

The PARTNER Study – stage 2 (2014-2017):

Estimating the risk of HIV transmission irrespective of sexual practice

Stage 2 of the PARTNER Study aims to define the risk of HIV transmission in gay sero-discordant couples who do not use condoms. The study comprises 75 clinics in 14 European countries, and is projected to run until March 2017. Approximately 950 gay couples will be enrolled.

A critical yet still unresolved public health question related to HIV is, whether HIV positive persons on antiretroviral treatment (ART) are still able to transmit HIV to their HIV seronegative sexual partner. The HPTN 052 study gave indications towards the answer to this, but without conclusive evidence for sexual partnerships having condom-less sex, due to the high reported (but unknown actual) levels of condom use. Additionally, HPTN 052 provided essentially no information on risk through anal intercourse irrespective of use of condoms. The PARTNER study is the only ongoing study worldwide able to comprehensively address the risk of HIV transmission in situations of sexual intercourse without condoms in general, and in particular in situations where a couple have anal intercourse.

In men-having-sex-with-men (MSM), receptive and, to a lesser extent, insertive condom-less anal intercourse is the major risk factor for HIV acquisition. There have been studies documenting per act estimates of HIV transmissibility for anal intercourse, but to date no data are available from observational cohorts or RCTs to determine HIV transmission rates for anal sex in MSM when the HIV positive partner is on ART. As the risk of HIV transmission in the absence of ART is greater for anal sex than for vaginal sex, the degree to which the HPTN 052 results in heterosexual couples can be extrapolated to MSM or to heterosexuals having anal sex is unknown. Only 37 couples (2%) enrolled in HPTN 052 were MSM and 96% of the participants reported regular condom use. Conversely, in the PARTNER study, to be eligible the participating couples have to report condom-less sex in the past month prior to enrolment into the study and only the couples continuing to report having sex without condom (despite advice to use a condom) will be included in the final risk analysis. As such, PARTNER is testing the most risky situations for potential transmission through vaginal or anal intercourse.

It is likely that an acceptable risk will be one that is at least twice an individual's life span i.e. 1 transmission per 200 years (meaning approximately four times an individual's sexually active life). In order to be able to show that the risk is very likely to be at this level or lower, 2000 person years are needed.

The PARTNER study is set out to define whether such an acceptable risk exists for sexual relationships that do not use condoms regularly or not at all. Table 2 summarizes the results of HPTN 052, the first stage of PARTNER that is funded and will continue until March 2014, and the second stage of PARTNER which remains unfunded but intends to define the risk of transmission via condom-less anal sex.



Implications from the PARTNER study for treatment as prevention in MSM

WHO, NIH and BHIVA refer to the PARTNER study as the only established study that can provide precise estimates of the rate of transmission of HIV in serodifferent MSM couples, where the positive partner is on ART. Hence, the PARTNER study aimed to be able to conclude on any difference in the magnitude of the effect of ART for HIV prevention between vaginal sex and anal sex.

More precise knowledge of transmissibility among sero-different MSM couples practicing condom-less intercourse will have major public health consequences in areas of the world where anal sex is a major route of forward transmission. Additionally, it will be important for the test and treat concept of reducing ongoing transmission to be able to provide concrete and direct evidence as part of informing MSM couples as well as heterosexual couples of the risks of infecting persons they have anal sex with.

PARTNER stage 2 can provide the necessary additional evidence required to inform potential scale up of ART for prevention in MSM, transgender women and others who have anal sex.

Support for PARTNER stage 2 will allow obtaining an estimate of the transmission rate with the same level of precision for anal intercourse as for vaginal intercourse.

Risk of transmission is likely to be highest for couples for which the positive partner is insertive and ejaculates. If PARTNER stage 2 can be completed, couple years for this are projected to grow from 282 to 726.

Comparison HPTN 052, PARTNER stage 1 and 2

Table 2: Comparison of results generated by HPTN 052, and projected for PARTNER stage 1 and 2

| | HPTN 052 | PARTNER stage 1 (by March 2014) | PARTNER stage 2 (by March 2017) |
|---|--|--|---|
| Number of serodiscordant couples | 1763 | App 1350 | App. 1780 |
| Number MSM couples | 37 | App. 500 | App .950 |
| Condom-less sex | 96% reported regular condom use 5-6% reported having unprotected sex prior to enrolment | Only couples reporting having sex without condom will be included in the final analyses. | Only couples reporting having (anal) sex without condom will be included in the final analyses. |
| PYFU overall | 1585 | 2015 | 3590 |
| PYFU eligible | 1145 ** | 1753* | 3124* |
| PYFU of condomless sex | Estimated <200 PYFU | 1753* | 3124* |



| | | | |
|---|--|--|--|
| MSM/Anal sex | 2% | 48% | 100% |
| PYFU from anal sex couples | Unknown < 50 | 879 | 2250 |
| PYFU receptive anal sex with ejaculation | Unknown | 282 | 726 |
| upper 95% confidence limit for Risk of transmission – overall | If no transmissions occur in the study: 1/54 couple years combined | If no transmissions occur in the study(**): 1/474 couple years combined | If no transmissions occur in the study (**): 1/847 couple years combined |
| upper 95% confidence limit for Risk of transmission – anal sex | If no transmissions occur in the study: 1/14 couple years anal sex | If no transmissions occur in the study (**): 1/238 couple years anal sex | If no transmissions occur in the study (**): 1/610 couple years anal sex |

* Eligibility criteria: HIV negative reporting condom-less sex; HIV+ VL<200 in the last year

** These numbers will be lower if one or more linked transmissions are observed (see table 1 above for details)

Funding the PARTNER Study

Funders of the PARTNER Study – stage 2 will have a unique opportunity to contribute to finally closing the discussion on transmission risk on ART with a definitive study on anal sex – and thereby support clarifying an essential public health problem and potential benefit of ART.