



Q and A - the PARTNER Study: new results from PARTNER 2

1. Study results

What is the PARTNER Study?

The PARTNER study is an international two-phase study that looked at whether HIV transmission occurs when an HIV positive person is on effective treatment (ART). This was defined as having a viral load less than 200 copies/mL.

PARTNER1 ran from 2010 to 2014 and PARTNER2 from 2014 to 2018. The study recruited and followed sero-different couples where one partner was HIV positive and on ART and the other partner was HIV negative. To enter the study, couples had to be not always using condoms. Many couples were already not using condoms on a regular basis and some couples had not been using condoms for many years.

The study was designed to provide estimates of the risk of HIV transmission risk from sex without condoms for both heterosexual and gay couples when the positive partner was on effective ART.

To be eligible for the study, the HIV positive person needed to be on HIV treatment (ART) at the time of enrolment.

The results from the PARTNER1 study (2010-2014)

From 2010 until 2014, the first phase of PARTNER recruited over 1100 couples from 14 different European countries. Two-thirds of the couples were heterosexual and one third were gay.

Results from PARTNER1 included 888 couples (548 heterosexual and 340 gay). During follow-up, couples had sex without condoms on average 37 times per year (median). Overall, gay couples reporting having sex without condoms approximately 22,000 times and heterosexuals approximately 36,000 times.

During PARTNER1, none of the HIV negative partners became positive from having sex with the HIV positive partner in their couple. This gave a rate of within-couple HIV transmission of zero. However as most of the couples were heterosexual the conclusion was less certain for sex between men than for heterosexual sex.

At the end of PARTNER1, the upper 95% confidence interval for transmission risk in heterosexual couples was 0.46 per 100 couple years of follow (CYFU), and for MSM couples it was 0.84 per 100 CYFU.



Why PARTNER2?

PARTNER therefore continued into a second phase, to provide the same level of evidence for gay couples than as for heterosexual sex.

Many of the gay couples from PARTNER1 continued in PARTNER2 and new gay couples were also recruited.

Phase 2 of the PARTNER study (2014-2018) continued to enrol and follow up gay couples only.

The results from the PARTNER2 study

Overall, PARTNER2 enrolled 972 gay couples (480 of whom were already followed in PARTNER 1 and 492 were newly enrolled). Of these, 783 couples provided 1596 eligible¹ couples years of follow up (CYFU), where the positive partner was on effective ART.

Couples had condomless sex a median of 43 times per year. During eligible follow-up, couples had sex 76,991 times without condoms.

As with PARTNER1, some of the HIV negative partners did become HIV positive but none of these cases was linked to their HIV positive partner so there were no cases of within couple HIV transmission. The rate of within-couple HIV transmission risk was zero.

Overall 15 HIV negative men became HIV positive between 2010-2018 (some during PARTNER 1). In all cases their HIV positive partner had a very different virus (i.e., phylogenetically unrelated).

The larger number of couples meant that the upper 95% confidence limit for gay men is now 0.23/100 CYFU.

What do these results mean?

PARTNER 2 now provides a similar level of confidence in the evidence for gay couples as for heterosexual couples in PARTNER 1 that risk of sexual transmission from a person with an undetectable viral load is effectively zero.

¹ Eligible couples year of follow up (CYFU) is the sum of time periods during which couples had condomless sex, the HIV positive partner had an undetectable viral load, and the HIV negative partner did not use PEP or PrEP.



2. Glossary

What does eligible couple years of follow up (CYFU) mean?

Eligible couples year of follow up (CYFU) is the sum of time periods during which couples had condomless sex, the HIV positive partner had an undetectable viral load (measured maximum 1 year before), and the HIV negative partner did not use PEP or PrEP.

Why does the study refer to confidence intervals? What do these mean in PARTNER2?

When estimating risk, scientists must allow for the fact that results may occur by chance due to the limited size of the study. This involves calculating an upper and a lower limit, containing possible values called the confidence interval (CI). In the study we calculated the point estimate of the transmission rate and the 95% CI. The 95% CI around our estimate is the range within which we are 95% certain that the true transmission rate lies, given the possible effects of chance.

In general, the larger the study, the more confident we can be that the results are genuine and not due to chance. In this type of study, the size of the study is measured by the total number of years people are followed for, rather than just the number of participants.

The results suggest that there is a small possibility that the absolute upper rate of transmission is as low as 0.23/100 CYFU (i.e. one infection per 433 years of condomless sex), which means we can conclude that the risk is essentially zero.

The estimated rate for condomless anal sex with ejaculation is also zero. This upper-limit for condomless anal sex with ejaculation was 0.57/100 CYFU. In other words, even if we have under-estimated the (zero) risk of transmission due to chance, in the worst-case scenario it would still take more than 177 years of anal sex with ejaculation for one transmission to occur in a sexual partnership.

What is a linked transmission?

A linked transmission is when a negative partner's new HIV infection is with a strain of the HIV virus that is highly related to that found in their HIV positive partner.

To investigate whether linked transmissions occurred in PARTNER, investigators at the University of Liverpool used a specialised method called phylogenetic analysis. This method examines whether the HIV viruses found in the blood of the two partners are closely related. If the negative partner became infected but the virus was genetically different from that found in the



positive partner, this is taken as an indication that the new infection was from a different source than the positive partner.

This is essential when looking at HIV transmission risk because many previous studies reporting transmission between sero-different couples found that 25%-50% of those cases of new infection were from people outside the main relationship. The genetic analysis is thus an essential part of the PARTNER study.

So far, the study has been able to show that although some HIV negative people have become HIV positive during the study period, none of the new infections was with a HIV virus similar to that found in their positive partner.

In PARTNER we have undertaken both standard and ultrasensitive testing to provide the phylogenetic evidence. It was thus concluded that these new infections were not from their respective partner in the PARTNER study.

How does the PARTNER study define 'undetectable viral load'?

In the PARTNER study, an undetectable viral load was defined as being less than 200 copies/mL.

Different hospitals use viral load test that have different low-level cut-off values. For example, this can be at 20 or 50 or 200 copies/mL depending on the study site.

How long does viral load remain undetectable after a viral load test?

Viral load results only give information about the viral load at the time the blood was taken. So long as someone continues to take treatment as prescribed, viral load is very likely to remain undetectable.

In most centres across Europe, a small percentage of patients who are on stable treatment have a viral load rebound above the suppressed level each year. This is largely thought to be related to difficulties with adherence. Viral load rebound in the context of continued good adherence to ART is extremely unlikely to occur. The PARTNER study used <200 copies as the cut off for virological suppression, which encompasses most minor VL blips seen in patients on ART.

3. Study design

An observational study

PARTNER study participants did not undergo any special medical treatment or intervention while in the study; for this reason, it is called an "observational" study.



Information about sexual behaviour was collected via questionnaires completed by study participants every six to 12 months and the HIV positive partner had HIV viral load testing and the negative partner HIV testing.

Where did the PARTNER2 study take place?

The PARTNER2 study has enrolled participants in 14 European countries: Austria, Belgium, Denmark, Finland, France, Germany, Ireland, Italy, Portugal, Spain, Sweden, Switzerland, The Netherlands, and UK.

In total, 55 clinics and hospitals participated in the PARTNER2 study.

How was the PARTNER study funded?

The second phase of PARTNER was funded by the National Institute of Health Research UK, ViiV Healthcare, Gilead Sciences, Augustinus Fonden and A.P. Møller Fonden and is sponsored by CHIP, Rigshospitalet. Additionally, funding for participation of the Swiss centres has been provided by the Swiss Office of Public Health. The study is coordinated cooperatively between CHIP, Rigshospitalet, University of Copenhagen, and University College London.

Who was running this study?

The PARTNER study was a collaboration involving independent researchers and scientists from Europe. The study Steering Committee included doctors, researchers and community advocates.

The PARTNER study Steering Committee:

Prof Andrew Phillips, University College London (UCL)

Prof Jens Lundgren, University of Copenhagen and Rigshospitalet,

Dr Alison Rodger, UCL

Tina Bruun, University of Copenhagen and Rigshospitalet,

Simon Collins, HIV i-Base

Prof. Pietro Vernazza, Kantonsspital St. Gallen

Dr. Vicente Estrada

Dr. Olaf Degen

Giulio Maria Corbelli, EATG

Dorthe Raben, University of Copenhagen and Rigshospitalet,

Dr Valentina Cambiano, UCL

Prof Anna Maria Geretti, University of Liverpool

Dr Apostolos Beloukas, University of Liverpool

Press contact:

Alison Rodger: Alison.rodger@ucl.ac.uk [+44 (0) 203 108 8515]

Jens Lundgren: jens.lundgren@regionh.dk [+45 40879303]