Profile of MDR/XDR-TB in South Africa based on laboratory data

Moscow 26 May 2010

Gerrit Coetzee
Tuberculosis and HIV

TB incidence per 100,000

- India: 168
- China: 100
- South Africa: 600
- Russian Fed.: 119
- Brazil: 60
- Zimbabwe: 601
- Indonesia: 239

HIV prevalence in TB

- India: 5.2%
- China: 0.5%
- South Africa: 58%
- Russian Fed.: 6.2%
- Brazil: 14%
- Zimbabwe: 60%
- Indonesia: 0.8%
TB notification/100k/yr

HIV prevalence in adults

All forms

SS+

TB notification/100k/yr

HIV prevalence in adults

Botswana

Kenya

Malawi

Tanzania

Uganda

Zimbabwe
WHO global TB control 2009

- SA: 5th highest total number incident cases
  (fuelled by HIV epidemic)
- SA: 4th highest total number MDR-TB reported 2007
### Table 3: Number of MDR-TB patients diagnosed by the NHLS by province per year

<table>
<thead>
<tr>
<th>PROVINCE</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>EASTERN CAPE</td>
<td>379</td>
<td>545</td>
<td>836</td>
<td>1,092</td>
<td>1,501</td>
<td>1,858</td>
<td>6,211</td>
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<tr>
<td>FREE STATE</td>
<td>116</td>
<td>151</td>
<td>198</td>
<td>179</td>
<td>381</td>
<td>253</td>
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<td>986</td>
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<td>583</td>
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<td>2,200</td>
<td>2,208</td>
<td>1,573</td>
<td>1,773</td>
<td>9,361</td>
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<td>40</td>
<td>77</td>
<td>91</td>
<td>185</td>
<td>204</td>
<td>656</td>
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<td>MPUMALANGA</td>
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<td>134</td>
<td>139</td>
<td>506</td>
<td>657</td>
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<tr>
<td>NORTH WEST</td>
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<td>397</td>
<td>363</td>
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<td>1,179</td>
<td>1,771</td>
<td>2,220</td>
<td>2,078</td>
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<tr>
<td>Grand Total</td>
<td>3,219</td>
<td>4,120</td>
<td>5,774</td>
<td>7,429</td>
<td>8,198</td>
<td>9,070</td>
<td>37,810</td>
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</table>
Table 4: Number of XDR-TB patients diagnosed by the NHLS by province per year

<table>
<thead>
<tr>
<th>PROVINCE</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>Grand Total</th>
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<tr>
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<td>181</td>
<td>254</td>
<td>1,298</td>
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<tr>
<td>LIMPOPO</td>
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<td>5</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td>17</td>
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<tr>
<td>MPUMALANGA</td>
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<td></td>
</tr>
<tr>
<td>NORTH WEST</td>
<td>1</td>
<td>5</td>
<td>9</td>
<td>4</td>
<td>4</td>
<td>13</td>
<td>36</td>
</tr>
<tr>
<td>NORTHERN CAPE</td>
<td>4</td>
<td>10</td>
<td>3</td>
<td>7</td>
<td>19</td>
<td>40</td>
<td>83</td>
</tr>
<tr>
<td>WESTERN CAPE</td>
<td>12</td>
<td>16</td>
<td>28</td>
<td>42</td>
<td>60</td>
<td>72</td>
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<tr>
<td>Grand Total</td>
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<td>298</td>
<td>464</td>
<td>458</td>
<td>488</td>
<td>594</td>
<td>2,387</td>
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</tbody>
</table>
Number of NEW MDR-TB PATIENTS per year

- 2004: 3000
- 2005: 4000
- 2006: 6000
- 2007: 8000
- 2008: 9000
- 2009: 10000

MDR-TB
XDR-TB
TB TIMEBOMB FOUND

Report in The Star sparks search for woman carrying deadly strain

A s the emergency vehicle drove through the gates of the hospital, a nurse exclaimed, "Thank God they found her!"

On the day that The Star broke the story of a woman in her 30s walking the streets with a highly infectious disease and possibly infecting scores of unsuspecting people, the Gauteng Health Department acted quickly to get her back into a hospital bed.

She had refused treatment on Monday and demanded to be discharged from the Pretoria Hospital in Pretoria. Health officials, accompanied by a police escort and a team from the Health Department's disaster management unit, surrounded the woman's home yesterday.

Clad with protective clothing, face masks and gloves, the team entered the ward 11 but she wasn't been cooperative. The nurses there said she was refusing to put on a mask," a nurse said.

The hospital's chief executive, Edna van Staden, however, told The Star last night: "She is here with us, she is happy and we are happy. That's all I can say."

So determined was the Health Department to stop the woman from spreading the infection that it had legal documents prepared beforehand and a police escort to escort her if she refused to go back to hospital.

The department refused to divulge the woman's identity or where she lived, fearing a backlash from her community.

"We have a legal team in Pretoria who had already prepared the necessary legal documents to get a High Court order, which would have forced the patient to go with the team," van Staden said.

"We had a police escort present,
Cape Flats gangs accused of drug-resistant TB drive-by coughing

LAVENDER HILL
Rapid response to XDR-TB
WHO Global Task Force on XDR-TB, October 2006

• Accelerate access to rapid tests for rifampicin resistance
• Adherence to WHO Drug Resistance Guidelines; improve programme management; access to MDR-TB drugs including DOT; HIV+ cases adequately treated and started on ART
• Implementation of IC measures, especially among HIV+
• Strengthen laboratory capacity to diagnose, manage and survey DR; rapid survey to determine size of XDR-TB problem
• Initiate information sharing strategies that promote prevention, treatment and control of XDR-TB
Deciphering the biology of *Mycobacterium tuberculosis* from the complete genome sequence


*Countless millions of people have died from TB and in the developing world it is a leading cause of death from chronic disease.

The complete genome sequence of the best characterised strain of *M. tuberculosis* has now been determined and analysed in order to improve our understanding of the genetic elements that contribute to the success of this pathogen. This is likely to lead to new targets for drug design.

4,411,529 bp  ≈ 4000 genes
Figure 1. Examples of GenoType MTBDRplus strips (Hain Lifescience, Nehren, Germany). (Lane 1) Mycobacterium tuberculosis, susceptible to isoniazid (INH) and rifampin (RIF). (Lane 2) M. tuberculosis, INH monoresistant (katG S315T1 mutation). (Lane 3) Multidrug-resistant tuberculosis (MDR TB), rpoB S531L mutation and katG S315T2 mutation. (Lane 4) MDR TB rpoB S531L mutation and katG S315T1 and inhA C15T mutations. (Lane 5) M. tuberculosis, RIF monoresistant (mutation in rpoB S50-533 region). (Lane 6) MDR TB, rpoB D-516V and katG S315T1 mutations. (Lane 7) MDR TB, rpoB S531L, and katG S315T2 mutations. (Lane 8) MDR TB, rpoB, D516V, katG S315T1 mutation and inhA mutation at -15/-16. (Lane 9) Uninterpretable result, no M. tuberculosis complex (TUB) band. (Lane 10) Negative control.
Table 5. Performance of MTBDRplus assay in detecting rifampicin, isoniazid and multidrug-resistance in ALL specimens

<table>
<thead>
<tr>
<th></th>
<th>Rifampicin</th>
<th>Isoniazid</th>
<th>Multidrug-resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, % (95% CI)</td>
<td>98.4% (95.3 – 99.7)</td>
<td>91.4% (87.2 – 94.6)</td>
<td>96.5% (92.1 – 98.9)</td>
</tr>
<tr>
<td>Specificity, % (95% CI)</td>
<td>99.1% (98.4 – 99.5)</td>
<td>99.7% (99.3 – 99.9)</td>
<td>99.7% (99.2-99.9)</td>
</tr>
<tr>
<td>Overall accuracy, % (95% CI)</td>
<td>99.0% (98.4 – 99.4)</td>
<td>98.5% (97.8 – 99.0)</td>
<td>99.4% (98.9 – 99.7)</td>
</tr>
<tr>
<td>PPV (95% CI)</td>
<td>0.927 (0.881 – 0.960)</td>
<td>0.982 (0.956 – 0.995)</td>
<td>0.965 (0.921 – 0.989)</td>
</tr>
<tr>
<td>NPV (95% CI)</td>
<td>0.998 (0.994 – 1.000)</td>
<td>0.985 (0.978 – 0.991)</td>
<td>0.997 (0.992 – 0.999)</td>
</tr>
</tbody>
</table>
Development of an Algorithm

• Simplify current algorithms
• Capacity of laboratories to inactivate sputum to PCR friendly state
• Cost to NTP should not increase
• Laboratory capacity/physical structure for LPA PCR
• Available technical skills
• At least provisionally confirm MDR phenotypically
• Technical problems eg amplicon contamination
From: +27836336965
Time: 07/07/06, 13:52:25
Good luck to the Springboks

From: +27824443500
Time: 07/07/06, 13:50:38

Dear TB printer and cellphone. This is a miracle that will improve the management of TB in South Africa and the rest of the first and second worlds.

From: +27836336965
Time: 07/07/06, 13:45:28
<table>
<thead>
<tr>
<th><strong>CLI</strong></th>
<th><strong>PA</strong></th>
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<tbody>
<tr>
<td><strong>NIC</strong></td>
<td><strong>TEN</strong></td>
</tr>
<tr>
<td>Clinic/Hospital/Disa Lab code: ____________________________</td>
<td>Patient Surname: ____________________________________</td>
</tr>
<tr>
<td>Hospital / Clinic number: ____________________________</td>
<td>Patient First Name: ____________________________</td>
</tr>
<tr>
<td>SMS report number: ____________________________</td>
<td>ID number: [ ] [ ] [ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Clinic fax number: ____________________________</td>
<td>Patient Telephone number: ____________________________</td>
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<tr>
<td>Copy results to: ____________________________</td>
<td>Patient Physical Address: ____________________________</td>
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<table>
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<tr>
<th><strong>SPECIMEN DETAILS</strong></th>
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<tbody>
<tr>
<td>Specimen type: [ ] Sputum</td>
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<tr>
<td>Date collected: ____________________________</td>
</tr>
<tr>
<td>Time collected: ____________________________</td>
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<table>
<thead>
<tr>
<th><strong>TB INVESTIGATION</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>TB Suspect:</td>
</tr>
<tr>
<td>No previous treatment [ ]</td>
</tr>
<tr>
<td>Patient currently on treatment for TB [ ]</td>
</tr>
<tr>
<td>Suspected MDR-TB relapse patient [ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>New TB Suspect</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>First visit: Specimen 1&amp;2 (frontloaded) [ ] Specimen 1 only (spot) [ ] Specimen 2 only (spot or overnight) [ ] Day 7 visit: Specimen 3 [ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>New TB Case</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Month 2 visit: End of intensive phase</td>
</tr>
<tr>
<td>Specimen 1&amp;2 (frontloaded) [ ] Specimen 1 only [ ] Specimen 2 only [ ]</td>
</tr>
<tr>
<td>Month 3 visit: Additional month intensive phase</td>
</tr>
<tr>
<td>Specimen 1&amp;2 (frontloaded) [ ] Specimen 1 only [ ] Specimen 2 only [ ]</td>
</tr>
<tr>
<td>Month 5/6 visit: 1 month prior to end of cont phase</td>
</tr>
<tr>
<td>Specimen 1&amp;2 (frontloaded) [ ] Specimen 1 only [ ] Specimen 2 only [ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>New TB Case Previously Treated</strong></th>
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</thead>
<tbody>
<tr>
<td>Month 3 visit: End of intensive phase</td>
</tr>
<tr>
<td>Specimen 1&amp;2 (frontloaded) [ ] Specimen 1 only [ ] Specimen 2 only [ ]</td>
</tr>
<tr>
<td>Month 7 visit: 1 month prior to end of continuation phase</td>
</tr>
<tr>
<td>Specimen 1&amp;2 (frontloaded) [ ] Specimen 1 only [ ] Specimen 2 only [ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>MDR-TB case</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial/Confirmatory MDR facility specimen [ ] Monthly follow-up specimen [ ] Months since treatment initiation [ ]</td>
</tr>
</tbody>
</table>
A Corporate Data Warehouse - why?

- Provide a single, consistent view of data
- Easy, quick access to data
- Improved quality of data
- Enhanced reporting
Approach

• Phase 1
  • Thusano Customer Portal

• Phase 2
  • Laboratory Information
Information Architecture

- **Region 1**: Lab 1, Lab 2, Lab 3, etc. (Pervasive DB)
- **Region 2**: Pervasive DB, Pervasive DB, Pervasive DB
- **Region 3, etc**: Pervasive DB, Pervasive DB

- **LIS Central Repository**: Pervasive (database)

- **Corporate Data Warehouse**: Thusano, Oracle 10G

- **Laboratory Information**: APPS (AR)

- **Oracle Financials**: Oracle 9G

- **Billing**
Laboratory Data

• Data Content
  – All demographic data
  – All test results
  – All drug susceptibility test results
  – Billing information

• Historical Data Load (1997 – 2007)
  Extracted data from Central Repository to flat files
  – Staged all data
  – Loaded data into subject area fact tables
  – Archived original data to persistent tables
  – Archived the flat files
Laboratory Data (Cont..)

- Current Data
  - Extracted daily/intra-daily into staging tables
  - Archive original data to persistent tables
  - Archive data to flat files
  - Load into subject area fact tables
Challenges

• Specimen centric lab system

• Inadequate / inaccurate demographic information

• No patient unique identifier
Patient Identification Process

HISTORY LOAD

Exact Match - Patient Name, Physical Address & DOB

Apply further cleansing (names & addresses) & Apply combination of rules

Visual Check / Update

12 Million TB Specimens

6,1 Million TB Specimens

4.6 Million TB Patients
User Access / Data Security

• Web enabled

• Internal Users
  – Access to data dependent on privileges e.g. TB Programme staff can only see TB data

• External Users
  – Access via secure internet connection (https)
User Interface

• Outbreak Notification via eMail

• Oracle Discoverer
  – Analytical grid reports / graphs

• MicroStrategy
  – Analytical reports/graphics
  – Management Dashboards
  – Integrated Microsoft Office functionality
  – Integrated spatial reports using MapInfo
Outbreak Notification

Isolates have been detected for the following pathogens:

- Gram Negative Diplococcus
- Neisseria Meningitidis
- Neisseria Meningitidis B/Escherichia Coli : Negative
- Bacillus Anthracis
- Gram Negative Cocci
- Gram Negative Diplococcus
- Neisseria Meningitidis
- Salmonella Typhi
- Vibrio Cholerae
- Neisseria Meningitidis A,C,Y,W135
- Positive
- Neisseria Meningitidis A,C,Y,W135
- Negative

CDW Portal Interface
Discoverer Report

### XDR Counts: Eastern Cape

**DTB0006 - XDRCounts**

**Last run:** May 12, 2008 2:19:25 PM GMT+2:00

#### XDR Volumes

**Sensitivity Status:** XDR

<table>
<thead>
<tr>
<th>Province</th>
<th>EASTERN CAPE</th>
<th>FREE STATE</th>
<th>GAUTENG</th>
<th>REGION A</th>
<th>JOHANNESBURG</th>
<th>WEST RAND DM</th>
<th>REGION B</th>
<th>REGION C</th>
<th>KWAZULU-NATAL</th>
<th>LIMPOPO</th>
<th>MPUMALANGA</th>
<th>NC</th>
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<tbody>
<tr>
<td>Health Region</td>
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<td>4</td>
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</table>

Total: 273
Summary Report (MicroStrategy)
Grid/Graph - (MicroStrategy)
Spatial – (MicroStrategy/MapInfo)
Drill – (MicroStrategy/MapInfo)
Future Development

• Enhance reporting for National Programmes

• Enhance spatial reporting

• Rollout to selected external users
THANK YOU