Addressing TB in a High HIV Prevalence Setting in Rural South Africa: the 3Is

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Outline

- Background on Tuberculosis and HIV epidemics
- South Africa & Tugela Ferry
- WHO 3Is
- Infection Control
- Intensive Case Finding
- Isoniazid Preventive Therapy
- Future Plans
M.tb & Global Epidemiology

- Mycobacterium tuberculosis
  - TB transmission occurs exclusively via airborne route
    - Coughing, sneezing, talking
    - Inhibited by UV light

- HIV infected patients are particularly susceptible
  - Diminished immune response
  - Complicates diagnosis and treatment
  - Increased morbidity and mortality

- 8.8 million new cases of TB in 2010
- 1.45 million deaths from TB in 2010
- 350,000 deaths in HIV infected patients

WHO, 2011
## Reported TB Cases
### United States, 1982–2010*

<table>
<thead>
<tr>
<th>Year</th>
<th>No.</th>
<th>Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>14,068</td>
<td>4.8</td>
</tr>
<tr>
<td>2006</td>
<td>13,732</td>
<td>4.6</td>
</tr>
<tr>
<td>2007</td>
<td>13,286</td>
<td>4.4</td>
</tr>
<tr>
<td>2008</td>
<td>12,905</td>
<td>4.2</td>
</tr>
<tr>
<td>2009</td>
<td>11,537</td>
<td>3.8</td>
</tr>
<tr>
<td>2010</td>
<td>11,182</td>
<td>3.6</td>
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</tbody>
</table>

*Updated as of July 21, 2011

*MMWR, 2012*
TB and HIV Globally

- 8.8 million incident TB cases (2010)
  - 13% HIV coinfection
    - 80% in Africa
  - 1.4 million deaths
    - 350,000 (25%) deaths among HIV infected
  - HIV status known in 24%
  - 440,000 cases of MDR TB (2008)

- 34 million PLWH (2010)
  - 68% in sub-Saharan Africa
  - 1.8 million deaths
  - 20-30% of eligible receiving antiretroviral therapy (ART)
Drug Resistant TB

- Multiple Drug Resistant (MDR) TB: resistance to isoniazid, rifampin

- XDR TB defined as: MDR plus resistance to a fluoroquinolone, and an injectable agent (amikacin, kanamycin, capreomycin)

- In 2005-06, 53 patients with XDR TB identified in Tugela Ferry, South Africa with 98% mortality within 16 days of obtaining culture
  - Now reported throughout South Africa and from 58 countries
  - South Africa has greatest case load
  - Jeopardizes TB & antiretroviral (ARV) rollouts globally

- Mortality from MDR TB: 73%
- Mortality from XDR TB: 82%

WHO, 2011
Gandhi, Lancet, 2006
Moodley, 2011
Multi Drug Resistant (MDR) TB

Global XDR TB
October 2011
South Africa - TB

- Population: 50,133,000 (2010)
- Incidence: 981 cases per 100,000/year
  - *U.S.: 3.6/100,000 per year*
- 5th in the world in TB cases
- 4th in the world of drug resistant TB cases
- 1st in the world in number of HIV/TB cases (36% of global burden)
- Estimated mortality from TB: 50%
- Diagnosis: AFB is the standard
  - Culture is not widely utilized, but increasing
The HIV and TB epidemics in South Africa
Tugela Ferry, Rural South Africa

- 180,000 traditional Zulu people
- 31% HIV antenatal prevalence
- 1074/100,000 TB incidence
- Extreme poverty
  - high employment (85%)
  - no electricity (70%)
  - no access to clean water (70%)
- Served by 350 bed district hospital
The 3Is

- World Health Organization TB control strategy

1. Infection Control

2. Intensive Case finding (ICF)

3. Isoniazid Preventative Therapy
Infection Control
TB Infection Control

- Nosocomial transmission of TB to patients and healthcare workers is well-described
  - XDR-TB epidemic in Tugela Ferry likely driven by nosocomial transmission
- Community transmission of XDR-TB estimated to predominate by 2012
  - Household contacts are at increased risk: 3.3% of MDR/XDR-TB patients concurrently have active TB
- Airborne Infection Control
  - Administrative Controls
  - Personal Protection
  - Environmental Controls

PROJECT: Effect of natural ventilation at the household level

Joshi et al., PLoS Medicine, 2006
Jarvis, Research in Microbiology, 1993
Basu et al., Proc Nat Academy Sci 2009
Vella et al, IJTL, 2011
WHO Policy on TB Infection Control, 2009
Shenoi et al., CID 2010
Intensive Case Finding
Intensive Case Finding

- Early diagnosis for both improved outcomes and decreased transmission
- Actively looking for TB cases instead of waiting passively for TB cases to come to the health care system

Areas of concern:
- Which tools to diagnose TB?
  - Symptoms only, sputum smear/culture, chest xray
- Which populations to screen?
  - HIV positive patients
- Where to screen them?
  - Inpatient wards, outpatient clinics
- Who will perform screening?
  - Dedicated staff, clinical vs. nonclinical
Intensive Case Finding

- Historical focus on TB case finding among known HIV patient populations
- Novel **Community-Based** Strategy

**Project: Community Based Intensive Case Finding (NIAID K23)**

- In conjunction with local Department of Health
- TB screening effort with integrated HIV services
  - Team of nurses, HIV counselors, field health workers
  - HIV testing with phlebotomy for CD4 cell count
  - TB symptom screen with sputum collection
  - Evaluation of clinical outcomes
- Congregate community sites

<table>
<thead>
<tr>
<th>Municipality events</th>
<th>Pension pay points</th>
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<tbody>
<tr>
<td>Home based care events</td>
<td>Taxi ranks</td>
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<tr>
<td>Prisons</td>
<td>Secondary schools</td>
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<td>Health fairs</td>
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Isoniazid Preventive Therapy (IPT)
Community Based ICF & IPT

- Isoniazid Preventive Therapy is recommended for all HIV+ persons, regardless of:
  - Age (Adults & children)
  - Pregnancy status
  - TB history
  - CD4 count
- Isoniazid daily for 6 months to reduce incidence of TB
  - Durability ~18 months
- Currently only being offered to those already in HIV care (CD4<350)

**Project: Implementation of IPT through ICF**
(CDC award)
Other Future Plans

- Rapid point of care CD4 count assay (NIAID R21)
  - Evaluation in community setting
  - Comparison to standard phlebotomized sample
  - Task shifting evaluation
Summary

- The WHO’s 3Is form a comprehensive platform for combatting TB
- We are developing and implementing community based interventions in all 3 areas:
  - Infection Control
  - Intensive Case Finding
  - Isoniazid Preventive Therapy
- Application at the community level is essential to early detection and interrupting transmission
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Questions?