Potential Solutions for Overcoming the Challenges in Measuring the Burden of TB Disease in Children

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“The time has come for the hidden epidemic of childhood tuberculosis to emerge from the shadow of adult tuberculosis and be seen as a neglected child health problem of considerable proportions in precisely those communities that do not have the resources to deal with it adequately.”
The Basic Conundrum of Childhood Tuberculosis

There has been a circular argument concerning childhood tuberculosis. Some have said that without evidence of under-diagnosis of tuberculosis in children there is no justification for allotting additional resources for diagnosis, treatment and prevention. However, the resources to adequately determine the burden of childhood tuberculosis [the evidence] have not been made available.
Why We Must Measure

“Measurement is the first step that leads to control and eventually to improvement. If you can’t measure something, you can’t understand it. If you can’t understand it, you can’t control it. If you can’t control it, you can’t improve it.”

— H. James Harrington
What Are Obtaining Accurate Measures of Childhood TB So Important?

- Allocation of resources within an NTP
- Allocation of resources along the health care spectrum: community workers and programs, clinics, hospitals
- Awareness among pediatric providers
- Recognition of the issue among child survival experts and planners – MDG 4 and 5
- Approaching and interesting funders for both grants and programs
- Attracting the attention of researchers
- Protect the human rights of children and families
ECONOMIC AND SOCIAL BURDEN OF TUBERCULOSIS FOR CHILDREN

- Direct treatment costs
- Inpatient or institutional treatment
- Lost earnings of the family
- Redirecting resources from other needs
- Withdrawal from school
- Stigmatization and discrimination
- Creation of orphans
Tuberculosis Orphans

**BOX 2.4**

Parental deaths caused by TB have created large numbers of orphans

Globally in 2009, there were an estimated 14 million (range, 13–15 million) children aged <15 years who were orphans as a consequence of a parental death caused by HIV/AIDS.¹ Of these children, an estimated 3.1 million (range, 2.7–3.5 million) had been orphaned as a result of a parental death from HIV-associated TB. There were also an estimated 6.5 million (range, 5.5–7.7 million) children who were orphans as a result of a parental death caused by TB among people who were HIV-negative.

In total in 2009, there were an estimated 9.7 million (range, 8.5–11 million) children who were orphans as a result of losing at least one of their parents to TB (including HIV-associated TB).

SOME REASONS WHY CHILDHOOD TUBERCULOSIS HAS BEEN NEGLECTED

- Inadequate data
- Difficulty confirming the diagnosis
- Children are rarely contagious  
  [public health “dead end”]
- Perception from TB policy makers that treating adults is enough
- Government programs fail to address children
- Lack of family centered contact tracing
- Perceived lack of scientific study and scrutiny
- Misplaced faith in the BCG vaccines
- Lack of industry support
- Inadequate advocacy by pediatricians
To estimate TB incidence among children, it was assumed that the ratio of notified to incident cases at the global level in 2011 (best estimate 66%, range 64%–69%) was the same for adults and children. On this basis, TB incidence among children was estimated at 490 000 (range, 470 000–510 000) in 2011, equivalent to about 6% of the total number of 8.7 million incident cases.

Limitations of the methods used include:

- The assumption that the ratio of notified to incident cases is the same for adults and children, in the absence of any data on levels of under-reporting of diagnosed cases for children and adults separately;
- The assumption that reported cases were true cases of TB. Misdiagnosis is possible, especially given the difficulties of diagnosing TB in children; and
- The proportion of cases among children may be different in countries for which age-disaggregated data are not available.
### CASE NOTIFICATIONS OF CHILDHOOD TUBERCULOSIS IN SELECTED HIGH-BURDEN COUNTRIES - 2011

<table>
<thead>
<tr>
<th>Country</th>
<th>Cases</th>
<th>&lt; 15 smear +</th>
<th>&lt; 15 smear -</th>
<th>&lt;15 %</th>
<th>Total Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afghanistan</td>
<td>26,853</td>
<td>669 [28]</td>
<td>1,753 [72]</td>
<td>9.0</td>
<td></td>
</tr>
<tr>
<td>Brazil</td>
<td>71,337</td>
<td>692 [36]</td>
<td>1,243 [64]</td>
<td>2.7</td>
<td></td>
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<tr>
<td>China</td>
<td>865,059</td>
<td>1,378 [25]</td>
<td>4,165 [75]</td>
<td>0.6</td>
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<tr>
<td>India</td>
<td>1,211,441</td>
<td>12,985 [26]</td>
<td>36,673 [74]</td>
<td>4.1</td>
<td></td>
</tr>
<tr>
<td>Pakistan</td>
<td>255,094</td>
<td>3,895 [22]</td>
<td>14,142 [78]</td>
<td>7.1</td>
<td></td>
</tr>
<tr>
<td>Viet Nam</td>
<td>98,462</td>
<td>95</td>
<td>------</td>
<td>?</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>2,890,527</strong></td>
<td><strong>23,444</strong></td>
<td><strong>92,691</strong></td>
<td><strong>4.0</strong></td>
<td></td>
</tr>
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</table>
Ten Truths About Childhood Tuberculosis

1. Adequate TB control for children requires a robust public health system.
2. We can prevent most childhood TB with simple, inexpensive measures.
3. Childhood TB can be found earlier when it is easier to treat.
4. Finding and treating adults with TB is not sufficient for controlling childhood TB.
5. BCG vaccines alone cannot control childhood TB.
Ten Truths About Childhood Tuberculosis

6. Some tests, like chest x-ray, are more important for children than adults.

7. Many adult TB cases arise from infection that occurred in childhood.

8. Childhood TB is a window into the effectiveness of tuberculosis control.

9. Almost all children with TB are treated with medications designed for adults.

10. Childhood TB is a neglected disease in most of the world.
New TB Tests Are Not Applied to Children- 2012

<table>
<thead>
<tr>
<th>Test</th>
<th># of published studies in children</th>
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<tbody>
<tr>
<td>FNA</td>
<td>140</td>
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<tr>
<td>Fluorescent microscopy</td>
<td>1</td>
</tr>
<tr>
<td>LED-FM</td>
<td>0</td>
</tr>
<tr>
<td>MODS</td>
<td>7</td>
</tr>
<tr>
<td>Line-probe assays</td>
<td>1</td>
</tr>
<tr>
<td>LAMP</td>
<td>0</td>
</tr>
<tr>
<td>GeneXpert</td>
<td>3</td>
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</table>
TRANSITIONS IN TUBERCULOSIS

- Susceptible
- Exposed
- Infected
- Diseased
- Sick
- Diagnosed
- Treated
- Cured

Prevent Infection
Prevent Disease
Register, Record, Report
Some Results from Contact Tracing Studies

Jaganath et al. Clin Infect Dis 2013 epub

- Study of 761 childhood household contacts of TB cases in Uganda
- ~ half of the contacts were children < 5 years of age
- Patients followed for 2 years
- 10% prevalence of TB disease among the children [71% were culture positive] – 16,400 per 100,000!!!
- No cases of disseminated disease [? Effect of early intervention]
- 483/490 [99%] children started on INH did not develop disease
- 2 TB cases while on IPT, one case after completion
- BCG was protective, esp. among children < 5 years of age
- Characteristics of index case not a/w disease in contacts
**Tuberculosis and latent tuberculosis infection in close contacts of people with pulmonary tuberculosis in low-income and middle-income countries: a systematic review and meta-analysis**

*Lancet Infect Dis* 2008; 8: 359–68

*Janina Morrison, Madhukar Pai, Philip C Hopewell*

<table>
<thead>
<tr>
<th></th>
<th>Total studies (n)</th>
<th>Pooled yield (95% CI)</th>
<th>Heterogeneity</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Active tuberculosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child contacts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 years</td>
<td>13</td>
<td>8.5% (7.4–9.7%)</td>
<td>&lt;0.001</td>
<td>88.8%</td>
</tr>
<tr>
<td>5–14 years</td>
<td>6</td>
<td>6.0% (4.7–7.5%)</td>
<td>0.064</td>
<td>43.5%</td>
</tr>
<tr>
<td>&lt;15 years</td>
<td>8</td>
<td>7.0% (6.0–8.0%)</td>
<td>&lt;0.001</td>
<td>88.3%</td>
</tr>
<tr>
<td>Adult contacts (&gt;15 years)</td>
<td>9</td>
<td>6.5% (5.7–7.4%)</td>
<td>&lt;0.001</td>
<td>70.1%</td>
</tr>
<tr>
<td><strong>LTBI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child contacts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 years</td>
<td>14</td>
<td>30.4% (28.6–32.3%)</td>
<td>&lt;0.001</td>
<td>94.4%</td>
</tr>
<tr>
<td>5–14 years</td>
<td>7</td>
<td>47.9% (45.5–50.4%)</td>
<td>&lt;0.001</td>
<td>96.0%</td>
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<tr>
<td>&lt;15 years</td>
<td>10</td>
<td>40.4% (38.7–42.2%)</td>
<td>&lt;0.001</td>
<td>97.8%</td>
</tr>
<tr>
<td>Adult contacts (&gt;15 years)</td>
<td>7</td>
<td>64.6% (62.9–66.2%)</td>
<td>&lt;0.001</td>
<td>98.7%</td>
</tr>
</tbody>
</table>

*Table 6: Pooled data for all active tuberculosis and LTBI among household contacts, by age*
ROADMAP FOR CHILDHOOD TUBERCULOSIS
Include the needs of children and adolescents in research, policy development and clinical practices

Collect and report better data, including data on prevention

Develop training and reference materials for health care workers

Foster local expertise and leadership

Do not miss critical opportunities for intervention

Engage key stakeholders

Develop integrated family-centred and community-centred strategies

Address research gaps

Meet funding needs for childhood TB

Form coalitions and partnerships to improve tools for diagnosis and treatment
NTPs and Childhood Tuberculosis

Box 3. A framework for improving childhood TB activities within national TB control programmes

- Know your epidemic
- Ensure that policies are evidence-based and relevant
- Identify priorities and gaps
- Engage in continuing surveillance
- Train health workers and implement care strategies for children with TB
- Conduct operational research
- Assess funding needs
- Assign responsibility and ensure accountability
- Take leadership and work in partnership with all stakeholders
- Collaborate and communicate across the entire health care sector
NTPs and Childhood Tuberculosis

Box 5. Steps to improve the diagnosis and care of children with TB identified by national TB control programmes from eastern and southern Africa at a meeting to discuss best practices in tuberculosis control, Kigali, Rwanda, 2010

- Adapt international strategies and develop national guidelines for diagnosing and treating children with TB.
- Operationalize the guidelines addressing childhood TB.
- Identify someone to champion the cause of children with TB.
- Establish a working group on childhood TB at each national TB programme, and identify a person at the programme who will develop links with paediatricians and national paediatric associations.
- Provide training about childhood TB, and incorporate it into continuing education on TB and TB/HIV coinfection.
- Incorporate activities to address childhood TB into annual plans and five-year strategic plans.
- Ensure that national TB programmes incorporate activities addressing childhood TB into their budgets.
- Include data on TB in children in routine reporting and in reviews of national TB programmes.
- Develop and implement operational research to determine the constraints and barriers to diagnosing and treating children.
- Implement research aimed at improving the diagnosis and treatment of children with TB and the care of children who are contacts of someone with TB.
Activities to Improve Childhood TB Epidemiology and Reporting

- Register/Notify every case of childhood TB by age, disease type, HIV status and treatment outcome
- Improve private sector reporting of children
- Improved contact tracing of index cases
- Add child contacts to TB treatment cards
- Promotion of case-based electronic recording and reporting systems, use of mobile technology in the field
- Implementation of national inventory surveys to measure under-reporting of childhood TB cases
- Improved diagnostics - Xpert
- Surveys of other programs that serve at-risk children
Integration of Childhood Tuberculosis Into Other Programs

Box 8. Programmes into which TB services can be integrated

- Integrated management of pregnancy and childbirth (IMPAC)
- Integrated management of childhood illness (IMCI)
- Integrated community case management (iCCM)
- Child HIV care programmes
- Prevention of mother-to-child transmission of HIV (PMTCT)
- Nutritional programmes for children
- Family planning and fertility services