Early ART Uptake and Adherence: The Tambua Mapema Plus Study

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Disclosures

• I have received research support from Gilead and Cepheid
Global HIV Testing and Treatment Cascade

HIV TESTING AND TREATMENT CASCADE, GLOBAL, 2020

- Additional gap to reaching the first 95: 1.9 million
- Gap to reaching the first 90: 2.3 million
- Additional gap to reaching the first and second 95s: 3.4 million
- Gap to reaching the first and second 90s: 3 million
- Additional gap to reaching the three 95s: 4.9 million
- Gap to reaching the three 90s: 2.7 million

Target of adherence interventions

Source: UNAIDS special analysis, 2021.
Acute HIV Infection (AHI)

- Acute HIV-1 infection, despite its short duration, can account for 10%–50% of all new HIV-1 transmissions, especially in persons who have multiple concurrent sex partners or high rates of partner change.

- “AHI is routinely missed in healthcare encounters, despite the presence of clinical, behavioral, and serological clues.”

Cohen NEJM 2011

Kim Powers and Mike Cohen AIDS 2014
HIV Testing Intervention

- Point-of-care HIV-1 Qual Test (Cepheid Xpert®) used for all samples
- Detects HIV-1 nucleic acid at levels >1,000 copies/mL
- Samples positive by HIV-1 Qual can be tested with standard HIV rapid tests to distinguish acute from chronic HIV infection

Systematic Review, Agutu PLoS One 2019
Tambua Mapema Plus Trial

- To conduct a proof-of-concept study to determine outcomes of a multi-component health facility-based intervention including
- HIV-1 RNA testing to identify undiagnosed acute (RNA+, rapid test-) and prevalent (RNA+, rapid test+) HIV infection in adults aged 18-39 years seeking care for symptoms, compared to standard care
- Newly diagnosed patients linked to HIV care and immediate treatment
- Partners notified and tested with the same “enhanced” HIV testing intervention, with linkage to ART or PrEP as indicated

R01 AI124968 (MPI Graham, Sanders)
Tambua Mapema Plus Eligibility

• Aged 18-39
• HIV negative or unknown HIV status
• Scoring ≥ 2 on AHI risk score
  • 1 point each for:
    ✓ age 18-29 years
    ✓ reported fever
    ✓ fatigue
    ✓ body pains
    ✓ diarrhea
    ✓ sore throat
  • 3 points for:
    ✓ genital ulcer disease
Stepped Wedge Design

Objectives:
- Use GeneXpert machines efficiently
- Capture baseline data at each site (3-6 months)
- Capture 6 months of intervention data at each site

<table>
<thead>
<tr>
<th>Clinic</th>
<th>0-3</th>
<th>4-6</th>
<th>7-9</th>
<th>10-12</th>
<th>13-15</th>
<th>16-18</th>
<th>19-21</th>
<th>22-24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site 1</td>
<td>O</td>
<td>O</td>
<td>I</td>
<td></td>
<td>I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Site 2</td>
<td>O</td>
<td>O</td>
<td>I</td>
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<td>I</td>
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<tr>
<td>Site 3</td>
<td>O</td>
<td>O</td>
<td>I</td>
<td>I</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Site 4</td>
<td>O</td>
<td>O</td>
<td>I</td>
<td>I</td>
<td></td>
<td></td>
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<td>Site 5</td>
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<td>I</td>
<td>I</td>
<td></td>
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</tr>
<tr>
<td>Site 6</td>
<td>O</td>
<td>O</td>
<td>I</td>
<td>I</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N enrolled</td>
<td>250</td>
<td>375</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>375</td>
<td>250</td>
<td>125</td>
</tr>
</tbody>
</table>

I = intervention period, N = number, O = observation period

Graham JMIR Res Protocols 2020
## Results – HIV Diagnoses

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Observation Period</th>
<th>Intervention Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled</td>
<td>1374</td>
<td>1500</td>
</tr>
<tr>
<td>Tested</td>
<td>352 (25.6%)*</td>
<td>1500 (100%)*†</td>
</tr>
<tr>
<td>Chronic infections</td>
<td>13</td>
<td>35</td>
</tr>
<tr>
<td>Acute infections</td>
<td>—</td>
<td>2</td>
</tr>
<tr>
<td>Total infections</td>
<td>13</td>
<td>37</td>
</tr>
<tr>
<td>Yield among enrolled</td>
<td>0.9%</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

* 92% of participants would have accepted an HIV test if offered  
† 5% of eligible individuals refused due to HIV testing requirement

- Odds of a new diagnosis: 2.2 (95% confidence interval: 1.4–3.5)
- 1 chronic HIV infection for every 40 patients tested and 1 AHI patient for every 750 patients tested

Agutu PLoS One 2021  
Sanders HIV Medicine 2022
Treatment and PNS Outcomes, 6 weeks

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Observation N=13</th>
<th>Intervention N=37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linked to ART</td>
<td>9 (69%)</td>
<td>33 (89%)</td>
</tr>
<tr>
<td>Enrolled in research cohort</td>
<td>—</td>
<td>30 (81%)</td>
</tr>
<tr>
<td>Accepted enhanced aPNS</td>
<td>—</td>
<td>16 (53%)</td>
</tr>
<tr>
<td>Partners named</td>
<td>10 (7 regular, 3 casual)</td>
<td>65 (39 regular, 26 casual)</td>
</tr>
<tr>
<td>Partners tested</td>
<td>3 (1 regular, 2 casual)</td>
<td>10 (8 regular, 2 casual)</td>
</tr>
<tr>
<td>Partners with chronic HIV</td>
<td>2</td>
<td>2 regular</td>
</tr>
<tr>
<td>Partners with acute HIV</td>
<td>—</td>
<td>0</td>
</tr>
<tr>
<td>Partners starting PrEP</td>
<td>—</td>
<td>4 regular</td>
</tr>
</tbody>
</table>

- More index cases were successfully linked to ART in the intervention period (p=0.05)
- Ratio of named partners to index 1.76, tested partners to index 0.27
- Disclosure and partner testing rates improved over follow-up
Patient Experiences

• “When I was tested, my viral load was high. Both of us [my wife and I] decided that I should take the drugs [ART] and use protection [condoms] to prevent transmission and a pregnancy. . . Starting medication immediately at least gives you time to change. . . to make up, what do we call this. . .? It helps with the acceptance [of HIV status].” — 36-year-old male, 1st clinic visit after ART initiation

• “I thought I was suffering from malaria and pneumonia. . . I was feeling tired, my stomach was aching, and I was just feeling pain all over. When I went to the chief’s clinic, . . . I was told that I was going to be (HIV) tested. I got to know my HIV status and I got HIV treatment.”— 24-year-old female, 1st clinic visit after ART initiation

Van der Elst PLoS One 2022
TMP Impact and Cost-Effectiveness

- Developed an agent-based network model of HIV-1 transmission using TMP data and Kenyan statistics
- Estimated potential population-level impact of a scaled-up TMP intervention over 10 years
- Three scenarios modeled:
  - Standard care (PITC at current rates)
  - Scaled-up opt-out rapid testing with similar uptake as the TMP intervention
  - The TMP testing intervention as applied in the trial
- Evaluated cost-effectiveness of each scenario from Kenyan government perspective over a 10-year time horizon

Hamilton JAIDS 2022, Babigumira BMJ Open 2022
Percentage of HIV-1-infected individuals aware of their status and percent diagnosed on treatment in Kenya over 10 years with current rates of PITC compared to four levels of TMP intervention uptake.
HIV-1 incidence in Kenya over 10 years with current rates of PITC compared to three levels of TMP intervention uptake

- Percentage of infections averted was 1.0% for scaled-up PITC versus 9.4% for TMP
- Identifying acute HIV AHI among symptomatic outpatients is superior to scaled-up PITC, resulting in >95% knowledge of HIV status, and would reduce new HIV infections in Kenya

Hamilton JAIDS 2022
Cost-Effectiveness Results

• Average per patient cost of POC NAAT was $214 compared with $173.6 for scaled-up PITC and $47.3 for standard PITC

• Mean DALYs accumulated per patient for POC NAAT were 0.160 compared with 0.176 for scaled-up PITC and 0.214 for standard PITC

• Incremental cost-effectiveness ratio (ICER) comparing POC NAAT to standard PITC was $3,098 per DALY averted

• Scaled-up PITC had no advantage (lower cost but less effective)

• Results were sensitive to disability weights for HIV/AIDS and costs of antiretroviral therapy

• TMP intervention offered to adults in Kenya was cost-effective and should be considered for inclusion as the standard of HIV testing

Babigumira BMJ Open 2022
What if we offered PrEP to those testing negative in *TMP* (97.5 of participants%)?

- Four scenarios modeled:
  - PrEP for uninfected participants in disclosed serodiscordant couples
  - PrEP for individuals with concurrent partnerships (≥2 partners at interview)
  - PrEP for all uninfected individuals
  - PrEP integrated into the enhanced PNS component of TMP

- Providing PrEP to uninfected individuals in serodiscordant, disclosed partnerships had no impact on the overall number of infections in this model, but disclosure was only 3% in main partnerships

- Providing PrEP for all uninfected individuals identified through TMP averted as much as 12.7% of new infections but was not efficient based (NNT 200)

- Providing PrEP to individuals with concurrent partnerships (2.8% of infections averted, NNT 22.5) and to uninfected partners identified through enhanced PNS (4.6% of infections averted, NNT 27.6) was most efficient based on numbers needed to treat

Hamilton, in submission
Limitations

• *TMP* was conducted in Kenya and modeling reflects the Kenyan epidemic – local situations may differ

• Recently available antigen-antibody tests less expensive (Determine Early Detect), may work as well and is cheaper

• Different targeting strategies to enhance HIV test positivity could improve results

• Partner services results were disappointing – this is a challenging area for future research!
Key Take-Home Messages

- The need for prevention-effective ART adherence starts at HIV acquisition
- Motivation to adhere to HIV treatment is increased during health-setting for symptoms and when viral load is high
- Missed opportunities for timely HIV diagnosis and linkage to ART are undermining progress towards the 95/95/95 goals
- Testing for AHI in healthcare settings is cost-effective and should be scaled up
- PrEP should be offered to patients testing negative in health facilities, and is most efficient when offered to those with HIV+ partners and those who report concurrent relationships
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