 100% condom use were less likely to have an HIV-1 transmission event. However, the acquisition of sexually transmitted diseases and the frequent occurrence of pregnancy during the study indicate that self-reported condom use was misleading, or that condoms performed imperfectly. To fully understand the efficacy of ART for HIV-1 prevention in persons who have unprotected sex requires a clinical trial that excludes the use of

condoms, but such a trial would be unethical. Our article did not offer a public health recommendation; rather, we noted the considerable public health potential of ART under the conditions we used. Finally, the degree to which the results we observed in heterosexual couples can be extrapolated to men who have sex with men is simply unknown.

Tao and colleagues comment on the potential for increased risk-taking sexual behavior after the initiation of ART, citing self-reported behavior; this has been a source of intense study for many years, with variable results.¹ An increase in risky sexual behavior is unlikely to substantially alter the prevention benefit of ART.² However, the unlinked transmission of HIV-1 in partners of treated subjects in our study and other studies warrants special attention. Transmitted drug resistance has been recognized worldwide⁴ and can compromise treatment of HIV-1. In our study, all subjects were treated with effective ART regimens, and these regimens were switched in participants with virologic failure. ART can reduce HIV-1 transmission only with durable suppression of HIV-1. The durability of HIV-1 suppression and longer-term transmission risks will be studied during continuation of the HPTN 052 trial.

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Since publication of their article, the authors report no further potential conflict of interest.

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