Estimating TB burden

Philippe Glaziou
World Health Organization
Accra, Ghana
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.

TB incidence decline in the Netherlands

Chemotherapy introduced

10% decline per year

- 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

- Incident, all
- Notified
- Incident, HIV-pos

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

7 years
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
- Prophylactic treatment, Post-exposure vaccine
- BCG (limited efficacy)
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:
-3%/yr

Prevalence:
-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 |

Selected recent studies of 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

Many detected cases *not* reported

GOOD

All detected cases reported
Capture-recapture in 45 seconds

Assuming independence between events A and B,

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

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

\[ N = \frac{N_A \times N_B}{N_{AB}} \]
An augmented model for 3 lists

• For an incomplete $2^3$ contingency table

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

$$u_{12} I(i = j = 1) + ... + u_{123} I(i = j = k = 1)$$

• 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, under-reporting = 16%
473 additional cases estimated (394–565)
How else can we estimate incidence?
From prevalence surveys estimates of prevalence

$I \approx \frac{Prevalence}{duration}$

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

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

- $P = \text{prevalence untreated}$
- $N = \text{on treatment}$
- $r = \text{removal rate}$
- $t = 2 \text{ / year}$
- $d = \text{duration}$

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?
Estimating incidence from case notifications in Vietnam

- Notification rate, all forms
- Smear positive
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

- Brazil: Vital Registration (modelled)
- China: Repeat mortality surveys, Sample VR
- Japan: Modelled VR
- Republic of Korea: Modelled 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