Tuberculosis Inventory Study in Indonesia 2016-2017

TB Inventory Study Team
Glion, 1 May 2018
Background
Introduction (1)

• Indonesia among top 5 countries with the highest TB burden
• TB incidence estimated 1,020,000 cases per year (Global TB Report 2017)
• Number of TB case notified: 360,565 (National TB database, 2016)
• Low contribution of private sectors in case notification of TB (NSP 2016-2020)
• 56% of people found on TB treatment were not reported to SITT (National Prevalence Survey, 2013-2014)
• Protocol development workshop for TB inventory studies (September 2014): China, Indonesia, Pakistan, Philippines, Viet Nam
Introduction (2)

• TB surveillance system (manual and electronic) in tiers: health center, district, province and national

• Web and case based TB information system (SITT) started in 2014, mainly covers all public health centers and some government hospitals

• Web and case based DR TB information system (eTB Manager) started in 2009 in 93 PMDT sites Nationally

• Health Minister decree No. 67/2016: mandatory for all health facilities to notify TB cases (excluding laboratories)
Objectives
Objectives

• Main objective
  • To estimate the level of under-reported TB cases in the National Surveillance System (SITT and eTB Manager)

• Specific objectives
  • To quantify the level of under-reporting of TB cases put on treatment to the national surveillance systems, PHC and Non PHC, public and private
  • To understand the relative contribution of types of health facilities to TB treatment and TB under-reporting
  • To assess the difference in under-reporting by age, sex, geographical area and type of health facilities
Methods
Overview of Study Design and Analysis

• Sampling design: Stratified cluster sampling design
• Stratification: (1) Sumatera, (2) Java-Bali, and (3) Other
• Sample size of district = 23 (6 in Sumatra, 12 in Java-Bali, and 5 in other provinces)
• Probability proportional to population sampling of districts (clusters) followed by prospective collection of data for cases diagnosed by ALL health-care providers within selected districts for 3 months (1 Jan-31 Mar 2017)
• Record-linkage between the Inventory Study and NTP case based databases to estimate under-reporting
Sampled districts

Selected districts is 23 out of 514 districts
Covered about 10% of total population (260 millions)
Key study timelines

Protocol development (Sep 14 – Oct 15)
Funding secured (Oct 15)

Established Steering committee (June 16)

Study plan dissemination (central and district level) and Field team recruitment (June – Oct 16)

Mapping of health facility at sampled districts (Nov 16 – Jan 17)

Field team training (Nov 16)

Pilot study: Sukabumi and East Jakarta (August 16)

Data collection (Jan – April 17)
Data validation (July 17 – Jan 18)

Data processing and data analysis (Jan – Mar 18)

National dissemination of study results (April 18)
Data processing
Data processing steps

- Data entry
- Data cleaning
- Data standardization
- Deduplication
- Matching
- Data analysis

- The process was done using Stata, except incidence estimation was done using R statistics
- Deduplication and matching were done using probabilistic record linkage and manual review
Deduplication of IVS data

Original
- Public: 15,191
- Private: 6,701
- Laboratory: 1,035

Unique
- Public: 14,562
- Private: 6,557
- Laboratory: 1,010
Deduplication of NTP data

Original
- Q1: 10,996
- Q1 (neighbour): 30,266
- Q2: 9,708

Unique
- Q1: 10,844
- Q1 (neighbour): 29,733
- Q2: 9,536

E-TB: 1,253

Q1*: 605
Q2*: 648

SITT: 50,970

Q1*: 595
Q1: 78
Q2*: 635
Q2: 86

* Total Indonesia
Mapping of health facilities
Health facility mapping

Initial information
- List from Center of Data and Information, MOH (2015)
  Hospital: 195, PHC: 810
- List from DHO
  Clinic: 1,510
  Laboratory: 85
- List of from IMA
  Certified MD: 9,274

List development
- Health Facilities List: 11,874
  Hospital: 195
  PHC: 810
  Clinics: 1,510
  Certified MD: 9,274
  Lab: 85

Mapping process
- Found: 2,882
  Hospital: 156
  PHC: 707
  Clinics: 977
  GPs: 993
  Lab: 49
- Newly found: 1,325
  Hospital: 55
  PHC: 19
  Clinics: 546
  GPs: 660
  Lab: 45

- Enumerated: 4,207
- Eligible: 1,687 (40.1%)
- Participated: 1,681 (99.6%)
Enumerated, eligible\(^1\), and participated\(^2\) health facilities by type

1. At least one TB patient diagnosed or treated during the last three months
2. Informed consent provided
Results of analyses from IVS cases

Targeted study period Q1 2017
### Distribution of IVS cases by health facility

<table>
<thead>
<tr>
<th>Source</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total unique IVS cases</td>
<td>21,320</td>
</tr>
<tr>
<td>Non-Lab Public(^1)</td>
<td>14,562</td>
</tr>
<tr>
<td>Non-Lab Private(^2)</td>
<td>6,557</td>
</tr>
<tr>
<td>Laboratory(^3)</td>
<td>1,010</td>
</tr>
</tbody>
</table>

\(^1\) Puskesmas (PHC), hospitals, clinics  
\(^2\) Hospitals, clinics, GPs  
\(^3\) Public and private

---

**Source**

<table>
<thead>
<tr>
<th>PHC</th>
<th>Public hosp</th>
<th>Private hosp</th>
<th>Clinic</th>
<th>GP</th>
<th>Lab</th>
</tr>
</thead>
<tbody>
<tr>
<td>36.9%</td>
<td>27.4%</td>
<td>17.4%</td>
<td>8.0%</td>
<td>5.7%</td>
<td>4.6%</td>
</tr>
</tbody>
</table>
Distribution of IVS cases by age group

- **Public**:
  - 0-14: 8.9%
  - 15-64: 75.7%
  - 65+: 15.3%

- **Private**:
  - 0-14: 9.7%
  - 15-64: 66.6%
  - 65+: 23.7%

- **Laboratory**:
  - 0-14: 13.3%
  - 15-64: 77.1%
  - 65+: 9.6%

- **Total**:
  - 0-14: 9.4%
  - 15-64: 72.8%
  - 65+: 17.8%
Distribution of IVS cases by gender

- **Public**
  - Male: 56.6%
  - Female: 43.4%

- **Private**
  - Male: 55.4%
  - Female: 44.6%

- **Laboratory**
  - Male: 58.3%
  - Female: 41.7%

- **Total**
  - Male: 56.4%
  - Female: 43.6%
Distribution of IVS cases by region

Public
- Sumatera: 8.0%
- Jawa Bali: 12.2%
- Others: 79.8%

Private
- Sumatera: 4.2%
- Jawa Bali: 2.5%
- Others: 83.3%

Laboratory
- Sumatera: 6.4%
- Jawa Bali: 8%
- Others: 88.8%

Total
- Sumatera: 6.7%
- Jawa Bali: 1.8%
- Others: 81.6%
Distribution of cases by case type in each age group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Clinically diagnosed</th>
<th>BacteriologicallyConfirmed</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-14</td>
<td>97.5%</td>
<td>2.5%</td>
</tr>
<tr>
<td>15-64</td>
<td>43.0%</td>
<td>57.0%</td>
</tr>
<tr>
<td>65+</td>
<td>32.9%</td>
<td>67.1%</td>
</tr>
</tbody>
</table>
Distribution of cases by case type in each region

<table>
<thead>
<tr>
<th>Region</th>
<th>Clinically diagnosed</th>
<th>Bacteriologically Confirmed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatera</td>
<td>45.8%</td>
<td>54.2%</td>
</tr>
<tr>
<td>Jawa Bali</td>
<td>32.1%</td>
<td>67.9%</td>
</tr>
<tr>
<td>Others</td>
<td>48.1%</td>
<td>51.9%</td>
</tr>
</tbody>
</table>
Adherence to national guidelines of TB treatment by region and total:

Sumatera:
- FDC: 59.8%
- RHZE: 33.9%
- Others: 6.3%

Jawa Bali:
- FDC: 88.4%
- RHZE: 8.1%
- Others: 3.5%

Others:
- FDC: 73.3%
- RHZE: 22.2%
- Others: 4.5%

Total:
- FDC: 83.6%
- RHZE: 12.5%
- Others: 3.9%
Adherence to national guidelines of TB treatment by DOTS/ Non DOTS
IVS and NTP databases matching results
Selected districts and their neighbouring* for matching buffer

*Excluding neighbouring district with no geographical access to study districts (e.g. mountain separating 2 district)
Matching results of 4 data sources

<table>
<thead>
<tr>
<th>Source</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTP (Unique)</td>
<td>13,211</td>
</tr>
<tr>
<td>IVS (Unique)</td>
<td>21,320</td>
</tr>
<tr>
<td>IVS: Non-Lab Public¹</td>
<td>14,562</td>
</tr>
<tr>
<td>IVS: Non-Lab Private²</td>
<td>6,557</td>
</tr>
<tr>
<td>IVS: Laboratory³</td>
<td>1,010</td>
</tr>
<tr>
<td>NTP-IVS (Unique)</td>
<td>22,681</td>
</tr>
</tbody>
</table>

¹ Puskesmas (PHC), hospitals, clinics
² Hospitals, clinics, GPs
³ Public and private

Not shown in the Venn Diagram:
NTP & Lab (not in Public and Private) = 129
NTP & Private & Lab (not in Public) = 3
Under-reporting

(Weighted, stratified, clustered accounted for)
## Total and by facility type

<table>
<thead>
<tr>
<th>Facility type</th>
<th>Best estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>41% (36% - 46%)</td>
</tr>
<tr>
<td>Puskesmas</td>
<td>15% (11% - 20%)</td>
</tr>
<tr>
<td>Non-puskesmas</td>
<td>71% (61% - 79%)</td>
</tr>
<tr>
<td>Hospital</td>
<td>62% (52% - 72%)</td>
</tr>
<tr>
<td>Other (Clinics, GPs, Lab)</td>
<td>96% (92% - 98%)</td>
</tr>
</tbody>
</table>
By case type and by site of disease

<table>
<thead>
<tr>
<th>Case type</th>
<th>Best estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteriologically confirmed</td>
<td>21% (16% - 26%)</td>
</tr>
<tr>
<td>Clinically diagnosed</td>
<td>55% (49% - 61%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Site of disease</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>38% (33% - 44%)</td>
</tr>
<tr>
<td>Extra-pulmonary</td>
<td>58% (49% - 66%)</td>
</tr>
</tbody>
</table>
By age group and by sex

<table>
<thead>
<tr>
<th>Age group</th>
<th>Best estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>54% (44% - 64%)</td>
</tr>
<tr>
<td>&gt;=15</td>
<td>39% (34% - 44%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>Best estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>41% (36% - 47%)</td>
</tr>
<tr>
<td>Female</td>
<td>41% (36% - 46%)</td>
</tr>
</tbody>
</table>
By geographical area

<table>
<thead>
<tr>
<th>Geographical area</th>
<th>Best estimate (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatera</td>
<td>40% (24% - 59%)</td>
</tr>
<tr>
<td>Bali/Java</td>
<td>42% (18% - 47%)</td>
</tr>
<tr>
<td>Other</td>
<td>39% (28% - 51%)</td>
</tr>
</tbody>
</table>
Risk factors for TB under-reporting  
(Logistic regression, weighted, stratified & clustered accounted for)

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinic. vs bact. (ref)</td>
<td>4.8 (3.4 - 6.8)</td>
<td>4.5 (3.1 - 6.5)</td>
</tr>
<tr>
<td>Extra pulm. vs Pulm. (ref)</td>
<td>2.2 (1.5 - 3.3)</td>
<td>1.4 (0.9 - 2.2)</td>
</tr>
<tr>
<td>Child vs adult (ref)</td>
<td>1.8 (1.3 - 2.6)</td>
<td>1.0 (0.7 - 1.5)</td>
</tr>
<tr>
<td>Male vs female (ref)</td>
<td>1.0 (0.9 - 1.1)</td>
<td>1.1 (1.0 - 1.2)</td>
</tr>
</tbody>
</table>
Capture-recapture*

(To estimate undetected TB cases and extrapolate to total TB incidence)

*Additional analysis not originally part of protocol
## Estimate of undetected cases

<table>
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<tr>
<td>IVS (Unique)</td>
<td>21,320</td>
</tr>
<tr>
<td>IVS: Public(^1)</td>
<td>14,747</td>
</tr>
<tr>
<td>IVS: Private(^2)</td>
<td>7,323</td>
</tr>
<tr>
<td>NTP-IVS (Unique)</td>
<td>22,681</td>
</tr>
</tbody>
</table>

\(^1\) Puskesmas (PHC), hospitals, clinics, labs  
\(^2\) Hospitals, clinics, GPs, labs

- NTP: 4,902  
- IVS: 21,320  
- NTP-IVS: 13,211  

- Undetected cases?  
  - IVS-Public: 9,626  
  - IVS-Private: 4,371  
  - NTP: 197  

Undetected cases?
<table>
<thead>
<tr>
<th>Model</th>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>ntp + public + private + ntp<em>public + ntp</em>private + public<em>private + ntp</em>public*private</td>
</tr>
<tr>
<td>Model 2</td>
<td>ntp + public + private + public*private</td>
</tr>
<tr>
<td>Model 3</td>
<td>ntp + public + private + ntp*public</td>
</tr>
<tr>
<td>Model 4</td>
<td>ntp + public + private + ntp*private</td>
</tr>
<tr>
<td>Model 5</td>
<td>ntp + public + private</td>
</tr>
</tbody>
</table>
Estimates and Akaike Information Criterion (AIC) for optimal model selection

<table>
<thead>
<tr>
<th>Model</th>
<th>$b_0^*$</th>
<th>SE($b_0$)</th>
<th>95% CI</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>5,113.7</td>
<td>478.3</td>
<td>4,257.2 - 6,142.6</td>
<td>79.2</td>
</tr>
<tr>
<td>Model 2</td>
<td>1,087.7</td>
<td>33.1</td>
<td>1,024.7 - 1,154.4</td>
<td>3,670.6</td>
</tr>
<tr>
<td>Model 3</td>
<td>31,096.6</td>
<td>812.2</td>
<td>29,544.8 - 32,729.9</td>
<td>4,124.0</td>
</tr>
<tr>
<td>Model 4</td>
<td>3,340.8</td>
<td>71.0</td>
<td>3,204.6 - 3,482.8</td>
<td>12,732.3</td>
</tr>
<tr>
<td>Model 5</td>
<td>4,927.1</td>
<td>88.0</td>
<td>4,757.5 - 5,102.7</td>
<td>14,211.3</td>
</tr>
</tbody>
</table>

*Estimate of total undetected cases in 23 selected districts*
Capture-recapture to estimate the number of undetected cases

<table>
<thead>
<tr>
<th>NTP</th>
<th>4,902</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,361</td>
<td></td>
</tr>
<tr>
<td>555</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>4,371</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>9,626</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,669</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5,114 (18.4%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4,902</td>
</tr>
<tr>
<td>555</td>
</tr>
</tbody>
</table>

\[
\text{Estimate the number of undetected cases} = 5,114 (95\% \text{ CI: 4,257-6,143})
\]

\[
\text{Proportion of undetected cases} = \frac{5,114}{(5,114+22,681)} = 18.4\%
\]
National estimate of TB incidence

\[ \hat{I} = \frac{n}{(1 - u)} \frac{1}{1 - d} \]

- \( n \) is number of notified cases in 2017
- \( u \) is proportion of under reporting, \( u = 0.4128 \) (uncertainty, se = 0.0241)
- \( d \) is proportion of undetected cases, \( d = 0.1837 \), (uncertainty, se = 0.0279)
Summary of key results

• 1.681 health facilities from 23 districts participated in the study
• 21,320 TB cases were found in Q1 2017 from the study
  • 68% of cases in public facilities (56% PHC, 42% hospitals, 2% clinics)
  • 28% of cases in private facilities (59% hospitals, 22% clinics, 19% GPs)
  • 4% labs (22% public, 78% private)
• Overall under-reporting 41% (15% PHC, 62% hospital, 96% lab/GPs/clinics)
  • Clinically diagnosed, extra pulmonary and children are more likely to be under-reported
• Nationally more than 84% of TB cases are prescribed with treatment that adheres to national guidelines (regional differences exist)
• Half of incident TB cases are detected and reported to NTP and from the remaining “missing” cases 2/3 are detected but not reported and 1/3 not detected
Key lessons learned

• Exhaustive mapping of all health facilities that diagnose and treat TB must be kept up to date in every district
  • What is the best mechanism to ensure this?

• Participation of eligible health facilities was extremely high 99.6%
  • Successful model of engagement with different type of health facilities could be rolled out to the rest of the country

• Record linkage exercises to be routinely implemented
  • Deduplication of NTP databases
  • Matching with other sources of TB cases (SIRS, SIHA, BPJS, SRS)
Limitations

• Data collection could not be conducted in 6 health facilities from 2 districts due to difficult geographical access
• 1,361 TB cases that appear in SITT/eTB manager were not captured by IVS enumerators
• 3 labs from 3 districts refused to participate
• Probabilistic record linkage is not fail-proof (sensitivity analyses were conducted to investigate potential bias of results – not found to be the case)
• We did not include pharmacies in the sampling frame of the study
Acknowledgements

- NIHRD
- NTP
- TB Expert Committee
- District field teams
- Provincial and district health offices
- Medical associations (national and district)
- Hospital associations (national and district)
- Pusdatin
- WHO
- Technical partners
- Funding partners (Global Fund, TB Alliance)
Sensitivity analyses
Sensitivity analysis for NTP cases not found in IVS databases

Crude under-reporting

41.7%

Assuming no unmatched NTP records, crude under-reporting

38.0%
## Sensitivity analysis for laboratory data

<table>
<thead>
<tr>
<th></th>
<th>Match</th>
<th>Unique</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bact. (+)</td>
<td>165</td>
<td>53</td>
<td>218</td>
</tr>
<tr>
<td>Bact. (-)</td>
<td>131</td>
<td>661</td>
<td>792</td>
</tr>
<tr>
<td>Total</td>
<td>296</td>
<td>714</td>
<td>1,010</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Assumption</th>
<th>Est.</th>
<th>SE</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assuming 131+661 are false-negative (FN)</td>
<td>41%</td>
<td>2%</td>
<td>36% - 46%</td>
</tr>
<tr>
<td>Assuming 131 are FN and 661 are truly-negative (TN)</td>
<td>39%</td>
<td>3%</td>
<td>33% - 44%</td>
</tr>
<tr>
<td>Assuming 131+661 are TN</td>
<td>39%</td>
<td>3%</td>
<td>33% - 44%</td>
</tr>
</tbody>
</table>