Targets for global TB control
MILLENNIUM DEVELOPMENT GOALS
"to have halted and begun to reverse incidence.."

**Implementation (DOTS)** | **Target year**
---|---
Case detection | 70% | 2005
Treatment success | 85% | 2004/5

**Impact**

<table>
<thead>
<tr>
<th>Metric</th>
<th>Target</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>50% of ≈ 300/100K</td>
<td>2015</td>
</tr>
<tr>
<td>Deaths</td>
<td>50% of ≈ 30/100K (&lt;1m)</td>
<td>2015</td>
</tr>
<tr>
<td>Incidence</td>
<td>&lt;1 per million</td>
<td>2050</td>
</tr>
</tbody>
</table>
1. Measuring and estimating TB incidence
Direct measures of TB burden incidence and prevalence
Korean civil servants
Tubercle and Lung Disease 76, 534 (1995)

• Prevalence PTB 1990 \(\frac{241}{100K}\)
• Incidence PTB 1989-90 \(\frac{84}{100K/yr}\)

• Estimated duration = \(\frac{241}{84} = 2.9\) years
(bigger ratio for older age groups)
Where case notifications = true incidence
Four indirect measures of TB incidence

1. incidence TB = \frac{notifications}{proportion detected}

2. incidence TB = \frac{prevalence}{duration}

3. incidence TB = incidence infection \times Styblo ratio

4. incidence TB = \frac{deaths}{proportion cases dying (case fatality rate)}

Incidence, prevalence, deaths derived by rearranging 4 equations
4 steps to check accuracy and completeness of surveillance data

1. **Inventory** of, and cross-check, data from all possible sources, removing duplications

2. **Capture-recapture** techniques to estimate case detection from lists of patients that have been "captured" in different ways

3a. Consistency of case reports: **spatial and temporal variation**, to check for inconsistencies

3b. Consistency of case reports: **norms of TB epidemiology** and natural history
Completeness of case registrations

TB cases notified by compulsory (CSS) and Varese surveillance systems (VSS)

<table>
<thead>
<tr>
<th></th>
<th>VSS</th>
<th>CSS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cases notified</td>
<td>143</td>
<td>89</td>
</tr>
<tr>
<td>Duplicates</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>Not TB</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>True cases</td>
<td>121</td>
<td>76</td>
</tr>
</tbody>
</table>

(-37%)

Source: Migliori ERJ 8, 1252 (1995)
Capture-recapture method
Petersen 1896, Lincoln 1930 (ducks)

Take 2 independent samples from an unknown population of N (TB patients):

<table>
<thead>
<tr>
<th>Method 2</th>
<th>Method 1 e.g. lab register</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>Present Absent Total</td>
</tr>
<tr>
<td>Present</td>
<td>20 5 25</td>
</tr>
<tr>
<td>Absent</td>
<td>30 c b</td>
</tr>
<tr>
<td>Total</td>
<td>50 a N</td>
</tr>
</tbody>
</table>

N = 50×25/20 = 62.5

<table>
<thead>
<tr>
<th></th>
<th>a</th>
<th>b</th>
<th>c</th>
<th>CDR lab</th>
<th>CDR hosp</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>62.5</td>
<td>50</td>
<td>55</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>37.5</td>
<td>7.5</td>
<td>0.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>
Indonesia: why does the fraction of TB cases among suspects vary between provinces?
Morocco: consistent 40-60% smear+ across 16 regions

Proportion smear-positive

Oued Ed Laayoune Guelmim Souss Gharb Chaouia Marrakech Oriental Casablanca Rabat Doukala Tadla Meknès Fes Taza Tanger
1b. Assessing trends in TB incidence, and the impact of control
Cambodia: higher case rates among older people imply long-term epidemic decline

![Graph showing reported TB cases/100k in 2006 by age group and gender.]

- **Male**
- **Female**

The graph illustrates the reported TB cases per 100k inhabitants in 2006, categorized by age group and gender. The data indicates a trend of higher case rates among older people, which may suggest a long-term decline in the epidemic.
TB incidence is falling slowly in 95 of 135 countries, 1996-2005

Annual change incidence (up to % marked)
Morocco:
PTB incidence projected to 2015

on 1994 age-structure

on aging population
TB patients in Morocco

Mean age of adult patients (yr)

Men: $0.14 \pm 0.01$

Women: $0.15 \pm 0.02$
Morocco:

TB falling slowly in women, very slowly in men
Trends in case notification rates in Viet Nam, 1997-2004

Annual percentage change

Reported TB cases/100K/yr

15-24 25-34 35-44 45-54 55-64 65+ total

Men  Women  Total

Graph showing trends in case notification rates in Viet Nam from 1997 to 2004.
Average age of men 15-54 yrs with TB is falling in some countries.
TB trends: New Caledonia

All TB 9.4%/yr

Smear+ 8.2%/yr

Notification rate (per 100 000)

Notifications (new & relapse)

Notifications new smear-positive
Impact of DOTS in Peru

2. Measuring and estimating TB prevalence
When to do a prevalence survey

- **High burden** (e.g. among 22 HBC)
- **Uncertain burden**, in part because surveillance is weak
- **Potential for collecting other data** e.g. about where patients are diagnosed and treated
- **Logistically feasible** - terrain, population density, staff security, mobile X-ray, culture etc
- **Potential source of funds**: $100,000 - $1m
- **Potential for doing** 2 or more surveys (to measure change)
- **Participatory population**
The 6 national TB prevalence surveys carried out since 1995

<table>
<thead>
<tr>
<th>Country</th>
<th>Design</th>
<th>Number examined</th>
<th>Number active pulmonary cases (prevalence ± 95%CL, per 100,00)</th>
<th>Number culture-positive cases (prevalence ± 95%CL, per 100,000)</th>
<th>Number smear-positive cases (prevalence ± 95%CL, per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Republic of Korea 1995 28</td>
<td>Stratified, cluster randomized; Age ≥ 5 years; X-ray (miniature) screen</td>
<td>64 713</td>
<td>668 (1032 ± 80)[1]</td>
<td>142 (219 ± 37)[2] (culture+ and/or smear+)</td>
<td>60 (93 ± 24)</td>
</tr>
<tr>
<td>Philippines 1997 31</td>
<td>Stratified, cluster randomized; Age ≥ 10 years; X-ray screen</td>
<td>21 960</td>
<td>537 (4200 ± 330)[3]</td>
<td>124 (810 ± 88)</td>
<td>47 (310 ± 99)</td>
</tr>
<tr>
<td>China 2000 29</td>
<td>Stratified, cluster randomized; Age ≥ 3 months; Tuberculin/symptom/fluoroscopy screen</td>
<td>365 097</td>
<td>1340 (367 ± 28)</td>
<td>584 (160 ± 16)</td>
<td>447 (122 ± 14)</td>
</tr>
<tr>
<td>Cambodia 2002 50</td>
<td>Stratified, cluster randomized; Age ≥ 10 years; X-ray/symptom screen</td>
<td>22 160</td>
<td>580 (1916 ± 300)</td>
<td>271 (899 ± 165) (culture+ and/or smear+)</td>
<td>81 (269 ± 66)</td>
</tr>
<tr>
<td>Indonesia 2004 30</td>
<td>Stratified, cluster randomized; Age ≥ 15 years; Symptom screen</td>
<td>50 154</td>
<td>N/A</td>
<td>48 (186 ± 49)[4]</td>
<td>80 (104 ± 38)</td>
</tr>
<tr>
<td>Eritrea 2004 120</td>
<td>Stratified, cluster randomized; Age ≥ 15 years; No screen</td>
<td>18 152</td>
<td>N/A</td>
<td>N/A</td>
<td>15 (50 ± 30)</td>
</tr>
</tbody>
</table>
DOTS reduces prevalence of TB by 37% in less than a decade in China

DOTS Other

Prevalence culture+ TB/100,000

1990 2000

DOTS

Other
Progress towards MDGs in Indonesia
prevalence rate fell 4%/yr 1980-2004?

<table>
<thead>
<tr>
<th>Region</th>
<th>1980 regional surveys</th>
<th>2004 national survey</th>
<th>% fall 1990-2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatera</td>
<td>53%</td>
<td>192/100K</td>
<td></td>
</tr>
<tr>
<td>Java-Bali</td>
<td>74%</td>
<td>137/100K</td>
<td></td>
</tr>
<tr>
<td>KTI (East)</td>
<td>45%</td>
<td>227/100K</td>
<td></td>
</tr>
<tr>
<td>National</td>
<td>61%</td>
<td>115/100K</td>
<td></td>
</tr>
</tbody>
</table>
"Model DOTS Project" reduces TB prevalence in south India

Source: TRC Chennai

Graph showing the prevalence of TB from 1970 to 2003, with a steady decline of about 10% per year in the Model DOTS Project area (MDP). The graph includes data for male and female cases, with a focus on the decrease in prevalence over time.
Incidence cannot reliably be estimated from prevalence e.g. Cambodia?

prevalence ss+ + = incidence × weighted duration

<table>
<thead>
<tr>
<th>prevalence ss+ (survey)</th>
<th>269/100K in 2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>weighted duration DOTS</td>
<td>0.65 @1.0 year</td>
</tr>
<tr>
<td>non DOTS</td>
<td>0.10 @1.5 years</td>
</tr>
<tr>
<td>untreated</td>
<td>0.25 @2.0 years</td>
</tr>
<tr>
<td></td>
<td>= 1.3 years</td>
</tr>
</tbody>
</table>

Therefore: incidence ss+ = 269/1.3 = 207/100K/year

NB: usually wide range on estimates
3. Measuring and estimating TB mortality
Measuring and estimating TB deaths

Method 4: incidence TB = \frac{\text{deaths}}{\text{proportion cases dying (case fatality rate)}}

Three approaches
1. Incidence × case fatality (method 4)
2. Verbal autopsy (in sample vital registration)
3. Vital (death) registration
## Comparing unknowns

Cause of death from vital statistics (VSD) and verbal autopsy (VA) of 48,000 adult (≥ 25) deaths in Chennai, India: 1995-97

<table>
<thead>
<tr>
<th>Cause of death</th>
<th>Cause of death in VSD</th>
<th>Cause of death based on VA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (%)</td>
<td>F(%)</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>8319  (30)</td>
<td>5168  (25)</td>
</tr>
<tr>
<td>Tuberculosis (TB)</td>
<td>1399  (5)</td>
<td>372   (2)</td>
</tr>
<tr>
<td>Other Respiratory</td>
<td>1088  (4)</td>
<td>596   (3)</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>1163  (4)</td>
<td>1002  (5)</td>
</tr>
<tr>
<td>Infectious (ex Resp/TB)</td>
<td>584   (2)</td>
<td>303   (2)</td>
</tr>
<tr>
<td>Unspec med.</td>
<td>12291 (44)</td>
<td>11511 (56)</td>
</tr>
<tr>
<td>Other spec med.</td>
<td>1899  (7)</td>
<td>1045  (5)</td>
</tr>
<tr>
<td>Cause NA</td>
<td>983   (4)</td>
<td>634   (3)</td>
</tr>
<tr>
<td>Total deaths - med</td>
<td>27726</td>
<td>20631</td>
</tr>
</tbody>
</table>

**Source:** Jha, Gajalakshmi et al
Regional trends in TB death registrations

Few data from Asia & Africa, long reporting delays

Geometric mean TB mortality (per 100K)

TB mortality Philippines (per 100K)

- ex Soviet Union
- Central Europe
- Industrialized
- Latin America
- Rep. Korea
- Philippines
4. Measuring and estimating risk of TB infection
Tanzania 1983 to 1988

Egypt 1995 to 1997

Korea

0 to 20 years

0 to 9 years
Styblo's 1:50 rule and endemic (untreated) TB

Prevalence non-infectious TB
~ sputum smear-

Prevalence infectious TB
~ sputum smear+, 2yr

MTB infection

Infected with M. tuberculosis

\[
\text{Styblo } \frac{\text{incidence } \times 10^5}{\text{risk infection } \times 10^2} = \frac{1000}{(10 \times 2)} = 50
\]

Endemic TB 1 smear+ cases gives \(10 \times 2 \times 0.1 \times 0.5 = 1\) smear+ case
IRAQ
Notification rate varies 5-fold among governorates

- 1.43% infection
- 0.51% infection

Smear+ notifications/100K

ALDEWANIA
AL-NAJAF
AL-MUTHANNA
WASIT
AL-BASRAH
MESAN
BAGHDAD
BABIL
KURKOK
THE-QAR
SALAH ADDEN
NINAWA
DIYALA
AL-ANBAR

0.51% infection
1.43% infection

IRAQ
Notification rate varies 5-fold among governorates

Smear+ notifications/100K

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MESAN
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BABIL
KURKOK
THE-QAR
SALAH ADDEN
NINAWA
DIYALA
AL-ANBAR

0.51% infection
1.43% infection
Tuberculin skin test responses in household contacts of active TB cases

979 children, median age 7yr, Istanbul

Source: Bakir et al 2006
5. Summary
Measuring TB burden and the impact of control

- **Routine surveillance** the ultimate tool for evaluating TB epidemiology and control; completeness of reporting to be formally examined in all countries
- Disease **prevalence surveys** best for measuring prevalence (and change), not incidence
- **Tuberculin surveys** feasible where ARI high and BCG coverage low; better for comparisons (trends); Styblo's rule defunct
- **TB death registrations** need to be improved in all countries with high TB burden, and compared with data from NTPs; **verbal autopsy** needs validation
"By 2015, every country should be able to assess progress in control by evaluating the time trend in incidence, and the magnitude of reductions in either TB prevalence or deaths."