HPTN 071 (PopART)  
Treatment for prevention: a new paradigm for HIV control

JOINT IMPAACT/HPTN MEETING
MAY 8 2013, WASHINGTON DC
ACKNOWLEDGEMENTS

- Sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) under Cooperative Agreements # UM1 AI068619, UM1-AI068617, and UM1-AI068613

- Funded by:
  - The U.S. President's Emergency Plan for AIDS Relief (PEPFAR)
  - The International Initiative for Impact Evaluation (3ie) with support from the Bill & Melinda Gates Foundation
  - NIAID, the National Institute of Mental Health (NIMH), the National Institute on Drug Abuse (NIDA)
ART for prevention: background

• HIV incidence continues to be unacceptably high in many countries in Africa
• Lack of proven effective HIV prevention strategies
• Unless incidence can be reduced dramatically it will become increasingly difficult over time to sustain effective ART services
• Risk of HIV transmission closely correlated with HIV viral load and ART can be used to reduce HIV viral load and hence infectivity
• Current guidelines limit ART to those with late-stage HIV infection (CD4<350) but most transmission occurs before that
Universal test and treat intervention

- Promote universal HIV voluntary counselling and testing at regular intervals
- All those diagnosed HIV positive are started on ART immediately
- Mathematical models show immediate increase in numbers needing treatment but in medium-term, HIV incidence and prevalence are reduced dramatically
- In long-term, numbers needing ART are reduced.
Why is a trial needed?

- Not known whether a UTT intervention can be delivered with high uptake and acceptability
- Many uncertainties in model parameters
- Population-level impact of (feasible) intervention package is not known
- Many potential adverse effects, such as toxicity, drug resistance, sexual risk disinhibition, HIV-related stigma, overload of health services
- A rigorously designed trial can measure the costs and benefits of this strategy and provide reliable evidence on cost-effectiveness for health policy makers
HPTN 071
The PopART Study
Hypothesis

Universal voluntary HIV testing with appropriate combination prevention offered to all those testing HIV negative - in addition to immediate ART for all those testing HIV positive - will have a substantial impact on HIV incidence at population level.
PopART Intervention Package

- Universal voluntary HIV testing delivered annually through door-to-door, home-based testing
- Active linkage to care, referral and support for retention/adherence by CHiPs for the following:
  - Voluntary medical male circumcision for HIV-ve men
  - PMTCT for HIV+ve pregnant women
  - HIV treatment and care for all HIV+ve individuals
  - Promotion of sexual health and TB services
  - Condom provision
- Immediate ART offered at health center for all testing HIV+ve

CHiPs = Community HIV-care Providers
Trial Design: three-arm, two-country, cluster-randomized trial

- 21 clusters (communities): 12 in Zambia, 9 in South Africa
- Average of ~50,000 in each cluster (~50% adults)
- Incidence measured in *Population Cohort*: 2,500 adults in each cluster, followed up after 1, 2 and 3 years

<table>
<thead>
<tr>
<th>Arm A (7 sites)</th>
<th>Arm B (7 sites)</th>
<th>Arm C (7 sites)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full PopART</td>
<td>PopART <em>but</em> CD4&lt;350</td>
<td>Standard of Care</td>
</tr>
</tbody>
</table>
- Clusters matched into triplets by HIV prevalence: 4 triplets in Zambia, 3 in S Africa
- Clusters randomly allocated to 3 study arms within each matched triplet
- Restricted randomisation used to ensure balance on ART uptake, population size and HIV prevalence
Objectives

• Primary Objective
  – To measure the impact of the PopART intervention in reducing HIV incidence
  – Measured in a cohort of 52,500 adults over 3 years
Objectives

- Secondary Objectives
  - Uptake of intervention components
  - Retention in HIV care
  - Sexual risk behaviour
  - HIV-related stigma
  - HIV disease progression and death
  - TB case notification rate
  - HSV-2 incidence
  - ART Toxicity
  - ART adherence and viral suppression *
  - Community viral load *
  - ART drug resistance *

See Table 10 of Protocol for further details

* if further funding obtained
Parameter values assumed for the model of the impact of the intervention for central and optimistic target scenarios, and projected impact on HIV incidence in Arms A and B compared with Arm C, assuming intervention roll-out over a 6-month time period.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Central Target</th>
<th>Optimistic Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual coverage of test and treat campaign</td>
<td>70%</td>
<td>75%</td>
</tr>
<tr>
<td>Treatment failure &amp; drop-out rate, per year</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Effectiveness of ART in blocking transmission</td>
<td>90%</td>
<td>95%</td>
</tr>
<tr>
<td>Take up of male circumcision when offered</td>
<td>50%</td>
<td>50%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Arm A</th>
<th>Arm B</th>
<th>Arm A</th>
<th>Arm B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact on cumulative incidence (3 years)</td>
<td>58%</td>
<td>25%</td>
<td>66%</td>
<td>29%</td>
</tr>
<tr>
<td>Impact on cumulative incidence (2 first years)</td>
<td>54%</td>
<td>23%</td>
<td>62%</td>
<td>27%</td>
</tr>
<tr>
<td>Impact on HIV incidence during Year 1</td>
<td>45%</td>
<td>19%</td>
<td>53%</td>
<td>23%</td>
</tr>
<tr>
<td>Impact on HIV incidence during Year 2</td>
<td>63%</td>
<td>28%</td>
<td>72%</td>
<td>33%</td>
</tr>
<tr>
<td>Impact on HIV incidence during Year 3</td>
<td>68%</td>
<td>31%</td>
<td>76%</td>
<td>36%</td>
</tr>
</tbody>
</table>

Zambia

South Africa
Progress with trial implementation

- October 2012: Approval of Version 1.0 of protocol
- December 2012: Conditional approval of life-of-project budget
- November 2012 - January 2013: Ethical approval by LSHTM, CDC, University of Stellenbosch (awaited from University of Zambia)
- December 2012: Start of formative research
- February 2013: Public randomisation ceremony in Lusaka and Cape Town
- April 2013: First meeting of DSMB
- June 2013: Start of intervention and population cohort enrolment in Zambia and S Africa
PMTCT

Assessing the Impact of Universal Test-and-Treat on HIV-free infant survival in HPTN-071
## PMTCT WHO options by cluster

<table>
<thead>
<tr>
<th>Clusters</th>
<th>Arm A</th>
<th>Arm B</th>
<th>Arm C</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Zambia</td>
<td>S Africa</td>
<td>Zambia</td>
<td>S Africa</td>
</tr>
<tr>
<td>Option B+</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Option B</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>
Proposed Studies (Under Discussion)

To study:

• The effectiveness & cost-effectiveness of Option B/B+ delivered within the PopART model on infant HIV-free survival

• The effect of the PopART model on uptake of Option B/B+, linkage and retention in care and adherence to triple ART regimens

• To collect data on maternal health on triple ART and selected infant birth outcomes
**Design**

*Expanded population cohort* (PC36+): any women in household where a PC cohort member resides

*Population cross-sectional survey* (PX): random sample of additional 250 households/cluster (different from PC): any women in those households

Mothers in HH (if pregnant within last 36 m) consented, interviewed (birth outcome, HIV care) and offered HIV test and infant HIV tested by heel-prick.
Thanks to

• Sarah Fidler
• Helen Ayles
• Nulda Beyers

And all members of the HPTN 071 Study Team!
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