

OHTN EVIDENCE REVIEW:

HIV sexual transmission risk by people with suppressed HIV viral load

Key message

The best available research evidence shows that the risk of sexual HIV transmission from a person living with HIV who is on antiretroviral therapy (ART) and has achieved a suppressed HIV viral load in their blood for at least six months is extremely low (negligible).

Background

A recent consensus statement developed by the Prevention Access Campaign in the United States¹ is prompting public re-consideration of the question of HIV and infectiousness. The “undetectable equals untransmittable” (U=U) statement says that “people living with HIV on ART with an undetectable viral load in their blood have a negligible risk of sexual transmission of HIV. Depending on the drugs employed it may take as long as six months for the viral load to become undetectable. Continued and reliable HIV suppression requires selection of appropriate agents and excellent adherence to treatment. HIV viral suppression should be monitored to assure both personal health and public health benefits”¹.

This statement is not the first discussion of whether or not the full suppression of viral load by antiretroviral therapy completely eliminates the risk of sexual transmission of HIV. In a widely publicized 2008 article known as the Swiss Statement, the Swiss National AIDS Commission stated that a person living with HIV who has a suppressed viral load “cannot pass on the virus through sexual contact” if three conditions are met: 1) the HIV-positive individual is fully complying with antiretroviral therapy and is being monitored by a physician; 2) their viral load has been undetectable for at least six months;

and 3) the HIV-positive individual does not have any other sexually transmitted infections².

Studies of HIV transmission risk within serodiscordant couples provide important information about the risk of sexual transmission of HIV. The most comprehensive systematic review to evaluate rates of sexual HIV transmission between heterosexual serodiscordant couples when the HIV-positive partner was fully suppressed in blood was published in 2013³. The authors suggested that there was a “minimal risk” of sexual HIV transmission among heterosexual serodiscordant couples when the HIV-positive partner was fully virally suppressed on antiretroviral therapy³. Several additional cohort studies have stated these conclusions even more strongly, including the PARTNER study (Partners of People on Antiretroviral Therapy—A New Evaluation of the Risks), which included both heterosexual and same sex HIV-serodiscordant couples where the HIV-positive partner is virally suppressed⁴. The PARTNER study’s estimate of the overall transmission rate was “zero.”

This evidence brief examines the scientific literature regarding the risk of sexual transmission of HIV by a person with a suppressed HIV viral load[†].

[†] Studies referenced use the terms “suppressed,” “undetectable” and “below the limit of detection” interchangeably to describe the impact of antiretroviral therapy on viral load. For the purpose of this document, we are using the term “suppressed.”

Methods

We searched Medline (including In-Process & Other Non-Indexed Citations) using a combination of text term HIV and [text terms (ART or cART or ARV* or antiretroviral* or anti-retroviral* or anti-viral* or antiviral* or treatment as prevention) or MeSH terms (Anti-HIV Agents or Anti-Retroviral Agents or Antiretroviral Therapy, Highly Active)] and text terms [(sex* adj partner*) or couples or serodiscord* or sero-discord* or discord* or infectiousness or infectivity or prevent* transmission* or transmission rate* or prevent* HIV transmission* or probability of HIV transmission or prevent* HIV-1 transmission* or HIV diagnoses or HIV diagnosis]. Reference lists of identified literature reviews and systematic reviews were also searched. All searches were conducted on February 9, 2017 and results limited to English articles published from 2007 to present.

The search yielded 3,204 references from which 12 studies were included. Sample sizes of primary studies ranged from 81 to 1,763 couples.

Only primary studies quantifying sexual HIV transmission risk reduction through antiretroviral therapy in virologically suppressed individuals have been included.

No restrictions were made based on study jurisdictions, but systematic reviews, literature reviews, meta-analyses, modelling studies, commentaries, editorials, and studies focusing on viral load in the genital tract (rather than in blood plasma) were excluded.

Main findings

The majority of evidence on the impact of suppressed viral load on HIV transmission comes from cohort studies (n=9). Other study designs include: one randomized controlled trial^{5,6}, one case study⁷, and one cross sectional study⁸.

The vast majority of studies (9 of 12) examining the impact of undetectable and/or suppressed plasma HIV viral load on sexual transmission were conducted among heterosexual couples. Three studies included men who have sex with men – one case study⁷, one cohort study with 38% same sex couples⁴, and one ongoing cohort study exclusively focusing on gay men⁹.

Studies with no linked[‡] HIV sexual transmission after six months of viral suppression

HIV Prevention Trials Network trial 052

The 2011 analysis of the HIV Prevention Trials Network trial 052 (known as HPTN 052) is the only randomized controlled trial to assess antiretroviral therapy and HIV transmission risk among serodiscordant couples (97% heterosexual)⁵. HPTN 052 enrolled 1,763 serodiscordant couples between 2005 and 2010 at 13 study sites in nine countries (Botswana, Kenya, Malawi, South Africa, Zimbabwe, Brazil, India, Thailand, US).

The final study analysis, published in 2016, included more than five years of follow-up assessing the durability of antiretroviral therapy for the prevention of HIV transmission⁶. In total, among 1,763 serodiscordant couples enrolled in HPTN 052, only eight linked partner HIV infections were diagnosed after the participant had started antiretroviral therapy^{6,10}. In four cases, the partner was diagnosed with HIV infection less than 90 days after the participant started antiretroviral therapy. In these cases, further analysis suggested that all four infections probably occurred before the participant was virally suppressed^{6,11}. In the other four cases, partner infection occurred after antiretroviral therapy failed^{6,10,11}. Thus none of the linked infections were observed when the HIV-infection was stably suppressed⁶.

The PARTNER study

The PARTNER study included both heterosexual and same sex HIV-serodiscordant couples where the HIV-positive partner was virally suppressed⁴.

Conducted at 75 clinical sites in 14 European countries starting in 2010, this study analyzed 888 serodiscordant couples who reported over 58,000 condomless sex acts during follow-up. The study found no HIV transmission events.

Unlike HPTN 052 (in which reported condom use was around 95%)^{5,6}, all couples in this study practiced condomless sex and over a third of participants were men who have sex with men (38%, n=340). Over 1,238 couple-years of follow-up (median follow-up 1.3 years), 11 HIV-negative partners became HIV-positive, but none of these transmissions were linked. More than 100 transmissions would have been expected in the

‡ Genetic linkage of partner infections is assessed by phylogenetic analysis. No linkage indicates that the HIV-positive partner was not the likely source of the infection. A linked infection indicates that the HIV-positive partner was most likely the source of the infection.

men who have sex with men group if the HIV-positive partner had not been taking antiretroviral therapy^{4,12}.

Opposites Attract

Opposites Attract – an ongoing study of 234 serodiscordant couples in three countries (Australia, Thailand and Brazil) – began in 2012 and is the only study that has been focused entirely on men who have sex with men⁹.

In total, 88 couples reported 5,905 acts of condomless anal intercourse. As of December 2014, no linked HIV transmissions were reported⁹.

Other examples

Five additional studies found similar results as above – no linked HIV sexual transmission after six months of viral suppression:

1. A study of 93 heterosexual HIV serodiscordant couples from Brazil (between 2000 and 2006) demonstrated no transmissions among the 41 participants who were taking antiretroviral therapy (median: 22 months) and were virally suppressed¹³.
2. A 2011 study based in Uganda followed 28 heterosexual couples where the HIV-positive partner was virally suppressed¹⁴.
3. A 2013 French study examined 81 heterosexual women who had suppressed viral loads for over six months⁸ and routinely had unprotected sex (on average 13 times a month, over a 46-month period). No male partners acquired HIV infection even though 37% of the women participants had detectable HIV in the cervicovaginal fluid.
4. A 2015 Spanish prospective cohort study examined heterosexual transmission of HIV among 202 heterosexual couples (93% of virally suppressed) between 1989 and 2010¹⁵⁻¹⁷. No HIV infections were detected among their sexual partners even though 58% of couples reported unprotected sexual acts¹⁷.
5. A 2015 Chinese study followed 753 serodiscordant heterosexual couples for five years (2007–2012): 596 HIV-positive individuals received antiretroviral therapy¹⁸. Among participants who were virally suppressed, no new HIV infections were observed. Five new infections were observed among participants who were not virally suppressed¹⁸.

Studies with possible phylogenically-linked HIV sexual transmissions after viral suppression is achieved.

1. The first report documented a 2004 transmission linked to the primary partner in a serodiscordant gay couple in Germany despite the HIV-positive partner having achieved viral suppression⁷. However, documentation of the HIV-negative partner's last negative test result was lacking and therefore the judgment was based on the HIV-negative partner's recollection of an anonymous HIV test from five years earlier⁷. As a result, the HIV transmission event could have occurred before or shortly after antiretroviral therapy was initiated by the HIV-positive partner^{19,20}.
2. A 2011 study from Uganda entitled Highly Active Antiretroviral Therapy as Prevention (HAARP) followed 586 heterosexual couples, of which the HIV-positive partner was virally suppressed, between 2009 and 2011²¹. All couples received antiretroviral therapy (median duration at enrollment 2.3 years, median at follow-up: 1.5 years). In total, only two transmissions were genetically linked (with partners having been on antiretroviral therapy for nine and 65 months, respectively). The study authors did note that viral load measurements could have been taken up to six months prior to the date of the HIV-negative partners' seroconversion and therefore may have missed episodes of high viremia which may have caused the transmission events to occur²¹.
3. Another 2011 Ugandan study estimated HIV transmission from HIV-infected adults after six months of antiretroviral therapy^{22,23}. One linked seroconversion occurred among 62 serodiscordant partners²³. It is not clear if the HIV-positive was in fact virologically suppressed at the time of seroconversion.
4. A 2013 study from rural China followed 471 monogamous heterosexual serodiscordant couples over a two-year period (2009–2011). One linked transmission occurred when the HIV-positive partner was virally suppressed²⁴. The authors note this could be the result of the HIV-positive person not being virologically suppressed for at least six months.

Suggested citation

Globerman J, Gogolishvili D, Rourke SB. Evidence Review: HIV sexual transmission risk by people with suppressed HIV viral load. Ontario HIV Treatment Network: Toronto, ON; May 2017.

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