The Cost-effectiveness of Treatment as Prevention: Analysis of the HPTN 052 Trial

Supported by NIAID R01 AI058736 and HPTN 052
Early ART compared to delayed ART conferred a 96% relative reduction in linked HIV transmissions among serodiscordant couples.
Objective
Collaboration: HPTN 052/CEPAC-International

• To project the cost-effectiveness of early compared to delayed ART for treatment and prevention in serodiscordant couples

• We conducted analyses for two countries, South Africa, and India to assess regional differences in value
Methods: CEPAC-International Model

- CEPAC-International Model
  - Mathematical model of HIV natural history and treatment
  - Clinical and resource utilization data from South Africa and India
  - Cohort and ART efficacy parameters from HPTN 052 trial
• Projects transmission events from index cases
  – Allows for transmission between 1° and outside partners
  – Accounts for 1st- and 2nd-order transmissions from the index case
  – Flexible structure allows input variation in:
    • Duration of partnerships
    • Activity outside primary partnerships
    • Transmission by viral load

Methods: Transmission Module in CEPAC
Methods: Two Strategies

1) Delayed ART (CD4 <250/µl)
2) Early ART (at presentation)

• Evaluate outcomes in:
  – Clinical benefit, cost and transmissions
  – 5-year and lifetime horizons
## Model Input Parameters: Cohort, Treatment, and Transmission

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Input</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean CD4 (cells/μL)</td>
<td>449</td>
</tr>
<tr>
<td>48-wk virologic suppression</td>
<td>92%</td>
</tr>
<tr>
<td>Loss to follow-up rate (/100 py)</td>
<td>3.4</td>
</tr>
<tr>
<td>Average partners (/mo)</td>
<td>1.011</td>
</tr>
<tr>
<td>Transmission rate (/100 py)</td>
<td>0.103-1.483</td>
</tr>
</tbody>
</table>
## Model Input Parameters: Costs (2011 US$)

<table>
<thead>
<tr>
<th></th>
<th>South Africa</th>
<th>India</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART (/mo)</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>OI treatment</td>
<td>300-1,000</td>
<td>40-300</td>
</tr>
<tr>
<td>Routine care</td>
<td>20-200</td>
<td>10-30</td>
</tr>
<tr>
<td><em>per capita</em> GDP*</td>
<td>8,100</td>
<td>1,400</td>
</tr>
</tbody>
</table>

*WHO thresholds:
- “Very cost-effective”: <1x *per capita* GDP
- “Cost-effective”: <3x *per capita* GDP

1WHO Global Price Reporting Mechanism
## Model Input Parameters:
**Costs (2011 US$)**

<table>
<thead>
<tr>
<th></th>
<th>South Africa</th>
<th>India</th>
</tr>
</thead>
<tbody>
<tr>
<td>ART (/mo)</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>OI treatment</td>
<td>300-1,000</td>
<td>40-300</td>
</tr>
<tr>
<td>Routine care</td>
<td>20-200</td>
<td>10-30</td>
</tr>
<tr>
<td><strong>per capita GDP</strong></td>
<td><strong>8,100</strong></td>
<td><strong>1,400</strong></td>
</tr>
</tbody>
</table>

**WHO thresholds:**
- “Very cost-effective”: <1x *per capita* GDP
- “Cost-effective”: <3x *per capita* GDP
Results:
Survival for South Africa

- Early ART: 93%
- Delayed ART: 84%
- No ART: 55%

Graph showing survival rates over years since presentation-to-care.
Results:
Transmission Rates, 5 yrs, South Africa

Transmissions/1,000 patients/year vs. Years since presentation-to-care.
## Results:
### Cost-effectiveness, 5 yrs, South Africa

<table>
<thead>
<tr>
<th>Life expectancy* (years)</th>
<th>Costs (USD 2011)</th>
<th>ICER† ($/YLS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Delayed ART</strong></td>
<td>4.3</td>
<td>4,850</td>
</tr>
<tr>
<td><strong>Early ART</strong></td>
<td>4.6</td>
<td>4,830</td>
</tr>
</tbody>
</table>

*Of 5.0 possible years
†Including projected survival losses and cost increases associated with 1\textsuperscript{st}- and 2\textsuperscript{nd}-order transmissions
Results:
Transmission Rates, Lifetime, South Africa

Transmissions/1,000 patients/year

Years since presentation-to-care

- Early ART
- Delayed ART
- No ART
Results:
Cumulative Transmissions, South Africa

- Early ART
- Delayed ART
- No ART
## Results:
Cost-effectiveness, Lifetime, South Africa

<table>
<thead>
<tr>
<th></th>
<th>Life expectancy (years)</th>
<th>Costs (USD 2011)</th>
<th>ICER† ($/YLS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Delayed ART</strong></td>
<td>13.3</td>
<td>15,970</td>
<td>--</td>
</tr>
<tr>
<td><strong>Early ART</strong></td>
<td>15.2</td>
<td>16,320</td>
<td>530</td>
</tr>
</tbody>
</table>

†Including projected survival losses and cost increases associated with 1\textsuperscript{st}- and 2\textsuperscript{nd}-order transmissions

*per capita* GDP for South Africa: $8,100
## Results:
### Cost-effectiveness, India

<table>
<thead>
<tr>
<th></th>
<th>Life expectancy (years)</th>
<th>Costs (USD 2011)</th>
<th>ICER† ($/YLS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>5-year horizon</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed ART</td>
<td>4.4*</td>
<td>1,810</td>
<td>--</td>
</tr>
<tr>
<td>Early ART</td>
<td>4.6*</td>
<td>2,170</td>
<td>1,840</td>
</tr>
<tr>
<td><strong>Lifetime horizon</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed ART</td>
<td>14.2</td>
<td>6,840</td>
<td>--</td>
</tr>
<tr>
<td>Early ART</td>
<td>15.8</td>
<td>7,840</td>
<td>530</td>
</tr>
</tbody>
</table>

*Of 5.0 possible years

per capita GDP for India: $1,400

†Including projected survival losses and cost increases associated with 1st- and 2nd-order transmissions
Different Costs of HIV Care

South Africa, early ART

India, early ART

*“Other care costs” include labs, routine care, OI prophylaxis, and treatment for HIV-related events
## Sensitivity Analyses

<table>
<thead>
<tr>
<th>Treatment and Cost</th>
<th>Transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Initial mean CD4</td>
<td>• Duration of primary relationships</td>
</tr>
<tr>
<td>• ART starting criteria</td>
<td>• Rate of new partner acquisition</td>
</tr>
<tr>
<td>• Loss to follow-up rates</td>
<td>• Acute infection transmissibility</td>
</tr>
<tr>
<td>• ART efficacy</td>
<td>• Acute infection duration</td>
</tr>
<tr>
<td>• Long-term suppressive durability of ART</td>
<td></td>
</tr>
<tr>
<td>• OI incidence rates</td>
<td></td>
</tr>
<tr>
<td>• OI treatment and routine care costs</td>
<td></td>
</tr>
</tbody>
</table>
Sensitivity Analyses: Transmission

• 5-year horizon: early ART greatly reduces transmissions compared to delayed ART
  • *Robust* to changes in all parameters examined

• Lifetime horizon: early ART moderately reduces cumulative transmissions compared to delayed ART
  • *Sensitive* to changes in ART efficacy and long-term durability of suppression
Sensitivity Analyses: Cost-effectiveness

• 5-year horizon: early ART is cost-saving in South Africa and cost-effective in India
  • Sensitive to changes in all treatment- and cost-related parameters: variations made early ART very cost-effective in both settings

• Lifetime horizon: early ART is very cost-effective in both countries
  • Robust to changes in all parameters examined
Limitations

• Specific to the HPTN 052 trial; not necessarily generalizable to non-trial settings, or to individuals not in regular partnerships
• Excluded productivity and other non-medical benefits of transmission prevention
• Transmissions beyond 2\textsuperscript{nd}-order from the index case excluded; likely have a minimal effect on cost-effectiveness results
Conclusions

- In serodiscordant couples – with ART efficacy and behavior data from HPTN 052 – early ART will prevent transmissions in the short-term.
- In South Africa, over the short term, early ART may be cost-saving.
- Early ART for serodiscordant couples is very cost-effective, regardless of country, ART efficacy, or behavior.
The Cost-effectiveness of Treatment as Prevention: Analysis of the HPTN 052 Trial

Rochelle Walensky, MD, MPH
Eric Ross
Nagalingeswaran Kumarasamy, MBBS, PhD
Robin Wood, FCM, MMed, DTM&H
Farzad Noubary, PhD
A. David Paltiel, PhD, MBA
Yoriko Nakamura
Sheela Godbole, MD
Mina Hosseinipour, MD, MPH
James Hakim, MD
Johnstone Kumwenda, FRCP
Joseph Makhema, MB, ChB, FRCP
Lisa Mills, MD, MSc
Ravindre Panchia, BSc, MBBCh

Ian Sanne, MBBCh, FCP, DTM&H
Milton Weinstein, PhD
Elena Losina, PhD
Ken Mayer, MD
Beatriz Grinsztejn, MD, PhD
Jose Pilotto, MD, PhD
Suwat Charayalertsak, MD, DrPH
Breno Santos, MD
Ying Chen, PhD
Lei Wang, PhD
Xin Li, PhD
Marybeth McCauley, MPH
Theresa Gamble, PhD
Susan Eshleman, MD, PhD
Estelle Piwowar-Manning, BS MT

Leslie Cottle, BA
Irving Hoffman, PA, MPH
Joe Eron, MD
Joel Gallant, MD, MPH
Susan Swindells, MD
Taha Taha, MBBS, PhD
Karin Nielsen-Saines, MD, MPH
David Celentano, ScD, MHS
Max Essex, DVM, PhD
Vanessa Elharrar, MD, PhD
David Burns, MD, MPH
George R. Seage III, DSc, MPH
Myron Cohen, MD
Kenneth Freedberg, MD, MSc

Supported by NIAID R01 AI058736 and HPTN 052