

Serotype Replacement Following Pneumococcal Conjugate Vaccine Introduction

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Serotype Replacement Following PCV Introduction



- What is serotype replacement?
- What has been the experience in different populations?
- What drives shifts in serotypes?

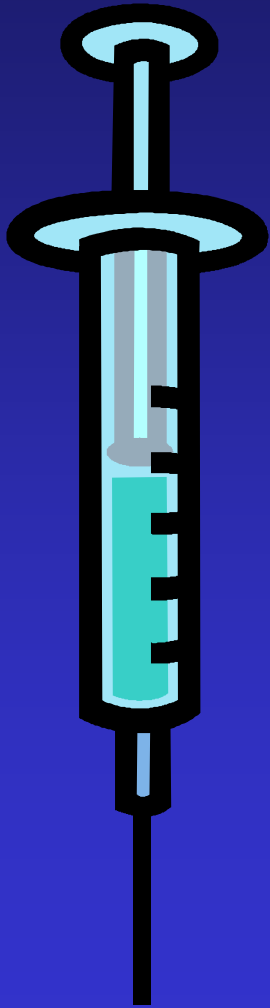
Replacement

(ri' pleys munt)

1. [n] a person or thing that takes or can take the place of another
2. [n] an event in which one thing is substituted for another

www.hyperdictionary.com

Pneumococcal Conjugate Vaccines



- Poly- or oligosaccharides of a small number of serotypes (7, 10, or 13 currently licensed)
- Conjugated to carrier proteins
- Provide serotype-specific protection (limited cross protection-- e.g., serotype 6B-6A)
- Does PCV use lead to changes in disease burden for rest of the 91 (or so) serotypes?

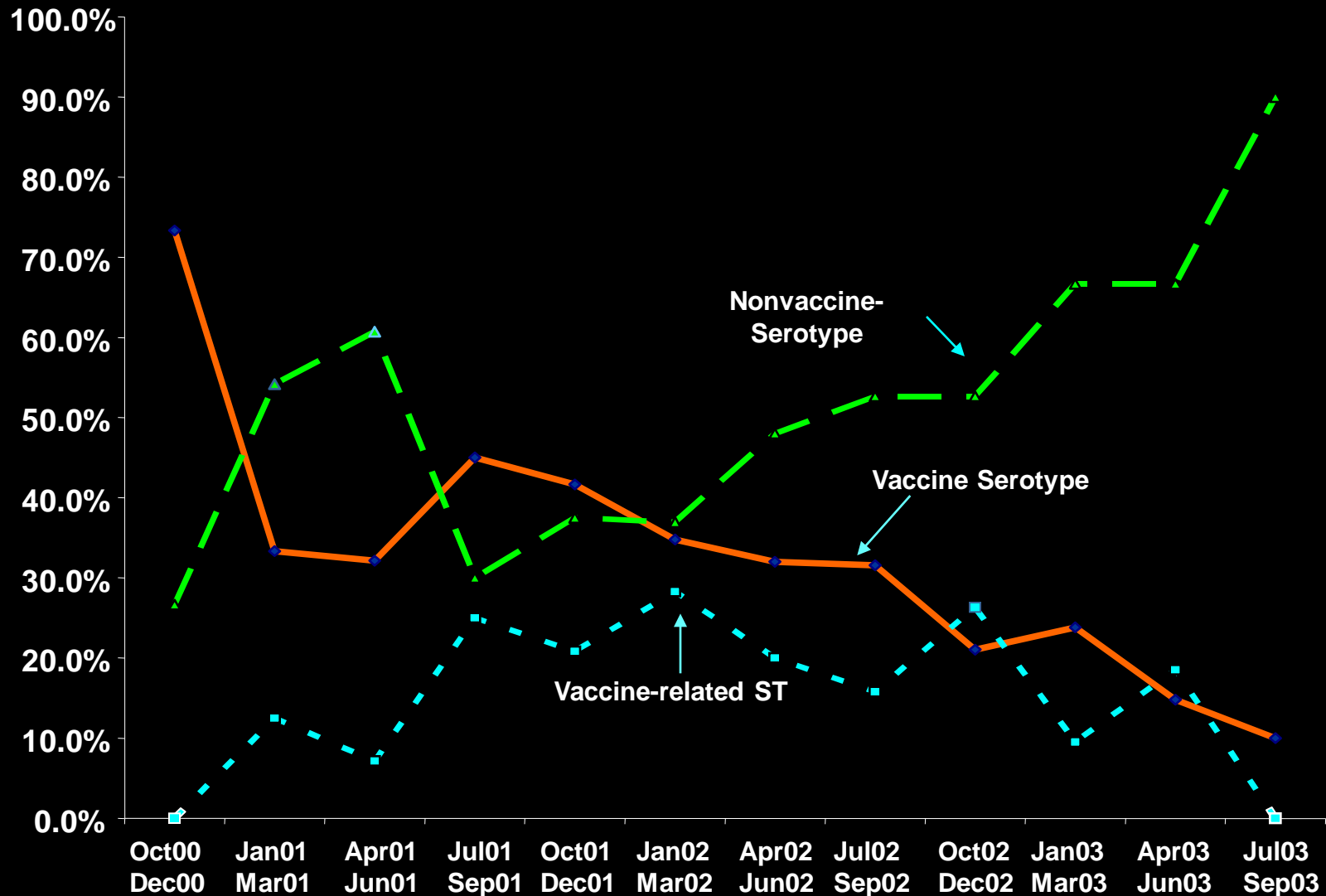
Factors Affecting Serotype Distribution

Factor	Timeframe		
	Months	Years	Decades
Vaccination	+	+	
Outbreaks/epidemics	+	+	
Surveillance methods	+	+	
Blood culturing practices	+	+	
Population immune status		+	
Antibiotic use		+	
Change in age distribution		+	+
Improved socioeconomic conditions		+	+
Strain evolution or capsular switch		+	+

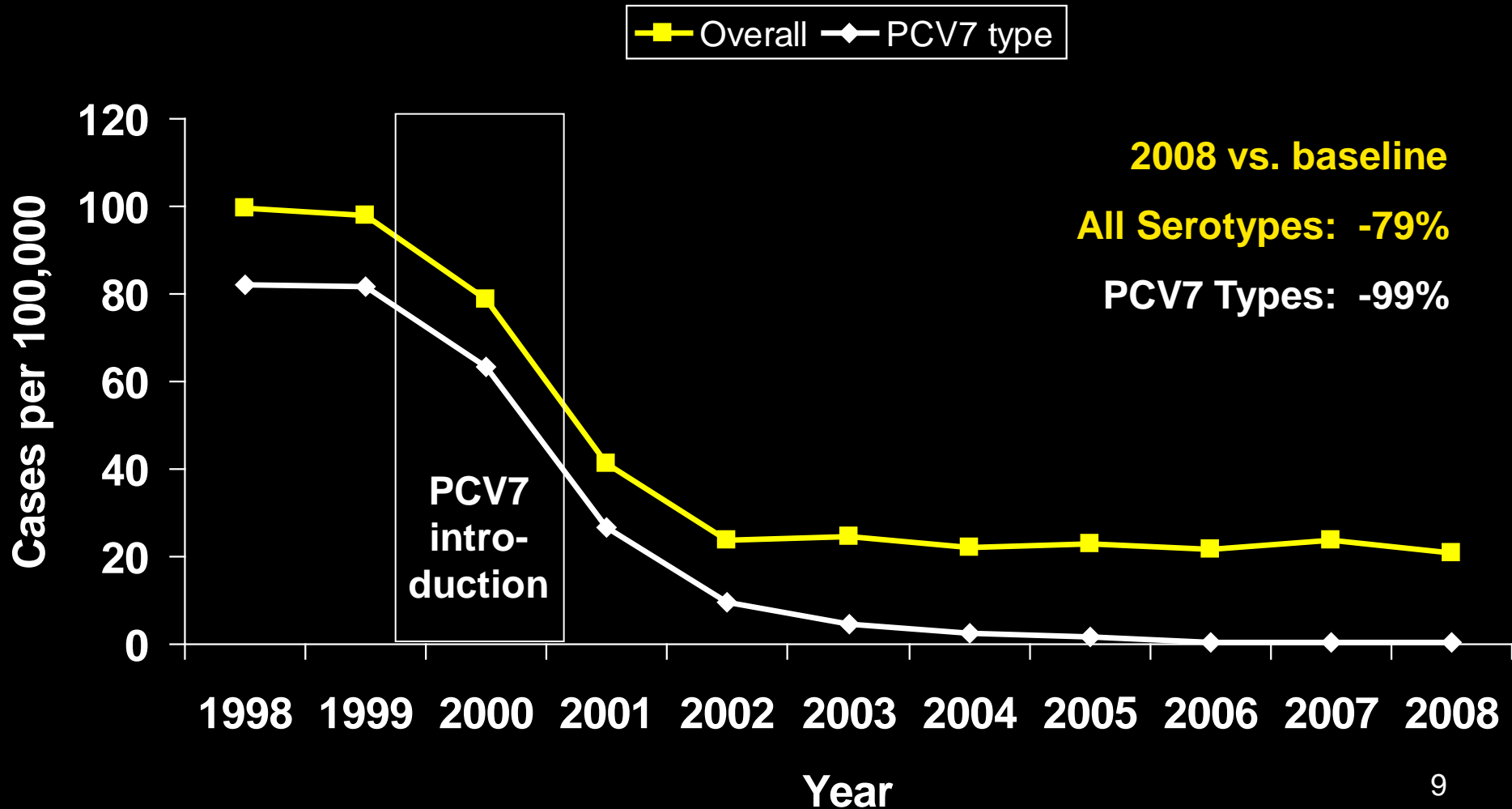
Pneumococcal Conjugate Vaccine Introduction in the U.S.

Feb 2000	7-valent vaccine (Prevnar™) licensed on 4-dose schedule
Mid-late 2000	Recommended for all children <2, high risk 2-4 years Government purchasing Rapid increase in use
Aug 2001- Sept 2004	Intermittent shortages
2006	87% coverage with 3+ doses among children 19-35 months

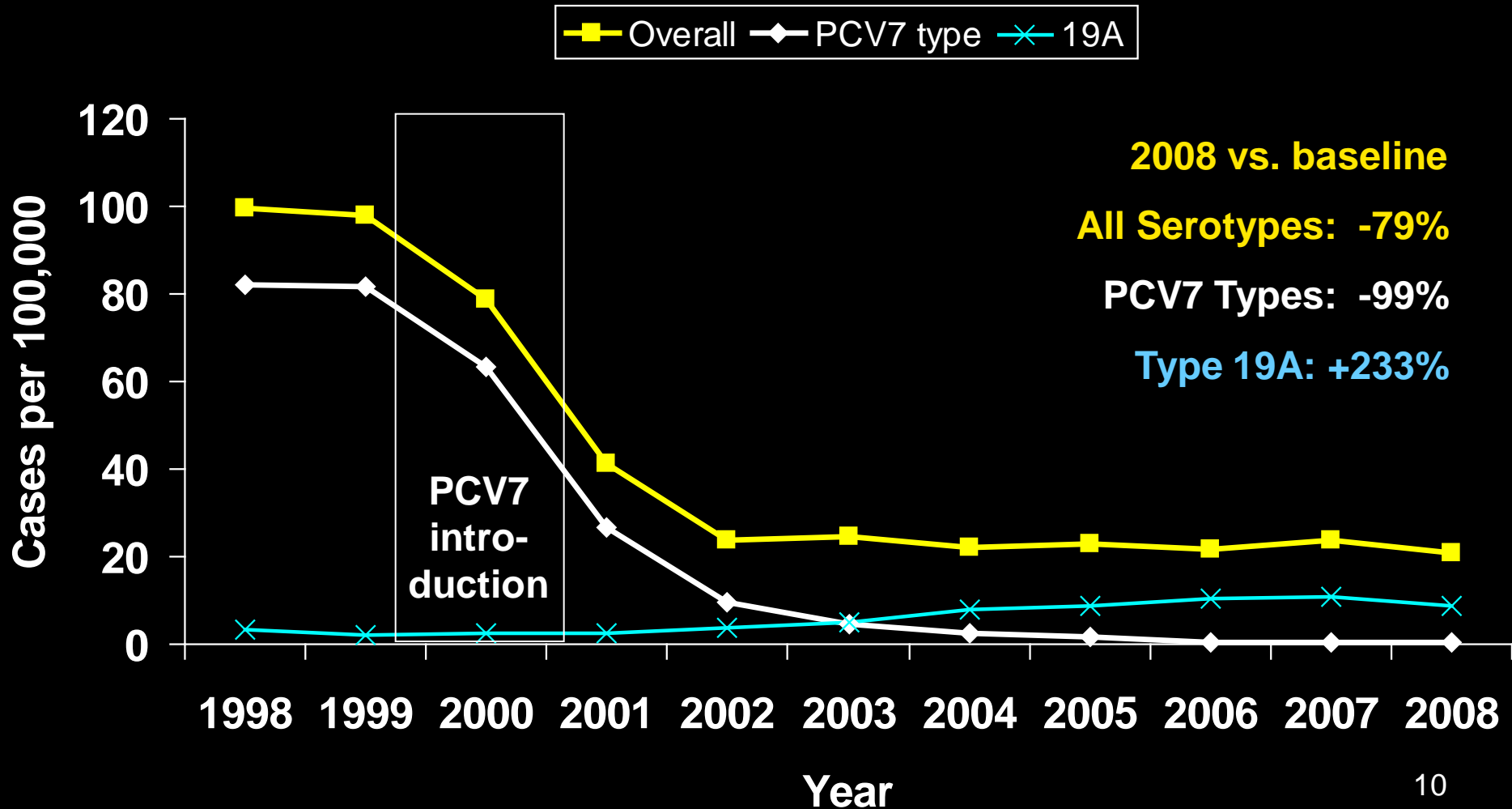
Pneumococcal carriage following introduction of PCV7 by serotype and quarter, 2000-2003



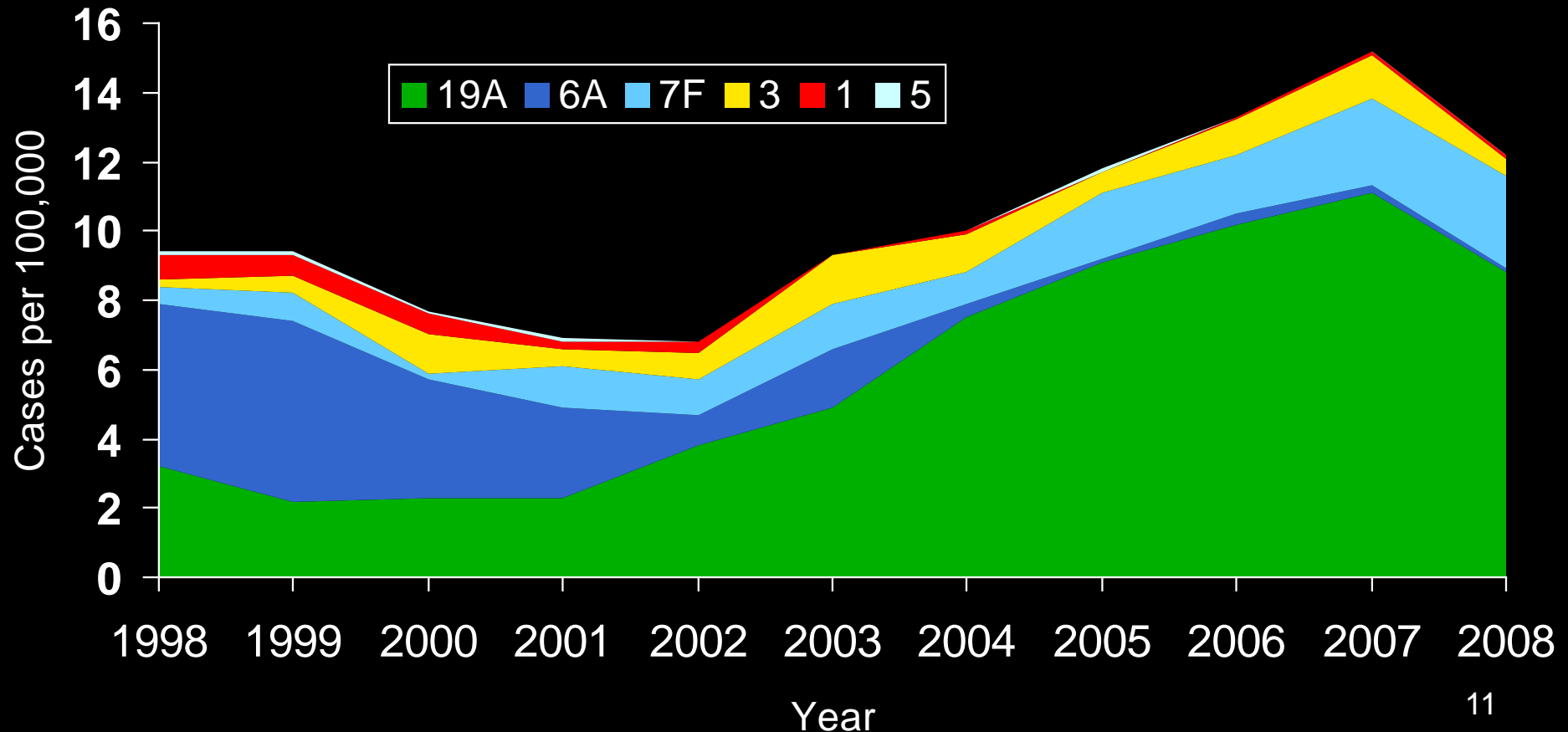
Rates of invasive pneumococcal disease among children <5 years, 1998-2008



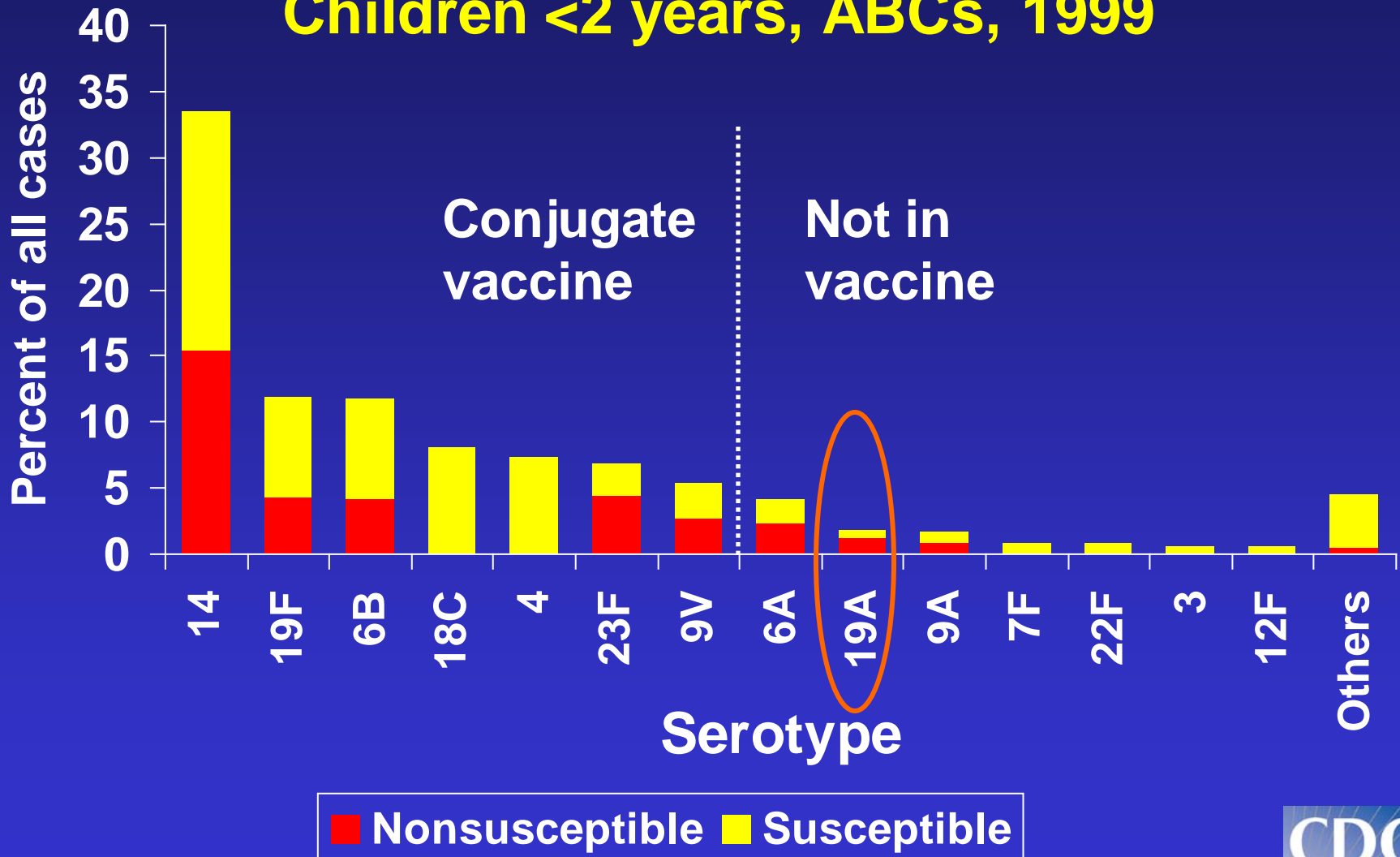
Rates of invasive pneumococcal disease among children <5 years, 1998-2008



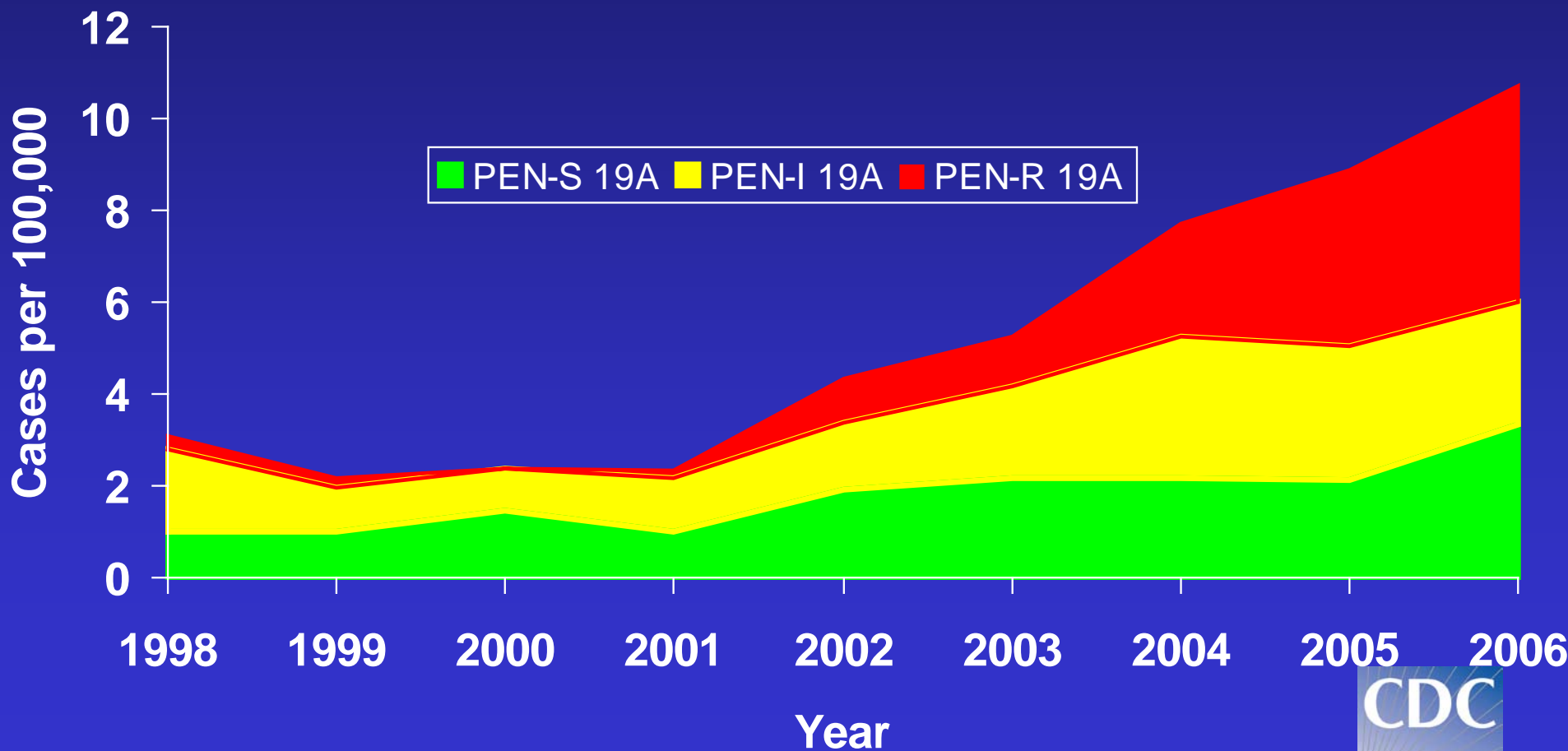
Rates of invasive pneumococcal disease caused by 6 serotypes unique to PCV13, children <5 years, ABCs, 1998-2008



Distribution of Pneumococcal Serotypes by Frequency and Penicillin Resistance Children <2 years, ABCs, 1999



Rates of serotype 19A IPD among children aged <5 years, by penicillin susceptibility, 1998-2006



Increasing incidence of 19A in settings without PCV7 use



South Korea

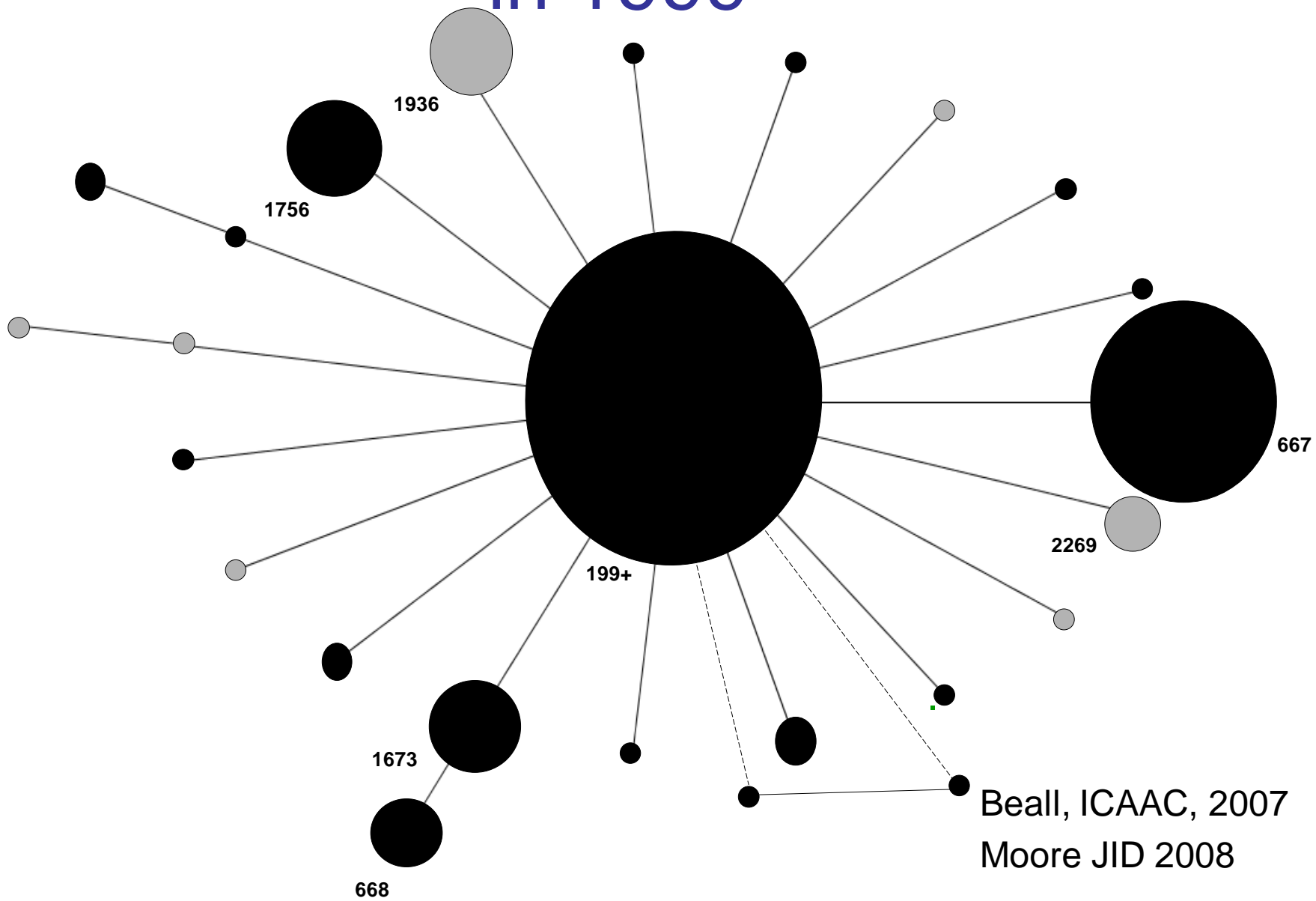
- 538 isolates 1991-2006 from children <5
- Proportion of 19A increased (0% 1991-4 to 20-26% 2000-6); 19F decreased
- PCV7 coverage <25%
- *Choi EH et al Emerg Infect Dis 2008;14:275-281*



Israel

- 4,449 otitis media isolates 1999-2006 from children <5
- 63% increase in 19A among Bedouin children (8-10% 1999/2001 to 13-15% 2002-6)
- Linked to 2 multidrug resistant clones
- No PCV7 use
- *Dagan R et al ICAAC 2007 Abstract G-1001*

Clonal structure of serotype 19A based on MLST of 528 strains in 2005



**Cause of
invasive disease**

(Robinson et al, JAMA
2001)

**Common in
carriage**

(Brueggemann et al, JID
2003)

**Associated with
antibiotic
resistance**

(Pai et al, JID 2005)

**Why has serotype
19A increased?**

**New clones
emerging in the
absence of
vaccination**

(Dagan et al. ICAAC 2007)

**Evidence of
capsular
switching**

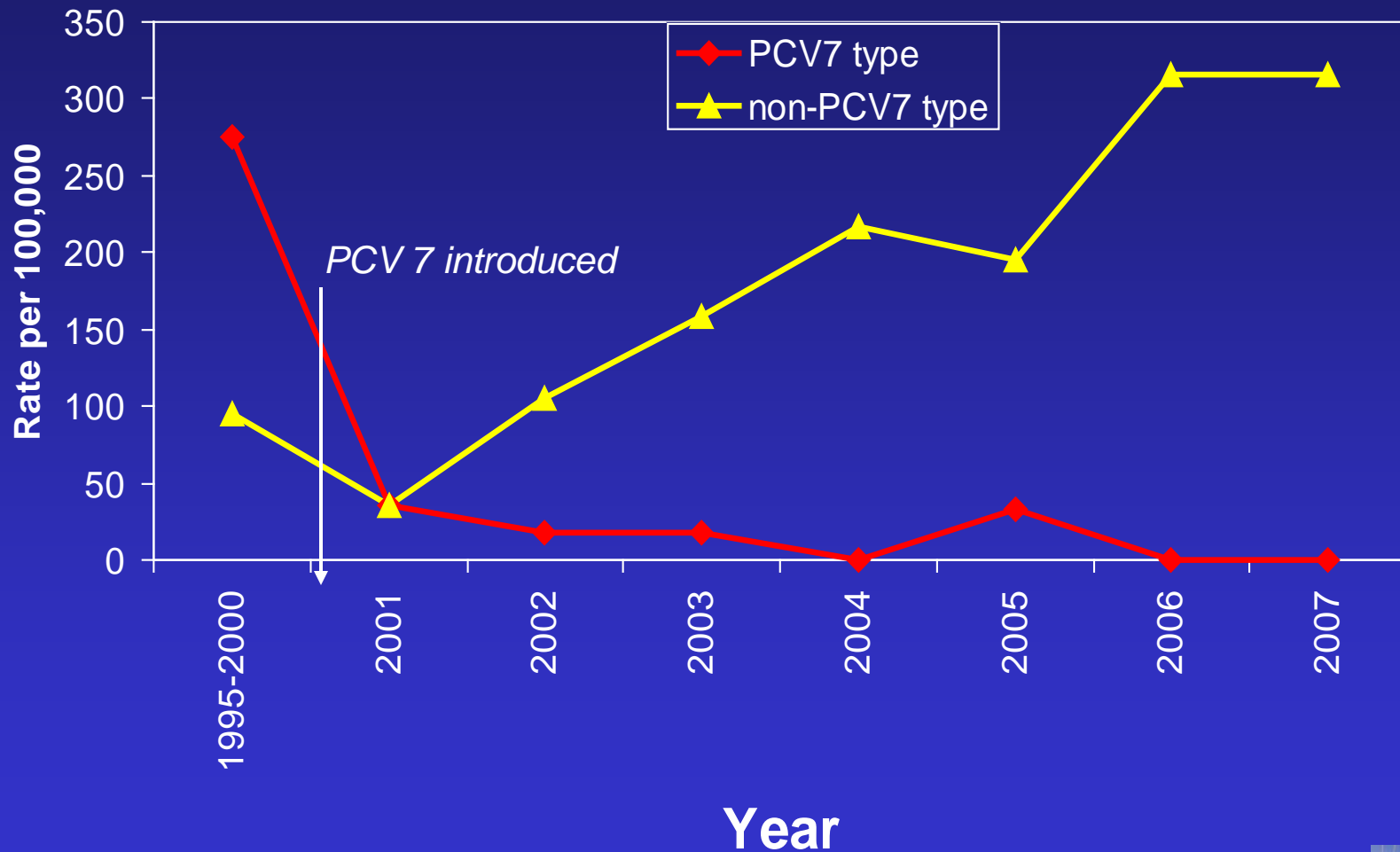
(Brueggemann et al,
PLoS Pathogen In press)

**PCV7 not
effective
against type
19A IPD**

(Whitney et al. Lancet
2006)

**Key point: Multiple factors are contributing to observed
increases in serotype 19A disease**

Invasive Pneumococcal Disease Rates Alaska Native Children < 2 yrs old

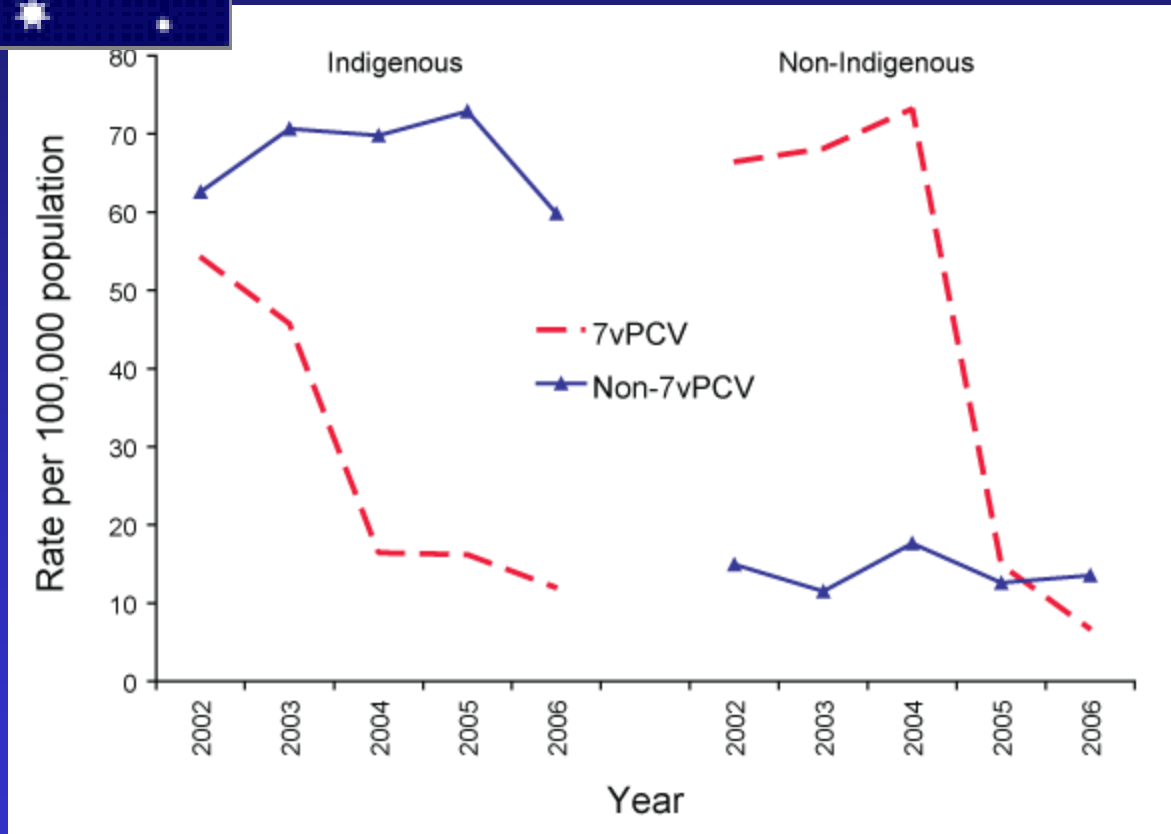
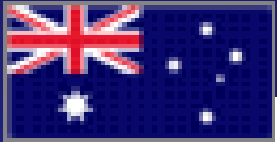


Slide Courtesy of AIP





Invasive pneumococcal disease in children <2 years by serotype and indigenous status Australia, 2002 to 2006



- Indigenous 2001 3+PPV
- All kids 2005 3+0
- Catch up both groups <2 yrs

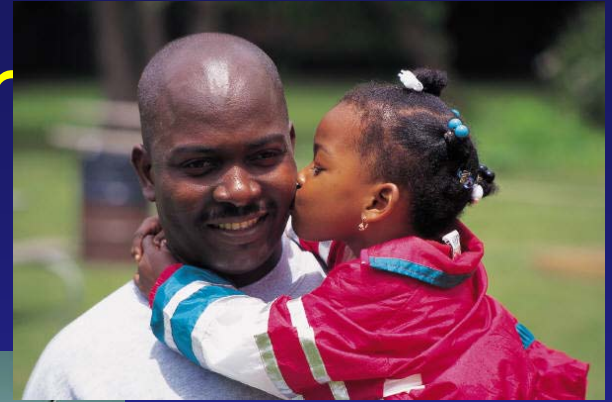
Roche PW CDI Vol 32:1;March 2008

<http://www.health.gov.au/internet/main/publishing.nsf/content/cda-pubs-cdi-cdicur.htm>

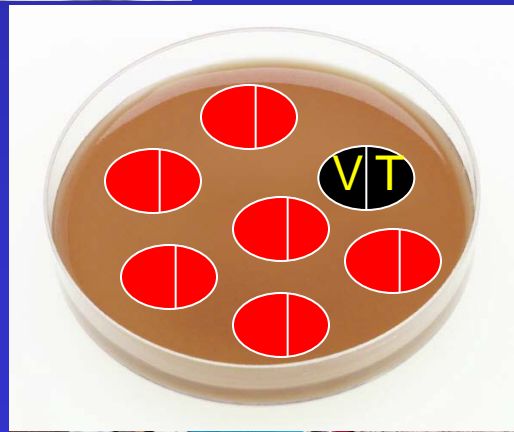
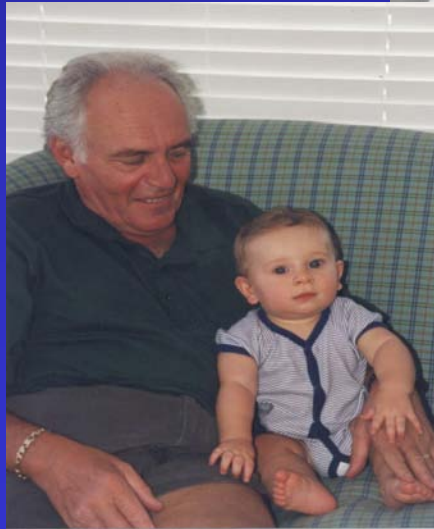


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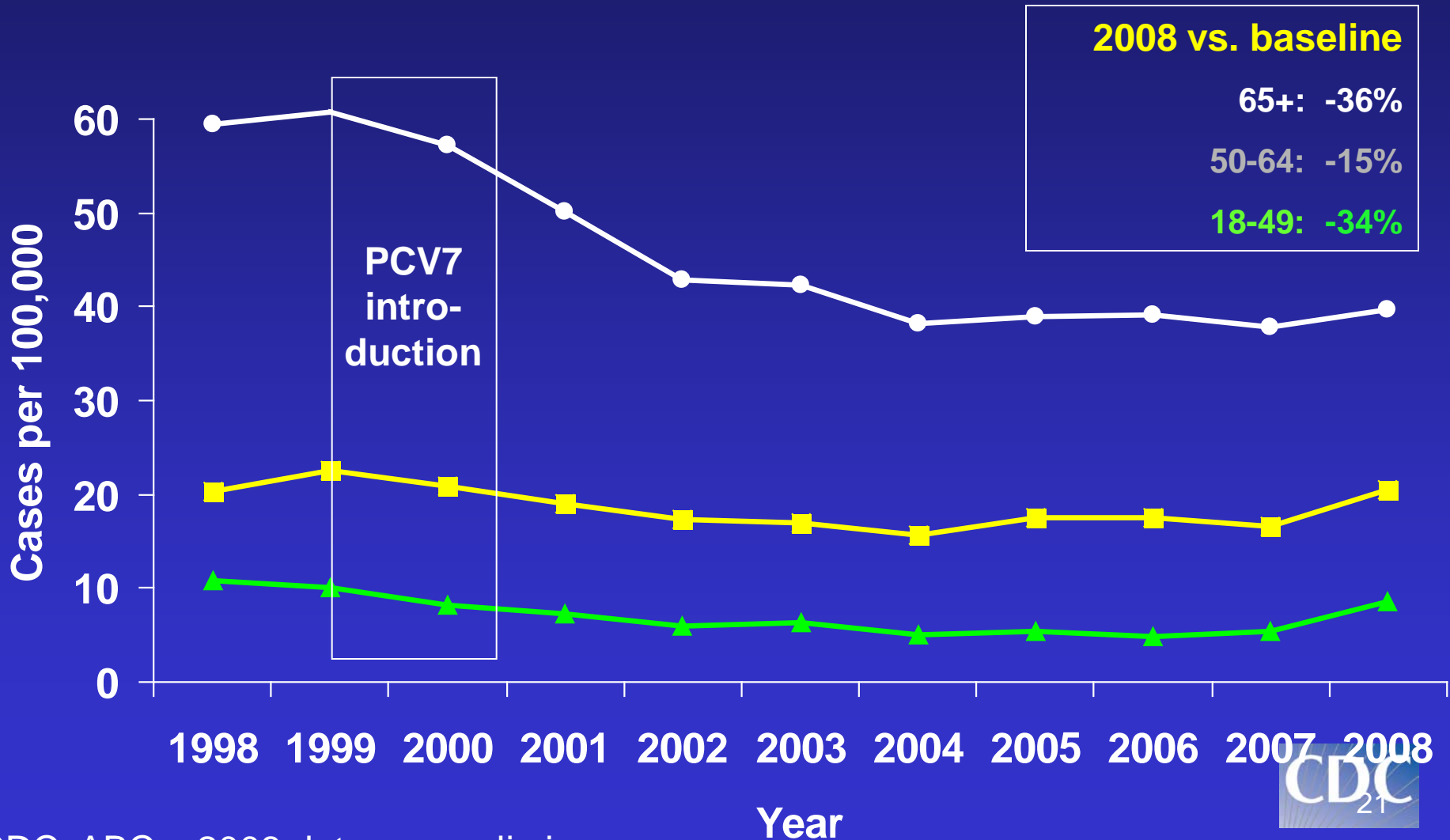
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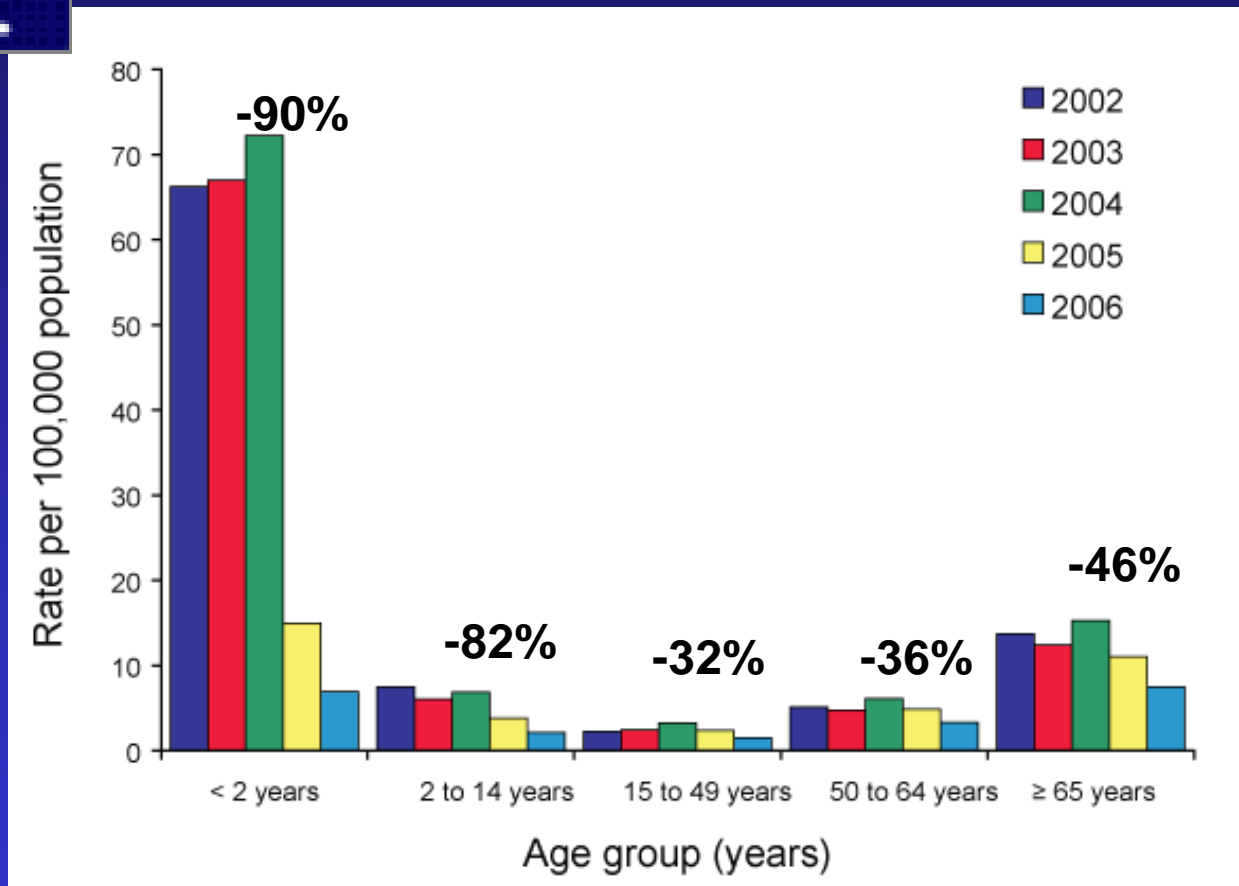
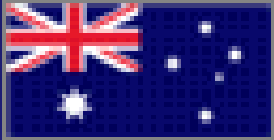
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Rates of IPD caused by all serotypes among adults ≥ 18 years-old, ABCs 1998-2008



Rates of invasive pneumococcal disease caused by PCV7 serotypes by age group Australia, 2002 to 2006



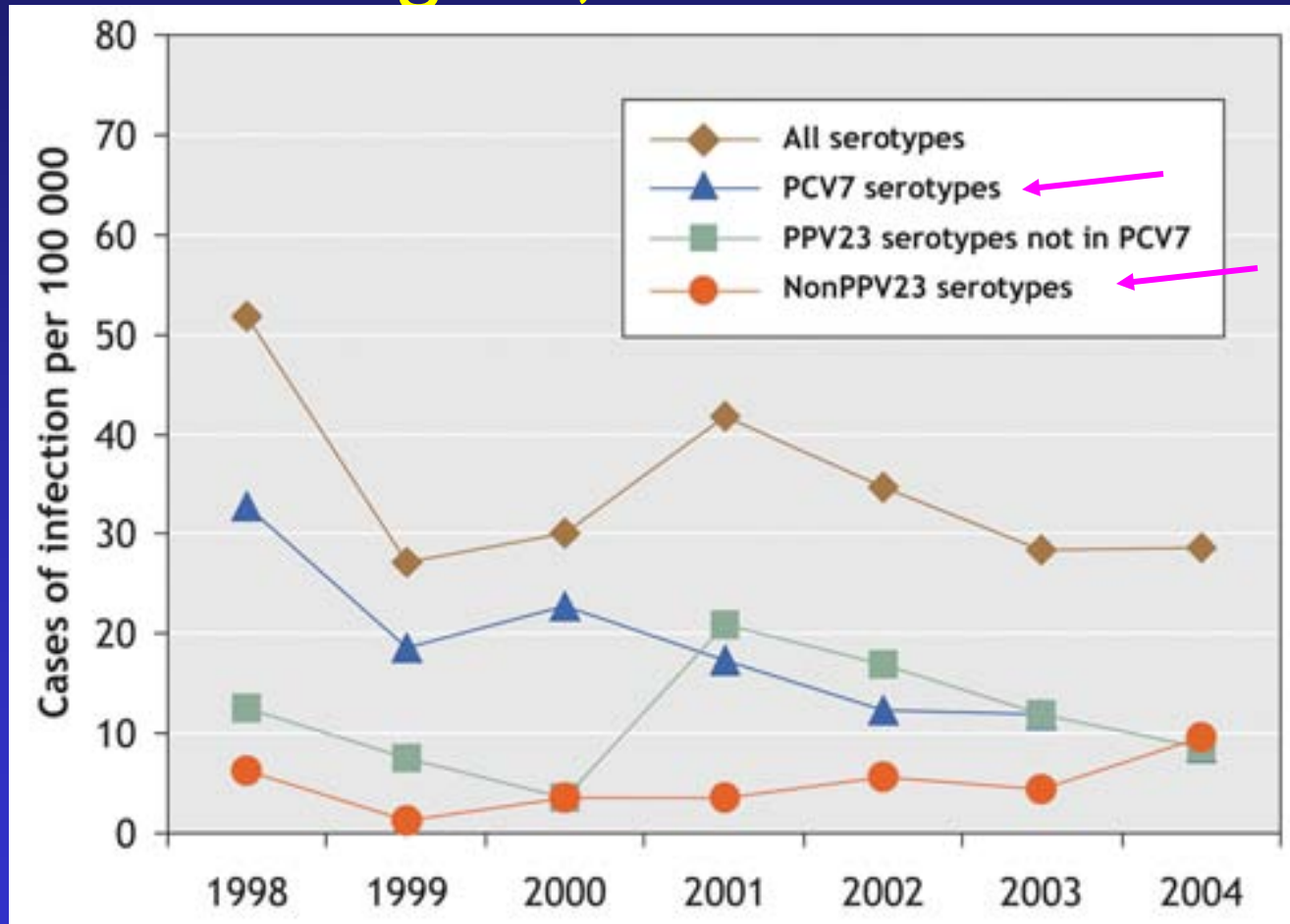
Routine PCV7
with catch-up
January 2005

Roche PW CDI Vol 32:1; March 2008

<http://www.health.gov.au/internet/main/publishing.nsf/content/cda-pubs-cdi-cdicur.htm>

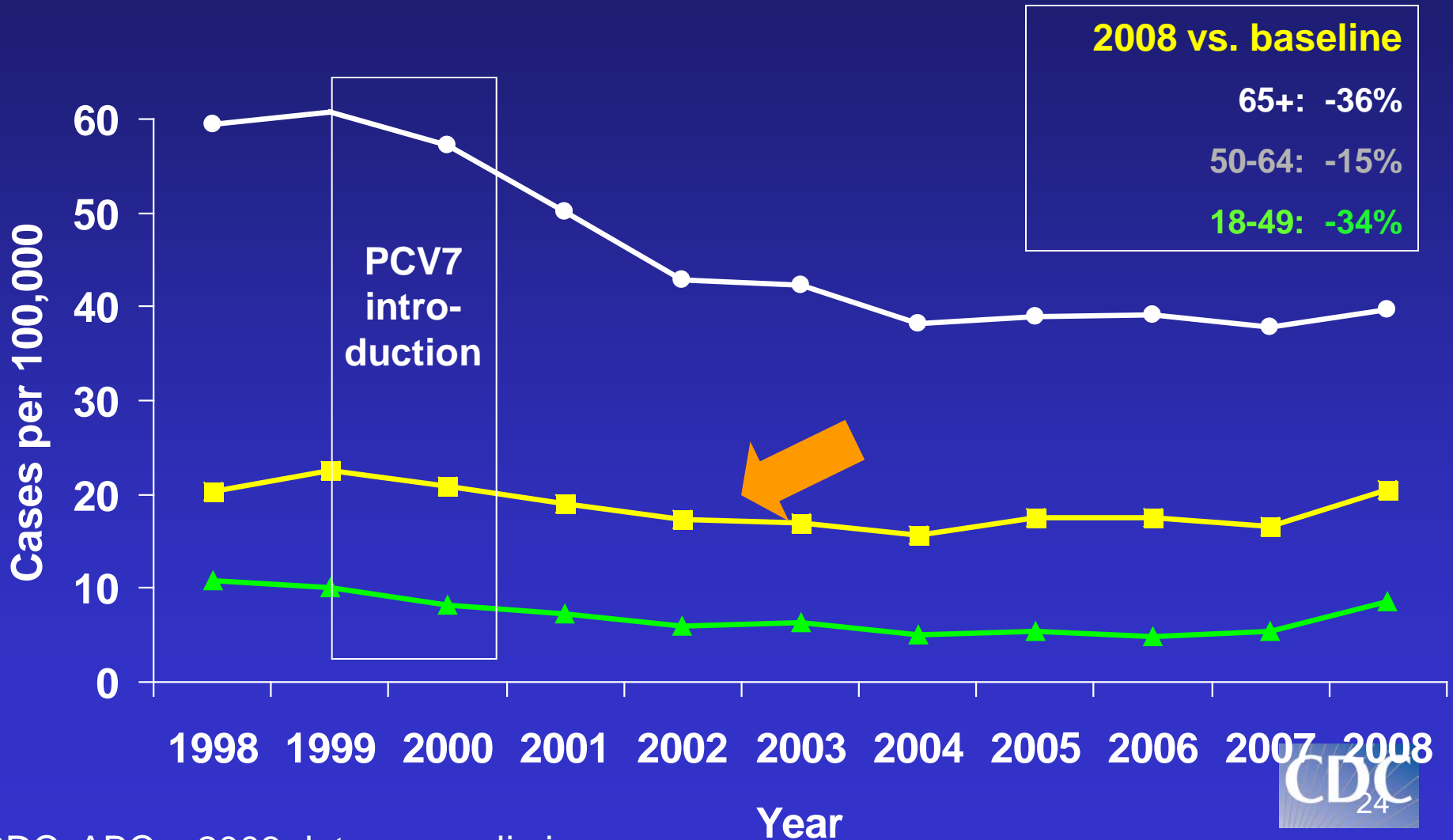


Changes in IPD in ≥ 65 yo, Calgary Region, Canada

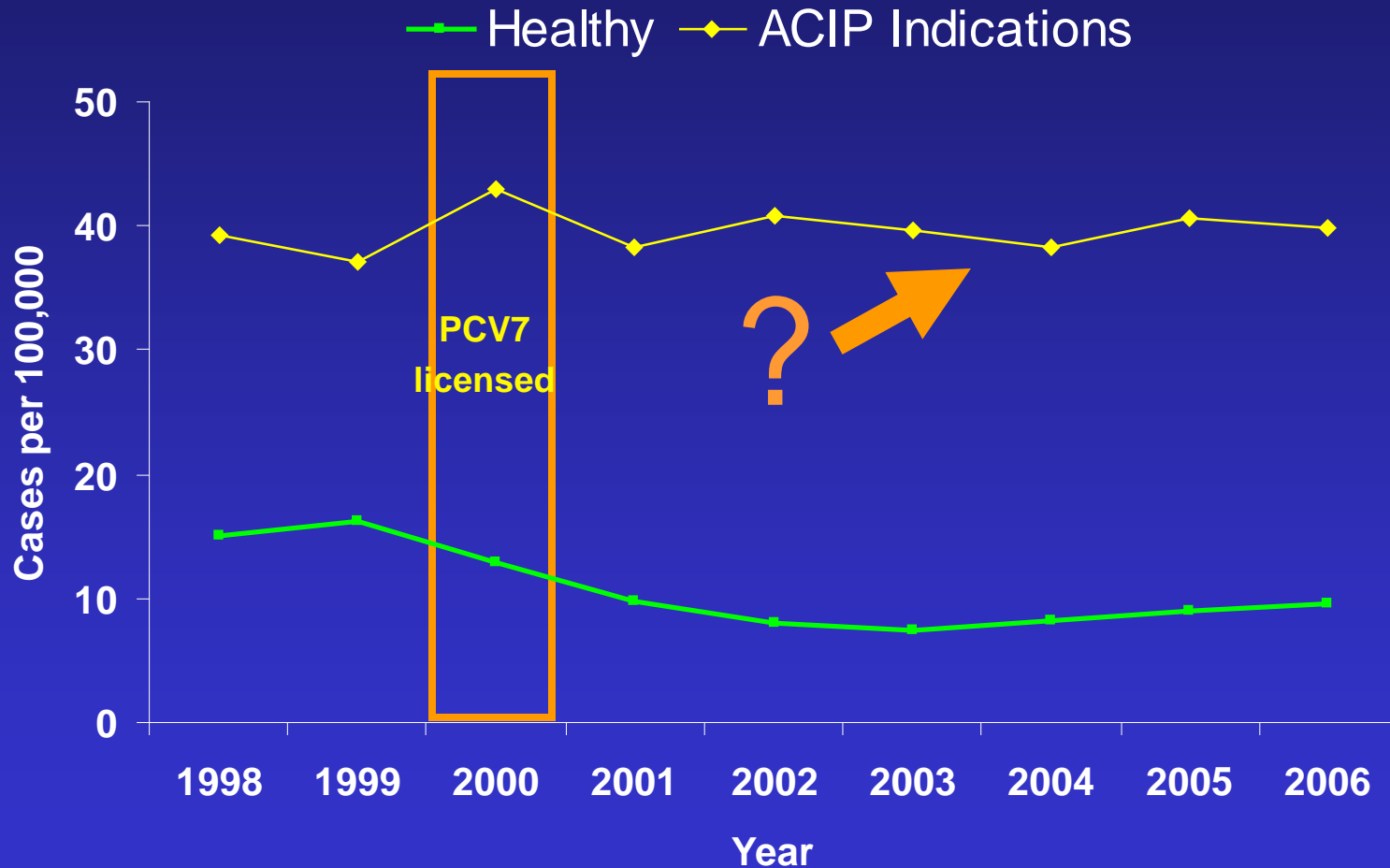


Kellner J, Canadian Medical Association Journal Jan 3 2006

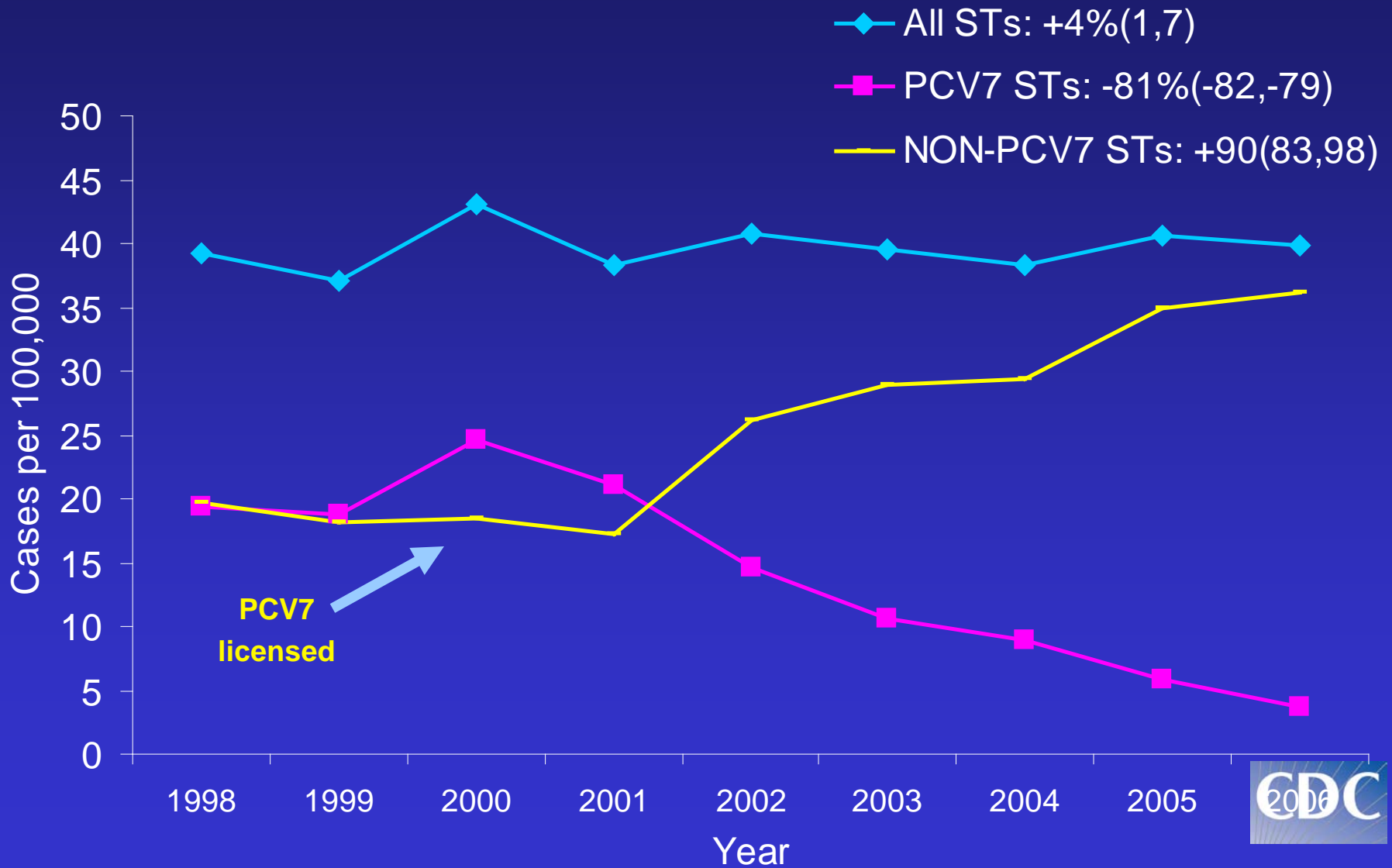
Rates of IPD caused by all serotypes among adults ≥ 18 years-old, ABCs 1998-2008



Invasive pneumococcal disease among adults 50-64 years with and without chronic illnesses (PPV23 indications)



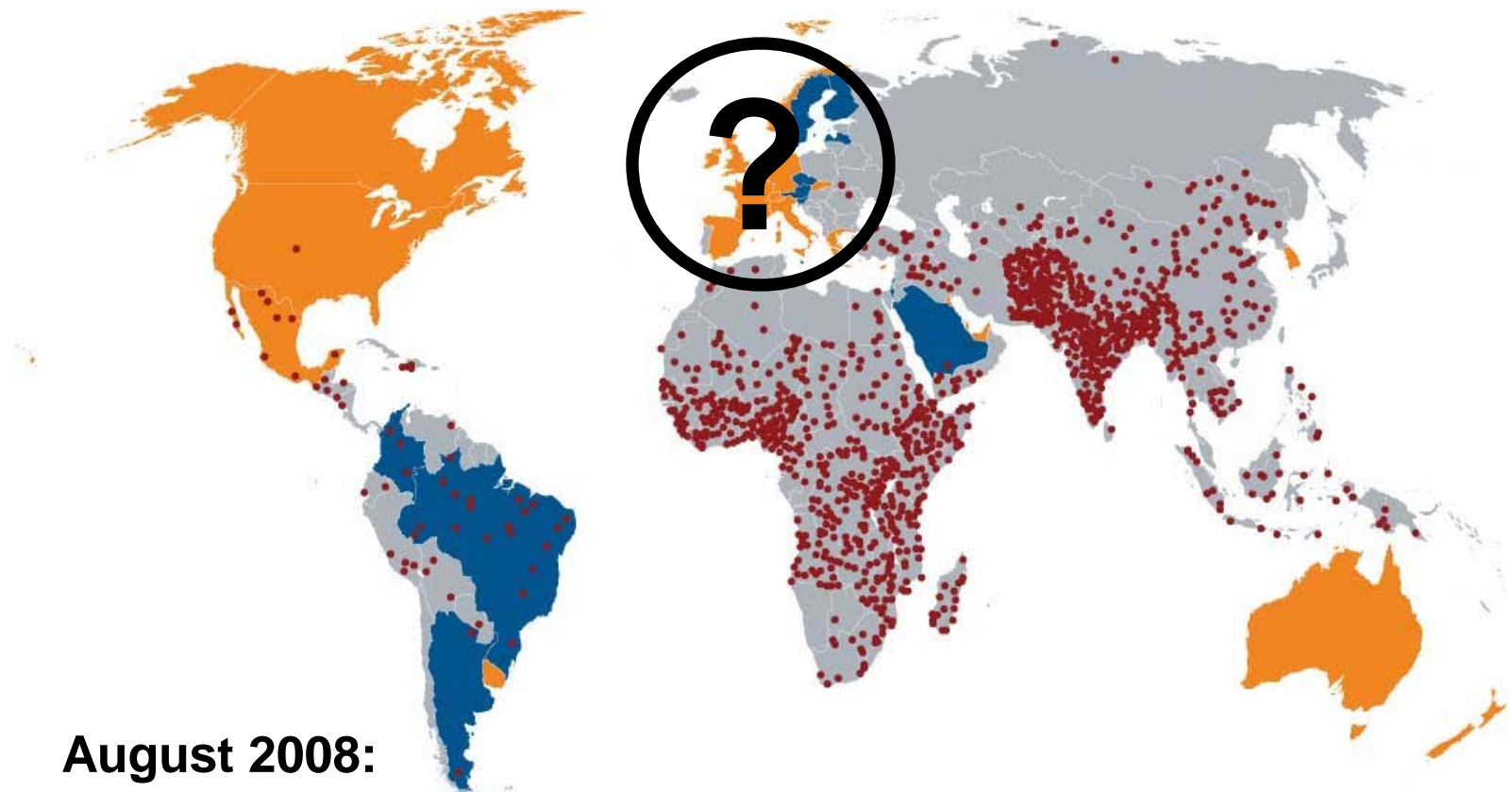
Incidence of invasive pneumococcal disease among 50-64 year olds with any ACIP indication



Summary: Replacement in Early-Adopting Countries

- In general population of children in U.S., Canada, and Australia – vaccine benefits vastly outweigh replacement disease
 - Exception: Alaska Natives living in remote area
- For adults, studies of overall indirect benefits are mixed
 - Yes: U.S. (including HIV+), Australia
 - No: Canada, Indigenous populations, chronically ill U.S. adults
- 19A main (only?) significant replacement strain
- Strain, environmental, and host factors may all contribute to amount of replacement
- Caveat: results vary by syndrome

Global Status of PCV7, 2000-2008

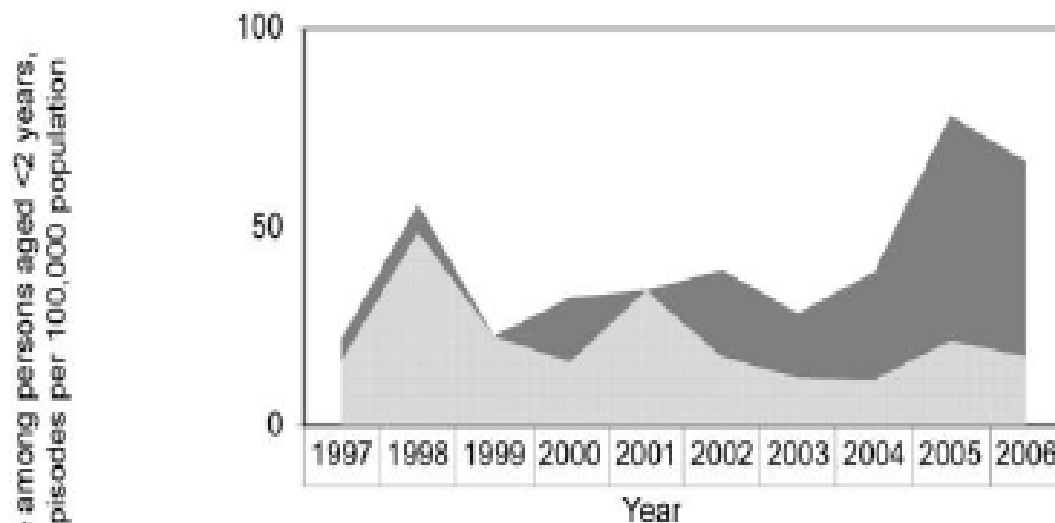


August 2008:
PCV7 licensed in 90/193 WHO member states
Routine or widespread use in 26 (13%)

■ Universal introduction ■ High-risk group introduction ■ No introduction

Pneumonia deaths in children > 5
• 1 Dot = 1,000 deaths

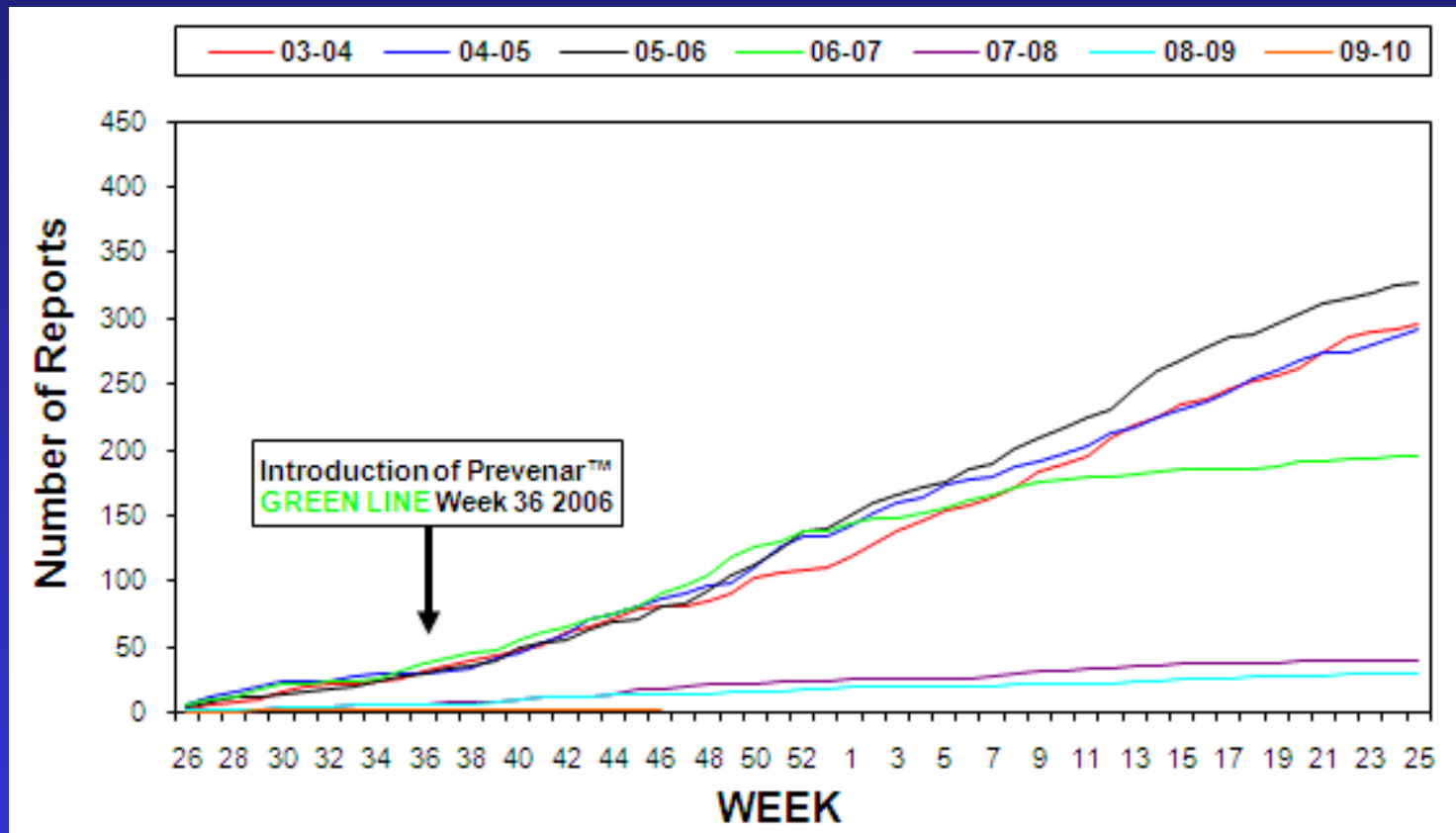
Emergence of invasive pneumococcal disease caused by nonvaccine serotypes in the era of 7-valent conjugate vaccine—Barcelona, Spain



TOTAL	22.0	55.7	22.7	32.2	34.0	39.1	28.3	38.6	78.0	66.4
■ Non-PCV7S	5.5	7	0	16.1	0	21.7	16.2	27.0	58.7	48.9
■ PCV7S	16.5	48.7	22.7	16.1	34	17.4	12.1	11.6	21.3	17.5

- Single hospital
- PCV7 introduced for high risk June 2001; 2006 coverage ~50%
- 198 episodes over 10 years
- Increase in blood cultures
- Authors relate NVT increase to vaccine use

Invasive Pneumococcal Disease Caused by PCV7 Serotypes Children 0-2 Years in England and Wales

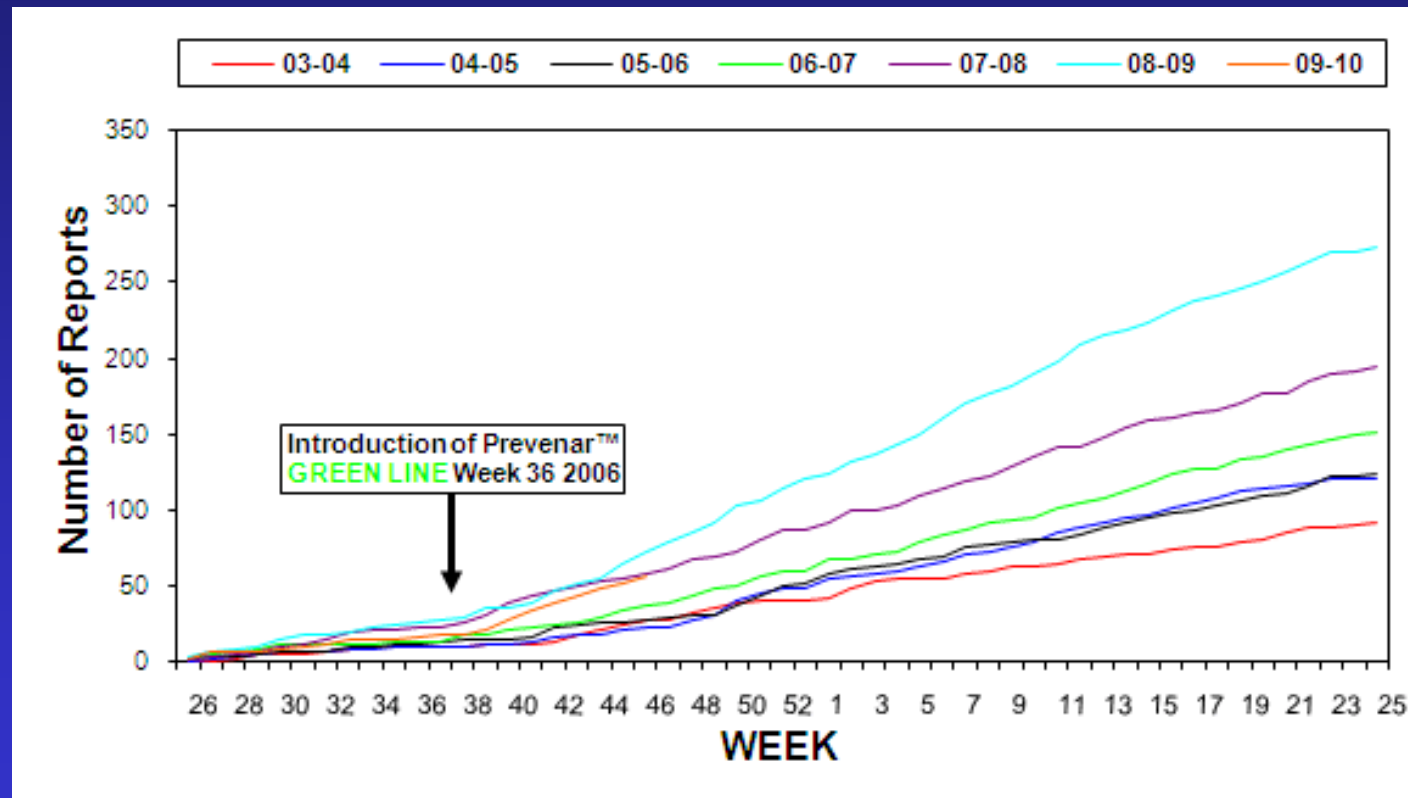


http://www.hpa.org.uk/infections/topics_az/pneumococcal/IPDcumulNvacc.htm

Accessed 4 December 2009



Invasive Pneumococcal Disease Caused by Non-vaccine Serotypes Children 0-2 Years in England and Wales



http://www.hpa.org.uk/infections/topics_az/pneumococcal/IPDcumulNvacc.htm

Accessed 4 December 2009



Unanswered questions

- What is happening in Europe?
- How do we sort the contribution of vaccination from other factors that drive serotype changes?
- What will happen in developing countries?
- What will be the effects of next generation conjugates?