Scaling-up TB/HIV

HIV-TB SOTA
Washington DC
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TB CAP/KNCV
Outline - key areas

- Global TB/HIV epidemiology/progress
- TB/HIV clinical management issues
- TB/HIV scale up – policies / evidence
- Summary / recommendations
Global situation 2007
TB/HIV

**HIV/AIDS burden**
- 33 million with HIV globally
- 2.7 million newly infected in 2007
- 3.4 million on ART
- In high prev. areas, five new HIV infections for every two people newly added on treatment

**TB burden**
- 9.27 million (139 per 100,000);
  - Estimated death 1.77 million (27 per 100,000)
- HIV-associated TB 1.4 million,
  - Estimated death 0.5 million (23% of all HIV deaths)
HIV Prevalence in New TB Cases - 2007
Management of TB/HIV co-infection

- High mortality during first 2 months
  - ART should be initiated earlier (CD4 < 350 cells/mm³), if possible during the intensive phase of TB treatment

- Early ART initiation has challenges
  - High pill burden
  - Drug-drug interaction
  - Toxicity
  - IRIS
Recommended ART for patients with active TB (WHO)

- First-line ART regimen
  - 2 NRTIs plus 1 NNRTI (EFV)
  - Use of triple NRTIs

- Second-line ART: Limited PI options for pts on TB regimen with R.
  - Use of additional amounts of boosted ritonavir with some PIs (SQV/r or LPV/r)
  - Replacement of rifampicin with rifabutin.
Rifabutin

- Added on WHO EML for use in HIV+ TB pts on 2nd line ART - ritonavir-boosted PIs
- Equally safe / effective as rifampicin
- Little effect on PI serum concentration
- Cost-effective in combination with the standard dose of boosted-PIs.
IRIS

- **Paradoxical TB-IRIS**
  - Pts on TB treatment and start ART
  - 1-4 weeks after ART initiation
  - Major risk factors:
    - Low CD4 count, Disseminated TB
    - Short interval between TB treatment and ART

- **Unmasking TB-IRIS (ART Associated TB)**
  - High incidence during first 3 months of ART.
  - Severe pulmonary TB, TB abscess, neurological manifestations...
  - High mortality (>{20%}) during first year of ART.
WHO 2009 TB guidelines - draft
Treatment of TB (TB/HIV)

- New TB (PTB and EP) cases: 2HRZE / 4HR
- 2HRZE/6HE regimen should be phased out
- Optimal dosing is daily throughout the course
- In high INH resistance continuation phase: 4HRE
- All previously treated patients: culture and DST
- Failures with DR likelihood: empiric MDR regimen
Collaborative TB/HIV activities

A. Establish the mechanism for collaboration
   A.1. TB/HIV coordinating bodies
   A.2. HIV surveillance among TB patient
   A.3. TB/HIV joint planning
   A.4. TB/HIV monitoring and evaluation

B. To decrease the burden of TB in PLWHA - 3 I’s
   B.1. Intensified TB case finding (ICF)
   B.2. Isoniazid preventive therapy (IPT)
   B.3. TB infection control in health care and other settings (IC)

C. To decrease the burden of HIV in TB patients
   C.1. HIV testing and counselling
   C.2. HIV preventive methods
   C.3. Cotrimoxazole preventive therapy
   C.4. HIV/AIDS care and support
   C.5. Antiretroviral therapy to TB patients.
## HIV testing and treatment
**Global 2007 (WHO)**

<table>
<thead>
<tr>
<th>Region</th>
<th>TB patients tested for HIV, thousands (%)</th>
<th>% of tested TB patients HIV +</th>
<th>% of identified TB patients on CPT</th>
<th>% of identified TB patients on ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>492 (37)</td>
<td>51</td>
<td>66</td>
<td>29</td>
</tr>
<tr>
<td>AMR</td>
<td>114 (49)</td>
<td>13</td>
<td>36</td>
<td>77*</td>
</tr>
<tr>
<td>EMR</td>
<td>4.2 (1.1)</td>
<td>12</td>
<td>35</td>
<td>65*</td>
</tr>
<tr>
<td>EUR</td>
<td>169 (35)</td>
<td>2.5</td>
<td>52</td>
<td>16</td>
</tr>
<tr>
<td>SEAR</td>
<td>122 (5.5)</td>
<td>15</td>
<td>37</td>
<td>17</td>
</tr>
<tr>
<td>WPR</td>
<td>95 (6.6)</td>
<td>7</td>
<td>45</td>
<td>28</td>
</tr>
<tr>
<td><strong>Global</strong></td>
<td><strong>996 (16)</strong></td>
<td><strong>30</strong></td>
<td><strong>63</strong></td>
<td><strong>30</strong></td>
</tr>
</tbody>
</table>
Implementation of IPT 2005-2007

2005 (10 countries, 26000 cases)

2006 (25 countries, 27000 cases)

2007 (45 countries, 29000 cases)
Scaling up the 3 I’s
ICF, IPT, IC

Cross-cutting challenges (global consensus)

- Policies and guidelines (3 I’s)
- HR capacity - trained staff.
- Weak M&E system – Ownership? R&R?
- Tools/strategy to scale up ICF & IPT
- TB-IC policy and implementation
- Laboratory/Health systems capacity
- Commitment/collaboration NTP/NACP
  - Priority setting
- Integration - centralized ART services vs decentralized TB services
**Intensified TB Case Finding**

- **High CFR for HIV-infected TB pts**
  - 25-50% during TB treatment
  - >50% deaths occur within 2 months

- **Early diagnosis vital**
  - Reduces transmission and case-fatality
  - Improve safety of ART initiation
  - Improve uptake of IPT

- **Challenges:**
  - Diagnosis difficult (AFB, X-ray, clinical)
  - Evidence-based approach to TB screening
WHO policy on TB case finding

- TB screening of PLHIV using at least a simple set of questions
- A referral system between HIV and TB services.
- TB screening among PLHIV at health facilities, contacts, those at high risk for HIV, and congregate settings.
TB preventive therapy

- IPT – effective, safe and feasible (WHO)

- The role of ART & IPT in TB prevention has become more evident

- But concerns
  - Durability of protection
  - Effectiveness of TB screening
  - Drug resistance risk
  - Adherence
**Widespread ART is associated with decline in TB prevalence**

*Cape Town IAS 2009*

<table>
<thead>
<tr>
<th></th>
<th>HIV Negative</th>
<th>HIV Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current Notified</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB</td>
<td>0.7%</td>
<td>0.7%</td>
</tr>
<tr>
<td><strong>Previously</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undiagnosed TB</td>
<td>0.5%</td>
<td>0.4%</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>1.2%</td>
<td>1.1%</td>
</tr>
</tbody>
</table>

*Middelkoop K et al. Widespread ART is associated with decline in TB prevalence.*

5th IAS Conference on HIV Treatment, Pathogenesis and Prevention, Cape Town, abstract WeLBB105, 2009.
TB incidence in HIV infected patients in Rio – impact of ART and IPT

Incidence rate of tuberculosis for primary exposure categories.

<table>
<thead>
<tr>
<th>Exposure category</th>
<th>IR (per 100 PY)</th>
<th>Incidence rate ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naive</td>
<td>4.01 (3.40–4.69)</td>
<td>1.0 (REF)</td>
</tr>
<tr>
<td>ART only</td>
<td>1.90 (1.66–2.17)</td>
<td>0.48 (0.39–0.59)</td>
</tr>
<tr>
<td>IPT only</td>
<td>1.27 (0.41–2.95)</td>
<td>0.32 (0.10–0.76)</td>
</tr>
<tr>
<td>Both</td>
<td>0.80 (0.38–1.47)</td>
<td>0.20 (0.09–0.91)</td>
</tr>
<tr>
<td>Total</td>
<td>2.28 (2.06–2.52)</td>
<td></td>
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</tbody>
</table>

IPT, HAART and TB risk in HIV infected adults in SA – prospective study

Incidence rate of tuberculosis for primary exposure categories.

<table>
<thead>
<tr>
<th>IPT &amp; HAART history</th>
<th>IR (per 100 PY)</th>
<th>Incidence rate ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naive</td>
<td>7.1 (6.2–8.2)</td>
<td>REF</td>
</tr>
<tr>
<td>HAART only</td>
<td>4.6 (3.4–6.2)</td>
<td>0.65 (0.46–0.91)</td>
</tr>
<tr>
<td>IPT only</td>
<td>5.2 (3.4–7.8)</td>
<td>0.73 (0.44–1.13)</td>
</tr>
<tr>
<td>IPT and HAART</td>
<td>1.1 (0.2–7.6)</td>
<td>0.15 (0.004–0.85)</td>
</tr>
</tbody>
</table>

### TB drug susceptibility after IPT

**IAS 2009 - Thibela TB***

<table>
<thead>
<tr>
<th></th>
<th>First episode</th>
<th>Re-treatment episode</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TB after IPT group</td>
<td>Control cluster</td>
</tr>
<tr>
<td><strong>Any INH resistance</strong></td>
<td>7/58 (12.1%)</td>
<td>12/182 (6.6%)</td>
</tr>
<tr>
<td><strong>MDR-TB</strong></td>
<td>1.58 (1.7%)</td>
<td>6/182 (3.3%)</td>
</tr>
</tbody>
</table>

- **TB episode with drug resistance in TB after IPT group not significantly different from those in comparison group**

- **Most TB episodes after IPT have good treatment outcome.**

- **Data don’t support concerns about drug resistance following IPT**

*TB treatment outcomes and drug susceptibility in individuals previously exposed to INH preventive therapy in a high HIV prevalent setting – South Africa. Poster + oral presentation IAS 2009*
ICF and IPT scaling up
HIV/AIDS implementers - ICAP Moz

TB screening for ICF - ART facilities

- Used active TB symptom screening tool.
- Progressive increase in the proportion of HIV patients screened for TB at enrollment:
  - 26% (587/2,219) patients at 5 facilities in Q1 2007
  - 58% (4,614/8,023) patients at 32 facilities in Q4 2008

Conclusion

- Enhancing TB case finding using TB screening at ART facilities is feasible.
- Screening tool improves data collection as well as management and follow-up of co-infected patients.
- Challenge was high number of suspects – sensitivity??
- Recommend - screening tools evaluation and validation
Responding to adherence challenge to IPT
Urban ART facility - ICAP Mozambique

- **IPT implementation**
  - INH made available at general pharmacy
  - ART facility chosen for IPT
  - National TB screening tools used
  - Doctors: prescribe IPT
  - Nurses: focal point + monthly followup
  - First month – only 38% (13/34) went to IPT follow-up, but 57% defaulters returned for ART not IPT

- **Response:**
  - Strengthened counseling of patients pre-IPT and during follow-up
  - “IPT” recorded on patient card and file envelope in addition to the IPT register
  - More healthcare staff involved in patient follow-up – patients better tracked
### Lessons Learnt

- **IPT in ART facility is feasible**
- **Intensive patient counseling improves adherence**
- **If pts return for first follow-up visit, rarely miss further visits**
- **Combining IPT & ART visits can reduce IPT missed visits and delays**

## First 6 months of IPT implementation July – December 2008

<table>
<thead>
<tr>
<th>Month</th>
<th>Patients adherent + follow up</th>
<th>Defaulters to follow-up visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 2</td>
<td>38% (13/34) 62% (21/34)</td>
<td>57% (12/21) to ART visit not IPT visit</td>
</tr>
<tr>
<td>Month 3</td>
<td>78% (42/54) 22% (12/54)</td>
<td>45% with delay</td>
</tr>
<tr>
<td>Month 6</td>
<td>91% (99/109) 9% (10/109)</td>
<td>32% with delay</td>
</tr>
</tbody>
</table>
WHO policy on TB prevention

- HIV services should provide IPT as essential package of care for PLHIV when active tuberculosis is safely excluded for 6-9 months
  - Mandatory CXR (WHO/UNAIDS 1998 policy)
  - PPD skin test is not a requirement
- Rifampicin and pyrazinamide containing regimens are contraindicated
- Information about isoniazid preventive therapy should be made available to all people living with HIV
TB preventive therapy / IPT summary

- ART reduces TB incidence, but TB remains high after ART.
- IPT reduces TB incidence (also during ART) and is cost-effective and safe.
- Strategies to implementation and adherence need to be enhanced.
- New drugs for shorter treatment and probably longer protection?
- New tools for more accurate Dx of latent TB and to exclude active disease.
Global efforts – ongoing

- WHO-CDC meta-analysis: sensitive clinical algorithm to screen TB in PLHIV
- Standardized evidence-based guidelines to TB screening and prevention (IPT) among PLHIV.
- Research on shorter and effective TB preventive regimens. (CREATE…)
- Community case finding strategy for TB (Eg. ZAMBART Project)
**TB-IC policy in health care facilities (WHO 2009)**

- **Organisation and systems**
- **Administrative controls**
  - Triage, cough etiquette, minimise hospital stay
- **Environmental controls**
  - Ventilation (natural and mechanical)
  - UV radiation
  - Health facility design and renovation
- **Personal protective interventions**
  - Respirators
  - Prevention and care package for HIV positive health workers
TB/HIV M&E

- Revised 2009
- Indicators (2004) reduced from 20 to 12
- Including 2 new indicators
TB/HIV research agenda
Cape Town July’09

- Clinical challenges of Dx & Rx of TB in PLHIV:
  - TB IRIS, PI+Rifamycins
  - TB and early mortality in PLHIV

- MDR-TB/HIV
  - Early DR diagnostic strategy and tools
  - Best treatment models – community or hospital
  - TB-IC strategies and tools

- Pediatric TB in HIV infected children
  - Better diagnostic tools for TB in co-infected children
  - Maternal interventions to reduce risk in children
  - Safe and effective vaccine for TB in HIV+ and HIV-

- Preventing TB in PLHIV
  - Impact of ART on TB prevention
  - Community case finding for TB
  - TB-IC effectiveness of strategies
Conclusions/Recommendations

- Scaling up TB care in HIV/AIDS settings a gap
- ICF: priority and gateway to TB care for PLHIV
- IPT: feasible/effective but has to be linked to ICF
- Engage HIV stakeholders to scale up TB/HIV.
- ART scale up key to reducing TB and mortality
- Enhance effectiveness - “evidence based”
- Define benchmarks and targets for countries
- Focus on efficiency and sustainability of programs