



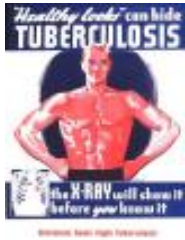
# The challenges of eliminating tuberculosis

Christopher Dye

World Health  
Organization



Pre 2015: dynamics and control of TB



Drug resistance as part of the TB challenge



Post 2015: TB elimination and “sustainable development”

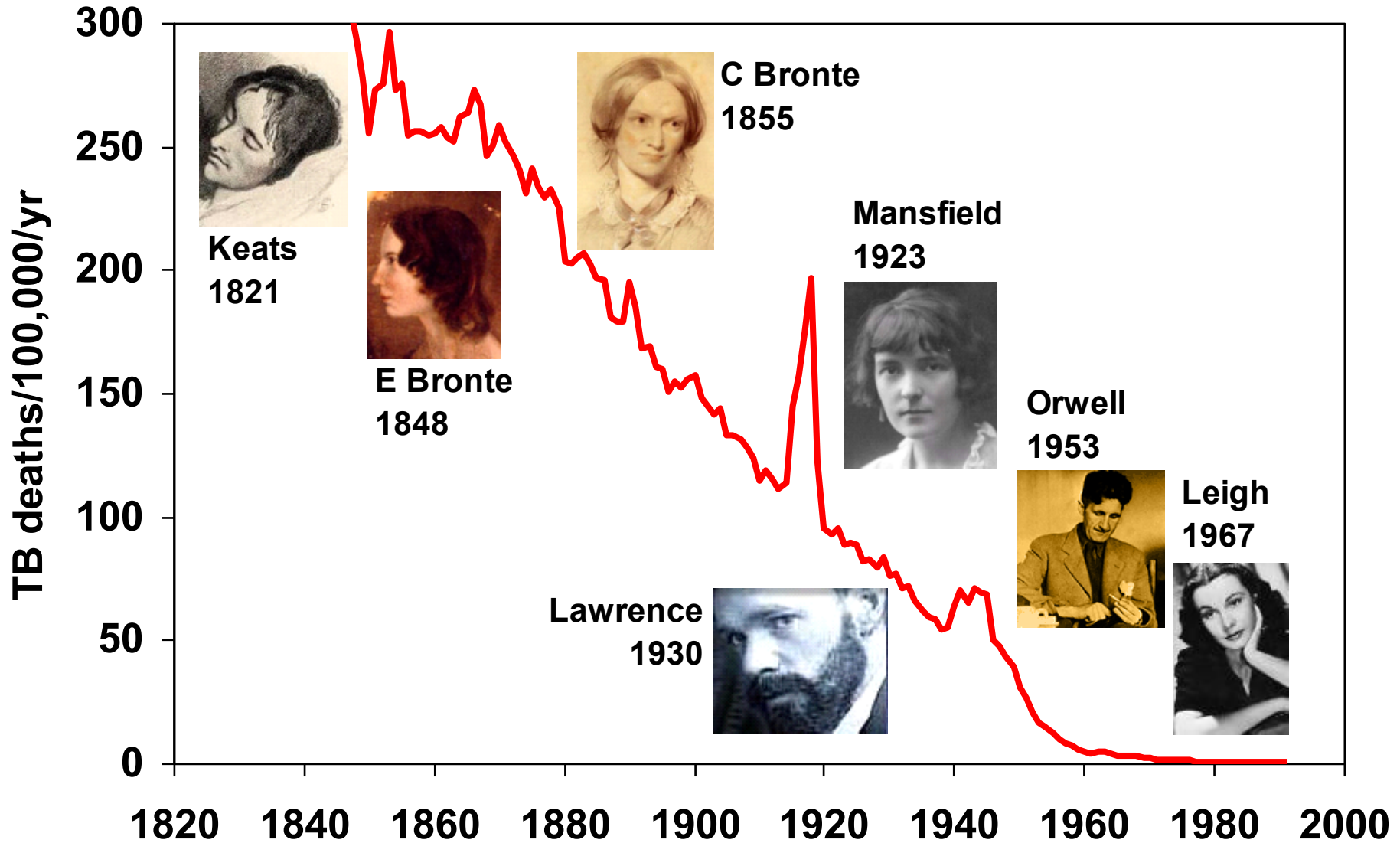


Pre 2015:  
dynamics and control  
of TB



# Britain beat TB in the 19th and 20th centuries?

## Much of the (slow) decline preceded drugs

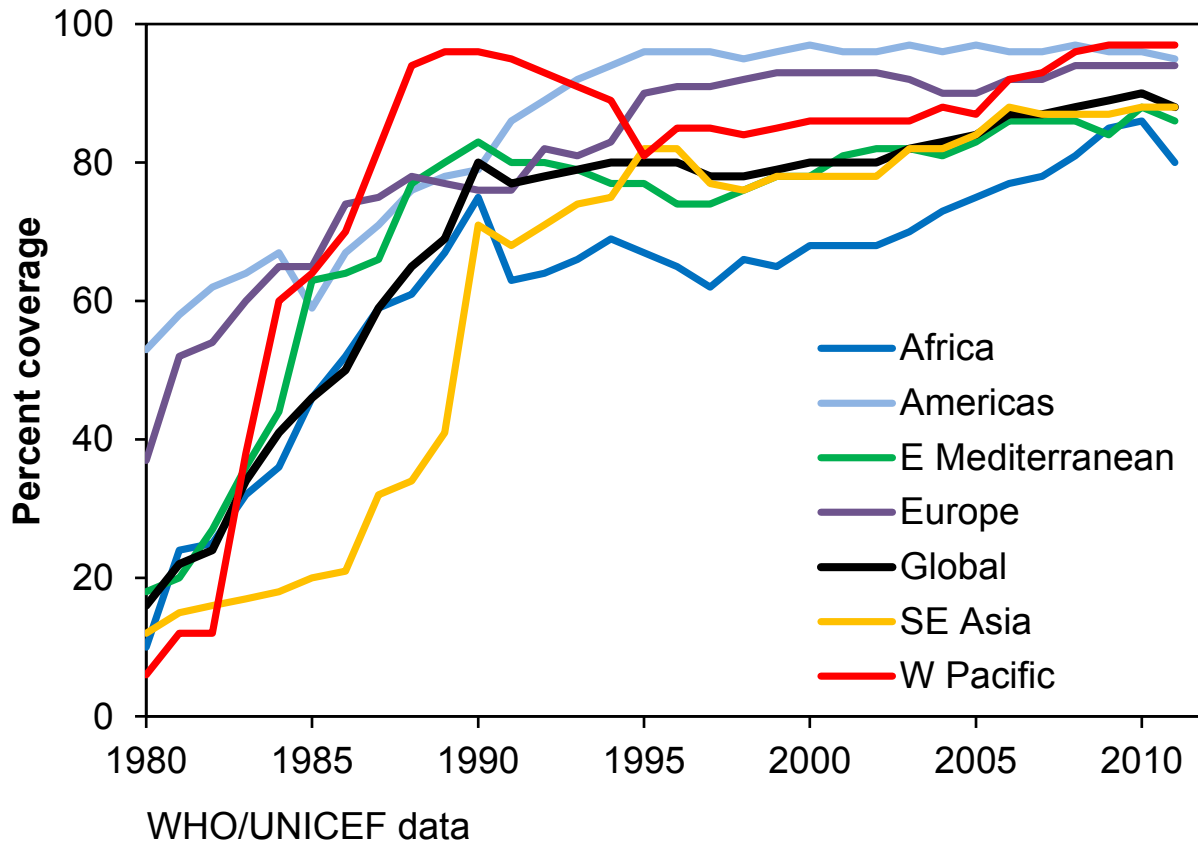


# BCG: the jab since 1921

~100M doses to infants annually in >150 countries with vaccination policy

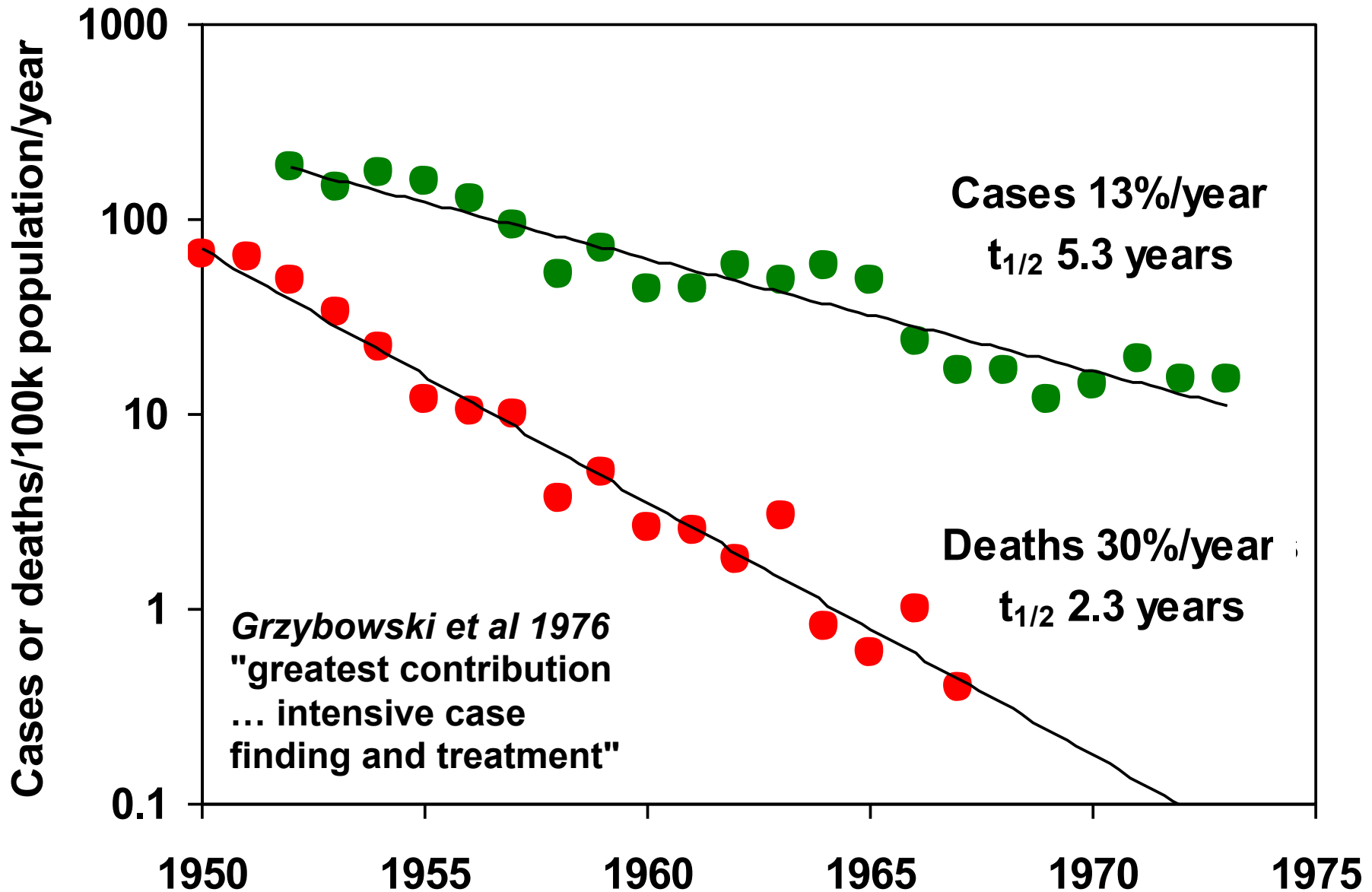
protects children from meningeal and disseminated TB, not adults from pulmonary TB

High BCG coverage across all WHO regions





# Tuberculosis in Alaskan Eskimos







# Global burden of TB

**All forms of TB**

**HIV-associated TB**

**Multidrug-resistant TB**

**Estimated incidence, 2013**

**Estimated number of deaths, 2013**

**9.0 million**  
(8.6–9.4 million)

**1.1 million\***  
(1.0–1.3 million)

**1.1 million**  
(1.0–1.2 million)

**360,000**  
(310,000–410,000)

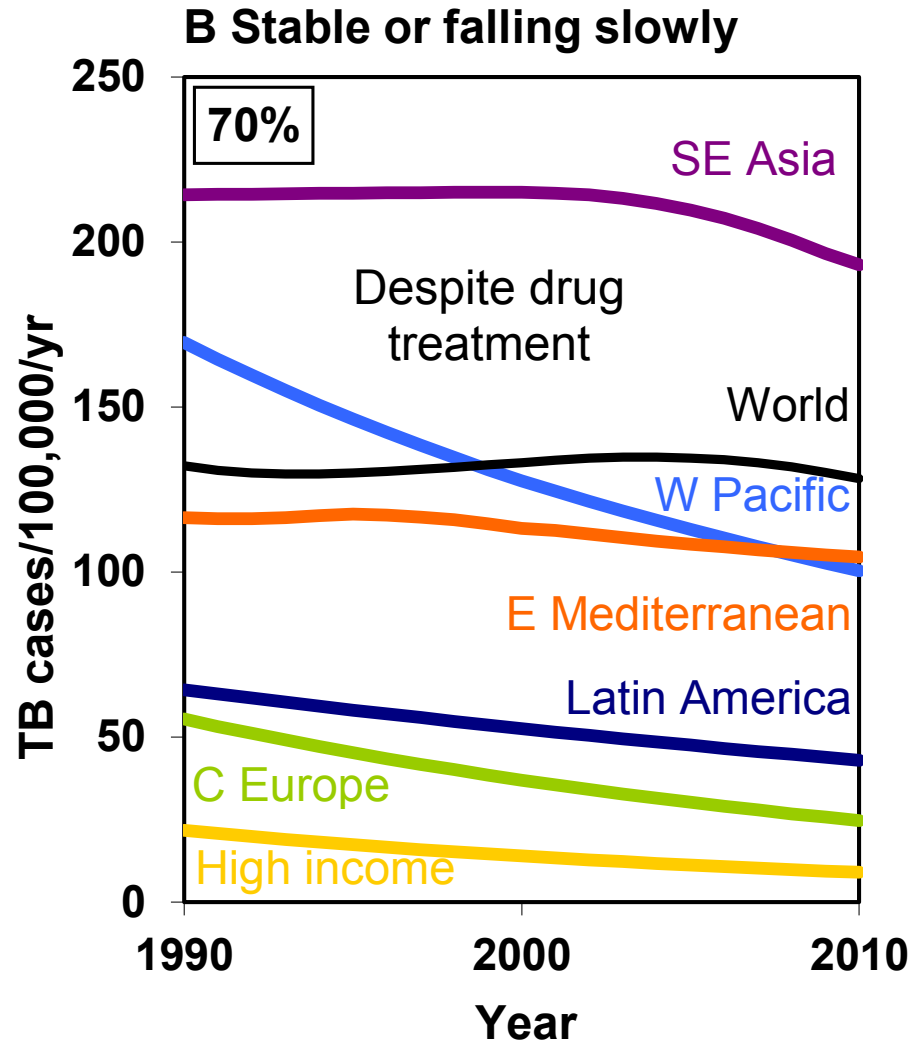
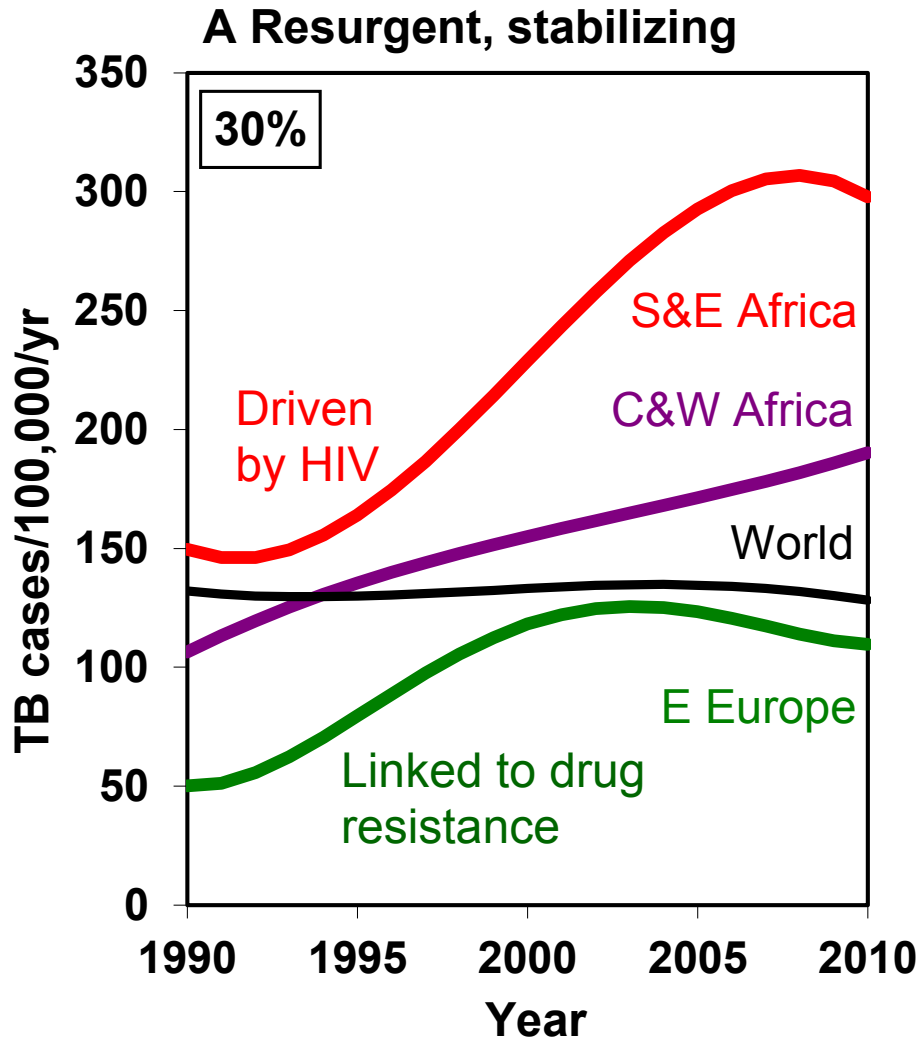
**480,000**  
(350,000–610,000)

**210,000**  
(130,000–290,000)

4-5%

20%

# TB case rate stable or falling after epidemics peak in **Africa** and **Europe**





Develop a global partnership for development



Eradicate extreme poverty and hunger



Achieve universal primary education



Ensure environmental sustainability

# 2015

## MILLENNIUM DEVELOPMENT GOALS



Promote gender equality and empower women



Combat HIV/AIDS, malaria and other diseases



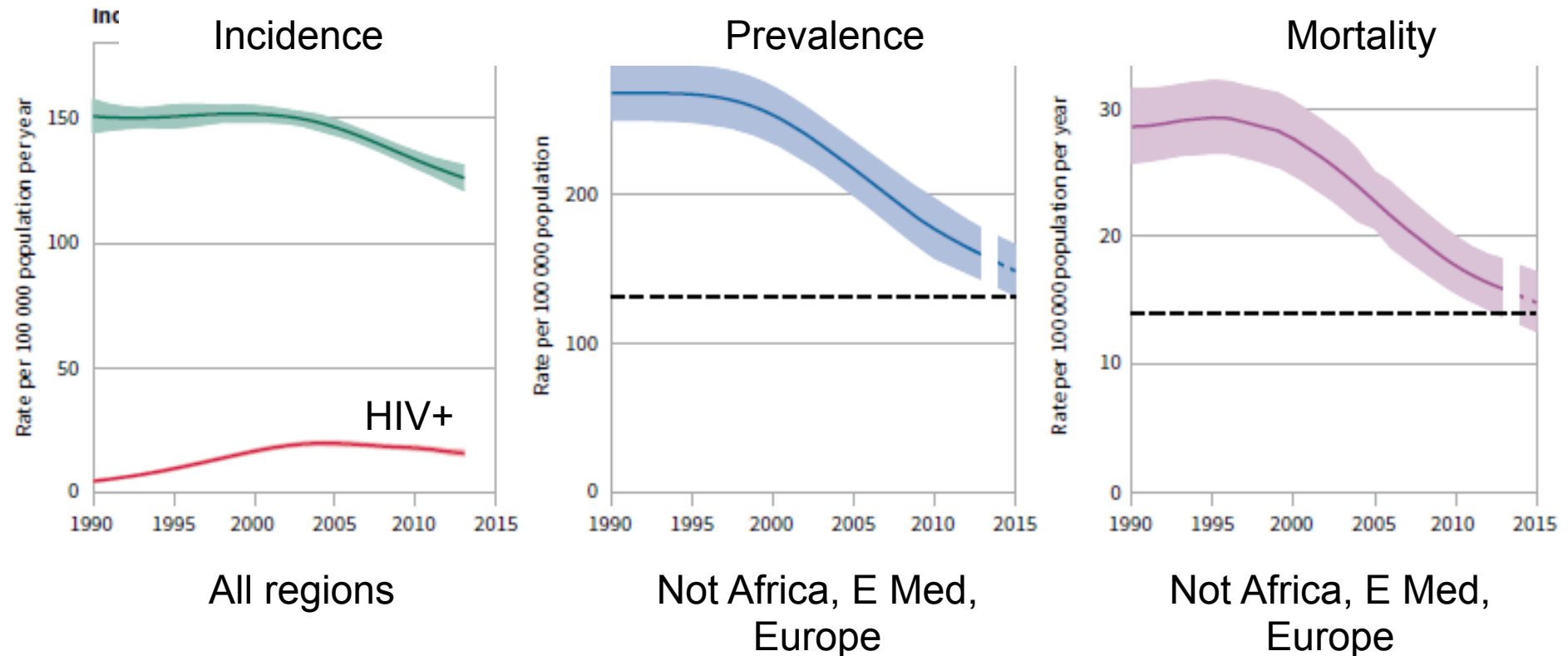
Improve maternal health



Reduce child mortality

# TB MDGs by 2015?

Stop TB targets: falling incidence, halve prevalence and death rates 1990-2015





# Dynamics of drug resistant TB

# **MDR-TB AND XDR-TB**

## **Multidrug-resistant tuberculosis**

### **MDR-TB**

Resistant to at least isoniazid and rifampicin

## **Extensively drug-resistant TB**

### **XDR-TB**

Resistant to isoniazid and rifampin, plus any fluoroquinolone and at least 1 of 3 injectable second-line drugs (amikacin, kanamycin or capreomycin)

## **Totally drug-resistant TB**

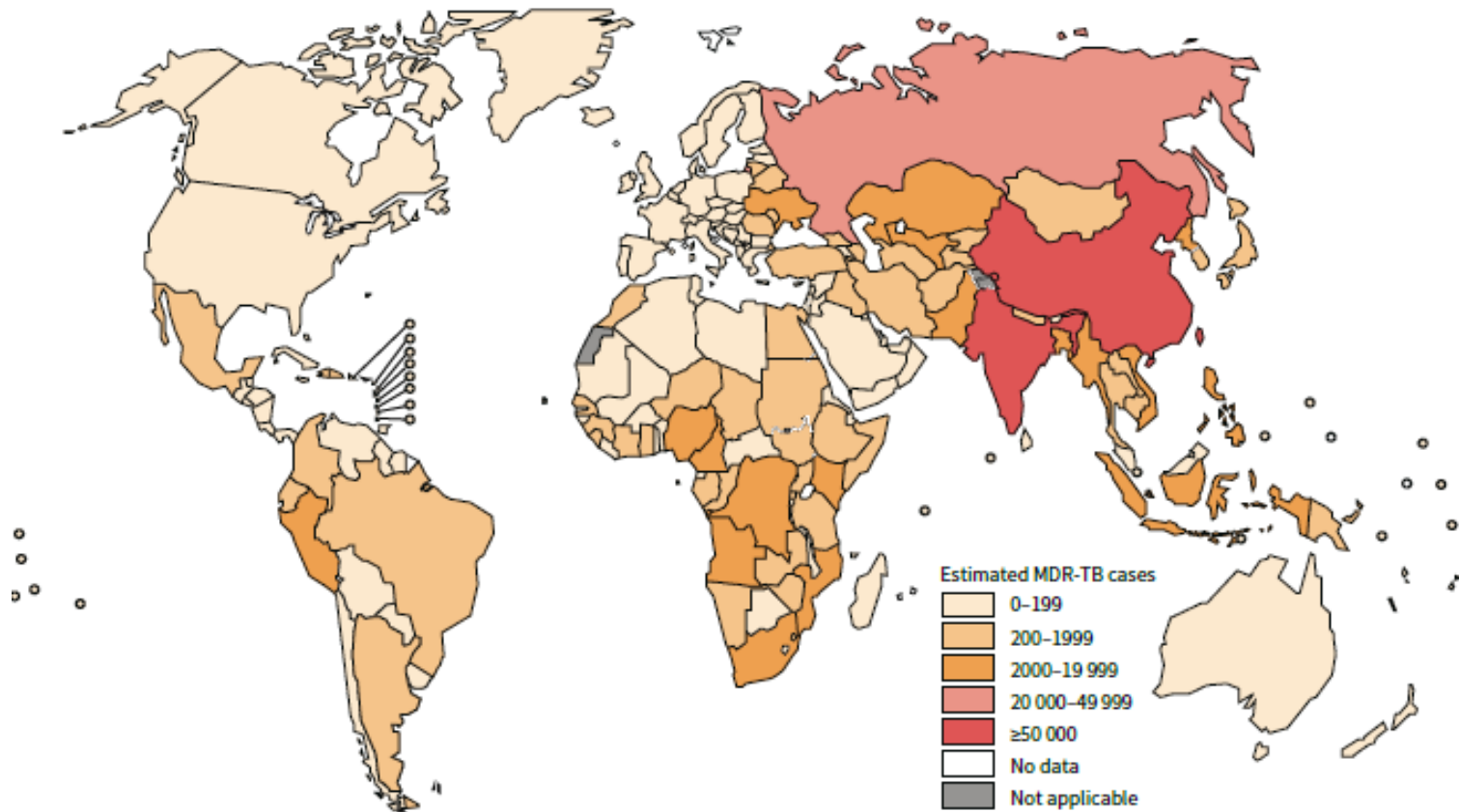
### **TDR-TB**

Informal, undefined by susceptibility tests

# Drug resistant TB worldwide

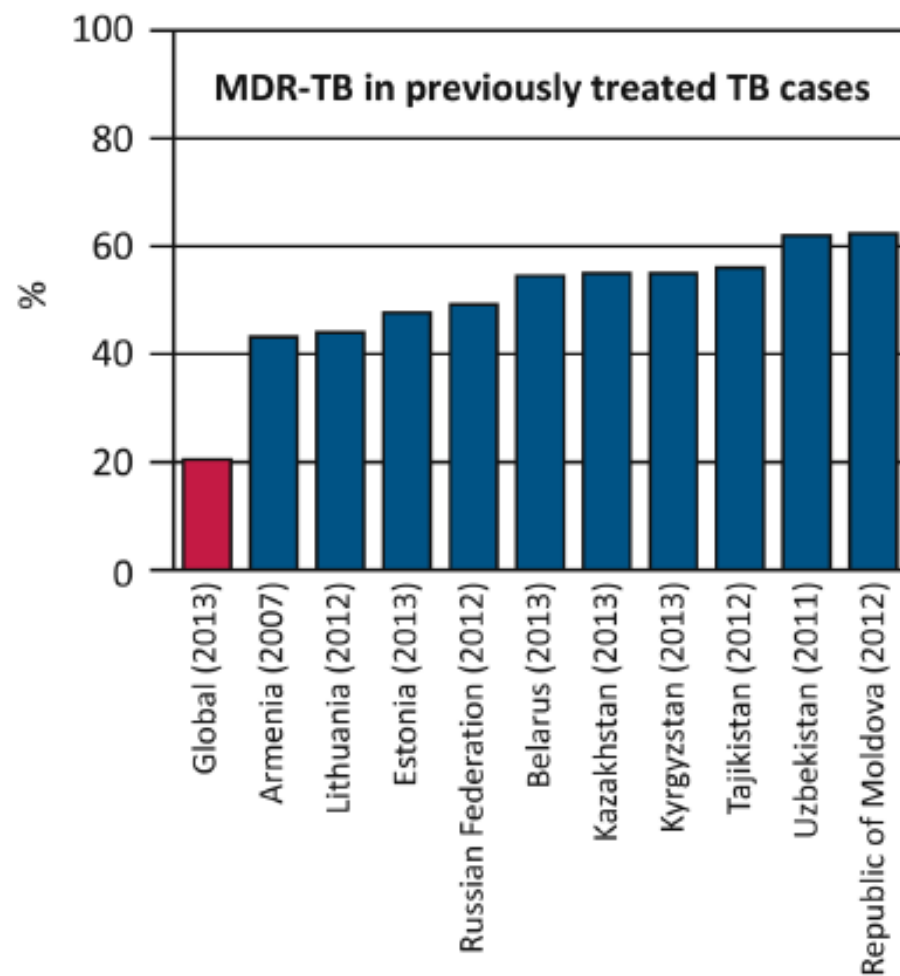
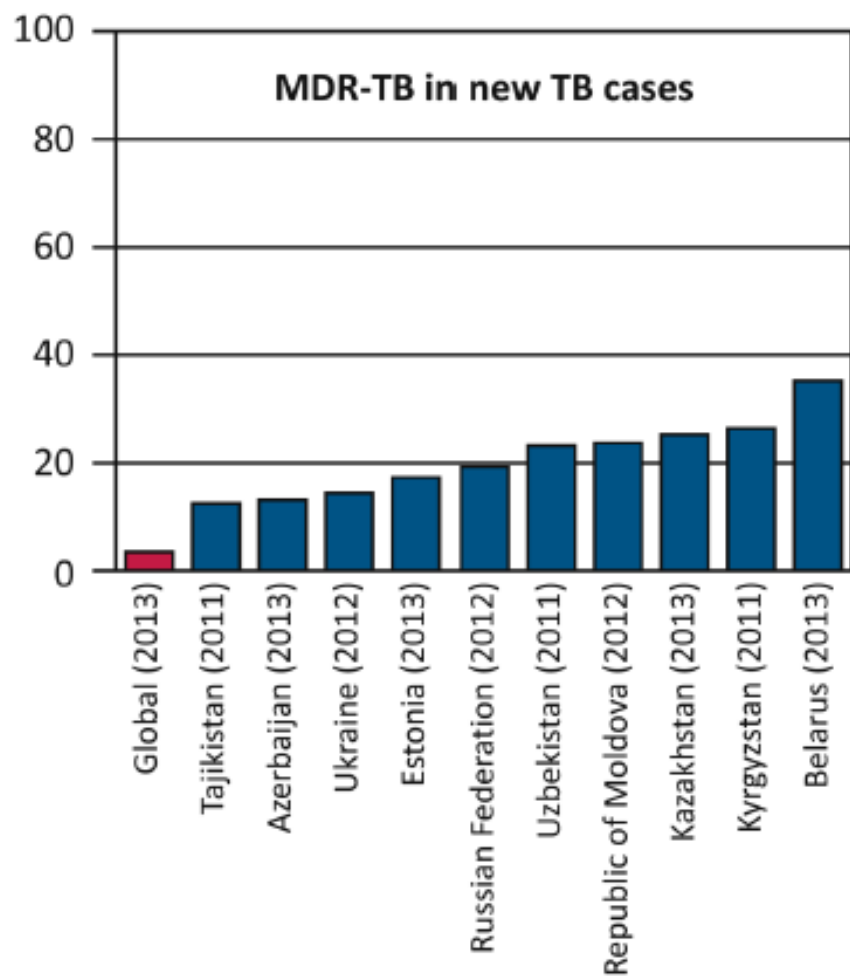
>50% cases of MDR-TB in China, India, Russia

ESTIMATED NUMBER OF MDR-TB CASES AMONG NOTIFIED TB PATIENTS, 2013



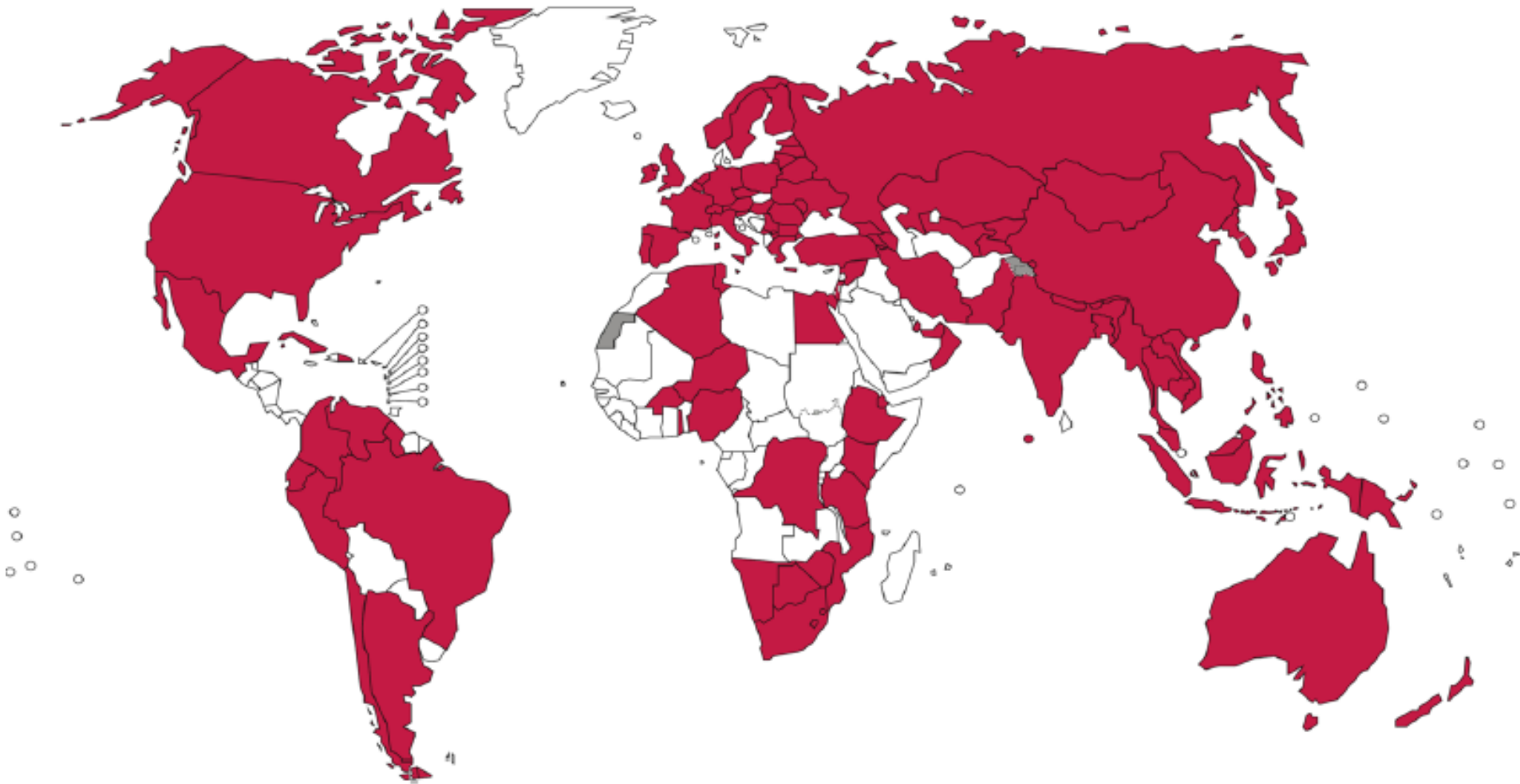
≈ 480,000 cases MDR-TB in 2013  
4-5% new cases, 20% recurrent cases

# Percentage of new and previously treated TB cases with MDR-TB globally and in the top 10 countries, 2014





# Countries that notified at least one case of XDR-TB



>85 countries by 2014

**300 000** of 480,000



detected

cases of MDR-TB estimated among TB patients reported by national TB programmes in 2013

Only 10% of MDR-TB cases known to be successfully treated

**136 000**

diagnosed



patients eligible for MDR-TB treatment

(136 000 out of 300 000) were detected and reported in 2013

**97 000**

treated



people with TB were started on second-line treatment for MDR-TB in 2013, leaving many patients on waiting lists for treatment

Poor practice promotes the evolution of resistance?

cured

**48%**

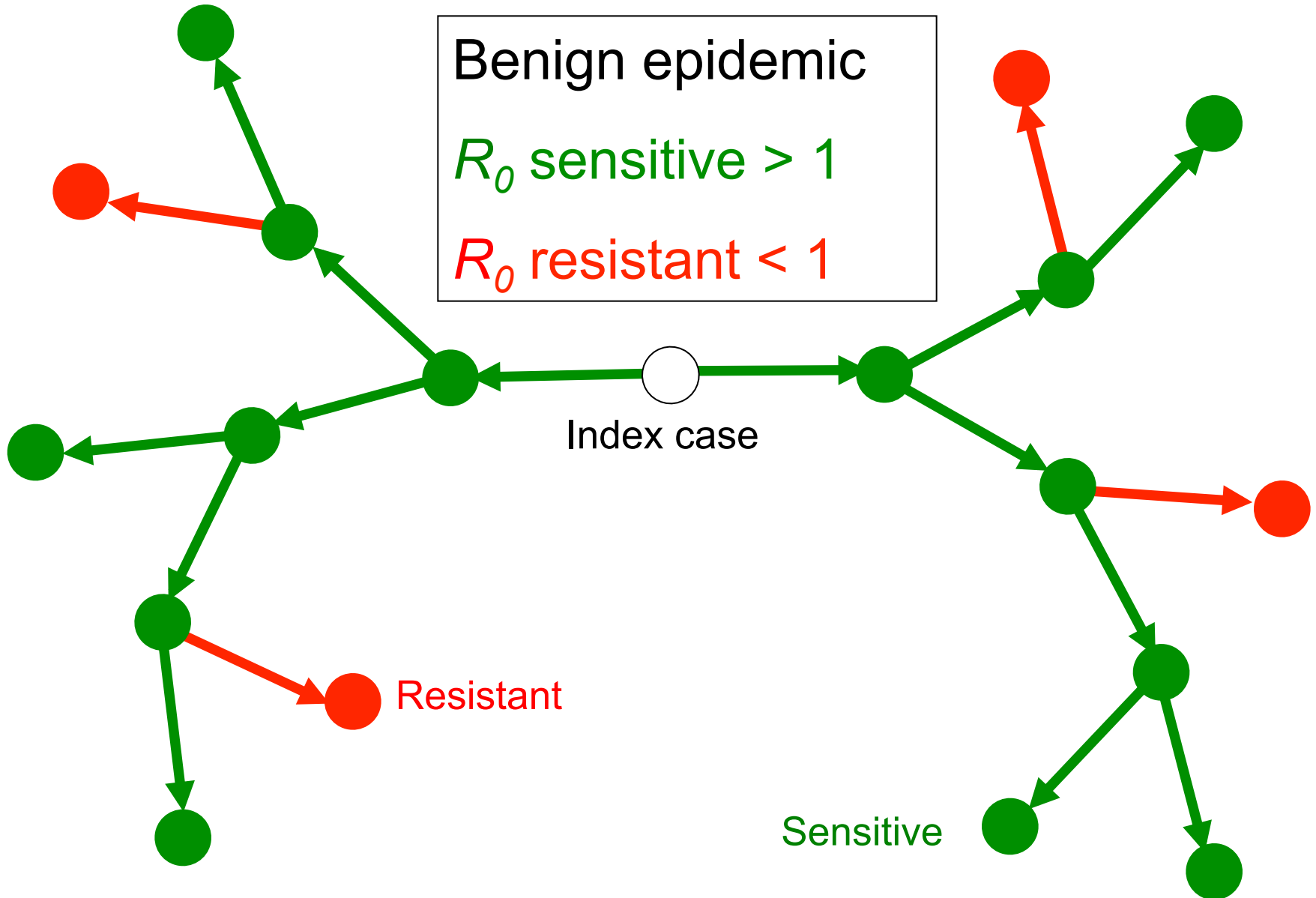
of MDR-TB patients globally had a successful treatment outcome

Five out of the 27 high MDR-TB countries achieved a treatment success rate of  $\geq 70\%$

Six criteria govern long-term dynamics of drug-sensitive and drug-resistant TB, based on case reproduction numbers

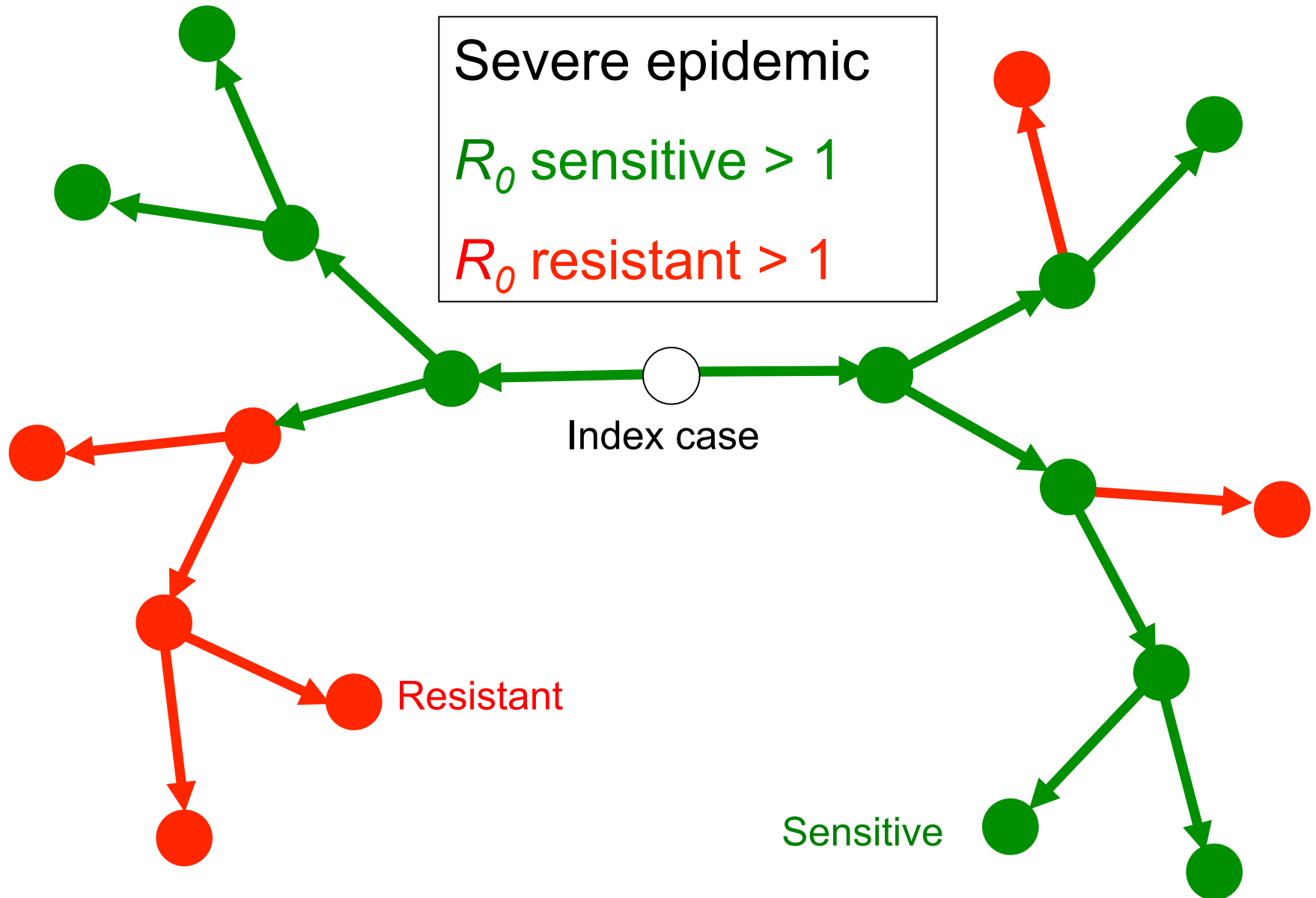
Condition on $R_{0S}$	Condition on $R_{0R}$	Outcomes	
		Number of cases	Fraction new cases resistant
$< 1$	$< R_{0S}$	Extinction of S and R	Falling
	$> R_{0S}$	Extinction of S and R	Rising
	$> 1$	Extinction of S; R persists in self-sustaining transmission cycles	Rising to fixation
$> 1$	$> R_{0S}$	Extinction of S; R persists in self-sustaining transmission cycles	Rising to fixation
	$< R_{0S}$	Persistence of S and R	Rising then steady
	$< 1$	Extinction of S, persistence of R	Rising then steady but low

# Stop **production** of resistant cases



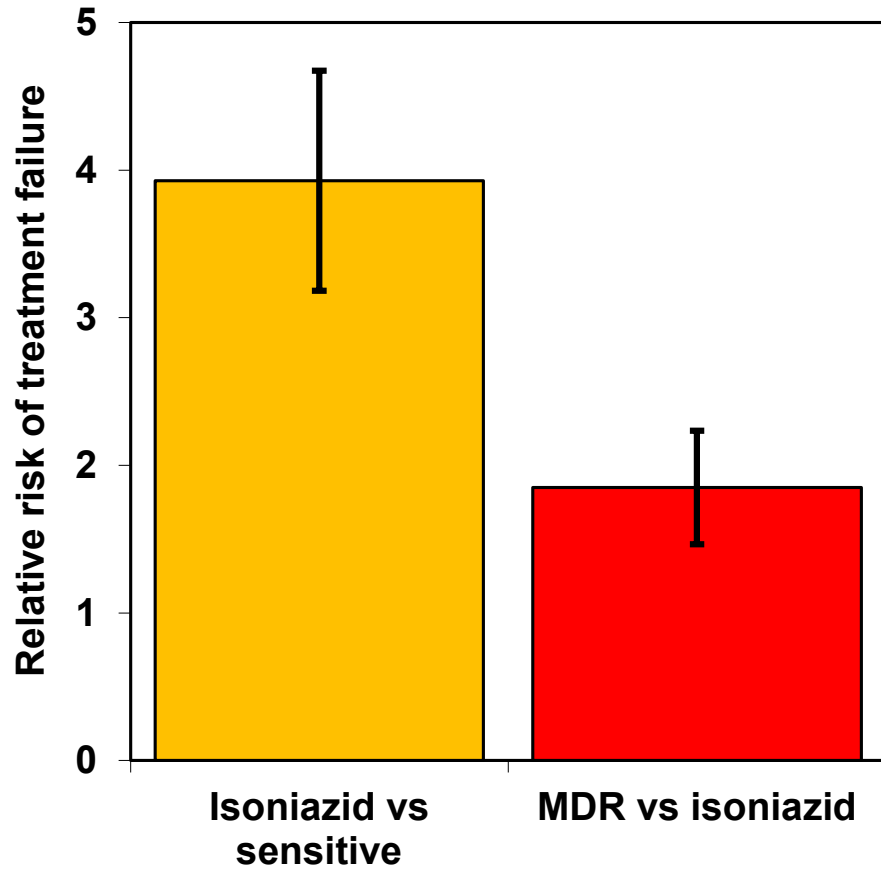


# Stop production and reproduction of resistant cases

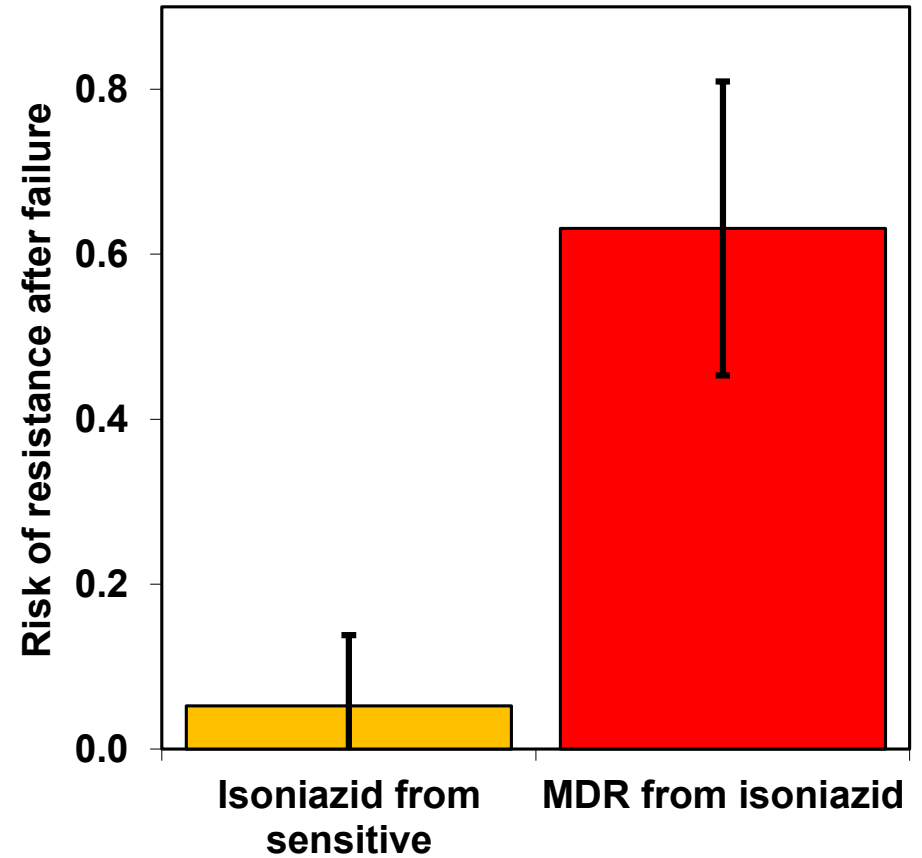


# Two factors that determine the evolution of drug resistant TB strains

## Treatment Rx failure

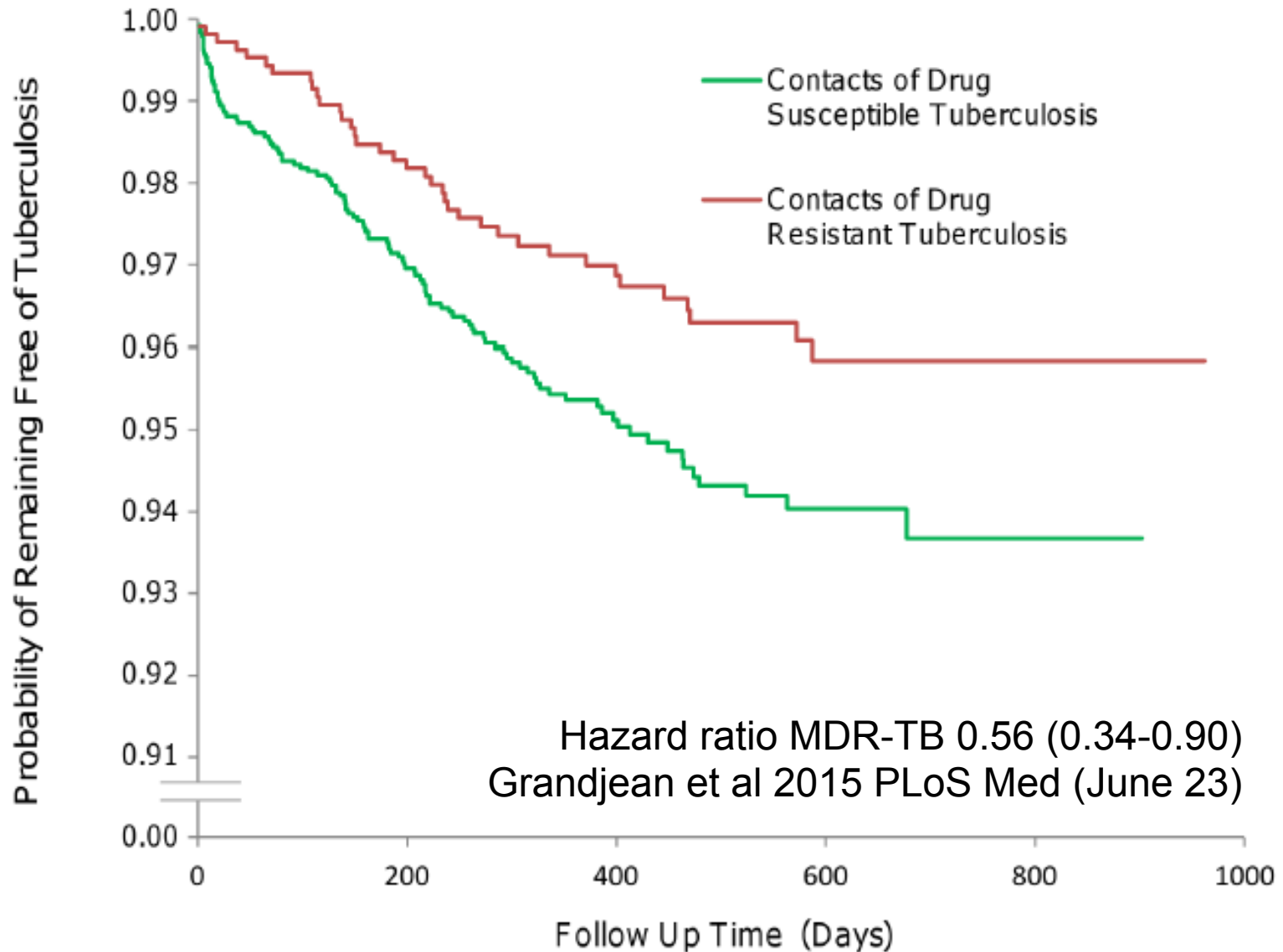


## Resistance after Rx failure

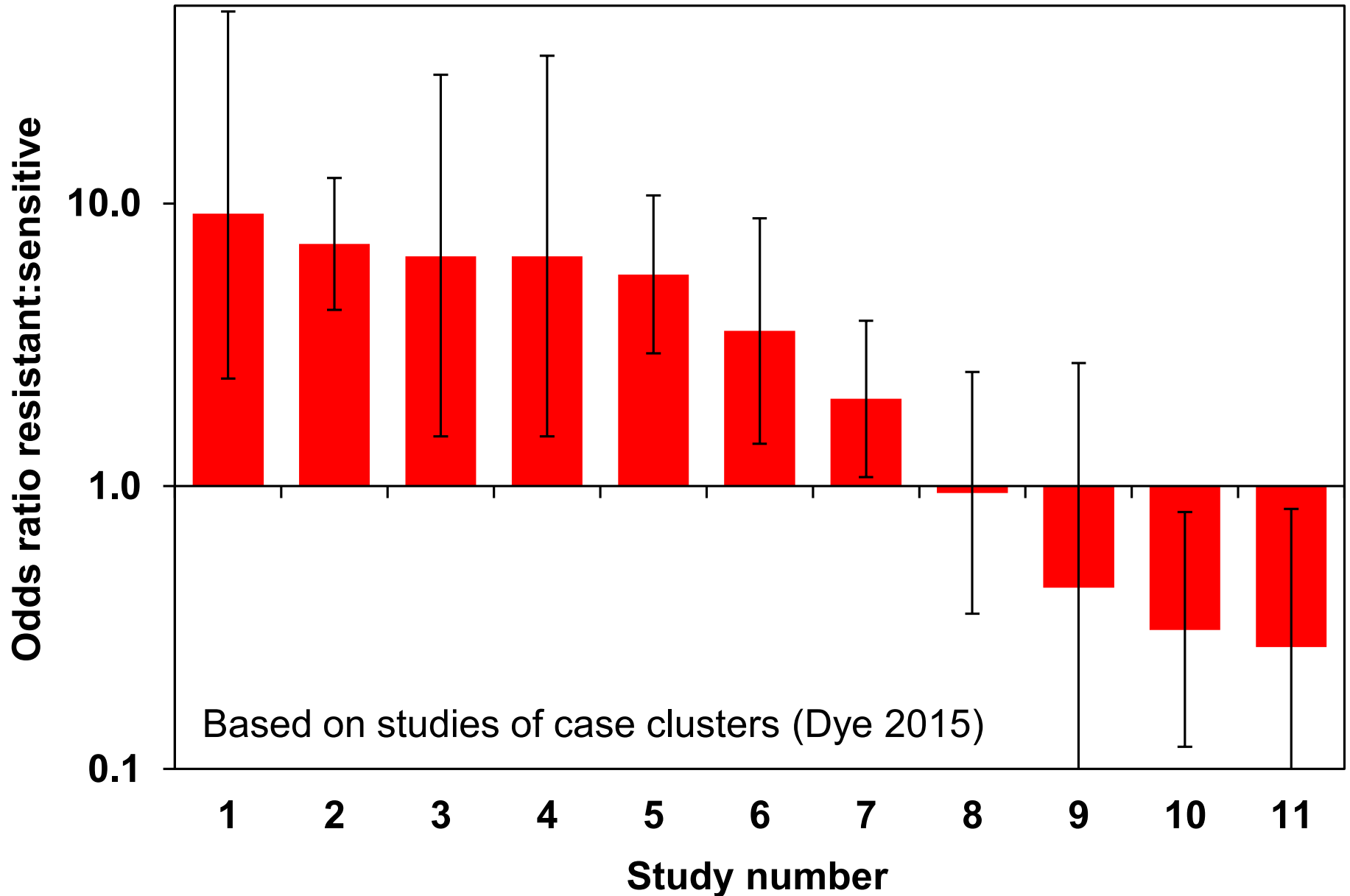


Data pooled from 138 surveys in 118 countries

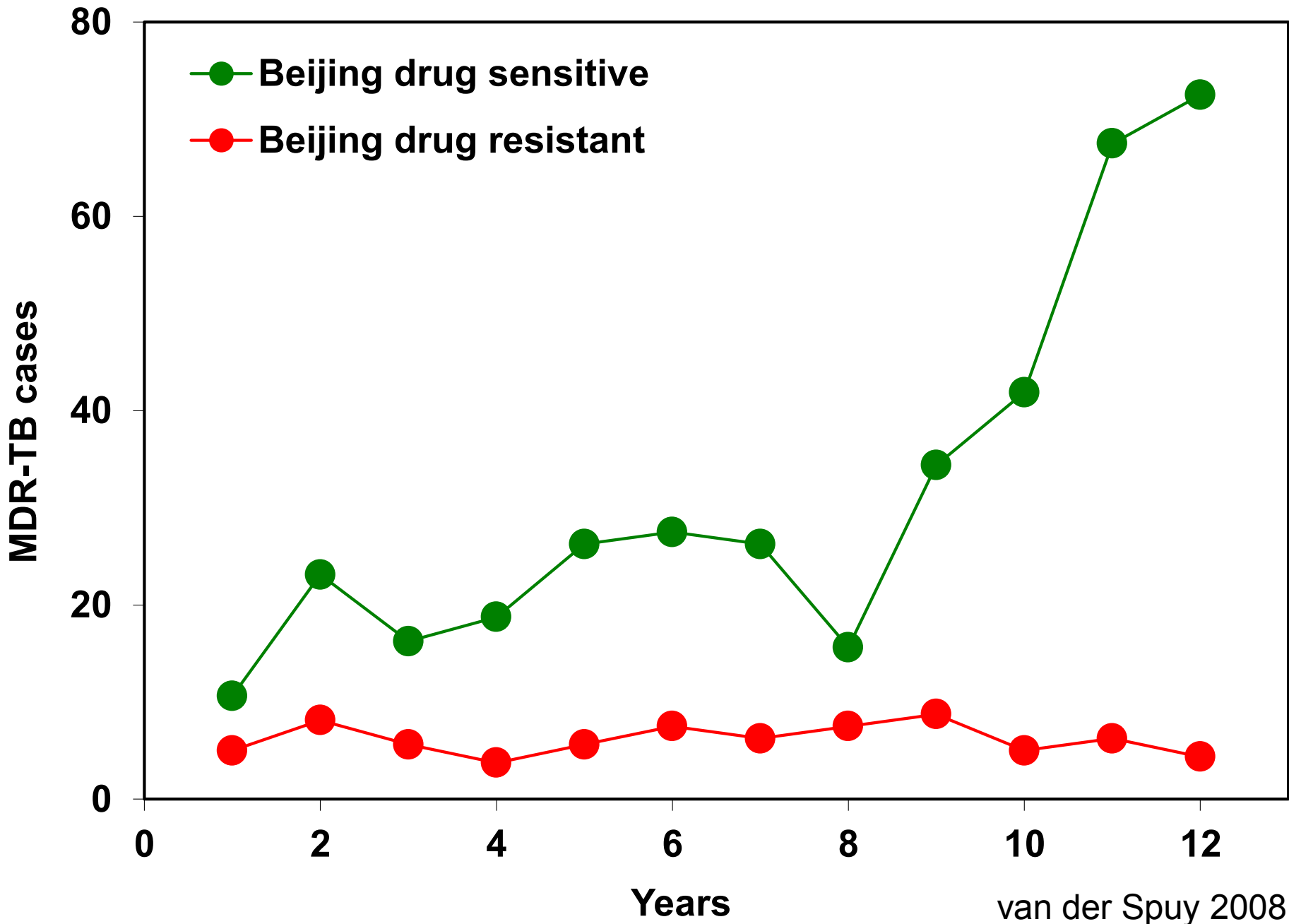
# MDR-TB half as “fit” as drug susceptible TB in Peruvian households



# Relative fitness of MDR-TB strains: not just biology

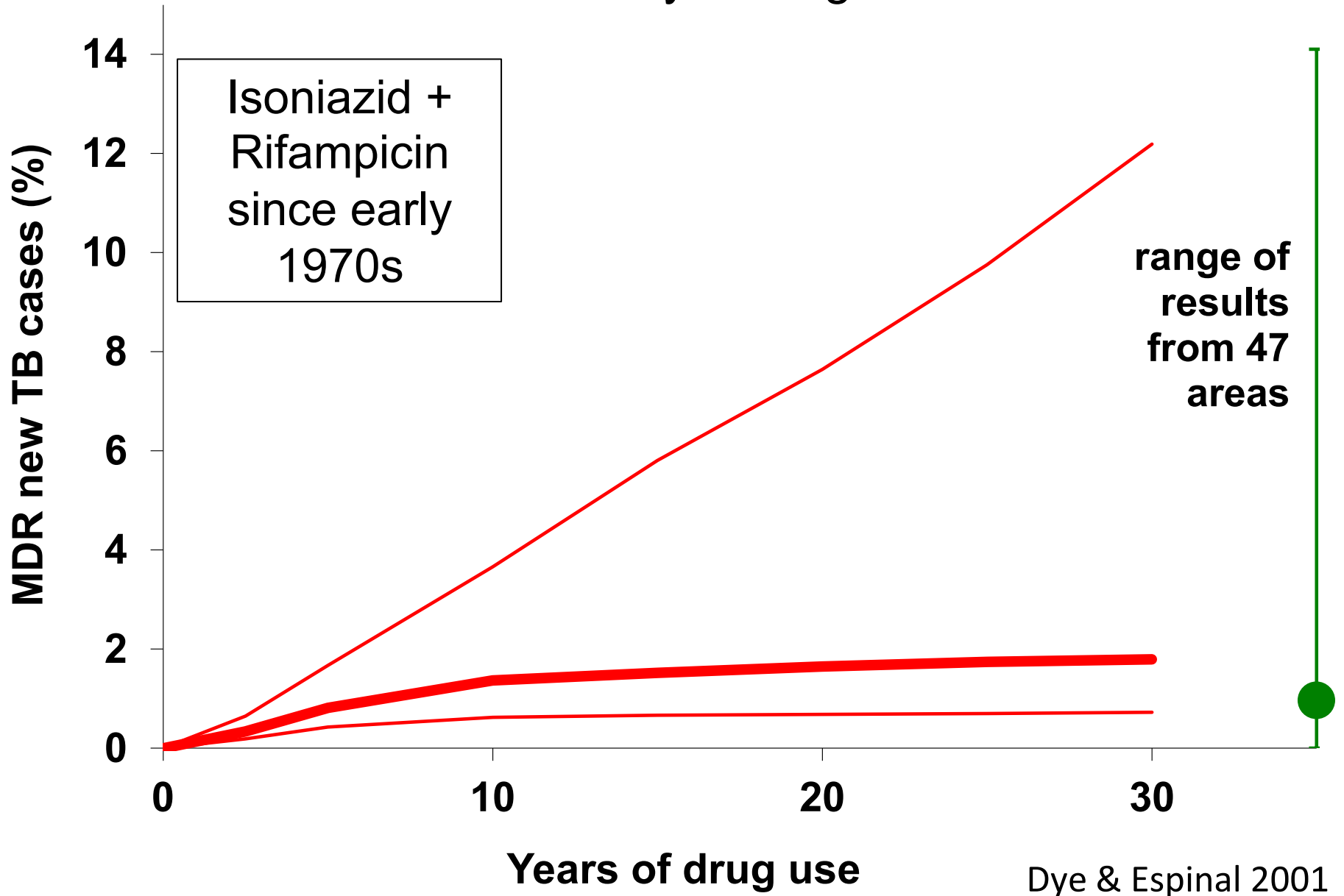


# Beware preconceptions: MDR-TB in Cape Town



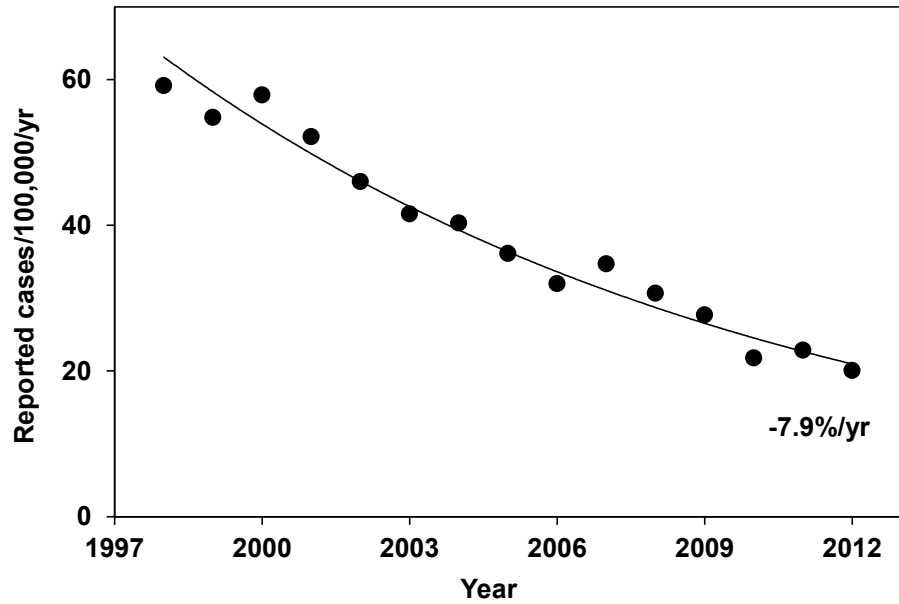
# Forecasting the future of MDR-TB

15 years ago

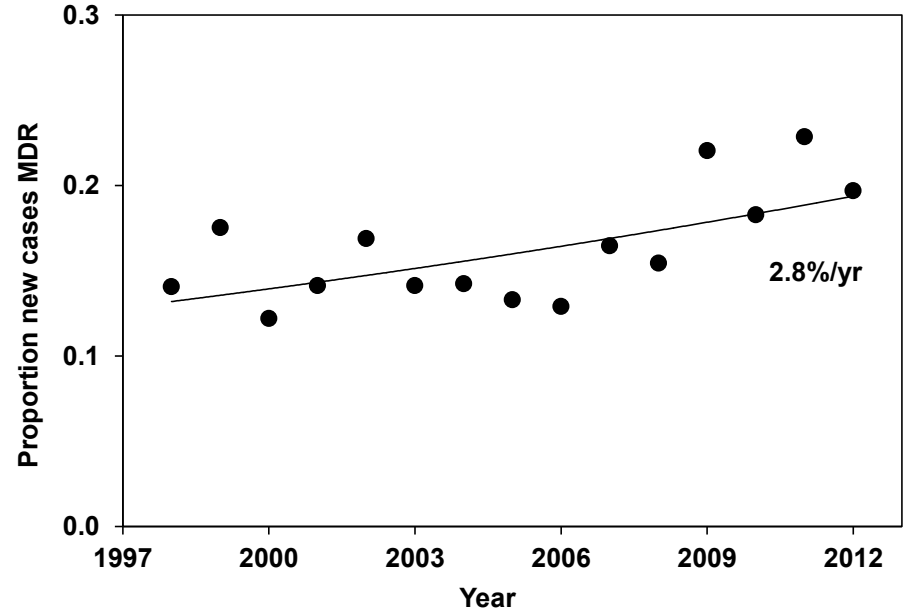


# Contrasting dynamics of resistance: E Europe

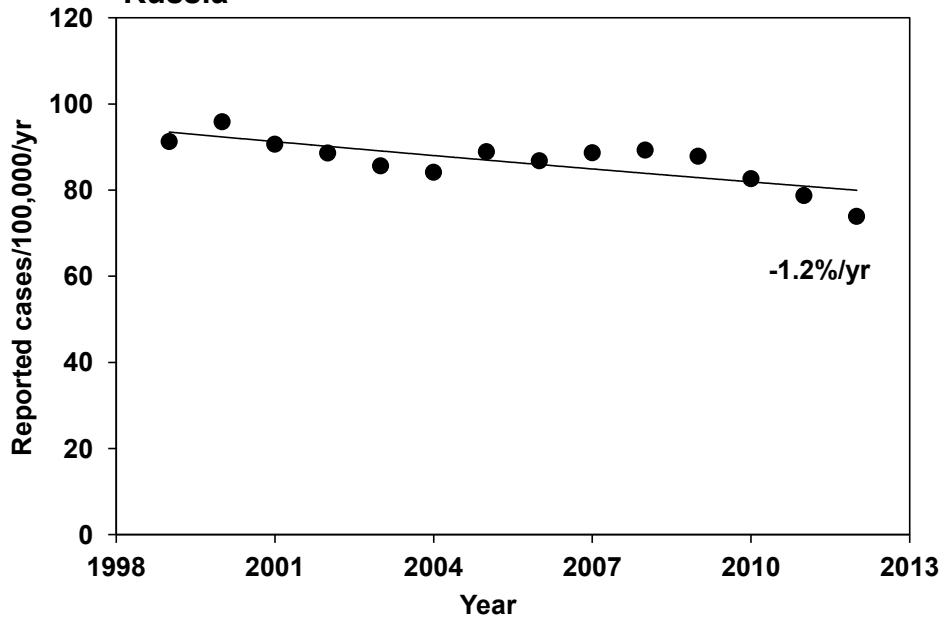
## Estonia



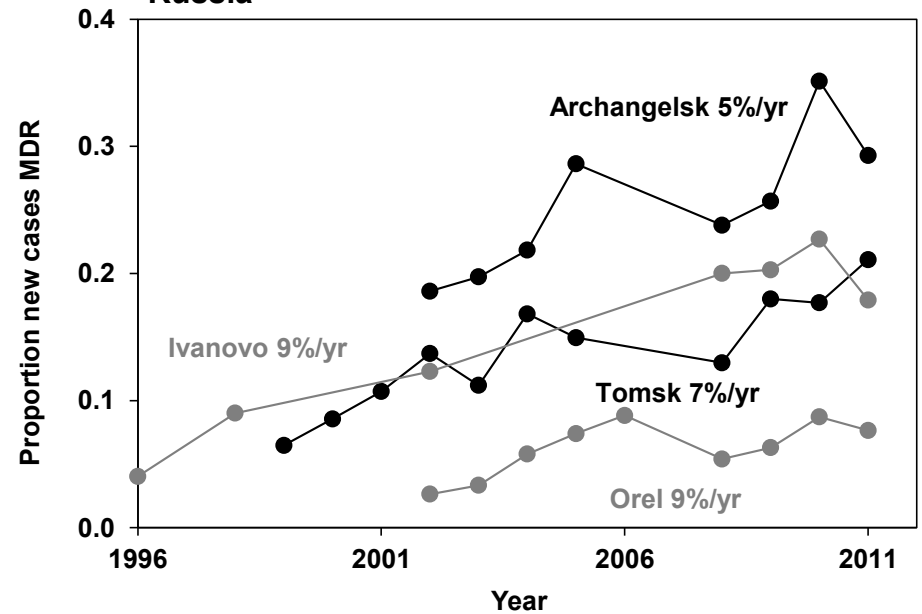
## Estonia



## Russia

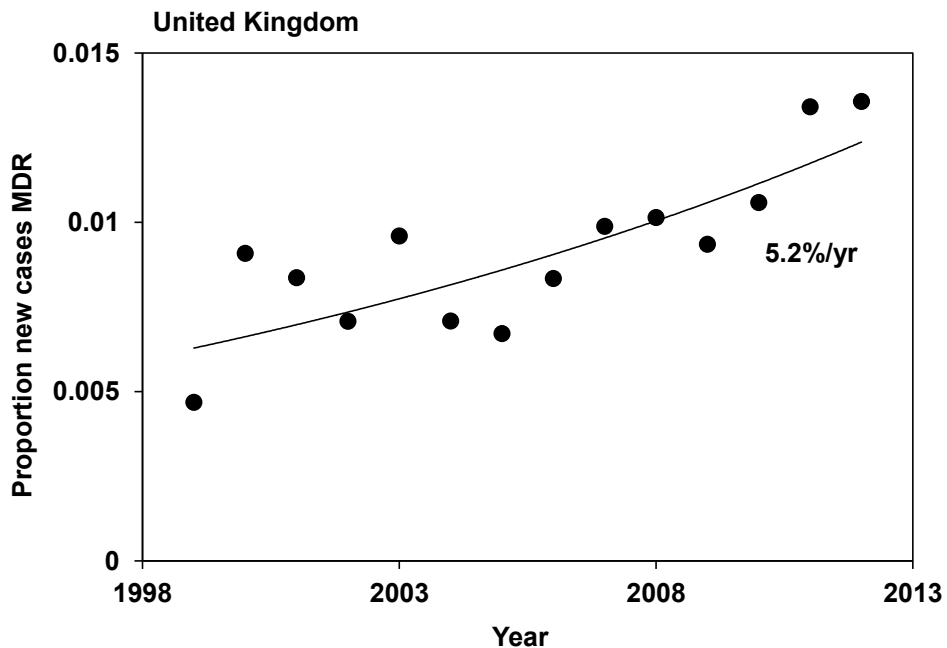
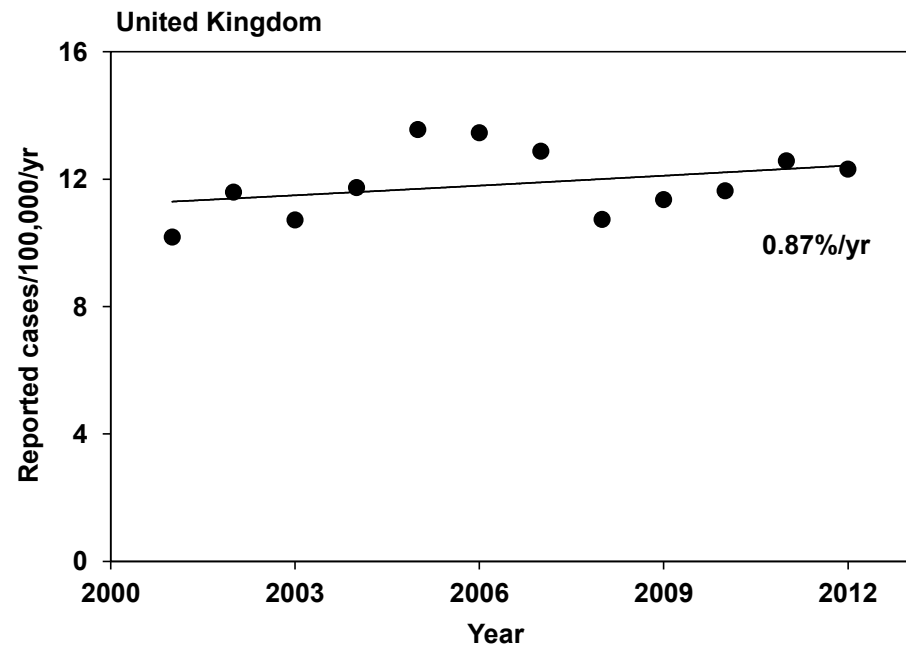
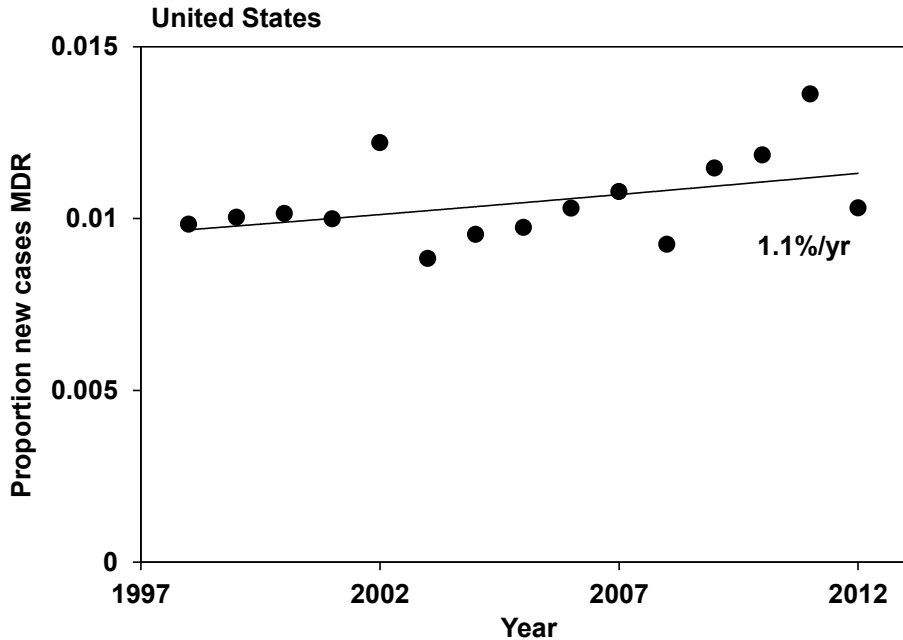
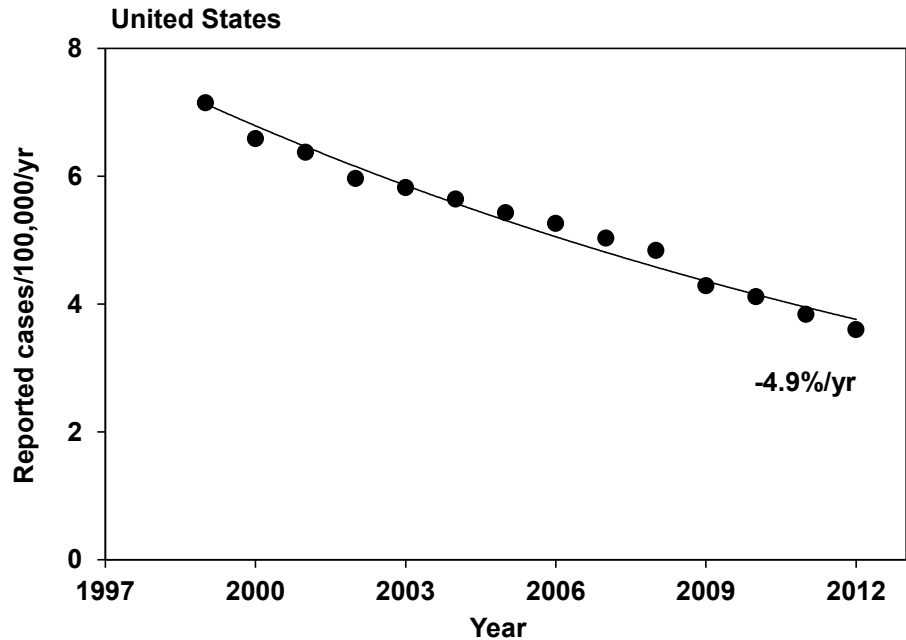


## Russia

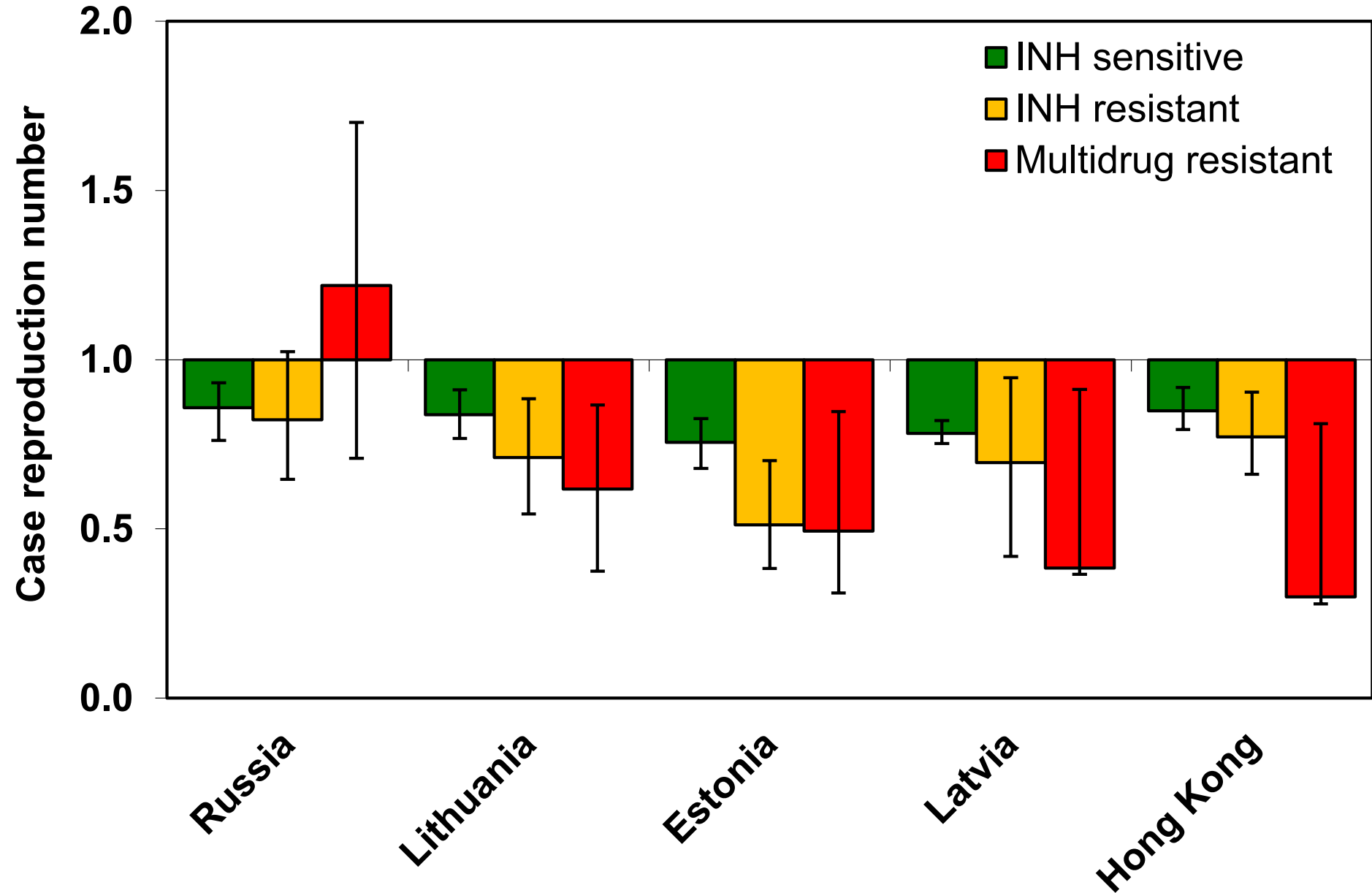




# Contrasting dynamics of resistance: low incidence



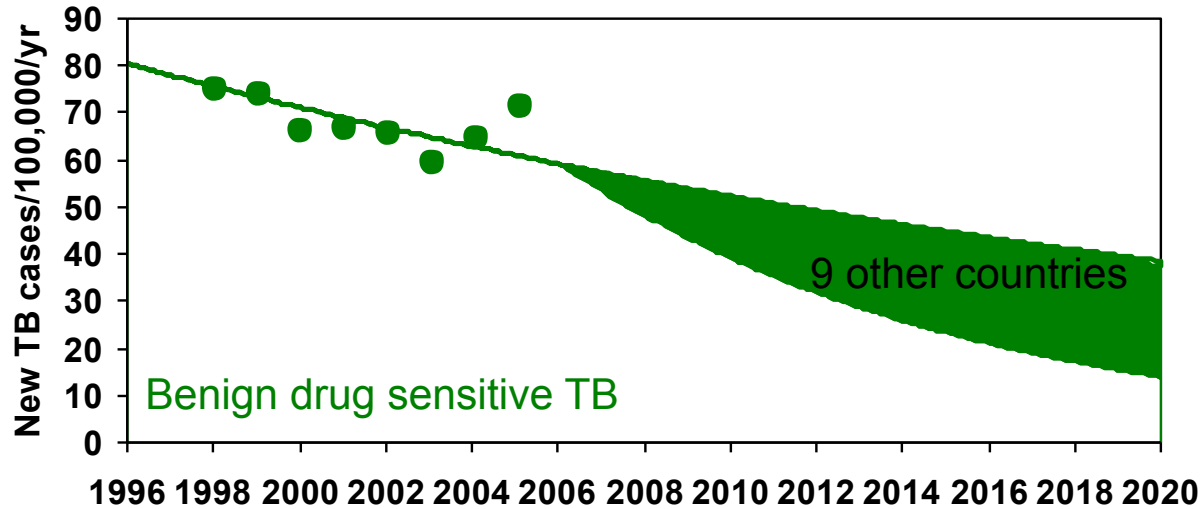
# Case reproduction numbers for sensitive and resistant TB mostly < 1



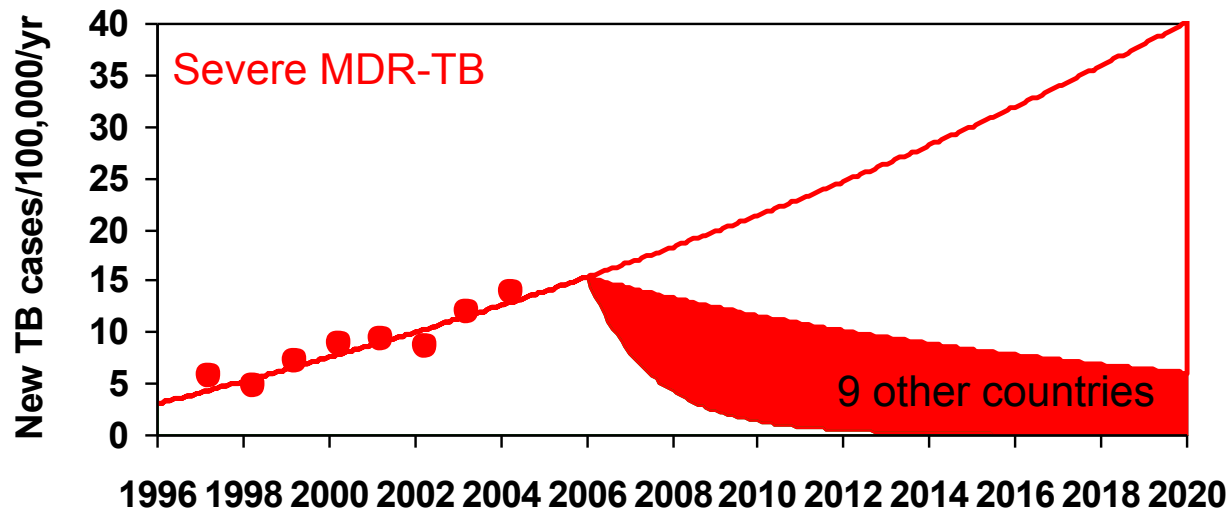
# Reversing the spread of MDR-TB

possible now, but will not eliminate TB by 2050

Treat drug-sensitive TB to maximize fall in incidence



Treat MDR-TB to interrupt self-sustaining transmission



After 2015:  
Sustainable  
Development Goals



2010 MDG Summit

Post-2015 Development  
Agenda

SUSTAINABLE  
DEVELOPMENT  
GOALS  
Environment,  
poverty, health on  
same agenda



2012 Rio+20

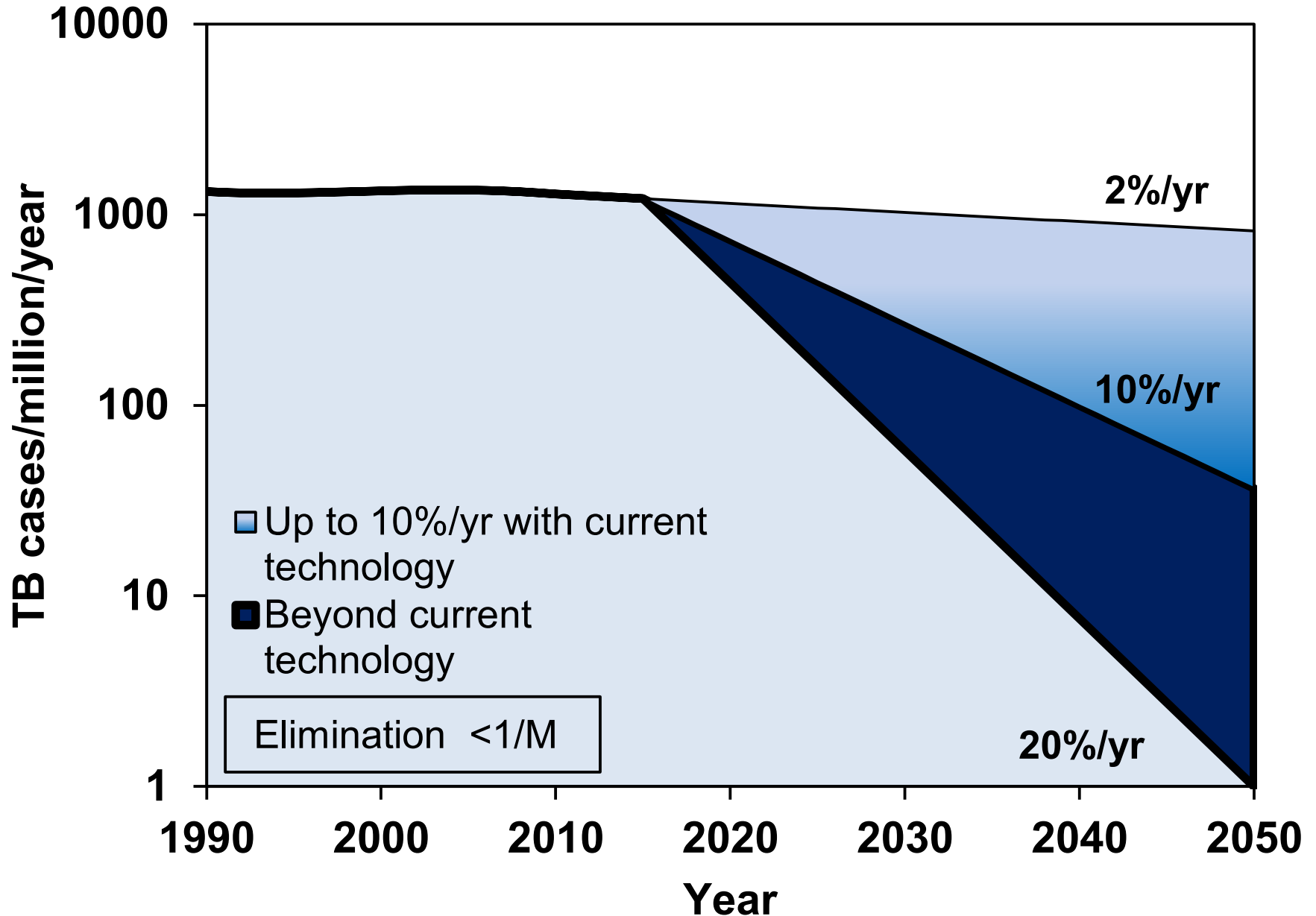
Mandate for the SDGs

17 PROPOSED GOALS AND  
TARGETS

3. Attain healthy life for all at  
all ages

By 2030, **end the epidemics  
of AIDS, tuberculosis, malaria  
and neglected tropical  
diseases** and combat  
hepatitis, water-borne  
diseases and other  
communicable diseases.

# TB cases: elimination by 2050?

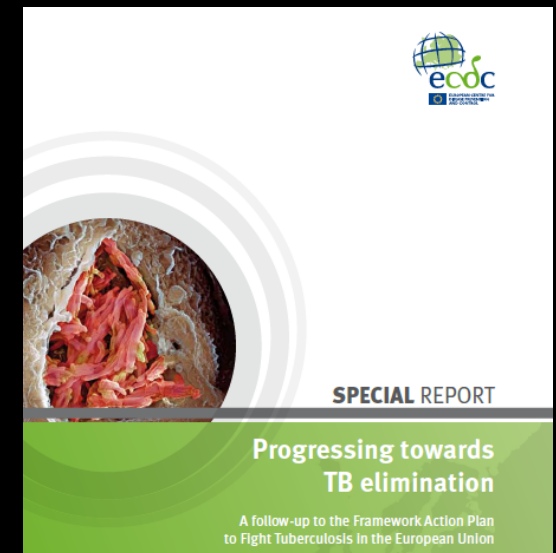


# United States of America

A Call for Action on the  
Tuberculosis  
Elimination Plan for  
the United States

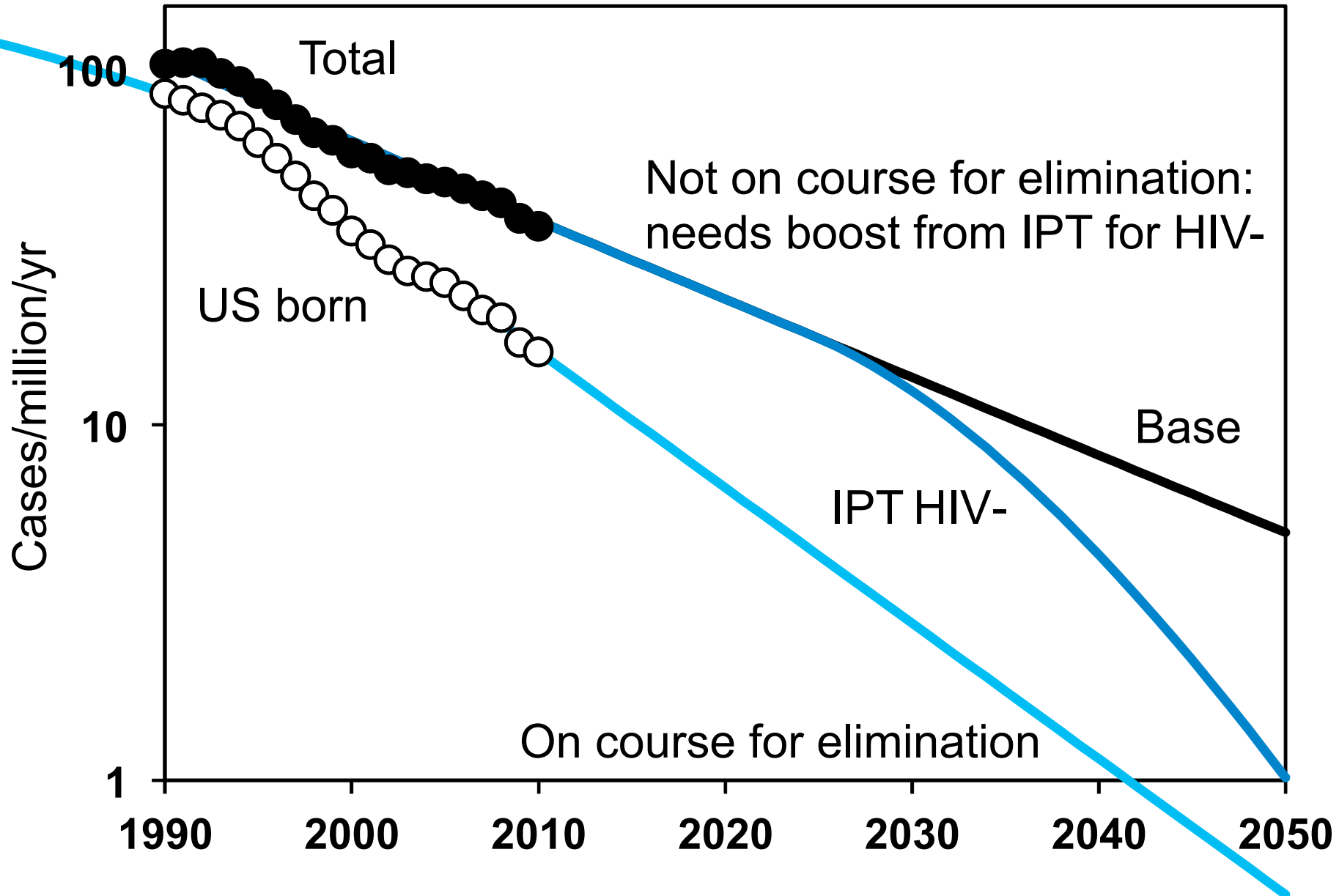


## Europe



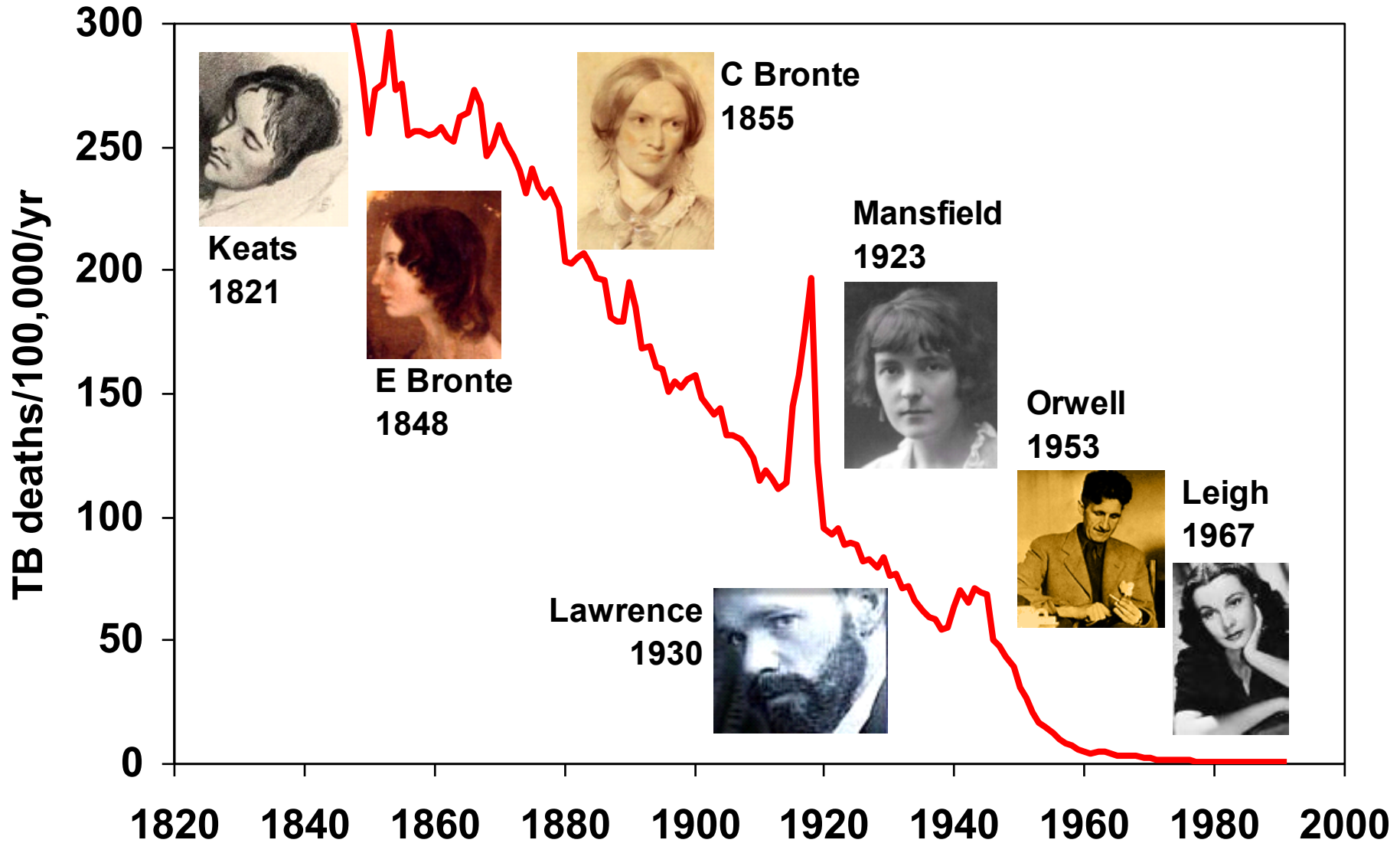


# USA: eliminate TB by 2050

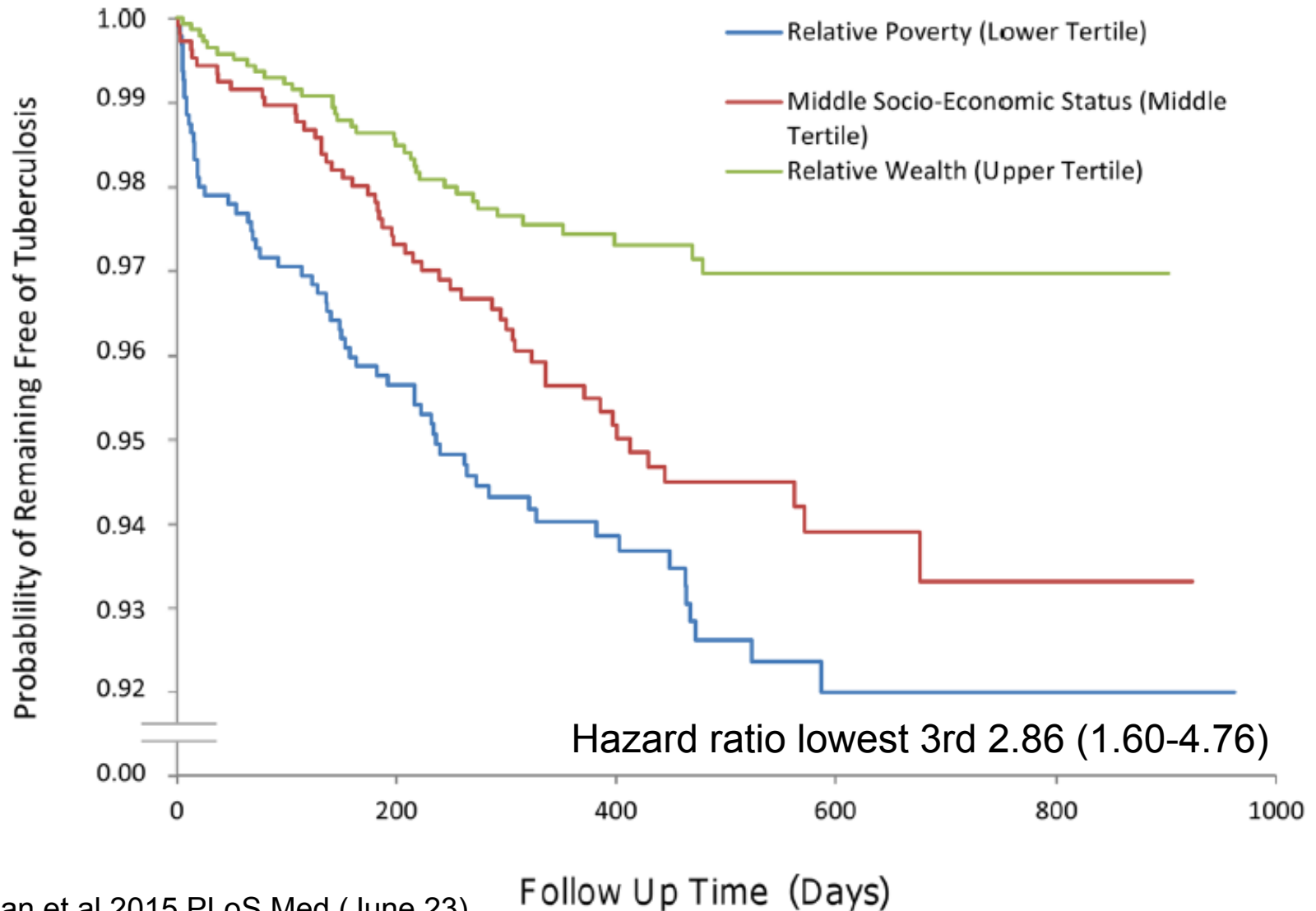


# Britain beat TB in the 19th and 20th centuries?

## Much of the (slow) decline preceded drugs



# Three times the risk of TB in poorest Peruvian households



# TB, universal health coverage and sustainable development

	MILESTONES		TARGETS	
	2020	2025	SDG* 2030	END TB 2035
<b>Reduction in number of TB deaths</b> compared with 2015 (%)	35%	75%	<b>90%</b>	<b>95%</b>
<b>Reduction in TB incidence rate</b> compared with 2015 (%)	20%	50%	<b>80%</b>	<b>90%</b>

UHC

**TB-affected families facing catastrophic costs due to TB (%)**

0%

0%

**0%**

**0%**

# The challenges of eliminating tuberculosis

## The epidemic

- 9 million new cases in 2014
- Falling 1-2%/yr << 20%/yr needed for elimination
- No country on course to elimination target

## Drug resistance

- 0.5M new cases MDR-TB each year - stable
- XDR-TB in 85+ countries – trends unknown
- Spread of drug resistance resistance is preventable and (slowly) reversible
- DR-TB not the main obstacle to TB elimination

## Elimination

- “integrating social wisdom into biotechnology” (cf Dubos)

# The Population Biology of Tuberculosis

Christopher Dye