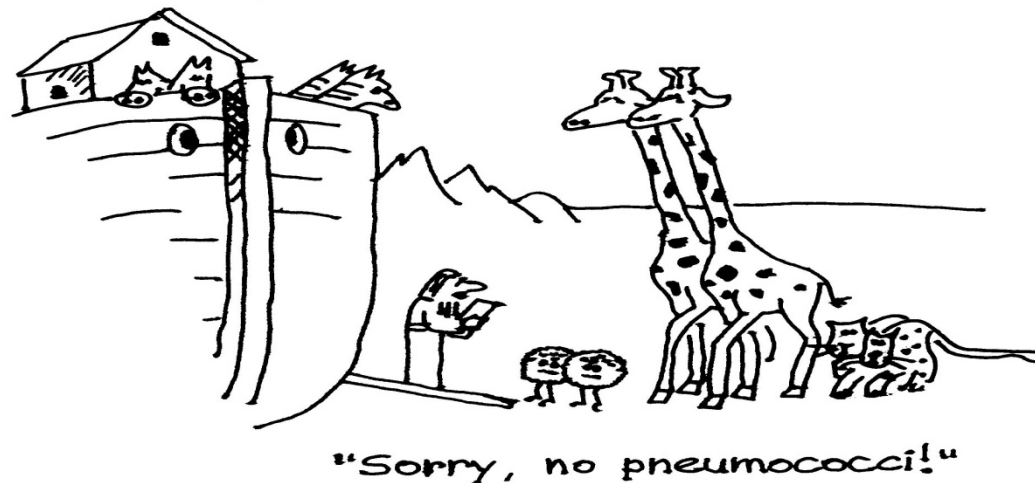


The impact of the pneumococcal conjugate vaccine on pneumococcal disease



**Reinier Veenhoven
ESSOP 2009 Maribor**

Outline

- Introduction to pneumococcal nasopharyngeal carriage and disease
- Impact of the 7-valent pneumococcal conjugate vaccine on pneumococcal disease (RCT's)
- Importance of pneumococcal disease surveillance
- 10- or 13-valent pneumococcal conjugate vaccine?
- Conclusions

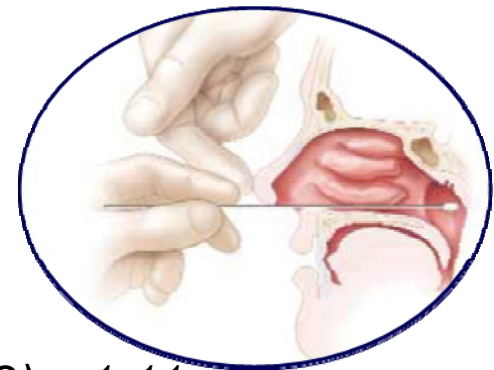
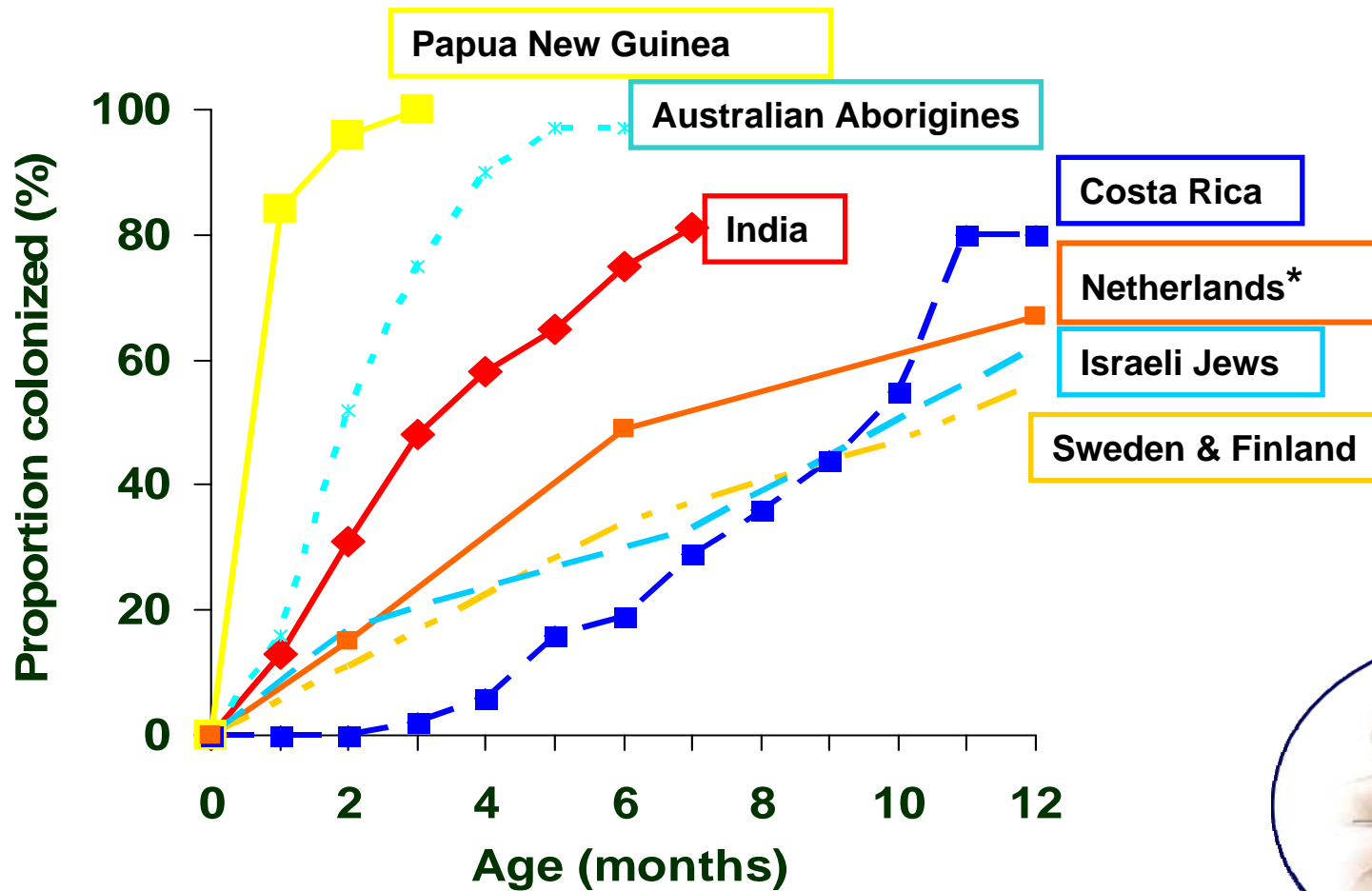


Streptococcus pneumoniae



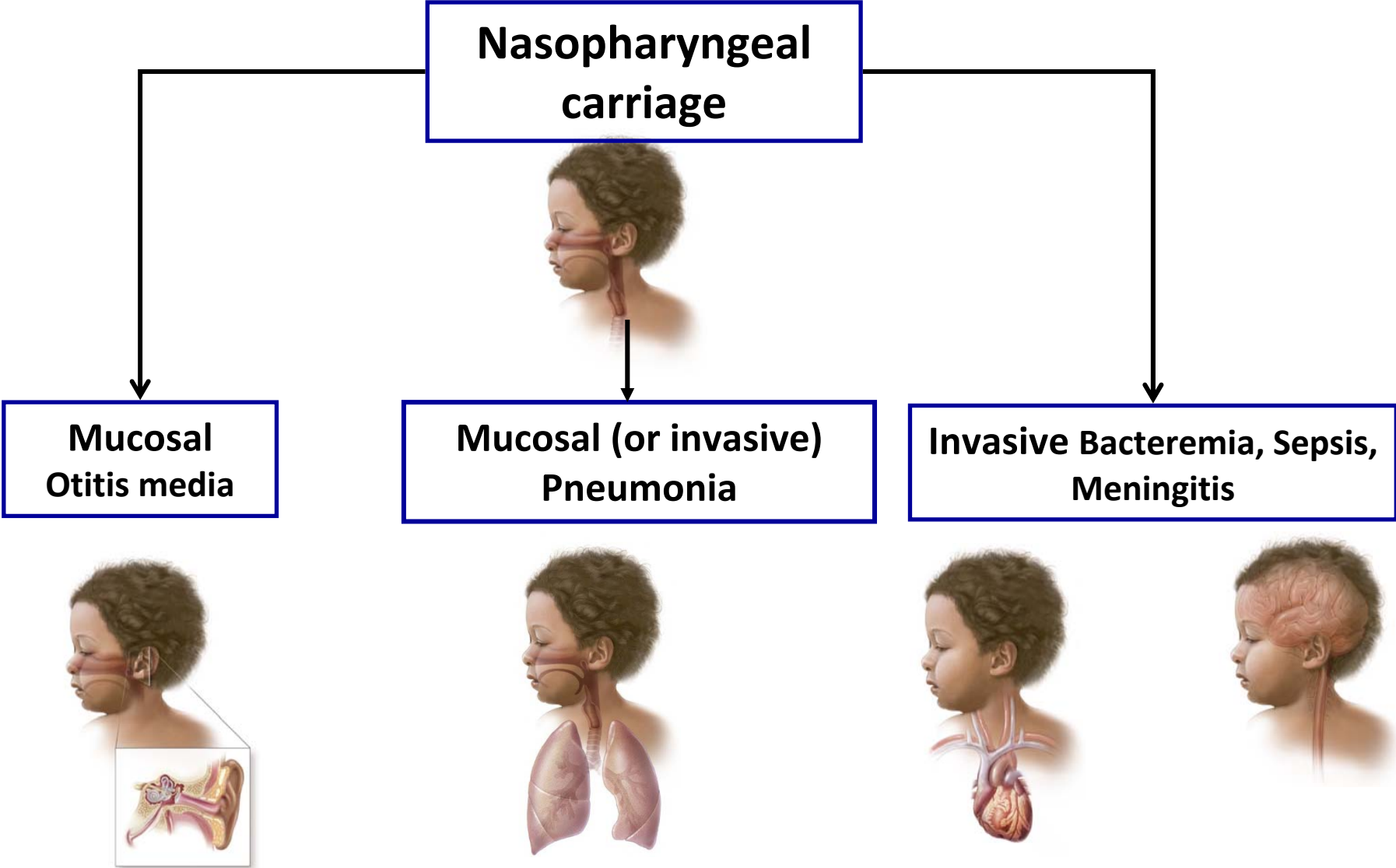
- 91 different pneumococcal serotypes
- A serotype is defined by its polysaccharide capsule
- Antipolysaccharide Ab's are protective

Nasopharyngeal pneumococcal colonization in infants over the world



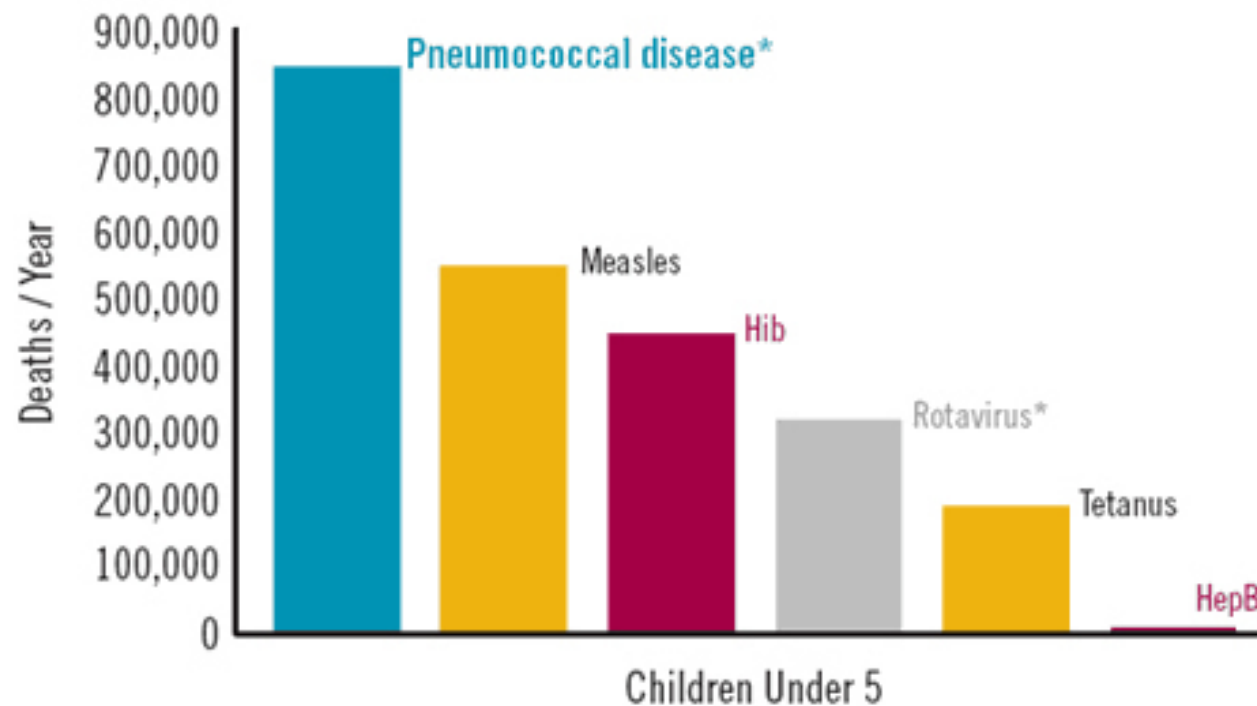
Adapted from O'Brien et al. *Pediatr Infect Dis J.* 2003; 22(2): e1-11

Pneumococcal Disease



Adapted from www.pneumoadip.org

Leading causes of vaccine-preventable death in children <5 years old



Source: WHO official mortality rates — June 2003

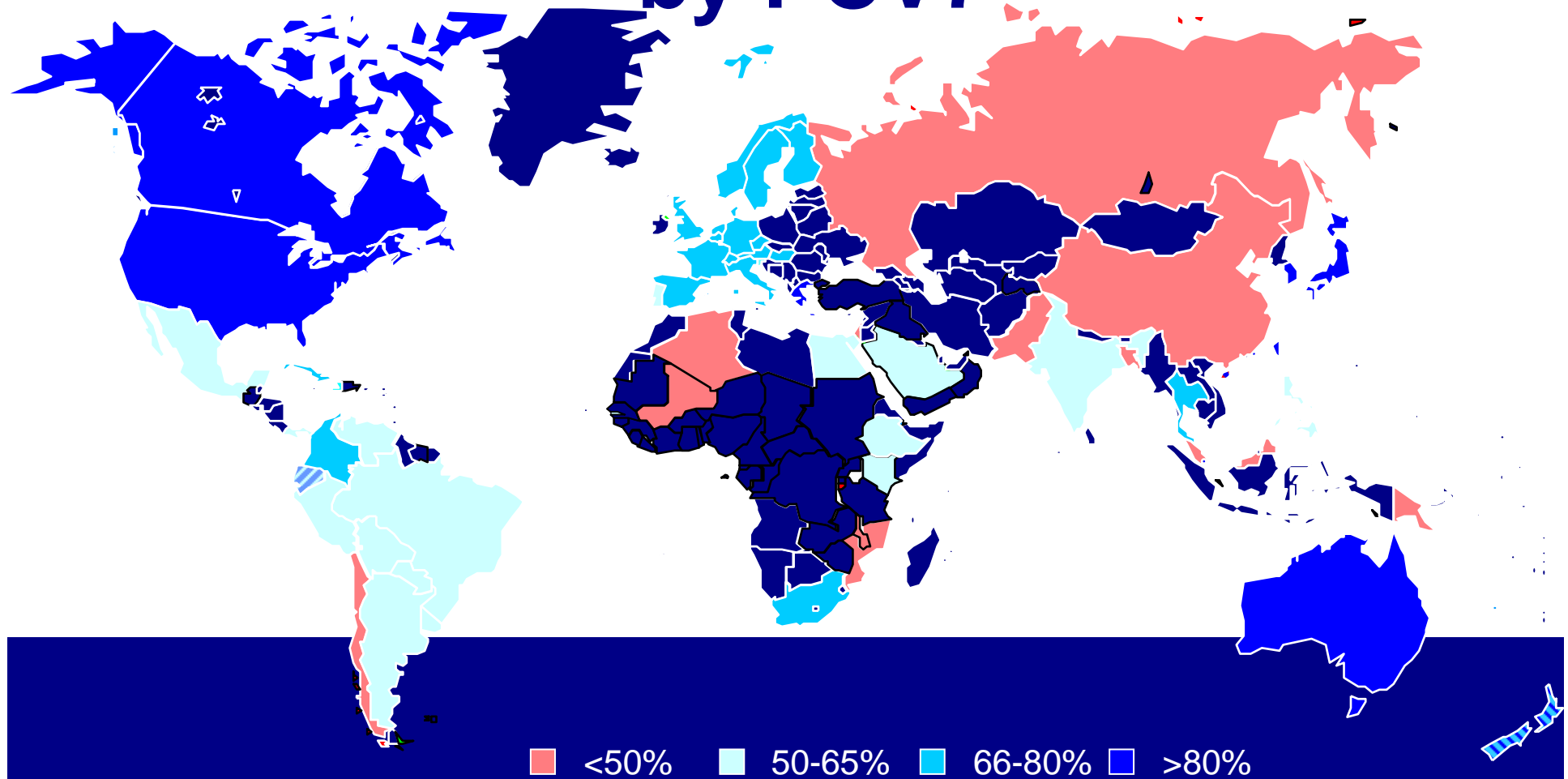
* Provisional estimates

Licensed pneumococcal vaccines



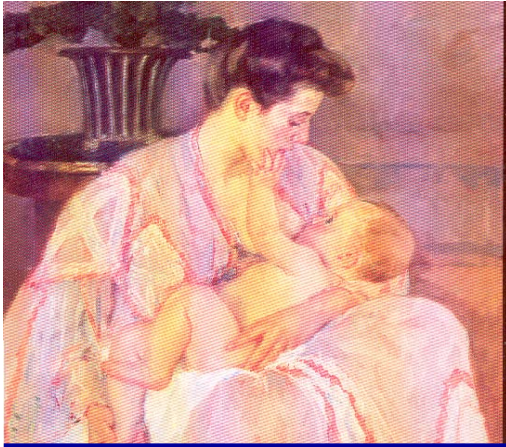
- **1977: 23-valent PPV**
 - not effective < 2 years of age
 - poorly immunogenic
- **2000: 7-valent PCV (4,6B,9V,14,18C,19F,23F)**
 - carrier protein (CRM197)
 - from 2 months: Ab's and Memory
- **2009: 10-valent PCV (+ 1,5,7F)**
 - protein D carrier (Non-typable *H. influenzae*)

IPD in < 5 years: percentage of disease due to serotypes covered by PCV7



*pre-PCV7-CRM introduction & Assuming GB – GA cross reactivity

Adapted from Hausdorff, Brueggemann, Hackell, Scott "Pneumococcal Serotype Epidemiology" in PNEUMOCOCCAL VACCINES: THE IMPACT OF CONJUGATE VACCINES (ASM Press 2008)



Efficacy RCT's PCV-7 Infants (0-24 months)

USA, Black et al. PIDJ 2000

South Africa, Klugman et al, NEJM 2003

Finland, Eskola et al, NEJM 2001

IPD

- All pneumococci
- Vaccine serotypes

USA

SA

HIV-

HIV+

89%

42%*

53%

94%

83%

65%

Pneumonia

(confirmation by X-ray)

23-32%

20%

13%*

AOM

- All otitis episodes
- *Culture MEF:
 - VT-SP
 - Non-VT SP

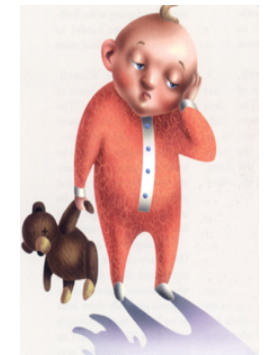
USA/Finland*

6-7 %

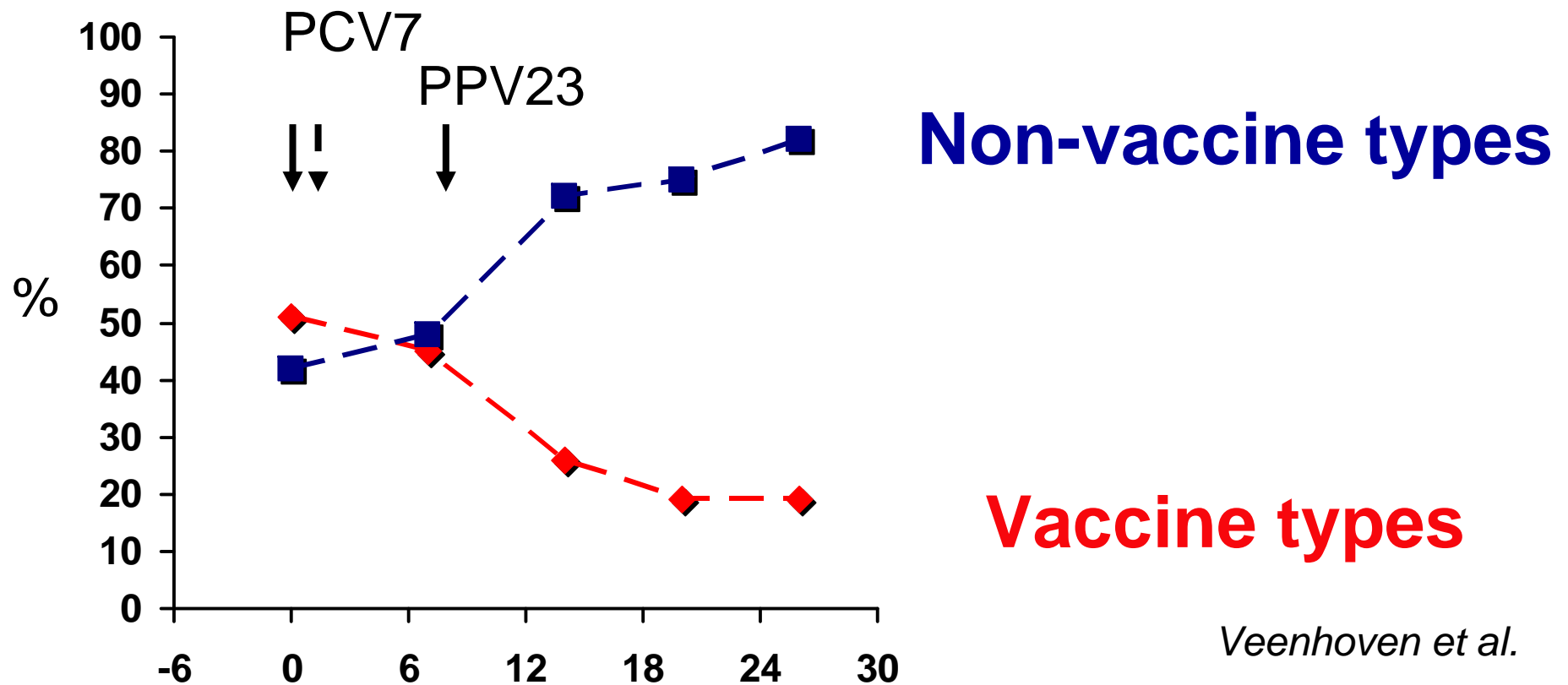
57 %

+33 %

(replacement disease)



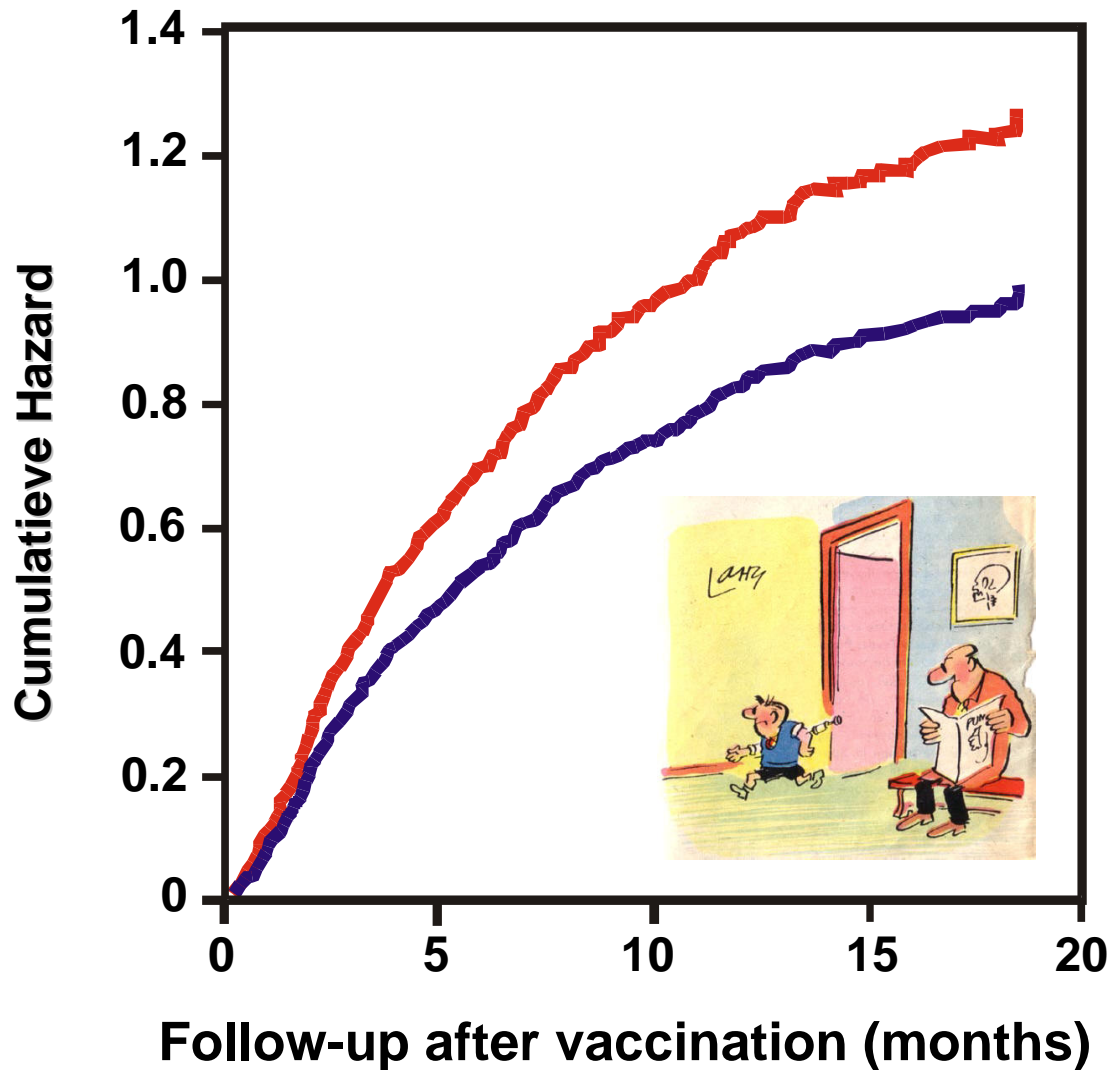
Replacement at the nasopharyngeal level. Dutch rAOM trial (age 12-24 months)



Veenhoven et al.

CID 2004

Dutch trial rAOM (400 children, 1-7 yrs)



**Pneumococcal
vaccination**

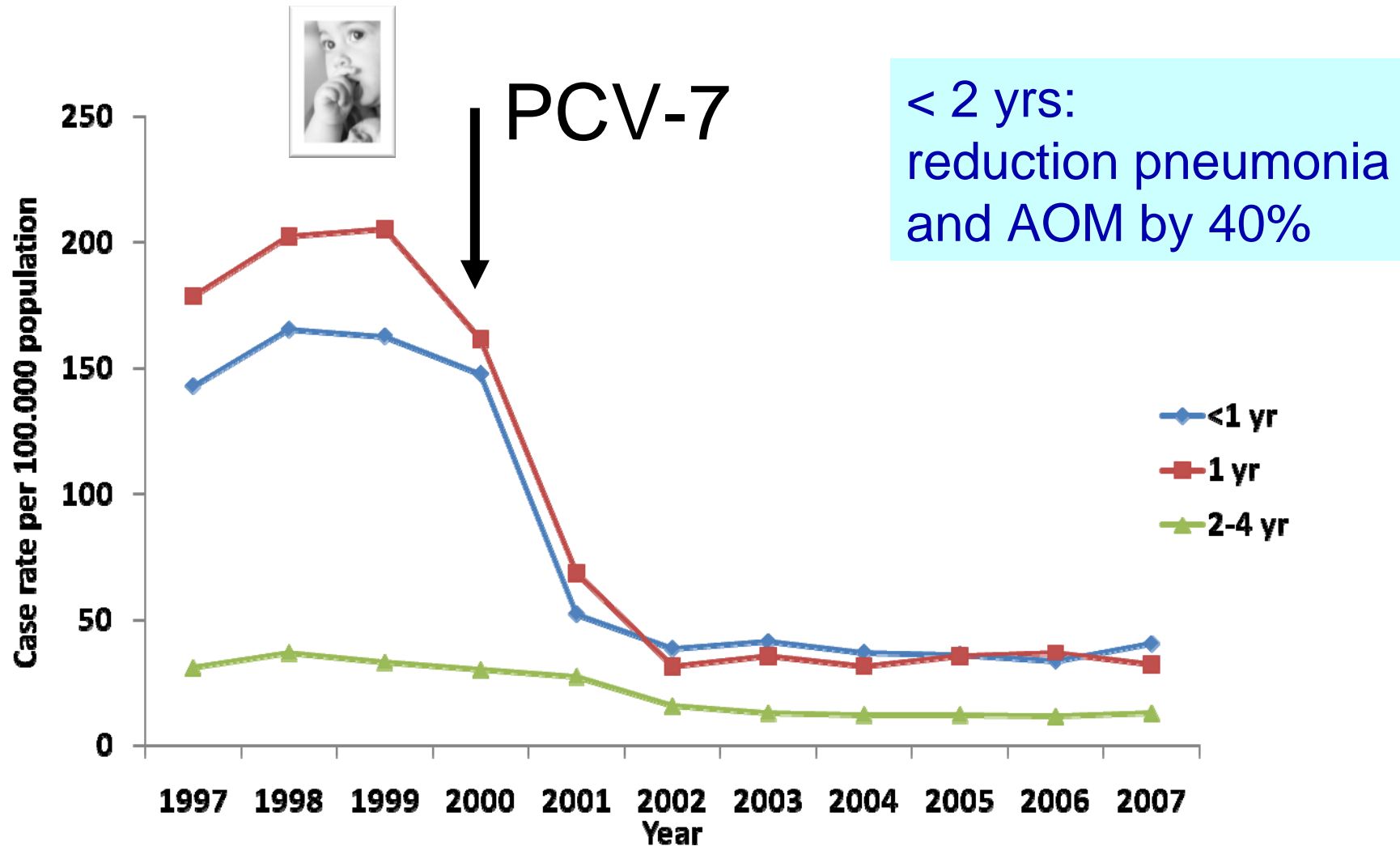
**Control
group**

S.aureus ↑

*Veenhoven et al.
Lancet 2003*

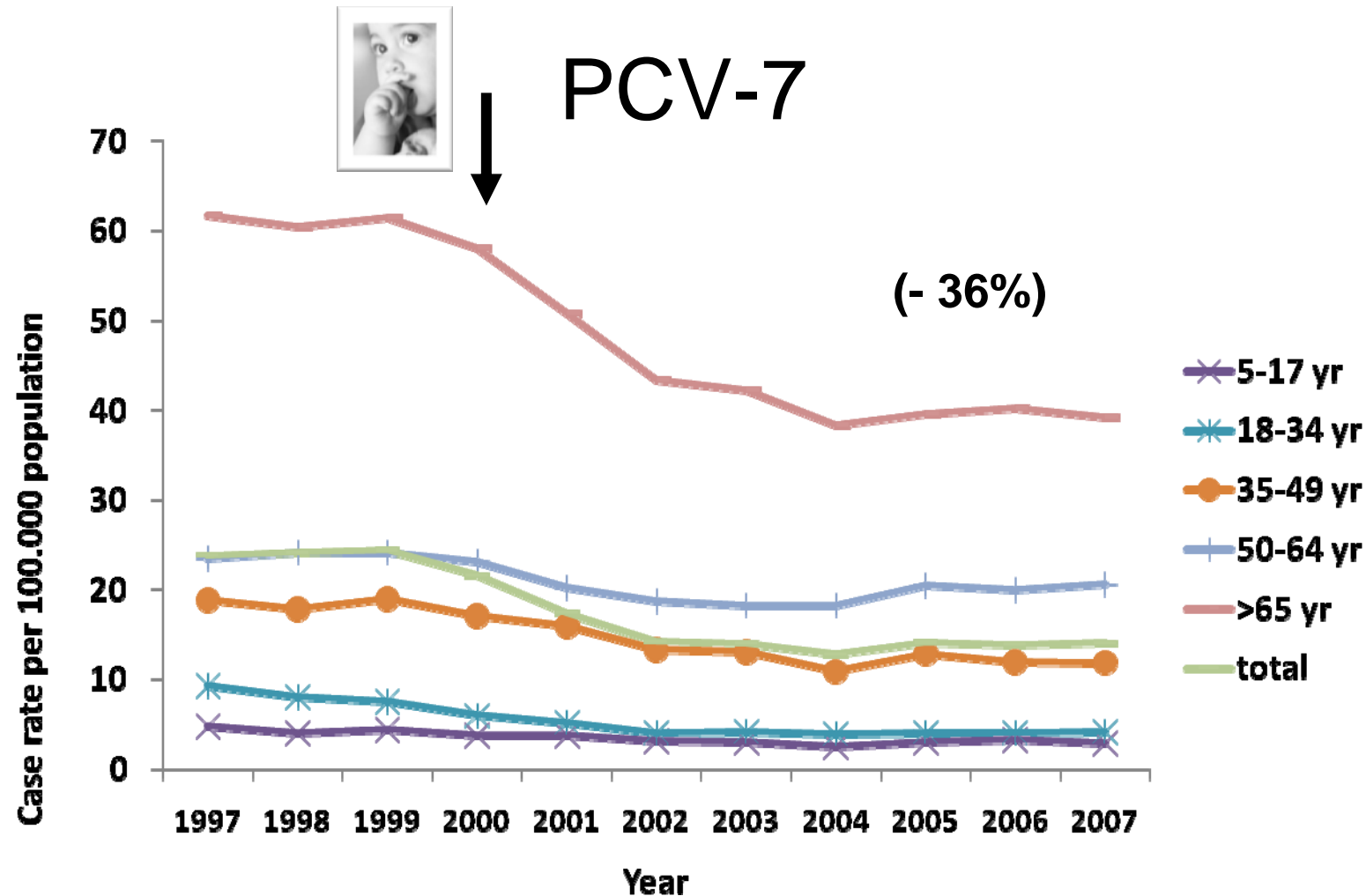
USA: Effect in target age group

IPD case rate < 5 yrs



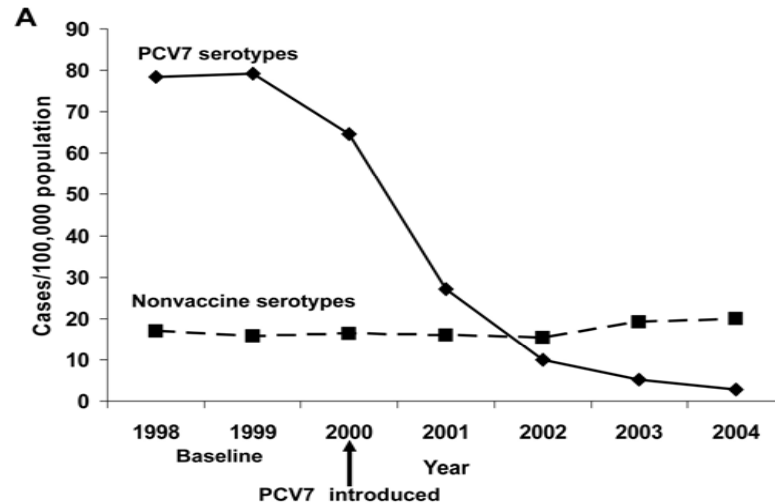
Source: CDC

USA: Herd effect in other age groups (IPD Case rate >5 yrs)

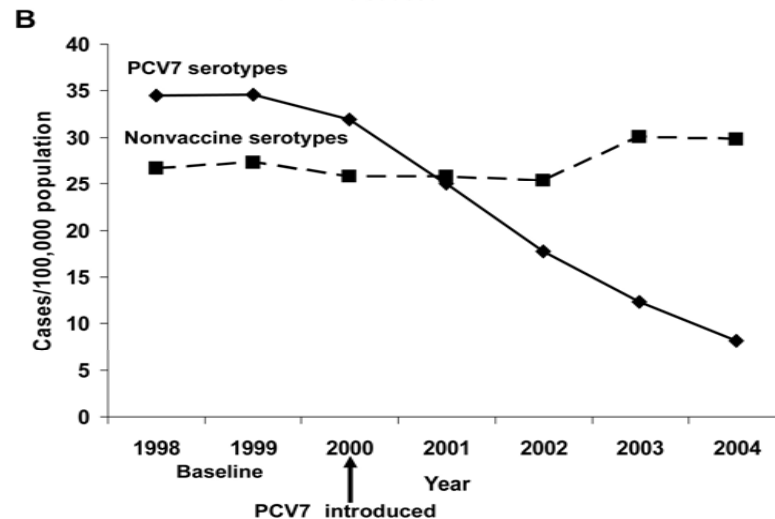


Source: CDC

USA: IPD replacement disease

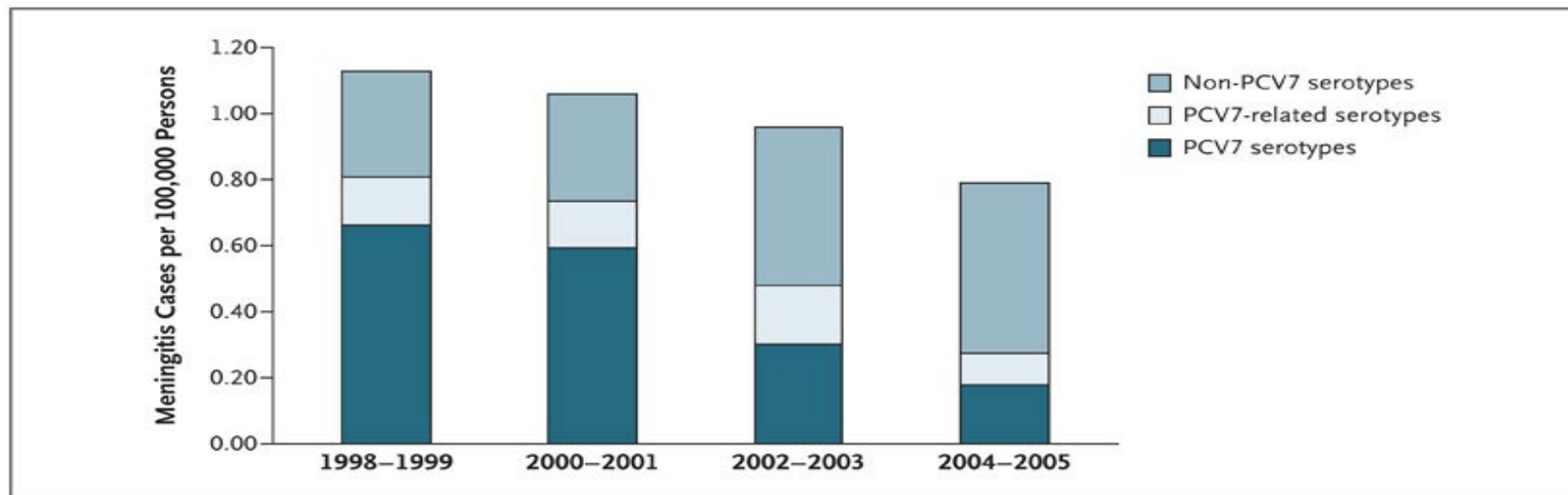


Age < 5 years
(RR 1.2, P<0.01)



Age > 65 years
(RR 1.1, P<0.05)

USA: direct and indirect effect of PCV7 on SP meningitis (all ages -30%)



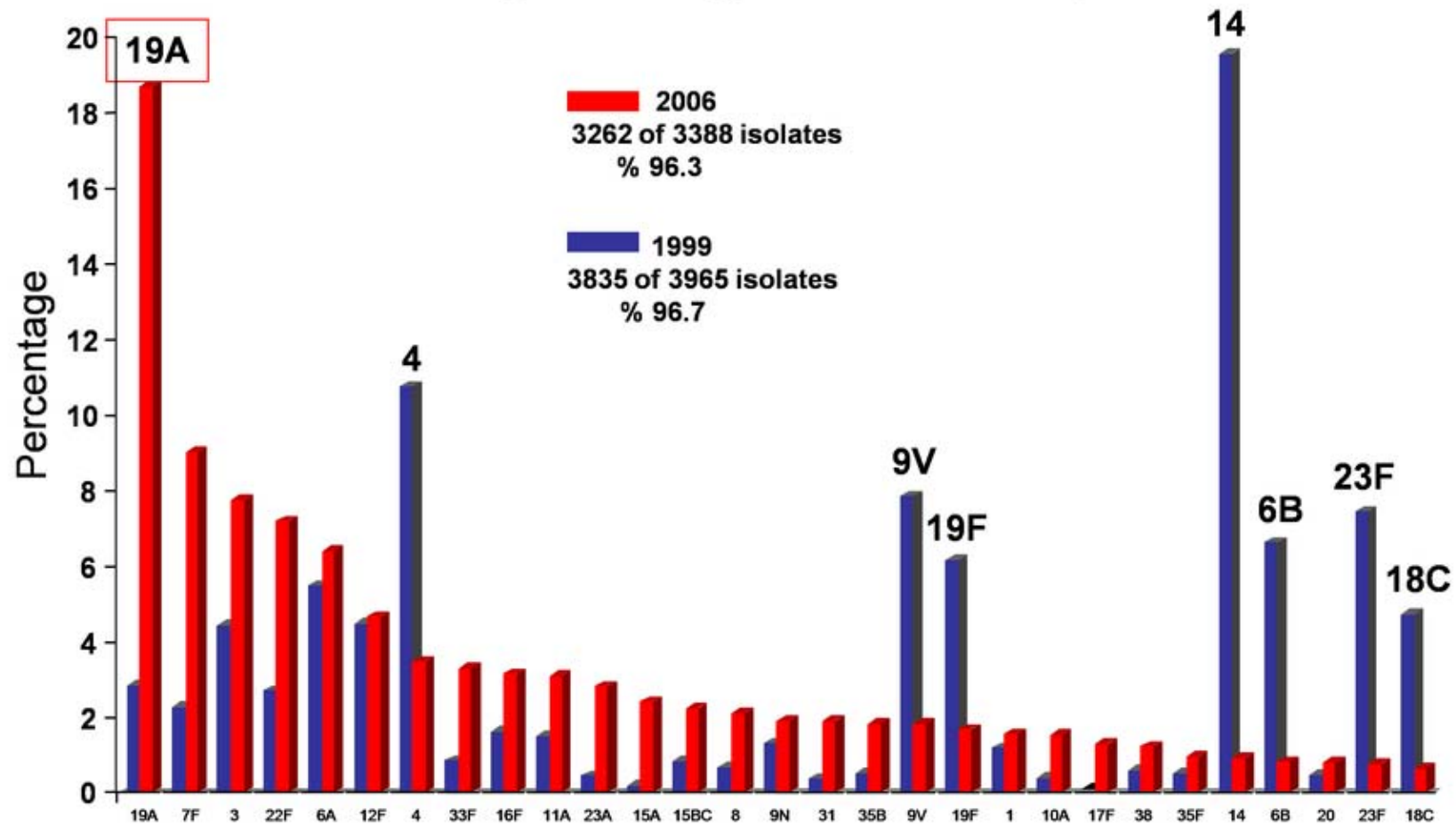
< 2 jaar (-64%):

VT disease reduction by 7.61 cases per 100.000

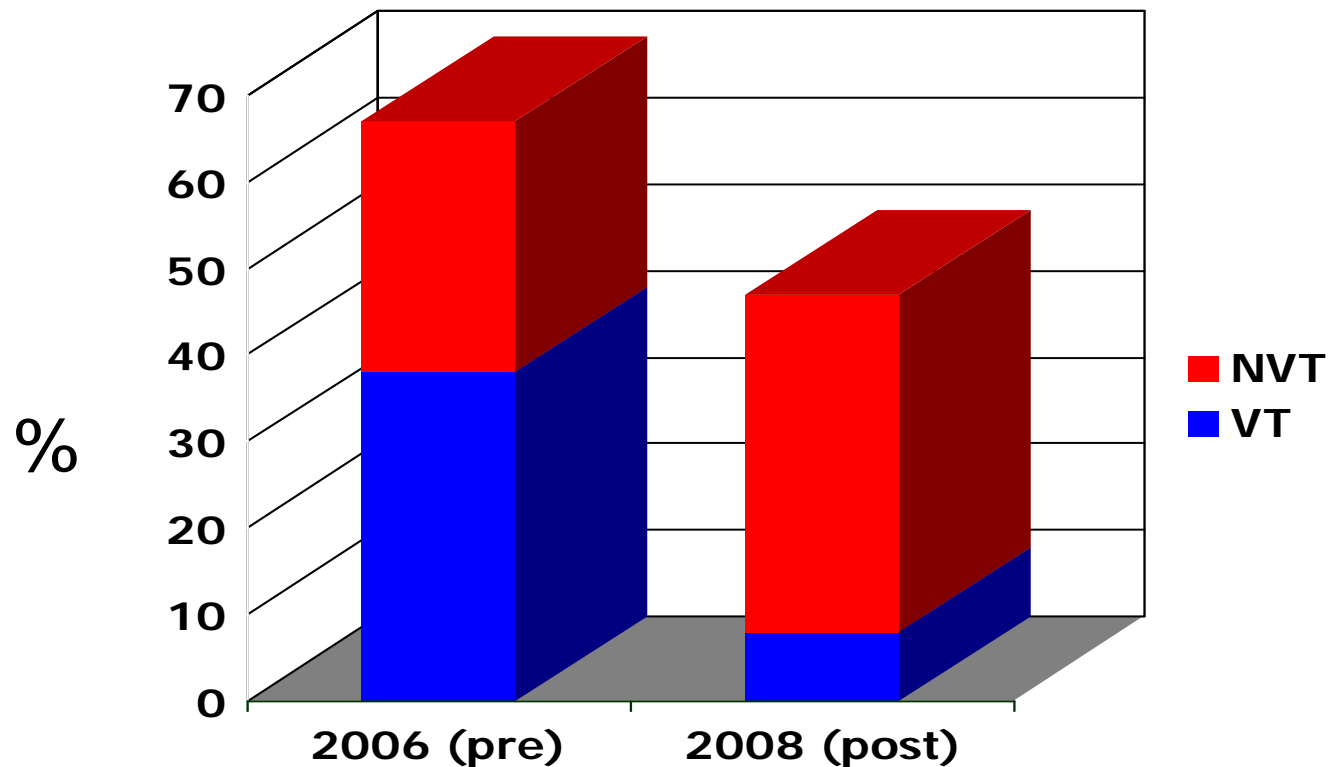
NVT disease increase of 2.10 cases per 100.000

Serotype distribution in US pre- and post-PCV7 (all ages)

Dramatic change in serotype distribution in post-PCV7 era

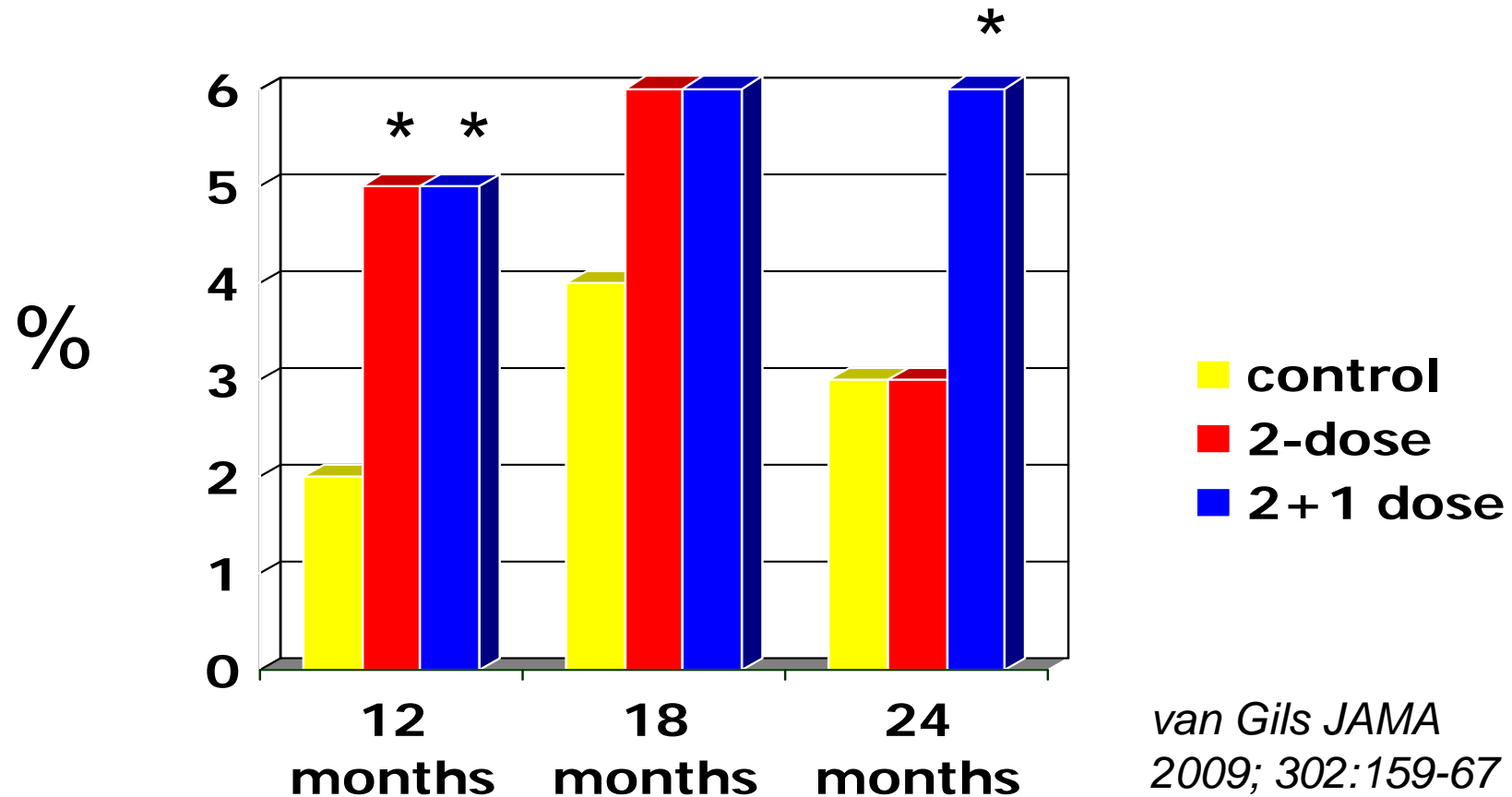


The Netherlands: Serotype distribution at the NP level prior to and after introduction of PCV-7 at the age of 11 months

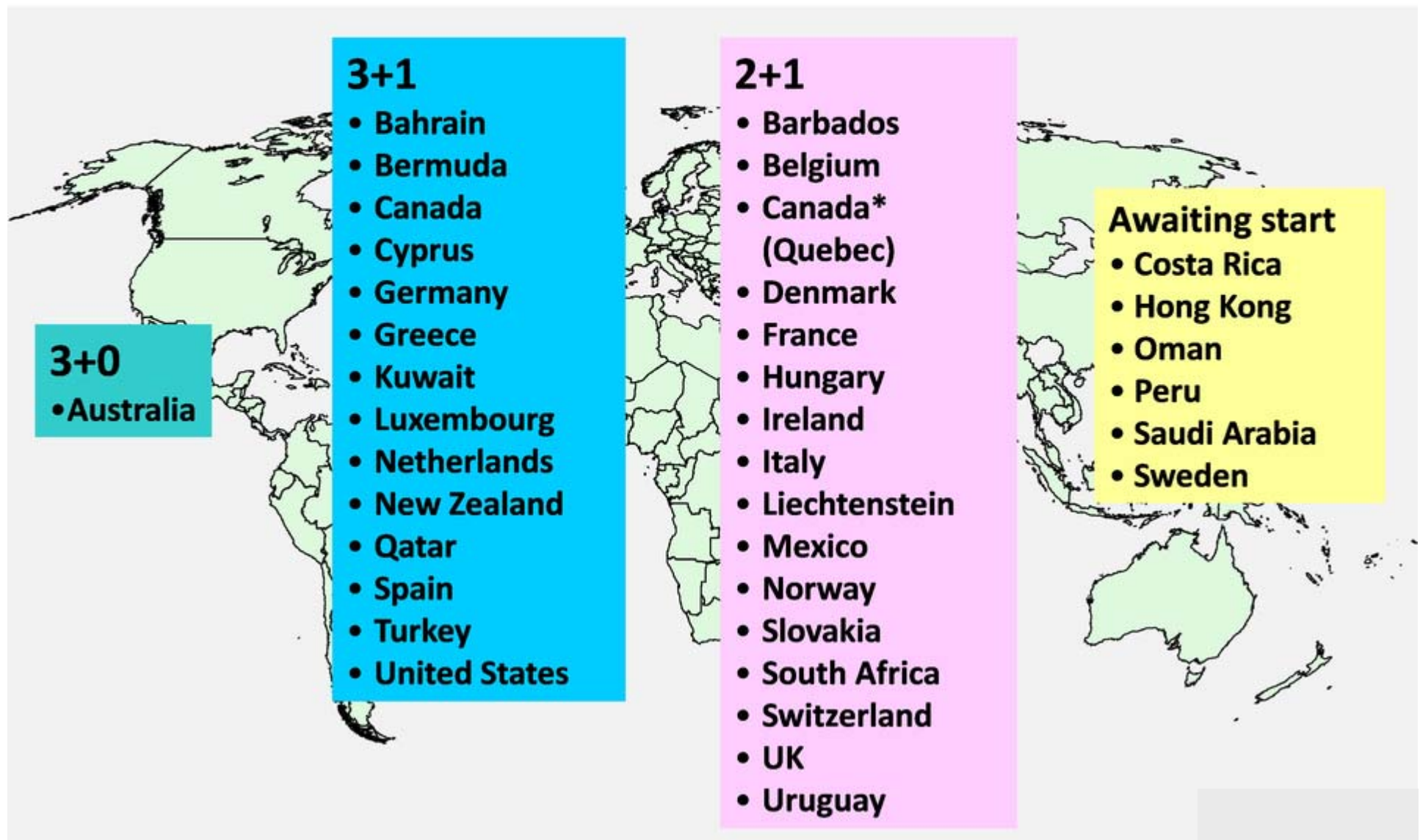


van Gils and Spijkerman

Dutch trial: Serotype 19A at the nasopharyngeal level after 2 and 2+1 dose PCV7



PCV7 worldwide: commercialized in 88 countries, of which 30 have a national infant vaccination program



Data other countries as compared to USA

Differences in:

- **IPD Coverage by vaccine**

Vaccine types: USA 80% and Europe 60-70%

- **IPD incidence < 2 years:**

*- USA 188/100.000 vs The Netherlands 34.5/100.000
(Different method of blood culture)*

- Rates for meningitis more similar

- **Vaccine uptake:**

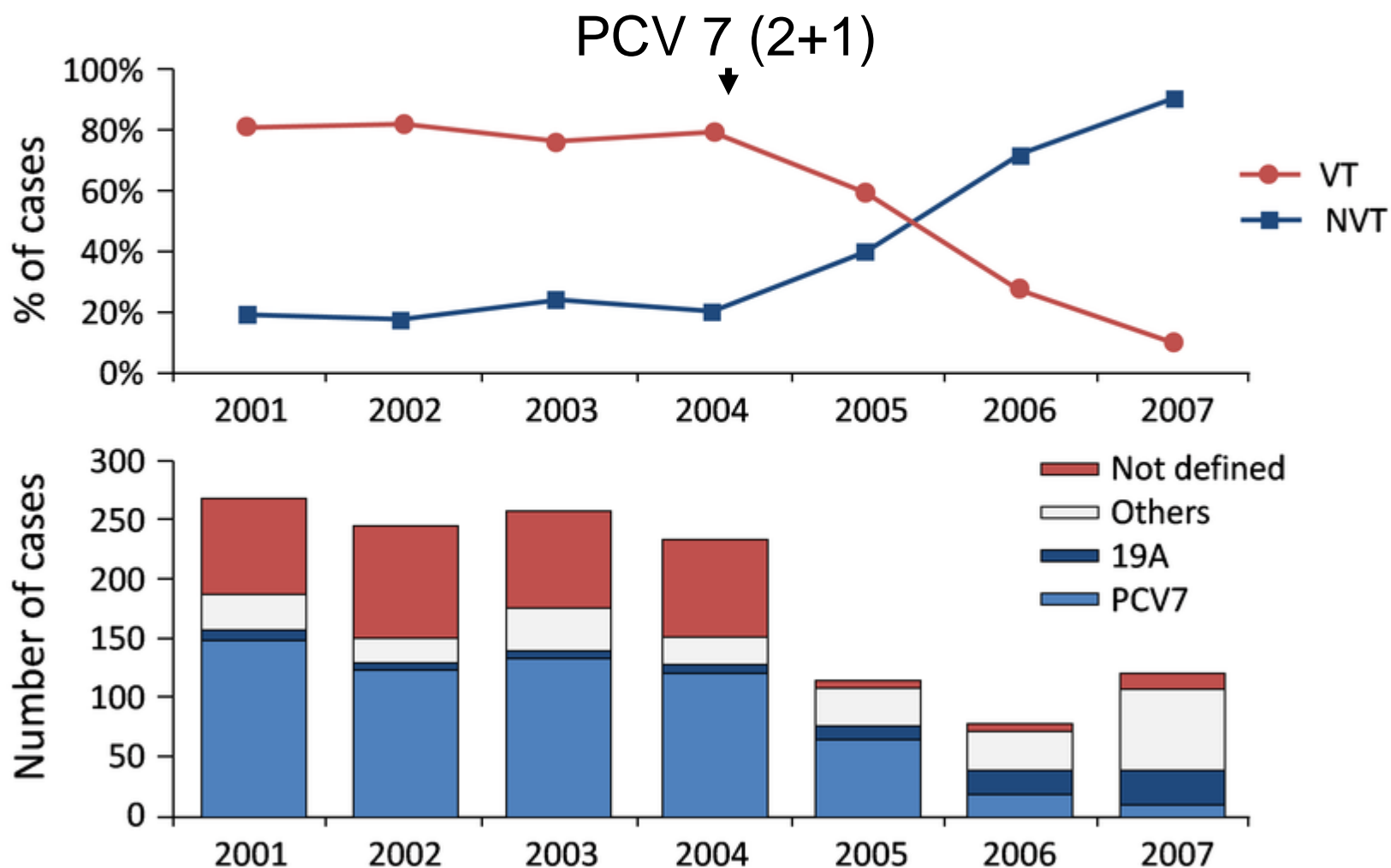
- USA 2001-03 shortage

- The Netherlands > 95% coverage directly after introduction in NIP



Cases of VT- and NVT-IPD

Quebec, 2001–2007; children 0–4 years

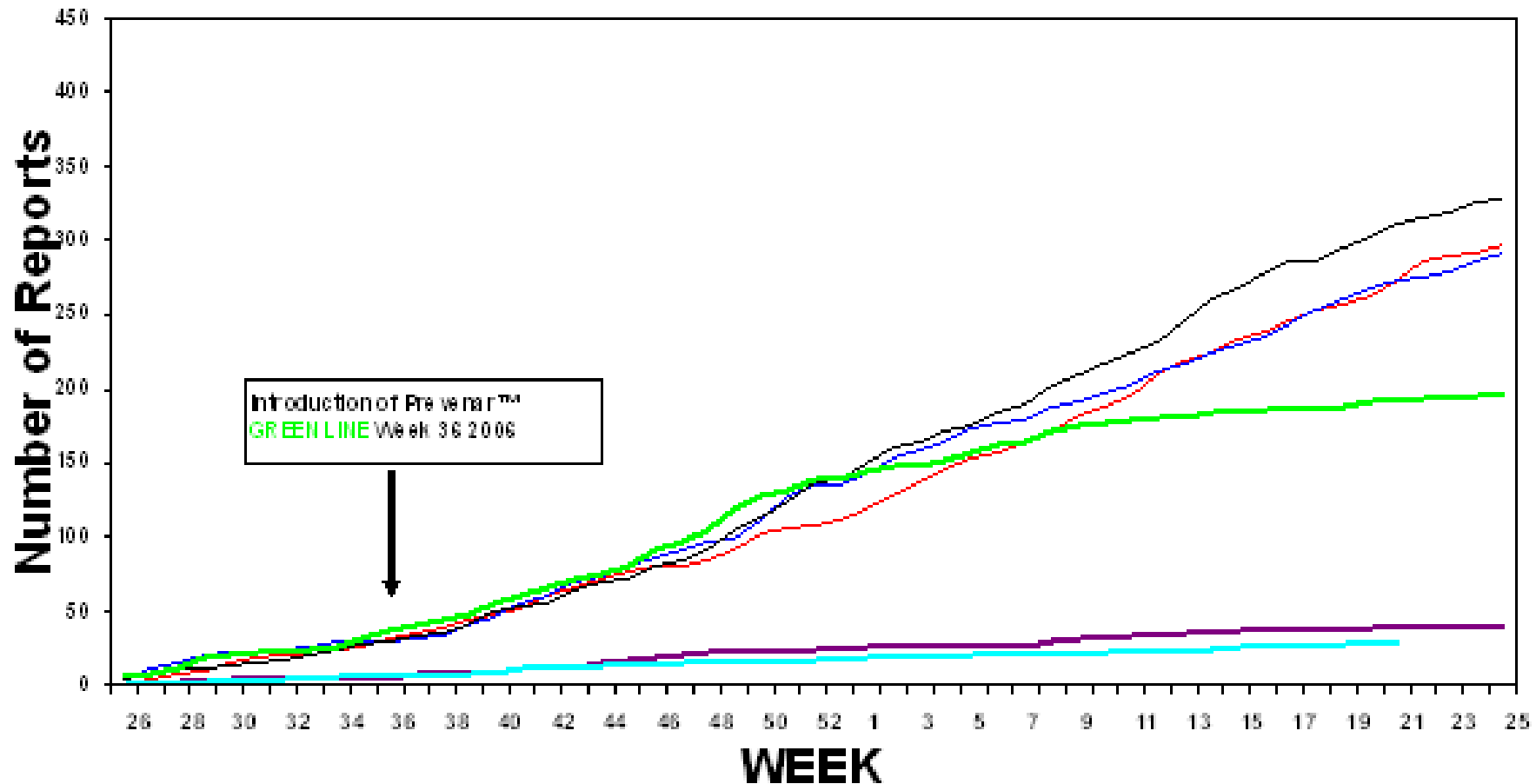




Cumulative number of VT-IPD cases in children <2 yrs

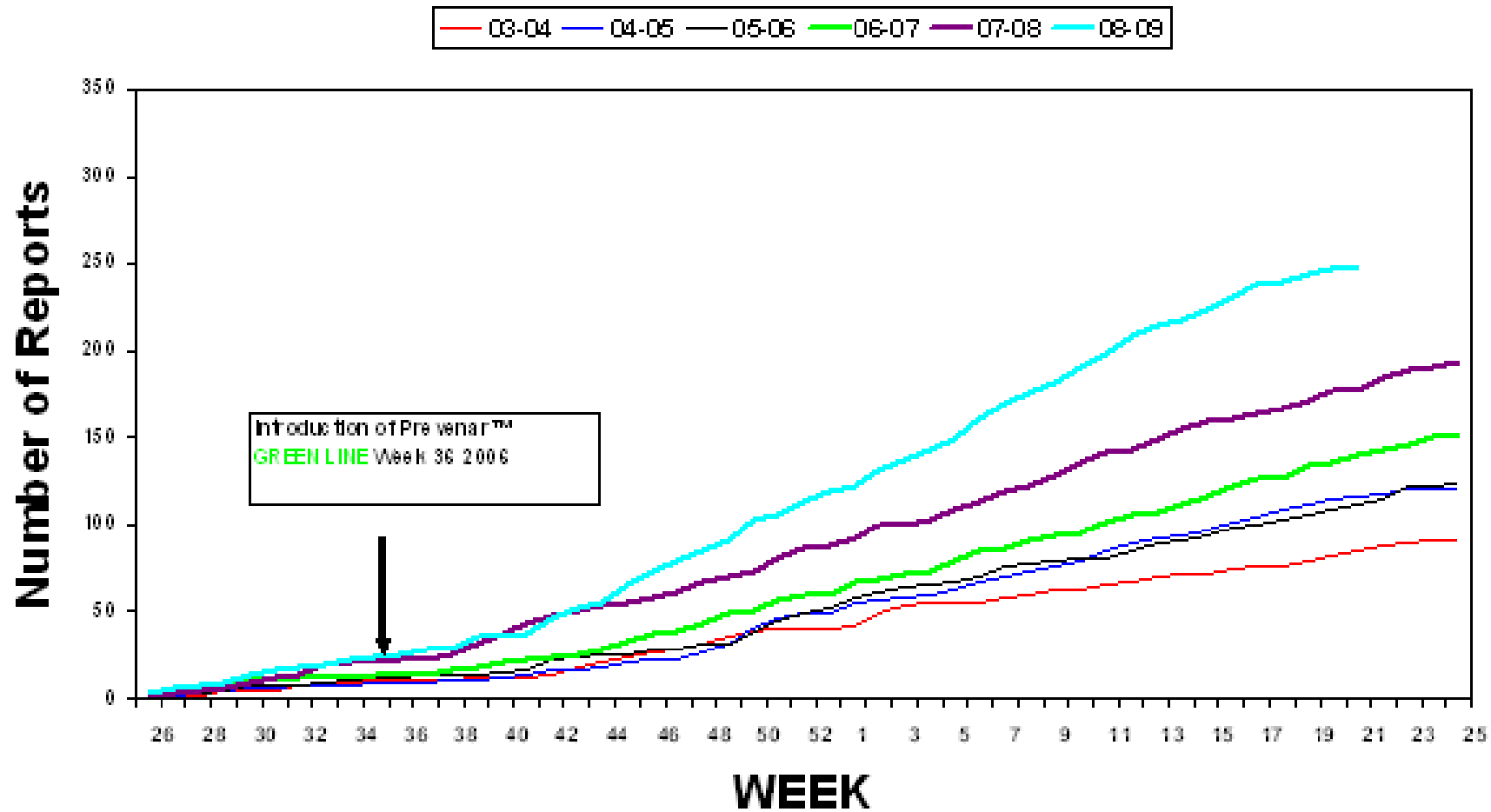
2006: 2+1 schedule (2, 4, 13 mo)

03-04 04-05 05-06 06-07 07-08 08-09





Cumulative number of NVT-IPD cases in children <2 yrs

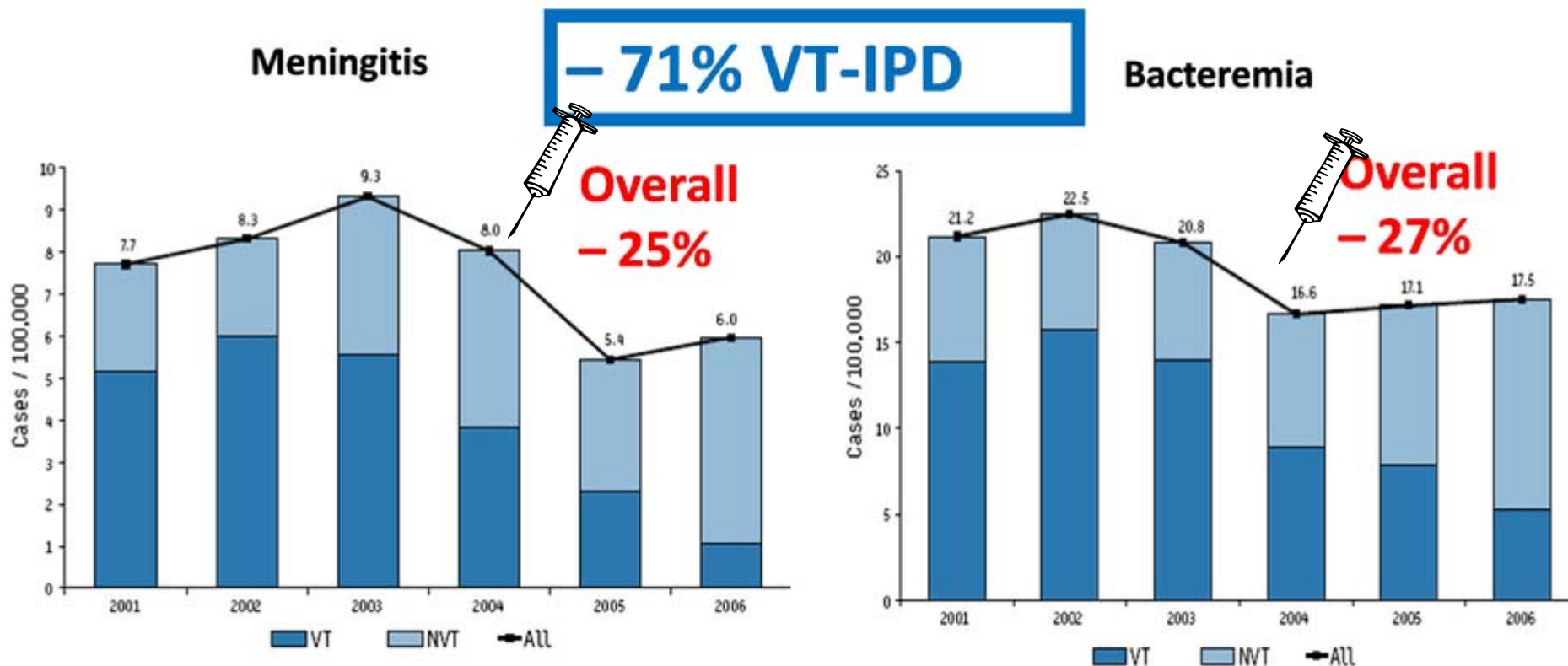


France

IPD incidence by serotype
(VT/NVT) ; children <2 years



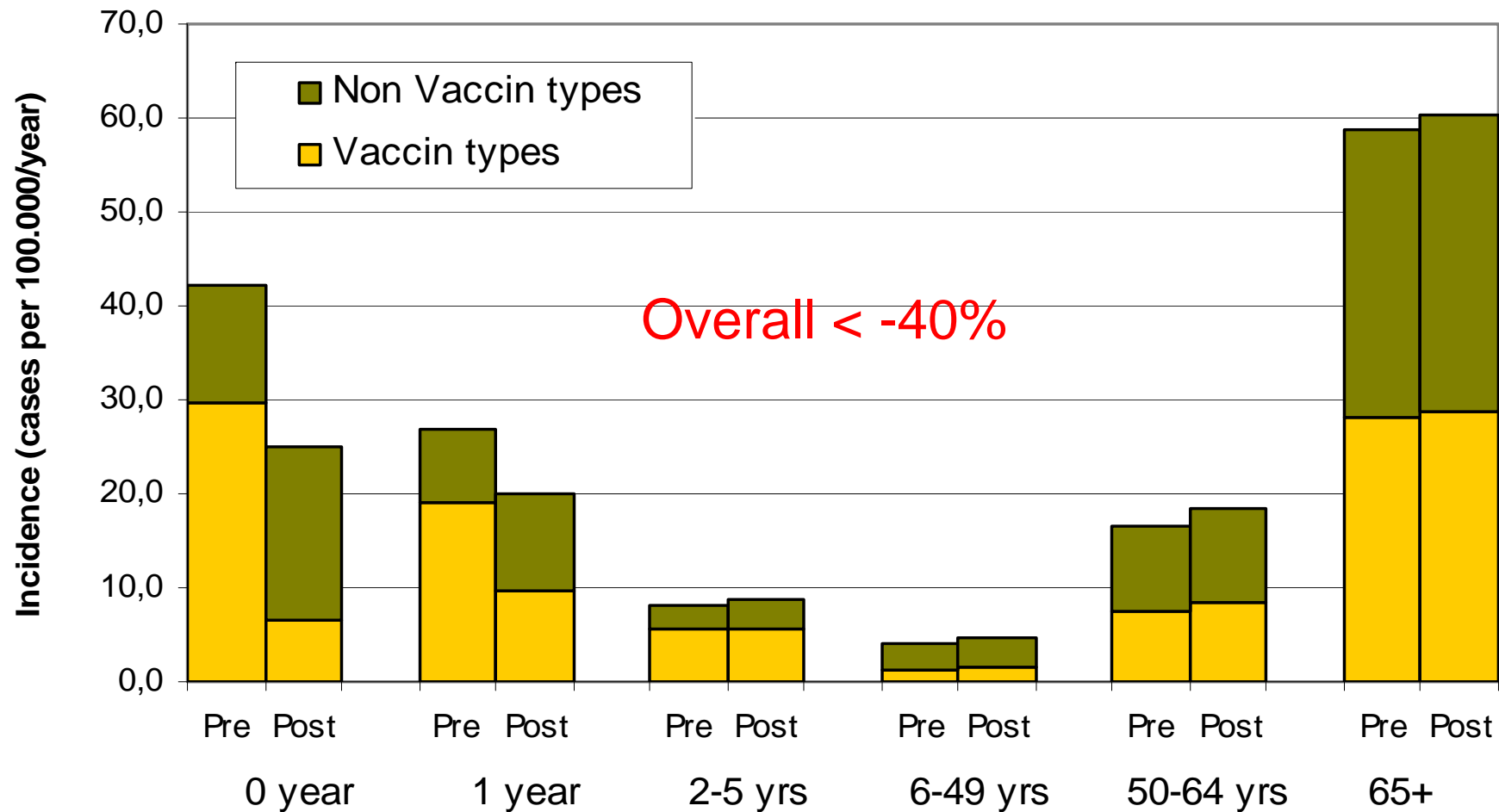
2001–2006; *Epibac net*



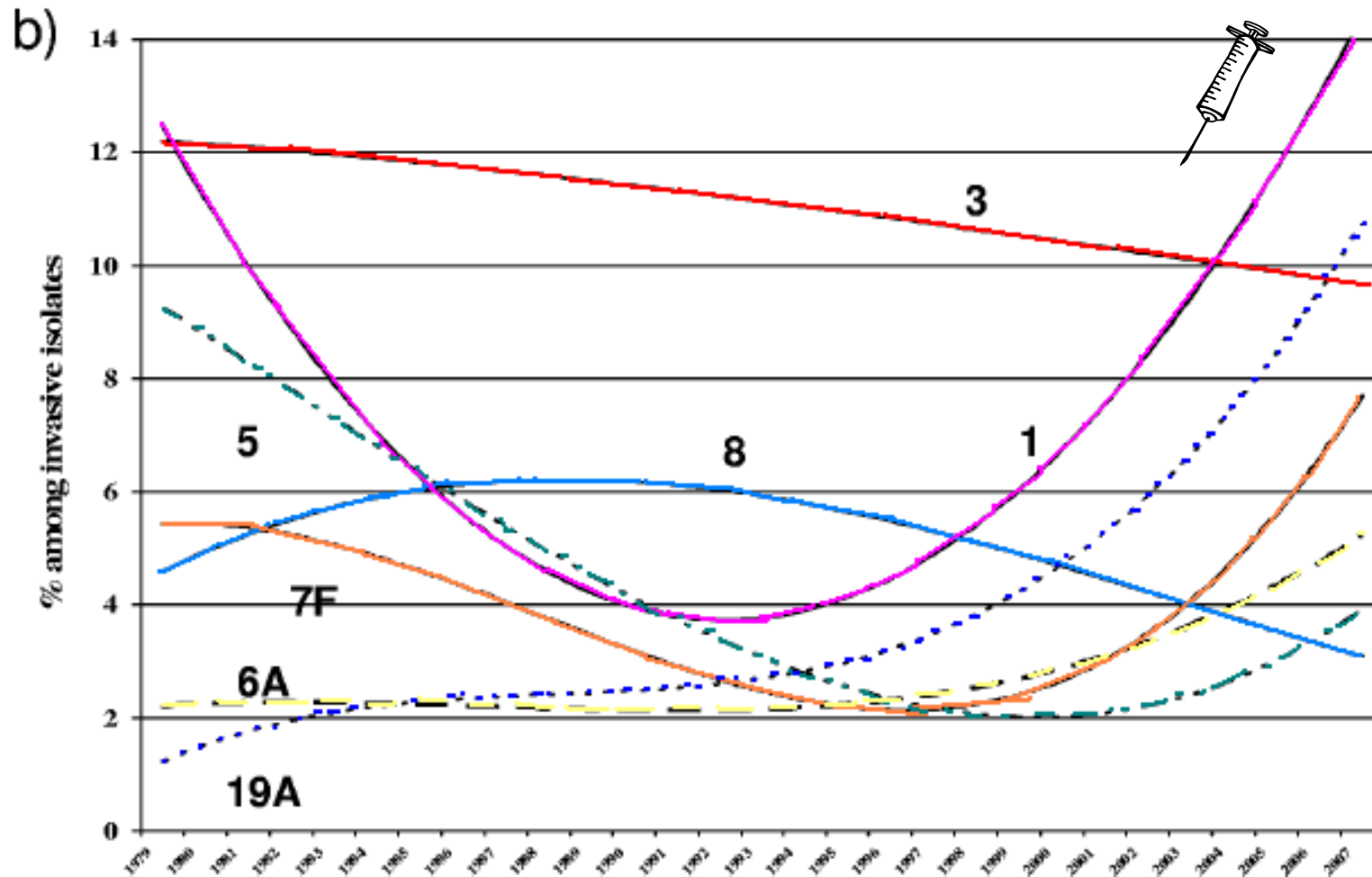
NO indirect effect observed so far



IPD in the Netherlands June 2004 - May 2008: PCV7 2006 in NIP (coverage > 95%)



Temporal trends in other serotypes (Spain, 1979-2007)



Post-marketing OMA in USA



- Replacement by NVT- SP 6A(6C?) and 19A
- Increase ntHi, Moraxella catarrhalis

Pichichero et al. PIDJ 2007; 26:S12-6

Mahjoud et al. Arch Pediatr 2008;15:1713-6

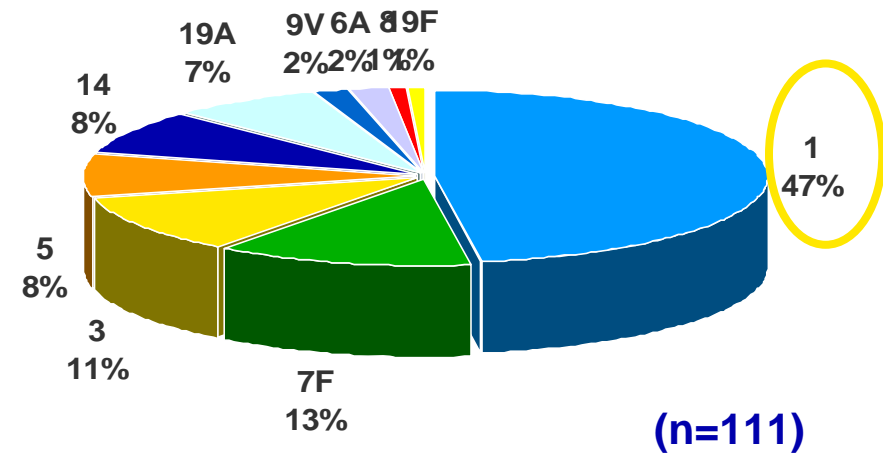
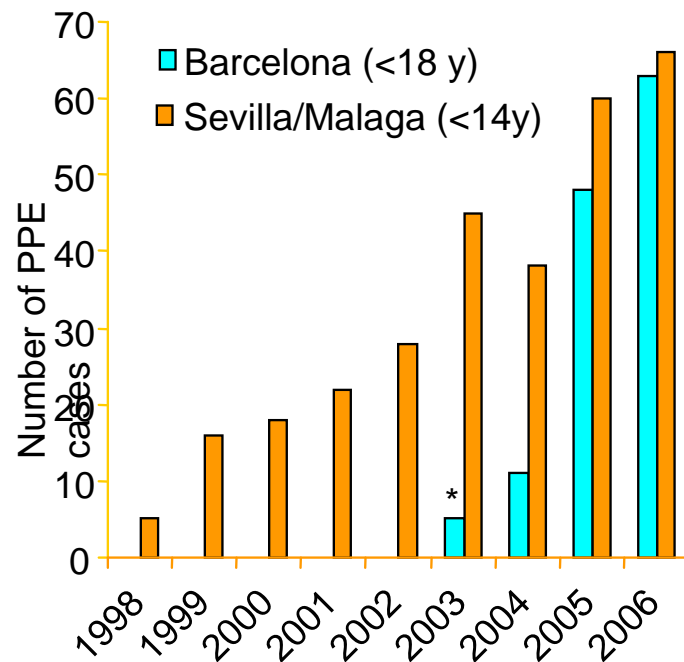
Mastoiditis:

- incidence in Texas increases (19A), course more complicated

Ongkasuwan et al. Pediatrics 2008;122:34-9

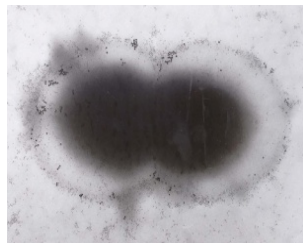
Importance of serotype specific incidence but also serotype specific disease and severity

Complicated pneumonias / parapneumonic empyemas in Spanish children are especially associated with the serotype 1 (25-69%)

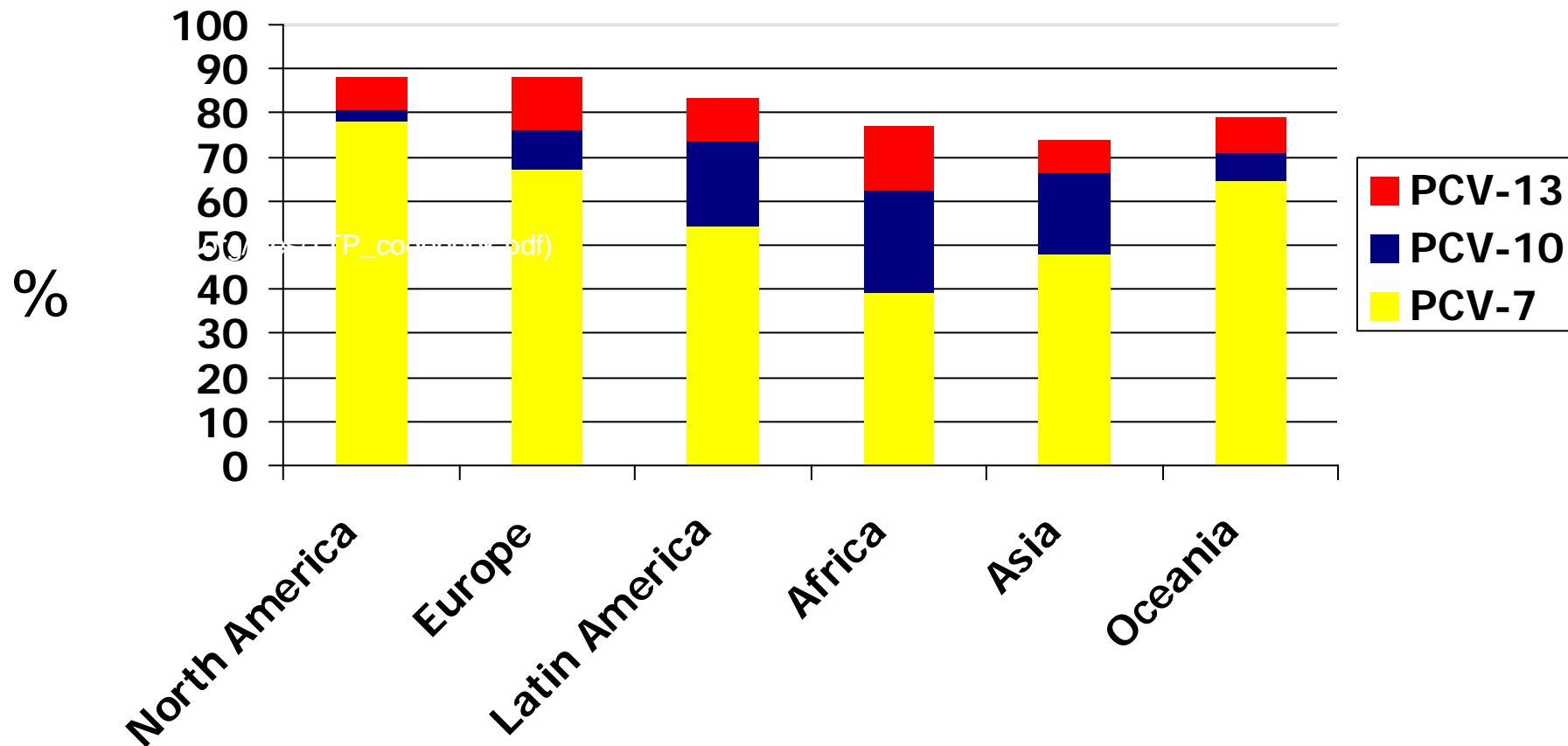


Serotype composition of pneumococcal conjugate vaccines

7-valent	10-valent	13-valent
4	4	4
6B	6B	6B
9V	9V	9V
14	14	14
18C	18C	18C
19F	19F	19F
23F	23F	23F
	1	1
	5	5
	7F	7F
		3
		6A
		19A



Theoretical serotype coverage PCV-7,-10,-13





Tsjech study with PCV11 (Protein D carrier) *Prymula et al, Lancet 2006*

RCT, n=5000, vaccination at 3,4,5, 12-15 months
Follow-up AOM episodes up to 24 months

Reduction of AOM

- | | |
|---|-------------|
| - VT-SP | 34%! |
| - <i>Non-typable haemophilus influenzae</i> | 53% |
| - <i>No replacement</i> | 35% ! |

Conclusions (1)

- **PCV-7 schedules provide adequate protection against invasive and mucosal (IPD>Pneumonia>AOM) pneumococcal disease**
- **Results IPD Europe < USA because of differences in vaccine coverage and a more substantial increase of IPD due to NVT serotypes**
- **Need for new conjugate vaccines that contain additional serotypes (PCV10/13)**

Conclusions (2)

- **The coupling of polysaccharides to proteins of other bacteria can further increase the effect of these vaccines.**
- **In the meantime surveillance of pneumococcal disease and nasopharyngeal carriage remains extremely important**

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**Thanks for
your attention**

"Are you PCV7-boostered?"