Paediatric TB: disease burden estimation and the opportunities it creates to strengthening surveillance

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Overview

• The WHO Global Task Force on TB Impact Measurement
  – Who are we?
  – What is our mandate and area of work?

• Background to estimates of disease burden for paediatric TB

• Epidemiological estimates of disease burden for paediatric TB: current rationale, strengths, limitations, next steps
  – Incidence
  – Mortality
  – Prevalence

• Opportunities to strengthening surveillance
WHO Global Task Force on TB Impact Measurement

www.who.int/tb/advisory_bodies/impact_measurement_taskforce

National TB Programmes of many countries & key technical and funding agencies

- To produce robust, rigorous, widely-endorsed assessment of whether 2015 targets are achieved at global level, regional and country levels

- To regularly report on progress towards impact targets in years leading up to 2015

- To strengthen national capacity in monitoring and evaluation of TB control
2015 targets for global TB control

- Halt and reverse incidence (MDG 6, Target 6.c)

- Halve prevalence and mortality rates compared with baseline of 1990
3 strategic areas of work
(defined December 2007, 2nd Task Force meeting)

1. **National TB prevalence surveys** in 22 (+) global focus countries

2. **Strengthening surveillance** of TB cases and deaths in all countries

3. **Periodic review and revision of methods** used to translate surveillance and survey data into estimates of disease burden
What do we offer to countries?
Regional and country workshops moving away from expert knowledge promoting direct measurement.

Quantify the burden of TB

Monitoring effectiveness of control programs by quantifying trends.

<table>
<thead>
<tr>
<th>Estimates of TB burden* 2011</th>
<th>NUMBER (thousands)</th>
<th>RATE (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (excludes HIV+TB)</td>
<td>65 (29-120)</td>
<td>27 (12-48)</td>
</tr>
<tr>
<td>Prevalence (includes HIV+TB)</td>
<td>680 (310-1,200)</td>
<td>281 (130-489)</td>
</tr>
<tr>
<td>Incidence (includes HIV+TB)</td>
<td>450 (370-540)</td>
<td>187 (155-222)</td>
</tr>
<tr>
<td>Incidence (HIV+TB)</td>
<td>15 (11-20)</td>
<td>6.2 (4.4-8.3)</td>
</tr>
<tr>
<td>Case detection, all forms (%)</td>
<td>70 (59-85)</td>
<td></td>
</tr>
</tbody>
</table>
Why are paediatric disease burden estimates important?

• How big of a problem paediatric TB really is?

• Are interventions aiming to have an impact on disease burden working?

• Competing health priorities; appropriate investment and funding allocation

• Addressing neglect of paediatric TB

• Evidence-based advocacy
Background to paediatric disease burden estimates

• What makes the estimates problematic?
  – Lack of gold-standard, point-of-care, diagnostic tool
  – Scarcity of robust, nationwide data
  – Neglect of recording and reporting of "non-infectious" TB cases among children

• What will improve estimates?
  – Global momentum for childhood TB

• WHO-led effort in collaboration with the Childhood TB Subgroup (since March 2011)
  – First set of estimates in 2012, updated in 2013
  – Collaboration with TB Alliance, STEP TB (since January 2013)
WHO TB data collection system

- TB case notifications collected online on an annual basis

- Disaggregated by
  - new/retreated status;
  - TB case type: SP, SN, EP;
  - age & sex.

### TABLE 1.1

**Reporting of data in the 2013 round of global TB data collection**

<table>
<thead>
<tr>
<th>WHO REGION OR SET OF COUNTRIES</th>
<th>COUNTRIES AND TERRITORIES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NUMBER</td>
</tr>
<tr>
<td>African Region</td>
<td>46</td>
</tr>
<tr>
<td>Eastern Mediterranean Region</td>
<td>23</td>
</tr>
<tr>
<td>European Region</td>
<td>54</td>
</tr>
<tr>
<td>Region of the Americas</td>
<td>46</td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td>11</td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td>36</td>
</tr>
<tr>
<td>High-burden countries (HBCs)</td>
<td>22</td>
</tr>
<tr>
<td>World</td>
<td>216</td>
</tr>
</tbody>
</table>

*Countries that did not report by the deadlines were mostly low-incidence countries in Western Europe.*

2.16 New pulmonary smear-negative/smear-unknown/smear-not done TB cases by age and sex, 2009 calendar year (number of patients)

*Time-changes in the distribution of cases by age and sex are analyzed by WHO to understand trends in disease burden and gaps in the performance of TB surveillance*

If you have data by age and sex that do not fit this framework (e.g., different age groups), please provide the data that you do have in the "Remarks" section.
Incidence *data source* (2012)
Incidence *estimation* (2012)

Estimated notifications: **349 000**

Global Case Detection Rate: **66% (64%-69%)**

Estimated incidence: **530 000 (510 000 – 550 000)**

6% of total 8.6 million incident cases are children

**TABLE B2.2.3**

*New TB case notifications in 2012, by case type and age disaggregation*

<table>
<thead>
<tr>
<th></th>
<th>SMEAR-POSITIVE</th>
<th>SMEAR-NEGATIVE(^a)</th>
<th>EXTRAPULMONARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total notifications</td>
<td>2 568 789</td>
<td>1 935 971</td>
<td>817 462</td>
</tr>
<tr>
<td>Countries disaggregating by age</td>
<td>2 551 136</td>
<td>1 597 530</td>
<td>678 953</td>
</tr>
<tr>
<td>Countries not disaggregating by age</td>
<td>17 653</td>
<td>338 441</td>
<td>138 509</td>
</tr>
<tr>
<td>(% total notifications disaggregated)</td>
<td>(99%)</td>
<td>(83%)</td>
<td>(83%)</td>
</tr>
<tr>
<td>Number of countries that reported notifications disaggregated by age (number of HBCs)(^b)</td>
<td>204 (22)</td>
<td>184 (14)</td>
<td>184 (14)</td>
</tr>
<tr>
<td>Total childhood notifications from countries disaggregating by age</td>
<td>46 488</td>
<td>163 477</td>
<td>91 308</td>
</tr>
<tr>
<td>Total estimated childhood notifications among all countries</td>
<td>349 000</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) This includes reported cases for whom smear results were unknown or not done.

\(^b\) An additional nine countries reported zero TB cases for 2012 and three countries had not reported data to WHO by July 2013.
**Incidence**

**strengths, limitations**

**Strengths**
- Making use of a global, annually available data source: TB notifications

**Limitations**
- Assumed gap between notifications and real incidence is the same for children as for adults
- No adjustment made for misdiagnosis. Each notified case is assumed to be true case of TB
- Assume 0 paediatric cases among case type unknown and retreatments
Incidence

next steps

**Short-term**

- Complementary mathematical modelling work
  - novel approach to estimating incidence
  - disaggregation by HIV status
- Generation of new, nationwide data (particularly on informing the gap between notifications and real incidence)

**Longer-term**

- Promote the use of case-based electronic recording and reporting and strengthening links outside the NTP network e.g. paediatricians (getting to the under-reported)
- TB integration in MCH programmes (getting to the under-diagnosed)
Quantifying the level of under-reporting

nationwide inventory studies

Under-reporting: \( \frac{(199+99+9)}{1980} = 16\% \)

An estimated additional cases 473 (394 – 565)
A modelling approach to estimating the burden of paediatric TB

Pete Dodd (University of Sheffield)
& James Seddon (Imperial College London)

Ongoing complementary analytical work to increase our understanding and build a richer, more consistent picture
Mortality data source (2012)

Countries (in orange) for which TB mortality is estimated using measurements from vital registration (n=121) systems and/or mortality surveys (n=2, India and Viet Nam)

* VR data from South Africa and Zimbabwe are not used due to miscoding of HIV as TB deaths
Mortality estimation (2012)

- Underlying cause of death is TB (excludes TB deaths among PLHIV)
  - ICD-10: codes A15-A19
  - ICD-9: codes 010-018
- Adjust reported $d$ deaths from VR: $d_a = \frac{d}{c(1-g)}$
  where $c$ denotes system coverage and $g$ proportion of ill-defined causes
- For countries with VR data: use adjusted reported paediatric TB deaths $d_a$
- For countries without VR data: use an ecological statistical model to predict the ratio of paediatric to adult adjusted TB deaths

74 000 (59 000 – 90 000) TB deaths (HIV-negative)

8% of total 940 000 TB deaths (HIV-negative)
Mortality strengths, limitations

**Strengths**

- **National** vital registration systems with standard coding of cause of death, reporting data to WHO [annually](#)

**Limitations**

- All countries used in model are middle to high income
- Uncertainty of estimates is not fully propagated
- Possible under-estimation due to miscoding of TB deaths (e.g. pneumonia, malnutrition, HIV/AIDS)
- The only available VR data from Africa, that from South Africa and Zimbabwe, are not used due to the miscoding of HIV as TB deaths
Mortality

next steps

• Additional analytical work
  – Further develop the ecological model
  – Mathematical modelling (e.g. TB deaths in HIV co-infected children)

• Collaboration with CHERG*: investigate options to quantify the miscoding of TB deaths in VR systems (e.g. due to pneumonia, malnutrition, HIV/AIDS)

• Investigate options for "correcting" VR data from South Africa and Zimbabwe

• Advocate for the development of and investment in VR systems
  – Allows for a direct measurement of mortality: level of & time trends
  – Serving many health programmes, not only TB
  – Interest from funding agencies: Global Fund investment in VR, part of HIS strengthening grants (e.g. Indonesia)

* UNICEF & WHO's Child Health Epidemiology Reference Group
National TB prevalence surveys (15+ years)

Overview of global progress

12 completed 2008-2012, an additional 17 to be completed 2014-17

- Repeat survey done
- Repeat survey planned
- 1 survey done
- Survey ongoing
- Survey planned 2013 or 2014
Field operations

(100-200 participants/day
5-7 days/cluster)

- **Census collection**
- **Group instructions to participants**
- **Reception and interview screening**
- **Chest X-ray screening**
- **Chest X-ray reading**
- **Sputum specimen collection for those screened positive**
- **Result for all and exit**
### National prevalence surveys that included children in the past

<table>
<thead>
<tr>
<th>NATIONAL SURVEYS*</th>
<th>Age group</th>
<th>Participants N (%1)</th>
<th>S+2 cases N (%1)</th>
<th>S+2 rate per 100,000</th>
<th>B+3 cases N (%1)</th>
<th>B+3 rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>China 1990</td>
<td>0 -14</td>
<td>401,997 (28)</td>
<td>30 (2)</td>
<td>7</td>
<td>51 (2)</td>
<td>13</td>
</tr>
<tr>
<td>China 2000**</td>
<td>0 -14</td>
<td>89,295 (24)</td>
<td>6 (1)</td>
<td>7</td>
<td>11 (2)</td>
<td>12</td>
</tr>
<tr>
<td>Cambodia 2002**</td>
<td>10 -14</td>
<td>4,591 (21)</td>
<td>3 (4)</td>
<td>65</td>
<td>4 (1)</td>
<td>87</td>
</tr>
<tr>
<td>Philippines 1997</td>
<td>10–19</td>
<td>4,989 (31)</td>
<td>6 (9)</td>
<td>120</td>
<td>18 (10)</td>
<td>361</td>
</tr>
<tr>
<td>Philippines 2007</td>
<td>10–19</td>
<td>6,728 (29)</td>
<td>1 (2)</td>
<td>15</td>
<td>11 (7)</td>
<td>163</td>
</tr>
<tr>
<td>Republic of Korea 1990</td>
<td>5-19</td>
<td>16,468 (34)</td>
<td>2 (3)</td>
<td>12</td>
<td>5 (4)</td>
<td>30</td>
</tr>
<tr>
<td>Republic of Korea 1995</td>
<td>5-19</td>
<td>19,005 (29)</td>
<td>1 (2)</td>
<td>5</td>
<td>2 (1)</td>
<td>11</td>
</tr>
</tbody>
</table>

*Pulmonary TB with CXR screening; ** Additional symptoms screening; ¹ Over total survey population; ² Smear-positive; ³ Bacteriologically-confirmed (smear and/or culture positive)

### Survey's in the 2000's
- Heterogeneous age groups, difficult to pool
- 20-29% of the sample size to detect 1-4% S+ and 2-7% B+ cases
### Why not include children in prevalence surveys?

<table>
<thead>
<tr>
<th>Item</th>
<th>Current design</th>
<th>Adding children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevalence estimate</strong></td>
<td>Bacteriologically-confirmed TB among 15+ in the general population</td>
<td>- A more accurate estimate among the total population</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Still imprecise estimate of prevalence among children</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>Typically about 50,000-70,000</td>
<td>- 20% increase if 10+ included</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- 60-100% increase if 0-14 included</td>
</tr>
<tr>
<td><strong>Screening algorithm</strong></td>
<td>CXR and symptoms</td>
<td>- CXR problematic in children</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- No reliable test for tuberculous infection</td>
</tr>
<tr>
<td><strong>Confirmation of TB</strong></td>
<td>Sputum smear microscopy and culture (with supporting CXR evidence)</td>
<td>- Invasive and uncomfortable diagnostic procedures</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Referral hospital for follow-up diagnosis and treatment required</td>
</tr>
<tr>
<td><strong>Budget</strong></td>
<td>- USD 1-2 million in Asia</td>
<td>- Prolonged cluster operations</td>
</tr>
<tr>
<td></td>
<td>- USD 2-4 million in Africa</td>
<td>- Inclusion of pediatrician</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Larger sample size</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Additional equipment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Referral hospital incidentals and transportation</td>
</tr>
</tbody>
</table>
Prevalence

next steps

• Data source does not exist at global level

• With current tools the WHO Global Task Force on TB Impact Measurement does not recommend the inclusion of children in nationwide prevalence surveys of pulmonary TB

• No disease burden estimate of paediatric TB prevalence is currently produced

• Global sentinel sites for stand-alone prevalence surveys among children?

• Is there room for contact tracing studies instead?

• Deterministic model to estimate prevalence
Current status of direct measurement

**TB incidence and mortality**

**Incidence**
(notification data)

**Mortality**
(vital registration data)

Clearly a long way to go
Opportunities to identifying strengths & gaps in national TB surveillance systems

- **Checklist of standards & benchmarks**
  - To assess a national surveillance system's ability to accurately measure TB cases and deaths
  - To identify gaps that need to be addressed

- **Completed with accompanying user guide & ready for roll-out January 2013**
  - 10 standards to assess if notification and VR data provide direct measure of TB incidence and mortality
  - 3 supplementary standards: *HIV-related TB, drug-resistant TB and TB in children*
  - Benchmarks for each standard to allow assessment of whether standard is met or not

- **Now being rolled out**
  - 7 countries to date, 8 planned
    - GF high burden/impact countries prioritized
    - Linked to "impact analyses", programme reviews
    - M&E investment plans to close surveillance gaps
1. Invest in routine information systems and surveys

2. Link to/build on programme or "mini" reviews
   - Strengthen epi/impact analysis component of reviews
   - Invest based on results of epi/impact analyses and systematic assessments of routine surveillance
   - M&E investment plans

3. Epi/impact analyses essential part of developing concept note in new funding model

Funding allocation based on directly measurable (as opposed to estimated) indicators

* Global Fund's Technical Evaluation Reference Group
Investment plan to strengthen surveillance, Indonesia (total budget US 1 million excl. VR)

<table>
<thead>
<tr>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Vital registration (VR): maintaining and scaling up the nationally-representative sample VR system</td>
</tr>
<tr>
<td>- Inventory study to measure the level of underreporting</td>
</tr>
<tr>
<td>- Capacity building for data management and statistical analysis – through attending courses and extra staffing at the central level</td>
</tr>
<tr>
<td>- Implementation of the Service Availability and Readiness Assessment Tool and health facility data quality assessment</td>
</tr>
<tr>
<td>- Assessment of the Integrated Tuberculosis Information System (SITT) Phase 2 in 2014</td>
</tr>
<tr>
<td>- Implementing mandatory notification policy</td>
</tr>
<tr>
<td>- Analysis of available mortality data</td>
</tr>
<tr>
<td>- Drug resistance survey or sentinel surveillance</td>
</tr>
<tr>
<td>- Nationally representative survey of HIV prevalence among TB patients</td>
</tr>
<tr>
<td>- Corrective actions required to compile all the reports from Papua</td>
</tr>
</tbody>
</table>
Available relevant guidance to countries

Guide on inventory studies to measure TB under-reporting (2012)
Among all health providers including paediatricians

Electronic recording and reporting guide (2011)
Case-based information allows NTPs to perform "know-your-epidemic" type of analyses including age of ALL cases
Objectives

1. To review available data and highlight gaps
2. To review analytical methods and epidemiological indicators
3. To define and prioritise specific actions that can be taken by TB Alliance, WHO, and other participating organizations
4. To catalyse efforts to strengthen routine surveillance and promote consensus in disease burden estimation
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- National TB Control Programmes
- Global TB Programme
- Stop TB Partnership Secretariat
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- UNITAID
- DfID
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