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Pneumococcal Infection

PPV introduced for “at risk” 1996

PCV7 introduced for “at risk” 2002

PCV7 introduced to childhood schedule 2008

PCV13 replaced PCV7 in 2010

NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the Summary of Product Characteristics of the vaccines. When this occurs, the recommendations in these guidelines, which are based on current expert advice from NIAC, should be followed.

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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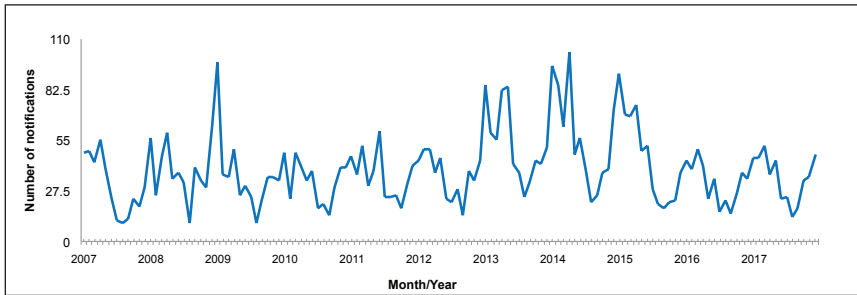
and 13 (PCV7 and PCV13) vaccines occurred. In 2017 (January - September), the 10 most commonly implicated serotypes in Ireland were 8, 12, 19A, 22F, 15A, 9N, 3, 24F, 33F and 11A (in order of frequency).

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).

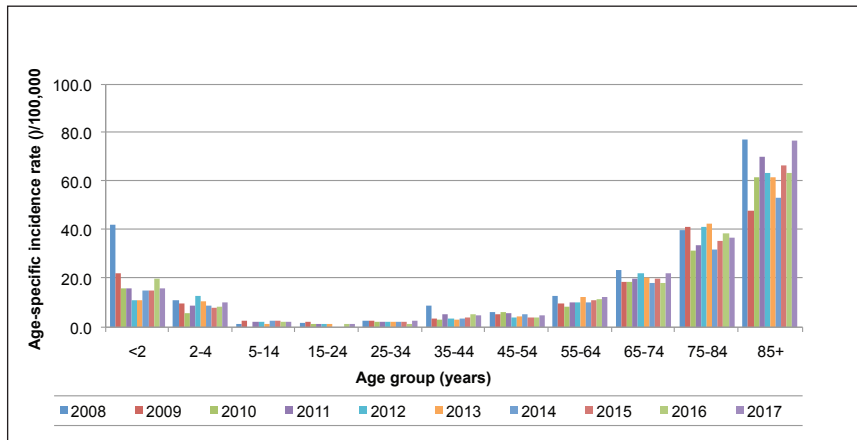
Source: HPSC



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).

Figure 16.2 Age-specific incidence rates of confirmed invasive pneumococcal disease (IPD) notifications, 2008-2016

Source: HPSC



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.

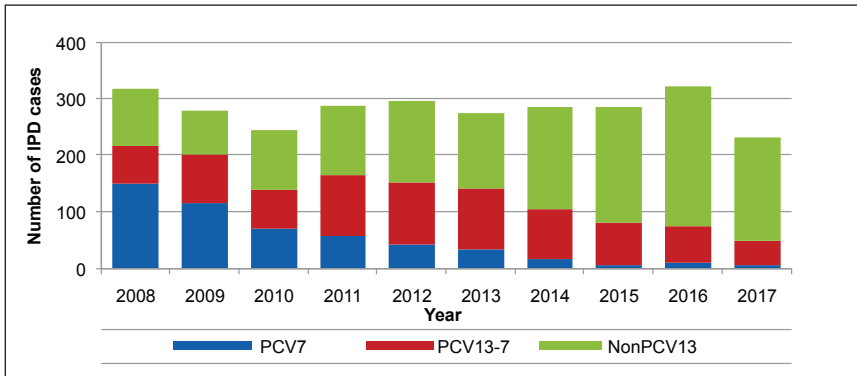
*PCV 7 serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F

**PCV 13 serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19 A, 19F, 23F

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Figure 16.3 Number of IPD cases in all ages due to serotypes covered by PCV7, PCV13, and non PCV13 serotypes, 2008-2016.

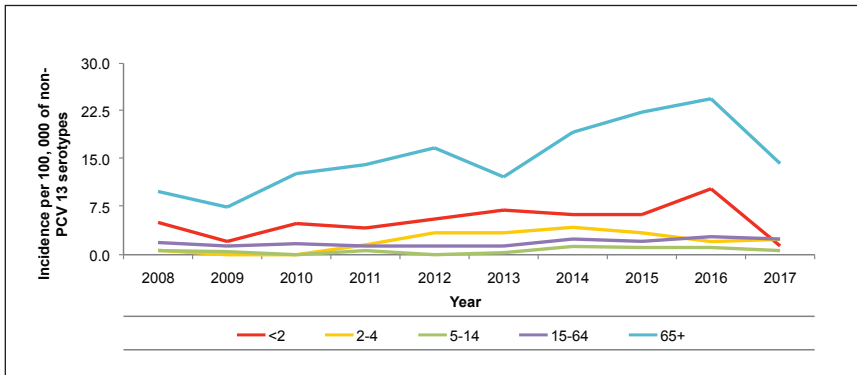
Source: HPSC, from Irish Pneumococcal Reference Laboratory



Cases of non-PCV vaccine serotypes have increased in those aged >65 years from 2008 - 2016 (Figure 16.4).

Figure 16.4 Age specific incidence rates of confirmed IPD notifications due to non PCV13 serotypes, 2008-2016.

Source: HPSC from Irish Pneumococcal Reference Laboratory



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 HPRAs website www.hpra.ie

A list of vaccines currently available from the National Cold Chain Service can be found at www.immunisation.ie

Pneumococcal vaccines should be stored at $+2$ to $+8^{\circ}\text{C}$.

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).

* 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

High risk (Group A)	Medium risk (Group B)
<ul style="list-style-type: none"> • Asplenia, hyposplenia (including splenectomy, sickle cell disease, haemoglobinopathies, and coeliac disease) • Cancer patients under hospital supervision • Chronic renal disease or nephrotic syndrome • Cochlear implant candidates and recipients • Complement deficiency (particularly C1-C4) • CSF leaks (congenital or complicating skull fracture or neurosurgery) • Haematopoietic stem-cell transplant • Immunosuppressive conditions (e.g. some B- and T-cell disorders, HIV infection, leukaemia, lymphoma), and those receiving immunosuppressive therapies¹ or corticosteroids (see Chapter 3). • Intracranial shunt • Solid organ transplant 	<ul style="list-style-type: none"> • Children under 5 years of age following invasive pneumococcal disease • Chronic heart, lung, or liver disease • Diabetes mellitus requiring insulin or oral hypoglycaemic drugs • Down syndrome • Occupational exposure to metal fumes (i.e. welders) • Smokers and alcoholics

¹Individuals 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

	High risk (Group A)		Medium risk (Group B)	
	PCV ¹	PPV23	PCV	PPV23
6 weeks - <24 months	Routine schedule	1 dose at ≥ 2 years of age	Routine schedule ²	1 dose at ≥ 2 years of age
2 - <5 years	If unvaccinated, 2 doses	1 dose ≥ 2 months after PCV	If unvaccinated, 1 dose ²	1 dose ≥ 2 months after PCV
5- <18 years	If unvaccinated, 1 or 2 ³ doses ⁴	1 dose ≥ 2 months after PCV	If unvaccinated, 1 dose	1 dose
18 - <65 years	1 or 2 ³ doses	1 – 2 ⁵ doses ≥ 2 months after PCV	None	2 doses, with 2 nd dose at ≥ 65 years, ≥ 5 years after 1 st dose)
≥ 65 years	1 or 2 ³ doses	1 dose ≥ 2 months after PCV	None	1 dose

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

² 1 additional dose if had IPD, irrespective of vaccine history

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

⁴ If fully vaccinated with PCV7 give 1 dose of PCV13

⁵ 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.

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.

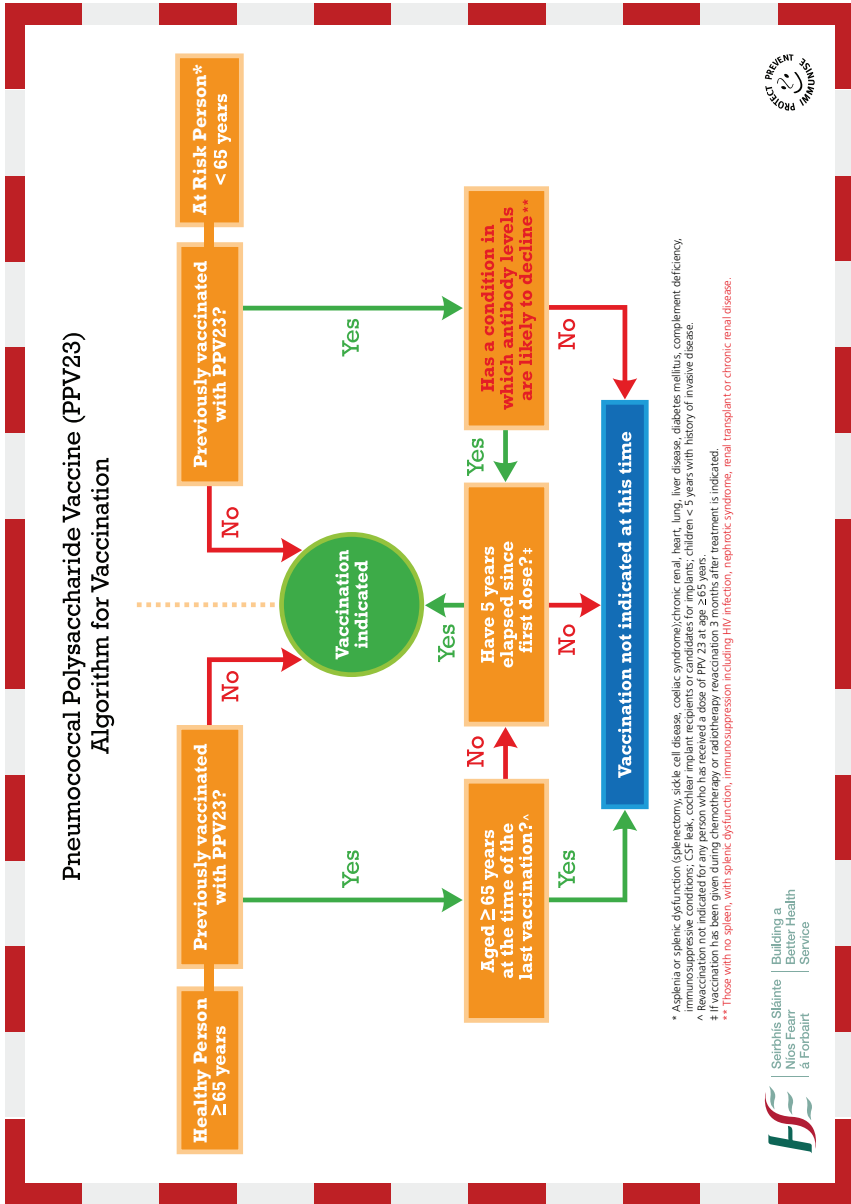


Figure 16.5 Pneumococcal polysaccharide vaccination algorithm Adapted from NIO

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