Drug resistance surveillance: global overview and latest development

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World Health Organization

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Drug resistance surveillance in the World Health Assembly

"Surveillance means the systematic ongoing collection, collation and analysis of data for public health purposes and the timely dissemination of public health information for assessment and public health response as necessary"
Source: International Health Regulations (2005), adopted by the 58th World Health Assembly

All Member States to "achieve universal access to diagnosis and treatment of multidrug-resistant and extensively drug-resistant tuberculosis", including by means of "strengthening health information and surveillance systems to ensure detection and monitoring of the epidemiological profile of multidrug-resistant and extensively drug-resistant tuberculosis and monitor achievement in its prevention and control"
Source: 2009 World Health Assembly resolution WHA62.15

Drug resistance surveillance is crucial for planning and monitoring of scale-up of MDR-TB treatment
The Global Project on anti-TB drug resistance surveillance

Objectives:
- To estimate the magnitude of drug resistance
- To determine trends

Main technical Partners:
- Project hosted by WHO
- SRLs, US CDC, The Union, KNCV, ECDC, RIT-Japan

Main donor Agencies:
- USAID, The Global Fund, PEPFAR, (Lilly MDR-TB partnership)
History of the Global Project on anti-TB drug resistance surveillance

1st ed. DRS guidelines

Global Project launched

1994

1st global DRS report

SRLN launched

1997

2nd global DRS report

2000

3rd global DRS report

2003 2004

4th global DRS report

2008

3rd ed. DRS guidelines

2009

M/XDR-TB report

2010

4th ed. DRS guidelines

2012

2012 global TB report

Guidelines for surveillance of drug resistance in tuberculosis

Guidelines for surveillance of drug resistance in tuberculosis

Guidelines for surveillance of drug resistance in tuberculosis

Guidelines for surveillance of drug resistance in tuberculosis

Global Tuberculosis Report 2012
Objectives of drug resistance surveillance

- To estimate the magnitude of drug resistance
- To determine trends
Coverage of surveillance data on anti-TB drug resistance, 1994–2011 - I

- Data available from 135 out of 194 Members States (70%)
  - 63 countries rely on surveillance systems
  - 72 countries rely on periodic surveys

- Trends data available from 71 countries (751 country-year data points)
<table>
<thead>
<tr>
<th>Country</th>
<th>2008</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afghanistan</td>
<td>No data</td>
<td>Completed in 2010</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>No data</td>
<td>Completed in 2011</td>
</tr>
<tr>
<td>Belarus</td>
<td>No data</td>
<td>Completed in 2011</td>
</tr>
<tr>
<td>Bulgaria</td>
<td>No data</td>
<td>Completed in 2010</td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>No data</td>
<td>Completed in 2011</td>
</tr>
<tr>
<td>Nigeria</td>
<td>No data</td>
<td>Completed in 2011</td>
</tr>
<tr>
<td>Pakistan</td>
<td>No data</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Tajikistan</td>
<td>No data</td>
<td>Completed in 2011</td>
</tr>
<tr>
<td>DR Congo</td>
<td>1999</td>
<td>No more recent data</td>
</tr>
<tr>
<td>India</td>
<td>9 States</td>
<td>1 additional State in 2011</td>
</tr>
<tr>
<td>Indonesia</td>
<td>2 Provinces</td>
<td>1 additional Province in 2010</td>
</tr>
<tr>
<td>Russian Federation</td>
<td>4 Oblasts</td>
<td>17 additional Oblasts</td>
</tr>
<tr>
<td>Azerbaijan</td>
<td>2007</td>
<td>Planned for 2013</td>
</tr>
<tr>
<td>Uganda</td>
<td>1997</td>
<td>Completed in 2011</td>
</tr>
<tr>
<td>Ukraine</td>
<td>2006</td>
<td>Planned for 2013</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>2005</td>
<td>Completed in 2011</td>
</tr>
<tr>
<td>Brazil</td>
<td>1996</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Cambodia</td>
<td>2007</td>
<td>No more recent data</td>
</tr>
<tr>
<td>China</td>
<td>2007</td>
<td>Planned for 2013</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>2005</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Kenya</td>
<td>1995</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Mozambique</td>
<td>2007</td>
<td>No more recent data</td>
</tr>
<tr>
<td>Myanmar</td>
<td>2007</td>
<td>Planned for 2013</td>
</tr>
<tr>
<td>Philippines</td>
<td>2004</td>
<td>Ongoing</td>
</tr>
<tr>
<td>South Africa</td>
<td>2002</td>
<td>Ongoing</td>
</tr>
<tr>
<td>Thailand</td>
<td>2006</td>
<td>No more recent data</td>
</tr>
<tr>
<td>UR Tanzania</td>
<td>2007</td>
<td>No more recent data</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>2006</td>
<td>No more recent data</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>1995</td>
<td>Planned for 2013</td>
</tr>
<tr>
<td>Armenia</td>
<td>2007</td>
<td>Moving towards routine surveillance</td>
</tr>
<tr>
<td>Georgia</td>
<td>2007</td>
<td>Routine surveillance</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>2001</td>
<td>Routine surveillance</td>
</tr>
<tr>
<td>Moldova</td>
<td>2006</td>
<td>Routine surveillance</td>
</tr>
<tr>
<td>Estonia</td>
<td>Routine surveillance</td>
<td>Routine surveillance</td>
</tr>
<tr>
<td>Latvia</td>
<td>Routine surveillance</td>
<td>Routine surveillance</td>
</tr>
<tr>
<td>Lithuania</td>
<td>Routine surveillance</td>
<td>Routine surveillance</td>
</tr>
</tbody>
</table>
Proportion of MDR among new TB cases, 1994-2011

Global estimate: 3.7% (2.1-5.2)
Proportion of MDR among previously treated TB cases, 1994-2011

Global estimate: 20% (13-16)
MDR-TB cases estimated to occur among notified pulmonary TB cases, 2011

Global estimate: 310,000 (220,000-400,000)
84 countries reported at least one XDR-TB case by mid-2012

Global estimate: XDR in MDR TB cases: 9.0%; FQL res in MDR-TB cases: 14.5%
Association between MDR and HIV
Overall no statistically significant association

<table>
<thead>
<tr>
<th>Country</th>
<th>year</th>
<th>New cases</th>
<th>Previously treated cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cases with DST results (H +R)</td>
<td>% MDR (95% CI)</td>
</tr>
<tr>
<td>Botswana</td>
<td>2008</td>
<td>924</td>
<td>2.5 (1.5-3.5)</td>
</tr>
<tr>
<td>Mozambique</td>
<td>2007</td>
<td>1102</td>
<td>3.5 (2.2-4.8)</td>
</tr>
<tr>
<td>Namibia</td>
<td>2008</td>
<td>1054</td>
<td>3.8 (2.7-5.1)</td>
</tr>
<tr>
<td>Swaziland</td>
<td>2009</td>
<td>352</td>
<td>7.7 (4.8-10.5)</td>
</tr>
<tr>
<td>Belarus</td>
<td>2011</td>
<td>934</td>
<td>32.3 (29.7-35.6)</td>
</tr>
<tr>
<td>Estonia</td>
<td>2008</td>
<td>272</td>
<td>15.4 (11.4-20.3)</td>
</tr>
<tr>
<td>Latvia</td>
<td>2008</td>
<td>684</td>
<td>12.1 (9.8-14.8)</td>
</tr>
<tr>
<td>Republic of Moldova</td>
<td>2008</td>
<td>1,212</td>
<td>24.8 (22.4-27.4)</td>
</tr>
<tr>
<td>Ukraine</td>
<td>2006</td>
<td>1,003</td>
<td>16.0 (13.7-18.4)</td>
</tr>
</tbody>
</table>
Association between MDR-TB and sex
Overall no statistically significant association

- Higher odds among female TB patients have been previously observed in South Africa and in certain western settings (Netherlands, US, Australia)

- Data from recent surveys in Namibia and Swaziland show higher odds among female TB patients:
  - Namibia - Odds ratio: 1.5 (1.0-2.3)
  - Swaziland - Odds ratio: 1.8 (1.1-2.7)

- Higher odds have been observed among male TB patients in Lithuania, Ukraine (Donetsk)
Association between MDR-TB and age
ORs for MDR-TB in children compared to adults

- Wide range: 0.3 (95% CI 0.0-3.3) to 5.8 (95% CI 0.8-44.0)

- Higher odds of harbouring MDR-TB strains in children compared to adults in Germany, Namibia, South Africa, United Kingdom, United States

- No association between MDR-TB and age in the other countries
Objectives of drug resistance surveillance

- To estimate the magnitude of drug resistance
- To determine trends
Time trends in MDR-TB in selected settings, 1996-2010

- **Rep. of Korea**: 7.4% per year, 10.9% per year
- **Botswana**: 0.3% per year, 19.4% per year
- **Peru**: -3.3% per year, 4.3% per year
- **Russian Federation, Arkhangelsk Oblast**: 0% per year, 3.7% per year
- **Russian Federation, Tomsk Oblast**: -2.4% per year, 2.4% per year
- **Russian Federation, Orel Oblast**: -4.0% per year, 6.6% per year
- **Latvia**: -5.5% per year, -4.9% per year
- **Estonia**: -7.4% per year, -5.5% per year
- **United States**: -5.1% per year, -5.4% per year
Global and regional trends in MDR-TB, 1994-2011

<table>
<thead>
<tr>
<th>WHO REGION</th>
<th>ANNUAL CHANGE</th>
<th>ANNUAL CHANGE LOW ESTIMATE</th>
<th>ANNUAL CHANGE HIGH ESTIMATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>African</td>
<td>5.6%</td>
<td>-7.5%</td>
<td>18.7%</td>
</tr>
<tr>
<td>Americas</td>
<td>0.2%</td>
<td>-17.1%</td>
<td>17.5%</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>-0.7%</td>
<td>-23.5%</td>
<td>22.0%</td>
</tr>
<tr>
<td>Europe</td>
<td>3.5%</td>
<td>-4.8%</td>
<td>11.9%</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>-1.3%</td>
<td>-31.4%</td>
<td>28.8%</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>-4.5%</td>
<td>-12.7%</td>
<td>3.8%</td>
</tr>
<tr>
<td><strong>GLOBAL</strong></td>
<td><strong>-0.3%</strong></td>
<td><strong>-14.7%</strong></td>
<td><strong>14.1%</strong></td>
</tr>
</tbody>
</table>

- Trends data available from 71 countries
- Regional and global trends difficult to predict
Update in current drug resistance surveillance work
Ongoing or ready-to start surveys in 2013

- Azerbaijan
- Bolivia
- Bhutan
- Burkina Faso
- China
- Ethiopia
- India
- Iraq
- Kenya
- Mongolia
- Myanmar
- North Sudan
- Pakistan

- Papua New Guinea
- Philippines
- Rwanda
- South Africa
- Thailand
- Tunisia
- Turkey
- Turkmenistan
- Ukraine
- Venezuela
- Vietnam
- Zimbabwe
Status of DRS in countries attending this workshop

<table>
<thead>
<tr>
<th>Country</th>
<th>Latest survey</th>
<th>Plans for new survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethiopia</td>
<td>2005</td>
<td>Ongoing: enrollment ongoing.</td>
</tr>
<tr>
<td>Gambia</td>
<td>2000</td>
<td>None</td>
</tr>
<tr>
<td>Ghana</td>
<td>None</td>
<td>To start in 2014-2015.</td>
</tr>
<tr>
<td>Kenya</td>
<td>1995</td>
<td>To start in 2013.</td>
</tr>
<tr>
<td>Malawi</td>
<td>2011</td>
<td>Completed. Final results available.</td>
</tr>
<tr>
<td>Nigeria</td>
<td>2011</td>
<td>Completed. Final results available.</td>
</tr>
<tr>
<td>Pakistan</td>
<td>None</td>
<td>Ongoing: enrollment ongoing.</td>
</tr>
<tr>
<td>Rwanda</td>
<td>2005</td>
<td>To start in 2013.</td>
</tr>
<tr>
<td>South Africa</td>
<td>2001</td>
<td>Ongoing: enrollment ongoing.</td>
</tr>
<tr>
<td>Thailand</td>
<td>2006</td>
<td>Ongoing: enrollment completed.</td>
</tr>
<tr>
<td>Uganda</td>
<td>2011</td>
<td>Completed. Final results available.</td>
</tr>
<tr>
<td>Zambia</td>
<td>2010</td>
<td>Completed. Final results to be disseminated.</td>
</tr>
</tbody>
</table>
Surveillance project on resistance to PZA and fluoroquinolones

- All patients enrolled in population-based drug resistance surveys
- 5 countries: Azerbaijan, Bangladesh, Belarus (Minsk Oblast), South Africa (2 provinces), Vietnam
- China and India also engaged
- Both phenotypic and genotypic testing
- To be concluded by mid 2014
- Funded by BMGF
Challenges in anti-TB drug resistance surveillance

Organization/logistics:

- Dedicated human resources at NRL and NTP
- Duration of 1-2 years
- Specimen's transport within the country (from clinics to NRL)
- Specimen's transport outside the country (from NRL to SRL)

Laboratory:

- Capacity for culture and DST
- Workload at NRL

Funding:

- Minimum of US$ 200,000-300,000 for sample size of ≈ 1,200
Future of anti-TB drug resistance surveillance - I

Utilization of molecular technologies to accelerate baseline coverage and measure trends:

- Line Probe Assays: already used in Nigeria & Tanzania

- Xpert MTB/RIF: already used in Pakistan and planned to be used in Cameroon, Eritrea, Ivory Coast, Papua New Guinea, Senegal & Zimbabwe
Future of anti-TB drug resistance surveillance - II

The future technology for drug resistance surveillance:

- High throughput (sequencing technology)
- Include at least RIF, INH, FQL, 2nd-line injectable, PZA
- Hosted at NRL
- Linked to patient's care
THANK YOU

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