MDR-TB : key issues

WHO Civil Society Task Force Seminar on TB
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What forms of drug-resistant TB?

- **Rifampicin-resistant TB (RR-TB)** = TB bacteria that are resistant to at least rifampicin, one of the most effective anti-TB medicines. These patients need second-line treatment similar to MDR-TB patients.

- **Multidrug-resistant TB (MDR-TB)** = TB bacteria that are resistant to at least isoniazid and rifampicin, the two most effective anti-TB drugs. These patients need second-line treatment.

- **Extensively drug-resistant TB (XDR-TB)** = MDR-TB that is also resistant to any fluoroquinolone and any of the second-line anti-TB injectable agents (i.e. amikacin, kanamycin or capreomycin). These patients have much more limited options for curative treatment.
RR-TB and non RR-TB patients

Resolve + Incident RR (acquired)

Deaths non RR RR

Prevalent TB

Incident TB non RR RR

non RR RR

on tx
The global TB situation

### Estimated incidence, 2014

- **All forms of TB**: 9.6 million (9.1–10.0 million)
- **HIV-associated TB**: 1.2 million (1.0–1.3 million)
- **Multidrug-resistant TB**: 480,000 (360,000–600,000)

### Estimated number of deaths, 2014

- **All forms of TB**: 1.1 million* (1.0–1.3 million)
- **HIV-associated TB**: 390,000 (350,000–430,000)
- **Multidrug-resistant TB**: 190,000 (120,000–260,000)

* Excluding deaths attributed to HIV/TB

Source: WHO Global Tuberculosis Report 2015
Why is rifampicin resistance (RR-TB) important?

Global treatment outcomes in three groups of TB patients

- **New TB cases, 2011 [2610821]**
  - Cured: 90%
  - Treatment completed: 8%
  - Died: 2%
  - Treatment failed: 1%
  - Loss to follow up: 0%
  - Not evaluated: 0%

- **Retreatment TB cases, 2011 [601904]**
  - Cured: 85%
  - Treatment completed: 10%
  - Died: 3%
  - Treatment failed: 1%
  - Loss to follow up: 0%
  - Not evaluated: 0%

- **MDR-TB cases, 2010 [34281]**
  - Cured: 80%
  - Treatment completed: 15%
  - Died: 5%
  - Treatment failed: 1%
  - Loss to follow up: 0%
  - Not evaluated: 0%
Why is rifampicin resistance (RR-TB) important?

Typical regimen duration in months

- not RR-TB, "first line"
- RR-TB, shorter regimen
- RR-TB, longer regimens
Why is rifampicin resistance (RR-TB) important?

Non RR-TB -> R, H, E, Z

RR-TB ->

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<thead>
<tr>
<th>GROUP A</th>
<th>Fluoroquinolones</th>
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<tr>
<td></td>
<td>Levofloxacin</td>
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<td>Moxifloxacin</td>
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<td>Gatifloxacin</td>
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<th>GROUP B</th>
<th>Second-line injectable agents</th>
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<tr>
<td></td>
<td>Amikacin</td>
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<td></td>
<td>Capreomycin</td>
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<td>Kanamycin</td>
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<td>(Streptomycin)</td>
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<th>GROUP C</th>
<th>Other Core Second-line Agents</th>
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<tr>
<td></td>
<td>Ethionamide / Prothionamide</td>
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<td>Cycloserine / Terizidone</td>
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<td>Linezolid</td>
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<td>Clofazimine</td>
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<th>GROUP D</th>
<th>Add-on agents (not core MDR-TB regimen components)</th>
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- Global Project launched
- SRL network launched
- 1st ed. DRS guidelines
- 2nd ed. DRS guidelines
- 3rd ed. DRS guidelines
- 4th ed. DRS guidelines
- 5th ed. DRS guidelines
- 1994
- 1997
- 2000
- 2003
- 2004
- 2008
- 2009
- 2010
- 2015
Progress in global coverage of surveillance data on drug resistance, 1994-2015
Percentage of new TB cases with MDR-TB

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Percentage of previously treated TB cases with MDR-TB

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MDR-TB cases estimated to occur among notified pulmonary TB cases, 2014
Countries that notified at least one case of XDR-TB

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DR-TB RESPONSE
End TB Strategy

Pillars & Principles

- Integrated, patient-centered TB care and prevention
- Bold policies and supportive systems
- Intensified research and innovation

- Government stewardship and accountability, with monitoring and evaluation
- Building a strong coalition with civil society and communities
- Protecting and promoting human rights, ethics and equity
- Adaptation of the strategy and targets at country level, with global collaboration
WHO guidance on treatment & management of drug-resistant TB, 1996-2016
RR-/MDR-TB notification and enrolment

MDR-TB cases and additional rifampicin-resistant TB cases detected (orange) compared with TB cases enrolled on MDR-TB treatment (turquoise), global trend and trend in 30 high MDR-TB burden countries, 2009–2014.
Outcomes of XDR-TB treatment

XDR-TB cohorts 2012, by WHO Region*

*number of cases observed shown next to the bars

*World Health Organization (WHO) Programme

END TB
Number of **bedaquiline** treatments* delivered for M/XDR–TB as part of expanded access, compassionate use or normal programmatic use by end 2015

white=no information

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<tr>
<th>Treatments</th>
<th>&lt;4</th>
<th>4–39</th>
<th>40–199</th>
<th>200–799</th>
<th>800+</th>
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WHO Member States reporting use = 69

High MDR–TB burden countries reporting use = 22

*Data provided to WHO by Janssen in March 2016; one treatment usually corresponds to one patient

**Source:** WHO/GTB (as on 6 June 2016; provisional data subject to change)

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Countries that had used delamanid for the treatment of M/XDR–TB as part of expanded access, compassionate use or under normal programmatic conditions by the end of 2015

white=no information

Countries/settings reporting use = 38
High MDR–TB burden countries reporting use = 15
*Data provided to WHO by Otsuka in April 2016
(provisional data subject to change)

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Even if most TB patients in the world are not drug-resistant, the burden of MDR-TB in the world poses a formidable challenge to the prospect of controlling TB. More resources need to be committed in future to ensure that targets are reached.

Coverage of DST for TB patients remains low and thus a minority of drug-resistant TB patients are detected and notified. Information remains incomplete.

Progress has been achieved in recent years in scaling-up MDR-TB care. However, in 2014, detection of MDR-TB appears not to have increased globally compared with 2013 and less than 40% of the estimated cases eligible for MDR-TB treatment among known TB patients were started on treatment.
Conclusions (2)

- In certain countries, a sizeable gap has developed between diagnostic and enrolment capacity, leading to waiting lists for MDR-TB treatment.
- Treatment of MDR-TB is complicated and less effective than for drug-susceptible TB. Countries need to place more MDR-TB patients on adequate treatment.
- Country reporting of surveillance and monitoring data continues to improve. However, efforts need to take better advantage of available information & communication technologies to collect data efficiently and provide managers with indicators for timely action.
Patient care
Surveillance
Programme management
eLearning
FIVE PRIORITY ACTIONS TO ADDRESS THE GLOBAL MDR-TB CRISIS

1. Prevent the development of drug resistance through high quality treatment of drug-susceptible TB
2. Expand rapid testing and detection of drug-resistant TB cases
3. Provide immediate access to effective treatment and proper care
4. Prevent transmission through infection control
5. Increase political commitment with financing