Drug resistance surveillance: current status and latest innovations

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Objectives:

- To estimate the magnitude of drug resistance
- To determine trends in drug resistance over time

Main technical partners:

- Project hosted by WHO
- Supranational TB Reference Laboratories (SRLs), The Union, US CDC, KNCV, ECDC, RIT-Japan

Main donor Agencies:

- USAID, The Global Fund, PEPFAR, BMGF
1. Coverage of surveillance
2. Latest surveillance data
3. Visions for the future
1. Coverage of Surveillance
The Global Project, 1994-2014

- Global Project and SRL network launched
- 1st global DRS report
- 2nd global DRS report
- 3rd global DRS report
- 4th global DRS report
- M/XDR-TB report
- 2014 TB report

- 1994
- 1st ed. DRS guidelines
- 1997
- 1997
- 2nd ed. DRS guidelines
- 2000
- 2000
- 3rd ed. DRS guidelines
- 2003
- 2004
- 4th ed. DRS guidelines
- 2008
- 2009
- 2010
- 2010
- 5th ed. DRS guidelines under development
- 2014
Progress in global coverage of surveillance data on drug resistance, 1994-2014
Progress in global coverage of surveillance data on drug resistance, 1994-2014
Number of national drug resistance surveillance country-year data points, 1994-2014
2. Latest surveillance data
Current MDR-TB situation

**THE MDR-TB SITUATION**

- **480,000** people estimated to have developed MDR-TB in 2013
- **210,000** people died due to MDR-TB in 2013
- **3.5%** proportion of new cases with MDR-TB unchanged in recent years but some countries have serious epidemics
Proportion of new TB cases with MDR-TB, 2014

GLOBAL: 3.5%
EURO: 14%
Proportion of previously treated TB cases with MDR-TB, 2014

GLOBAL: 20.5%
EURO: 44%
Proportion of all TB cases with resistance to isoniazid but not rifampicin, 1994-2014

9.5%
Countries that notified at least one case of XDR-TB by the end of 2013

Proportion of MDR-TB cases with XDR-TB = 9%
3. Visions for the future
Limitations of surveys

■ Difficult to repeat at regular intervals
  Limited understanding of time trends worldwide

■ Surveys are mostly targeting NTP facilities
  Limited understanding of drug resistance in the private health sector

■ Drug susceptibility testing limited to rifampicin and isoniazid, plus fluoroquinolones and injectable agents on MDR-strains
  Not useful for investigating feasibility of introducing new drugs and regimens
Next steps for strengthening surveillance

- Incorporating molecular technologies into surveys, including Xpert MTB/RIF and high throughput sequencing technologies
- Expanding the range of drugs to be tested
- Establishing sentinel surveillance systems for monitoring trends
UPDATE: 5th edition of WHO guidelines, 2014
Xpert MTB/RIF in surveys

- Reduces logistic challenges for sample transport
- Reduces demands on laboratory (expertise and time)
- Limitation: depending on testing algorithm, cannot investigate other resistance patterns not associated with rifampicin resistance
- Used in surveys in Pakistan, Papua New Guinea, Senegal
- Planned for DR Congo, Eritrea, Ivory Coast, Zimbabwe
Xpert MTB/RIF in surveys

Conventional

1200-1500 cultures

Xpert MTB/RIF

100 cultures
Surveillance systems for trends over time

Indications
- For countries with recent national survey data (3-5yrs)
- To monitor trends in resistance over time

Approach
- Sentinel sites chosen purposively, unlike national surveys
- Testing of consecutive patients during a given time period until target sample size is reached
- Repeated annually
- Rapid molecular technologies

Limitations
- Data are **not** nationally representative
- Data cannot be extrapolated to other areas
Conclusions

- Require more country-specific drug resistance surveillance data (more countries, more drugs, more data points)

- Need to trial new approaches to surveillance in drug resistance (particularly to assess time trends and burden of drug resistance in the private health sector)

- Increase reliance on molecular technologies