

# Management of the febrile child in the era of an expanded immunisation program

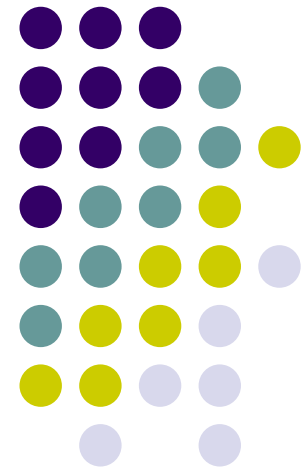
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# Fever without focus

- Children beyond neonatal period (>2 mths)
- Relatively well
- Fever > 38°C core temp (aural, rectal)
- No obvious focus

# JR

- 13 month old
- Previously well
- Immunisations UTD





# JR

- Presented to ED with 24 hour history of fever
- Reduced intake
- Adequate wet nappies

## O/E

- Temp 39.2°C
- Not too unwell. Cap refill 2 sec. Well hydrated
- No obvious focus

# RT



## Ix

- FBE – WCC 11.3, N 7, L 4
- CRP – 15
- Blood cultures – pending
- Clean catch urine – nothing on microscopy

# RT



- Did the investigations help us?
- What do we do now?



# Epidemiology of fever

- 20-30% of all children's visits to EDs
- 4-6 episodes in 1<sup>st</sup> 2yrs of life
- Majority of episodes caused by viral or minor bacterial infections
- Small proportion have occult bacteraemia
- Very small proportion develop serious focal sequelae



# Occult bacteraemia

- 10-15% in the 90s  
*(Arch Pediatr Adolesc Med 1998; 152: 624-8)*
- 3% following Hib vaccine  
*(Arch Pediatr Adolesc Med 2002;156:512-7)*
- 3.4% at RCH, Melbourne, 1996-7  
*(MJA 1999; 170: 475-8)*



# Occult bacteraemia

- *S. pneumoniae* – 60-85%
- *H. influenzae* – 5-20%
- *N. meningitidis*
- *S. aureus*
- *E. coli*
- Group A streptococcus
- *Salmonella* spp



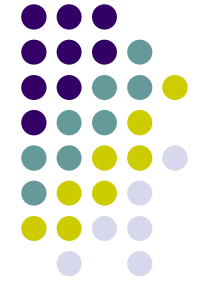
# Risk of invasive disease

- *H. influenzae* – 25%
- *S. pneumoniae* – 1-4%
  
- Overall – ~2%

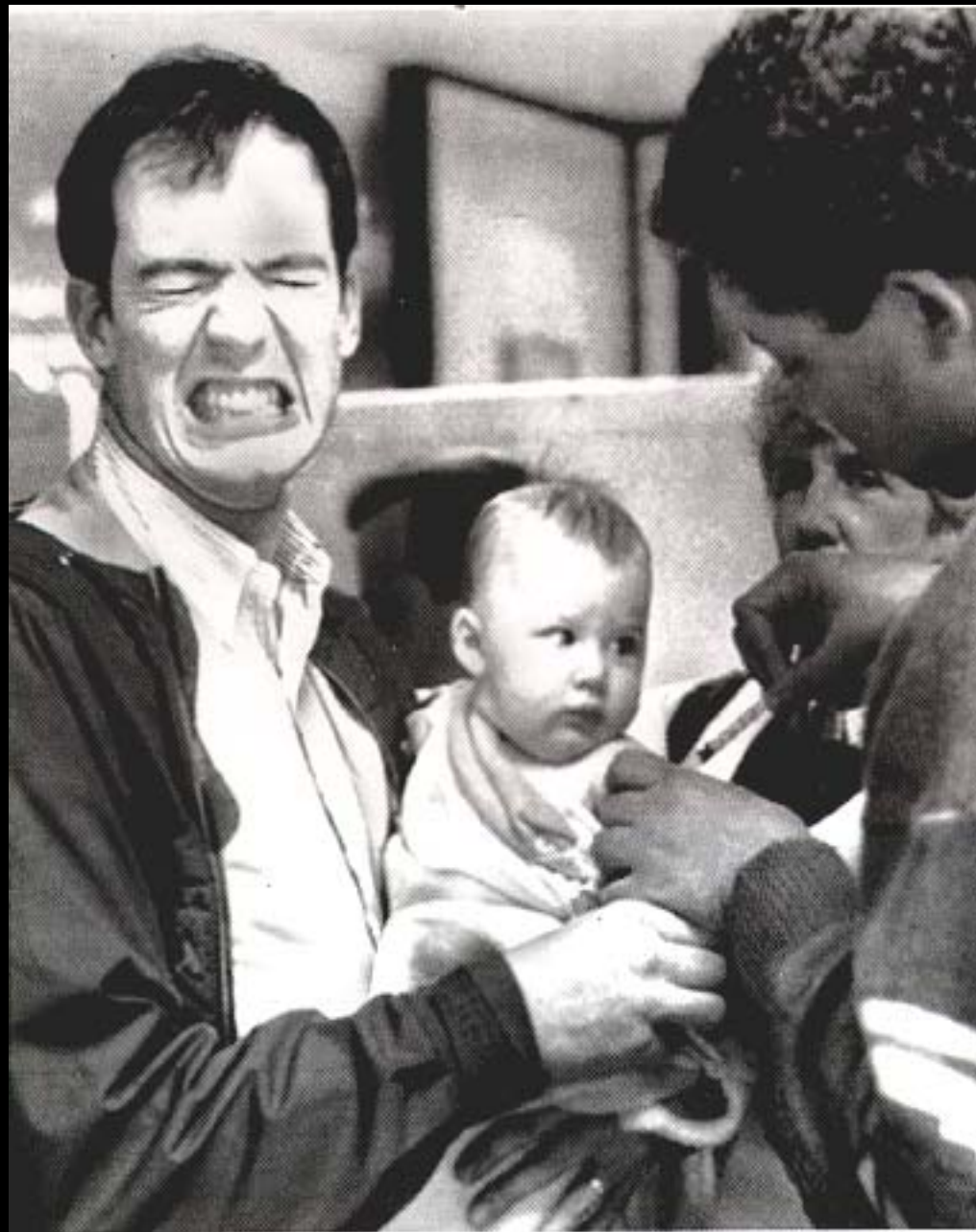
*Pediatrics. 2000;106;505-511*

*Arch Pediatr Adolesc Med. 2004;158:671-5*

# Introduction of vaccines into routine schedule



- Hib vaccine 1993
- MenC vaccine 2003
- Conj pneumococcal vaccine (7vPCV) 2005
- VZV vaccine, IPV 2005
- Rotavirus, HPV vaccines 2007



Age	Vaccine
Birth	<ul style="list-style-type: none"> <li>• Hepatitis B (hepB) <sup>a</sup></li> </ul>
2 months	<ul style="list-style-type: none"> <li>• Hepatitis B (hepB) <sup>b</sup></li> <li>• Diphtheria, tetanus and acellular pertussis (DTPa)</li> <li>• <i>Haemophilus influenzae type b (Hib)</i> <sup>c,d</sup></li> <li>• Inactivated poliomyelitis (IPV)</li> <li>• Pneumococcal conjugate (7vPCV)</li> <li>• Rotavirus</li> </ul>
4 months	<ul style="list-style-type: none"> <li>• Hepatitis B (hepB) <sup>b</sup></li> <li>• Diphtheria, tetanus and acellular pertussis (DTPa)</li> <li>• <i>Haemophilus influenzae type b (Hib)</i> <sup>c,d</sup></li> <li>• Inactivated poliomyelitis (IPV)</li> <li>• Pneumococcal conjugate (7vPCV)</li> <li>• Rotavirus</li> </ul>
6 months	<ul style="list-style-type: none"> <li>• Hepatitis B (hepB) <sup>b</sup></li> <li>• Diphtheria, tetanus and acellular pertussis (DTPa)</li> <li>• <i>Haemophilus influenzae type b (Hib)</i> <sup>c</sup></li> <li>• Inactivated poliomyelitis (IPV)</li> <li>• Pneumococcal conjugate (7vPCV) <sup>e</sup></li> <li>• Rotavirus <sup>j</sup></li> </ul>
12 months	<ul style="list-style-type: none"> <li>• Hepatitis B (hepB) <sup>b</sup></li> <li>• <i>Haemophilus influenzae type b (Hib)</i> <sup>d</sup></li> <li>• Measles, mumps and rubella (MMR)</li> <li>• Meningococcal C (MenCCV)</li> </ul>
12-24 months	<ul style="list-style-type: none"> <li>• Hepatitis A (Aboriginal and Torres Strait Islander children in high risk areas) <sup>f</sup></li> </ul>
18 months	<ul style="list-style-type: none"> <li>• Varicella (VZV)</li> </ul>
18-24 months	<ul style="list-style-type: none"> <li>• Pneumococcal polysaccharide (23vPPV) (Aboriginal and Torres Strait Islander children in high risk areas) <sup>g</sup></li> <li>• Hepatitis A (Aboriginal and Torres Strait Islander children in high risk areas)</li> </ul>
4 years	<ul style="list-style-type: none"> <li>• Diphtheria, tetanus and acellular pertussis (DTPa)</li> <li>• Measles, mumps and rubella (MMR)</li> <li>• Inactivated poliomyelitis (IPV)</li> </ul>
10-13 years <sup>h</sup>	<ul style="list-style-type: none"> <li>• Hepatitis B (hepB)</li> <li>• Varicella (VZV)</li> </ul>
12-13 years <sup>i</sup>	<ul style="list-style-type: none"> <li>• Human Papillomavirus (HPV)</li> </ul>
15-17 years <sup>i</sup>	<ul style="list-style-type: none"> <li>• Diphtheria, tetanus and acellular pertussis (dTPa)</li> </ul>



*“And here’s a lollipop  
for being so brave”*

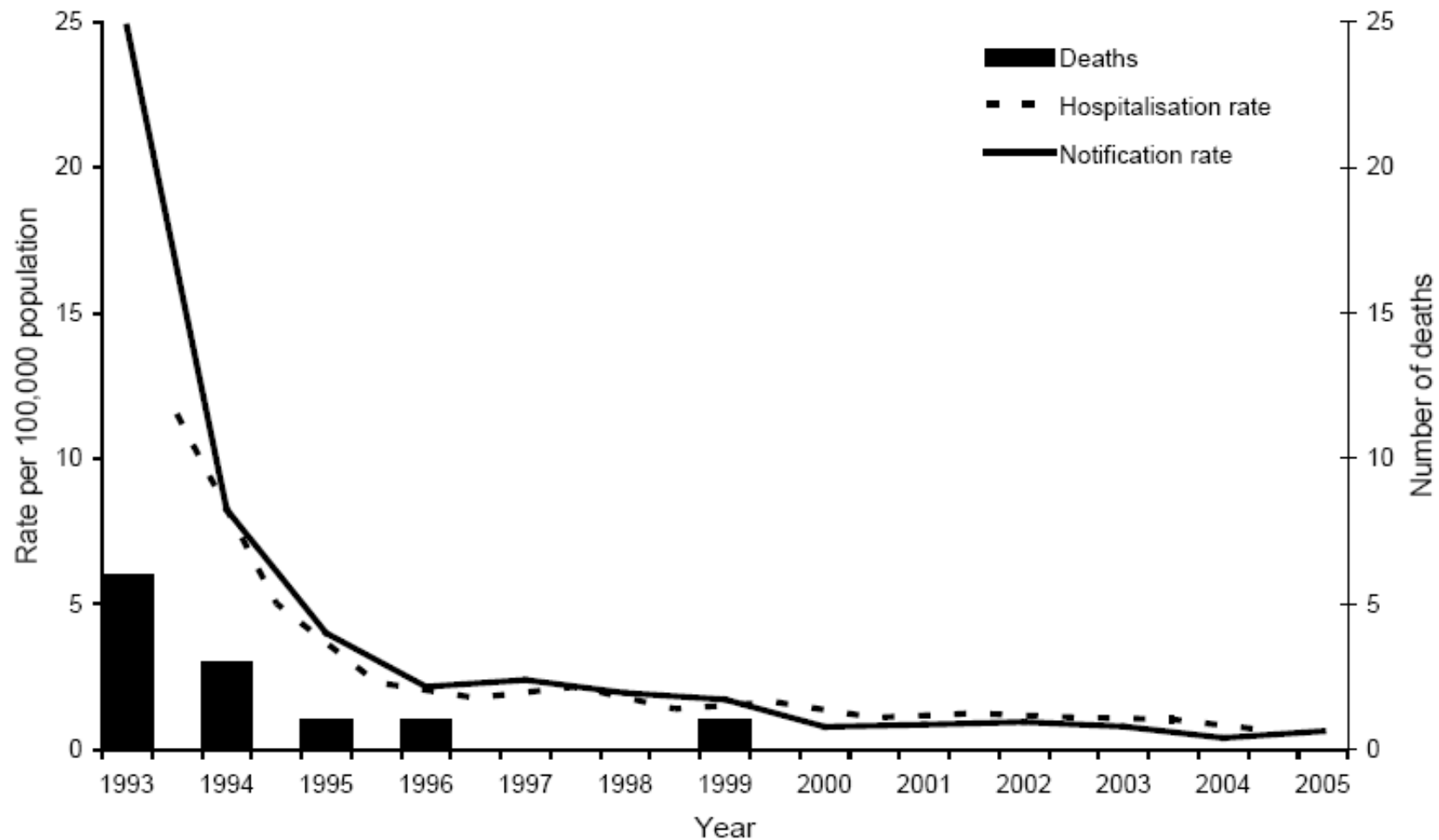
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# Impact of routine Hib immunisation in Australia

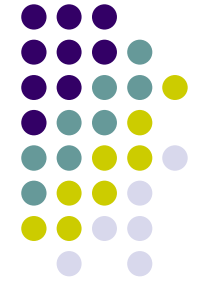


- Notified cases of Hib disease reduced >90%
  - 502 in 1992 → <15 per year now
- Reduction particularly marked in Indigenous children
- Similar impressive ↓ in other countries with routine childhood vaccination

# Impact of routine Hib immunisation in Australia



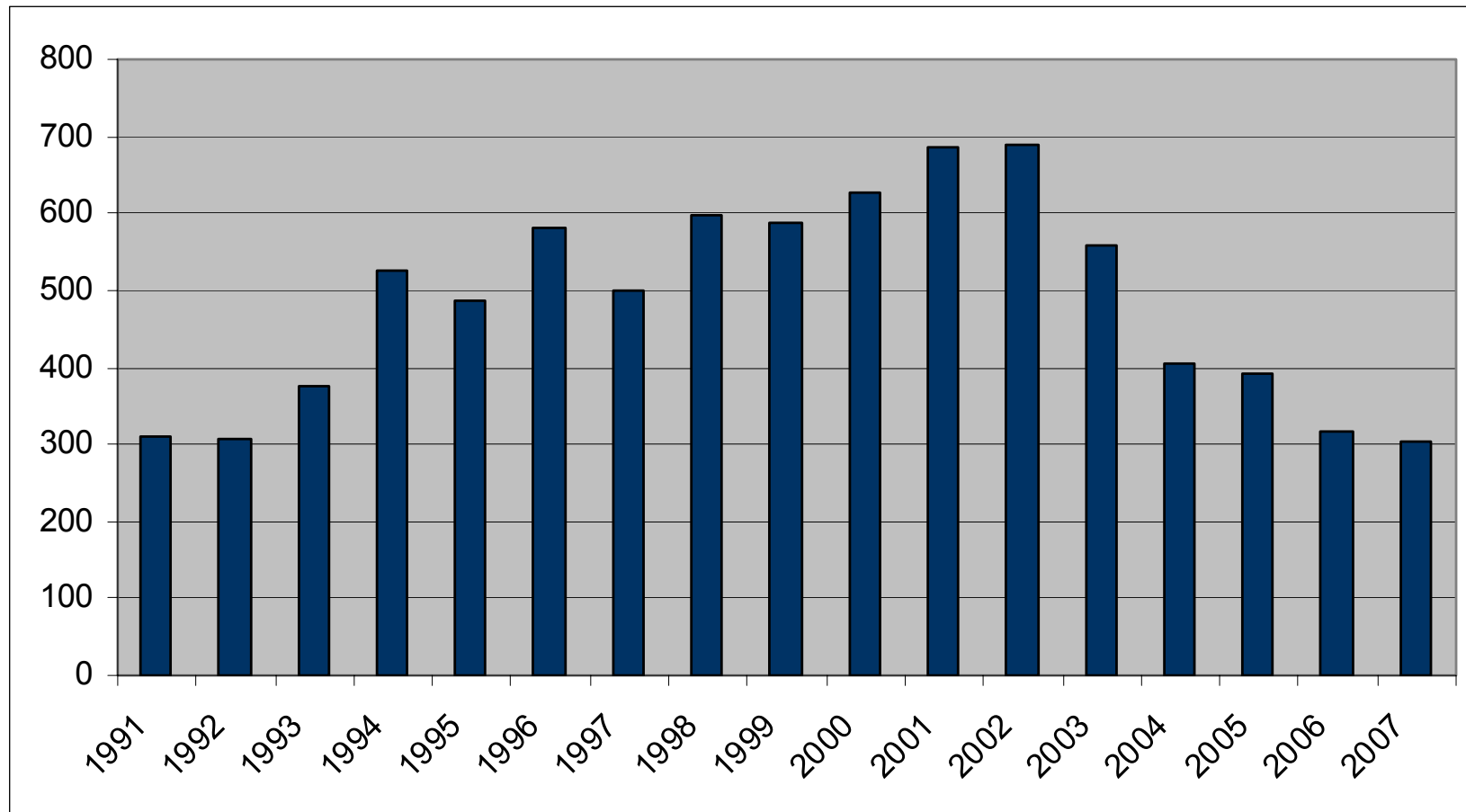
# Meningococcal C conjugate vaccines



- Meningitec<sup>®</sup>, Menjugate<sup>®</sup> and NeisVac-C<sup>®</sup>
- Serogroup C polysaccharide conjugated to protein carrier
  - CRM197 (Menjugate and Meningitec)
  - Tetanus toxoid (NeisVac-C)

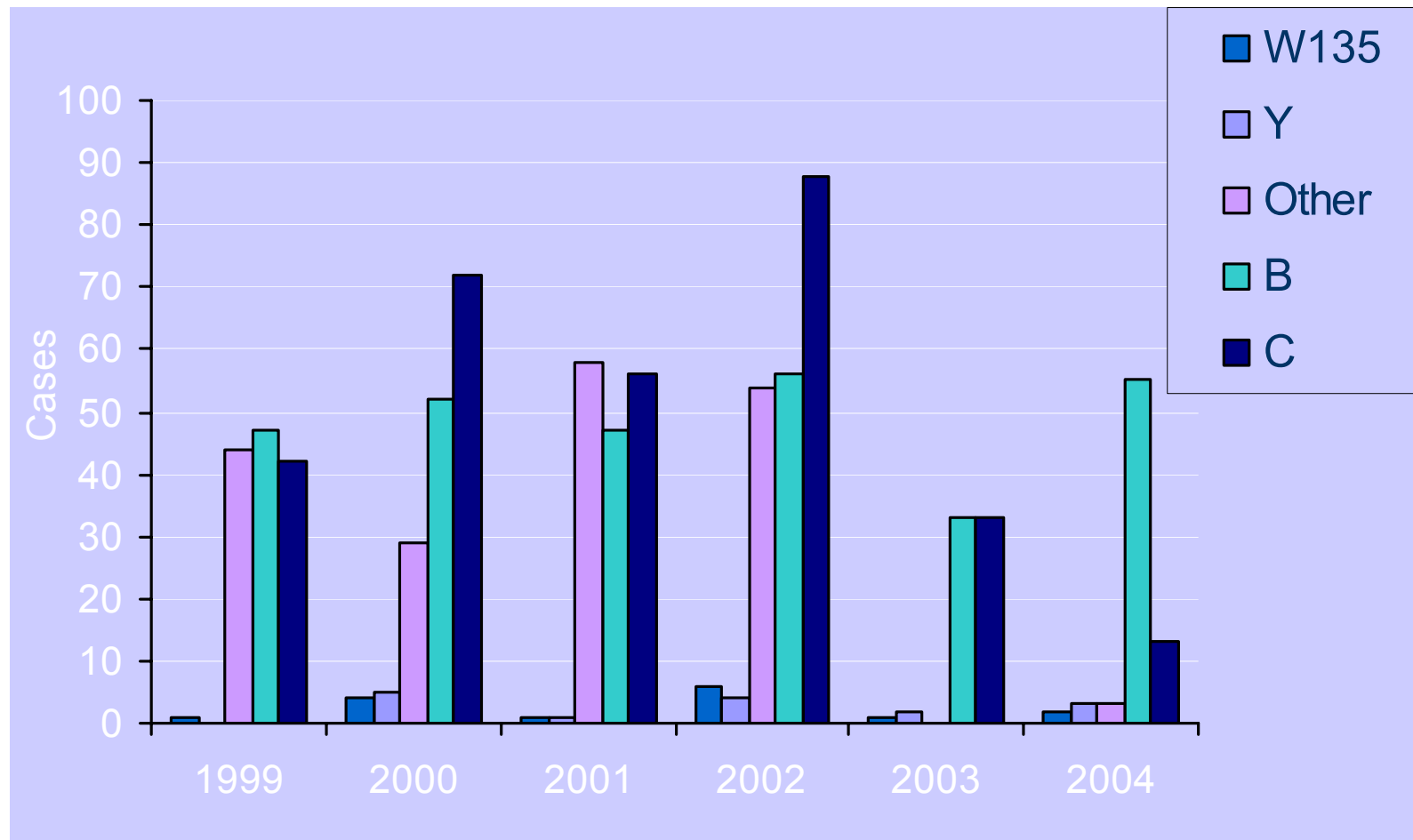


# Meningococcal infection notifications, Australia 1991-2007



*Commun Dis Intell. 2007;31:185–194.*

# Meningococcal serogroups, Victoria, 1999-2004



*Commun Dis Intell 2005;29:149–158*

# Invasive meningococcal disease, Australia, 2006 by age and serogroup



Serogroup	Age group						Total
	<1	1-4	5-14	15-19	20+	NS	
B	52	41	21	40	59	4	217
C	2	0	3	4	17		26
Other	2	3	1	5	16	1	28
Total	56	44	25	49	92	5	271

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<15yo: 91% serogroup B, 4% serogroup C

# Invasive meningococcal disease, Australia, 2006 by age and serogroup



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>15yo: 71% serogroup B, 15% serogroup C,  
15% other serogroups

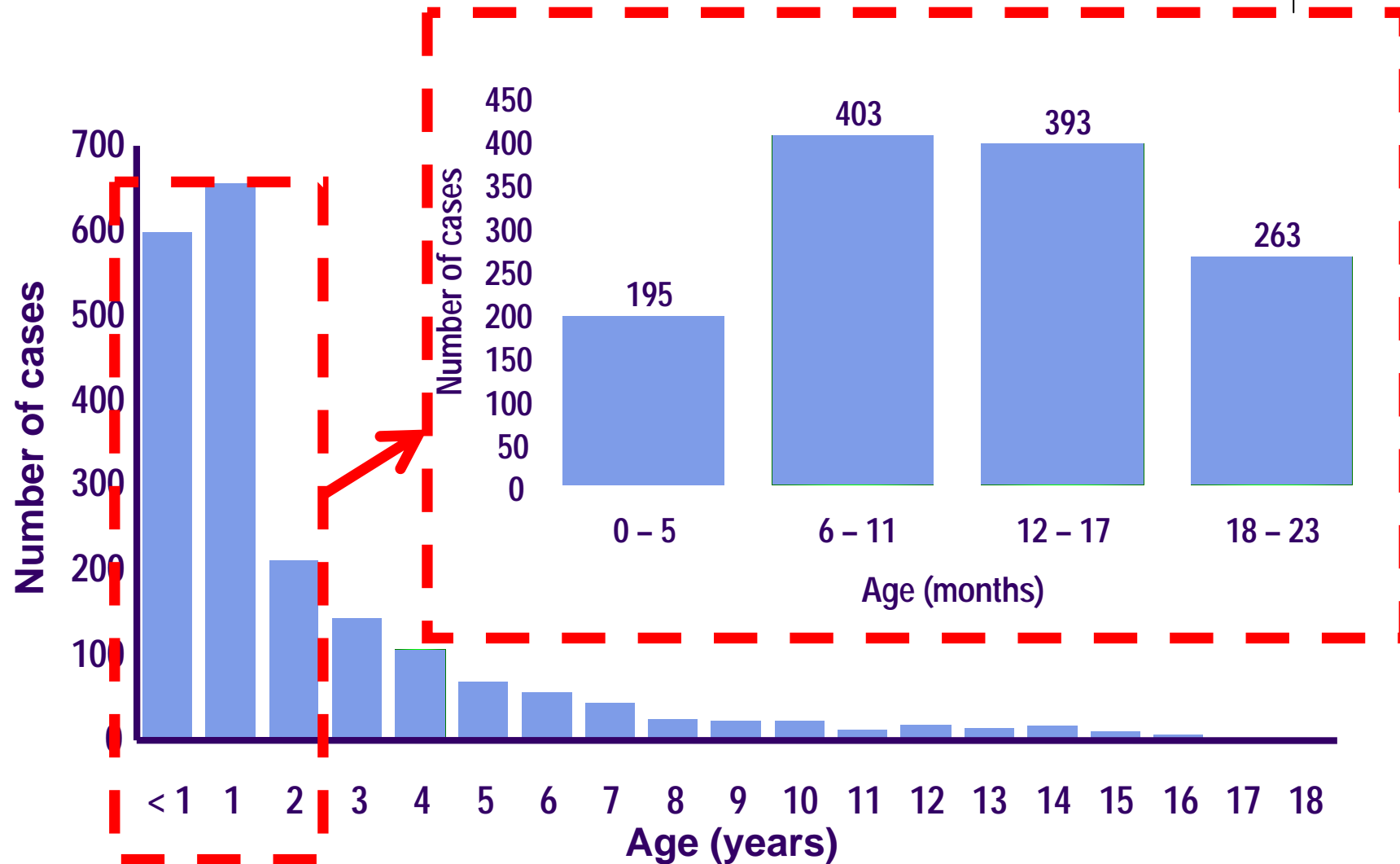


## Serotypes of *S. pneumoniae*

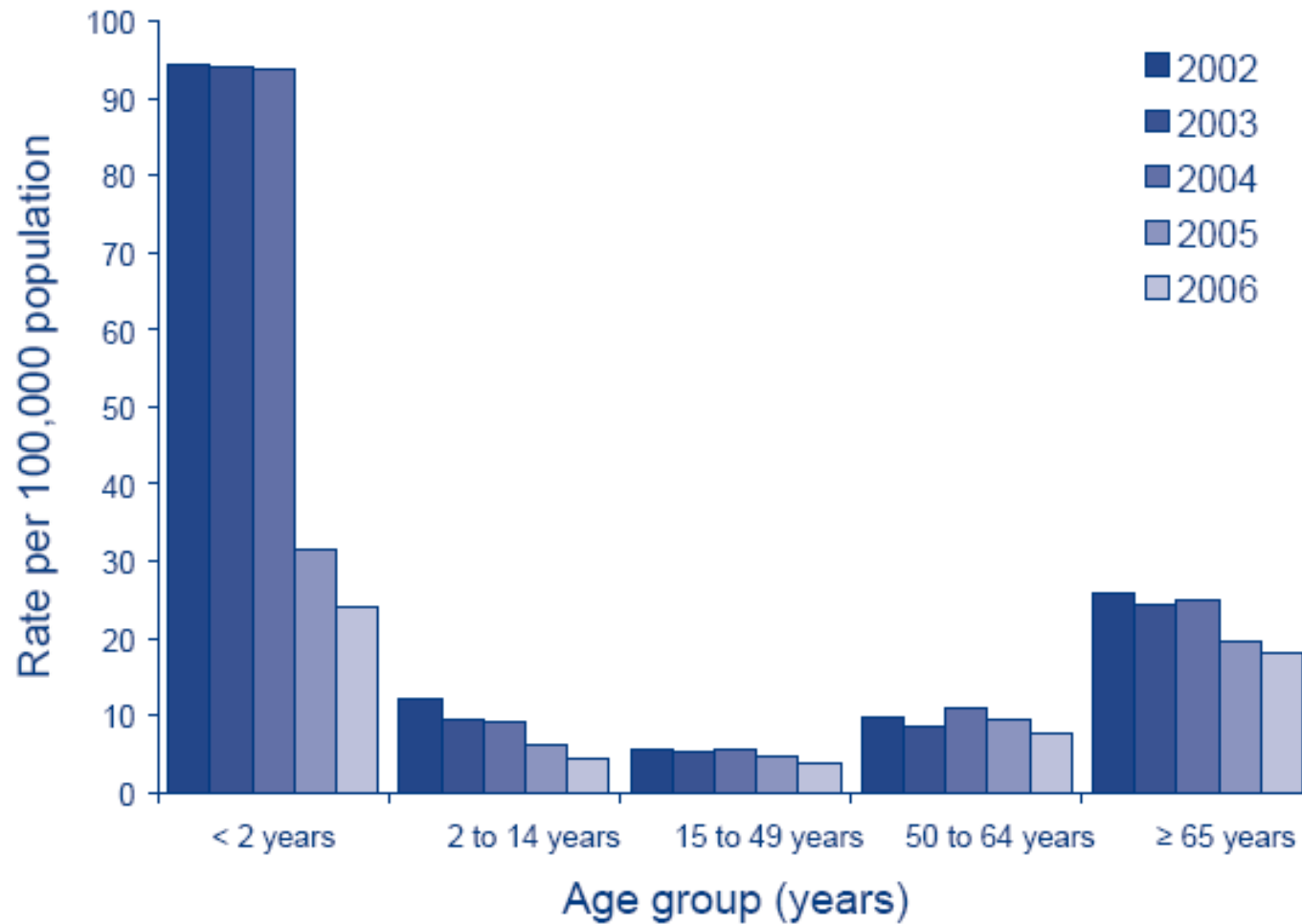
- Over 90 serotypes
- Limited cross-reactivity among some serotypes
- 10 most common serotypes cause 62% of disease worldwide
- In Australia, 7 serotypes cause ~84% of invasive cases
- Common serotypes vary with age & by country

# Age distribution of invasive infections

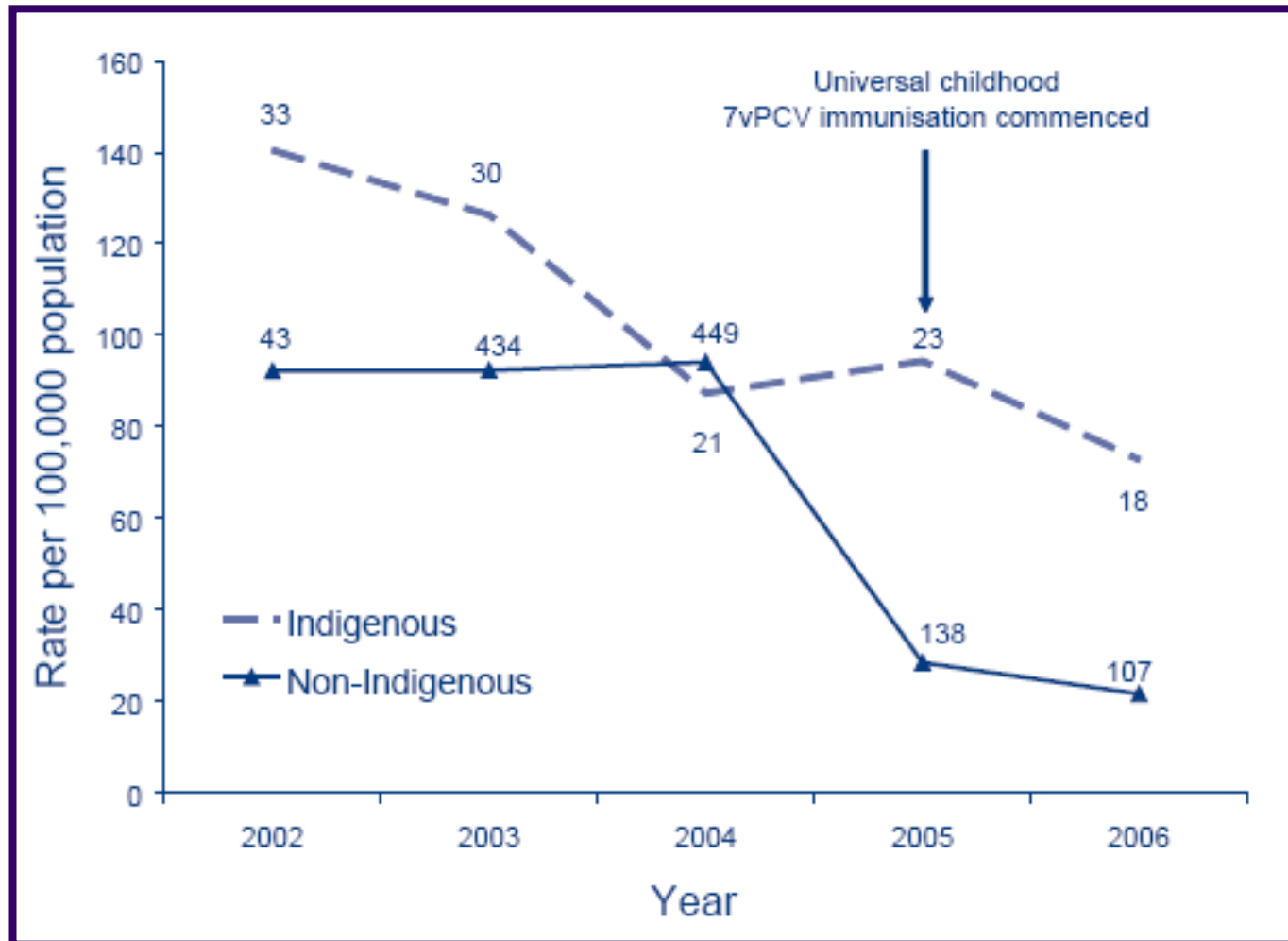
*Scheifele et al. Clin Infect Dis. 2000;31:58-64*



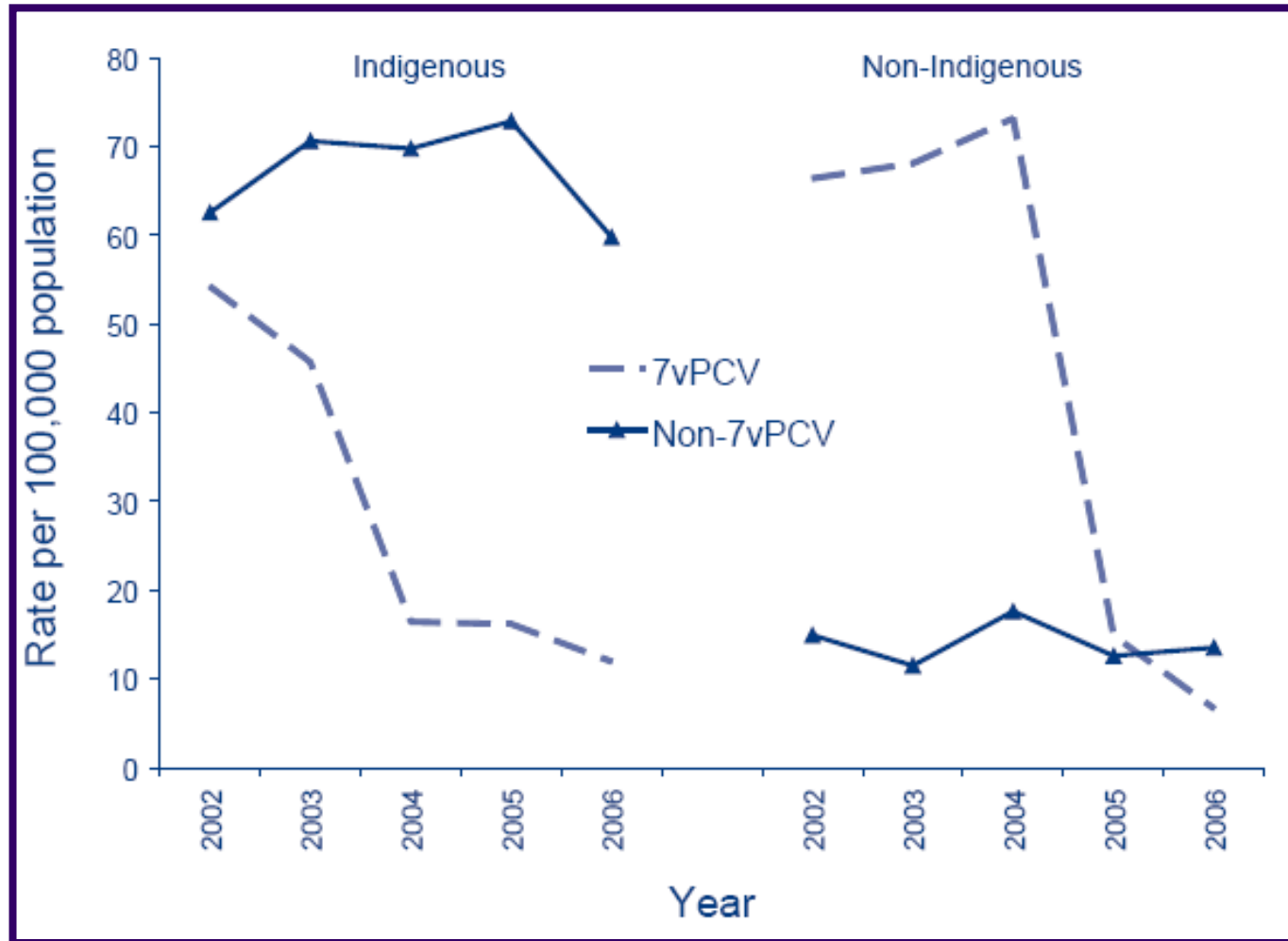
# Invasive pneumococcal disease (IPD), Australia, 2002 - 2006



# Rates of IPD in children <2yo, Australia, 2002-06



# Rates of IPD in children <2yo, 7-valent vs non-7-valent serotypes





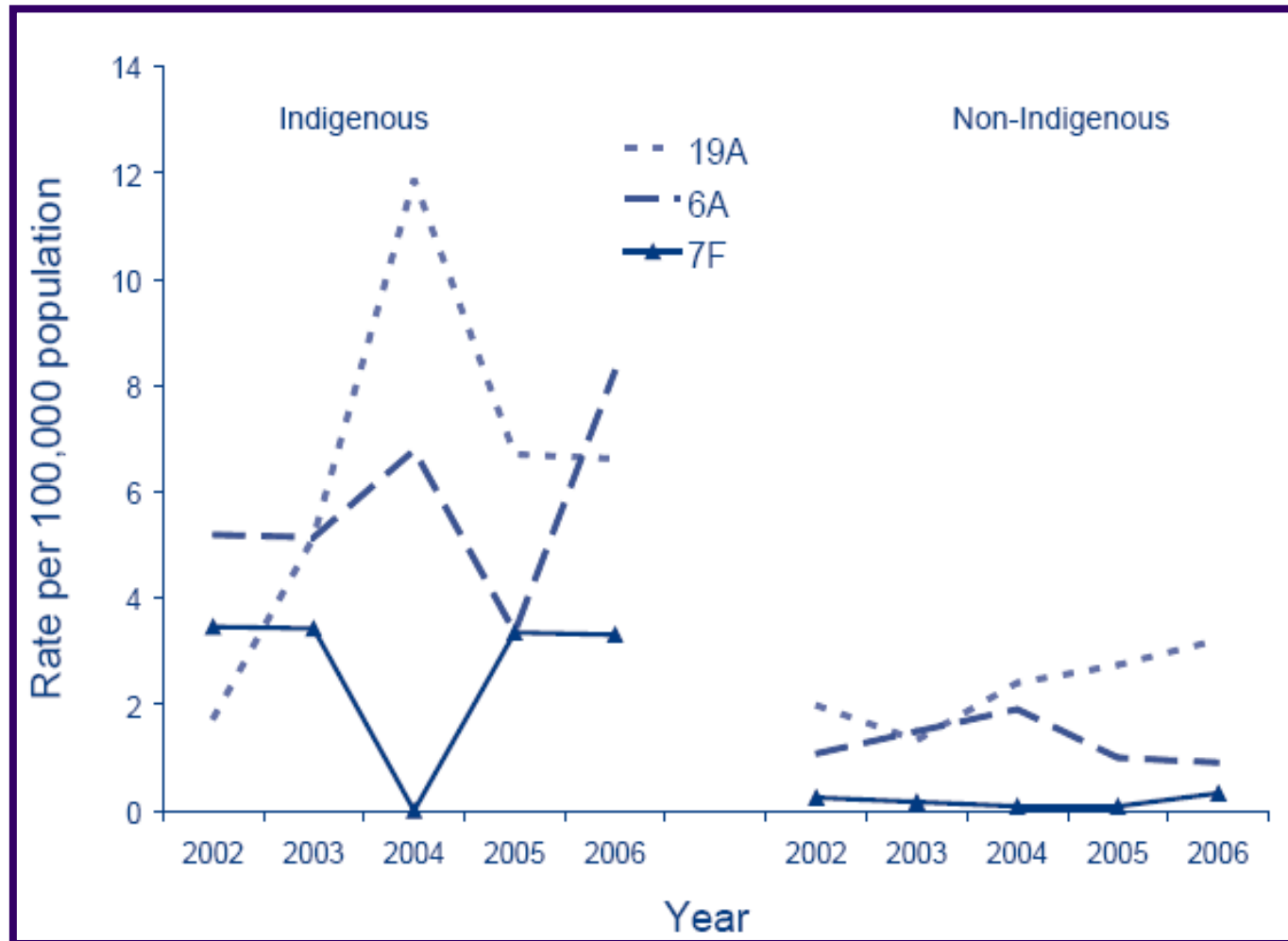
# Serotype replacement

- 7vPCV introduced in US in 2000
- Emergence of replacement pneumococcal disease, partic serotypes 19A and 7F
- 19A
  - 9<sup>th</sup> most common serotype causing IPD before 7vPCV → now most common
  - > 60% have reduced susceptibility to penicillin

*JID. 2008; 197:1016-27*

*JAMA. 2007;297:1784–92*

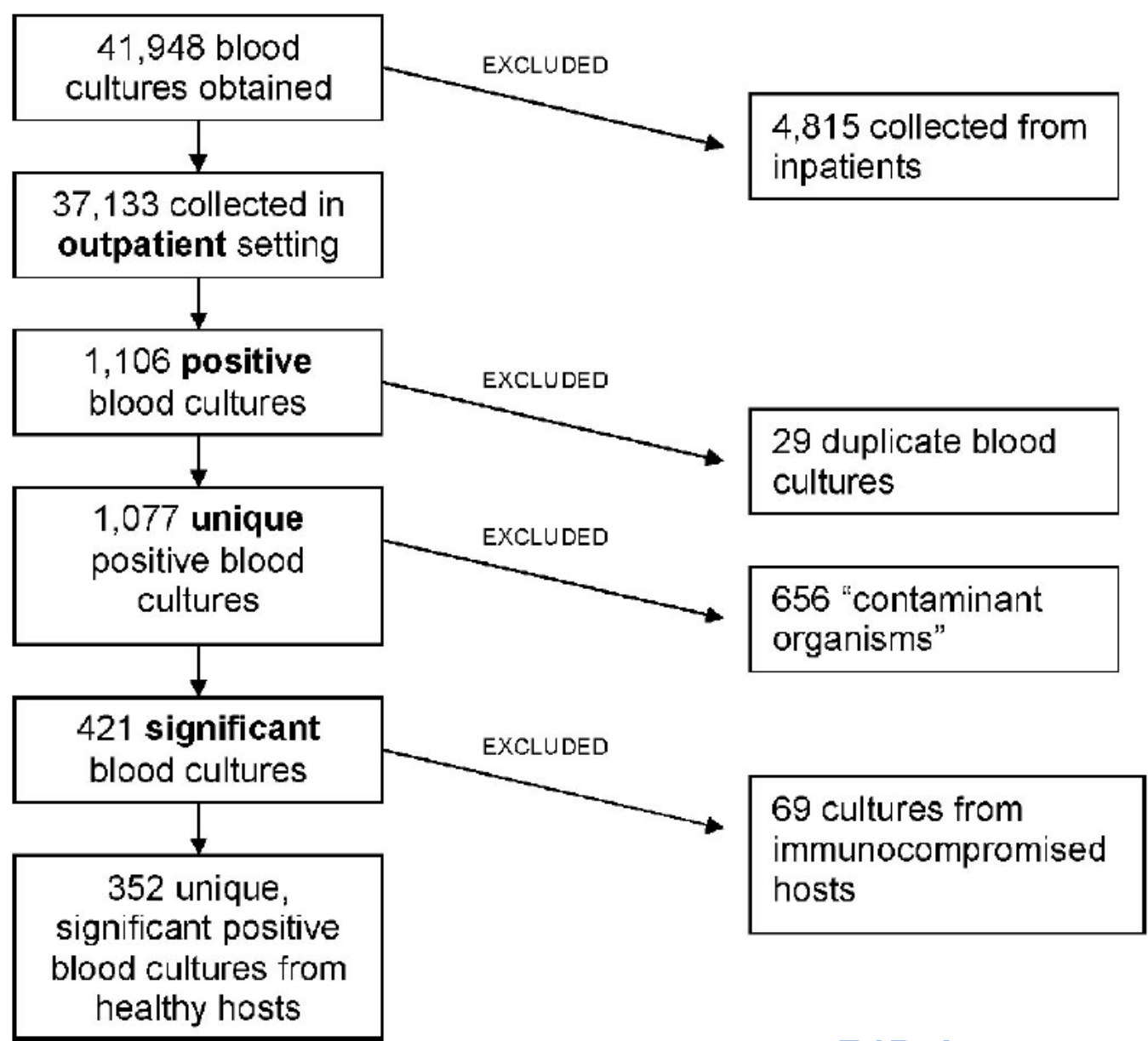
# ? Serotype replacement, Australia Children < 5yo, 2002 - 06



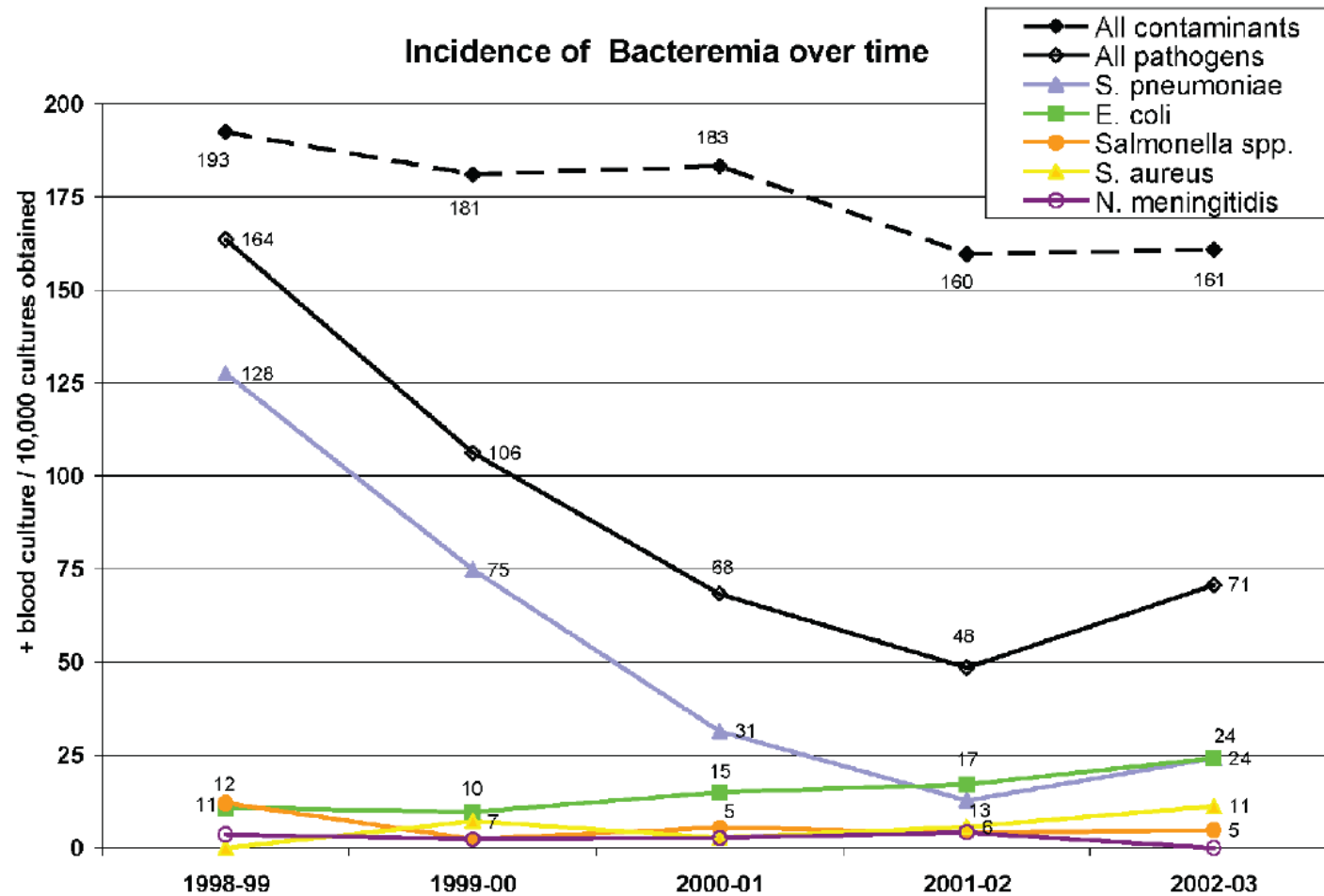
# Epidemiology of bacteraemia



- Kaiser Permanente
- Retrospective case series of all blood cultures collected on children age 3 months–3 years 1998 – 2003
- Universal conjugate pneumococcal vaccine program from 2000



# Incidence of bacteremia in children aged 3mths – 3yo



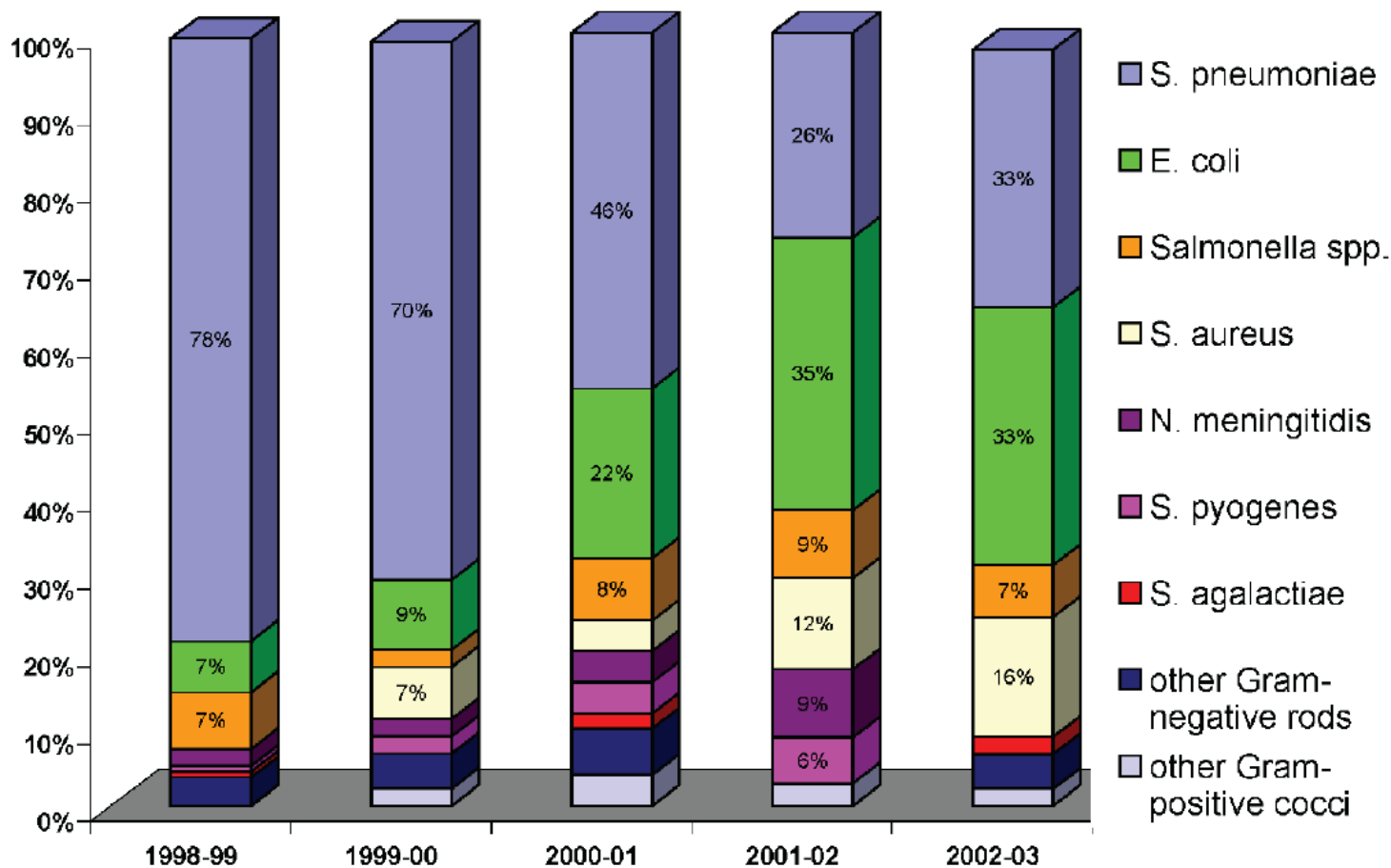
# Incidence of bacteremia in children aged 3mths – 3yo



**TABLE 1.** Pathogenic Organisms Identified in Blood Cultures Obtained From Previously Healthy Children Ages 3 Months–3 Years Presenting to Outpatient Settings at Kaiser Permanente Northern California From 1998 to 2003

Organism	Year 1	Year 2	Year 3	Year 4	Year 5
<i>Streptococcus pneumoniae</i>	106 (79)*	62 (70)	23 (46)	9 (26)	15 (34)
<i>Escherichia coli</i>	9 (7)	8 (9)	11 (22)	12 (35)	15 (34)
<i>Salmonella</i> spp.	10 (7)	2 (2)	4 (8)	3 (9)	3 (7)
<i>Staphylococcus aureus</i>	0	6 (7)	2 (4)	4 (12)	7 (16)
<i>Neisseria meningitidis</i>	3 (2)	2 (2)	2 (4)	3 (9)	0
<i>Streptococcus pyogenes</i>	1 (1)	2 (2)	2 (4)	2 (6)	0
<i>Streptococcus agalactiae</i>	1 (1)	0	1 (2)	0	1 (2)
Other Gram-negative rods <sup>†</sup>	5 (4)	4 (5)	3 (6)	0	2 (5)
Other Gram-positive cocci <sup>‡</sup>	0	2 (2)	2 (4)	1 (3)	1 (2)
Total pathogenic organisms	135 (100)	88 (100)	50 (100)	34 (100)	44 (100)
Total contaminant organisms	160	150	134	112	100
Pathogen bacteremia rate <sup>§</sup>	1.62%	1.06%	0.68%	0.48%	0.71%
Contaminant-pathogen ratio	1.2:1	1.7:1	2.7:1	3.3:1	2.3:1

# Incidence of bacteremia in children aged 3mths – 3yo





# Occult bacteraemia

- 10-15% prior to Hib vaccine  
*(Arch Pediatr Adolesc Med 1998; 152: 624-8)*
- 3% following Hib vaccine  
*(Arch Pediatr Adolesc Med 2002;156:512-7)*
- 3.4% at RCH, Melbourne, 1996-7  
*(MJA 1999; 170: 475-8)*



# Occult bacteraemia now

- <1% since Hib, meningococcal + pneumococcal vaccines

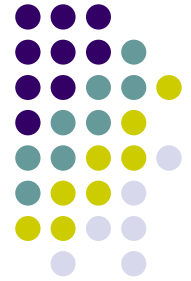
*Ann Emerg Med.* 2000; 36: 602-14

*Arch Pediatr Adolesc Med.* 2004; 158: 671-5

*PIDJ.* 2006;25: 293–300

# Risk of invasive disease now

- ?? ~0.5%



# JR

- 13 month old
- Previously well
- Immunisations UTD
- Fever without focus
- Did investigations help us?
- What do we do now?



