Key Points

- The Opposites Attract Study was an observational cohort study of male homosexual serodiscordant couples conducted in Australia, Brazil and Thailand.

- The study has released its final results on whether HIV treatments reduce the risk of the HIV-positive partner in homosexual male serodiscordant couples passing on HIV to the negative partner.

- The results found that there were no “linked” HIV transmissions within these couples. That is, no HIV-negative partner contracted HIV from his HIV-positive study partner, despite nearly 17 thousand reported acts of condomless anal intercourse within couples.

- There were over 12 thousand reported acts of anal intercourse that were protected only by undetectable viral load (that is, condomless anal intercourse when the HIV-negative partner was not taking PrEP), and there were still no linked transmissions. This indicates that condomless sex with an undetectable viral load is safe.
Previous research in “Treatment as Prevention”

Previous research in heterosexual serodiscordant couples has shown that early antiretroviral treatment of the HIV-positive partner was associated with a 96% reduction in the risk of transmitting HIV to their HIV-negative partner. This idea of reducing the risk of HIV transmission through HIV-positive people being on treatments is widely known as “treatment as prevention” or “TasP”. In this study there were no “linked” transmissions in couples where the HIV-positive partner had undetectable viral load, and the only linked transmissions were in very early treatment before reaching undetectable viral load, or after treatment stopped being fully effective.

However, there is much less evidence for homosexual couples. Opposites Attract is one of only two studies ever to be conducted that explores this research question in gay men. The other study is called PARTNER, which is currently being conducted in Europe and the UK. In July 2016, the PARTNER Study reported its Phase 1 results, showing that there were no HIV transmissions within serodiscordant couples where the HIV-positive partner had undetectable viral load and who were having sex without condoms with each other. However, statistical uncertainty meant that for anal sex without condoms among gay male couples, the HIV transmission risk could be between 0% and 0.89% per year, or between 0% and 2.70% per year for HIV-negative men who take the receptive role in anal sex. The PARTNER Study is currently running Phase 2 of the study, which involves a larger number of gay couples only. The final results will be reported in the next couple of years. Depending on what happens with transmission, this could narrow the range of statistical uncertainty further.

What was the Opposites Attract Study?

Opposites Attract was an observational cohort study of homosexual male serodiscordant couples, that is, where one partner in the couple is HIV-positive and the other partner is HIV-negative.

The key research question of the study was: To what extent do HIV treatments in the HIV-positive partner reduce the risk of HIV transmission to the HIV-negative partner in these couples?

Opposites Attract enrolled gay male serodiscordant couples in three Australian cities (Sydney, Melbourne, Brisbane), and in Rio de Janeiro, Brazil, and Bangkok, Thailand. The couples were followed-up over time, visiting their study clinic at least two times per year. All couples were provided with HIV transmission education prior to enrolment. The HIV-positive partner did not need to be taking HIV treatments for the couple to participate. While the couples needed to be having regular anal sex with each other to enrol, there were no requirements about condom use: Some couples always used them, while others sometimes or never used them. There were also no restrictions on whether or not the HIV-negative partner could use pre-exposure prophylaxis (PrEP). So, this meant that the study was a good representation of what HIV prevention in sexually-active male serodiscordant couples looks like in the real world.

At each visit, the HIV-positive partner had his viral load tested, and the HIV-negative partner was tested for HIV antibodies. Both partners were also tested for sexually transmissible infections, and they both completed a questionnaire.

The study began recruiting in early 2012 in Australia, and in May 2014 in Brazil and Thailand. In total, the study enrolled 358 couples, with 343 of these attending at least one follow-up visit. Follow-up of couples ended on 31 December 2016.
What did the Opposites Attract Study find?

The study recruited a total of 358 gay male serodiscordant couples: 157 of these couples were from Australia, 96 were from Rio de Janeiro, and 105 were from Bangkok. Of the total 358 couples enrolled, the final analysis focused only on the 343 couples who had attended at least one follow-up visit by the end of the study. These couples were in the study for an average time of just over one-and-a-half years. A total of 591 couple-years of follow-up were included in the analysis. “Couple-years of follow-up” means the cumulative total amount of time that all the couples were in the study.

There were no “linked” HIV transmissions in these couples. A “linked” transmission is where genetic analysis of the virus shows that the HIV came from the HIV-positive partner in the couple to his HIV-negative partner. So, no HIV-negative man in the study contracted HIV from his HIV-positive study partner.

Because we found no “linked” transmissions, the focus of the analysis becomes about how confident we are that the zero rate of transmission we observed in the study is actually “true”. Even though the transmission rate in Opposites Attract was zero, there is a statistical chance that the “true” transmission rate could be higher.

We found that for anal sex without a condom when the HIV-positive partner had undetectable viral load (defined as less than 200 copies per mL), the “true” risk of transmission could be between zero and 1.56% per year, with a very small chance that the per-year risk could be higher. The couples in Opposites Attract reported over 12 thousand acts of condomless anal sex when the HIV-positive partner had undetectable viral load and the HIV-negative partner was not on PrEP.

This is an exciting result and provides further evidence to add to previous studies that HIV transmission when someone’s viral load is undetectable is extremely unlikely, if not impossible.

There were 3 new infections in initially HIV-negative partners during follow-up, all from outside sexual partners, which equated to an incidence rate of 0.5% per year. This is quite a low incidence rate. Even though the incidence rate was fairly low, this means that HIV-negative partners who are having condomless sex with outside partners should consider going on PrEP.

However, the most important point is that we found an HIV transmission rate of zero within the Opposites Attract Study couples.

Is it safe to have anal sex without condoms if the HIV-positive partner has undetectable viral load?

In homosexual and heterosexual couples, there has never been a recorded case of HIV transmission from an HIV-positive person to their HIV-negative sexual partner when the HIV-positive partner had undetectable viral load.

Between Opposites Attract and the PARTNER Study, there have now been a combined 34,911 acts of condomless anal sex reported in gay couples when the HIV-positive partner had undetectable viral load and the HIV-negative partner was not taking PrEP. We can now be confident that condomless sex with undetectable viral load is a form of safe sex.

However, it is important to remember that when the HIV-positive partner is in the first six months of starting HIV treatment, it can take a little bit of time for the viral load to become undetectable. There have been some cases overseas in heterosexuals where transmission happened when the HIV-positive partner was on treatment but was not yet undetectable. So, during the first six months of treatment and until the viral load is undetectable, it is best to use condoms or for the HIV-negative partner to take PrEP. It is also important to monitor and treat sexually transmitted infections.
What else did the analysis find out?

Some other interesting results were:

- 73.5% of HIV-positive partners took HIV treatments the entire time they were in the study, while 24.8% started treatment during follow-up, and only 1.8% did not take any HIV treatments.

- 75.2% of HIV-positive partners consistently had undetectable viral load throughout the whole study period.

- By the end of the study, 32.1% of HIV-negative partners had taken daily PrEP at some point during follow-up.

- 73.8% of couples had condomless anal sex with each other during the study.

- 63.0% of the HIV-negative partners reported having sex with a partner outside the relationship during the study, and 38.5% reported any condomless sex with outside partners.

What happens now?

Opposites Attract has contributed important data showing that HIV treatments and undetectable viral load reduce the risk of HIV transmission in gay male serodiscordant couples.

The study has now ended, and the final result will be published in an academic journal. Additionally, the PARTNER Study will report on its final results from Phase 2 (following only the gay male couples) in the next couple of years.

Along with this main result, we will also be analysing and publishing other findings from the study over the next couple of years.

These will include:

- The combination of methods that couples used to prevent HIV transmission;

- Relationship agreements about monogamy and non-monogamy;

- Communication and agreements about viral load within couples;

- Whether viral load in blood is the same as viral load in semen; and

- Attitudes about TasP and PrEP.

These findings will be interesting and important, as there is currently little information published about gay male serodiscordant couples generally.
Who conducted the Opposites Attract Study?

The study was coordinated by the Kirby Institute at the University of New South Wales, in Sydney, Australia. In Australia, the study was conducted in 13 clinics, which were a mixture of private general practices, sexual health centres, and HIV specialist clinics. In Bangkok, it was conducted at the Thai Red Cross AIDS Research Centre, and in Rio de Janeiro, at the Evandro Chagas Institute of Clinical Research.

The study was overseen by a steering committee including researchers, clinicians and staff from clinical sites, and community partner organisations, and received ethical approval from five different ethics committees.

How was the Opposites Attract Study funded?

The study received funding from the Australian National Health and Medical Research Council (NHMRC), the Foundation for AIDS Research (amfAR), ViiV Healthcare, and Gilead Sciences.

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This study has been approved by the St Vincent's Hospital (ref. no. HREC/11/SVH/170), Alfred Hospital (proj. no. 80/12), Prince Charles Hospital (ref. no. HREC/13/QPCH/70), Instituto de Pesquisa Clinica Evandro Chagas (ref. no. 490.884) and Chulalongkorn University (study code TRC029) human research ethics committees.