HPTN 071 (PopART)
Population Effects of Antiretroviral Therapy to Reduce HIV Transmission

IMPACT OF UNIVERSAL TESTING AND TREATMENT IN ZAMBIA AND SOUTH AFRICA:
RESULTS OF A COMMUNITY-RANDOMIZED TRIAL
CROI: SEATTLE
6 MARCH 2019

U.S. NATIONAL INSTITUTES OF HEALTH:
National Institute of Allergy and Infectious Diseases
National Institute of Mental Health
National Institute on Drug Abuse
Background

- Universal testing and treatment (UTT) proposed as strategy to achieve steep reductions in HIV incidence
- Can UTT be delivered in practice in generalized epidemics in sub-Saharan Africa?
- What impact on HIV incidence can be achieved?
- Previous UTT trials have shown inconclusive results
  - SEARCH & TasP trials found no impact
  - BCPP found 30% reduction (borderline significance)
- We report primary results of HPTN 071 (PopART)
**Study Design**

- **Arm A**: Full PopART intervention including immediate ART irrespective of CD4 count
- **Arm B**: PopART intervention except ART initiation according to current national guidelines
- **Arm C**: Standard of care at current service provision levels including ART initiation according to current national guidelines

2,500 random sample from each community (aged 18-44) Population Cohort (N=52,500) Followed up annually for 36 months
21 Communities
7 per arm (A, B & C)

12 in Zambia
9 in S Africa

Total population ~1M
CHiPs Door-To-Door Intervention

- Universal HIV counselling and testing
- VMMC referral
- PMTCT referral
- STI screening
- TB screening
- Condoms

CHiPs: Community HIV-care Providers

Repeat Visits to Clients Living with HIV

Door-to-Door Delivery of Intervention

Including HIV Testing/Retesting

Referral to Clinic
Study Timeline

<table>
<thead>
<tr>
<th>CHiPs Intervention</th>
<th>Population Cohort</th>
<th>Primary Analysis Period</th>
<th>ART Eligibility, Arm A</th>
<th>Zambia ART Eligibility, Arms B&amp;C</th>
<th>SA ART Eligibility, Arms B&amp;C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R1</td>
<td>PC0</td>
<td>UNIVERSAL ART</td>
<td>CD4 &lt;350</td>
<td>CD4 &lt;500</td>
</tr>
<tr>
<td></td>
<td>R2</td>
<td>PC12</td>
<td>UNIVERSAL ART</td>
<td>CD4 &lt;500</td>
<td>CD4 &lt;500</td>
</tr>
<tr>
<td></td>
<td>R3</td>
<td>PC24</td>
<td>UNIVERSAL ART</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>PC36</td>
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</table>
PC enrolment and follow-up

**PC0**
- Enrolled: 38,474

**PC12**
- Terminated: 5,191 (13%)
- Retained: 25,289 (66%)
- Missed: 7,994 (21%)

**PC12N**
- Enrolled: 5,014

**PC24**
- Terminated: 5,043 (13%)
- Retained: 25,195 (66%)
- Missed: 8,059 (21%)

**PC24N**
- Enrolled: 4,813

**PC36**
- Terminated: 10,566 (28%)
- Retained: 27,501 (72%)
<table>
<thead>
<tr>
<th></th>
<th>Arm A N = 12,671</th>
<th>Arm B N = 13,404</th>
<th>Arm C N = 12,399</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>28%</td>
<td>29%</td>
<td>30%</td>
</tr>
<tr>
<td>Age: 18 – 24</td>
<td>40%</td>
<td>39%</td>
<td>40%</td>
</tr>
<tr>
<td>25 – 34</td>
<td>39%</td>
<td>39%</td>
<td>38%</td>
</tr>
<tr>
<td>35 – 44</td>
<td>21%</td>
<td>23%</td>
<td>22%</td>
</tr>
<tr>
<td>HIV Prevalence: Overall</td>
<td>21%</td>
<td>21%</td>
<td>22%</td>
</tr>
<tr>
<td>Men</td>
<td>12%</td>
<td>11%</td>
<td>12%</td>
</tr>
<tr>
<td>Women</td>
<td>25%</td>
<td>25%</td>
<td>27%</td>
</tr>
<tr>
<td>HSV2 Prevalence: Overall</td>
<td>44%</td>
<td>43%</td>
<td>46%</td>
</tr>
<tr>
<td>ART (self-reported coverage in HIV+)</td>
<td>33%</td>
<td>41%</td>
<td>35%</td>
</tr>
<tr>
<td>Viral suppression (HIV+; 75/community)</td>
<td>56%</td>
<td>57%</td>
<td>54%</td>
</tr>
<tr>
<td>Medical Male Circumcision</td>
<td>17%</td>
<td>16%</td>
<td>19%</td>
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</tbody>
</table>
Delivery of intervention: ART coverage in arm A & B communities at end of trial

Overall Coverage
Arm A: 81%
Arm B: 80%
Primary outcome

- HIV incidence in Population Cohort
- Between PC12 and PC36 (pre-specified)
- Time of infection imputed for seroconverters who were not seen at PC12 and/or PC24
- Impact comparing Arm A vs C, and Arm B vs C
- Using methods for matched cluster-randomized trials
## Primary analysis: Incidence in PC12-PC36

<table>
<thead>
<tr>
<th></th>
<th>Arm A</th>
<th>Arm B</th>
<th>Arm C</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV Incidence</strong></td>
<td>198/12,990 (1.45%)</td>
<td>157/14,149 (1.06%)</td>
<td>198/12,563 (1.55%)</td>
</tr>
<tr>
<td>(geometric mean of community incidence rates)</td>
<td></td>
<td></td>
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<tr>
<td><strong>Adjusted Rate Ratio</strong></td>
<td>0.93 (0.74, 1.18)</td>
<td>0.70 (0.55, 0.88)</td>
<td>1</td>
</tr>
<tr>
<td>(95% CI)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Incidence compared to</strong></td>
<td>7% reduction</td>
<td>30% reduction</td>
<td></td>
</tr>
<tr>
<td>Arm C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>0.51</td>
<td>0.006</td>
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Adjusted for age category, sex and baseline community HIV prevalence.
Reported numbers include imputation for PC12 and PC24 missed visits.
## Viral suppression at PC24

<table>
<thead>
<tr>
<th></th>
<th>Arm A</th>
<th>Arm B</th>
<th>Arm C</th>
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</thead>
<tbody>
<tr>
<td><strong>Viral suppression</strong></td>
<td>1531/2159 (72%)</td>
<td>1318/1891 (68%)</td>
<td>1480/2183 (60%)</td>
</tr>
<tr>
<td><strong>Adjusted prevalence ratio</strong></td>
<td>1.16 (0.99, 1.36)</td>
<td>1.08 (0.92, 1.27)</td>
<td>1</td>
</tr>
<tr>
<td>VS compared to Arm C</td>
<td><strong>16% increase</strong></td>
<td><strong>8% increase</strong></td>
<td></td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>0.07</td>
<td>0.30</td>
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Adjusted for age category, sex.
HPTN 071 (PopART) Summary

• PopART achieved the first two UNAIDS 90-90 targets in arms A and B
• High rates of viral suppression achieved
• PopART with ART according to local guidelines (Arm B) reduced HIV incidence by 30% in these high burden settings (from 1.6% to 1.1%).
• Lack of an effect in the full intervention arm (Arm A), where universal treatment was delivered ahead of change in guidelines, was surprising and not explained by lower rates of viral suppression.
• Further analysis of quantitative, qualitative and phylogenetic data in progress to explore and explain this dissonant finding.
• Community-based services for *universal* HIV testing and linkage are a key component of combination prevention in the global effort to achieve effective HIV control.
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), and the National Institute on Drug Abuse (NIDA) all part of the U.S. National Institutes of Health (NIH)
The HPTN 071 Study Team, led by:

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Dr. Helen Ayles
Dr. Nulda Beyers
Dr. Peter Bock

Government Agencies:

PEPFAR Implementing Partners:
HIV Incidence by community (PC12-PC36)

7% reduction

30% reduction