

# TB elimination: the quest for the seemingly impossible

[m.w.borgdorff@amc.uva.nl](mailto:m.w.borgdorff@amc.uva.nl)

# Overview

- **Setting the stage**
  - Definition of TB elimination
  - Current status and trends in EU
  - Time scale for achieving elimination
  - Key elements in natural history of TB
- **Country example: The Netherlands**
  - Trends in (molecular) epidemiology
  - Scope for accelerating progress towards elimination
  - Operational changes with reducing incidence
- **Scope for accelerating elimination in EU/EEA**
  - Current control methods
  - Additional options with available tools
  - New tools
- **Conclusions**

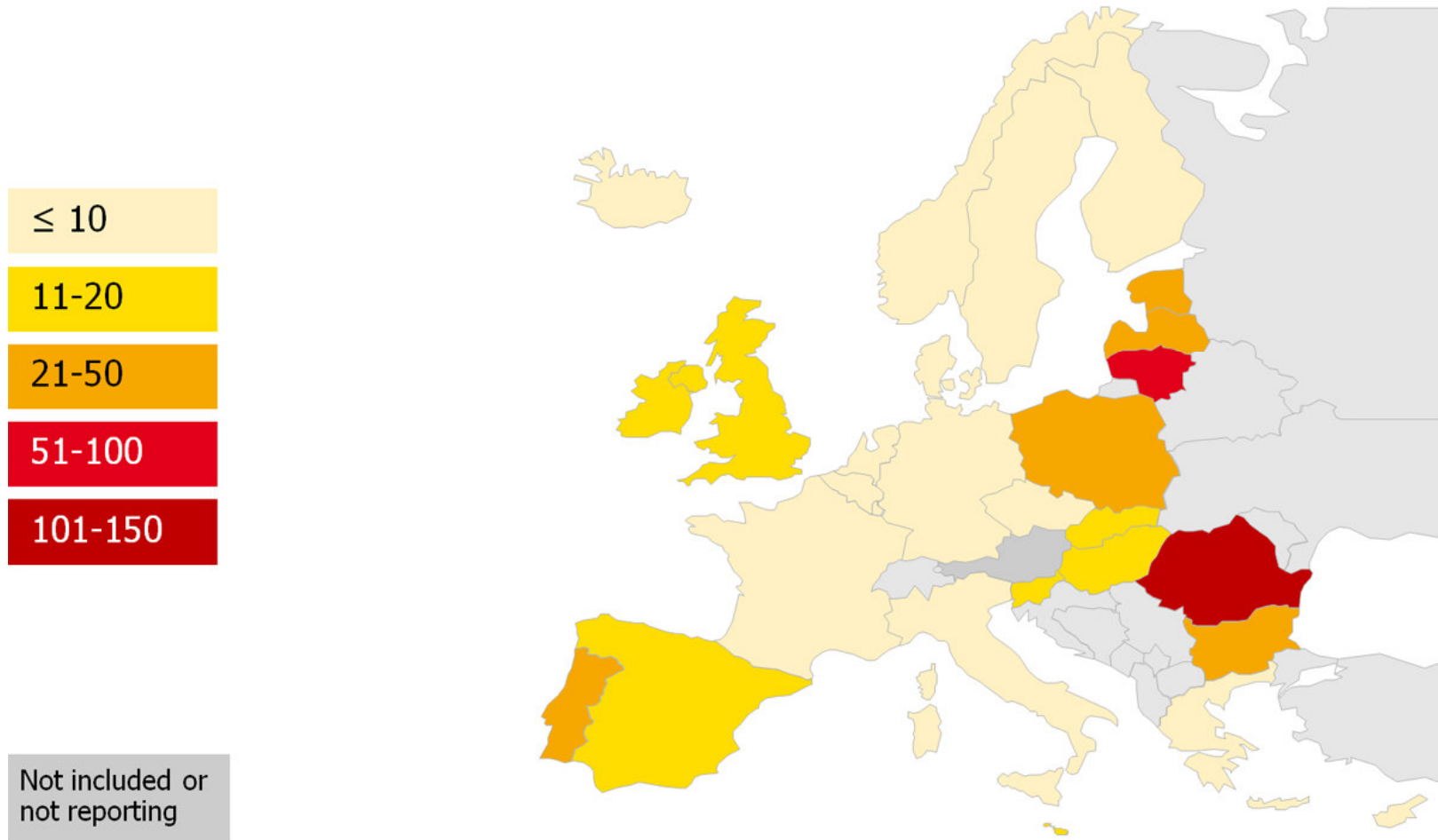
# Definition of TB elimination

- Reduction to zero of the prevalence of an infectious disease in human or animal host(s)
  - Globally: eradication
  - Limited geographic area: elimination
- TB elimination: incidence  $< 1$  per million
  - CDC: all TB<sup>1</sup>
  - Styblo: smear-positive TB only<sup>2</sup>
- Elimination phase: incidence  $< 20/100,000$ <sup>2</sup>

1. CDC. MMWR 1989;38 (S3):1-25.

2. Styblo. Bull IUATLD 1990;65:49-55.

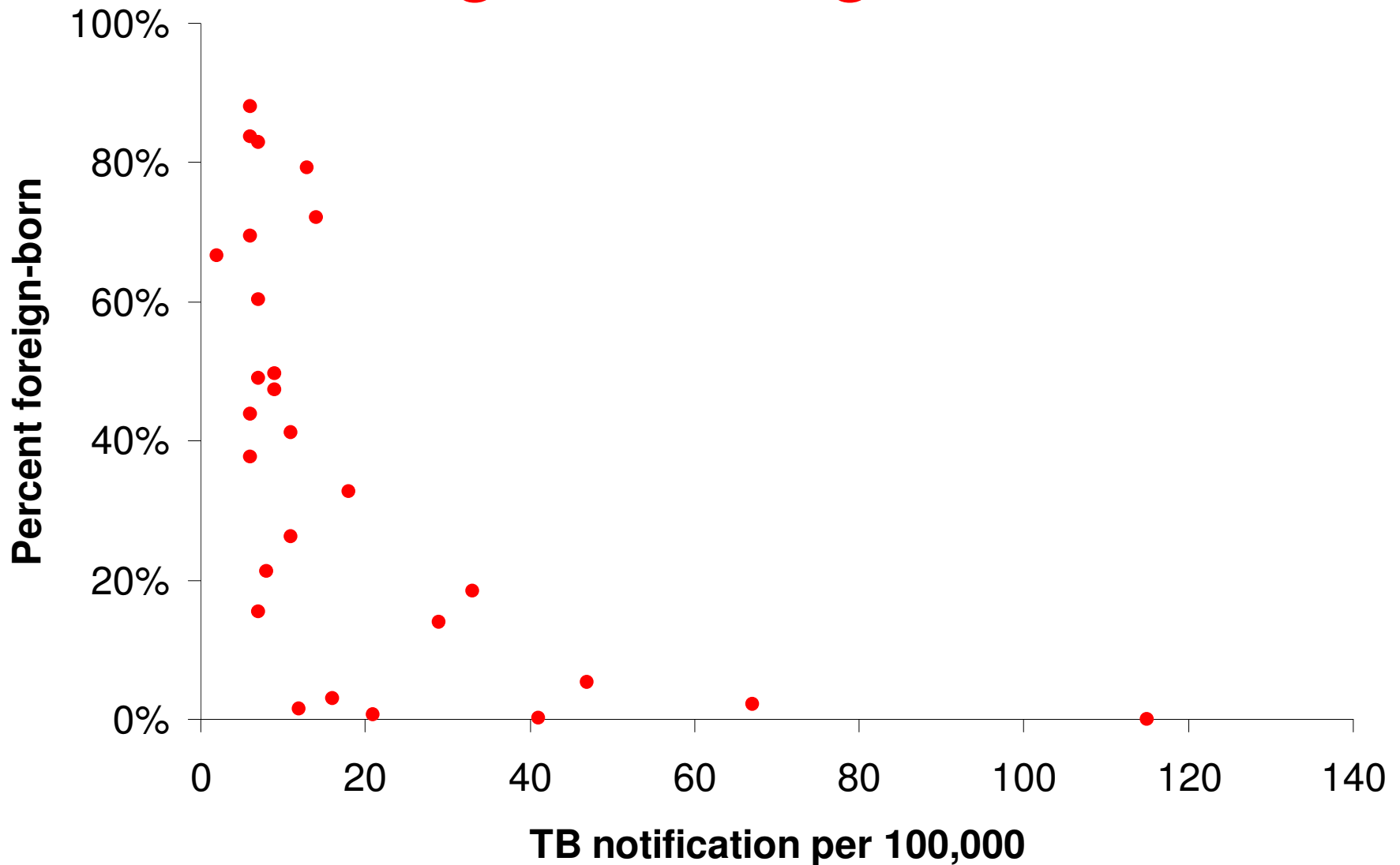
# TB rates in the EU/EEA



Mean 16.7/100,000, maximum 115.1/100,000.

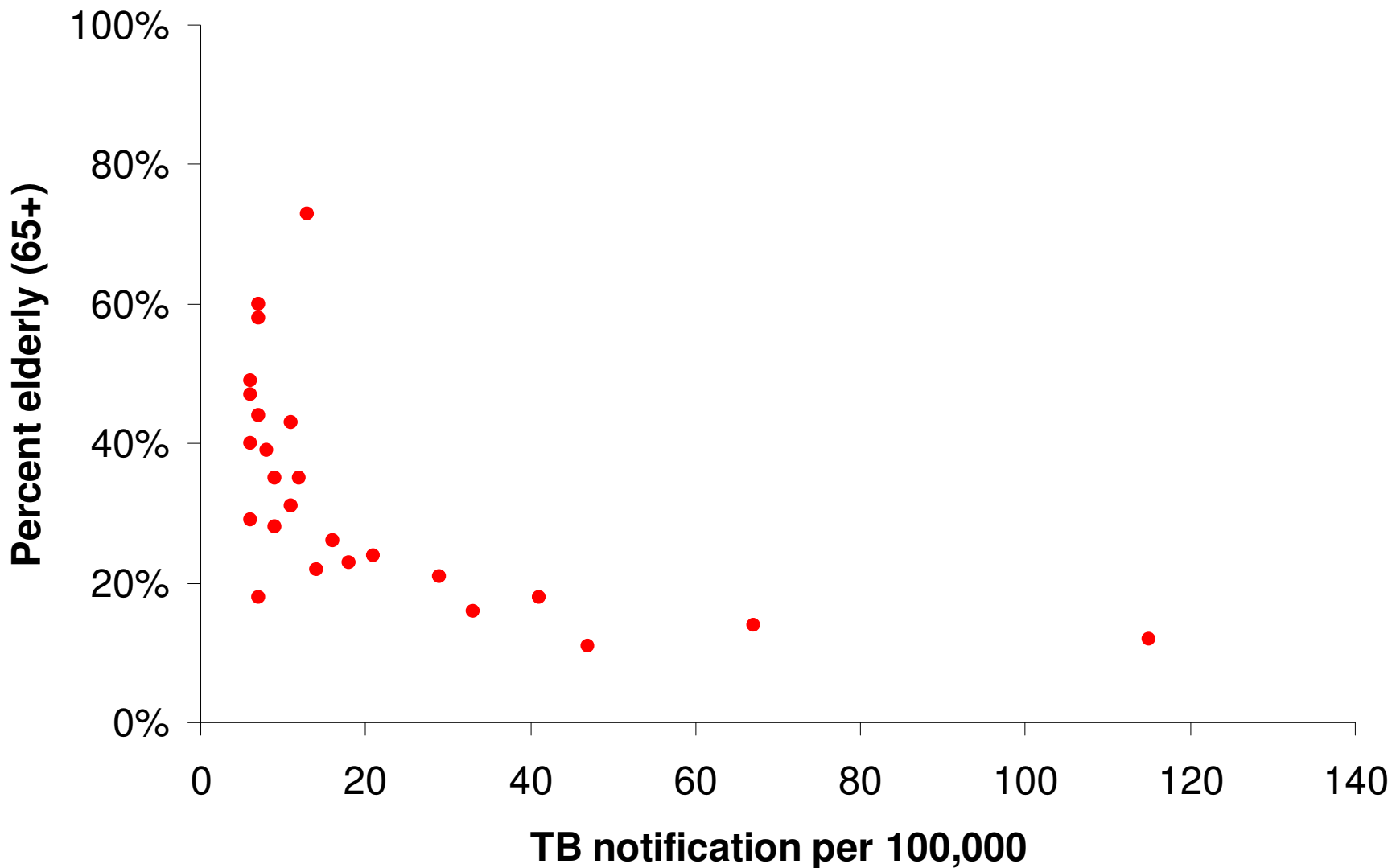
Source: ECDC 2010

# Proportion of TB cases in the EU among the foreign-born



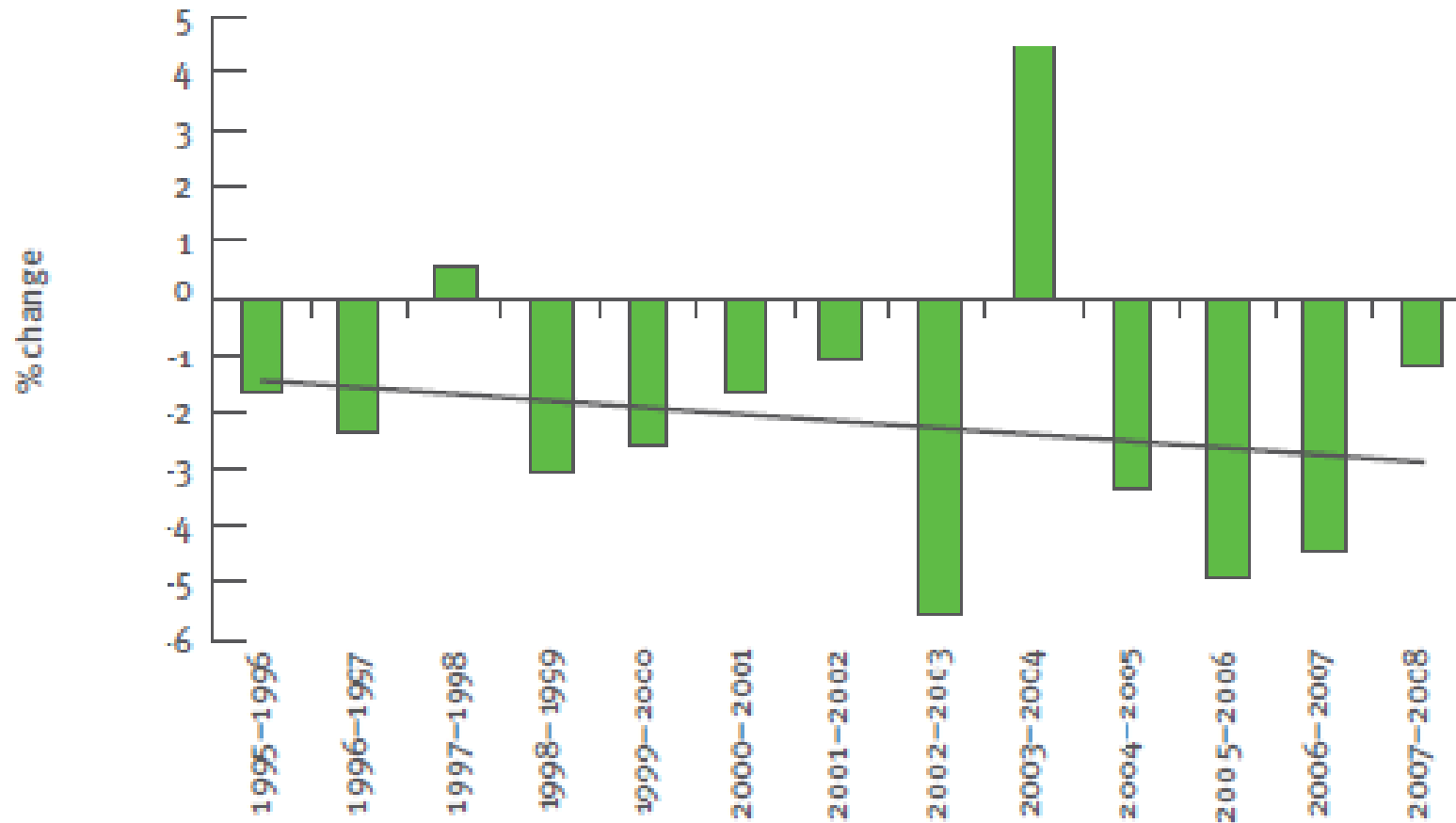
Source: ECDC 2010

# Proportion of TB cases in the EU among the elderly



Source: ECDC 2010

# TB rates of decline in the EU



Mean decline 2004-2008 -3.3%, Median -2.4%, IQR -4.7% to +0.8%.

Source: ECDC 2010

# Years to elimination depending on current status and rate of decline

Incidence per 100,000 at start

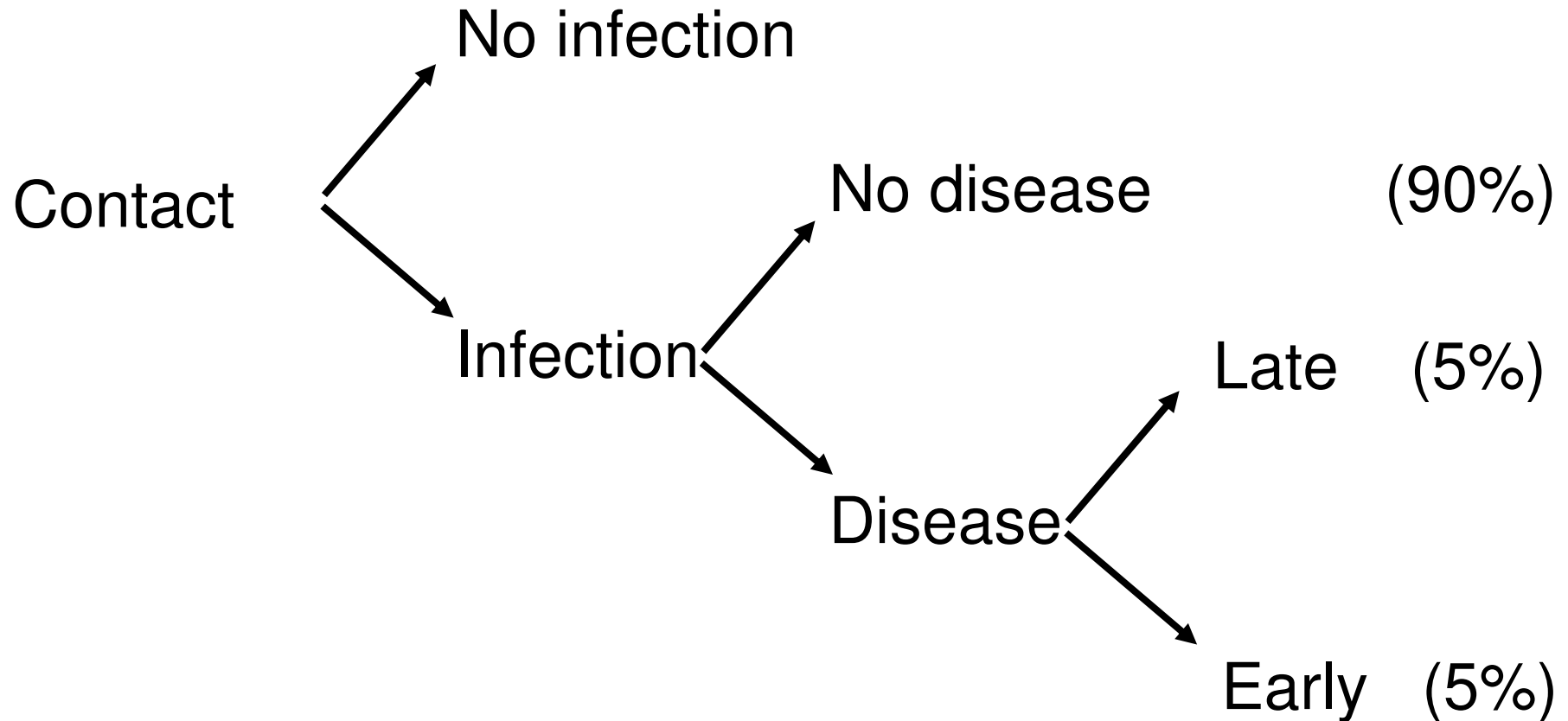
	5	10	20	40	80
Decline per year					
25%	14	17	19	21	24
12,5%	30	35	40	45	51
6,3%	61	72	83	93	104
3,1%	124	146	167	189	211
1,6%	249	293	337	381	425
0,8%	499	588	676	764	853

1. Rate of decline much stronger determinant than status at the start
2. With current rates of decline elimination at least decades away



# Natural history of tuberculosis

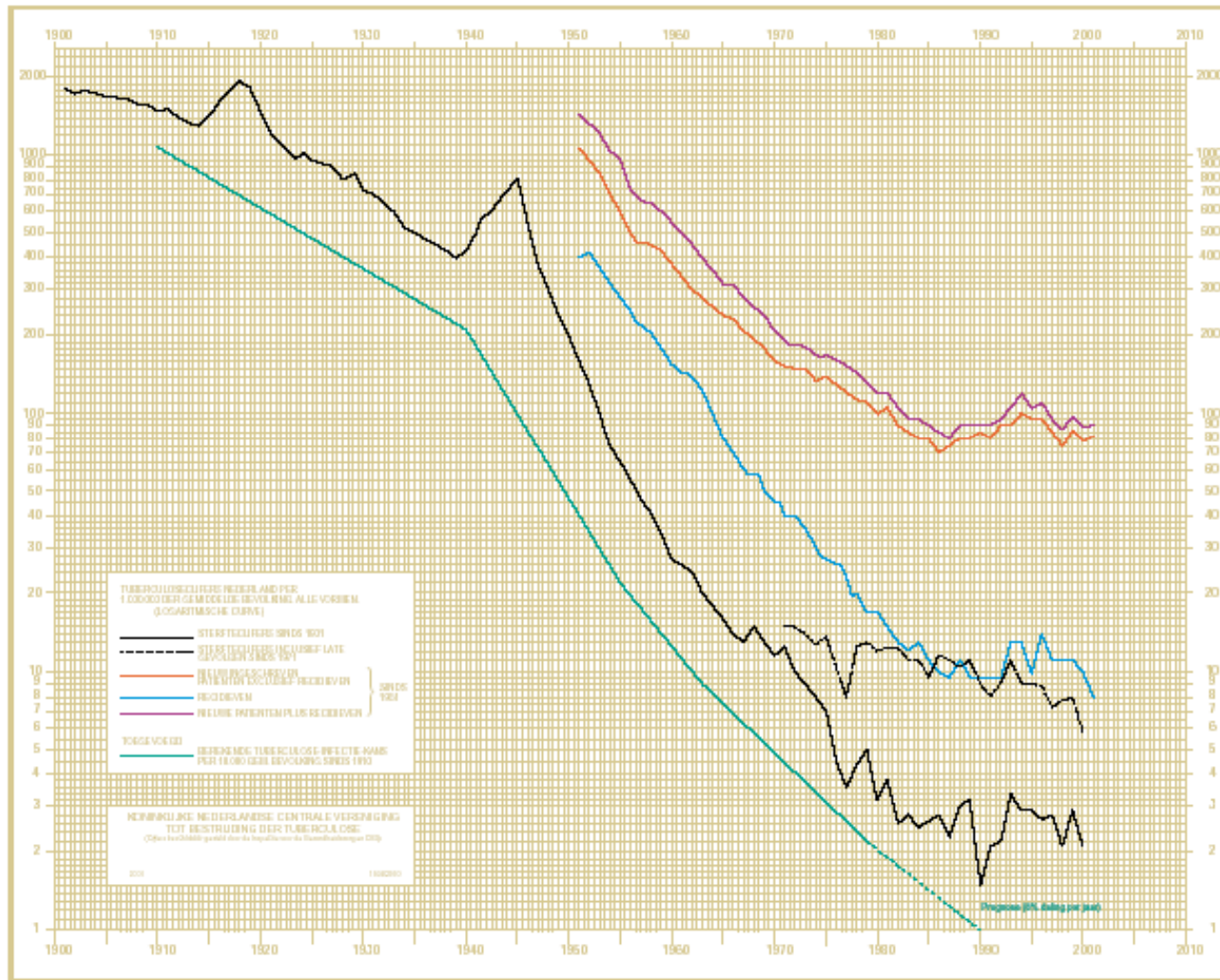
---



# Overview

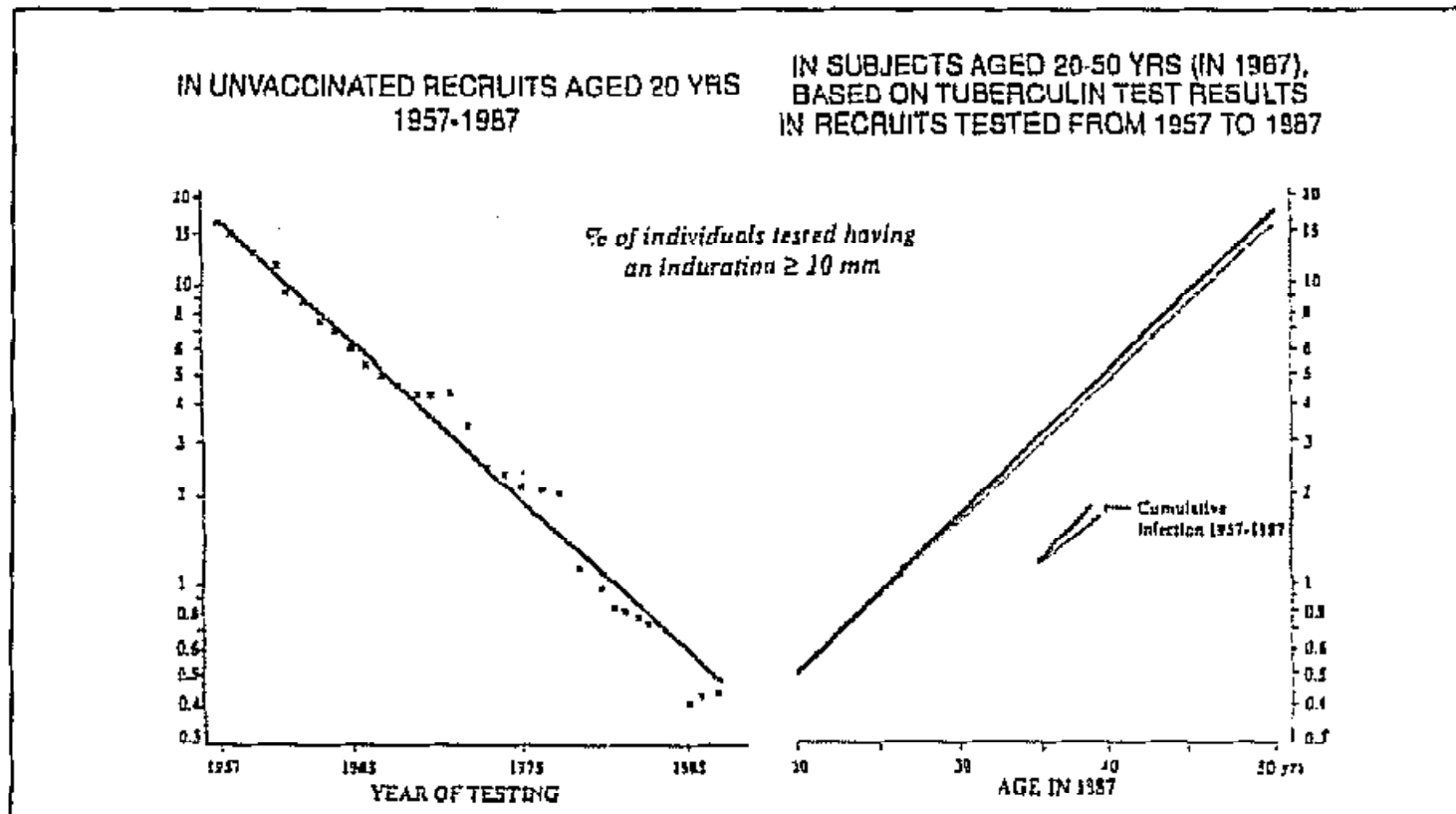
- **Setting the stage**
  - Definition of TB elimination
  - Current status and trends in EU
  - Time scale for achieving elimination
  - Key elements in natural history of TB
- **Country example: The Netherlands**
  - Trends in (molecular) epidemiology
  - Scope for accelerating progress towards elimination
  - Operational changes with reducing incidence
- **Scope for accelerating elimination in EU/EEA**
  - Current control methods
  - Additional options with available tools
  - New tools
- **Conclusions**

# Country example: The Netherlands



Source: KNKV Tuberculosis Foundation

# Prevalence of infection by age in 1987



*Figure III. Prevalence of tuberculous infection in the Netherlands.*

# When can tuberculosis elimination be expected in The Netherlands?

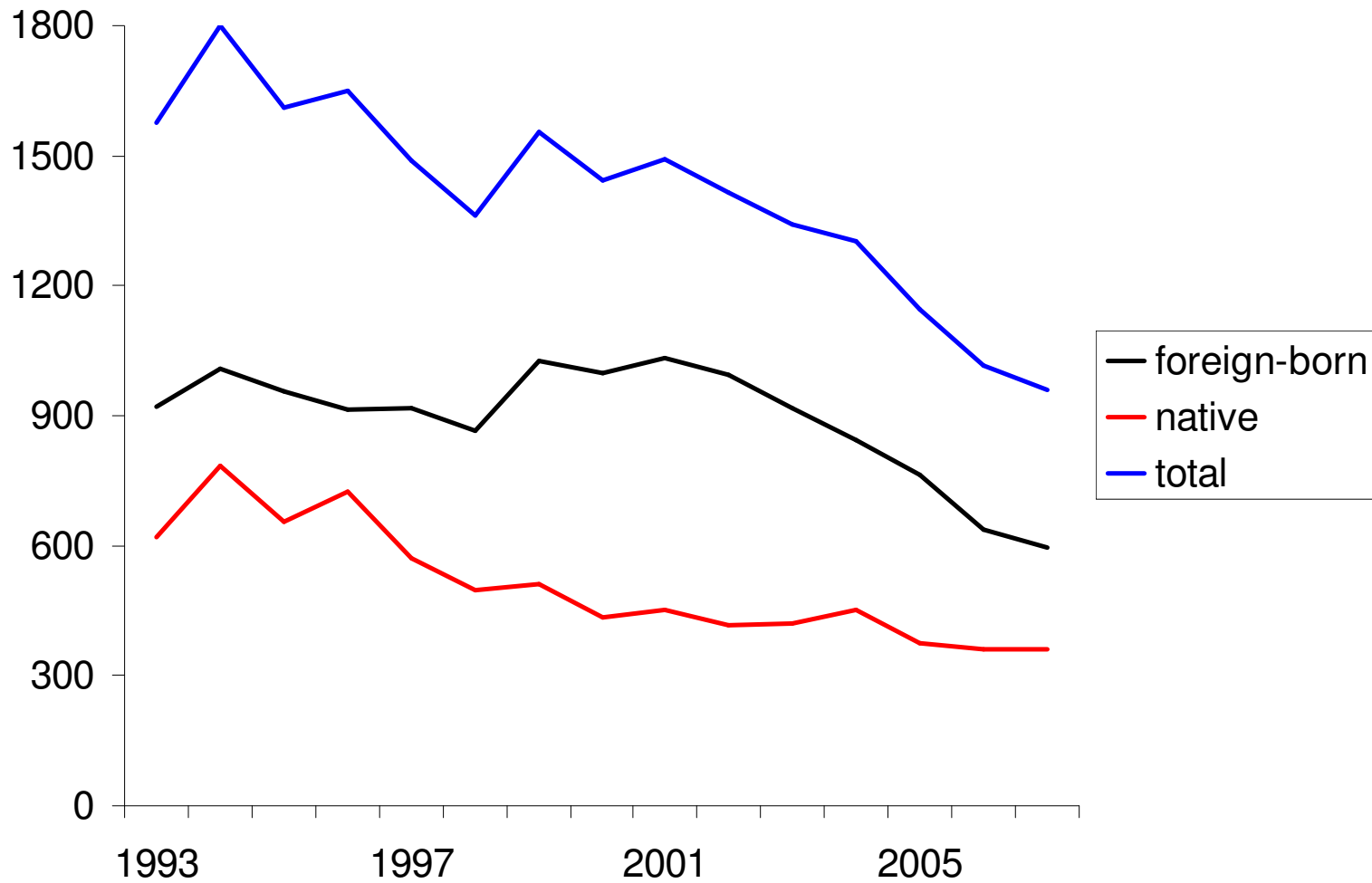
- 1990: not before 2025 if defined as prevalence of infection  $< 1\%$  and dependent on impact of immigration<sup>1</sup>
- 2002 and 2008: not by 2030 if defined as incidence  $< 1$  per million. Delay compared with Styblo in part attributed to impact of immigration<sup>2,3</sup>

1. Styblo. Bull IUATLD 1990;65:49-55.

2. Wolleswinkel-van den Bosch et al. Int J Tuberc Lung Dis 2002;6:130-6.

3. van Leth et al. Ned Tijdschr Geneeskd 2008;152:616-21.

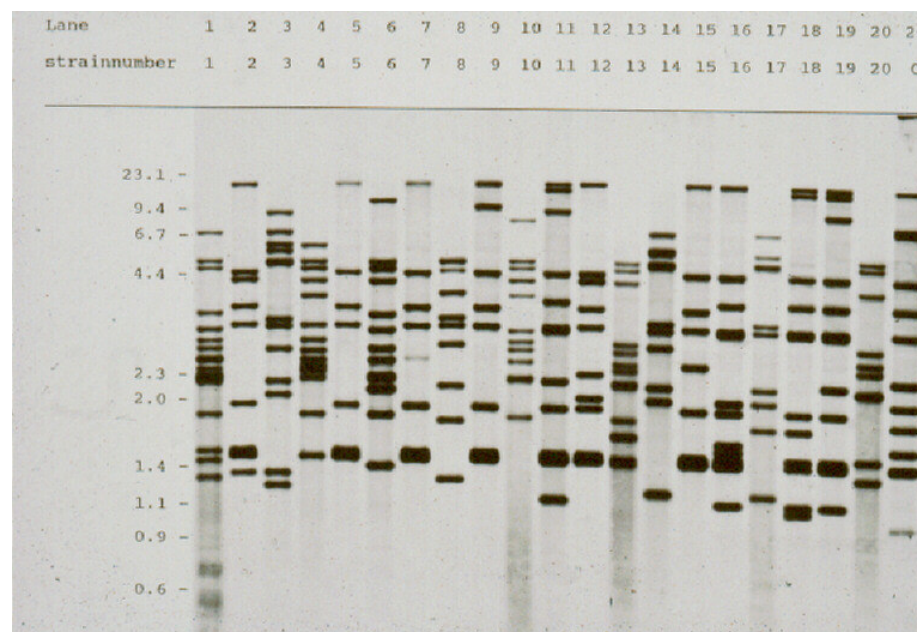
# TB notifications in The Netherlands (1993-2007)



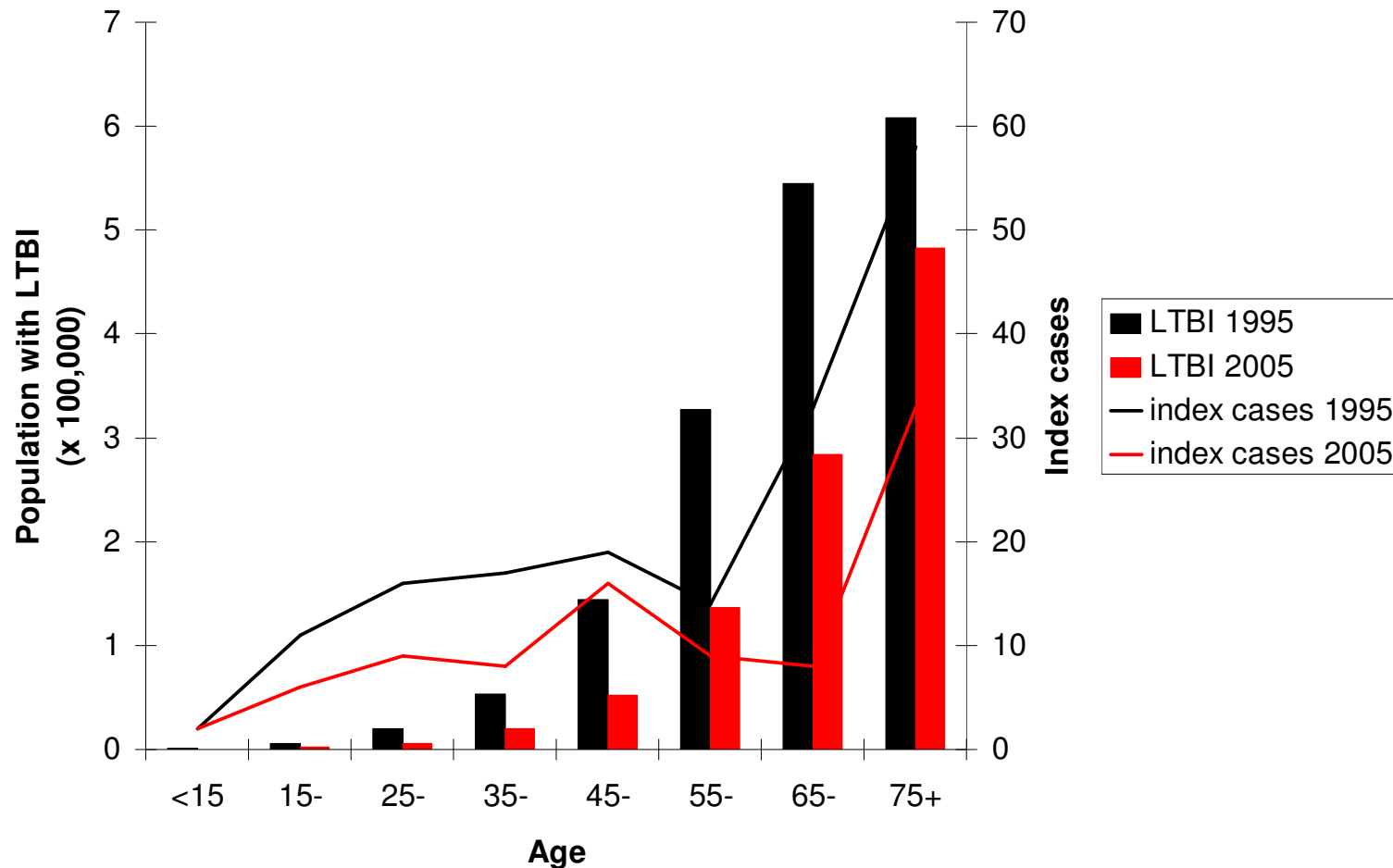
Source: KNKV Tuberculosis Foundation

# Molecular epidemiology of TB in The Netherlands, 1995-2005

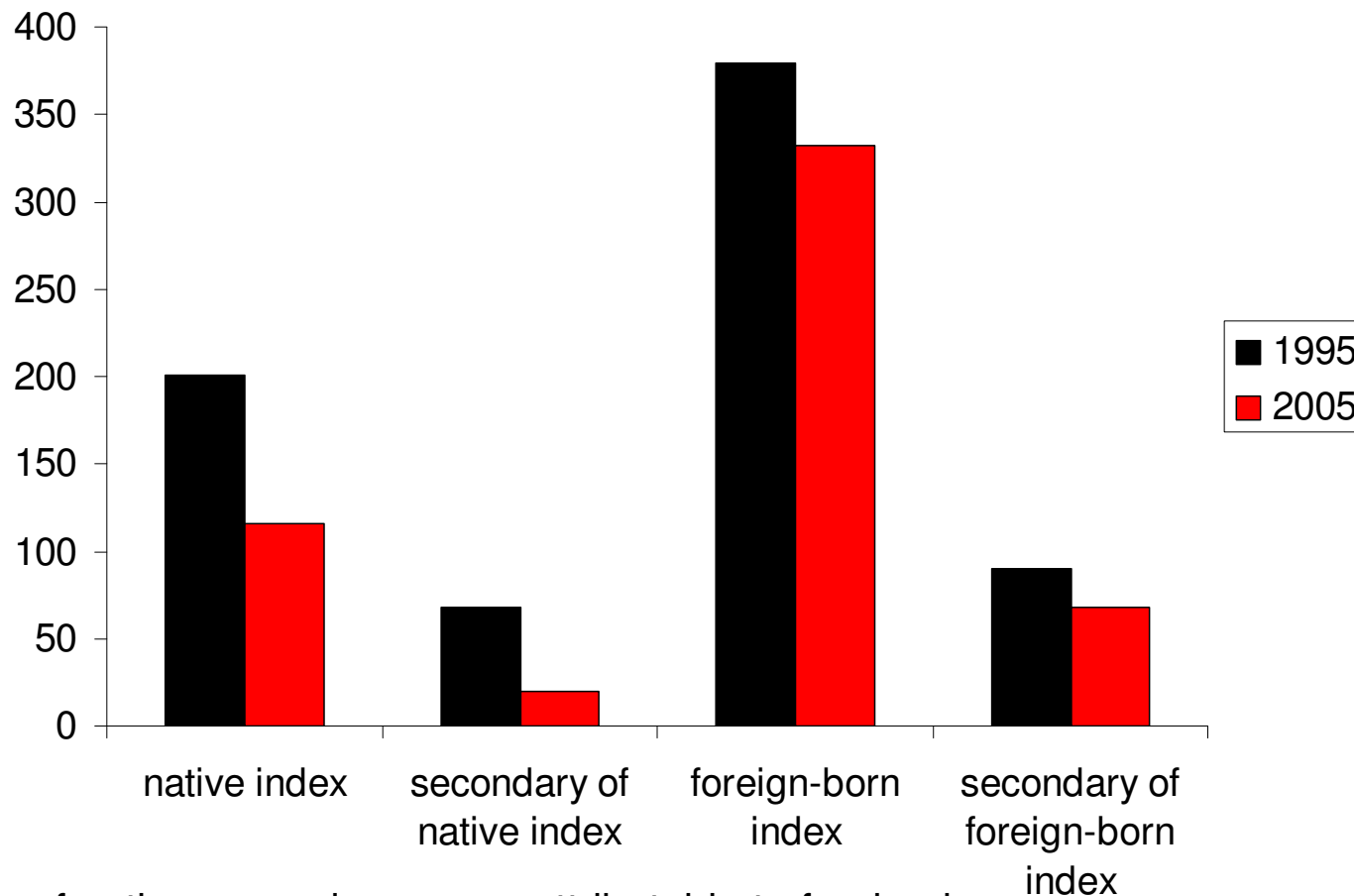
- In period 1993-2007 12,222 patients in TB register and with genotyping data
- Index defined as case with PTB and genotype not observed in previous two years



# Incidence index cases and prevalence of LTBI

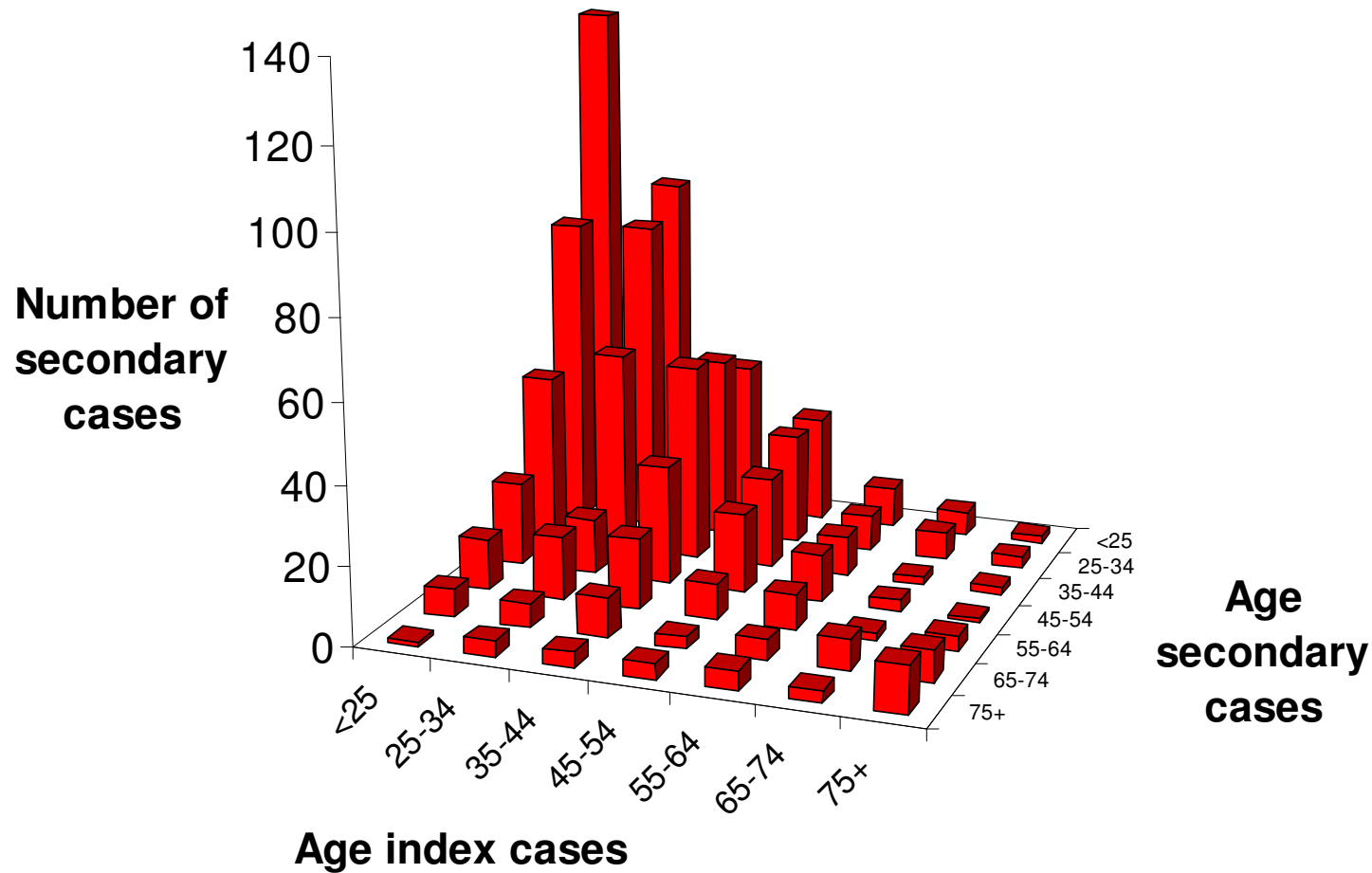


# Change from 1995 to 2005



Proportion of native secondary cases attributable to foreign-born source case:  
29% in 1995 and 50% in 2005

# Recent transmission



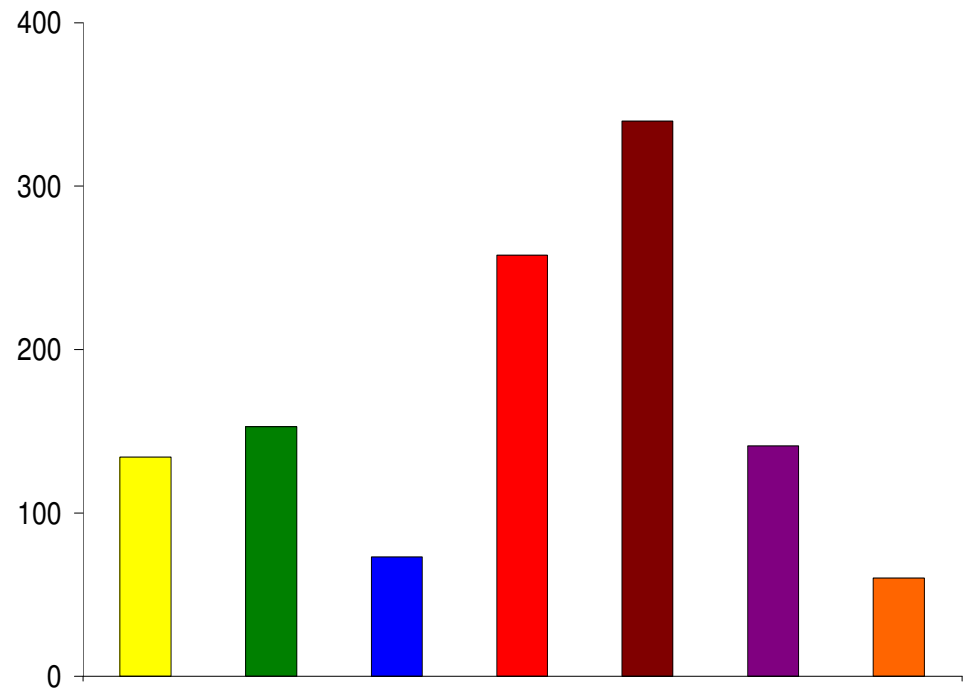
# Prediction of outbreaks (>4 cases within 2 years)

Probability (%) of development of a large cluster within 2 years determined by the characteristics of the first 2 cases in a cluster episode					
Time between 1 <sup>st</sup> and 2 <sup>nd</sup> case	Number of the first 2 cases with:  Age <35 years old	Number of first 2 cases with:  Origin from sub-Saharan Africa	Number of first 2 cases that:  Live in an urban area		
			None	1	2
0-3 months	None	None	4%	5%	<b>11%</b>
		1	4%	6%	<b>12%</b>
		2	9%	<b>11%</b>	<b>22%</b>
	1 or 2	None	<b>15%</b>	<b>19%</b>	<b>35%</b>
		1	<b>17%</b>	<b>21%</b>	<b>38%</b>
		2	<b>30%</b>	<b>36%</b>	<b>56%</b>
> 3 months	None	None	1%	1%	2%
		1	1%	1%	2%
		2	1%	2%	4%
	1 or 2	None	3%	3%	8%
		1	3%	4%	9%
		2	6%	8%	<b>16%</b>

Increase in probability of a large cluster episode in comparison to the background prevalence of a large cluster

	1-2 times increased probability
	≥ 2 - 3 times increased probability
	≥ 3 - 5 times increased probability
	≥ 5 times increased probability

# Scaling up TB control in The Netherlands



Notified patients 2009

Source: KNCV Tuberculosis Foundation

# Overview

- **Setting the stage**
  - Definition of TB elimination
  - Current status and trends in EU
  - Time scale for achieving elimination
  - Key elements in natural history of TB
- **Country example: The Netherlands**
  - Trends in (molecular) epidemiology
  - Scope for accelerating progress towards elimination
  - Operational changes with reducing incidence
- **Scope for accelerating elimination in EU/EEA**
  - Current control methods
  - Additional options with available tools
  - New tools
- **Conclusions**

# Current control methods

- Passive case finding and treatment
- Active case finding among risk groups (e.g., homeless, drug users, HIV infected, recent immigrants)
- Preventive therapy among contacts and risk groups
- BCG vaccination

Broekmans et al. Eur Respir J 2002;19:765-75.

Lönroth et al. Lancet 2010;375:1814-29.

# Additional options with available tools

Explore expansion of:

- Active case finding among risk groups<sup>1-5</sup>
- Preventive therapy among the foreign-born, in particular from sub-Saharan Africa and South-East Asia<sup>5</sup>
- Support global TB control in order to reduce TB among the foreign-born<sup>6</sup>

1. Broekmans et al. Eur Respir J 2002;19:765-75. 2. De Vries et al. Am J Respir Crit Care Med 2007;176:201-7.  
3. Bothamley et al. Eur Respir J 2008;32:1023-30. 4. Cain et al. JAMA 2008;300:405-12.  
5. Liu et al. N Engl J Med 2009;360:2406-15. 6. Schwartzman et al. N Engl J Med. 2005;353:1008-20.

# Development of new tools

- New diagnostics: rapid diagnosis including of multidrug resistance<sup>1</sup>
- New drugs<sup>2</sup>:
  - shorter curative and preventive therapy
  - expanding scope for preventive therapy to the foreign-born and elderly
  - tackling multidrug resistant TB
- New vaccines<sup>3</sup>: better efficacy against pulmonary tuberculosis in adults
  - target groups would ideally include the foreign-born and elderly (*post-exposure vaccine*)

1. Wallis et al. Lancet 2010;375:1920-37.

2. Nuermberger et al. Respirology 2010;15:764-78.

3. Beresford et al. Clin Infect Dis 2010;50 Suppl 3:S178-83.

# Conclusions

- TB elimination in EU/EEA is likely to be decades away
- Options to accelerate progress towards TB elimination include:
  - Fully implement current strategies, explore options for intensified case finding and preventive therapy
  - Development of new tools, in particular new drugs for preventive therapy and post-exposure vaccines aiming at immigrants and the elderly
  - Support global TB control given the impact of TB among the foreign-born on TB epidemiology in the EU/EEA