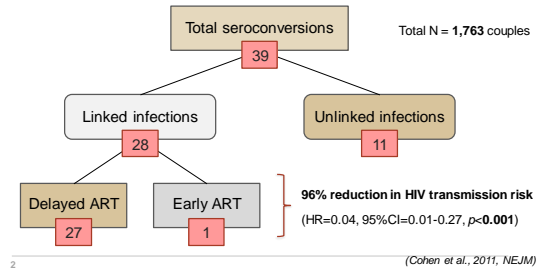**K**irby **I**nstitute

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
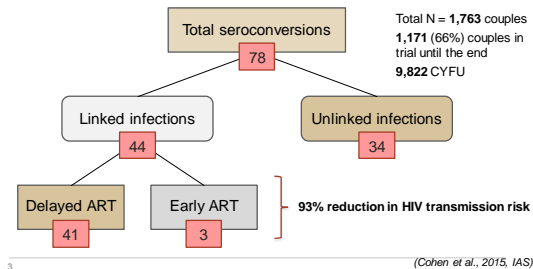16 September 2015

Background

HIV Treatment as Prevention: HPTN 052

Total N = **1,763** couples

96% reduction in HIV transmission risk
(HR=0.04, 95%CI=0.01-0.27, *p*<**0.001**)

(Cohen et al., 2011, NEJM)

Background

HIV Treatment as Prevention: HPTN 052

Total N = **1,763** couples
1,171 (66%) couples in trial until the end
9,822 CYFU

93% reduction in HIV transmission risk

(Cohen et al., 2015, IAS)

Background

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.

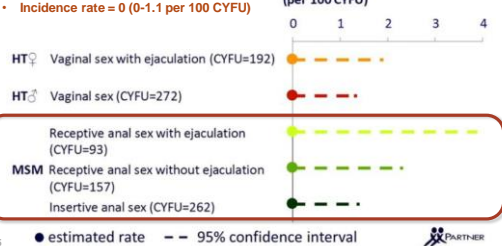- What is the case in homosexual men?

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)

HT♀ Vaginal sex with ejaculation (CYFU=192)

HT♂ Vaginal sex (CYFU=272)

MSM
- Receptive anal sex with ejaculation (CYFU=93)
- Receptive anal sex without ejaculation (CYFU=157)
- Insertive anal sex (CYFU=262)

● estimated rate   – – 95% confidence interval

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 (CLAI) 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?

8

Opposites Attract Study Methods
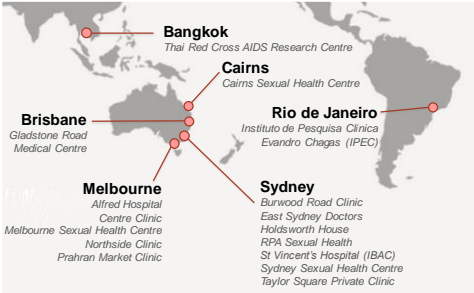
Study Design

- 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.

9

Opposites Attract Study Methods

Study Sites

Bangkok
Thai Red Cross AIDS Research Centre

Cairns
Cairns Sexual Health Centre

Brisbane
Gladstone Road Medical Centre

Rio de Janeiro
Instituto de Pesquisa Clínica Evandro Chagas (IPEC)

Melbourne
*Alfred Hospital
Centre Clinic
Melbourne Sexual Health Centre
Northside Clinic
Prahran Market Clinic*

Sydney
*Burwood Road Clinic
East Sydney Doctors
Holdsworth House
RPA Sexual Health
St Vincent's Hospital (IBAC)
Sydney Sexual Health Centre
Taylor Square Private Clinic*

10

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

Andrew E Grulich, Benjamin R Bavinton, Fengyi Jin, Garrett Prestage, Iryna Zablotska, Beatriz Grinsztejn, Nittaya Phanuphak, Richard Moore, and Kersten K Koelsch, on behalf of the Opposites Attract Study Group

---

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.

12

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.

13

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.

14

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.

15

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%

16

Interim Analysis Results

Relationship Characteristics at Baseline

- Length of relationship:

Pie chart: 5 or more years: 29%; 12 months or less: 38%; 1 to 5 years: 33%

- **70.4%** of couples lived together full-time.

- **98.0%** described each other as 'partner', 'husband' or 'boyfriend'

17
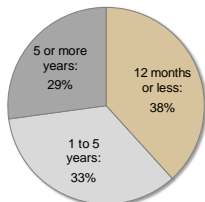
Interim Analysis Results

Sex and CLAI with Outside Partners

- Any sex with outside partners in previous 3 months:

Bar chart: Total 43%, Australia 48%, Brazil 32%, Thailand 15%

- Any CLAI with outside partners in previous 3 months:

Bar chart: Total 22%, Australia 27%, Brazil 11%, Thailand 0%

18

3

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:

Total	84%
Australia	89%
Brazil	84%
Thailand	38%

Total	83%
Australia	88%
Brazil	84%
Thailand	38%
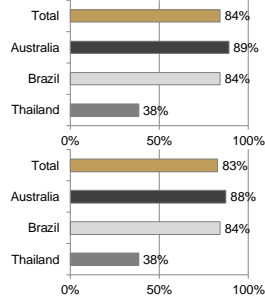
19

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

20

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.

21

Interim Analysis Results

HIV Incidence

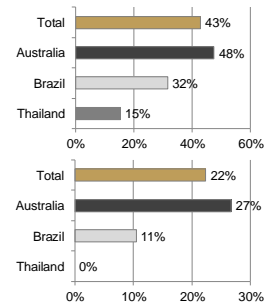| Type of condomless anal intercourse (CLAI) reported by HIV-negative partner	Linked trans-missions (n)	Couple-years of follow up (CYFU)	No. of CLAI acts	Incidence rate per 100 CYFU (97.5% CI)
Overall	0	149.96	5,905	0 (0-2.46)
Any CLAI	0	90.83	5,905	0 (0-4.06)
Insertive CLAI	0	77.87	3,569	0 (0-4.74)
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)

22 *(Grulich et al., 2015, CROI)*

Interim Analysis Results

HIV Incidence

Type of condomless anal intercourse (CLAI) reported by HIV-negative partner	Linked trans-missions (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)

23 *(Grulich et al., 2015, CROI)*

Interim Analysis Results

HIV Incidence

Type of condomless anal intercourse (CLAI) reported by HIV-negative partner	Linked trans-missions (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)

24 *(Grulich et al., 2015, CROI)*

4

UNSW

Interim Analysis Results

HIV Incidence

Type of condomless anal intercourse (CLAI) reported by HIV-negative partner	Linked trans-missions (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)

25

(Grulich et al., 2015, CROI)

UNSW

Interim Analysis Results

HIV Incidence

Type of condomless anal intercourse (CLAI) reported by HIV-negative partner	Linked trans-missions (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)

26

(Grulich et al., 2015, CROI)

UNSW

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.

27

UNSW

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.

28

UNSW

Acknowledgements

amfAR

Australian Government
National Health and Medical Research Council

29