Estimates of TB incidence, prevalence and mortality

Philippe Glaziou
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A short history of TB estimations

• Tuberculin surveys to measure TB burden (Annual Risk of Infection → Incidence)
• World Bank estimates of incidence 1993 (based on ARI), rescaled (WHO, 1996)
• *Corbett et al. Archives Internal Medicine 2003.* TB/HIV estimates
• Country-specific updates: special surveys, including disease prevalence surveys, re-analysis of existing data
Incidence: main methods

- Reference year: 1997 global consultation process. 64 country estimates updated later.
- Of proportion of cases being notified (expert opinion)

\[ l = \frac{N}{r} \]

\[ N = \text{notifications / year}, \ r = \text{case detection ratio} \]

- From surveys of infection

\[ \frac{l}{\lambda} \approx \frac{l \times 10^5}{2 \times 10 \times l \times 10^2} = 50 \]

\[ \lambda \text{ denotes the percent risk of TB infection, } l \text{ is expressed per 100,000/year} \]

This approximation does not hold everywhere
Incidence: other methods

- From **disease prevalence surveys**
  \[ I = \frac{P}{d} \]
  \( P = \text{prevalence}, \ d = \text{weighted duration} \)

- From **mortality data** (vital registration)
  \[ I = \frac{m}{f} \]
  \( m = \text{deaths}, \ f = \text{case fatality rate} \)

- **Capture re-capture**, \( \geq 3 \) lists required, log-linear model to estimate cases not in any list, after adjusting for dependencies
Main source of information (reference year)

<table>
<thead>
<tr>
<th>Best source</th>
<th>Number of countries (2007)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expert opinion</td>
<td>177</td>
</tr>
<tr>
<td>Survey of infection</td>
<td>19</td>
</tr>
<tr>
<td>Mortality (VRS)</td>
<td>3</td>
</tr>
<tr>
<td>Disease prevalence survey</td>
<td>12</td>
</tr>
<tr>
<td>Capture re-capture</td>
<td>2</td>
</tr>
</tbody>
</table>

In Eastern and Central Europe, all incidence estimates were based on expert opinion, mostly between 1997 and 1999.
Trends in incidence

• Assumed to mirror trends in time-series of country notifications
  – exponential regression fit to data
  – moving average filter
  – constant case detection ratio in some small countries

• Assumed to mirror trends in regional time-series of case notifications:
  – exponential regression (AFR low-HIV, LAC, SEA, WPR)
  – moving average filter (AFR high-HIV, CEU, EEU, EMR, High-income)
Trends in incidence (cont)

- Trends in annual risk of infection (repeat infection surveys)
- Flat trend (zero slope) when data are too difficult to interpret. E.g. Iraq, Pakistan
- Trends in mortality (Brazil, South Africa)

None of the above 3 methods applied in CEUR and EEUR countries
Russia: trends from notifications

Russian Federation incidence (all) 1990-2007

Russian Federation notifications (all) 1990-2007
Moldova: trends from the subregion

Republic of Moldova incidence (all) 1990-2007

Republic of Moldova notifications (all) 1990-2007
Subsets of incident cases

- HIV-positive
- Multi-drug resistant TB
Increase in HIV testing coverage

- **National surveys** of HIV in TB
  - 7 countries (up from 2 last year)

- **HIV sentinel surveillance** systems
  - 8 countries

- **Provider Initiated HIV Testing and Counselling** (where tested/new > 50%)
  - 49 countries (up from 13 last year)
PITC times series in 11 countries
Measurements of TB/HIV incidence

• Empirical measurements from 64 countries (7 national surveys, 8 sentinel surveillance, 49 provider-initiated HIV testing data with > 50% of new TB cases tested for HIV)

\[ \rho = \frac{l^+/N^+}{l^-/N^-} \]

\[ \rho \left( \frac{l}{l^+} - 1 \right) = \frac{N}{N^+} - 1 \]

\[ t = \frac{l^+}{l} = \frac{h\rho}{1 + h(\rho - 1)} \]

\( t = l^+/l \); proportion HIV-positive among incident TB; \( h = N^+/N \), HIV in general population (UNAIDS); \( r \), Incidence rate ratio
Predicting the incidence rate ratio
Prediction of TB/HIV incidence

• Linear model of logit-transformed $t$ using logit-transformed $h$, slope constrained to 1

\[
\rho = \frac{t(1-h)}{h(1-t)} \\
\log \left( \frac{t}{1-t} \right) = \beta_0 + \log \left( \frac{h}{1-h} \right) \\
\rho = e^{\beta_0}
\]
Three estimates of incidence rate ratio

- **High HIV (>1%)**
  \[ \rho = 20.6 \]
- **Med HIV (0.1-1%)**
  \[ \rho = 26.7 \]
- **Low HIV (<0.1%)**
  \[ \rho = 36.7 \]
Global burden of TB/HIV
TB/HIV summary

- 1.4m incident TB infected with HIV (15% of 9.3m)
- 63% of total TB/HIV estimated indirectly (104 countries) through the IRR method: need to scale up TB/HIV surveillance
- Impact of ART on IRR unclear: need to measure directly incidence of
- TB in patient enrolled in care cohorts and estimate TB IRR of patients on ART
Multidrug Resistant TB

- Direct measurements in 113 countries (new cases), of which 102 countries also have measurements on retreatment cases

\[ m = \sum_{i=n,r} \pi_i \cdot c_i \]

\[ c_r = \frac{r}{n} \cdot c_n \]

with \( \pi = \text{Pr}(\text{MDR} \mid \text{new}) \), \( c = \text{incident cases (new or retreatment)} \), \( r = \text{reported retreatment episodes} \) and \( n = \text{notified new cases} \)
MDR-TB (cont)

- In countries with no direct measurement, $p$ predicted from models with indirect predictors such as Gross National Income, retreatment ratio $r/n$; % HIV in TB
- Model predictions should be replaced with measurements from quality surveillance data
Other estimates

• Prevalence
• Mortality
Methods in Central & Eastern Europe

Notifications

\[ \div \text{case detection rate} \]

Incidence

\[ \times \text{case fatality rate} \]
\[ \times \text{disease duration} \]

Mortality

Prevalence
All incident cases

IRR or direct data

HIV+ve

smear-positive (45%)

DOTS

nonDOTS

untreated

smear-negative (55%)

DOTS

nonDOTS

untreated

HIV-ve

smear-positive (35%)

DOTS

nonDOTS

untreated

smear-negative (65%)

DOTS

nonDOTS

untreated
Mortality

• From incidence, $M = I.f$

• Assumed values for $f$
  – DOTS < non-DOTS < untreated
  – DOTS and HIV(+): $f = 0.1$
  – Untreated:
    • s(+), HIV(+): $f = 0.83$
    • s(-) HIV(+): $f = 0.74$
    • s(+), HIV(-): $f = 0.7$
    • s(-) HIV(-): $f = 0.2$

• No adjustment for ART or MDR/TB
Trends in mortality (excl. HIV+)
## Measured and predicted mortality

<table>
<thead>
<tr>
<th>Region</th>
<th>VR report</th>
<th>WHO estimated</th>
<th>$\frac{WHO\ estimated}{VR\ report}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>74,550</td>
<td>432,224</td>
<td>17%</td>
</tr>
<tr>
<td>America</td>
<td>7,864</td>
<td>39,040</td>
<td>20%</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>0</td>
<td>107,294</td>
<td>0%</td>
</tr>
<tr>
<td>Europe</td>
<td>59,213</td>
<td>60,631</td>
<td>98%</td>
</tr>
<tr>
<td>South-East Asia</td>
<td>4</td>
<td>517,668</td>
<td>&lt;0.01%</td>
</tr>
<tr>
<td>Western Pacific</td>
<td>7,633</td>
<td>288,765</td>
<td>2.6%</td>
</tr>
<tr>
<td><strong>World</strong></td>
<td>149,264</td>
<td>1,445,662</td>
<td>10%</td>
</tr>
</tbody>
</table>
Limitations of estimation methods

• No systematic analysis of trends
• No disaggregation by age and sex
• No forward projections
• Direct measurements of mortality (from VRS) under-used
• No sub-national estimates of TB burden
Methods in Central and Eastern Europe, in summary

- Incidence for a reference year (mostly 1997 and 1999), from expert opinion
- Time-series of incidence are calculated forward and backward, to cover 1990-2007
- Prevalence and mortality derived from incidence
Other predictors of changes in incidence

- HIV
- Economic development, trends in GDP
Impact of HIV on TB (Africa high-HIV)
Increase in estimated TB incidence in Eastern Europe (1990-2007)
Trends in GDP and TB, Eastern Europe
During this workshop, we would like to

• review the quality of surveillance data
• review and update assumptions
• update estimation methods
  – assessment of trends
  – changes in case finding efforts
  – changes in predictors of incidence (e.g. HIV, GDP, MDR?)
• update estimates of incidence, prevalence and mortality