Pneumococcal vaccination in UK: an update

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Immunisation Department
Health Protection Agency Centre for Infections
Leading infectious causes of mortality, 2000 WHO estimates

**Deaths (millions)**

<table>
<thead>
<tr>
<th>Cause</th>
<th>&lt; 5 years old</th>
<th>&gt; 5 years old</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumonia</td>
<td>3.5</td>
<td>2.7</td>
</tr>
<tr>
<td>AIDS</td>
<td>2.2</td>
<td>1.7</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>2.2</td>
<td>1.1</td>
</tr>
<tr>
<td>TB</td>
<td>1.7</td>
<td>0.9</td>
</tr>
<tr>
<td>Malaria</td>
<td>1.1</td>
<td>0.9</td>
</tr>
<tr>
<td>Measles</td>
<td>0.9</td>
<td></td>
</tr>
</tbody>
</table>

**S. pneumoniae:**

~1.6 million deaths, including ~800,000 child deaths

Source: WHO
Inability to mount immune response to capsule

Waning immunity
Non-immune factors
Burden of Pneumococcal disease
Hospital Episode Statistics (HES) England

Source: Melegaro et al
Proportion of hospitalised pneumococcal cases reporting co-morbidity (1, 2-4 and 5+ diagnoses)

Source: Melegaro et al
Case-fatality ratio by age of IPD, pneumococcal pneumonia and lobar pneumonia

Source: Melegaro et al
Burden of Pneumococcal disease

GP consultation rate for CAP and OM

Source: Melegaro et al
Pneumococcal polysaccharide vaccine

Produced from purified capsular polysaccharide;
Current vaccine contains 23 of the serotypes responsible for disease;

Protects against invasive disease:
– BUT
– poor antibody responses in young children;
– do not induce immunologic memory, short term protection;
– hyporesponsiveness on revaccination
– do not protect against non-invasive diseases e.g. otitis media;
– do not reduce nasopharyngeal carriage.
Pneumococcal conjugate vaccines

Pneumococcal conjugate vaccine contains 7 of the serotypes responsible for disease;
Seek to prevent invasive and non-invasive (pneumonia and otitis media) disease.

• effective in young children;
• induce long-term memory;
• reduce Pnc carriage and induce herd immunity.
Coverage of vaccine serotypes in England and Wales by age: 7-valent conjugate and 23-valent polysaccharide vaccine

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>&lt;5yrs</th>
<th>5-64 yrs</th>
<th>64+ yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-valent</td>
<td>74.2</td>
<td>42.3</td>
<td>55.4</td>
</tr>
<tr>
<td></td>
<td>(85.8)</td>
<td>(51.2)</td>
<td>(66.9)</td>
</tr>
<tr>
<td>23-valent</td>
<td>97.4</td>
<td>96.2</td>
<td>96.3</td>
</tr>
</tbody>
</table>

Figures in ( ) based on assumption of full cross protection between serotypes within serogroups.
Evolution of pneumococcal vaccination strategy in England and Wales

Polysaccharide vaccine (23-valent) licensed in 1989:
1992 until 2003 recommended for risk groups ≥2 year olds
post 2003 also recommended for elderly (≥65 years)

Conjugate vaccine (7-valent) licensed in 2001:
post 2002 recommended for risk groups <2 years old
post 2004 recommended for risk groups <5 years old
post 2006 recommended for all infants
Risk groups for whom vaccine indicated

- asplenics (including sickle cell & coeliac disease);
- chronic lung disease;
- chronic heart disease;
- chronic renal disease;
- chronic liver disease (including cirrhosis);
- diabetes mellitus;
- immunocompromised (disease or treatment);
- HIV infection (at any stage);
- persons with cochlear implants.
Meta-analysis of polysaccharide vaccine efficacy for IPD (Melegaro et al. 2004)

Little or no evidence of efficacy against pneumonia (not shown)

Limited evidence for efficacy against IPD in non-high risk individuals (left-hand panel & other studies)

Little or no evidence of efficacy against IPD in high risk population (right hand panel)
Polysaccharide vaccine coverage in high-risk population and all elderly >65 years, General Practice Research Database, 1989-2003
New polysaccharide programme for the elderly, England and Wales

from 20th August 2003:
all people ≥ aged 80 years

from 1st April 2004:
extended to all ≥ aged 75 years

from 1st April 2005:
extended to all ≥ aged 65 years
Enhanced pneumococcal surveillance

PPV coverage:

• 10 year historical coverage & previous 12 months uptake from GPs
  – From August 2004 for 80+
  – From April 2005 for 75-79
  – From April 2006 for 65-74

Enhanced IPD surveillance:

• All serotyped IPD cases followed with GP to ascertain:
  - immunisation history;
  - outcome of infection;
  - underlying risk factors.
US pneumococcal conjugate vaccine efficacy trial: 2/4/6 months + 12 month booster

PCV efficacy against

- Invasive disease vaccine serotypes (ST) 97.4%
- Invasive disease vaccine ST 1+ dose 85.7%
- Lobar pneumonia 73%
- Any pneumonia with abnormal CXR 33%
- Any otitis media episode 8.9%
- Recurrent OM 11.9%
- Ear tube placement 20.1%
Finnish Prevenar Efficacy Trial against Serotype-specific Culture-confirmed Acute Pneumococcal Otitis Media (AOM) in Infants and Children

<table>
<thead>
<tr>
<th>Condition</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodes due to vaccine related serotypes</td>
<td>51% (27 to 97)</td>
</tr>
<tr>
<td>Any culture confirmed pneumococcal AOM</td>
<td>34% (21 to 45%)</td>
</tr>
<tr>
<td>AOM irrespective of aetiology</td>
<td>6% (-4 to 16%)</td>
</tr>
<tr>
<td>Episodes due to non-vaccine serotypes</td>
<td>-33% (-80 to 1)</td>
</tr>
</tbody>
</table>

Eskola J, et al NEJM 2001
Invasive Pneumococcal Disease Rates by Age and Year
Children <5 Years, ABCs, 1998-2003

2003 vs baseline
- 77% (<1 yr)
- 83% (1 yr)
- 64% (2 yr)
- 60% (3 yr)
- 48% (4 yr)

Source: ABCs (August 2003), Observed Rates
Sites: CA (SF co), CT, GA (20 co), MD (6 co), MN (7 co), NY (7 co), OR (3 co)
Design of infant trial, UK
PCV/PPV given concomitantly with DTaP₃/Hib-TT + MCC- CRM

9V Conj at 2mths

9V Conj at 3 mths

9V Conj at 4 mths

23V Poly at 1yr

9V Conj at 1yr
Serotype-specific IgG GMCs after 3 doses (at 2/3/4 months) or 2 doses (at 2 and 4 months) of conjugate in UK infants compared with USA schedule*

Source: Miller et al.

*Data from Black et al PIDJ 2000
Vaccination schedule in the UK 2006

Primary immunisation

2 months
Diphtheria-tetanus-acellular pertussis, inactivated polio vaccine and *Haemophilus influenzae* type b

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>2 months</th>
</tr>
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<tbody>
<tr>
<td>DTaP-Hib-IPV</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal conjugate vaccine</td>
<td></td>
</tr>
<tr>
<td>PCV</td>
<td></td>
</tr>
</tbody>
</table>

3 months
Diphtheria-tetanus-acellular pertussis, inactivated polio vaccine and *Haemophilus influenzae* type b

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP-Hib-IPV</td>
<td></td>
</tr>
<tr>
<td>Meningococcal group C conjugate</td>
<td></td>
</tr>
<tr>
<td>MenC</td>
<td></td>
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</tbody>
</table>

4 months
Diphtheria-tetanus-acellular pertussis, inactivated polio vaccine and *Haemophilus influenzae* type b

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>4 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTaP-Hib-IPV</td>
<td></td>
</tr>
<tr>
<td>Meningococcal group C conjugate</td>
<td></td>
</tr>
<tr>
<td>MenC</td>
<td></td>
</tr>
<tr>
<td>Pneumococcal conjugate vaccine</td>
<td></td>
</tr>
<tr>
<td>PCV</td>
<td></td>
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13 months
Measles-mumps-rubella

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>13 months</th>
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</thead>
<tbody>
<tr>
<td>MMR</td>
<td></td>
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</table>
Vaccination schedule in the UK 2006
(continued)

**Booster immunisation**

12 months

*Haemophilus influenzae* type b – Hib-MenC
Meningococcal group C conjugate

13 months

**Pneumococcal conjugate vaccine** PCV

3½-5 years

Diphtheria-tetanus-acellular pertussis DTaP-IPV or dTaP/IPV
and inactivated polio vaccine

Measles-mumps-rubella MMR

13-18 years

Tetanus-low dose diphtheria Td-IPV
and inactivated polio vaccine
Cumulative Weekly Number of Reports of Invasive Pneumococcal Disease Due To One of the Serotypes Not Present in Prevenar™ for Children Aged 0 - 2 Years in England and Wales by Epidemiological Year: July - June (2003 to Date)
Cumulative Weekly Number of Reports of Invasive Pneumococcal Disease Due To One of the Seven Serotypes Present in Prevenar™ for Children Aged 0-2 Years in England and Wales by Epidemiological Year: July-June (2003 to Date)
Current issues

Impact and effectiveness of current programme
Pneumococcal clusters
Emergence of non-7-valent PCV serotypes
Pneumococcal vaccine development:
- 10-valent and 13-valent vaccines in advanced stages of testing
- At least one ‘common protein’ candidate approaching large-scale clinical evaluation
Acknowledgments

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