HIV transmission risk through condomless sex in gay couples with suppressive ART: The PARTNER2 Study extended results in gay men

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AIDS 2018

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Disclosure slide

No conflicts of interest

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Background

- There is clear evidence, particularly in heterosexual couples, of the dramatically reduced risk of HIV transmission from condomless sex with suppressive ART
- Zero cases of HIV transmission in gay male sero-different couples reported in recent observational studies (PARTNER1 and Opposites Attract)
- However with CYFU accumulated in PARTNER1, upper 95% confidence limit of the rate for gay men was 0.84 /100 CYFU (compared to 0.46/100 CYFU in heterosexual couples).
- The aim of PARTNER2 was to provide more precise estimates of transmission risk in gay partnerships in this context

Cohen et al. NEJM, 2016; Rodger et al. JAMA, 2016; Grulich et al. Lancet HIV, 2018

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PARTNER Study

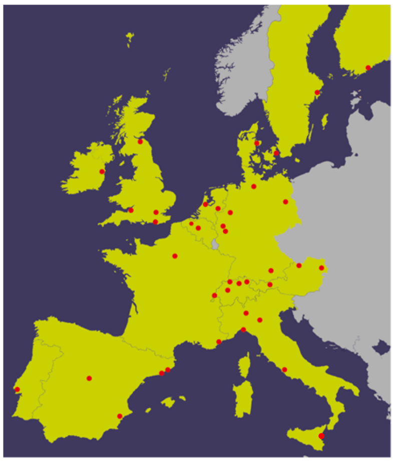
(Partners of people on ART: a New Evaluation of the Risks)

Design: observational multi-centre study of HIV serodifferent couples (MSM and HT) in which the positive partner is on ART in 75 European clinical sites:

- **Phase 1:** 2010-2014 (HT+MSM)
- **Phase 2:** 2014-2018 (MSM only)

Primary Aim

- To follow serodifferent partnerships that have penetrative sex without using condoms where the HIV-positive partner is on ART with a plasma HIV-1 RNA load <200 copies/mL to study risk of HIV transmission through anal sex in the absence of condom use



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Study Procedures

- Informed consent included explicit reference to the fact that HIV negative men knew their partner is HIV positive
- Study data collected at baseline and every 6 -12 months,
    - Confidential sexual behaviour questionnaires completed by each partner
    - HIV testing for the negative partner
    - HIV viral load measurement for the positive partner

	HIV Positive Partner	HIV Negative Partner
Questionnaire data	Demographics	Demographics
	Sexual behaviour with study partner	Sexual behaviour with study partner
	STI diagnosis	STI diagnosis
	STI symptoms	STI symptoms
	IVDU	IVDU
	ART adherence	HIV testing history Knowledge partner VL PEP/PrEP use Sexual behaviour with other partners
Clinical Data	HIV VL testing ART use STI diagnosis CD4 count	HIV testing

Study Procedures

- Eligible couple years of follow-up (CYFU) formed of periods of time between HIV tests in which:
    - Couples had condomless sex together during the time period
    - No reported PEP or PrEP use by the HIV negative partner
    - Plasma HIV-1 RNA load <200 copies/mL in HIV positive partner within last 12 months at all points in the period
    - Follow-up occurred before 30th April 2018 (censoring date)

- We report the rate of within-couple phylogenetically linked transmissions during eligible CYFU

Sequencing and Phylogenetic Analysis

- HIV-1 *pol* and *env* sequences were obtained from either plasma or PBMCs by Sanger sequencing,[1] complemented by deep sequencing by Illumina in a subset[2]
- Maximum likelihood (ML) and Bayesian Markov Chain Monte-Carlo (MCMC) inferences were determined with RAxML-HCP2 v8 and Mr Bayes v3.2.6, respectively
- Controls: i) the 10 closest GenBank sequences, ii) replicate partners' sequences, and iii) sequences from confirmed HIV-transmission pairs[3]
- Criteria for linking infections was monophyletic clustering with high statistical support e.g bootstrap value ≥0.90 (ML) or a posterior probability ≥0.95 (MCMC), and a pairwise genetic distance of ≤0.015 nucleotide substitutions per pol site[1]

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1. Rodger et al. JAMA, 2016 2. Geretti et al, JAMA, 2016. 3. Beloukas et al. Virus Res, 2012.

Eligible Couple Years of Follow Up

- Overall 972 gay couples were recruited, of which 783 couples contributed 1596 eligible CYFU
- Reasons CYFU are not eligible (n=477):
  - Reported no CL sex (32%)
  - Use of PEP/PrEP (24%)
  - VL not available (18%)
  - Missing data on whether CL sex reported (18%)
  - VL>200 copies/mL (5%)
  - No HIV test in negative partner (3%)

HIV negative partner characteristics

At study entry	
Age, median (IQR, n=759)	38 (31-45)
White ethnicity (%, n=768)	687 (89%)
Years condomless sex, median (IQR)	1.0 (0.4-2.9)
During follow up	
Years in the study, median (IQR)	1.6 (0.9-2.9)
Diagnosed with STI, %	23%
Condomless sex with other partners, %	37%
Condomless sex acts per year, median (IQR)	43 (19-74)
Estimated total number condomless sex acts	76,991

HIV positive partner characteristics

At study entry	
Age, median (IQR; n=758)	40 (33-46)
Years on ART, median (IQR)	4.0 (2.0-9.0)
Self-reported adherence >=90%, %	98%
Self report undetectable VL, %	93%
During follow-up	
Missed ART for more than 4 consecutive days, %	2%
Diagnosed with STI, %	27%

New HIV infections in negative partners

- 15 initially HIV-negative MSM partners became HIV-positive
    - 11 reported recent condomless sex with others
- Samples collected from partners in each couple a median of 0 months' apart (IQR 0.0-5.9)
- Viral sequences recovered successfully from all couples: 15/15 (100%) for *pol* and 13/15 (87%) for *env*
- All new infections phylogenetically NOT related to the initially positive partner's virus

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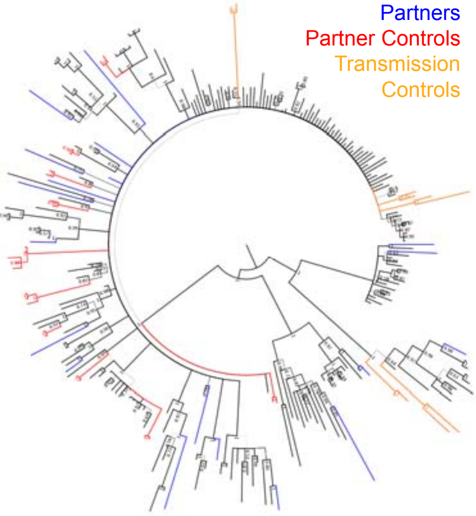
Phylogenetic tree of *pol* subtype B sequences

- The 15 HIV-positive partners all had subtype B infection; 6 of the 15 seroconverting partners acquired non-B infections
- None of the partners' sequences (blue) clustered together
- The study partner controls (red) and the control sequences from confirmed transmission pairs (orange) always clustered together with high supports
- The controls pairwise genetic distance was 0.004 (IQR: <0.001, 0.007), whilst the partners' *pol* sequences showed a median pairwise genetic distance of 0.068 (IQR: 0.060, 0.086).



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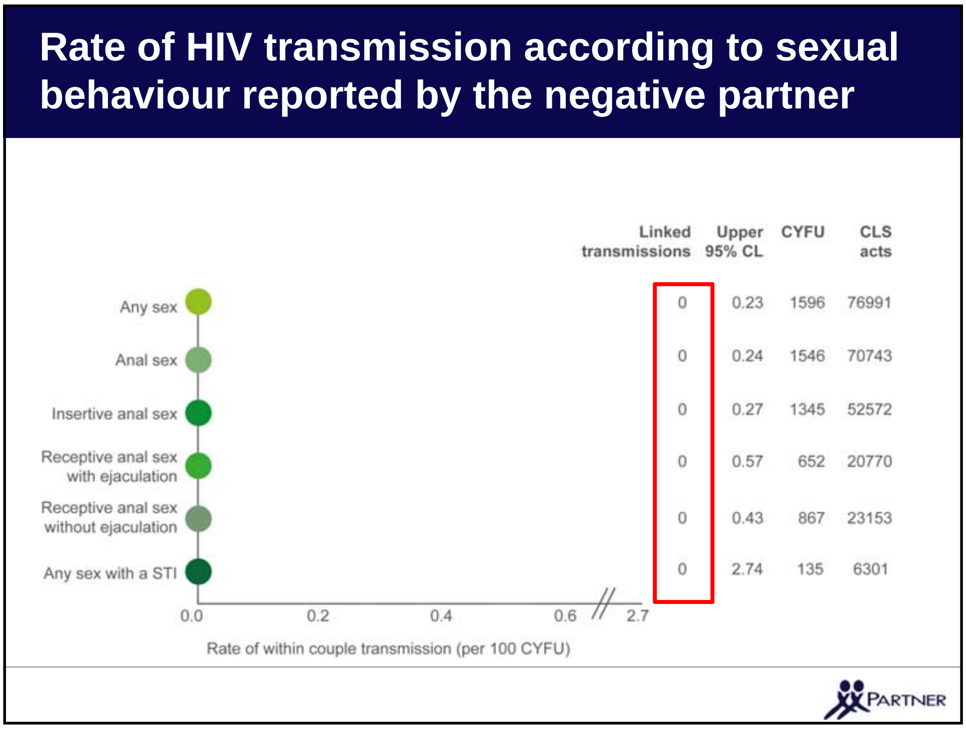
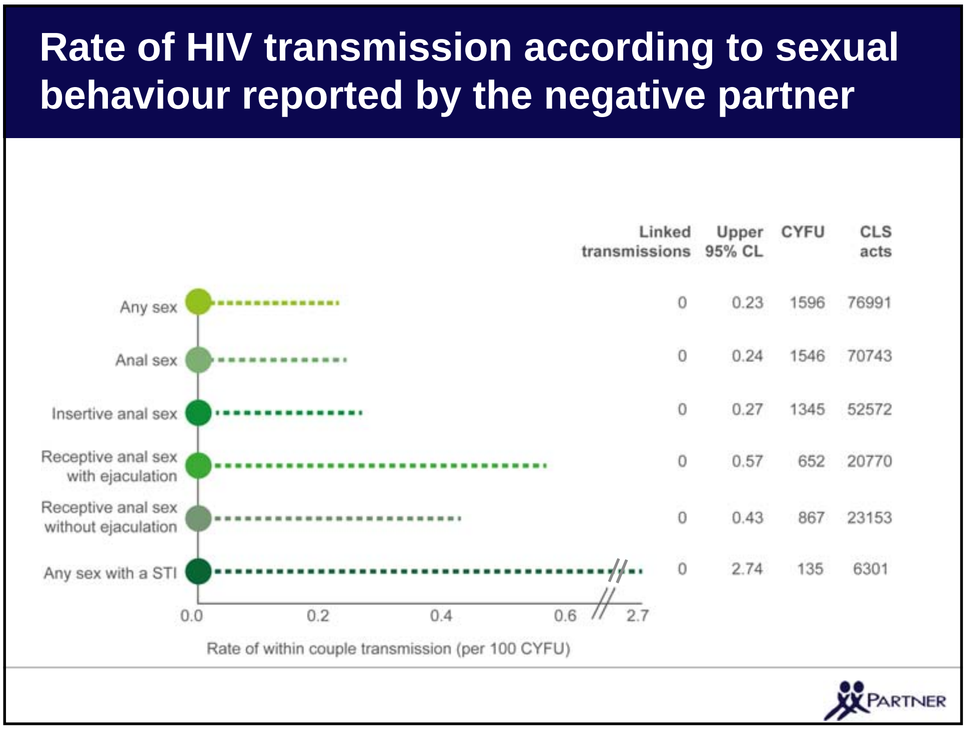


Rate of HIV transmission according to sexual behaviour reported by the negative partner

	Linked transmissions	Upper 95% CL	CYFU	CLS acts
Any sex	0	0.23	1596	76991
Anal sex	0	0.24	1546	70743
Insertive anal sex	0	0.27	1345	52572
Receptive anal sex with ejaculation	0	0.57	652	20770
Receptive anal sex without ejaculation	0	0.43	867	23153
Any sex with a STI	0	2.74	135	6301



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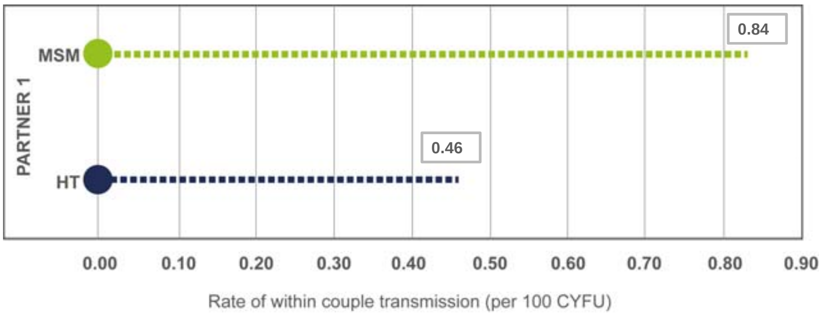
Upper 95% CI around estimated rate of zero HIV transmissions: PARTNER 1 compared to PARTNER 1&2



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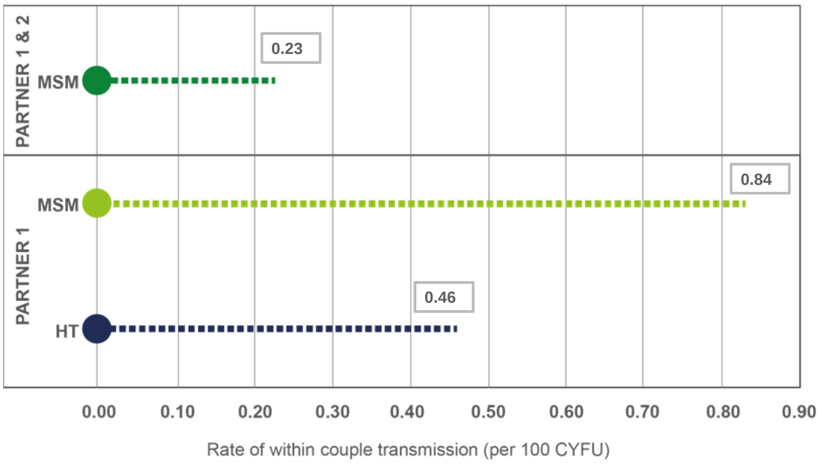

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Conclusions

- Among serodifferent gay couples who had sex 77,000 times without condoms with undetectable viral load, we found zero linked transmissions during almost 1600 CYFU
- Our results give equivalence of evidence for gay men as for heterosexual couples and indicate that the risk of HIV transmission when HIV viral load is suppressed is effectively zero
- **U**ndetectable = **U**ntransmissable

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PARTNER2 Study Sites

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