Update on drug resistance surveillance

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6th MDR-TB Working Group meeting
Tbilisi, Georgia
20-22 September 2007
Outline

- History and Objectives of the Global Project
- Principles
- Issues in DRS
- New Guidelines
- Coverage and content report 4
- Future
History

- 1994 WHO/IUATLD Global project on drug resistance
- 1994 WHO/IUATLD Supranational Laboratory Network

Objectives

- Implement standardized methods to generate comparable data
- Estimate the magnitude of drug resistance globally
- Determine trends
- Evaluate TB programmes
- Data to inform policy decisions; MDR-TB management, Laboratory
- Regimen evaluation
Principles of Anti-Tuberculosis Drug Resistance Surveillance

1. Sample accurately represents population under study
   - Representative group of new TB cases
   - Representative group of previously treated TB cases
   - Examples: surveillance, 100%, cluster, population proportionate cluster, sentinel

2. Quality assured laboratory results
   - Supranational Laboratory Network:
     26 laboratories, coordinating center, PT and QA

3. Differentiation between new and previously treated cases
   - treatment history
   - clinical records
What does the global project do?

- Provides assistance (directly, through consultant) in survey design, protocol development
- Reviews protocols
- Assists in linking of SRL
- Provides monitoring of survey where necessary
- Assist in data analysis where needed
- Provides tools (guidelines, software)
- Collects and analyzes global data, and produces estimates.
Coverage of Anti-Tuberculosis Drug Resistance Surveillance

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Global Project on Anti-TB Drug Resistance Surveillance

1994-2004 109 settings surveyed in 90 countries

Global Estimate of MDR-TB

424,203
(95% CI, 376,019–620,061) incident cases in 2004
Estimated deaths 110,000
4.3%
(95% CI, 3.8%–6.1%) of all TB cases notified in 2004

Coordinating Centre

- Americas: 5
- African region: 2
- Europe: 11
- South East Asia: 2
- Western Pacific: 5
- Eastern Mediterranean: 1

SRLN
TB SUPRANATIONAL REFERENCE LABORATORY NETWORK
The supranational reference laboratory network - 2007

- 26 Laboratories
- >100 proficiency panels a year
- > 50 countries rechecking, SLD DST for 15
- > 25 laboratories receiving on site training
- Introducing SLD into proficiency testing panels
- All regions plan to expand SRLN
- Regional and sub-regional Global Fund proposals
- SLCS working towards better coordination/integration of SRLN, consultants, other lab networks
Labs participating in proficiency testing for DST of first line drugs in the Russian Federation

- St. Petersburg RIPP
- CTRI RAMS
- RIPP MMA
- RIPP MMA Molecular
- FCS Ministry of Justice
- YaTRI Yakutia
- Obolensk State Scientific Centre
- NTRI Novosibirsk
- Yekaterinburg URIPP
- Penitentiary laboratory

Not yet participating:
- 1 round
- 2 rounds
- 3 rounds
Issues in Anti-TB Drug resistance Surveillance and testing

- Generally under financed (average 20-50k)
- Capacity limits repeated surveys, thus poor trend determination in countries conducting surveys.
- Wide CI's around surveys, trend determination problematic (3-5 year intervals)
- Absence or slow integration of HIV testing and SLD DST, molecular techniques
- Few settings have assessed sm- population
- Surveillance systems changing over time, shifting to diagnostic reporting in some settings
- Laboratory capacity, safety and performance largest obstacle
Issues in Anti-TB Drug resistance Surveillance

- No assessment of private sector or chronic pool.
- Representative sample sizes of retreatment cases difficult to achieve and difficult to compare between countries
- Better differentiation of sub-categories of retreatment
- Classification of patients prone to errors requires validation in all settings
- Weaknesses in rechecking in some settings because of shipment and customs issues.
- Absence of IRB or ethical review board
- No capacity to determine true acquired resistance
Successes of the Global project

- Comparable drug resistance data from 100+ countries
- Robust data on new cases
- Designed an international EQA system for DST
- Has identified high prevalence *emergency settings
- Strengthened lab networks
- Strengthened transport networks
- Good platform for OR (transport, classification, outcome)
- Useful preparatory exercise for MDR-TB treatment programmes
Interim guidelines

- Flexible approaches to provide more programmatically relevant data
  - Routine culture/DST to all cases gold standard
  - Periodic surveys among new cases, routine culture/DST to retreatment
- Larger samples for new and retreatment
- Retreatment by subcategory (relapse, RAD, RAF, retreatment other)
- Stronger QA of patient classification, and data management
- Consideration of ethical issues (treatment, testing)
- Inclusion of HIV where possible (primarily for patient benefit)
- SLD DST on all R resistant isolates at a minimum (at SRL in most places)
- Stronger section on transport
- Supplement surveys with
  - surveys of risk populations
  - longer term epidemiological studies (explore sentinel surveys)
  - use of molecular methods (under pilot)
  - platform for OR
- Better financing of survey protocols and work done at SRLs
- Analysis done in conjunction with notification and other programmatic data (better retreatment data)
Two models

Continuous surveillance (routine diagnosis)
- Conduct periodic surveys to verify routine data collection.
- Focus on QA of lab, and standardized classification and interpretation.
- Ultimately goal is to monitor drug resistance through routine diagnostic DST data.
- In EUR routine MDR-TB data reported to WHO already correlate well with survey data.

Survey data
- 100% retreatment, periodic surveys among new
- Sentinel, or open cluster
- Molecular
### 4th report coverage

<table>
<thead>
<tr>
<th>Region</th>
<th>4th settings</th>
<th>Not previously reported</th>
<th>1994-2007</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>5 settings (5 countries)</td>
<td>Ethiopia, Madagascar*, Rwanda, Senegal, Tanzania*</td>
<td>31 settings (23 countries)</td>
</tr>
<tr>
<td>AMR</td>
<td>11 settings (11 countries)</td>
<td>Costa Rica, Guatemala (final), Paraguay</td>
<td>21 settings (21 countries)</td>
</tr>
<tr>
<td>EMR</td>
<td>7 settings (7 countries)</td>
<td>Syria, Lebanon, Jordan</td>
<td>9 settings (9 countries)</td>
</tr>
<tr>
<td>EUR</td>
<td>41 settings (37 countries)</td>
<td>Georgia, Armenia, Azerbaijan (Baku), Spain (Aragon), Ukraine (Donetsk), Russian Federation Archangelsk, Uzbekistan (Tashkent)</td>
<td>45 settings (39 countries)</td>
</tr>
<tr>
<td>SEAR</td>
<td>9 settings (6 countries)</td>
<td>India (Gujarat state), India (3 districts) Indonesia (Miimeka province), Myanmar,Sri Lanka</td>
<td>14 settings (6 countries)</td>
</tr>
<tr>
<td>WPR</td>
<td>19 (16 countries)</td>
<td>China (Beijing, Shanghai, Inner Mongolia, Heilongjiang, Macao SAR), Philippines, Fiji, Vanuatu,Guam, Northern Marianas, and Solomon islands.</td>
<td>27 settings (18 countries)</td>
</tr>
<tr>
<td>Total</td>
<td>92 settings (86 countries)</td>
<td>37 settings (29 countries)</td>
<td>147 (116 countries)</td>
</tr>
</tbody>
</table>
**Expected in the 4th report**

<table>
<thead>
<tr>
<th><strong>Trends (3+ data points)</strong></th>
<th>All countries with routine culture DST (Nepal, Thailand, Russian oblasts, Cuba, Poland, Korea, Uruguay)</th>
<th>52 settings (49 countries with 3 or more data points)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV</strong></td>
<td>Argentina, Cuba, Honduras, Barcelona, Archangelsk RF, Tomsk RF, Donetsk, Ukraine, Uruguay, Costa Rica.</td>
<td>9 settings</td>
</tr>
<tr>
<td><strong>SLD DST</strong></td>
<td>Rwanda, Argentina, US, Canada, Latvia, Armenia, Georgia, Azerbaijan, 2 Russian oblasts, China Macao SAR, Hong Kong SAR, Japan, Australia, Singapore, Ukraine Donetsk (partial), (Gujarat, India, Thailand) (dataset from EuroTB 10 countries)</td>
<td>~17 (+10 EuroTB) Not in time: Ethiopia, Senegal, Madagascar, Morocco, Yemen, Nepal, Sri Lanka, Tanzania, Philippines, Tashkent, Uzbekistan</td>
</tr>
<tr>
<td><strong>Retreatment by sub-category</strong></td>
<td>Senegal, Honduras, Cuba, Syria, 1 oblast Russia, Georgia, Nepal, Macao SAR, Morocco, Gujarat, India (?)</td>
<td>~10 settings</td>
</tr>
<tr>
<td><strong>Prison sector</strong></td>
<td>Azerbaijan, Armenia, Georgia, Cuba</td>
<td>4 settings</td>
</tr>
</tbody>
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Future

- Meeting in 2008 to review current methods
- Development of a variety of protocols
- Pilot new methods
- Scale up of and access to culture/DST and/or molecular methods
- Increased incorporation of HIV testing and SLD DST, and OR built in
- Better link to treatment programmes
Acknowledgements

- Participating National TB programmes
- Participating laboratories
- EuroTB
- Supranational Reference Laboratories
- Coordinating SRL, Antwerp, Belgium (UNION)
- Subgroup on Laboratory Strengthening
- Partners assisting design and implementation (KNCV, CDC, JATA, MSF)
- WHO regional and country offices
- Donors and financial support (Eli Lilly, USAID, Global Fund, TBCAP)