

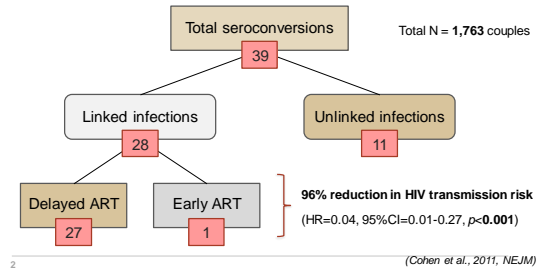


HIV Transmission in Male Serodiscordant Couples in Australia, Thailand and Brazil

Benjamin Bavinton, Fengyi Jin, Garrett Prestage, Iryna Zablotska, Beatriz Grinsztejn, Nittaya Phanuphak, Richard Moore, Kersten Koelsch, Andrew Grulich for the Opposites Attract Study Group
16 September 2015

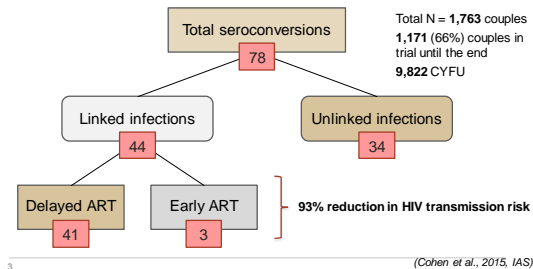
Background

HIV Treatment as Prevention: HPTN 052



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HIV Treatment as Prevention: HPTN 052

- No linked transmissions occurred when the HIV-positive partner was virally suppressed.
- Of the 8 linked infections that occurred when the HIV-positive partner was taking ART:
 - 4 infections were diagnosed shortly after the HIV-positive partner started ART (i.e. not yet virally suppressed)
 - 4 infections were diagnosed after ART failure
- In heterosexuals, TasP is effective and durable.
- What is the case in homosexual men?

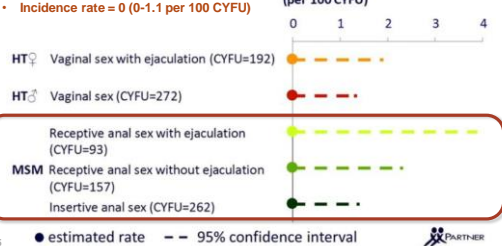
Background

HIV Treatment as Prevention: PARTNER

(Rodger et al., 2014, CROI)

- 308 CYFU in MSM in total
- Incidence rate = 0 (0-1.1 per 100 CYFU)

Rate of within couple transmission (per 100 CYFU)




Background

HIV Treatment as Prevention: Research Gaps

- More data are needed on homosexual serodiscordant couples.
 - Precision of confidence intervals if transmission rate remains 0 per 100 person-years.
 - Data from lower-to-middle income countries.
 - Durability of TasP in homosexual couples.
- Data are still limited on new sexual partnerships (<1 year).





OPPOSITES ATTRACT
THE STUDY OF RELATIONSHIPS BETWEEN HIV POSITIVE AND NEGATIVE GAY MEN



Opposites Attract Study Methods

Study Aims


1. Does HIV treatment/undetectable viral load reduce HIV transmission in anal sex?
2. How do gay men use viral load to negotiate condomless anal intercourse (CAI) within serodiscordant relationships?
3. Do STIs modify the relationship between viral load and HIV transmission?
4. Sub-Study: Is semen viral load related to transmission?
 - What is the correlation between viral load in blood and semen?



Opposites Attract Study Methods

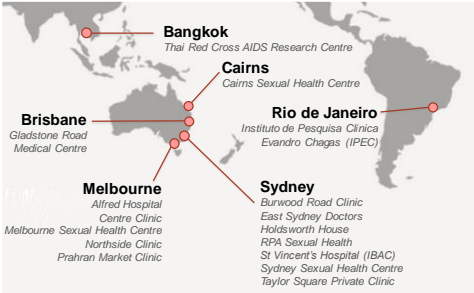
Study Design

- Prospective longitudinal cohort study.
- Unit of recruitment is a couple comprising two men in an ongoing sexual relationship where one is HIV-positive and the other HIV-negative at baseline.
- Couples attend at least 2 clinic visits per year:
 - Viral load and CD4 in HIV-positive partners
 - HIV antibody tests in HIV-negative partners
 - Tests for sexually transmissible infections in both partners.
- Both partners complete a questionnaire at each clinic visit.
- Phylogenetic analysis conducted for the interim analysis and at the end of the study.





Opposites Attract Study Methods

Study Sites



- Bangkok**: Thai Red Cross AIDS Research Centre
- Cairns**: Cairns Sexual Health Centre
- Brisbane**: Gladstone Road Medical Centre
- Melbourne**: Alfred Hospital, Centre Clinic, Melbourne Sexual Health Centre, Northside Clinic, Prahran Market Clinic
- Rio de Janeiro**: Instituto de Pesquisa Clínica Evandro Chagas (IPEC)
- Sydney**: Burwood Road Clinic, East Sydney Doctors, Hobsbawth House, RPA Sexual Health, St Vincent's Hospital (IBAC), Sydney Sexual Health Centre, Taylor Square Private Clinic

HIV Transmission in Male Serodiscordant Couples in Australia, Thailand and Brazil

Andrew E. Grulich,¹ Benjamin R. Bavinton,¹ Fengju Jin,¹ Garrett Prestage,¹ Jirana Zablotoka,¹ Beatrix Grinstead,² Nattaya Phansuphak,³ Richard Moore,⁴ and Franklin A. Koelsch,⁵ on behalf of the Opposites Attract Study Group

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Background

Typical prospective studies have demonstrated that HIV transmission is greatly reduced by heterosexual HIV serodiscordant couples when the HIV-positive partner is receiving combination antiretroviral therapy (ART) and has undetectable viral load. Comparative data in homosexual male serodiscordant couples are extremely limited.

We report a pre-specified interim analysis of the relationship between undetectable viral load and HIV transmission in an ongoing, observational, cohort serodiscordant study of homosexual male serodiscordant couples from three sites in Australia (Sydney, Melbourne, and Brisbane), in Bangkok, Thailand, and in Rio de Janeiro, Brazil.

Method

Homosexual male serodiscordant couples reporting regular anal intercourse with each other were recruited through internet sites. Detailed information on sexual risk behaviours was collected at each visit from the HIV-negative partner. HIV-negative partners were tested at baseline and followed for HIV antibodies and sexually transmitted infections (STIs), and HIV-positive partners were tested for HIV viral load and STIs. HIV incidence rates were calculated per couple-year of follow-up (CYPY).

Using penicillin-urea methods, and stratified by whether alternative forms of condoms and lubrication (CAI) were reported, undetectable viral load was defined as less than 200 copies per millilitre. One-sided confidence intervals were calculated using the exact Poisson method. Linear HIV transmission in couples was defined by phylogenetic analysis.

Results

By December 2014, 254 homosexual male serodiscordant couples were enrolled: 138 from Australia, 52 from Bangkok and 64 from Rio de Janeiro. Median age was 30.1 years for HIV-negative partners and 35.9 years for HIV-positive partners. Over one-third of couples (38.7%) had been having sex with each other for less than 12 months, while 22.0% and 28.4% had been having sex with each other for 1-5 years and for over 5 years, respectively.

There were a total of 1502 CYPY in 132 couples with at least one follow-up visit when 5% (42/274) were in a non-condomless relationship. At baseline, 86.2% (91/274) couples partners were on ART and 100% (274/274) had undetectable viral load. 371 (25%) partners were 11.2% in HIV-positive partners and 88.8% in HIV-negative partners.


There were 363 CYPY in periods where CAI was reported with a total of 1,866 acts of CAI in 89 couples. There were six blood HIV transmissions. The upper end of the 95% confidence interval of the transmission rate was 4.26 per 100 CYPY for periods in which CAI was reported, and 6.46 per 100 CYPY for periods in which no CAI was reported.

Conclusions

There were no blood HIV transmissions in 1502 CYPY in these homosexual male serodiscordant couples, despite rates in an historical study of CAI. The upper confidence limit of the transmission rate during follow-up in periods where CAI was reported was 4.26 per 100 CYPY. These data add to emerging evidence that the rates of HIV transmission in homosexual male serodiscordant couples is very low when the HIV-positive partner is on ART and has undetectable viral load. Further follow-up of a larger sample size is required to accurately determine any residual risk, and the Opposites Attract Study continues to recruit and follow-up homosexual male serodiscordant couples.

Type of intercourse without a condom reported by	Linked episodes (n)	Couple years of follow-up (CYPY)	No. of CAI acts	Incidence rate per 100 CYPY (95% CI)
Overall	0	149.56	5,965	0 (0-2.46)
Any CAI	0	92.53	3,905	0 (0-2.05)
Intensive CAI	0	77.87	3,589	0 (0-4.74)
Respective CAI	0	57.08	2,337	0 (0-6.46)
Any CAI when HIV <200 copies	0	88.59	3,620	0 (0-4.16)
Any CAI when HIV <200 copies	0	2.00	237	0 (0-164.31)



¹CAI when HIV <200 copies was reported: 1% (6/624)



Opposites Attract Study Methods

Interim Analysis

- The Study Protocol specified that an interim analysis of the main study outcome (i.e. HIV infection in the HIV-negative partner) would be conducted halfway through follow-up.
- The analysis was conducted in December 2014.
- Phylogenetic analysis of blood samples from couples where the negative partner had acquired HIV was led by Angie Pinto, Kersten Koelsch and Tony Kelleher.
- Behavioural data were analysed by Ben Bavinton, Jeff Jin and Andrew Grulich.



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Opposites Attract Study Methods

Statistical Analysis

- Incidence rates were calculated per couple-year of follow-up (CYFU) using person-year methods, and stratified by whether different forms of condomless anal intercourse (CLAI) were reported.
- 'Undetectable viral load' was defined as <200 copies/mL.
- One-sided 97.5% confidence intervals (CI) were calculated using the exact Poisson method.

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Opposites Attract Study Methods

Phylogenetic Analysis

- Researchers were blinded to study identification, behavioural data and partnerships.
- Comparison reference sequences obtained from:
 - Routinely performed resistance testing of *pol* gene in 19 recent locally derived seroconverters and stored *env* sequences from 9 randomly selected treatment experienced patients.
 - A third reference cohort included 11 routinely collected *pol* sequences from a geographically distant region of Sydney.
- Viral subtypes were determined using Stanford Resistance database.
- Maximum likelihood and neighbour joining methods were performed as well as bootstrap analysis using 1000 replicates for each phylogenetic inference.

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Interim Analysis Results

Enrolments, Visits, and Couple-Years

- By December 2014, 234 couples were enrolled:
 - 135 (57.7%) in Australia
 - 52 (22.2%) in Bangkok
 - 47 (20.1%) in Rio de Janeiro
- 152 couples (65.0%) had attended at least one follow-up visit.
- This analysis includes 149.96 couple-years of follow-up time within these 152 couples.

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Interim Analysis Results

Baseline Demographics

	HIV-Positive n=152	HIV-Negative n=152
Median Age	35.9 years	36.1 years
Gay Identity	93.1%	93.4%
Full-Time Employment	51.8%	61.2%
University Education	47.3%	54.1%

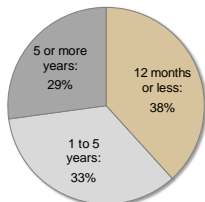
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Interim Analysis Results

Relationship Characteristics at Baseline

- Length of relationship:
 - 70.4% of couples lived together full-time.
 - 98.0% described each other as 'partner', 'husband' or 'boyfriend'



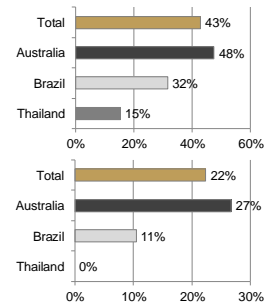
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Interim Analysis Results

Sex and CLAI with Outside Partners

- Any sex with outside partners in previous 3 months:
- Any CLAI with outside partners in previous 3 months:



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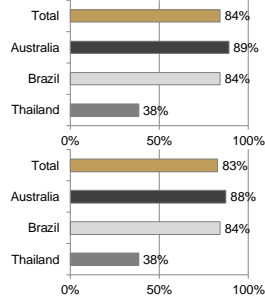
Interim Analysis Results

ART and Viral Load

- HIV-positive partners taking ART:

Thailand's ART guidelines changed in October 2014. More HIV-positive partners are going on ART during follow-up.

- HIV-positive partners with viral load of less than 200 copies per mL:



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Interim Analysis Results

STI Prevalence

	HIV-Negative Partner		HIV-Positive Partner	
	N	%	N	%
All (n=152)	10	6.6	17	11.2
Australia (n=120)	6	5.0	12	10.0
Brazil (n=19)	3	15.8	3	15.8
Thailand (n=13)	1	7.7	2	15.4
Gonorrhoea	5	3.3	6	4.0
Chlamydia	1	0.7	9	5.9
Syphilis	4	2.6	5	3.3
Rectal	5	3.3	11	7.2
Urethral	0	0.0	1	0.7

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Interim Analysis Results

Condomless Anal Intercourse within Couples

- At baseline, total of 54.6% of HIV-negative partners reported 'any CLAI' with his HIV-positive partner in the previous 3 months.
- Significant differences between countries:

Country	Percent	Odds Ratio	95% CI	p-value
Australia	68.1	Ref.	--	<0.001
Brazil	45.5	0.39	0.21-0.74	
Thailand	29.0	0.18	0.09-0.38	

Proportions were similar during follow-up.

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Interim Analysis Results

HIV Incidence

Type of condomless anal intercourse (CLAI) reported by HIV-negative partner	Linked transmissions (n)	Couple-years of follow up (CYFU)	No. of CLAI acts	Incidence rate per 100 CYFU (97.5% CI)
Overall	0	149.96	5,905	0 (0-2.46)
Any CLAI	0	90.83	5,905	0 (0-4.06)
Insertive CLAI	0	77.87	3,569	0 (0-4.74)
Receptive CLAI	0	57.08	2,337	0 (0-6.46)
Any CLAI when VL <200 copies	0	88.59	5,656	0 (0-4.16)
Any CLAI when VL >200 copies	0	2.00	237	0 (0-184.31)

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(Grulich et al., 2015, CROI)

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(Grulich et al., 2015, CROI)

Conclusion

- No linked HIV transmissions in 150 CYFU in these homosexual male serodiscordant couples, despite nearly 6,000 acts of CLAI.
- The incidence rate of linked HIV transmissions is 0 per 100 CYFU.
 - Statistically, the true risk lies between 0 and 4.16 per 100 CYFU in couples having CLAI where the HIV-positive partner has undetectable viral load.
- Combining the interim data from *Opposites Attract* and *PARTNER* means the upper limit of the confidence interval around 0 is less than 1 per 100 CYFU in these couples.
- These data add to emerging evidence that the rate of HIV transmission in homosexual male serodiscordant couples is very low when the HIV-positive partner is on ART and has undetectable viral load.

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Conclusion

- Further follow-up of a larger sample size is required to accurately delineate any residual risk.
- The *Opposites Attract Study* continues to recruit and follow-up homosexual male serodiscordant couples.
 - Recruitment continues until March 2016
 - Follow-up continues until December 2016
 - Reporting on the final transmission result in the first half of 2017.

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Acknowledgements

All Study Participants

Study Investigators: Andrew Grulich, Garrett Prestage, Ilyna Zabelska, Fangqi Jin, David A Cooper, Anthony Kelleher, David Wilson, Kersten Koelsch, Christopher Fairley, Kathy Triffitt, Sean Emery, Beatrix Grinsztejn, Nittaya Phanuphak

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All Recruiting Clinicians

Laboratory: Kate Marlin, Doris Chibo, Bertha Fadri, Shayla Shamin, Brooke Berry, Sandro Nazari, Tippawan Pankam, Angie Pinto

Site Coordinators/Staff: Colette Cashman, Jess Costa, Sian Edwards, Ruth Khallil Friedman, Shruti Gupta, Peta Hermit, Shane Hewitt, Julie Hoffman, Piranun Hongchokiet, Voki Ieroklis, Helen Kent, Helen Lau, Karen McRae, Simpson Nonenoy, Elizabeth Odgers, Janine Roney, Egidio Saingiao, Nicky Sharp, Julie Silvers, Rachel Woolstencroft, David Youds

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