Pneumokokken Conjugaatvaccin voor kinderen: wie wordt er beter van?

Prof Dr EAM Sanders
UMCUtrecht

14 juni 2011
Invasive pneumococcal disease following introduction of Prevenar™ for children

- Introduction
- The USA experience after PCV-7 implementation for children
- What happened in Europe? *Dutch and UK experience?*
- What drives replacement disease?
- Next generation vaccines
- Summary
The pneumococcal problem
Pneumococcal disease is the leading cause of vaccine-preventable death in children <5 years old worldwide.

- 90% Pneumococcal pneumonia
- 7% meningitis

> 90% in developing countries

Source: WHO official mortality rates — June 2003
* Provisional estimates
Acute respiratory infections: the leading infectious cause of death


*HIV-positive people who have died with TB or acute respiratory infections included among AIDS deaths

Gepresenteerd op de 2de Nederlandse Infectieziektendag
Zeist, 14 juni 2011
Invasive pneumococcal disease incidence in the Netherlands by age over 2004-2006

- 50% meningitis
  - 10% mortality

- 80% invasive pneumonia
  - 30-40% mortality

Comorbidity


Gepresenteerd op de 2de Nederlandse Infectieziektendag
Zeist, 14 juni 2011
Pneumococcal reservoir = human nasopharynx
Pneumococcal carriage and age

Carriage rate (%)

- preschool: 60%
- primary school: 30%
- high school: 20%
- adults: 10%
- elderly: 0%


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Zeist, 14 juni 2011
Pneumococcal disease

- Acute Otitis Media
- Pneumonia
- Sepsis
- Meningitis

Direct spread

asymptomatic colonization

Blood stream

bacteremia

Adapted from www.pneumoadip.org
Pneumococcal conjugate vaccine; the solution?
Streptococcus pneumoniae is surrounded by a polysaccharide capsule

- Capsule protects against immune system
- Anticapsular antibodies protect against disease and carriage
- > 90 serotypes based on capsular polysaccharide structure
First licensed protein polysaccharide conjugate vaccine covers 7 pediatric serotypes: 7-valent vaccin Prevnar™

North American Children < 5 years before introduction PCV-7

Global IPD serotypes 10 serotypes ~ 80% IPD

Source: Kate O’Brien GSP
PCV-7 licensure study: California Kaiser Permanente PCV7 Trial on Invasive Pneumococcal Disease

North America (37,868 infants), RCT 3+1-dose series

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pnc-CRM7</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meningitis</td>
<td>–</td>
<td>5 (1 died)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Bacteremic pneumonia</td>
<td>1</td>
<td>8 (1 died)</td>
</tr>
<tr>
<td>Bacteremic cellulitis</td>
<td>–</td>
<td>1</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>1</td>
<td>29</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>49 (2)</td>
</tr>
</tbody>
</table>

Vaccine-serotype IPD 97.4% (95% CI: 82.7 to 99.9%)

Pneumococcal conjugate vaccine and nasopharynx: Overall pneumococcal carriage remains similar
The USA experience after 2000
Rates of invasive pneumococcal disease among children <5 years, 1998-2007

Overall

2007 vs. baseline
All Serotypes: -76% (-79, -73)

22-25 cases per 100,000

Estimated using annual variability between 2003-08

Courtesy C. Whitney, CDC
Rates of invasive pneumococcal disease among children <5 years, 1998-2007

2007 vs. baseline
PCV7 Types: -99% (-100,-99)

PCV7 introduction

<1 case per 100,000

Courtesy C. Whitney, CDC
Rates of invasive pneumococcal disease among children <5 years, 1998-2007

PCV7 introduction

2007 vs. baseline
Non-Vaccine Types: +37% (+14,+64)

23 cases per 100,000

Courtesy C.Whitney, CDC
Serotype 19A up to 40% of invasive pneumococcal disease among children <5 years, 1998-2007

Overall PCV7 type non-Vaccine type 19A

2007 vs. baseline

19A: +312% (+178,+511)

11 cases per 100,000

C. Whitney, CDC
Gepresenteerd op de 2de Nederlandse Infectieziektendag
Zeist, 14 juni 2011
Rates of IPD caused by all serotypes among adults ≥65 years-old, ABCs 1998-2008

2008 vs. Average 1998-99

Percent change (95% CI)

PCV7: -93 (-91, -95)
NVT: +33 (+11, +60)*
All: -42 (-37, -47)

*Estimated using annual variability between 2003-08
Indirect Herd effect in other age groups
IPD Case rate in adults (ABCs 1998-2007)

Lexau et al. JAMA 2004 and unpublished data
USA herd effect → PCV7 cost-effective in The Netherlands (2005 report of Health Council)
Rijksvaccinatieprogramma, kinderen geboren van 1 April 2006: 3+1 schema. géén “catch-up”

<table>
<thead>
<tr>
<th>Fase</th>
<th>Leeftijd</th>
<th>Injectie 1</th>
<th>Injectie 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fase 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 maanden</td>
<td>HepB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 maanden</td>
<td>DKTP-Hib</td>
<td>PCV-7</td>
<td></td>
</tr>
<tr>
<td>3 maanden</td>
<td>DKTP-Hib</td>
<td>PCV-7</td>
<td></td>
</tr>
<tr>
<td>4 maanden</td>
<td>DKTP-Hib</td>
<td>PCV-7</td>
<td></td>
</tr>
<tr>
<td>11 maanden</td>
<td>DKTP-Hib</td>
<td>PCV-7</td>
<td>MenC</td>
</tr>
<tr>
<td>14 maanden</td>
<td>BMR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fase 2</td>
<td>4 jaar</td>
<td>DKTP</td>
<td></td>
</tr>
<tr>
<td>Fase 3</td>
<td>9 jaar</td>
<td>DTP</td>
<td></td>
</tr>
</tbody>
</table>

Gepresenteerd op de 2de Nederlandse Infectieziektendag Zeist, 14 juni 2011
Invasive pneumococcal disease in the Netherlands 2010
Number of Dutch IPD cases in children <5 years of age, stratified according to PCV7-vaccine and non-vaccine serotypes.

Data based on IPD cases from 9 sentinel lab’s that cover ~25% of Dutch population

De Greeff et al, ESPID June 2011
Number of IPD cases in persons >5 years of age, stratified according to the PCV-7 and non-PCV7 serotypes.

Data based on IPD cases from 9 sentinel lab’s that cover ~25% of Dutch population.

De Greeff et al, ESPID June 2011
UK PCV-7 Experience; England & Wales 2006-2010
Cumulative number of PCV-7-VT-IPD cases in children <2 yrs (HPA) June 2004/5 – July 2010

September 2006:
PCV-7: 2+4+13 months
Catch up: 1 dose for <2 year

August 5, 2010 http://www.hpa.org.uk
Cumulative number of Non-PCV-7 vaccine IPD cases in children <2 yrs 2003/4- March 2010

September 2006:
PCV-7: 2+4+13 months
Catch up: 1 dose for <2 year

Reference: http://www.hpa.org.uk
IPD incidence in England and Wales by serotype: children < 5 yrs old (2/4/13 month schedule) in 2009

Change 2008/9 vs 2005/6;  All IPD - 40% (-48, -30)
VT -92% (-94, -89);  NVT +88% (+23, +187)

Change 2008/9 vs predicted incidence in 2008/9;  All IPD -51% (-60, -41)
VT -93% (-95, -90);  NVT +35% (-22, +134)

Courtesy Liz Miller, HPA
IPD incidence PCV-7 VT- and NVT-IPD cases in persons >65 yrs

England and Wales 65+ yrs olds

Change 2008/9 vs 2005/6; All IPD -5% (-83, +8)
VT -59% (-65, -53); NVT +47% (+22, +78)

Courtesy Liz Miller, HPA
Invasive pneumococcal disease rates per 100,000 according to age in the pre-PCV-7 years


www. HPA data ; Rodenburg et al. Emerging Infect dis 2010
Incidence of invasive pneumococcal disease in children aged <5 years after PCV7 introduction

<table>
<thead>
<tr>
<th>IPD &lt; 5 years</th>
<th>USA 98/99 vs 06/07</th>
<th>England and Wales (2004/05 vs 08/09)</th>
<th>Netherlands 2004/06 vs 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>All IPD</td>
<td>-76%</td>
<td>- 40% (-51% **)</td>
<td>-60%</td>
</tr>
<tr>
<td>All VT-IPD</td>
<td>-99%</td>
<td>- 92%</td>
<td>-92%**</td>
</tr>
<tr>
<td>All NVT IPD</td>
<td>+37%</td>
<td>+ 88% (+35% **)</td>
<td>+22%**</td>
</tr>
<tr>
<td>All IPD hospitalized *</td>
<td>-59%</td>
<td>-40%</td>
<td>-60%</td>
</tr>
<tr>
<td>NVT hospitalized *</td>
<td>+102%</td>
<td>+ 88%</td>
<td>+22%**</td>
</tr>
<tr>
<td>NVT meningitis</td>
<td>+78%</td>
<td>+91%</td>
<td>+45%**</td>
</tr>
<tr>
<td>NVT non-hospitalized</td>
<td>- 9%</td>
<td>?</td>
<td>?</td>
</tr>
</tbody>
</table>

* Pilishvili et al. JID 2010

** after corrections for trends in time

*** preliminary data
IPD incidence in England and Wales without (A) and with adjustments for trends in case ascertainment (B)

After adjustments overall IPD in all ages 2009/2010 is 10.6 per 100,000 versus 16.1 per 100,000 in 2000-2006. Overall reduction all ages 33%

Miller et al, Lancet 2011, May 27
Pneumococcal meningitis between 1998/99 and 2004/05 (all ages, USA)

Decline in meningitis < 5 years in 2004-5 vs 98/99 is -60%

Hsu et al. NEJM 2009
Key points

• Despite replacement disease, overall reduction in IPD in children in developed countries with mature PCV7 programmes is still substantial (50%-60%)

• Hospitalised IPD cases in UK and meningitis in USA benefit by 30% (all ages)

• The decline in UK IPD is estimated to be 19% versus 42% in the USA

• In the Netherlands the vaccine benefit in individuals >5 yrs of age appears low due to replacement by NVT serotypes
Comorbidity at age 50-64 yrs
Invasive pneumococcal disease among adults 50-64 years with and without chronic illnesses (PPV23 indications)

C. Whitney, CDC, 2010

Gepresenteerd op de 2de Nederlandse Infectieziektendag
Zeist, 14 juni 2011
Similar incidence of invasive pneumococcal disease among 50-64 year olds with any ACIP indication

PCV7 licensed

C. Whitney, CDC, 2010
Key points IPD in adults

- Vaccinating young children shifts serotypes causing disease in adults

- Overall indirect benefit in USA adults for invasive disease
  - General population young adults, 65+
  - The Netherlands individuals > 5 years less (-5%)

- Benefits also not demonstrated also in USA for adult
  - Noninvasive pneumonia
  - Chronically ill baby boomers
Are replacing serotypes predictable by carriage monitoring?
Serotype distribution in US pre- and post-PCV7 (all ages)

Dramatic change in serotype distribution in post-PCV7 era

USA: 19A, 7F, (3), 22F
UK: 19A, 7F, 22F, 1
NL: 1, 19A, 22 F
Randomised controlled study PCV-7 in 1000 infants age 6 months-24 months

Cumulative carriage of 19A in 848 children

Cumulative proportion with 19A acquisition

* P < 0.05 versus unvaccinated controls

- 2+1-dose group
- 2-dose group
- control group

Van Gils et al. JAMA, Sept 8, 2010:

Randomised controlled study PCV-7 in 1000 infants age 6 months-24 months

Cumulative carriage of 19A in 848 children

Van Gils et al. JAMA, Sept 8, 2010:

Gepresenteerd op de 2de Nederlandse Infectieziektendag Zeist, 14 juni 2011
Sequence type distribution of serotype 19A in carriage in unvaccinated controls and PCV-7 vaccinated children and 19A IPD cases in children aged 0-2 years in 2005-2008

Nasopharynx controls

Nasopharynx PCV-7 vaccinees

19A IPD in children

Van Gils et al. JAMA Sept 8, 2010
Pneumococcal carriage monitoring in the Netherlands pre-PCV7, after 3 and 4.5 years in children and adults

* p-value <0.05 vs unvaccinated
Colonizing serotypes before, after 3 and 4.5 years following PCV7 introduction in Dutch NIP in groups of 330 children aged 24 months

Serotypes 1 and 7F are invasive serotypes and almost not encountered in carriage studies

Gepresenteerd op de 2de Nederlandse Infectieziektendag
Zeist, 14 juni 2011
UK IPD between 2000-2010; Increase of 7F, 19A, 22F. Decrease of 8, 9N and decrease of 1 in 5-64 and ≥65 years.

Liz Miller, Lancet 2011
Do all serotypes cause similar disease/mortality?
Serotype-dependent mortality in Denmark 1937-2007 in persons > 5 years without comorbidity

Multivariate logistic regression analysis of serotype-specific 30-d mortality associated with IPD in patients aged 5 y or older with low comorbidity level (Charlson 0) (n=9,059).

OR estimates controlled for age (in years), sex, IPD focus (meningitis or bacteremia), time at diagnosis (in decades), alcoholism-related conditions. The reference group was patients with IPD caused by serotype 1 in each group. ORs were calculated for serotypes with ≥50 IPD cases only.

Next generation Pneumococcal conjugate vaccines
## Serotype composition of pneumococcal conjugate vaccines

<table>
<thead>
<tr>
<th></th>
<th>7-valent</th>
<th>10-valent</th>
<th>13-valent</th>
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<tbody>
<tr>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>6B</td>
<td>6B</td>
<td>6B</td>
<td>6B</td>
</tr>
<tr>
<td>9V</td>
<td>9V</td>
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<td>14</td>
<td>14</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td>18C</td>
<td>18C</td>
<td>18C</td>
<td>18C</td>
</tr>
<tr>
<td>19F</td>
<td>19F</td>
<td>19F</td>
<td>19F</td>
</tr>
<tr>
<td>23F</td>
<td>23F</td>
<td>23F</td>
<td>23F</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>7F</td>
<td></td>
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<td>7F</td>
</tr>
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<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>6A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>19A</td>
</tr>
</tbody>
</table>

- Poly-or oligosaccharides
- Geconjugeerd aan een dragereiwit
- Vaccinatie leidt tot serotype-specifieke bescherming
Number of IPD cases in children <5 years of age, stratified according to the serotypes covered by the different conjugated vaccines. (June 04-June 2010)
Number of IPD cases in persons >5 years of age, stratified according to the serotypes covered by the conjugated vaccines.
Summary

- In a general population of children vaccine benefit vastly outweighs replacement disease.

- For adults, studies of overall indirect benefits are mixed:
  - Yes USA, Australia, UK
  - No Netherlands, Canada, Indigenous populations, chronically ill US adults

- 19A main (only?) significant replacement strain? What about 22F? 15B/C?
Unanswered questions

• How do we sort out the contribution of vaccination from other factors that drive serotype change?

• What will happen in developing countries?

• What will be the effect of next generation conjugate vaccines?
  • What will happen to highly invasive serotypes like 1 and 7F with respect to disease and herd effects?

• What will happen to other colonizing bacteria like *H. influenzae* or *Staphylococcus aureus*?
Participating families
Cooperating Entadministraties
Cooperating well-baby clinics

Financiering: Ministerie van Volksgezondheid, Welzijn en Sport
**S. Aureus** more in spontaneous draining ears in PCV-7 vaccinated children with recurrent otitis media

RCT in The Netherlands to study effect of PCV7 on recurrent OMA

<table>
<thead>
<tr>
<th></th>
<th>Pneumococcal vaccination</th>
<th>Control vaccination</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of children with at least one AOM episode</td>
<td>107</td>
<td>101</td>
<td></td>
</tr>
<tr>
<td>Number of AOM episodes at which MEF obtained</td>
<td>92</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>MEF obtained by</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous drainage</td>
<td>71</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Myringotomy</td>
<td>21</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Culture confirmed as</td>
<td>13</td>
<td>19</td>
<td>0.22</td>
</tr>
<tr>
<td><em>S pneumoniae</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCV7 pneumococcal serotypes</td>
<td>4</td>
<td>8</td>
<td>0.21</td>
</tr>
<tr>
<td>Other pneumococcal serotypes</td>
<td>9</td>
<td>11</td>
<td>0.44</td>
</tr>
<tr>
<td><em>H influenzae</em></td>
<td>21</td>
<td>23</td>
<td>0.64</td>
</tr>
<tr>
<td><em>M catarrhalis</em></td>
<td>8</td>
<td>6</td>
<td>0.62</td>
</tr>
<tr>
<td>Group A streptococcus</td>
<td>6</td>
<td>4</td>
<td>0.75</td>
</tr>
<tr>
<td>Negative cultures</td>
<td>32</td>
<td>35</td>
<td>0.53</td>
</tr>
<tr>
<td>Others (all from spontaneously draining ears)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>P aeruginosa</em></td>
<td>9</td>
<td>6</td>
<td>0.46</td>
</tr>
<tr>
<td><strong>S aureus</strong></td>
<td>26</td>
<td>9</td>
<td><strong>0.002</strong></td>
</tr>
</tbody>
</table>

MEF=middle ear fluid.
Higher colonization rates of *S. aureus* after PCV7 implementation

- *S. aureus* doubled at 11 months in randomised controlled trial (reduced doses)
- *S. aureus* increased 4.5 years after 3+1 PCV7 introduction

**Parents**

<table>
<thead>
<tr>
<th>PCV7</th>
<th>12 mo</th>
<th>24 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Co</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>2+1</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PCV7</th>
<th>11 mo</th>
<th>24 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre</td>
<td>3y</td>
<td>4.5 y</td>
</tr>
<tr>
<td>Post</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Post</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>

*van Gils et al. PlosOne 2011 (in press)*
Carriage of *S. aureus* doubles at 12 months in PCV7 vaccinated children as compared to controls: Dutch Randomized Control Trial

S. aureus in NP swabs before and after 3 and 4.5 yrs following introduction of PCV7 in Dutch NIP

Nasopharyngeal S. Aureus

Parents

Infants

11 months
24 months

Carriage (%)

Pre 3y Post 4.5y Post

Pre 3y Post 4.5y Post

Pre 3y Post 4.5y Post

0 10 20 30 40

11 Months 24 Months Parents

* aOR >1 compared to controls
S. aureus one of the dominant bacterial pathogens in severe respiratory infections in young children

Mahdi SA et al; CID July 2000

Gepresenteerd op de 2de Nederlandse Infectieziektendag
Zeist, 14 juni 2011
Research questions

- What is the effect of < 4 times PCV-7 injections on nasopharyngeal pneumococcal carriage
  - *Herd effect*
  - *Replacement by other non-vaccine serotypes*
- What is the effect of PCV-7 vaccinations on other nasopharyngeal bacteria/pathogens?
- What happens with co-morbidity?
- What happened after introduction of PCV-7 in Europe with invasive disease?
- What can we expect from new vaccines?
Carriage of *S.pneumoniae* serotypes in vaccinated children at 11-12 and 24 months of age before and three years after introduction of 3+1 PCV7

*P* <0.05 compared to control group
Overall IPD in ≥ 65 year olds from 34.8 to 28.2 per 100,000 (−19%)

VT –IPD -81%
NVT-IPD + 48%
Increase of 7F, 19A, 22F
Decrease of 8, 9N and decrease of 1 in 5-64 and ≥65 years
Carriage of PCV7 versus non-PCV7 serotypes in vaccinated children and their parents before and three years after introduction of 3+1 PCV7

* P <0.05 compared to control group
Carriage of \textit{S.aureus} is significantly higher in parents of vaccinated children three years after introduction of PCV7.
Carriage of *H. influenzae* is significantly higher in vaccinated children at 11-12 and 24 months and their parents three years after introduction of 3+1 PCV7.
Carriage of *M. Cattharalis* in vaccinated children at 11-12 and 24 months and their parents three years after introduction of 3+1 PCV7
Pneumococcal colonization 3 and 4.5 yrs after introduction of PCV7 in Dutch NIP

* aOR >1< compared to controls
H. influenzae colonization 3 and 4.5 yrs after introduction of PCV7 in Dutch NIP

aOR >1 compared to controls
M. catarrhalis colonization 3 and 4.5 yrs after introduction of PCV7 in Dutch NIP

* aOR >1 compared to controls
USA versus Europe

- USA IPD-rates in USA <2 yrs 188/100.000 versus 35-60/100.000 in the UK and The Netherlands (hospitalized children only, ≠ blood culture practices)
- Rates for meningitis more similar
- Coverage for 7 vaccine serotypes USA (80%) compared to Europe (60-70%)
- Differences in vaccine uptake?
  - Period of vaccine shortage in USA 2001-2003
- Surveillance (reduced in USA versus enhanced in UK following PCV7 introduction?)
Comparison of pre and post IPD non-vaccine type (NVT) incidence and % change in < 5 year olds by country

**USA versus England & Wales**

<table>
<thead>
<tr>
<th>Country</th>
<th>Outcome</th>
<th>Pre-PCV7</th>
<th>Post-PCV7</th>
<th>% change</th>
</tr>
</thead>
<tbody>
<tr>
<td>US ABC</td>
<td>All NVT IPD</td>
<td>16.8</td>
<td>22.1</td>
<td>+32%</td>
</tr>
<tr>
<td>1998/9 vs 2006/7</td>
<td>Outpatient</td>
<td>10.7</td>
<td>9.7</td>
<td>NS (-9%)</td>
</tr>
<tr>
<td>Pilishvili et al JID 2010</td>
<td>Hospitalised</td>
<td>6.1*</td>
<td>12.3</td>
<td>+102%</td>
</tr>
<tr>
<td></td>
<td>Meningitis</td>
<td>0.9</td>
<td>1.6</td>
<td>+78%</td>
</tr>
<tr>
<td>E&amp;W</td>
<td>All NVT IPD</td>
<td>7.8*</td>
<td>14.5</td>
<td>+86%*</td>
</tr>
<tr>
<td>average 2004/5 &amp;2005/6 vs 2008/9</td>
<td>Meningitis</td>
<td>1.1</td>
<td>2.1</td>
<td>+91%</td>
</tr>
</tbody>
</table>

* % less if corrected for upward trend in reporting

Overall reduction in hospitalised IPD in ABC surveillance 59%

Courtesy of Liz Miller, HPA
Comparison of pre and post IPD non-vaccine type (NVT) incidence and % change in < 5 year olds by country

**USA versus England & Wales**

<table>
<thead>
<tr>
<th>Country</th>
<th>Outcome</th>
<th>Pre-PCV7</th>
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<th>% change</th>
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<tbody>
<tr>
<td><strong>US ABC</strong></td>
<td>All NVT IPD</td>
<td>16.8</td>
<td>22.1</td>
<td>+32%</td>
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<tr>
<td>1998/9 vs 2006/7</td>
<td>Outpatient</td>
<td>10.7</td>
<td>9.7</td>
<td>NS (-9%)</td>
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<tr>
<td>Pilishvili et al JID 2010</td>
<td>Hospitalised NVT IPD</td>
<td>6.1*</td>
<td>12.3</td>
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<td>Meningitis</td>
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<td><strong>E&amp;W</strong></td>
<td>Hospitalized NVT IPD</td>
<td>7.8*</td>
<td>14.5</td>
<td>+86%*</td>
</tr>
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<td>E&amp;W average 2004/5 &amp;2005/6 vs 2008/9</td>
<td>Meningitis</td>
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<td>2.1</td>
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* % less if corrected for upward trend in reporting

ABC in USA overall reduction in *hospitalized* IPD 59%

**Gepresenteerd op de 2de Nederlandse Infectieziektendag Zeist, 14 juni 2011**

**Courtesy of Liz Miller, HPA**
Comparison of pre and post IPD non-vaccine type (NVT) incidence and % change in < 5 year olds by country

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<td>Australia 2002/4</td>
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Overall reduction in hospitalised IPD in ABC surveillance 59%

Courtesy Liz Miller, HPA
Estimated IPD incidence by serotype; children <2 years, 2001–2006

France

19A replacement
Capsule size is related to survival from phagocytosis (data not shown)

Capsule size is associated with #carbons/repeat unit (metabolic cost)
# carbons is related to carriage prevalence pre and post PCV-7

Weinberger D, Trzcinski K et al. PLoS Path 2009
Serotype dependent mortality is related to metabolic costs (carbons per polysaccharide unit) and capsule size in persons > 5 yrs

Carbos per polysaccharide unit versus severity of IPD for PCV-13 serotypes (Weinberger vs Harboe's ranks)

Weinberger and Trzcinski et al. PLoS Path 2009
Annual number of serotypes pre PCV7 (average 2004/5 & 2005/6) Vs post-PCV7 year 2008/9 by vaccine category < 5 year olds: England and Wales
Invasive pneumococcal disease in adults 18-64 years with HIV infection

All types -39%
Nonvaccine +48%
PCV7 -89%
Related -21%

A. Cohen poster P3.092
Comparison of pre and post IPD non-vaccine type (NVT) incidence per 100,000 and % change in < 5 year olds by country: *USA versus England & Wales*

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Overall reduction in hospitalised IPD in ABC surveillance 59%

*Courtesy of Liz Miller, HPA*
IPD incidence in UK before and after PCV7 in different age groups

Average adjusted incidence

< 2 yr
2-4 yr
5-14 yr
15-44 yr
45-64 yr
≥ 65 yr
All ages

PCV7 serotypes
Non-PCV7 serotypes

Courtesy E. Miller