

ICAP Journal Club



ICAP's Journal Club is designed to inform ICAP staff and colleagues of the latest scientific literature by providing a succinct summary and critical analysis of important studies, and by discussing the implications of the research on clinical work.

Article

Rodger AJ, Cambiano V, Bruun T, et al for the PARTNER Study Group. **Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study.** *Lancet*. Published online May 2, 2019. DOI: [https://doi.org/10.1016/S0140-6736\(19\)30418-0](https://doi.org/10.1016/S0140-6736(19)30418-0)

Study Summary

The PARTNER study was a prospective observational study that evaluated the risk of HIV transmission through condomless anal sex among serodiscordant men who have sex with men (MSM) couples when the HIV-positive partner was taking virally suppressive antiretroviral therapy (ART).

Study Setting

- Seventy-five clinical sites in 14 European countries.

Methods

- Phase 1 of the PARTNER study (PARTNER 1) enrolled serodiscordant heterosexual and MSM couples (2010–2014), whereas phase 2 of the study (PARTNER 2) only enrolled serodiscordant MSM couples (2014–2017). This article reports on results from MSM couples enrolled in both phases of the study.
- Serodiscordant male couples were eligible to participate if both partners were aged ≥ 18 years, reported having penetrative sex with each other without condoms in the prior month, expected to have sex again in the coming months, and if the HIV-positive partner was on ART and expected to remain on ART.
- Couples were followed until the end of the study period or until the partnership ended, the couple moved away, or either partner withdrew consent.
- Data were collected at baseline and every four to six months through self-completed questionnaires on sociodemographic characteristics, self-reported ART adherence, frequency and type of sexual activity between the partners, symptoms and diagnoses of other sexually transmitted infections (STIs), use of pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP), and injection drug use. HIV-negative partners were also asked about condomless sex with other partners and the HIV status of other partners if known.
- Information on the HIV-positive partners' ART regimen, CD4 cell count, and current and recent plasma viral load were recorded at baseline and each study visit.
- The HIV-negative partners were asked to test for HIV every six to twelve months with a combined antigen-antibody test.

- If an HIV-negative partner became HIV-positive, HIV-1 *pol* and *env* sequences were obtained from the seroconverted partner's plasma HIV-1 RNA and from the HIV-positive partner's peripheral blood mononuclear cells.
- The primary analysis was an estimation of the incidence rate of HIV transmission through condomless anal sex, calculated as the number of phylogenetically linked HIV infections during eligible couple-years of follow-up divided by eligible couple-years of follow-up.
- Couple-years of follow-up were eligible for inclusion in the analysis if couples had condomless sex during the period, PEP or PrEP was not reported by the HIV-negative partner, and the most recent viral load of the HIV-positive partner was <200 copies/milliliter and was measured within the past 12 months.
- Two-sided 95% confidence intervals (CIs) for the incidence rate of transmission were calculated to provide an estimate of the upper limit of transmission risk.

Study Population and Follow-up

- From September 2010 to July 2017, 972 MSM couples were recruited.
- Follow-up ended on April 30, 2018, at which point a total of 2,072 couple-years of follow-up were accrued, with an estimated dropout rate of 25 per 100 couple-years of follow-up.
- The most common reasons for dropping out of the study were the couple broke up (43%), consent was withdrawn (11%) and one or both partners moved away (7%). In 34% of the couples the reason for dropout was unavailable.
- A total of 1,593 couple-years, contributed by 782 couples, were eligible for inclusion in the analysis. The most common reasons for exclusion were no condomless sex reported (32% of couple-years), use of PEP or PrEP (24%), missing data on condomless sex (19%) and HIV viral load data were unavailable (18%).
- Median eligible years of follow-up per couple was 2.0 years (interquartile range [IQR] 1.1–3.5).
- The median age of the HIV-positive and HIV-negative partners at baseline was 40 years (IQR 33–46) and 38 years (IQR 31–45), respectively.
- The majority of participants were white (88% of HIV-positive partners, 89% of HIV-negative partners), and reported a college or university level of education (56% of HIV-positive partners, 58% of HIV-negative partners).
- At baseline, HIV-positive partners had been on ART for a median of 4.3 years (IQR 1.8–9.3) and 99% had a viral load <200 copies/milliliter.
- For 47% of eligible couple-years of follow-up, the HIV-positive partners were on non-nucleoside reverse transcriptase inhibitor-based regimens, for 25% they were on protease inhibitor-based regimens, and for 26% they were taking integrase inhibitors.

Primary Outcome

- Couples reported having condomless anal sex approximately 76,088 times during eligible couple-years of follow-up.
- Couples reported having condomless sex a median of 43 times per year (IQR 19–75).
- Fifteen of the initially HIV-negative partners became HIV-positive during eligible follow-up, but there were no within-couple phylogenetically linked transmissions.

- The estimated rate of transmission through condomless anal sex when the positive partner on ART had a viral load <200 copies/milliliter was zero, with an upper 95% CI limit of 0.23 per 100 couple-years of follow-up. This is equivalent to one transmission per 435 years of condomless sex.
- There were fewer eligible couple-years of follow-up during periods when either partner reported a STI, but no linked transmissions were reported. The upper 95% CI limit of the transmission estimate for periods when the HIV-negative partner had a STI was 3.17 per 100 couple-years of follow-up.

Critical Analysis

This large prospective observational study demonstrated that the risk of HIV transmission between serodiscordant MSM couples through condomless anal sex is effectively zero when the HIV-positive partner has a viral load value of <200 copies/milliliter.

The following points should be considered when interpreting the study findings:

- The median age of HIV-negative partners was 38 years, whereas the majority of HIV transmissions occur before the age of 25. Therefore, this study population might not represent those most at risk for HIV infection.
- Despite defining viral suppression as viral load <200 copies/milliliter, 96% of the eligible couple-years of follow-up were during a time when the HIV-positive partner had a most recent viral load of <50 copies/milliliter. Therefore, the evidence is not as strong for viral load values between 50 and 199 copies/milliliter.
- Only eight couple-years of follow-up of condomless sex were reported when the HIV-positive partner had been on ART for six months or less. Therefore, evidence is limited about transmission risk during this period.
- Sexual relationships outside of the primary partnership were common, with 37% of HIV-negative partners reporting condomless sex with other partners during follow-up, and 15 incident HIV infections acquired outside of the partnership were observed. Thus, additional HIV prevention interventions, such as pre-exposure prophylaxis (PrEP), may be warranted in this population.

Implications

This large observational study of serodiscordant MSM couples in Europe demonstrated that the risk of HIV transmission through condomless anal sex is effectively zero when the HIV-positive partner is virally suppressed. This contributes to the growing body of evidence that people living with HIV who achieve viral suppression are unable to transmit HIV to their sexual partners, in both heterosexual and MSM relationships. This study provides further support for the message of U=U (undetectable equals untransmittable), which can be used to promote the benefits of early HIV testing, early ART initiation, and ART adherence.

This article synopsis was written by Cassia Wells. Share your thoughts on this article or suggest an article for Journal Club by emailing her at caw2208@columbia.edu.