TB burden and treatment guidelines

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Global TB programme, WHO/HQ

Meeting of manufacturers
Copenhagen, Denmark, 23-26 November 2015
Outline

• Latest epidemiological data
• Global programme achievements
• Treatment guidelines recommendations for adults and children
• Future updates of guidelines and needs for more generic formulations
The Global Burden of TB - 2014

Estimated number of cases

- All forms of TB: 9.6 million
  - 1 million Children
  - 3.2 million women
  - 5.4 million men

- HIV-associated TB: 1.2 million (12%)

- Multidrug-resistant TB: 480,000

Estimated number of deaths

- All forms of TB: 1.5 million*
  - 140,000 children
  - 480,000 women
  - 890,000 men

- HIV-associated TB: 390,000

- Multidrug-resistant TB: 210,000

Source: WHO Global TB Report 2015

* Including deaths attributed to HIV/TB
Estimated TB incidence rates, 2014

- South-East Asia: 42%
- Western Pacific: 17%
- Africa: 28%
- E. Mediterranean: 8%
- Europe: 4%
- Americas: 3%

23% in India
10% each: Indonesia, China
### Adult TB regional estimates (2014)

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Estimated incidence</th>
<th>Estimated inc. low</th>
<th>Estimated inc. high</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>2 700,000</td>
<td>2 400,000</td>
<td>3 000,000</td>
</tr>
<tr>
<td>AMR</td>
<td>280,000</td>
<td>270,000</td>
<td>290,000</td>
</tr>
<tr>
<td>EMR</td>
<td>740,000</td>
<td>610,000</td>
<td>890,000</td>
</tr>
<tr>
<td>EUR</td>
<td>340,000</td>
<td>320,000</td>
<td>350,000</td>
</tr>
<tr>
<td>SEA</td>
<td>4 000,000</td>
<td>3 700,000</td>
<td>4 400,000</td>
</tr>
<tr>
<td>WPR</td>
<td>1 600,000</td>
<td>1 500,000</td>
<td>1 600,000</td>
</tr>
<tr>
<td>World</td>
<td>9 600,000</td>
<td>9 100,000</td>
<td>10 000,000</td>
</tr>
</tbody>
</table>
## Child TB regional estimates (2014)

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Estimated incidence</th>
<th>Estimated inc. low</th>
<th>Estimated inc. high</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>330,000</td>
<td>290,000</td>
<td>370,000</td>
</tr>
<tr>
<td>AMR</td>
<td>27,000</td>
<td>25,000</td>
<td>29,000</td>
</tr>
<tr>
<td>EMR</td>
<td>80,000</td>
<td>64,000</td>
<td>97,000</td>
</tr>
<tr>
<td>EUR</td>
<td>31,000</td>
<td>28,000</td>
<td>34,000</td>
</tr>
<tr>
<td>SEA</td>
<td>340,000</td>
<td>310,000</td>
<td>370,000</td>
</tr>
<tr>
<td>WPR</td>
<td>150,000</td>
<td>130,000</td>
<td>170,000</td>
</tr>
<tr>
<td><strong>World</strong></td>
<td><strong>1 000,000</strong></td>
<td><strong>900,000</strong></td>
<td><strong>1 100,000</strong></td>
</tr>
</tbody>
</table>
43 million lives saved
BETWEEN 2000 AND 2014

TB = 43m
HIV = 7.8m
Malaria = 7m

Ref: Global TB Control Report
2015
47% drop in TB mortality SINCE 1990

Most of the improvement is since 2000

47% decline since 1990

Rate per 100,000 population
TB/HIV global snapshot

Estimated HIV prevalence in new TB cases, 2014

74% of TB/HIV cases in Africa

Other co-morbidities emerging in other regions
MDR-TB: 3% of new TB cases globally

India, China, Russia, Pakistan and Ukraine have 62% of all MDR-TB cases
MDR-TB remains a public health crisis

480,000

Cases of MDR-TB estimated among TB patients reported by national TB programmes in 2013.

123,000

Patients reported with MDR-TB (136,000 out of 300,000) were detected in 2013.

111,000

People with TB were started on second-line treatment for MDR-TB in 2013, leaving many patients in waiting lists for treatment.

50%

Of MDR-TB patients globally had a successful treatment outcome.
Desired decline in global TB incidence rates to reach the 2035 targets

Optimize use of current & new tools emerging from pipeline, pursue universal health coverage and social protection

Introduce new tools: a vaccine, new drugs & treatment regimens for treatment of active TB disease and latent TB infection, and a point-of-care test

Current global trend: -1.5%/year

-10%/year by 2025

-5%/year

-17%/year
Impact: Estimated TB incidence rates (1990-2013)

## Progress at regional level

### Incidence rate falling

### Prevalence 50% reduction

### Mortality 50% reduction

<table>
<thead>
<tr>
<th>WHO Region</th>
<th>Incidence rate falling</th>
<th>Prevalence 50% reduction</th>
<th>Mortality 50% reduction</th>
<th>Case detection (%)</th>
<th>Treatment success (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>Target met</td>
<td>Target met</td>
<td>Target met</td>
<td>48</td>
<td>79</td>
</tr>
<tr>
<td>Americas</td>
<td>Target met</td>
<td>Target met</td>
<td>Target met</td>
<td>77</td>
<td>75</td>
</tr>
<tr>
<td>E Mediterranean</td>
<td>Target met</td>
<td>Target met</td>
<td>Target met</td>
<td>61</td>
<td>91</td>
</tr>
<tr>
<td>Europe</td>
<td>Target met</td>
<td>Target met</td>
<td>Target met</td>
<td>79</td>
<td>75</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>Target met</td>
<td>Target met</td>
<td>Target met</td>
<td>62</td>
<td>88</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>Target met</td>
<td>Target met</td>
<td>Target met</td>
<td>85</td>
<td>92</td>
</tr>
<tr>
<td>Global</td>
<td>Target met</td>
<td>Almost met</td>
<td>Not met</td>
<td>63%</td>
<td>86%</td>
</tr>
</tbody>
</table>

### Notes

1. Incidence falling in all 6 regions
2. All 3 "impact" targets already met: AMR, WPR and SEAR
3. Off track for prevalence and mortality: Africa, Europe
4. Treatment success needs improvement in EUR and AMR
Current treatment guidelines (adults and children)
WHO recommended regimens for treatment of TB

<table>
<thead>
<tr>
<th>Type of TB</th>
<th>Intensive phase treatment</th>
<th>Continuation phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients presumed or known to have drug-susceptible TB</td>
<td>2 months of HRZE (adults)</td>
<td>4 months of HR</td>
</tr>
<tr>
<td></td>
<td>2 months of HRZ (most children)</td>
<td></td>
</tr>
<tr>
<td>Confirmed or high likelihood of multidrug-resistant TB</td>
<td>8 months, for most of patients, of four second-line anti-TB drugs likely to be effective (including a parenteral agent), as well as pyrazinamide,</td>
<td>Completion of 20 months of total treatment duration with at least three anti-TB drugs likely to be effective as well as pyrazinamide</td>
</tr>
</tbody>
</table>

Previously recommended cat.II regimen with an addition of Streptomycin in the intensive phase is **no longer recommended by WHO**.
Anti TB drugs for treatment of DR-TB (including MDR-TB and XDR-TB)

<table>
<thead>
<tr>
<th>Group name</th>
<th>Anti-TB agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1: 1\textsuperscript{st} line oral</td>
<td>Isoniazid, Rifampicin, Ethambutol, Pyrazinamide, Rifabutine, Rifapentine</td>
</tr>
<tr>
<td>Group 2: Injectables</td>
<td>Streptomycin, Kanamycin, Amikacin, Capreomycin</td>
</tr>
<tr>
<td>Group 3 Fluoroquinolones</td>
<td>Levofloxacin, Moxifloxacin, Gatifloxacin</td>
</tr>
<tr>
<td>Group 4 Oral bacteriostatic 2\textsuperscript{nd} line</td>
<td>Ethionamide, Prothionamide, Cycloserine, Terizidone, PAS, PAS-Na</td>
</tr>
<tr>
<td>Group 5: Other with limited efficacy/or long term safety (including new agents)</td>
<td>Bedaquiline, Delamanid, Linezolid, Clofazimine, Amoxicillin/clavulanate, Imipenem/cilastatin, Meropenem, High-dose isoniazid, Thioacetazone, Clarithromycin</td>
</tr>
</tbody>
</table>
Short MDR-TB regimen

• An observational study in Bangladesh showed much better rates of treatment success using regimens having a duration of 12 months or less*

• WHO is advising countries to introduce short MDR-TB treatment regimens only in projects that adhere to the following criteria:
  – approval of the project by a national ethics review committee, ahead of any patient enrolment;
  – delivery of treatment under operational research conditions following international standards (including Good Clinical Practice and safety monitoring), with the objective of assessing the effectiveness and safety of these regimens;
  – monitoring of the MDR-TB programme using short regimens, and its corresponding research project, by an independent monitoring board set up by and reporting to WHO.


Treatment of latent TB infection
Currently recommended treatment regimens

- Treatment of LTBI (PLHIV, children < 5 years)
  - 6 months of Isoniazid
  - 9 months of Isoniazid
  - 3 months weekly rifapentine + isoniazid (12 dose regimen)
  - 3-4 months isoniazid + rifampicin
  - 3-4 months rifampicin alone

Contacts with MDR-TB

- Strict clinical observation and close monitoring for the development of active TB disease for at least two years is preferred over the provision of preventive treatment for contacts with MDR-TB cases.
Rational introduction of new drugs against MDR-TB
Future updates of treatment guidelines

- Q1-2 of 2016 – new guideline on treatment of drug resistant TB
- Q3 of 2016 – new guideline on treatment of drug susceptible TB
- Later 2016 – Consolidated guideline on treatment of TB (once the two above are approved for publication by WHO)
Ongoing studies and trials

• STREAM TB: clinical trial to evaluate shortened regimens for MDR-TB (The Union and UK MRC with funding from USAID)
• End TB project: use of new drugs in a regimen to shorten and simplify treatment of M/XDR-TB (PIH and MSF with funding from UNITAID)
Potential future changes that may affect manufacturers

- Need for more generic formulations of 2\textsuperscript{nd} line drugs for treatment of MDR-TB
  - Moxifloxacin/levofloxacin
  - Gatifloxacin
  - Linezolid
  - Clofazimine (currently used for treatment of leprosy; but increasing use in M/XDR-TB treatment)
  - Rifapentine – generic formulation not available; FDC with Isoniazid not available
Many thanks to all!