Targets for global TB control

MILLENNIUM DEVELOPMENT GOALS
"to have halted and begun to reverse incidence..

<table>
<thead>
<tr>
<th>Implementation (DOTS)</th>
<th>Target year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case detection 70%</td>
<td>2005</td>
</tr>
<tr>
<td>Treatment success 85%</td>
<td>2004/5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Impact</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence 50% of ≈ 300/100K</td>
<td>2015</td>
</tr>
<tr>
<td>Deaths 50% of ≈ 30/100K (&lt;1m)</td>
<td>2015</td>
</tr>
<tr>
<td>Incidence &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: 241/100K
- Incidence PTB 1989-90: 84/100K/yr

- Estimated duration = 241/84 = 2.9 years (bigger ratio for older age groups)
Where case notifications = true incidence

Reported TB cases/100,000/yr

USA
Netherlands
UK
Norway
Four indirect measures of TB incidence

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

2. incidence TB = \( \frac{\text{prevalence}}{\text{duration}} \)

3. incidence TB = incidence infection \( \times \) Styblo ratio

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

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 e.g. hospital register</th>
<th>Method 1 e.g. lab register</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Absent</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>N</td>
</tr>
</tbody>
</table>

N = 50×25/20 = 62.5
a = 62.5 - 50 = 12.5
b = 62.5 - 25 = 37.5
c = 62.5 - 55 = 7.5

CDR lab = 50/62.5 = 0.8
CDR hosp = 25/62.5 = 0.4
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
TB incidence is falling slowly in 95 of 135 countries, 1996-2005

> High income
> SE Asia & W Pacific
> Latin America
> E Mediterranean
> C&E Europe
> Sub-Saharan Africa

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

Incidence rate/100K on 1994 age-structure

Incidence rate/100K on aging population

on 1994 age-structure

on aging population
TB patients in Morocco

Women: 0.15 ± 0.02
Men: 0.14 ± 0.01
Morocco:
TB falling slowly in women, very slowly in men

Decline reported cases (%/person/yr)

- Urban
- Rural

Men Women
All forms
Men Women
Smear+
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

-8 -4 0 4 8

-8 -4 0 4 8

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

Men Women Total
Average age of men 15-54 yrs with TB is falling in some countries

![Graph showing the average age of men with TB in Viet Nam, Sri Lanka, Myanmar, and China over the years 1996 to 2004. The average age is decreasing over time in all countries.]
TB trends: New Caledonia

All TB 9.4%/yr

Smear+ 8.2%/yr
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
<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</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</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</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</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</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</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.

![Graph showing prevalence of TB over time with DOTS and Other categories.]

- DOTS: 200 in 1990, 150 in 2000
- Other: 170 in 1990, 180 in 2000
Progress towards MDGs in Indonesia
prevalence rate fell 4%/yr 1980-2004?
"Model DOTS Project" reduces TB prevalence in south India

source: TRC Chennai

fall ~10%/yr in MDP

[Graph showing prevalence rates over years for different groups (Male C+, Male S+, Female C+, Female S+).]
Incidence cannot reliably be estimated from prevalence e.g. Cambodia?

\[\text{prevalence ss} + = \text{incidence} \times \text{weighted duration}\]

<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

Three approaches

1. Incidence $\times$ case fatality (method 4)
2. Verbal autopsy (in sample vital registration)
3. Vital (death) registration

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

A few data from Asia & Africa, long reporting delays

**Geometric mean TB mortality (per 100K)**

<table>
<thead>
<tr>
<th>Year</th>
<th>ex Soviet Union</th>
<th>Central Europe</th>
<th>Industrialized</th>
<th>Latin America</th>
<th>Rep. Korea</th>
<th>Philippines</th>
</tr>
</thead>
<tbody>
<tr>
<td>1985</td>
<td>15</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>15</td>
<td>7</td>
</tr>
<tr>
<td>1990</td>
<td>10</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>1995</td>
<td>8</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>2000</td>
<td>6</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>2005</td>
<td>4</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
4. Measuring and estimating risk of TB infection
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

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

Smear+ notifications/100K

1.43% infection

0.51% infection

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

2005
2004
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."