

Abstract

Background High plasma HIV-1 RNA concentrations are associated with increased risk of HIV-1 transmission. Initiation of antiretroviral therapy (ART) reduces plasma HIV-1 concentrations, but little empiric data are available on the rate of sexual HIV-1 transmission from persons receiving ART. **Methods** 3381 African heterosexual HIV-1 serodiscordant couples were followed prospectively for up to 24 months. At enrollment, HIV-1 infected partners had CD4 counts ≥ 250 cells/mm³ and did not meet country guidelines for ART initiation; during follow-up, CD4 counts were measured every 6 months and ART initiated following national guidelines. HIV-1 uninfected partners were tested for HIV-1 every 3 months. We compared genetically-linked HIV-1 transmission rates by ART initiation. **Results** 349 (10%) HIV-1 infected partners initiated ART, at a median CD4 count of 198 cells/mm³. Only one of 103 linked HIV-1 transmissions was observed from an HIV-1 infected partner who had initiated ART corresponding to HIV-1 transmission rates of 0.37 versus 2.24 per 100 person-years for those who had initiated versus not initiated ART, respectively (adjusted incidence rate ratio 0.08, 95% confidence interval 0.002–0.57, $p=0.004$). After ART initiation, plasma HIV-1 RNA concentrations decreased significantly (from median 4.88 to <2.38 log₁₀ copies/mL, $p<0.001$) as did unprotected sex (6.2% of visits before to 3.7% of visits after ART initiation, $p=0.03$). Among those not on ART, the highest HIV-1 transmission rate (8.79 per 100 person-years) was from HIV-1 infected persons with CD4 counts <200 cells/mm³. In couples in which the HIV-1 infected partner had a CD4 ≥ 200 cells/mm³, 70% of transmissions occurred when plasma HIV-1 concentrations exceeded 50,000 copies/mL. **Conclusions** Among African heterosexual couples, ART initiation was followed by a 92% reduction in HIV-1 transmission risk, likely due to significantly reduced plasma HIV-1 levels, and was accompanied by increased self-reported condom use. The highest HIV-1 risk and greatest relative prevention benefit from ART was among couples in which the HIV-1 infected partner had CD4 counts <200 cells/mm³ or plasma HIV-1 RNA concentrations $>50,000$ copies/mL.