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, Karsten Koelsch, Andrew Grulich for the Opposites Attract Study Group

16 September 2015

HIV Treatment as Prevention: HPTN 052

Total N = 1,763 couples

Total seroconversions

Linked infections

Delayed ART

Early ART

Unlinked infections

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

93% reduction in HIV transmission risk

39

29

28

11

27

1

1,171 (66%) couples in trial until the end 9,822 CYFU

308 CYFU in MSM in total

Incidence rate = 0 (0-1.1 per 100 CYFU)

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)

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).

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).
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?

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.

Study Sites

- **Bangkok**
  - Thai Red Cross AIDS Research Centre
- **Cairns**
  - Cairns Sexual Health Centre
- **Brisbane**
  - Gladstone Road Medical Centre
- **Rio de Janeiro**
  - Instituto Pesquisa Clínica Evandro Chagas (IPEC)
- **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

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.
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.

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.

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.

Baseline Demographics

<table>
<thead>
<tr>
<th></th>
<th>HIV-Positive n=152</th>
<th>HIV-Negative n=152</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age</td>
<td>35.9 years</td>
<td>36.1 years</td>
</tr>
<tr>
<td>Gay Identity</td>
<td>93.1%</td>
<td>93.4%</td>
</tr>
<tr>
<td>Full-Time Employment</td>
<td>51.8%</td>
<td>61.2%</td>
</tr>
<tr>
<td>University Education</td>
<td>47.3%</td>
<td>54.1%</td>
</tr>
</tbody>
</table>

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'

Sex and CLAI with Outside Partners

• Any sex with outside partners in previous 3 months:

• Any CLAI with outside partners in previous 3 months:
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.

Interim Analysis Results

Interim Analysis Results

STI Prevalence

<table>
<thead>
<tr>
<th>Country</th>
<th>HIV-Negative Partner</th>
<th>HIV-Positive Partner</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>N (n=152)</td>
<td>N (n=152)</td>
</tr>
<tr>
<td>Australia</td>
<td>19 38%</td>
<td>23 84%</td>
</tr>
<tr>
<td>Brazil</td>
<td>38 15.8</td>
<td>12 10.0</td>
</tr>
<tr>
<td>Thailand</td>
<td>10 7.7</td>
<td>7 5.8</td>
</tr>
</tbody>
</table>

HIV Incidence

<table>
<thead>
<tr>
<th>Type of condomless anal intercourse (CLAI) reported by HIV-negative partner</th>
<th>Linked transmissions (n)</th>
<th>Couple-years of follow up (CYFU)</th>
<th>No. of CLAI acts</th>
<th>Incidence rate per 100 CYFU (97.5% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0</td>
<td>149.96</td>
<td>5,905</td>
<td>0 (0-2.46)</td>
</tr>
<tr>
<td>Any CLAI</td>
<td>0</td>
<td>90.83</td>
<td>2,905</td>
<td>0 (0-4.06)</td>
</tr>
<tr>
<td>Insertive CLAI</td>
<td>0</td>
<td>77.87</td>
<td>3,569</td>
<td>0 (0-4.74)</td>
</tr>
<tr>
<td>Receptive CLAI</td>
<td>0</td>
<td>57.08</td>
<td>2,337</td>
<td>0 (0-4.66)</td>
</tr>
<tr>
<td>Any CLAI when VL &lt;200 copies</td>
<td>0</td>
<td>88.59</td>
<td>5,656</td>
<td>0 (0-4.16)</td>
</tr>
<tr>
<td>Any CLAI when VL &gt;200 copies</td>
<td>0</td>
<td>2.00</td>
<td>237</td>
<td>0 (0-184.31)</td>
</tr>
</tbody>
</table>

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:

<table>
<thead>
<tr>
<th>Country</th>
<th>Percent</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>66.1</td>
<td>Ref.</td>
<td>0.21-0.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Brazil</td>
<td>45.5</td>
<td>0.39</td>
<td>0.21-0.74</td>
<td></td>
</tr>
<tr>
<td>Thailand</td>
<td>29.0</td>
<td>0.09</td>
<td>0.03-0.38</td>
<td></td>
</tr>
</tbody>
</table>

HIV Incidence

<table>
<thead>
<tr>
<th>Type of condomless anal intercourse (CLAI) reported by HIV-negative partner</th>
<th>Linked transmissions (n)</th>
<th>Couple-years of follow up (CYFU)</th>
<th>No. of CLAI acts</th>
<th>Incidence rate per 100 CYFU (97.5% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>0</td>
<td>149.96</td>
<td>5,905</td>
<td>0 (0-2.46)</td>
</tr>
<tr>
<td>Any CLAI</td>
<td>0</td>
<td>90.83</td>
<td>2,905</td>
<td>0 (0-4.06)</td>
</tr>
<tr>
<td>Insertive CLAI</td>
<td>0</td>
<td>77.87</td>
<td>3,569</td>
<td>0 (0-4.74)</td>
</tr>
<tr>
<td>Receptive CLAI</td>
<td>0</td>
<td>57.08</td>
<td>2,337</td>
<td>0 (0-4.66)</td>
</tr>
<tr>
<td>Any CLAI when VL &lt;200 copies</td>
<td>0</td>
<td>88.59</td>
<td>5,656</td>
<td>0 (0-4.16)</td>
</tr>
<tr>
<td>Any CLAI when VL &gt;200 copies</td>
<td>0</td>
<td>2.00</td>
<td>237</td>
<td>0 (0-184.31)</td>
</tr>
</tbody>
</table>
Interim Analysis Results

HIV Incidence

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

(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.
- 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.

Acknowledgements

All Study Participants

Study Investigators: Andrew Grulich, Garret Prestage, Iryna Zablotska, Fengyi Jin, Anthony Kahle, Craig Wilson, Kersten Knecht, Christopher Finlay, Kelly Triffle,/detail/Emery, Beate Gierschik, Wiphong Phromthap.

Project Leaders/Directors: Benjamin Bavinton

Research Assistant: Lara Cassar

Site Investigators: David Baker, Mark Bloch, Nicolas Doong, Jennifer Hoy, Anna McNulty, Richard Morris, Craig D’Orsi, Catherine Pollard, Silvia Rizzoli, Sun Jung, Tan, David Templeton.

All Recruiting Clinicians

Site Coordinating Staff: Cadita Cuthinan, Jason Costa, Sam Edis, Richard Freeman, Shuk Gopal, Peter Harvi, Shawn Heyl, Julia Hoffman, Penelope Hengsasmit, Volki Jevanes, Helen Kent, Helen Leu, Karen McRea, Sopropri Noerwong, Elizabeth Ogden, Jannine Romery, Egido Sampaio, Nang Shwe, Juka Stiven, Rachel Wollaston, David Yule.

Community Partners: ACON, VAC, Living Positive Victoria, HIV/AIDS Legal Centre.

Funders: National Health and Medical Research Council, Foundation for AIDS Research (amfAR).