Introduction

*Streptococcus pneumoniae* (*S. pneumoniae*, pneumococcus) is an important cause of serious infection, especially in young children, older adults and immunocompromised people. Invasive pneumococcal disease (IPD) is an illness characterized by the presence of *S. pneumoniae* in a normally sterile site (e.g. blood, cerebrospinal fluid, joint fluid or pleural fluid).

IPD mainly occurs in children under 5 years and those aged ≥65 years. Individuals with severe chronic disease or immunodeficiency are also at increased risk of this disease. Non-invasive manifestations of *S. pneumoniae* related disease include otitis media, sinusitis and bronchitis, i.e. mucosal infections.

Although more than 90 polysaccharide capsular serotypes of pneumococci are known, most infections are caused by a limited number of serotypes. The fact that relatively few serotypes cause most invasive disease has aided the development of effective vaccines. Following the introduction of pneumococcal conjugate vaccines into national programmes in Europe a marked decrease in the serotypes included in the pneumococcal conjugate 7
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and 13 (PCV7 and PCV13) vaccines occurred. In 2017 (January - September), the 10 most commonly implicated serotypes in Ireland were 8, 12, 19A, 22F, 15A, 9N, 3, 24F, 33F and 11A (in order of frequency).

Epidemiology

Pneumococcal infection is a leading cause of death worldwide. Mortality is highest in those who develop sepsis or meningitis. Pneumococcal meningitis case fatality rates of 11-16% were reported in Ireland between 2008—2016. Transmission is from person to person by droplet infection or direct contact with respiratory secretions of someone carrying the organism. Infection can occur at any time throughout the year but rates peak during the winter months (Figure 16.1).

Figure 16.1 Invasive pneumococcal disease (IPD) notifications in Ireland by month, 2007–2017. (Data for 2017 is provisional).
Source: HPSC

Each year the age specific incidence rates (ASIR) are highest among the elderly and young children. A decline in ASIR in the youngest age groups is evident in recent years (Figure 16.2).
PCV7* was introduced into the routine primary immunisation schedule in September 2008, with a catch up programme for children under 2 years of age. Since then the burden of notified confirmed cases of IPD has been reduced by 4%. The greatest reduction have been seen in young children, particularly in those aged <5 years (Figure 16.2). The decrease in this age group can largely be attributed to a 98% decline in IPD due to serotypes covered by PCV7 between 2008 (46 cases) and 2016 (1 case) (Figure 16.3). A decline of 50% in notifications of disease caused by the additional serotypes in PCV13 was also observed.

In December 2010 PCV13** vaccine replaced PCV7 in the Irish childhood immunisation programme. PCV13 includes antigens from the seven serotypes contained in PCV7 plus six additional serotypes.

Pneumococcal conjugate vaccines reduce the rates of nasopharyngeal colonisation by vaccine serotypes, thus decreasing the potential for transmission from vaccinated to unvaccinated persons.

*PCV 7 serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F
**PCV 13 serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19 A, 19F, 23F
Cases of non-PCV vaccine serotypes have increased in those aged >65 years from 2008 - 2016 (Figure 16.4).

**Clinical Manifestations**

Pneumococcal infection is the most common cause of bacteraemia, septicaemia, bacterial meningitis, pneumonia, sinusitis, and acute otitis media in children. It can also cause periorbital cellulitis, endocarditis, pericarditis, peritonitis, and soft tissue, bone and joint infection.
Pneumococcal meningitis case fatality rates of 11-16% were reported in Ireland in the years 2008-2016.

Transmission is from person to person by droplet infection or direct contact with respiratory secretions of someone carrying the organism. The incubation period varies by site of infection, and can be as short as 1-3 days.

**Management of cases, contacts, and outbreaks**

*Cases of invasive pneumococcal disease (IPD)*

Any case of invasive pneumococcal infection or lobar pneumonia believed to be due to *S. pneumoniae* should prompt a review of the patient’s history to establish whether they are in a risk group and have been vaccinated.

Unvaccinated at-risk patients should be offered pneumococcal vaccine (see section on recommendations for the use of pneumococcal vaccination).

All children under 5 years of age who have had IPD, even if not in a clinical risk group, should receive a dose of PCV13 irrespective of vaccine history followed by a dose of PPV23 2 months later (at or after 2 years of age).

*Contacts of cases*

Antibiotic prophylaxis is not indicated for close contacts of a case of invasive pneumococcal disease as such contacts are not normally at increased risk of pneumococcal infection. Clusters of invasive pneumococcal disease should be discussed with local Specialists in Public Health Medicine.

*Outbreaks*

Outbreaks of pneumococcal infection in institutional settings need prompt investigation. Control measures, including vaccination, may be appropriate; they should be discussed with local health-protection or infection-control teams.
Pneumococcal vaccines
There are two types of pneumococcal vaccine.

- **Pneumococcal conjugate vaccines (PCV)** contains polysaccharide antigens from 10 (PCV 10) or 13 (PCV 13) serotypes* conjugated to a protein. These have enhanced immunogenicity to their constituent antigens compared with the polysaccharide vaccine, with a better antibody response. They are immunogenic from 6 weeks of age. Conjugate vaccines are active against 75-90% of serotypes causing IPD in children, including a significant number of penicillin-resistant strains.

Conjugate vaccines induce higher affinity antibodies, longer-lasting antibody and memory responses, and booster vaccinations induce higher antibody levels.

- **Pneumococcal polysaccharide vaccine (PPV23)** contains purified capsular polysaccharide from 23 capsular types* of pneumococcus which account for up to 90% of IPD. It is indicated only for those ≥2 years of age, as an adequate antibody response does not develop in those <2 years of age.

An up-to-date list of authorised vaccines and SmPCs can be accessed on the HPRA website [www.hpra.ie](http://www.hpra.ie).

A list of vaccines currently available from the National Cold Chain Service can be found at [www.immunisation.ie](http://www.immunisation.ie)

Pneumococcal vaccines should be stored at +2 to +8°C.

**Dose and route of administration (PCV and PPV23)**
The dose is 0.5 ml given by intramuscular injection into the vastus lateralis muscle (anterolateral thigh) or the deltoid muscle.

**Recommendations**

1. **Primary and booster vaccination**
The course consists of 3 doses at 2, 6 and 13 months of age.
For children aged 6-< 24 months, if PCV and seasonal influenza vaccine are given at the same time, parents/carers should be advised of a small increased risk of fever and febrile convulsions. Separating the vaccines by one week may be advisable.

*Children aged ≥24 months* who are in particular at-risk groups should receive PCV (see Tables 16.1 and 16.2).

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* The following serotypes are contained in pneumococcal vaccines
  - **PCV10**: 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F
  - **PCV 13**: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F
  - **PPV23**: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, 33F
2. **Catch up vaccination**  
Children aged 12-<24 months of age who have not received PCV vaccine require 1 dose.

3. **Routine Adult Pneumococcal Vaccine**  
One dose of PPV23 is recommended for all aged 65 years and older.

4. **Vaccination of those at increased risk of pneumococcal infection**  
The following groups (Table 16.1) are at increased risk of invasive pneumococcal disease than the general population and often both PCV and PPV23 are recommended.

**Table 16.1: Conditions associated with an increased risk of invasive pneumococcal disease**

<table>
<thead>
<tr>
<th>High risk (Group A)</th>
<th>Medium risk (Group B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Asplenia, hyposplenia (including splenectomy, sickle cell disease, haemoglobinopathies, and coeliac disease)</td>
<td>• Children under 5 years of age following invasive pneumococcal disease</td>
</tr>
<tr>
<td>• Cancer patients under hospital supervision</td>
<td>• Chronic heart, lung, or liver disease</td>
</tr>
<tr>
<td>• Chronic renal disease or nephrotic syndrome</td>
<td>• Diabetes mellitus requiring insulin or oral hypoglycaemic drugs</td>
</tr>
<tr>
<td>• Cochlear implant candidates and recipients</td>
<td>• Down syndrome</td>
</tr>
<tr>
<td>• Complement deficiency (particularly C1-C4)</td>
<td>• Occupational exposure to metal fumes (i.e. welders)</td>
</tr>
<tr>
<td>• CSF leaks (congenital or complicating skull fracture or neurosurgery)</td>
<td>• Smokers and alcoholics</td>
</tr>
<tr>
<td>• Haematopoietic stem-cell transplant</td>
<td></td>
</tr>
<tr>
<td>• Immunosuppressive conditions (e.g. some B- and T-cell disorders, HIV infection, leukaemia, lymphoma), and those receiving immunosuppressive therapies(^1) or corticosteroids (see Chapter 3).</td>
<td></td>
</tr>
<tr>
<td>• Intracranial shunt</td>
<td></td>
</tr>
<tr>
<td>• Solid organ transplant</td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Individuals with primary immunodeficiency may have a suboptimal response to all vaccines. Pneumococcal vaccines are unlikely to be immunogenic in children with primary immune deficiencies involving significant B cell compromise who are receiving regular IVIG replacement therapy. However vaccination should be given as it may have some effect.

For vaccine types and schedule see Table 16.2.
## Table 16.2 Pneumococcal immunisation for those at increased risk of IPD

<table>
<thead>
<tr>
<th></th>
<th>High risk (Group A)</th>
<th>Medium risk (Group B)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PCV</strong>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>PPV23</td>
<td>PCV</td>
</tr>
<tr>
<td>6 weeks - &lt;24 months</td>
<td>Routine schedule</td>
<td>1 dose ≥2 years of age</td>
</tr>
<tr>
<td>2 - &lt;5 years</td>
<td>If unvaccinated, 2 doses</td>
<td>1 dose ≥2 months after PCV</td>
</tr>
<tr>
<td>5- &lt;18 years</td>
<td>If unvaccinated, 1 or 2 doses&lt;sup&gt;4&lt;/sup&gt;</td>
<td>1 dose ≥2 months after PCV</td>
</tr>
<tr>
<td>18 - &lt;65 years</td>
<td>1 or 2 doses&lt;sup&gt;3&lt;/sup&gt;</td>
<td>1 – 2&lt;sup&gt;5&lt;/sup&gt; doses ≥2 months after PCV</td>
</tr>
<tr>
<td>≥65 years</td>
<td>1 or 2 doses&lt;sup&gt;3&lt;/sup&gt;</td>
<td>1 dose ≥2 months after PCV</td>
</tr>
</tbody>
</table>

<sup>1</sup> HSCT recipients require 3 doses at 6, 8 and 12 months post-transplant

<sup>2</sup> 1 additional dose if had IPD, irrespective of vaccine history

<sup>3</sup> 2 doses 2 months apart if response may be blunted e.g. asplenia/ hyposplenia (see Chapter 3)

<sup>4</sup> If fully vaccinated with PCV7 give 1 dose of PCV13

<sup>5</sup> 2 doses 5 years apart if response may be blunted e.g. asplenia/ hyposplenia (see Chapter 3)

If both PCV and PPV23 are recommended, PCV should be given first, followed by PPV23 at least 2 months later. If PPV23 has been given first, wait at least 1 year before giving PCV.

Pneumococcal vaccination should if possible be completed ≥2 weeks prior to elective splenectomy or cochlear implant.

### 5. Cases of invasive pneumococcal disease (IPD)

Unvaccinated, or incompletely vaccinated, at-risk patients should be offered pneumococcal vaccine.

Following IPD in a child under 5 years of age, full blood count, immunoglobulin levels (including IgG sub classes) and complement levels should be checked.

All children aged <5 years who had IPD, even if not in a clinical risk group, should receive a further dose of PCV irrespective of vaccine history, followed by a dose of PPV23 two months later.
Booster doses of PPV23 (see Figure 16.5)

Booster doses are not recommended for immunocompetent people aged <65 years. The administration of a first dose of PPV23 may blunt the immune response to subsequent doses of both PPV23 and PCV13, such that antibody levels following a second vaccination, and possibly the magnitude of clinical protection, may be lower than following a first vaccination.

For individuals whose antibody levels are likely to decline more rapidly, (e.g. asplenia, hyposplenia, on immunosuppressants) one booster should be given 5 years after the first dose.

Adults aged ≥65 years should receive a dose of PPV23 if they received PPV23 more than 5 years previously and were less than 65 years of age at the time.

Those who received one dose of PPV23 at age ≥65 years should not receive a further dose regardless of immune status.

Contraindications (PCV13 and PPV23)
Anaphylaxis to any of the vaccine constituents.

Precautions (PCV13 and PPV23)
Acute severe febrile illness; defer until recovery.

If either vaccine has been given during chemotherapy or radiotherapy, revaccination ≥3 months after treatment is recommended (see Chapter 3).

PPV23 only: delay for at least 5 years after a previous dose of PPV23. Immunocompetent persons should only receive one dose of PPV23 before 65 years of age.

Pregnancy and breast feeding: Pneumococcal vaccines can be given to pregnant women in Group A, Table 16.1 if urgent protection is required. Breast-feeding women can be given either vaccine.
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Adverse reactions
A full list of adverse reactions may be found in the Summary of Product characteristics (SmPC). The following are common or very common adverse reactions.

PCV
Local: injection site pain, redness, swelling
General: fever

Diffuse swelling of the injected limb, sometimes involving the adjacent joint, may occur uncommonly.

PPV23
Local: injection site pain, tenderness, swelling, erythema
General: headache, tiredness, myalgia, fever, nausea, neck pain, upper respiratory infection, pharyngitis.

Immunisation (primary and revaccination) with PPV23 can result in moderate or severe pain and/or large induration at the injection site, especially if less than 5 years has elapsed since the first injection. Adverse events are more common following revaccination. In a trial in subjects ≥ 50 years of age, these side effects were reported by 10-19 % of subjects following primary vaccination and 30-35 % following revaccination. They do not respond to antibiotics.

B cell hyporesponsiveness to serotypes not included in PCV13 may occur after repeated doses of PPV23.
Pneumococcal Polysaccharide Vaccine (PPV23)
Algorithm for Vaccination

Healthy Person ≥65 years

Previously vaccinated with PPV23?

No

Yes

Aged ≥65 years at the time of the last vaccination?*

No

Yes

Have 5 years elapsed since first dose?*

No

Yes

Has a condition in which antibody levels are likely to decline**

No

Yes

Vaccination not indicated at this time

Vaccination indicated

Previously vaccinated with PPV23?

No

Yes

At Risk Person* < 65 years

Adapted from NIO

* Asplenia or splenic dysfunction (splenectomy, sickle cell disease, coeliac syndrome); chronic renal, heart, lung, liver disease; diabetes mellitus; complement deficiency; immunosuppressive conditions; CSF leak; cochlear implant recipients or candidates for implants; children < 5 years with history of invasive disease.

* Re-vaccination not indicated for any person who has received a dose of PPV 23 at age ≥ 65 years.

* If vaccination has been given during chemotherapy or radiotherapy re-vaccination 3 months after treatment is indicated.

** Those with no spleen, with splenic dysfunction, immunosuppression including HIV infection, nephrotic syndrome, renal transplant or chronic renal disease.
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Bibliography


Centers for Disease Control and Prevention (2016). PCV13 and diphtheria, tetanus, and acellular pertussis vaccine (DTaP) both increase risk of febrile seizure when given at the same time as the influenza vaccine. www.cdc.gov/vaccines/vpd/pneumo/hcp/administering-vaccine.html


