Eliminating tuberculosis: practical proposition or distant dream?

Christopher Dye

World Health Organization
TB control @

[DOTS-
sure cure for TB.]

stop

TB

THE END TB STRATEGY
WHO-IUATLD DOTS strategy (1990s)

1. Political and financial commitment
2. Diagnosis by sputum-smear microscopy
3. Treatment under direct and supportive observation (DOT)
4. Regular, uninterrupted supply of drugs
5. Standardized recording and reporting
Mission impossible: the End TB strategy

Tuberculosis eradication: renewed commitment and global investment required

*Helen Cox, Mark P Nicol
My main sources

The Population Biology of Tuberculosis
Christopher Dye

GLOBAL TUBERCULOSIS REPORT
2017
World Health Organization
Britain beat TB in the 19th and 20th centuries?

Much of the (slow) decline preceded drugs

Keats
1821

E Bronte
1848

C Bronte
1855

Mansfield
1923

Lawrence
1930

Orwell
1953

Leigh
1967

TB deaths/100,000/yr
England & Wales
Fall in TB cases and deaths 1914-2007

Case fatality (deaths/cases)
Cases or deaths
Year
Cases
Deaths
Case fatality

ESCMID eLibrary
© by author
"Model DOTS" accelerates TB decline in S India

Model: early Dx/Rx cuts transmission
Not model: hard to scale
Chemotherapy for tuberculosis

Vitamin A supplementation

Treatment of leukemia

Greater effectiveness

Lower cost

Environmental control of dengue

Cost per intervention or per intervention-year (dollars, log scale)

Increase in DALYs (log scale)
So why is TB decline so slow?

Fall incidence 2% and mortality 3% per year

Averting 53 million deaths 2000–2016: but millions of lives were lost
Why is TB case fatality at least ×2 too high?

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>HIV-</th>
<th>HIV+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases (M)</td>
<td>10.4</td>
<td>9.4</td>
<td>1.0</td>
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<tr>
<td>Deaths (M)</td>
<td>1.7</td>
<td>1.3</td>
<td>0.4</td>
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<tr>
<td>Case fatality (%)</td>
<td>16</td>
<td>14</td>
<td>36</td>
</tr>
</tbody>
</table>
TB deaths > HIV deaths (again)
How could we do better? Options for TB control

Uninfected → Latent
- 10 infections/case

Latent → Active
- Fast 5%
- Slow 5%
- Drug or vaccine

Active → Death 50%
- Drug Cure >85%

Vaccine

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How to eliminate TB by 2050
15M cases 5M deaths averted 2000-15 (WHO)

Cases and deaths prevented

- Up to 10%/yr with current technology
- Beyond current technology
- Elimination <1/M
- New tools 10%/yr
- UHC 10%/yr
- 20%/yr
- 2%/yr
What did the Millennium Development Goals do for health 2000-15?
# Sustainable Development Goals

<table>
<thead>
<tr>
<th>Goal</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>No Poverty</td>
</tr>
<tr>
<td>8</td>
<td>Decent Work and Economic Growth</td>
</tr>
<tr>
<td>9</td>
<td>Industry, Innovation and Infrastructure</td>
</tr>
<tr>
<td>11</td>
<td>Sustainable Cities and Communities</td>
</tr>
<tr>
<td>16</td>
<td>Peace, Justice and Strong Institutions</td>
</tr>
<tr>
<td>10</td>
<td>Reduced Inequalities</td>
</tr>
<tr>
<td>5</td>
<td>Gender Equality</td>
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<tr>
<td>4</td>
<td>Quality Education</td>
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<tr>
<td>17</td>
<td>Partnerships for the Goals</td>
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<tr>
<td>2</td>
<td>Zero Hunger</td>
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<tr>
<td>6</td>
<td>Clean Water and Sanitation</td>
</tr>
<tr>
<td>7</td>
<td>Affordable and Clean Energy</td>
</tr>
<tr>
<td>12</td>
<td>Responsible Consumption and Production</td>
</tr>
<tr>
<td>13</td>
<td>Climate Action</td>
</tr>
<tr>
<td>14</td>
<td>Life Below Water</td>
</tr>
<tr>
<td>15</td>
<td>Life on Land</td>
</tr>
</tbody>
</table>

**Inclusive Society**

**Shared Prosperity**

**Protected Environment**
What can the SDGs do for TB?

Individuals & Society

Economy

Environment

3 GOOD HEALTH AND WELL-BEING

Systems & Services
Universal Health Coverage

World Health Organization

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### Which top 10? Direct or indirect causes of death?

#### Deaths from CD, NCD & injuries

1. Ischaemic heart disease
2. Cerebrovascular disease
3. Lower respiratory infections
4. Neonatal preterm birth complications
5. Diarrhoeal diseases
6. Neonatal encephalopathy
7. HIV/AIDS
8. Road injuries
9. Malaria
10. COPD

#### Risk factors for death

1. High systolic blood pressure
2. Smoking
3. High fasting plasma glucose
4. High total cholesterol
5. Ambient particulate matter pollution
6. Diet high in sodium
7. High body-mass index
8. Diet low in whole grains
9. Diet low in fruits
10. Household air pollution from solid fuels

*Source: GBD 2015 (see also DCP3)*
Should we invest more in prevention?

Natl Health Accounts: low spending on prevention in relation to risk

Investment in services

<table>
<thead>
<tr>
<th>Service</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Cure</td>
<td>96.4%</td>
</tr>
<tr>
<td>Prevent</td>
<td>3.6%</td>
</tr>
</tbody>
</table>

Attributable Risk (minimum)

<table>
<thead>
<tr>
<th>Category</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Environment</td>
<td>16.7%</td>
</tr>
<tr>
<td>Behaviour</td>
<td>40.8%</td>
</tr>
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</table>

Percent of $7tn/yr spent on health

Source: Lerner/OECD
SDGs aim to put “health in all policies”
GREATER POLITICAL COMMITMENT URGENTLY NEEDED TO END TB

IN 2017

WHO GLOBAL MINISTERIAL CONFERENCE ON ENDING TB IN THE SUSTAINABLE DEVELOPMENT ERA IN MOSCOW, 16-17 NOVEMBER 2017

IN 2018

FIRST UN GENERAL ASSEMBLY HIGH-LEVEL MEETING ON TB IN 2018

BOTH HIGH-LEVEL EVENTS WILL BUILD MOMENTUM, DRIVE MULTISECTORAL ACTION AND ACCELERATE GLOBAL AND NATIONAL EFFORTS TO MAKE TB HISTORY

World Health Organization
END TB

Ending TB by 2030 means:

- **80%** drop in new TB cases
- **90%** drop in people dying of TB
- **100%** of TB-affected families protected from catastrophic costs

Through:

- **BETTER** care & prevention
- **BOLDER** policies & systems
- **BIGGER** investments in research & innovation

**IT’S ABOUT SAVING LIVES, TACKLING POVERTY AND INEQUITY**
“India can’t eliminate tuberculosis by 2025 without curbing smoking”  Quartz India
Indoor air pollution 3-4M deaths/year
Few at high risk, many at low risk

Prevalence of risk factor in target population

Relative risk

Population attributable fraction

0.05 0.2 0.4 0.6 0.8 0.9

Relative risk vs Prevalence of risk factor in target population
TB prevalence 5× higher among poorest in India but “poverty” suggests multiple interventions

Major risk factors
Low body mass index, indoor air pollution
But failure of TB control excluded!
Priority #1: Universal Health Coverage equity and economy underpinning UHC

Tedros Adhanom Ghebreyesus DG WHO

“The right of every individual to basic health services will be my top priority”
UHC as “The Affordable Dream”?
“India aims to eradicate tuberculosis by 2025, says PM Modi at Delhi End TB Summit”
100M poor and vulnerable families

up to $8000 per family per year for secondary and tertiary care hospitalization
The TB market in Bangalore
Diagnosis and treatment limited by health system

Data from Pantoja et al 2009
South-East Asia: India & Thailand
UHC necessary but not sufficient to cut TB transmission
inadequate political support for regulatory functions

poor technical and human capacity of regulatory bodies

private sector influence on regulatory policy and implementation
Eastern Europe: Estonia & Russia
Public health + TB Programme

Case notifications Russia (000s/yr)
Case notifications Estonia (/yr)
Year
Russia -2.0%/yr
Estonia -8.4%/yr

Estonia Primary Health Care
National TB Programme

© by author
Estonia is containing MDR-TB; Russia isn’t (yet) TB drug resistance can be reduced to low levels

![Graph showing MDR-TB cases reported in Estonia and Russia over years.](image-url)
Western Europe: Sweden & Hungary
Low incidence, high immigration, slow decline

Change in TB case notifications (%/yr)

TB cases foreign born (%)

R² = 0.58
TB HIV

Double Trouble

People with HIV Infection face a greater risk of also developing TB. Don’t take chances. Get tested.

Call your physician or county health department for a tuberculosis test today — especially if you know you’re HIV-infected.
Southern Africa: TB incidence cut mainly by ART? NB migration, mines and men: origins of high HIV

![Graph showing TB case notifications, HIV prevalence, and ART prevalence over years in Botswana. The graph indicates a significant drop in TB case notifications following the introduction of ART.](image-url)
Sustaining a national tuberculosis control programme during civil crisis: 6 years of experience in Syria
Middle East (Syria): resilience in civil war

![Graph showing the number of PTB cases per year in Syria, comparing national data with data from Aleppo and Damascus.](image)
Vaccination is easier than drug treatment

![Graph showing population coverage of BCG vaccination and drug treatment across countries ranked. The graph illustrates that BCG vaccination maintains higher coverage over time compared to drug treatment.]
India defeated polio … but not (yet) TB
The latest TB vaccine trial
BCG revaccination vs subunit vaccine H4:IC31

- Western Cape, South Africa
- Safe, immunogenic in adolescents
- Neither vaccine prevented initial infection
- **BCG revaccination**: prevented sustained QFT conversion (increased clearance or control of infection; VE 45% p=0.01)
- **H4:IC31**: modest effect in preventing sustained QFT conversion (VE 31% p=0.08)
“NIH experts call for transformative research approach to end tuberculosis” PR

Perspective Piece
Reimagining the Research Approach to Tuberculosis†

Anthony S. Fauci* and Robert W. Eisinger

doi:10.4269/ajtmh.17-0999
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Even USA needs more than current tools

On course for elimination

Not on course for elimination: needs boost from IPT for HIV-
$1.1bn funding gap for TB research

Treatment Action Group 2015

<table>
<thead>
<tr>
<th>Category</th>
<th>Unfunded</th>
<th>Funded</th>
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<tbody>
<tr>
<td>Basic science</td>
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<tr>
<td>Diagnostics</td>
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<tr>
<td>Drugs</td>
<td>0.29</td>
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<tr>
<td>Vaccines</td>
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<tr>
<td>Operational Research</td>
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The Next To Go

Fight Tuberculosis!

Red Cross Christmas Seal Campaign
Integrate biological wisdom into social technology (1952)

Integrate social wisdom into biotechnology (2015)

Avert 30M cases
7M deaths
2016-2030