Global Progress and Success of HIV/TB Collaborative Activities

Diane V. Havlir, MD
Professor of Medicine
University of California, San Francisco
Chair, WHO HIV/TB Working Group
HIV and TB: A deadly synergy from the start

TB defined AIDS

AIDS shaped TB
Why the slow response early on?

Scientific Gaps
- Diagnosis
- Epidemiology
- Use of ART
  - When to start ART
  - What to start
  - Immune reconstitution
- TB/HIV care delivery

Politics
- TB avoid HIV care
  - Overburdened
- HIV unwilling to treat TB
  - Overburdened
  - Access to TB drugs limited
- Funding silos for HIV and TB
Key Drivers of Progress 2002-2012

- **Policy** - WHO
- **Funding-investment** (PEPFAR, Global Fund)
- **Advocacy** - TAG, TB/HIV Working Group of the Stop TB Partnership
- **Research support** (NIH, ANRS, Gates)
- **Visibility** (IAC, CROI, UNAIDS)
Measuring Success

- **Processes**
  - HIV testing of TB patients
  - TB and septra treatment in HIV+ TB cases
  - ART in HIV+ TB cases
  - TB screening in HIV + patients
  - IPT in HIV + persons
  - ART in HIV + persons

- **Outcomes**
  - TB cases in HIV+ patients— 2002-2012
  - TB deaths in HIV+ patients— 2002-2012
  - Composite estimate of number of lives saved 2002-2012
Estimated lives saved 2005-2010 (with uncertainty interval in blue band)

Cumulative 2005-10 = 910,000 (800,000 – 1,100,000)
30 years later, TB is still the leading cause of death in HIV

<table>
<thead>
<tr>
<th>All forms of TB</th>
<th>Estimated number of cases</th>
<th>Estimated number of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.8 million</td>
<td>1.1 million</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HIV-associated TB</th>
<th>Estimated number of cases</th>
<th>Estimated number of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.1 million</td>
<td>350,000</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Multidrug-resistant TB (MDR-TB)</th>
<th>Estimated number of cases</th>
<th>Estimated number of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>650,000</td>
<td>150,000</td>
<td></td>
</tr>
</tbody>
</table>

Global Burden of TB 2009, WHO/STOP TB
We can do more

- New evidence that ART is extraordinarily effective to prevent TB
- New evidence that IPT can add to ART protection
- New evidence that early ART reduces mortality in TB patients
- New innovations in TB testing
- New TB drugs in the pipeline
- TB vaccines research moving forward

If we wait, the toll will continue to rise and we will have failed to put evidence into action.
If we act now, TB mortality rates will plummet.
Evidence from Malawi – Less TB with more ART

Zacharia, IJTLD, 2011
Clinical Studies show protection across wide CD4 range

<table>
<thead>
<tr>
<th></th>
<th>CD4 &lt;200</th>
<th>CD4: 200-350</th>
<th>CD4&gt;350</th>
</tr>
</thead>
<tbody>
<tr>
<td>Studies (n)</td>
<td>2</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Protection (%)</td>
<td>84</td>
<td>66</td>
<td>57</td>
</tr>
</tbody>
</table>

*Suthar et al 2012, PLoS Medicine*
HPTN 052: 40% reduction in probability of Death, AIDS or TB with immediate treatment

HR: 0.6 [0.4, 0.9], P=0.01

Cohen, NEJM, 2011
# Combined ART and IPT for greater impact

## Studies

<table>
<thead>
<tr>
<th>Studies</th>
<th>IPT alone</th>
<th>ART alone</th>
<th>ART plus IPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>68</td>
<td>52</td>
<td>80</td>
</tr>
<tr>
<td>South Africa</td>
<td>13</td>
<td>64</td>
<td>89</td>
</tr>
<tr>
<td>Botswana</td>
<td>65</td>
<td>67</td>
<td>97</td>
</tr>
</tbody>
</table>


ART has significant impact when combined with IPT
Early ART reduces death (CAMELIA) or death/AIDS (STRIDE, SAPIT)

Study and Fix and HIV/TB Care Cascade

UNDIAGNOSED + LOST TO FOLLOW UP = INADEQUATE CARE

Acquire TB → Diagnosed with TB → Prescribed adequate TB treatment → Begin ART (within 2 weeks of TB diagnosis) → Complete TB regiment + ART Adherence → Transition to long-term HIV care
TB Drug and Vaccine Development – HIV inclusive

New TB Drug Candidates

- TMC-207
- OPC-67683
- PA-824
- SQ-109
- PNU-100480
- AZD5847

Action

- Conduct drug interaction studies with new TB drugs and ART
- Include HIV patients in new TB drug clinical trials and permit ART
One vision: 2022

- Massive scale of ART and IPT
- A POC TB diagnostic test
- TB treatment – entirely new drugs
  - 2 weeks in duration
  - ART compatible
  - Effective for drug sensitive and drug resistant TB
- A TB vaccine in trial for HIV-and HIV+ persons

- HIV/TB cases reduced 10 fold and TB no longer the entry point for HIV diagnosis
- HIV/TB deaths reduced 10 fold
Acknowledgments

Special thanks to:

Haileyesus Getahun
Annabel Baddeley
Rueben Granich
WHO HIV and TB Dept
Tony Fauci
Mark Harrington
Mark Dybul
Moses Kamya
Becky Martinez

All those who care for HIV and TB patients
Global incidence of HIV-positive TB cases 1990-2010