Estimating TB burden

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Outline

• Basic facts about TB epidemiology
  – What should we expect with regards TB burden over time?
• Main indicators of TB disease burden
• Improving TB surveillance
TB has been with us for a very long time.


The graph shows a scatter plot with a trend line. The x-axis represents the date in years before present (BP), ranging from 40 to 5000. The y-axis represents the frequency of tuberculosis lesions in percent, ranging from 0% to 39%. The equation of the trend line is given as $y = 0.001x^{0.323}$ with an $R^2$ value of 0.059. The number of samples (N) is 99.
TB incidence decline in the Netherlands

Chemotherapy introduced

10% decline per year

Infection rate (10,000 year$^{-1}$)

- Incidence (reactivated cases excluded), since 1951
- Reactivated cases, since 1951
- Mortality, since 1901
- Risk of tuberculosis infection, since 1910

Slow decline in global TB burden

Number of new cases (million)

Rate falls 2%/yr
Why is global TB incidence declining so slowly?
Average lifetime risk of disease 5-15%*

World
7 billion

Infected
≈2.3 billion

Disease
≈9 million/yr

Slow death of the TB epidemic in Japan

- High case rates in old individuals
- Transmission nearly stopped
- 2 orders of magnitude
Aging TB epidemic in Japan

- High prevalence of infection in nearly all age groups
- High prevalence of infection in 30+ year old
- High incidence of disease in 60+ year old
### Selected determinants of TB

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infection</td>
<td>20 – 35</td>
</tr>
<tr>
<td>Under-nutrition</td>
<td>3.1 – 3.3</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.3 – 4.3</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>1.9 – 4.6</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>1.6 – 2.5</td>
</tr>
</tbody>
</table>

6-fold increase in notified TB in Kenya

HIV prevalence in 15–49 year-old in Kenya

TB incidence in Kenya

Incidence rate

Case notification rate
22 countries account for 80% of the global burden
Highest numbers of new cases in India and China (2011)
Highest incidence rates in Sub-Saharan Africa (2011)
TB driven by HIV in Sub-Saharan Africa (2011)
TB control principles

- Detect, treat and cure
- Isolation, infection control

Susceptible

- BCG (limited efficacy)

Infected

Prophylactic treatment, Post-exposure vaccine

TB disease
Impact of TB control on incidence

• Slow decline in global incidence 2%/year
  – Best decline with current tools 10%/year
    Post-exposure vaccine and/or safe prophylaxis to prevent reactivation of TB in 2+ billion needed to accelerate decline in incidence

• Mortality \((M)\) and Prevalence \((P)\) may temporarily decline faster than incidence

\[
M = \text{Incidence} \times \text{Case Fatality Ratio}
\]
\[
P \approx \text{Incidence} \times \text{disease duration}
\]
Decline in TB burden in Cambodia

Incidence

Prevalence

Rate per 100,000/year (log scale)

Rate per 100,000 pop (log scale)

-3%/yr

-7%/yr
Main indicators of TB burden

- Incidence
- Prevalence
- Mortality
Incidence

• National incidence surveys impractical

• **Best documented through state-of-the art TB surveillance.** Estimates are uncertain due to
  – Under-reporting
  – Under-diagnosis

• Estimation from tuberculin surveys not satisfactory
### Selected recent studies of under-diagnosis

**capture-recapture**
- Netherlands
- UK
- Egypt
- Syria
- Yemen
- Iraq

### under-reporting

**NO capture-recapture**
- USA (2 States)
- South Korea
- Taiwan
- India (study design not recommended in WHO guidelines)
- Vietnam (nested in the prevalence survey)
Under-reporting

BAD

Non-NTP cases

Many detected cases *not* reported

GOOD

All detected cases reported

Reported cases
Capture-recapture in 45 seconds

Assuming independence between events A and B,

\[ P(A \cap B) = P(A) \times P(B) \]

\[ \frac{N_{AB}}{N} = \frac{N_A}{N} \times \frac{N_B}{N} \]

\[ N = \frac{N_A \times N_B}{N_{AB}} \]

Total TB cases = \( N \)

\( N_A \)  \( N_{AB} \)  \( N_B \)

non-NTP  Reported
An augmented model for 3 lists

• For an incomplete $2^3$ contingency table

$$\log E(Z_{ijk}) = u + u_1 I(i = 1) + u_2 I(j = 1) + u_3 I(k = 1) +$$
$$u_{12} I(i = j = 1) + \ldots + u_{123} I(i = j = k = 1)$$

• Model with 8 terms
  – Number expected in all list ($u$)
  – 3 main effects, log odds of appearing in list 1, 2, 3
  – 3 two-factor interactions $u_{12}, u_{13}, u_{123}$
  – 1 three-factor interaction, assumed zero
Capture-recapture in Iraq

1980 detected, \textit{under-reporting} = 16\%

473 additional cases estimated (394–565)
How else can we estimate incidence?
From prevalence surveys estimates of prevalence

\[ I \approx \frac{\text{Prevalence}}{\text{duration}} \]

But, how do we measure disease duration?
Assuming stable state equilibrium,

\[ r^* P = t^* N \]
\[ d = r^{-1} \]

\( P \) = prevalence untreated
\( N \) = on treatment
\( r \) = removal rate
\( t \) = 2 / year
\( d \) = duration

but, ...

1. low precision of \( N/P \)
2. self-cure not accounted for
From mortality measurements (Vital registration or mortality surveys)

\[ I \approx \frac{\text{Mortality}}{\text{CFR}} \]

But, do CFR derived from literature reviews apply to all settings?
Contribution of PPM + active case finding in prisons
Trends in case notifications (log scale)

Underlying trends in incidence

NTP minus PPM and active case finding in prisons
TB determinants – approx. exponential growth of GDP/capita

Improved health system performance exponential decline in u5MR

Source: Global Health Observatory, WHO 2012
Assumptions about trends in incidence

- Notifications $N$ over 2007-2011 minus PPM run parallel to incidence on a log scale
- Decline in incidence affected by population aging (effect accounted for)
- Incidence *not attributable to HIV* in exponential decline
  - Exponential decline in u5MR (1990-2011)
  - Exponential increase in GDP/capita (1990-2011)
TB incidence attributable to HIV

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

\(h = \) HIV prevalence in general population (UNAIDS, 2012)
\(\rho = \) TB incidence rate ratio
\(t = \) HIV prevalence in TB (NTP 2012)
Assumptions about level in incidence (2007)

• **Under-reporting** $R$ from 2007 prevalence survey [1]
  – $R$ uncertainty range (7.1% - 20.3%)

• **Under-diagnosis** $D$ within plausible range for higher income countries with similarly good macro-indicators of health, e.g. Brazil
  – $D$ uncertainty range (5.6% - 35%)

• Incidence = $N / (R + D)$

1. Nguyen B Hoa et al. IED 2011;17:502-4
Estimated incidence rate in Vietnam, 1990-2011

Slight deceleration due to increasing HIV
Incidence *not* directly measured in most HBCs
Standards and benchmarks for assessing TB surveillance

• Goals
  – Assess ability to measure TB cases and deaths
  – Identify gaps that need to be addressed

• 13 standards and associated benchmarks
  – 9 on measurement of TB cases
  – 1 on measurement of deaths
  – 3 standards on special populations
  – All standards should be met
Prevalence surveys 1990 – 2015 (completed and planned)
Data on TB deaths (HIV-) from vital registration
Estimating mortality indirectly

- **Option 1**: ecological modelling using predictors among selected macro-economic and health indicators
- **Option 2**: $M = \text{incidence} \times \text{CFR}$
Uncertainty from modelling

Graphs showing the rate per 100,000 from 1990 to 2010 for Brazil, China, Japan, and Republic of Korea. The graphs show different models and Vital Registration (VR).
TB burden estimation in summary

• Best sources of data on TB burden are
  – **TB notifications** when data meet quality criteria and *under-reporting* low and documented
  – TB mortality from **Vital Registration with COD**
  – Prevalence from **national prevalence surveys**

• Impact assessment methods tailored to the existing data – document uncertainty and exercise care when using impact assessment for funding eligibility
Why is surveillance so important

• Estimates based on weak data are very uncertain
• Eligibility for funding should be based on measurable criteria and accurate measurements
• Planning, targeting and budgeting match actual needs
• Evaluation of programme performance based on accurate assessments
Global Fund evaluation strategy

- New evaluation strategy agreed by TERG*, 2012
- Contribution agreement for joint work by GF and WHO to implement strategy (health sector, TB, HIV, malaria)
- Building on ongoing programme reviews and evaluations together with partners
- Systematic assessment of routine surveillance and M&E capacity linked with M&E investment plans
- Emphasis on high impact, high priority countries (e.g. Indonesia)

* Global Fund's Technical Evaluation Reference Group