

4th Turkish Vaccine Day, 2009

Surveillance and its value for immunization

Ankara, Turkey

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General aspects of vaccination

- Vaccination has a short history when measured against the centuries during which man has sought desperately to rid himself of various plagues and pestilences
- Only in the 20th century: Routine vaccination of large populations started
- Despite its relative youth, since the time of Edward Jenner vaccination has controlled 12 major diseases



Edward Jenner



Louis Pasteur

Vaccination has controlled 12 major infectious diseases

- **At least in parts of the world:**
 - 1. Smallpox
 - 2. Diphtheria
 - 3. Tetanus
 - 4. Yellow fever
 - 5. Pertussis
 - 6. Haemophilus influenzae type b disease
 - 7. Poliomyelitis
 - 8. Measles
 - 9. Mumps
 - 10. Rubella
 - 11. Typhoid
 - 12. Rabies
- **In the case of smallpox, the dream of eradication has been fulfilled**
- **Cases of poliomyelitis have been reduced by 99%**



A typical case of variola major about 7 days after the onset of rash. (From the World Health Organization Smallpox Recognition Card)

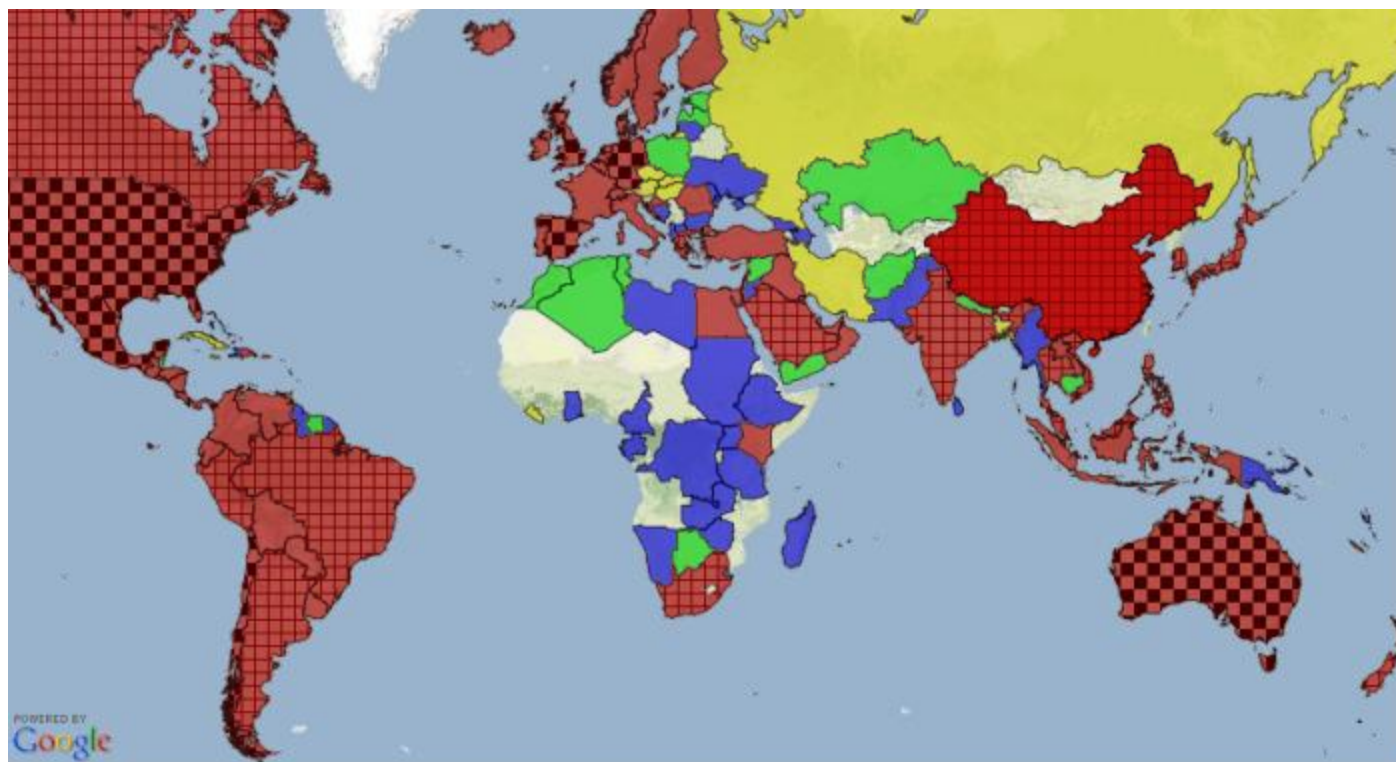
Historical perspective of surveillance (I)

- Surveillance is the collection, collation and analysis of data and the dissemination to those who need to know
- William Farr was one of the founders of the modern concept of epidemiology and health statistics (1837)
 - Development of highly relevant health indicators such as global and specific mortality rates (e.g. children under five mortality rate)
 - “importance of case definition to start with”
 - ‘Nomenclature is of as much importance in this department of inquiry as weights and measures in the physical sciences and should be settled without delay’.

Historical perspective of surveillance (II)

- In 1951, WHO issued the International Sanitary Regulations, requiring immediate notification of outbreaks of cholera, yellow fever and plague
- National and international surveillance of communicable diseases was supported by WHO since the 1960s
- Successful international surveillance is smallpox eradication achieved in 1979
- CDC established surveillances of specific diseases, with a centralized data collection, evaluation and dissemination across the U.S. states, in order to improve control of the disease
- In 2005, ECDC was established aimed to strengthen Europe's defenses against infectious diseases.
 - Mission: “to identify, assess and communicate current and emerging threats to human health posed by infectious diseases “

Global online surveillance: H1N1



- H1N1 Incidents 23:09 EDT 17 Aug 200... confirmed
- ⊗ above 10000
- H1N1 Incidents 23:09 EDT 17 Aug 200... confirmed
- between 1000 and 10000
- H1N1 Incidents 23:09 EDT 17 Aug 200... confirmed
- above 100
- H1N1 Incidents 23:09 EDT 17 Aug 200... confirmed
- between 26 and 100
- H1N1 Incidents 23:09 EDT 17 Aug 200... confirmed
- between 11 and 25
- H1N1 Incidents 23:09 EDT 17 Aug 200... confirmed
- between 1 and 10

FluTracker

Confirmed H1N1 cases by country (23:09 EDT 17 Aug 2009)

Created by Flu Tracker Admin on Aug 18, 2009
<http://flutracker2.rhizalabs.com/cbi/snapshot/page?concept=-fd000a02514fd3b510e41f48ff64800d2527fc1519f054d252db>

http://flutracker.rhizalabs.com/flu/by_country.html accessed September 2009

Leading Vaccine-preventable Cause of Child Death Worldwide (Children <5 Years)

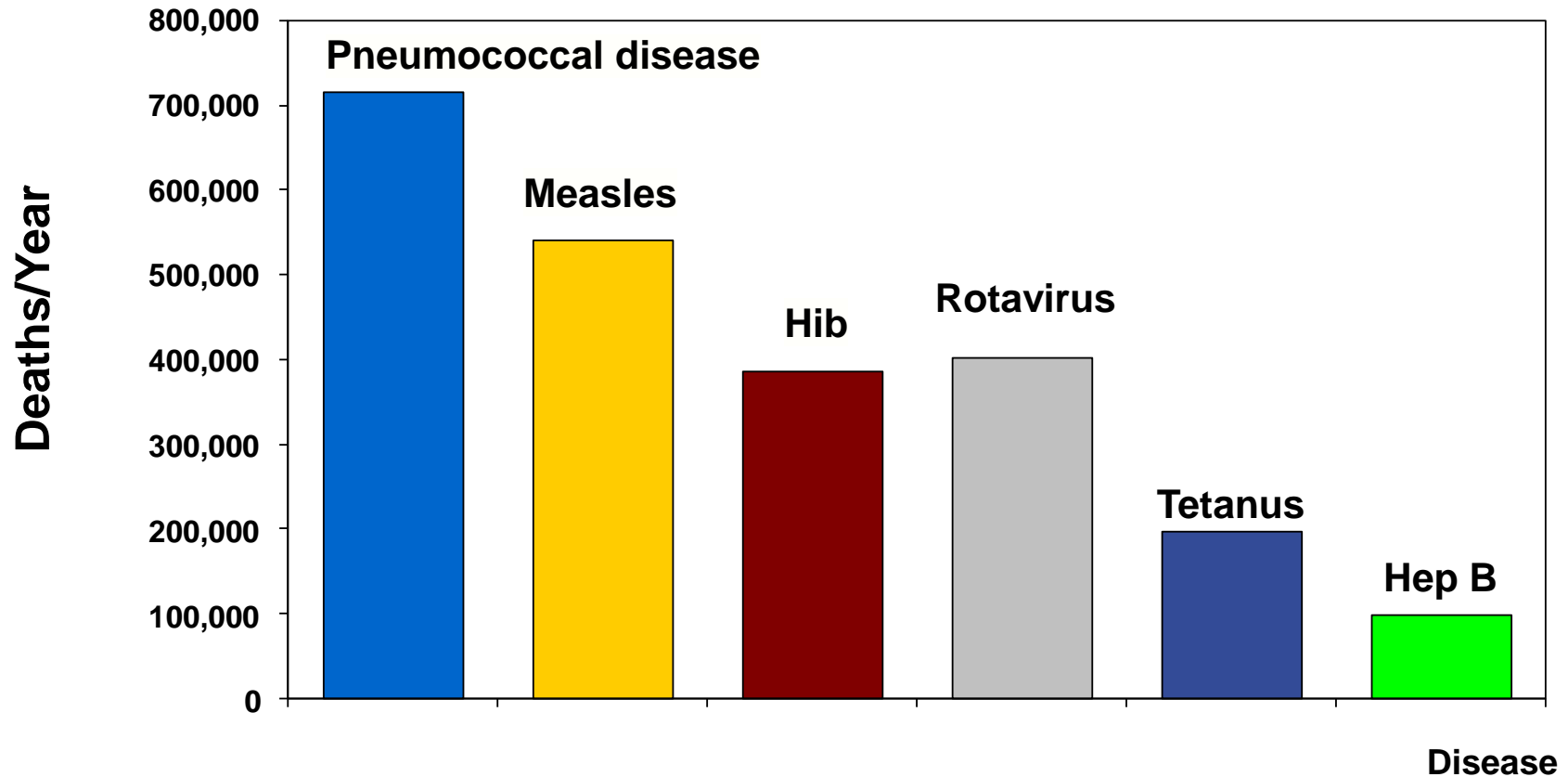
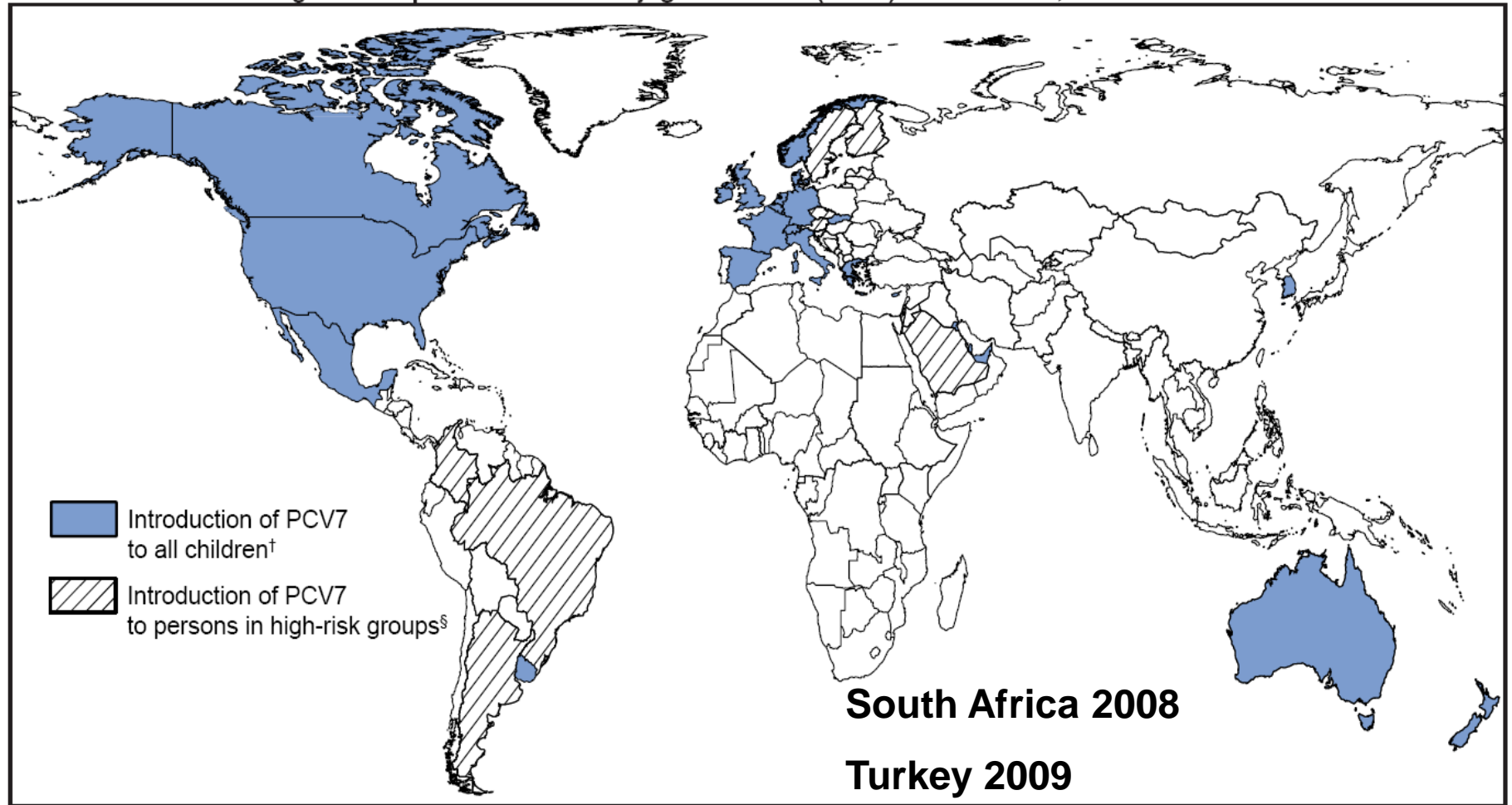


FIGURE. Countries using 7-valent pneumococcal conjugate vaccine (PCV7) — worldwide, 2008*

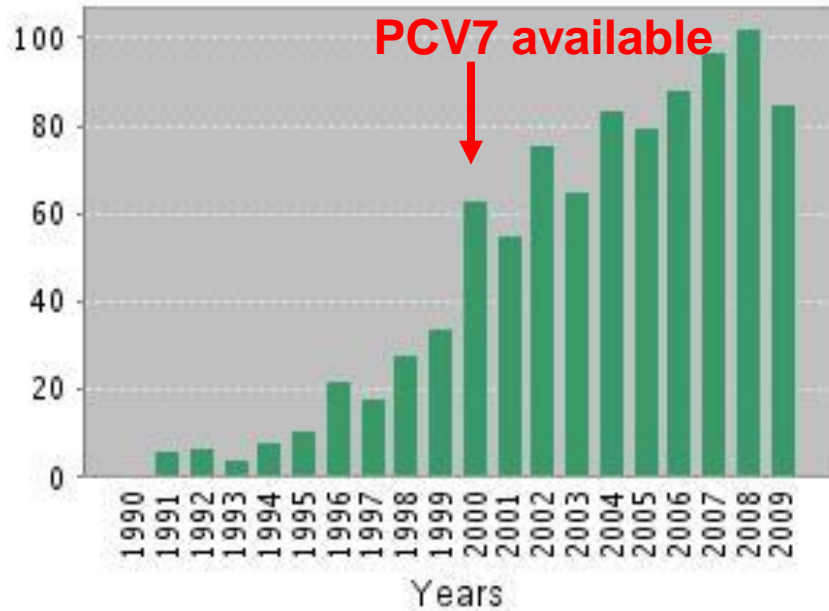


SOURCE: Database maintained by WHO, supplemented with data from other public and private sources, including the GAVI Alliance (formerly known as the Global Alliance for Vaccines and Immunizations), vaccine manufacturers, and country press releases.

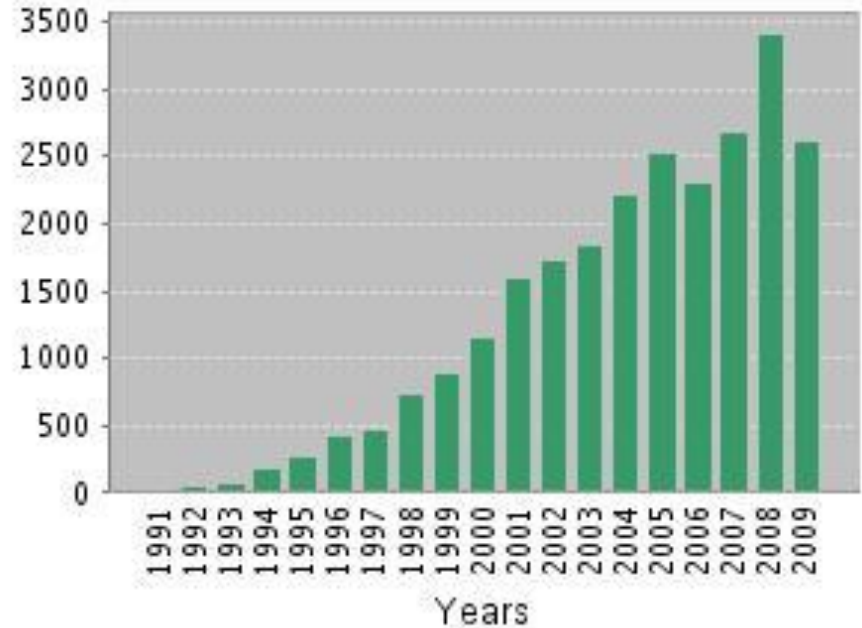
* As of August 2008.

Increasing scientific interest in pneumococcal surveillance

Published Items in Each Year



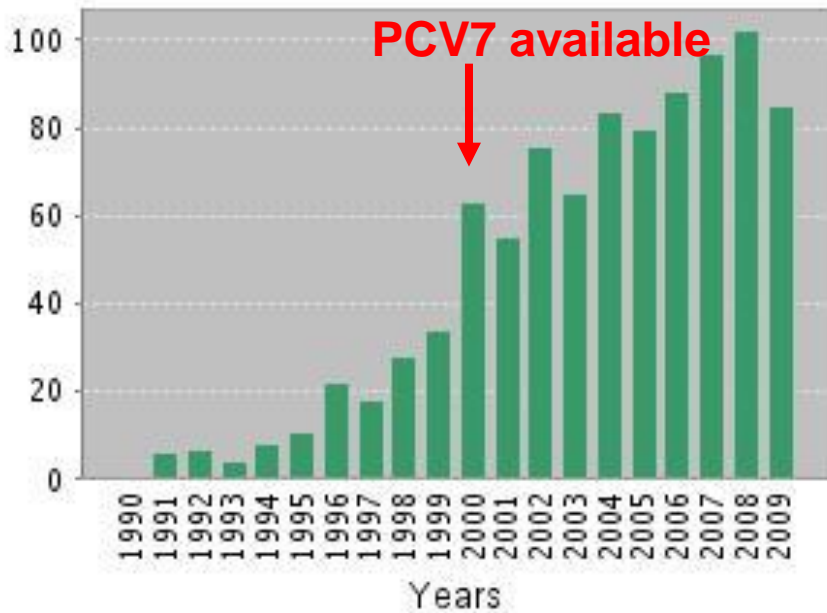
Citations in Each Year



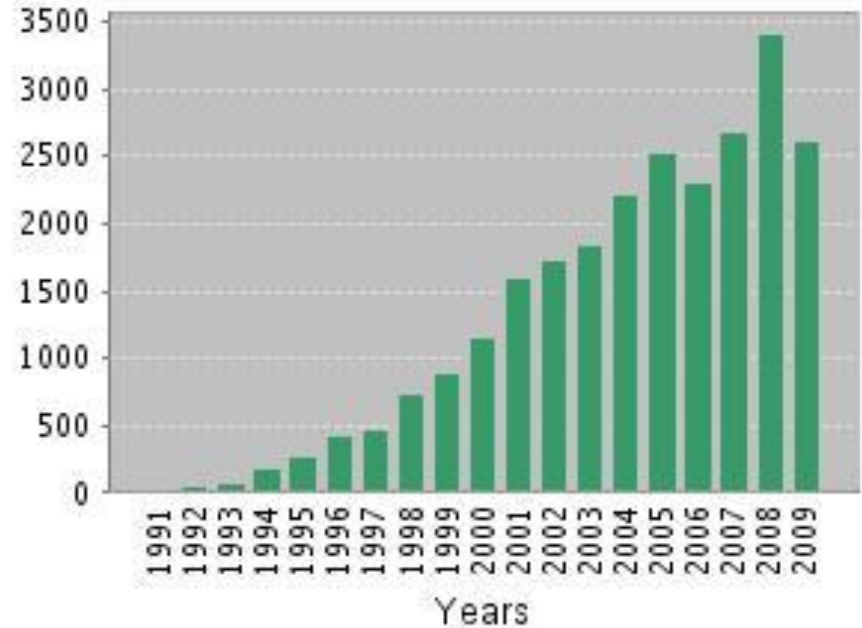
Keywords: pneumococcal and Surveillance

Increasing scientific interest in pneumococcal surveillance

Published Items in Each Year

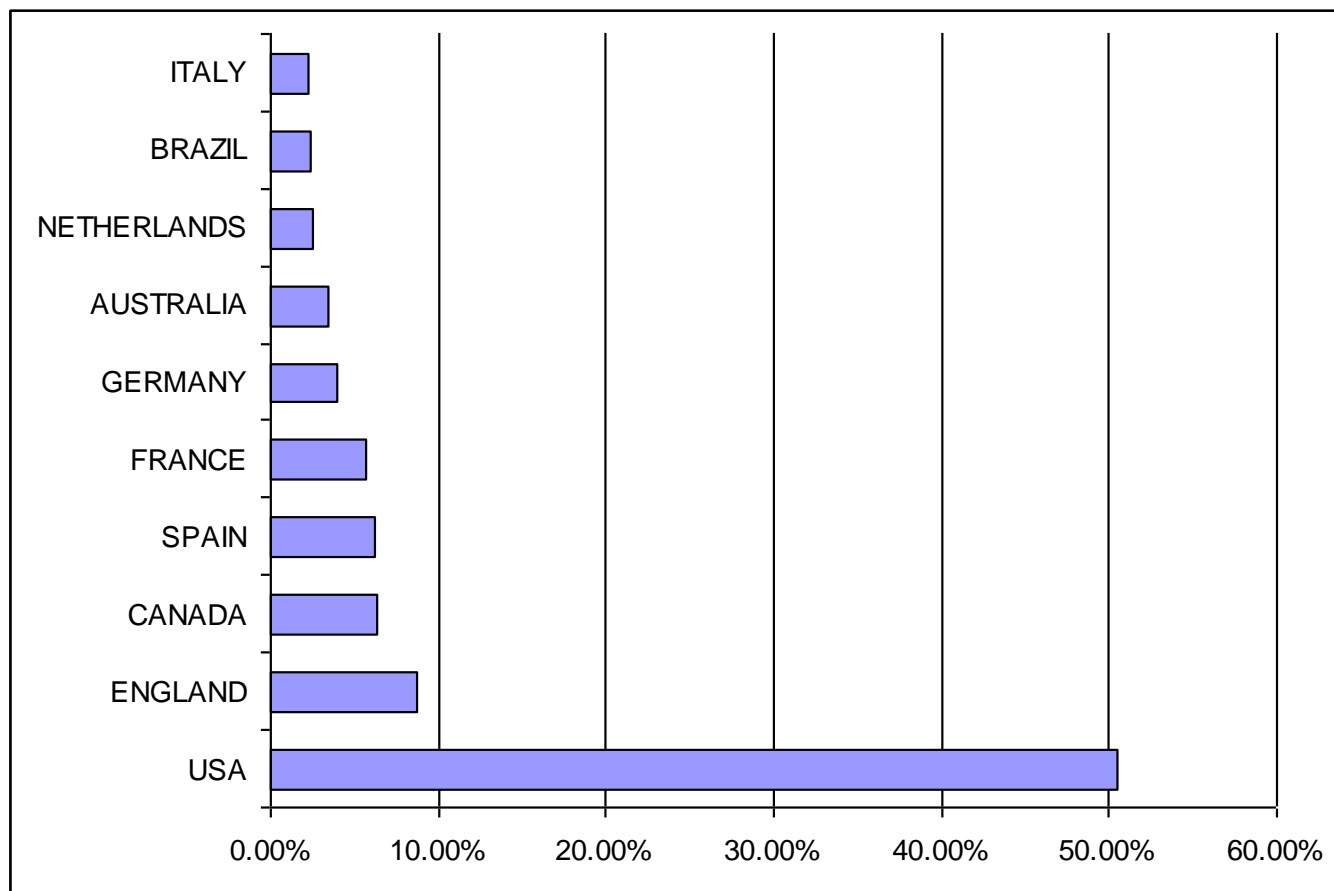


Citations in Each Year



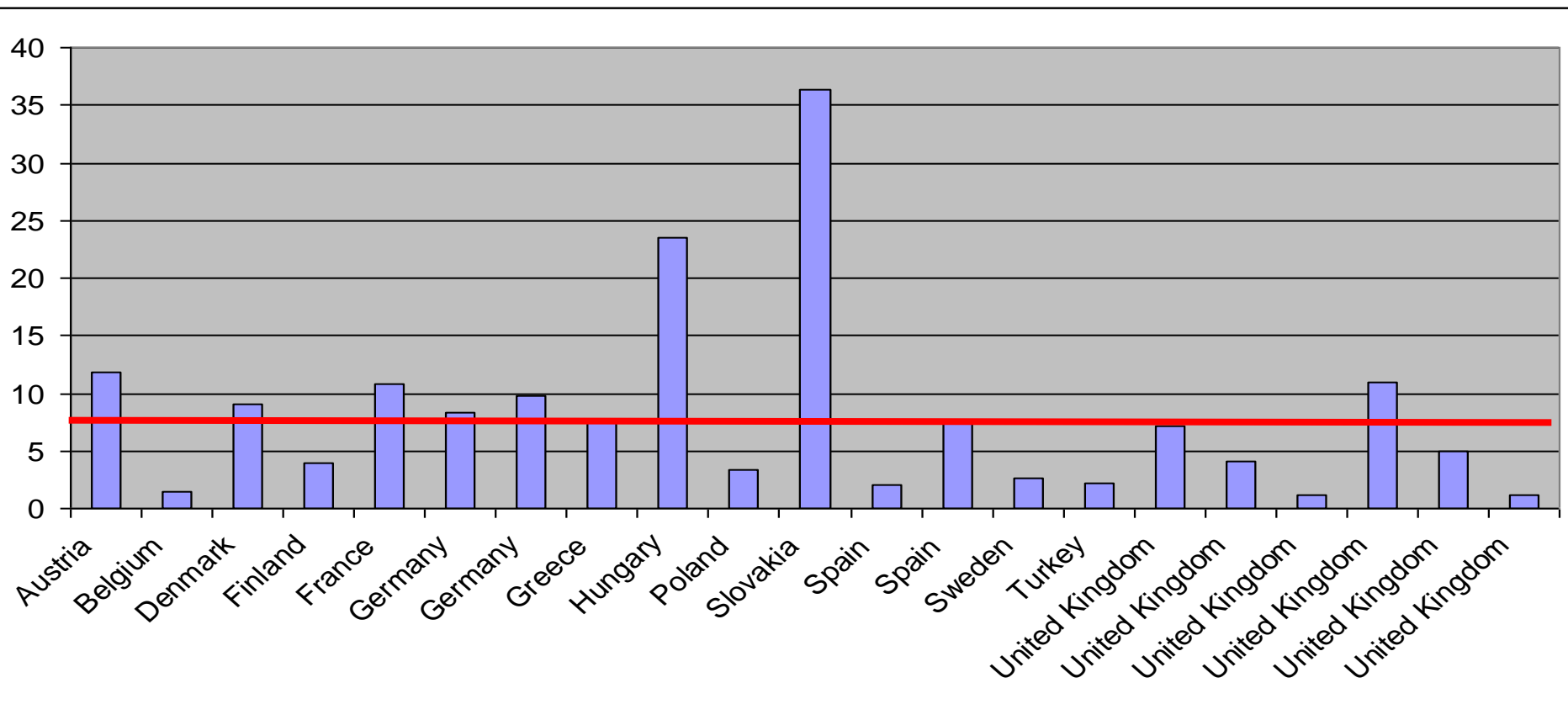
The availability of a preventive vaccine has created an interest in disease surveillance

From which countries does our current knowledge on pneumococcal surveillance come from?



The wide range of CFRs in pneumococcal meningitis reported from Europe: reality or surveillance bias?

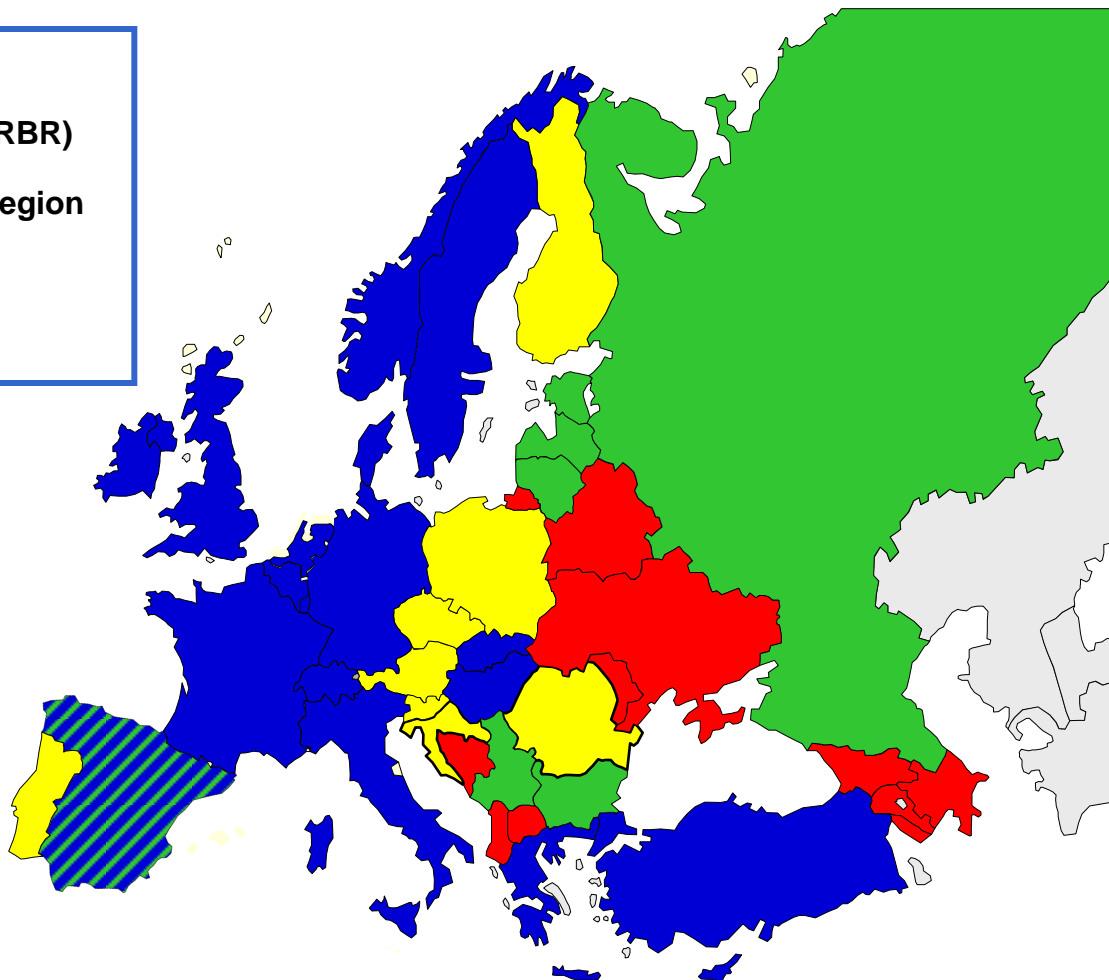
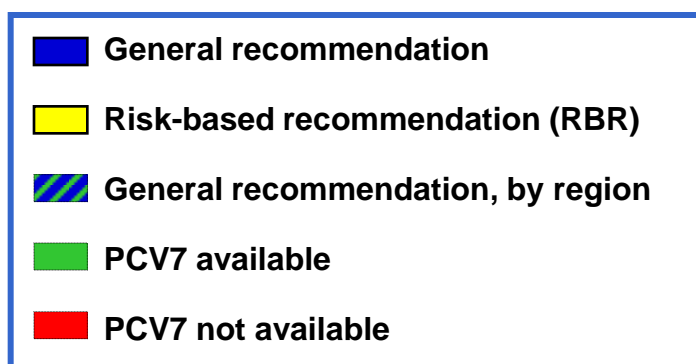
CFR (%)



Red line: mean CFR

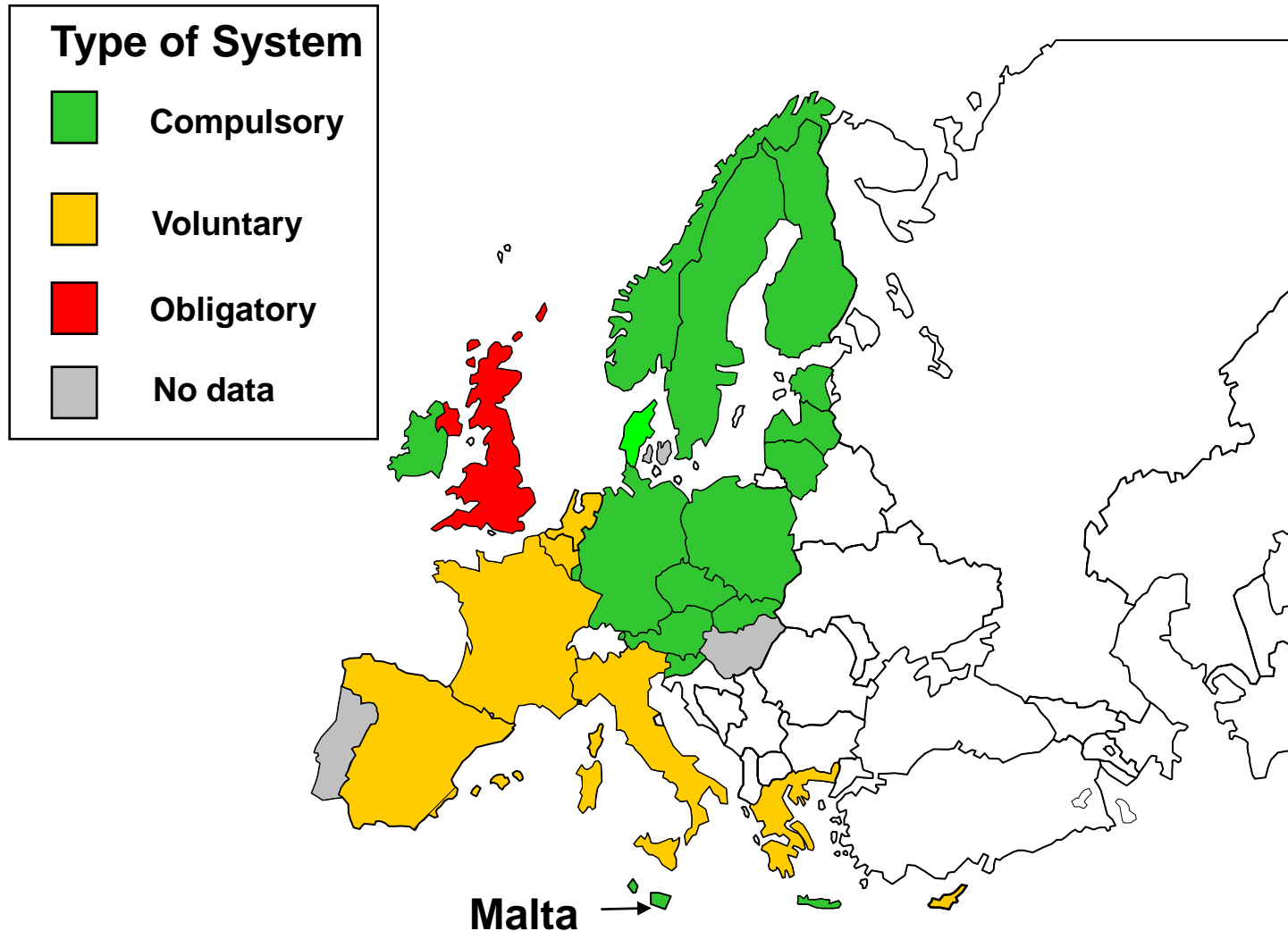
Countries

PCV7 introduction into national immunisation programmes (NIPs) in Europe



The First European Communicable Disease Epidemiological Report

Reporting systems for invasive pneumococcal disease

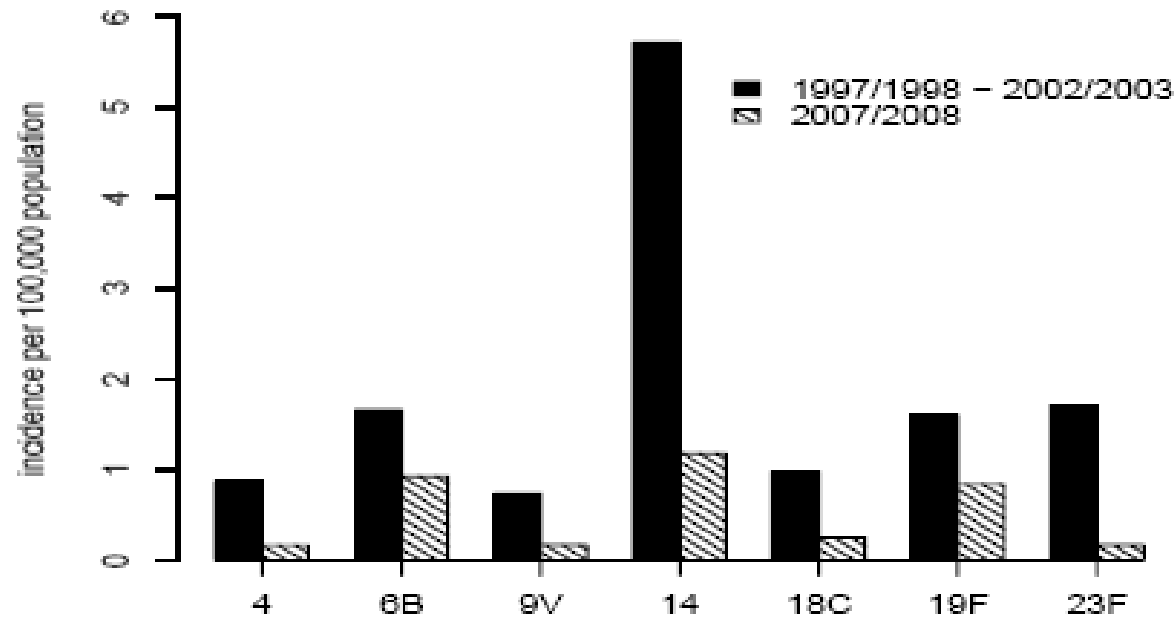


Based on The First European Communicable Disease Epidemiological Report

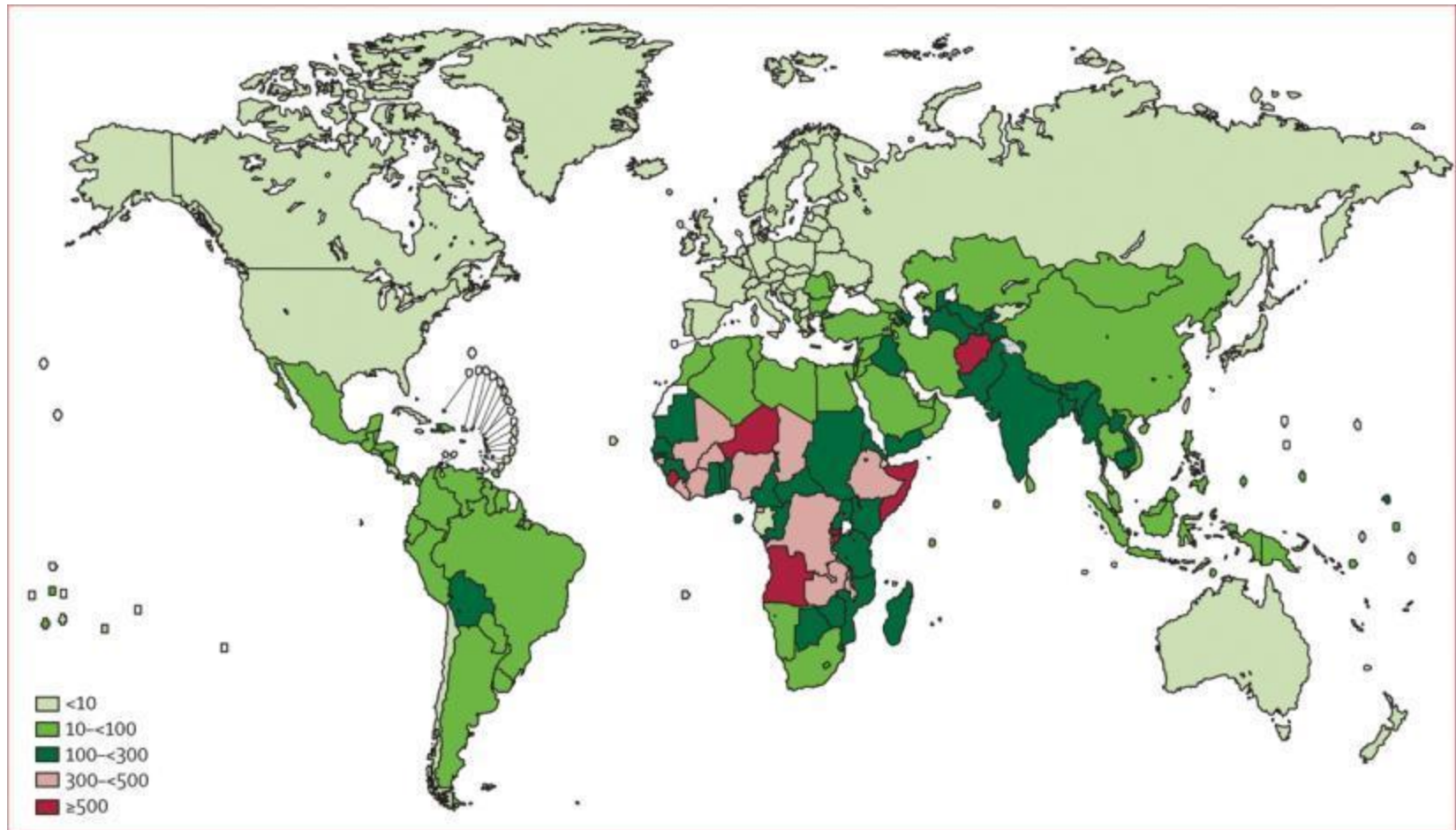
Editors: Andrew Amato-Gauci and Andrea Ammon, Stockholm, 7 June 2007
European Centre for Disease Prevention and Control, updated by R. R. Reinert; 11-2007

Reductions in the incidence of IPD in children < 2 yrs in Germany

A. Serotypes included in 7vPnC

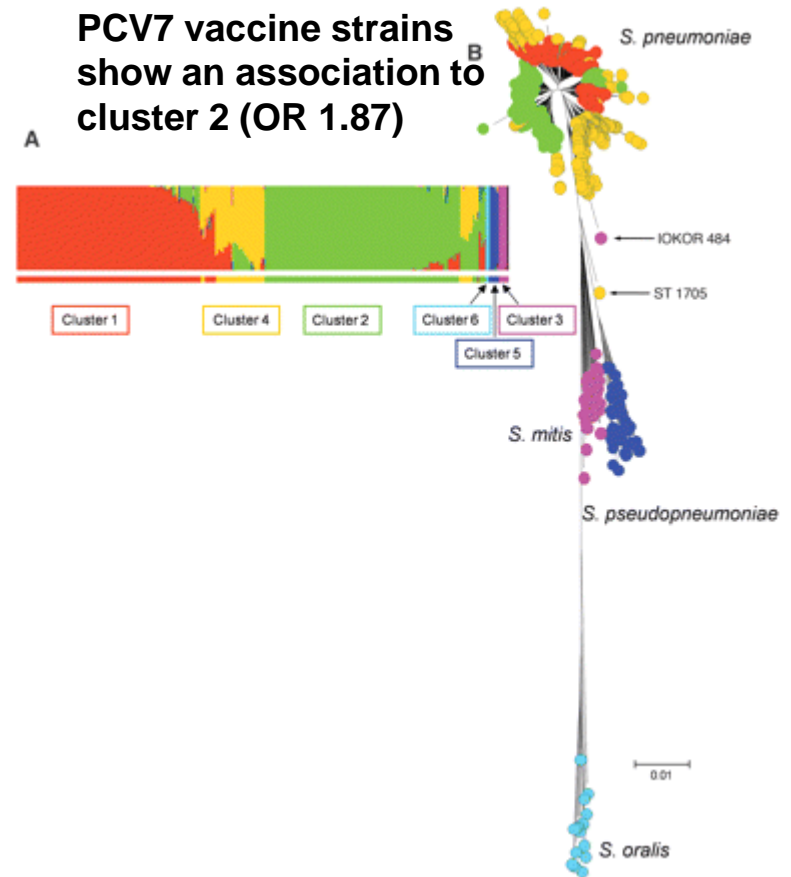


Pneumococcal mortality rate

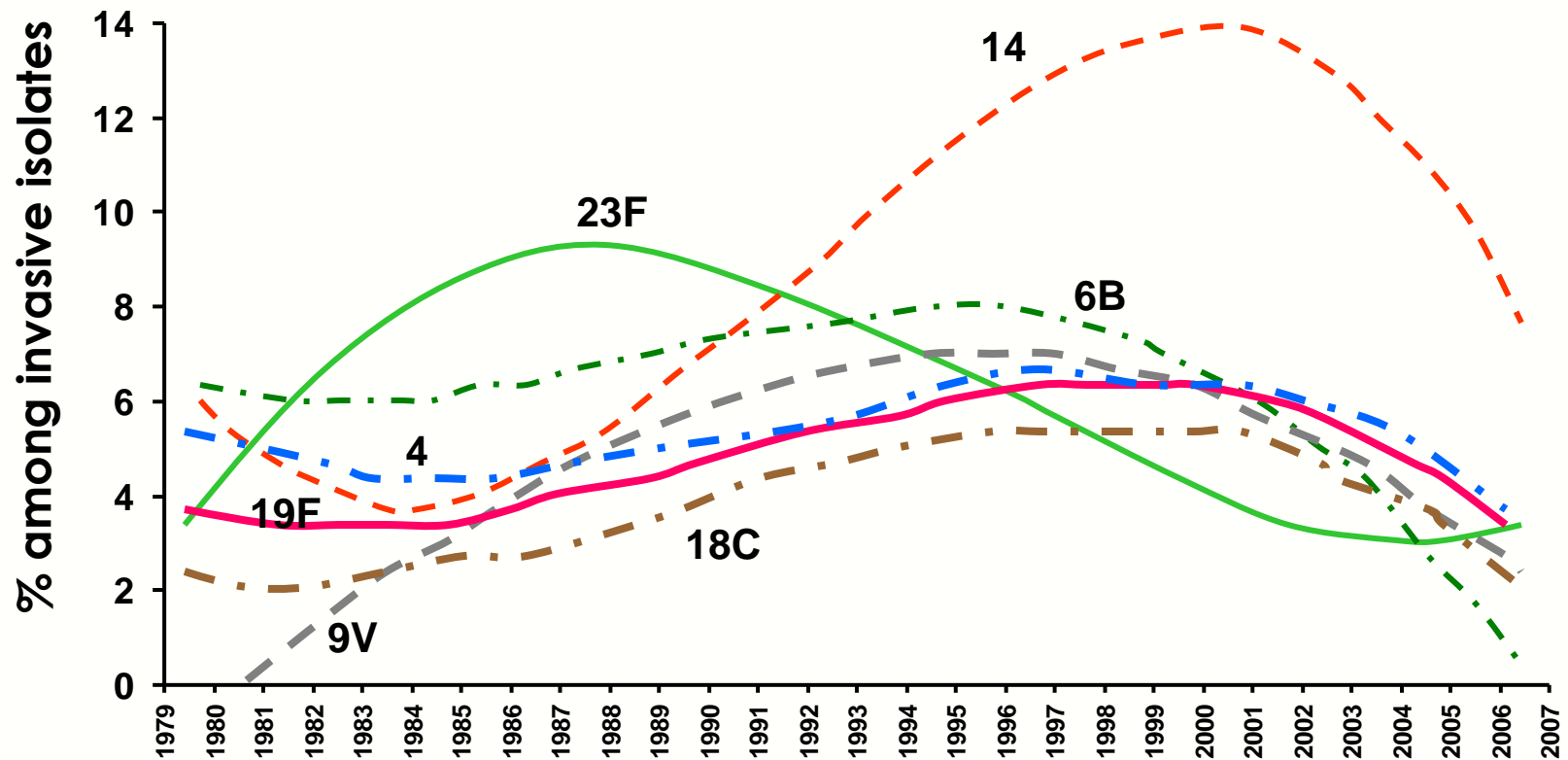


A challenge for the vaccine producers: Hyper-recombination, diversity, and antibiotic resistance in pneumococcus

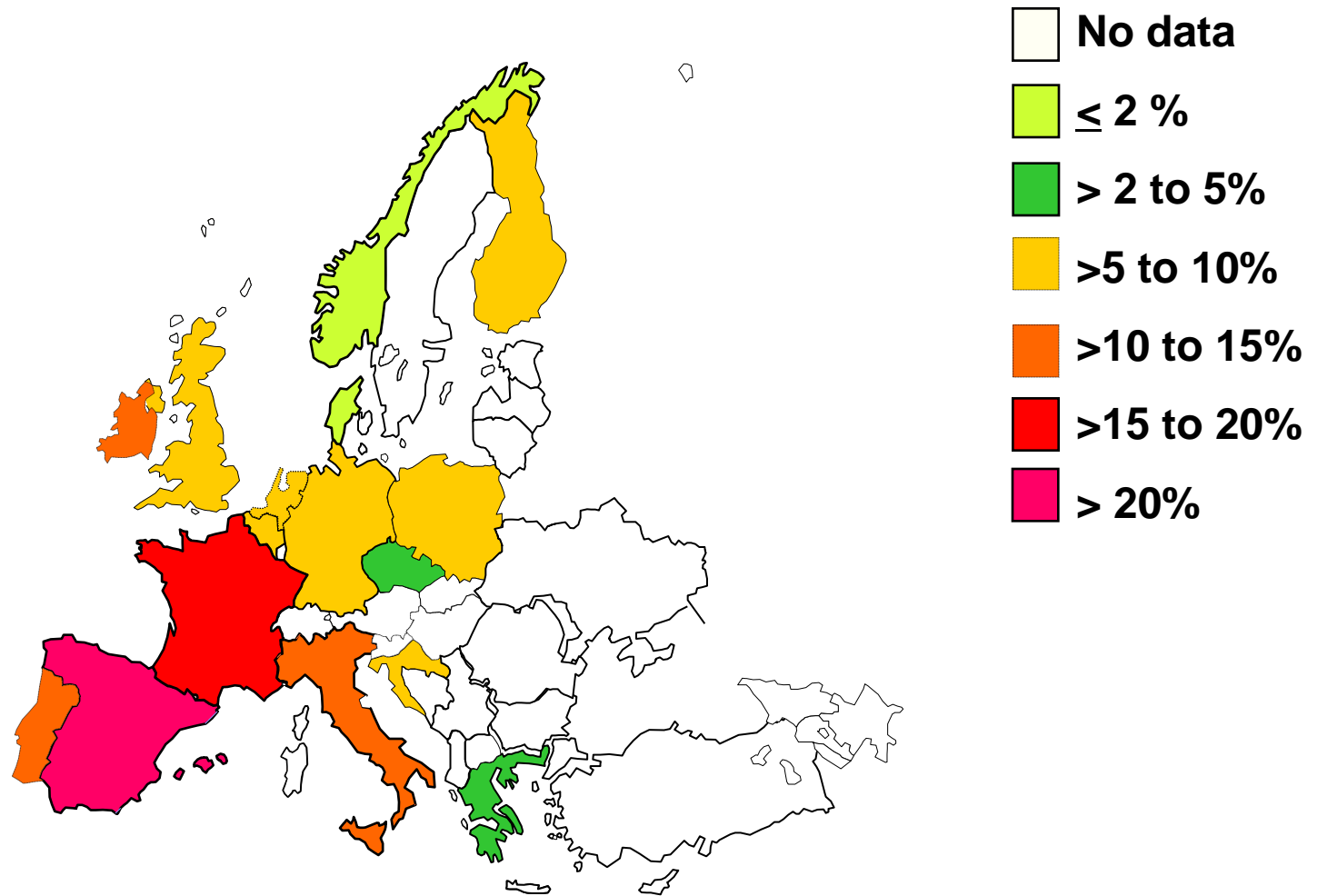
- Pneumococcal strains show evidence of past recombination with other pneumococci and with related species
- “ non vaccine serotypes may derive an ecological advantage from the removal of their competitors “
- General tolerance for foreign DNA, suggesting a hyper-recombinant state



Fluctuations of Pneumococcal 7-valent Vaccine Serotypes Over Time



Invasive pneumococcal disease in children due to serotype 19A in EUROPE , 2006-7



Post introduction surveillance can support the development of new vaccines addressing the changing epidemiology of pneumococcal disease

PCV7¹	CRM	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A
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PCV10²	PD, TT DT	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A
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PCV13^{3*}	CRM	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A
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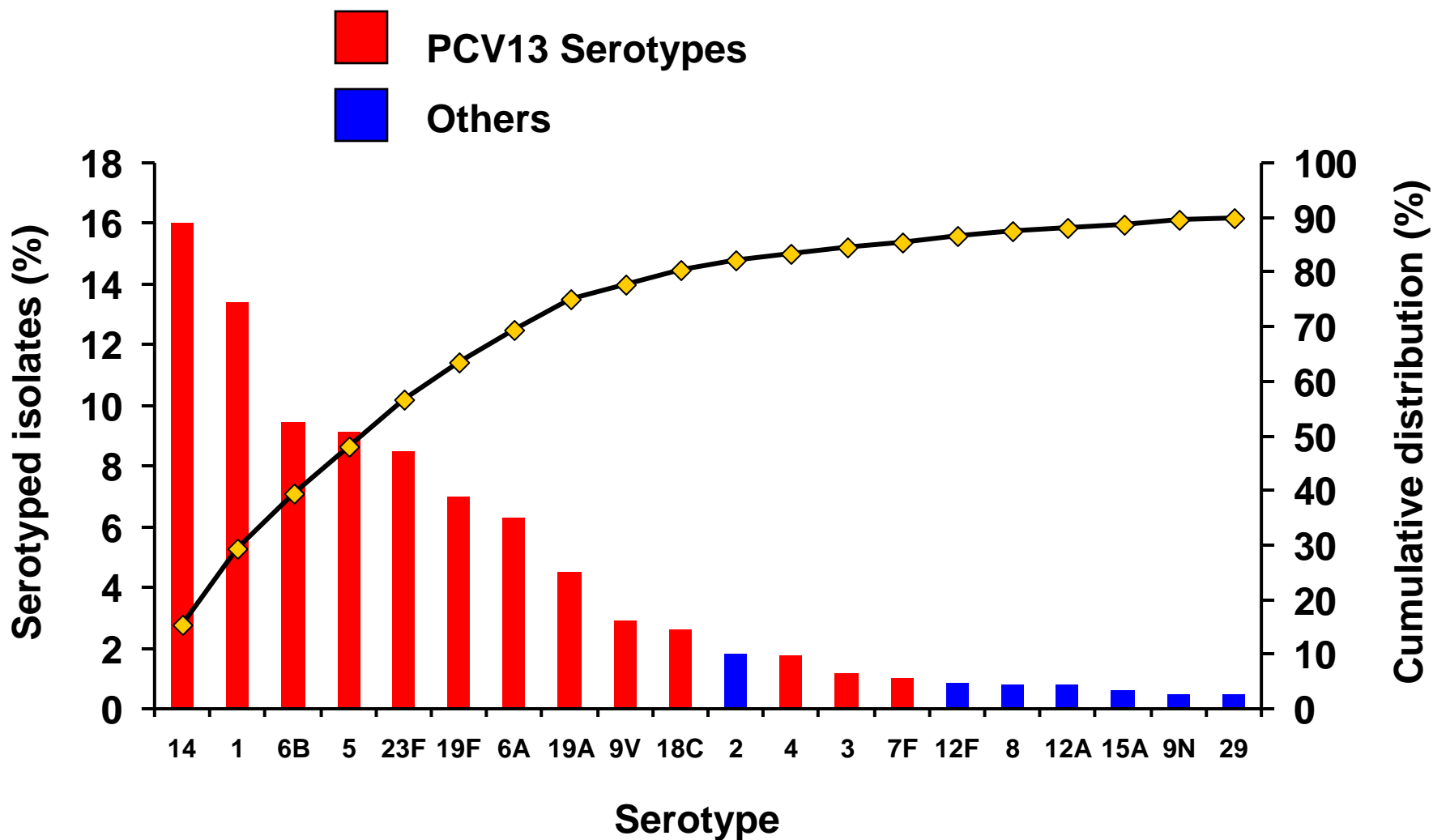
CRM = Diphtheria CRM₁₉₇

PD = *Haemophilus influenzae*-derived protein D, nontypeable *H. influenzae* carrier for all serotypes except 18C (tetanus toxoid) and 19F (diphtheria toxoid)

*Investigational vaccine, positive opinion by CHMP Sept 25th 2009

1. Prevenar. Summary of Product Characteristics.
2. Health Canada. Available at: http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/phase1-decision/drug-med/nd_ad_2009_synflorix_119056-eng.php. Accessed April 19, 2009.
3. Scott DA, et al. *Vaccine*. 2007;25:6164-6166.

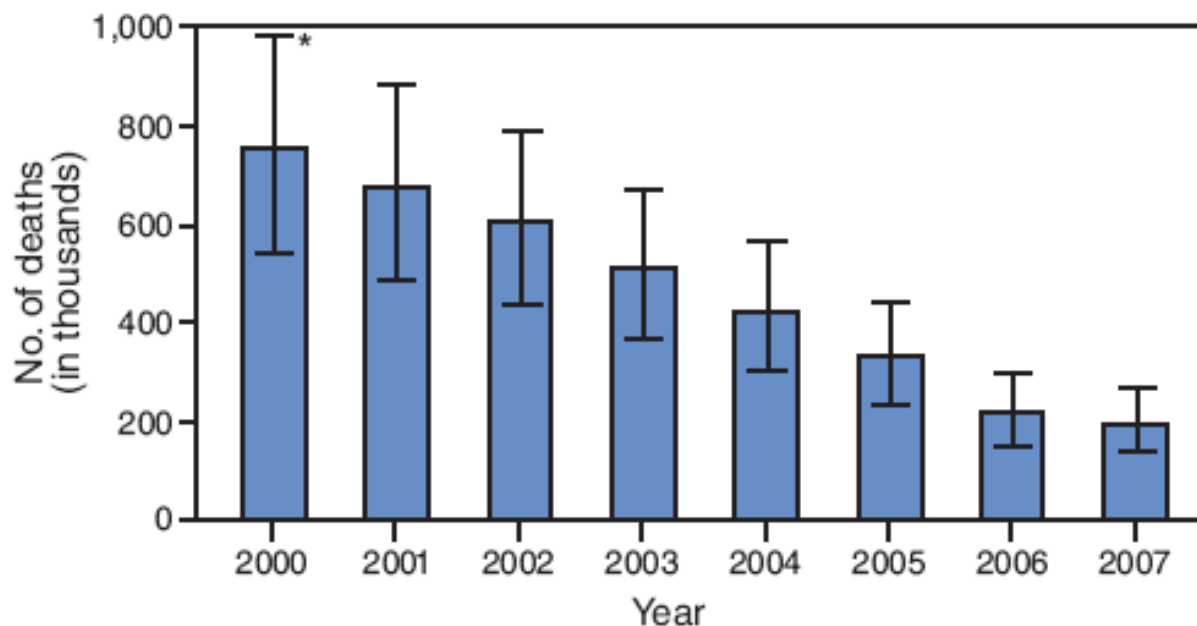
Global serotype distribution among children <5 years



Progress in Global Measles Control and Mortality Reduction, 2000-2007

- Despite the availability of a safe and effective vaccine since 1963, measles has been a major killer of children in developing countries
- At the World Health Assembly in 2008, all World Health Organization (WHO) member states reaffirmed their commitment to achieving a 90% reduction in measles mortality by 2010
- This WHO-UNICEF comprehensive strategy for measles mortality reduction focuses on 47 priority countries
- The strategy's components include
 - Achieving and maintaining high coverage (>90%)
 - Ensuring that all children receive a second opportunity for measles immunization
 - **Implementing effective laboratory-supported disease surveillance**
 - Appropriate clinical management for measles cases.

Progress in Global Measles Control and Mortality Reduction, 2000-2007



SOURCE: World Health Organization.

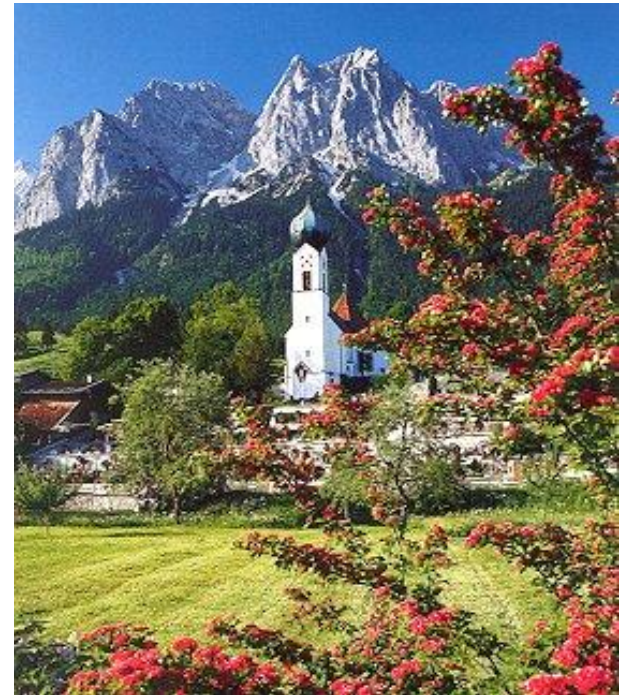
* 95% uncertainty interval. Based on Monte Carlo simulations that account for uncertainty in key input variables (i.e., vaccination coverage and case-fatality ratios).

Progress in global measles control and mortality reduction, 2000-2007

WHO region	% coverage with 1 st dose of measles vaccine		Decrease in measles deaths 2000-07		Proportion of estimated global decrease attributable to region/priority countries (%)
	2000	2007	No.	%	
Africa	56	74	350,000	89	63
America	92	93	-		
Eastern Mediterranean	73	84	86,000	90	16
Europe	91	94	-		
South-East Asia	61	73	99,000	42	18
Western Pacific	86	92	18,000	73	3
Total	72	82	553,000	74	100
47 priority countries	58	72	533,000	73	96

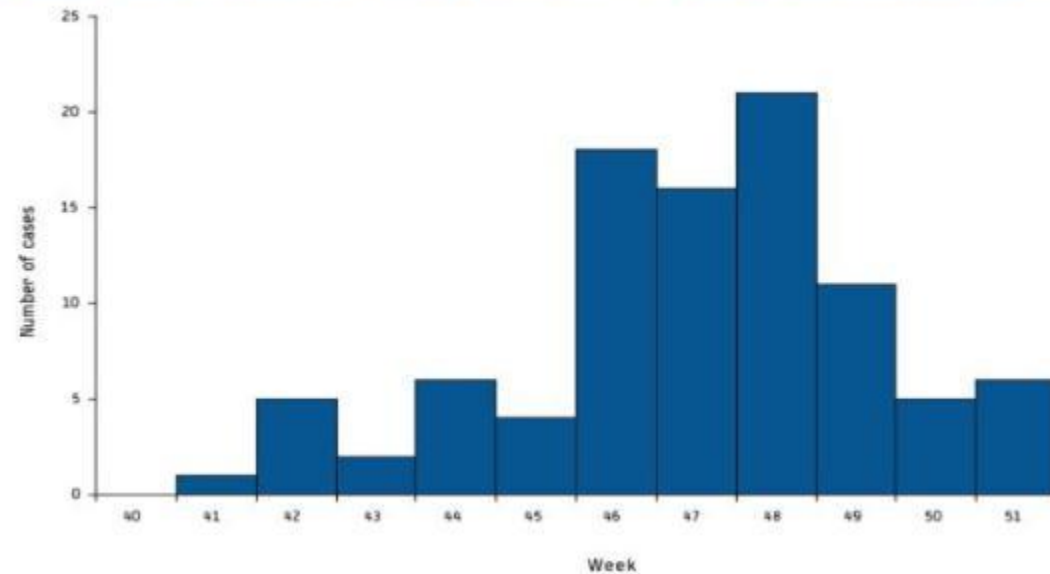
Source: MMWR 57, 2008

Southern Bavaria, Germany



Ongoing measles outbreak in Southern Bavaria, Germany

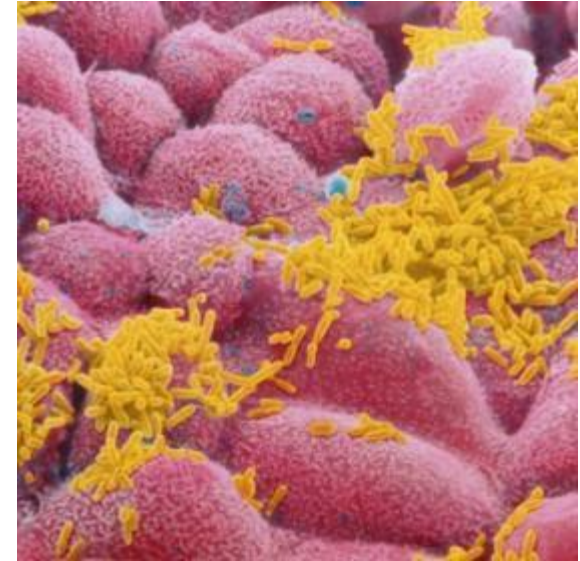
FIGURE 1
Measles cases in Bavaria, week 40-51, 2007, by week of notification (n=95)



“A total of 92 cases (97%) were unvaccinated. Two cases (aged 23 months and 16 years...) had received one documented dose of measles vaccine before exposure. No case had received two doses”

H. influenzae serotype B

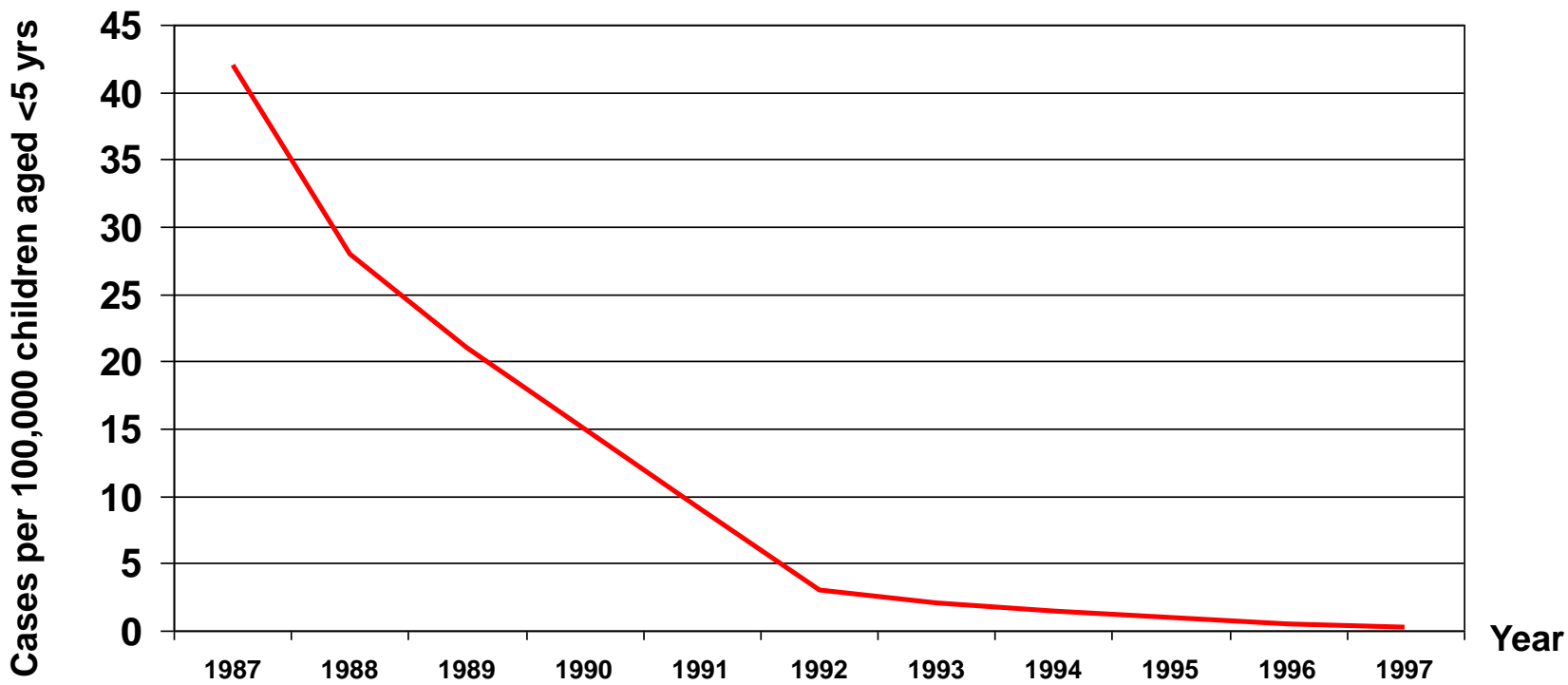
- **H. influenzae is responsible for significant morbidity and mortality worldwide, particularly in children under 5 years of age**
- **In the pre-vaccine era, 95% of serious disease was attributable to one serotype b (Hib)**



Electron micrograph of
Haemophilus influenzae

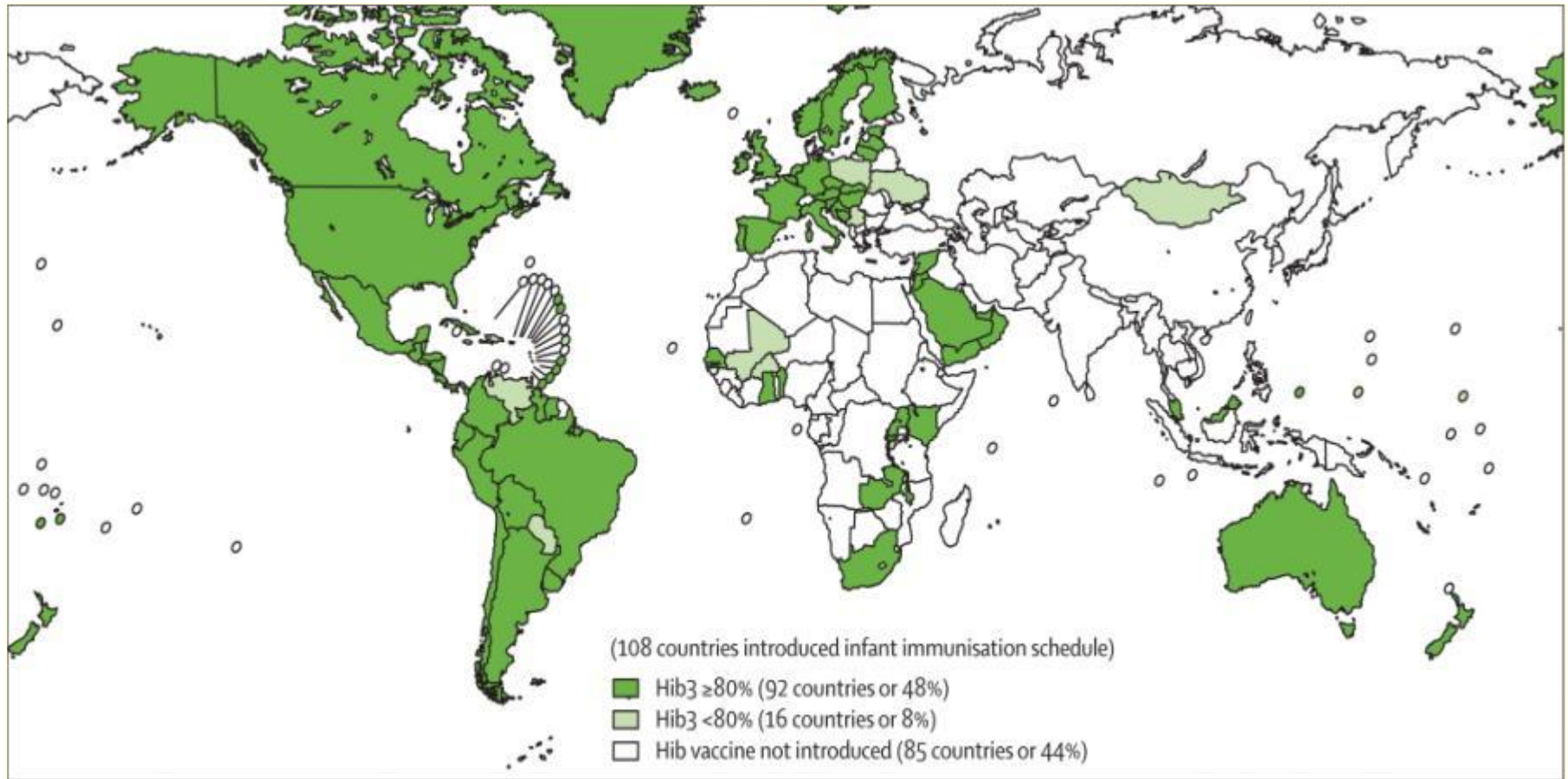
Routine use of Hib conjugate vaccines has resulted in a remarkable decline in Hib disease

Incidence of invasive H. influenzae disease in the United States, 1987-1997



Source: CDC MMWR 27, 1998

Countries that have introduced Hib vaccine and infant Hib coverage, 2006



From vaccine efficacy to effectiveness

Efficacy



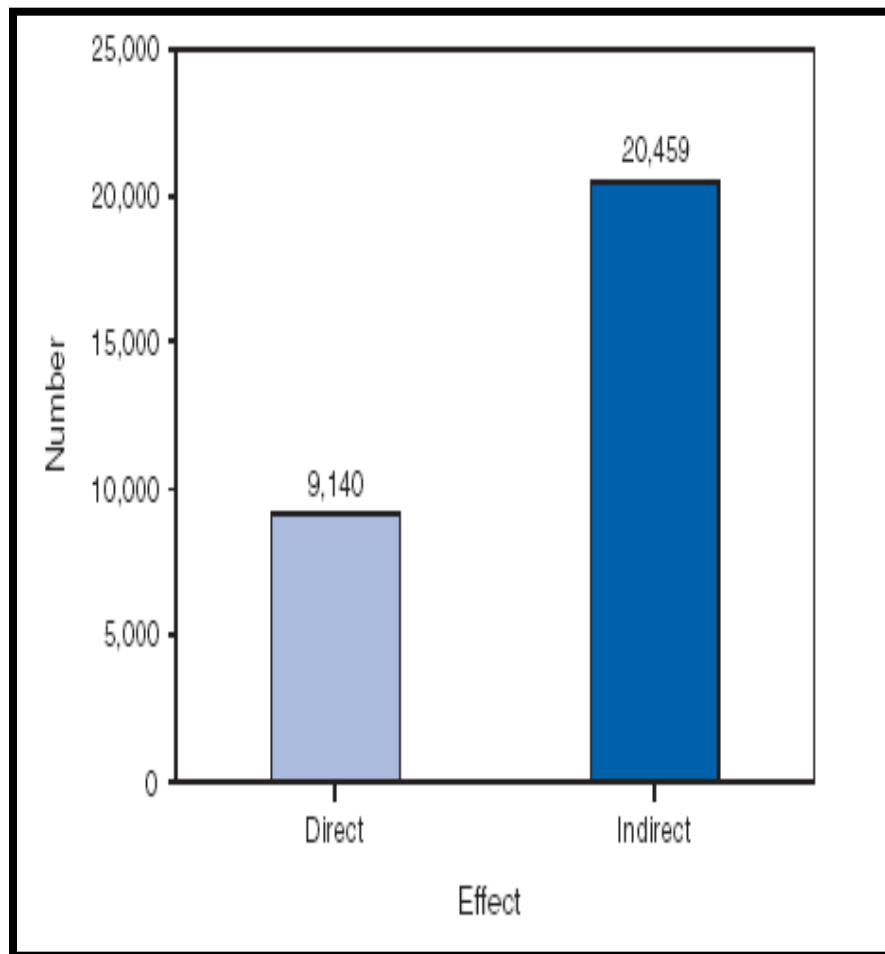
Schumacher, M. GP Canada 2003

Effectiveness



Beijing 2009

Vaccine-type IPD cases prevented directly and indirectly, USA, 2003



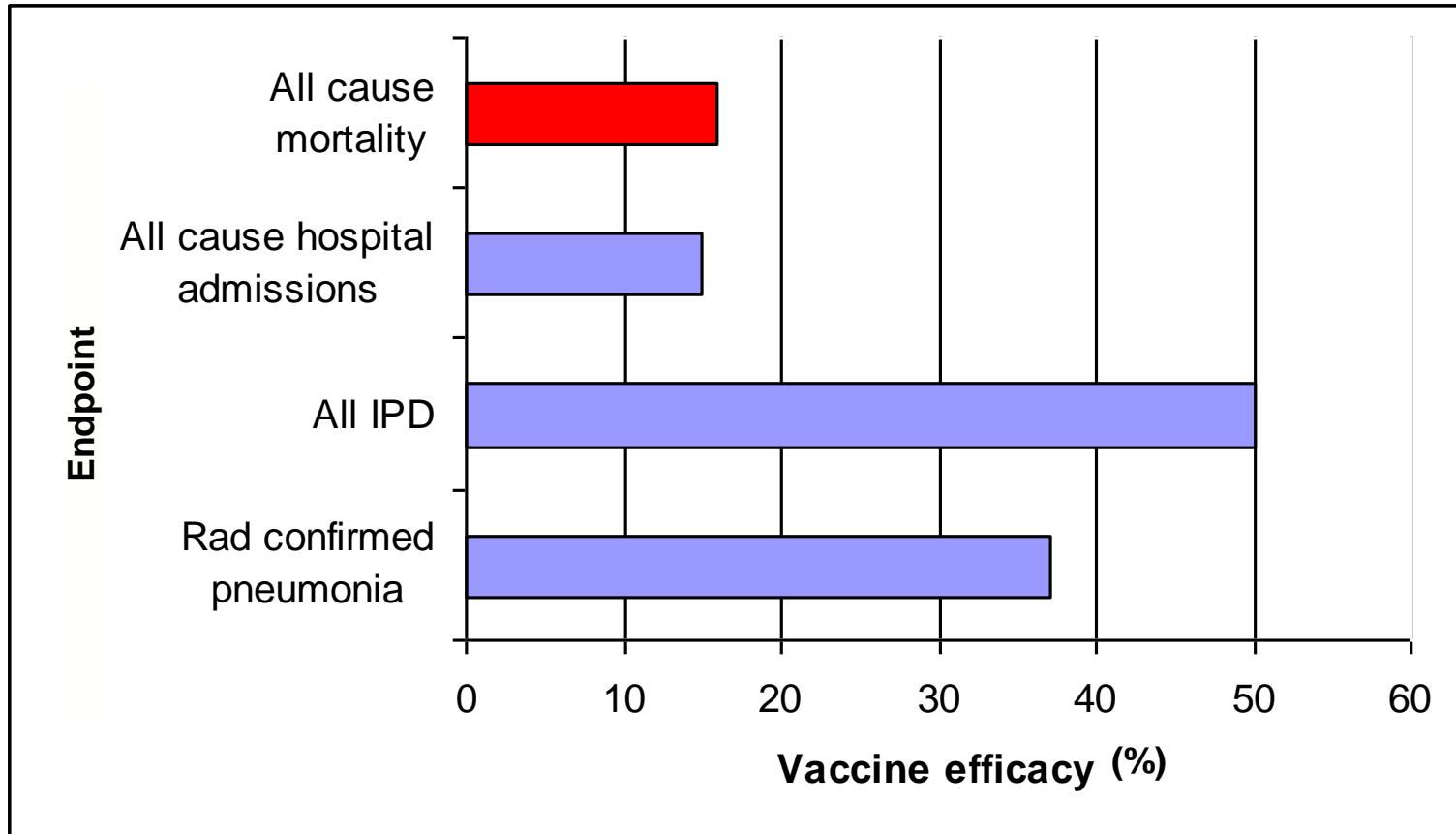
Direct VT IPD cases prevented in 2003

- (1998-1999 average number of VT IPD cases in children aged < 5 years) X (2003 PCV coverage with 3 doses [68.1%]) X (PCV7 effectiveness for VT IPD (93.9%))

Indirect VT IPD cases prevented in 2003

- (1998-1999 average number of VT IPD cases of VT IPD cases across all age groups – 2003 number of VT IPD cases across all age groups) – (2003 direct VT IPD cases prevented)

Reduction of « all cause » childhood mortality by vaccination: Clinical trial in The Gambia with PCV9



Conclusions

- Despite its relative youth vaccination has controlled 12 major communicable diseases
- The availability of solid surveillance data has accelerated the introduction of vaccines into National Immunization Programs
- But also vice versa: the availability of vaccines helps us to gain knowledge of infectious diseases
- Importance of surveillance for policy makers
 - Evidence-based recommendations
- **Disease surveillance & Vaccines: a productive marriage**