HIV and TB in Sub-Saharan Africa: Learning from a Catastrophic Collision

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Johns Hopkins University
A global view of HIV infection

38.6 million people [33.4–46.0 million] living with HIV, 2006
Increasing HIV seroprevalence among pregnant women in selected areas of Africa: 1988-2005

Source: US Census Bureau/WHO
### Global Burden of Tuberculosis
#### 2005 WHO Estimates

<table>
<thead>
<tr>
<th></th>
<th>Estimated number of cases</th>
<th>Estimated number of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>All forms of TB</td>
<td>8.8 million</td>
<td>1.6 million</td>
</tr>
<tr>
<td>Multidrug-resistant TB (MDR-TB)</td>
<td>424,000</td>
<td>116,000</td>
</tr>
<tr>
<td>eXtensively drug-resistant TB (XDR-TB)</td>
<td>27,000</td>
<td>16,000</td>
</tr>
</tbody>
</table>
Rising TB incidence in HIV+ gold miners in South Africa

Corbett EL et al. AIDS 2000;14:2759-68
Effect of ART on Risk of TB in HIV+ Patients in the Khayelitsha Cohort

Survival free of subsequent TB diagnosis

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Failed</th>
<th>Pre-ART</th>
<th>Failed</th>
<th>Survival</th>
<th>ART</th>
<th>Failed</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-ART</td>
<td>1333</td>
<td>301</td>
<td>433</td>
<td>84</td>
<td>162</td>
<td>51</td>
<td>180</td>
<td>76 (49-57)</td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ART</td>
<td>1243</td>
<td>165</td>
<td>493</td>
<td>32</td>
<td>187</td>
<td>45</td>
<td>76</td>
<td>85 (82-87)</td>
</tr>
</tbody>
</table>

Cox HR for ART vs pre-ART = 0.41 (0.38 – 0.51)

Logrank p<0.0001

Boulle et al., 9th International workshop in HIV Observational Databases – Budapest, April 2005
TB is the Most Common Opportunistic Infection in Patients Starting HAART

<table>
<thead>
<tr>
<th>Setting</th>
<th>TB Incidence in 90 d after HAART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Developing Countries</td>
<td>25.5/100 person years</td>
</tr>
<tr>
<td>Developed Countries</td>
<td>3/100 person years</td>
</tr>
</tbody>
</table>

M. Egger, CROI 2007
Killer TB tightens fatal grip

Despite indications that SA is in the forefront of infection, health minister tries to put a clamp on news and snubs global conference

By Chire Makwati

Bunumbi Phungulz was the latest victim of extreme drug-resistant \textit{MDR-TB}, a deadly strain of the disease that kills almost everyone who contracts it and is almost impossible to cure.

It was announced at an emergency international conference in Johannesburg this week that XDR-TB is being recorded across South Africa, Lesotho, Mozambique and Swaziland. Yet, while it appears to be a major problem in South Africa, nobody from the health department attended the seminar, having been reportedly ordered by Mantse Tshabalala-Msimang, the health minister, to stay away.

Tuberculosis is airborne and stays in the air for four hours after an infected person has left a room. Research completed this month in Mmabatho and announced by the Medical Research Council shows that multi-drug-resistant tuberculosis (MDR-TB), the parent of XDR-TB, is significantly more infectious than MDR-TB was first believed.

South Africa has the world's second worst rate of MDR-TB, with 0.8% cases 4 years of age and older. MDR-TB treatment is not administratively effective.

Prospect of an epidemic sets medics trembling

By Charlene Smith and Liz Clarke

At just one small hospital in Tugela Ferry, a site of the world's known XDR-TB cases, there are 587 cases of TB in the region. The number of patients is the highest in the country.

Dr Tony Moll of the Department of Health at Tugela Ferry said: "We have seen HIV in our community. We treat in our hospital TB cases of XDR-TB. Up to 80% of new cases are TB co-infected with HIV. A large proportion of deaths were attributed to AIDS, but a recent study from January 2006 to March 2006 shows that 71% of those receiving antiretroviral drugs also died from XDR-TB.

"Worldwide, there are 237 cases of XDR-TB. We picked up 55 cases in our small hospital alone. A child had no prior TB, died in 10 days and there were no prior treatments and 14% were newly infected with drug-resistant strains. We lost two health workers to XDR-TB.

"We can't afford to lose any more medical staff," said Moll. "South African health care is being overwhelmed.

A South African scientist who has supervised the clinical research and this week that "the use of new drugs has been extremely effective. In South Africa, because of the lack of treatment, the mortality rate is very high."

There are no alternative drugs available. According to Professor Louise Libas of the University of Kwazulu-Natal's School of Medicine, South Africa, the plights of the XDR-TB patients are almost hopeless without being diagnosed. All 16 patients are under treatment without having been diagnosed. All 16 patients are under treatment without having been diagnosed. All 16 patients are under treatment without having been diagnosed.

Dr Kunene Moyo, head of the Medical Research Council's TB programme, said: "South Africa is the epicentre of TB and HIV. HIV has the capacity to fast-track TB into an uncurable epidemic. If the epidemic gets out of control, we will not be able to control TB."

Professor Rob Wray, of the University of Johannesburg, said: "It is very difficult to deal with TB patients. It is very difficult to deal with TB patients. It is very difficult to deal with TB patients. It is very difficult to deal with TB patients.

"At the moment, we cannot say it is a "keystone" disease," said Wray. "At the moment, we cannot say it is a "keystone" disease."
A New Scourge: Extensively Drug Resistant TB (XDR)

• XDR TB
  – *Multidrug resistant TB* (MDR TB) is TB resistant to key first line drugs for treating TB (INH/rifampin)
  – *Extensively drug resistant TB* (XDR TB) is MDR TB that is also resistant to 2-3 of the second line drugs for TB (fluoroquinolones, “injectables”)
  – An epidemic of XDR TB has been detected in KwaZulu Natal, South Africa, among HIV+ patients
XDR TB in KwaZulu-Natal, South Africa, 2005-06

• Reports of high TB mortality in pilot HIV treatment program in Tugela Ferry, rural KZN, in 2005
• Cross-sectional study of TB suspects attending rural hospital
• 1539 TB suspects, 544 (35%) diagnosed with TB by culture
• 221/544 (41%) with MDR TB
  • 53/221 (24%, 10% of total) with XDR TB
    – 26 (49%) had no prior TB treatment
    – 44 tested for HIV, all infected
    – 52 (98%) died; 15 were on ARVs
    – Median survival = 16 days
• XDR TB now documented in 28 health care institutions throughout KNZ, ~350 cases

Gandhi et al., Lancet 2006; 368:1575-80; WHO 2007
Survival of Patients with XDR TB in Tugela Ferry, Kwa-Zulu Natal, South Africa

Gandhi et al., Lancet 2006; 368:1575-80
XDR TB: Back to the Magic Mountain?

- How widespread is XDR TB?
- What needs to be done to contain it?
- Can TB be controlled in an era of XDR?
HIV – leading infectious cause of death
TB – 2nd leading infectious cause of death

WHO 2005
Global Control of TB and of HIV
Tales of Failure with Some Rays of Hope

- What does the HIV response have that TB could benefit from?
- What does the TB response have that HIV could benefit from?
- How can HIV and TB control efforts work together to conquer both diseases?
Strengths of the HIV Response
(and what TB is lacking)

- Advocacy and commitment
- Money
  - PEPFAR: $15 billion → $30 billion
  - Global Fund for ATM
- Emphasis on individual needs and rights
- A big pipeline of new drugs, diagnostics and preventatives
- Willingness to innovate
President Mbeki, AZT/Nevirapine for pregnant women with HIV

© PHOTO, BOB HUFF
NIH Infectious Disease Spending
FY05 Actual (dollars in millions)

HIV/AIDS: 2,921
STDs/Herpes: 252
Smallpox: 187
Anthrax: 183
Influenza: 164
Tuberculosis: 158
Pneumonia: 154
Hepatitis C: 121
Malaria: 104

Courtesy of Mark Harrington, Treatment Action Campaign
People in sub-Saharan Africa on antiretroviral treatment as percentage of those in need, 2002–2005

Strengths of the TB Response (and what HIV is lacking)

- Public health approach with strong monitoring and evaluation
- Emphasis on community needs and rights
- Cheap drugs that can cure and prevent disease
- A plan to control the disease
  - STOP-TB Partnership – global buy-in
  - Epidemiologically based
  - Regional subplans
  - Timelines, benchmarks, budgets!
Stopping TB Now
The Stop TB Partnership
2006-2015

Actions for Life
TOWARDS A WORLD FREE OF TUBERCULOSIS

Stop TB Partnership
Total available funding and funding gaps for implementation, 2006-2015

b. Funding and funding gaps

Total needs: US$47.2 billion

- Gap
- Other donor funding
- GFATM
- Domestic funding

Year: 2006-2015
Key Financial Aspects of the Global Plan

- 80% of needs are for country-level activities
  - $44.3 billion
- 40% of country activities are for Africa
  - $19.4 billion
- Total gap is $31 billion, $11 billion for Africa
- TB/HIV gap is $3 billion
Planned achievements: Incidence

a. TB incidence rate by region, 2006-2015

- All regions
- Africa High
- Africa Low
- SE Asia
- E Europe
- E Med
- W Pacific
- L America
TB Strategies That Could Be Applied to HIV Care

- Adherence support
  - DOT for ART (DOT-HAART)
- Contact evaluations for patients who test HIV+ or for those starting HAART
- Registries and surveillance for incidence and outcomes of therapy
- A Global Plan that would control HIV with country benchmarks, timelines and budgets
HIV Strategies That Could Be Applied to TB Care

Resources and Research

• Presidential TB Initiative?
• Improved diagnostic tools
  – Culture for smear-negative and extrapulmonary TB
  – Drug susceptibility testing
• Better drugs, with vigorous drug-development program
  – Individualized regimens, especially for drug-resistant TB
Bringing Science to TB Control – What Technological Advances Could Improve TB Control?

• New TB diagnostics
  – Point of care tests, e.g., dipsticks

• New TB drugs
  – Drugs to shorten treatment
  – Drugs for MDR and XDR TB
  – Drugs that can be given with ARVs

• New TB vaccines
  – A vaccine that actually works!
Bringing Epidemiology to TB Control – What Public Health Strategies Could Improve TB Control?

- **TB diagnostics**
  - Make better use of existing technology
  - Active case finding to identify prevalent cases
- **TB drugs**
  - Use drugs that we know work, e.g., rifampin
  - Use TB preventive therapy
- **Infection control**
  - Prevent TB transmission in clinics and hospitals
Bringing HIV and TB Programs Together

- HIV testing of TB patients
  - In Africa, 50+\% of TB patients have HIV
- Screening for TB in HIV patients
  - 3\% of HIV+ pregnant women have *active* TB
  - 8\% of HIV VCT clients have *active* TB
- TB preventive therapy for HIV patients
  - Preventive therapy works but isn’t used
### Progress of the Global Plan to Stop TB (2006-2015)

<table>
<thead>
<tr>
<th>Activity</th>
<th>2006 Target</th>
<th>2005 Achievement</th>
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<tbody>
<tr>
<td>HIV Testing of TB patients</td>
<td>1.6 million</td>
<td>14%</td>
</tr>
<tr>
<td>TB screening of HIV patients</td>
<td>11 million</td>
<td>1.7%</td>
</tr>
<tr>
<td>INH preventive therapy for HIV patients</td>
<td>1.2 million</td>
<td>2%</td>
</tr>
</tbody>
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*WHO 2007*
Mission
To organize, implement and evaluate novel public health strategies to reduce tuberculosis incidence in populations with high rates of HIV and TB co-infection.

Funded by the Bill and Melinda Gates Foundation
<table>
<thead>
<tr>
<th>Study/Site</th>
<th>Intervention(s)</th>
<th>Design (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thibela TB SA Gold Mines</td>
<td>Mass TB preventive therapy</td>
<td>Cluster randomized trial (~60,000)</td>
</tr>
<tr>
<td>ZAMSTAR Zambia/South Africa</td>
<td>Intensive TB case finding, household interventions</td>
<td>Community randomized trial (~1 million)</td>
</tr>
<tr>
<td>THRio Rio de Janeiro</td>
<td>Preventive therapy and ARVs</td>
<td>Phased implementation trial (15,000)</td>
</tr>
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Thibela TB Study – Preventing TB in Miners
School drama on TB in Western Cape, SA

Community sputum collection depot
## Risk of TB in Brazilian HIV Patients by ART and INH Treatment Status

<table>
<thead>
<tr>
<th>Exposure category</th>
<th>Person-Years</th>
<th>TB Cases</th>
<th>Incidence Rate (per 100 PYs)</th>
<th>Incidence Rate Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Rx</td>
<td>3,865</td>
<td>155</td>
<td>4.01 (3.40-4.69)</td>
<td>1.0</td>
</tr>
<tr>
<td>ART only</td>
<td>11,627</td>
<td>221</td>
<td>1.90 (1.66-2.17)</td>
<td>0.48 (0.39-0.59)</td>
</tr>
<tr>
<td>IPT only</td>
<td>395</td>
<td>5</td>
<td>1.27 (0.41-2.95)</td>
<td>0.32 (0.10-0.76)</td>
</tr>
<tr>
<td>Both</td>
<td>1,253</td>
<td>10</td>
<td>0.80 (0.38-1.47)</td>
<td>0.20 (0.09-0.91)</td>
</tr>
<tr>
<td>Total</td>
<td>17,140</td>
<td>391</td>
<td>2.28 (2.06-2.52)</td>
<td></td>
</tr>
</tbody>
</table>

Golub et al., AIDS 2007
TB & HIV

FIND TB
Undiagnosed TB is common in PLWHIV

TREAT TB
Early treatment saves lives
Treatment reduces transmission

PREVENT TB
Isoniazid preventive therapy (IPT) works

CREATE
Consortium to Respond Effectively to the AIDS TB Epidemic
Implications for the World Bank

- TB remains neglected, under-funded and continues to ravage Africa, especially in PLWHIV
- Investment in TB services, integrated HIV/TB care programs and community level interventions urgently needed
- Operational research to improve the impact of new and existing services important
- Advocacy for changes in policy and practice required if scale up of TB interventions is to succeed
Gates Foundation Press Briefing on TB and HIV at the Bangkok AIDS Conference
July 15, 2004

“The world has made defeating AIDS a top priority. This is a blessing. But TB remains ignored. Today we are calling on the world to recognize that we can’t fight AIDS unless we do much more to fight TB as well.”

-Nelson Mandela