
15 Pneumococcal disease

Key information

Mode of transmission	Contact with respiratory droplets.
Incubation period	Asymptomatic nasopharyngeal carriage is common. The incubation period is variable and may be as short as 1–3 days.
Burden of disease	Particularly the young, the elderly and the immunocompromised.
Funded vaccines	All children aged under 5 years: PCV10 (Synflorix). Children and adults with eligible conditions: <ul style="list-style-type: none">• PCV13 (Prevenar 13)• 23PPV (Pneumovax 23).
Dose, presentation and route	All vaccines: <ul style="list-style-type: none">• 0.5 mL per dose• pre-filled syringe• intramuscular injection (23PPV may also be given subcutaneously).
Funded vaccine indications and schedule	PCV10 at ages 6 weeks, 3, 5 and 15 months, or age-appropriate catch-up. Children who started with PCV13 can continue with PCV10. PCV13 and 23PPV age-appropriate schedules for (re-)vaccination of children and adults with eligible conditions. PCV13 and 23PPV for testing for primary immune deficiencies.
Vaccine efficacy/effectiveness	For pneumococcal conjugate vaccines: reductions in pneumococcal disease and carriage of vaccine serotypes in vaccinated populations, plus herd immunity effects reducing pneumococcal disease in other age groups; some increases in disease caused by non-vaccine serotypes.
Precautions	There may be an increased risk of fever and febrile convulsions with concomitant PCV13 and influenza vaccine in children aged 6 months to under 5 years. 23PPV should not be given to children aged under 2 years due to the reduced immune response associated with polysaccharide vaccines.

15.1 Bacteriology

Streptococcus pneumoniae is a gram-positive diplococcus. It is ubiquitous, and many individuals carry the organism asymptotically in their upper respiratory tract.¹ There are over 90 identifiable serotypes of *S. pneumoniae*. Certain serotypes are more invasive or more associated with antibiotic resistance, and dominant serotypes vary by age and geographical distribution.

Table 15.1 summarises the serotypes contained in the pneumococcal conjugate (PCV) and polysaccharide (PPV) vaccines.

Table 15.1: Summary of pneumococcal vaccine serotype content

Vaccine	Serotypes
PCV7	Serotypes 4, 6B, 9V, 14, 18C, 19F, 23F
PCV10*	Includes: <ul style="list-style-type: none">• the serotypes contained in PCV7• plus serotypes 1, 5, 7F.
PCV13	Includes: <ul style="list-style-type: none">• the serotypes contained in PCV10• plus serotypes 3, 6A, 19A.
23PPV	Includes: <ul style="list-style-type: none">• the serotypes contained in PCV13 (except for 6A)• plus serotypes 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F.

* PCV10 contains serotype 19F, which elicits cross-reactive antibodies against serotype 19A.²

15.2 Clinical features

The human nasopharynx is the only natural reservoir of *S. pneumoniae*. Carriage rates in young children range up to 75 percent.³ Transmission of *S. pneumoniae* is by contact with respiratory droplets, and although nasopharyngeal colonisation precedes disease, most who are colonised do not develop invasive disease. The nasopharynx is a source of spread between individuals, and reduction of *S. pneumoniae* vaccine serotypes in children by vaccination results in less transmission to, and disease in, adults. Invasive pneumococcal disease (IPD) is the severe end of the pneumococcal disease spectrum and includes cases in which

S. pneumoniae has been isolated from a usually sterile site (such as blood, pleural fluid or cerebrospinal fluid). Major clinical syndromes are bacteraemic pneumonia, bacteraemia without a focus and meningitis; older adults most commonly have bacteraemic pneumonia while young children may have any of the three, with meningitis being the most severe.

Mucosal or non-invasive infection is extremely common, such as acute otitis media (the most common childhood bacterial infection), and sinusitis and pneumonia (without bacteraemia) in all age groups. The incubation period of *S. pneumoniae* infection is variable but may be as short as one to three days.

15.3 Epidemiology

15.3.1 Global burden of disease

Pneumococcal diseases are a common cause of morbidity and mortality worldwide, though rates of disease and death are higher in low-income countries than in high-income countries, with the majority of deaths occurring in sub-Saharan Africa and Asia.⁴ Along with the very old and very young, patients with underlying conditions have the highest rates of disease.

The WHO estimates that 476,000 (range 333,000–529,000) children aged under 5 years died from pneumococcal infections in 2008.⁴ Five percent of all-cause child mortality in 2008 was due to pneumococcal infections.

Global epidemiology since the introduction of PCV

Herd immunity

There is good evidence for the indirect (herd) effects of infant PCV immunisation on pneumococcal disease due to vaccine serotypes in the non-vaccinated population, especially in adults aged 65 years and older. This includes data showing reductions in the rates of IPD due to PCV7 serotypes in non-vaccinated groups in the US (for both adult pneumonia and IPD in adults),^{5, 6, 7} England and Wales,⁸ the Netherlands,⁹ Norway¹⁰ and Denmark¹¹ and New Zealand (see Figure 15.1). These herd effects

are due to decreased nasopharyngeal carriage of vaccine types in immunised children resulting in reduced transmission to unimmunised older children and adults. Although most of New Zealand data demonstrates the indirect effect on vaccine-type IPD (see Figure 15.2), there is also evidence of an all-age effect on non-bacteraemic pneumonia.¹² Data from Norway¹³ and Canada¹⁴ indicates further decreases in vaccine-type IPD in non-vaccinated populations (aged 5 years and older) after PCV13 replaced PCV7 on the infant immunisation schedule.

Impact of vaccination on non-invasive pneumococcal disease

The impact of pneumococcal conjugate vaccination on the large burden of non-invasive pneumococcal disease has been clearly demonstrated internationally in countries that have introduced these vaccines, particularly through reductions in childhood hospitalisations due to pneumonia.^{15, 16} Other impacts, such as on acute otitis media, are less clear and more difficult to measure accurately.¹⁷

15.3.2 New Zealand epidemiology

Pneumococcal disease occurs throughout the year, but is more common in the autumn and winter months.^{18, 19} Historically, the risk of disease is highest in infants and the elderly,^{20, 21} especially Māori and Pacific peoples.^{18, 20, 22} The introduction of PCV has substantially reduced the risk of IPD in vaccinated infants (see below).

Invasive isolates from cases of IPD are serogrouped and serotyped at ESR. Detailed surveillance information can be found on the ESR Public Health Surveillance website (www.surv.esr.cri.nz/surveillance/IPD.php).

Incidence and mortality

There were 447 IPD cases notified in 2015 (ESR, 1 February 2017). The notification rate was 9.7 cases per 100,000 population, a decrease from 2014 (10.8 cases per 100,000 population; 489 cases) and significantly lower than the 2009 peak rate of 16.2 per 100,000 population (697 cases).

Adults aged 85 years and older (53.7 per 100,000), 75–84 years (35.4 per 100,000), 65–74 years (25.8 per 100,000) and children aged under 1 year (16.9 per 100,000) had the highest rates of IPD (ESR, 1 February 2017). The age-standardised rates of IPD were highest for the Pacific peoples (31.3 per 100,000, 51 cases) and Māori (27.7 per 100,000, 107 cases) ethnic groups. The rates for these ethnic groups were, respectively, 4.3 and 3.8 times higher than the rate for the European/Other ethnic group (7.3 per 100,000, 259 cases).

IPD was recorded as the primary cause of death for 27 cases in 2015 (ESR, 1 February 2017). There were no deaths due to IPD in children aged under 5 years.

In 2015, the most commonly reported risk factor in cases aged under 5 years was premature birth (50.0 percent), and for cases aged 5 years and older it was having a chronic illness (55.2 percent).²³

New Zealand epidemiology since the introduction of PCV

PCV7 was introduced in June 2008, PCV10 in July 2011 and PCV13 in July 2014. From 1 July 2017, PCV10 will again be used on the routine Schedule (see Appendix 1 for the history of pneumococcal vaccination in New Zealand).

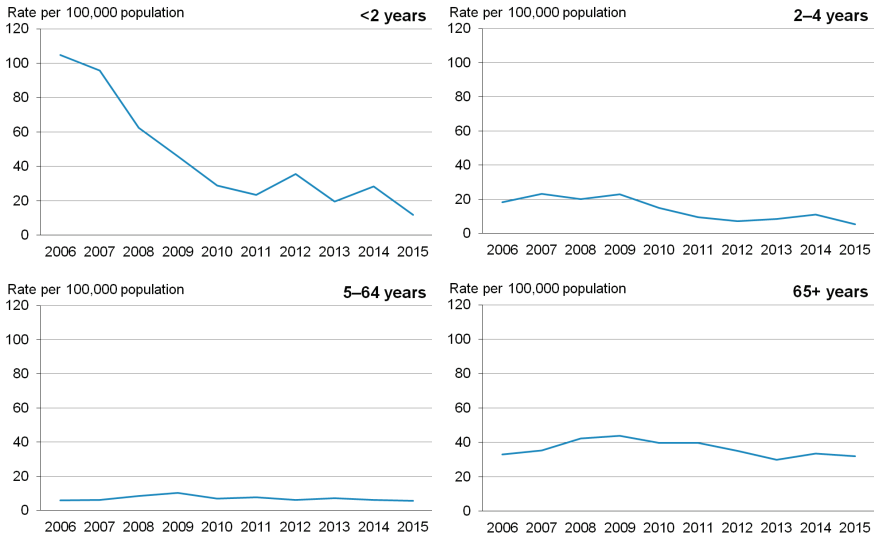
IPD incidence

There have been dramatic reductions in the incidence of IPD in the vaccine-eligible age groups in New Zealand since the introduction of PCV to the Schedule in 2008 (see Figure 15.1).

In New Zealand children aged under 2 years, the rate of IPD has decreased by 88 percent since the introduction of PCV to the Schedule: from an average annual rate of 100.3 per 100,000 for 2006/07²⁴ to 11.8 per 100,000 in 2015.²³ The impact on IPD caused by PCV7 serotypes in this age group is even greater (see Figure 15.2), with only one case of IPD in a child aged under 2 years due to a PCV7 serotype in 2015 (ESR, 1 February 2017).

Similar reductions were seen for IPD caused by PCV10 and PCV13 serotypes in children aged under 2 years (see Figure 15.2). The rate of IPD has also significantly decreased in children aged 2 to 4 years, for all-cause IPD (Figure 15.1) and IPD caused by PCV serotypes (Figure 15.2).

Figure 15.1: Rate per 100,000 of invasive pneumococcal disease by age group and year, 2006–2015



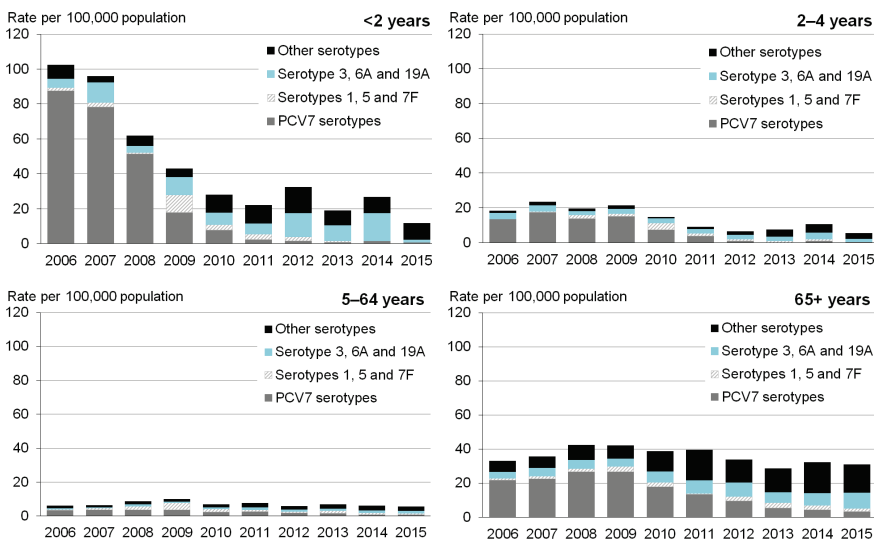
Notes:

PCV7 was introduced in 2008, PCV10 in 2011 and PCV13 in 2014.

IPD became a notifiable disease in 2008. Data presented from 2009 onwards is based on IPD notifications, and data prior to 2009 is from ESR's national laboratory-based surveillance of IPD.

Source: ESR

Figure 15.2: Rate per 100,000 population of invasive pneumococcal disease due to PCV7 serotypes, additional PCV10 types, additional PCV13 types and non-PCV types, by age group and year, 2006–2015



Notes:

PCV7 was introduced in 2008, PCV10 in 2011 and PCV13 in 2014.

'PCV7 serotypes' are cases due to serotypes covered by PCV7 (4, 6B, 9V, 14, 18C, 19F and 23F); 'Serotypes 1, 5 and 7F' are cases due to the additional serotypes contained in PCV10; 'Serotypes 3, 6A and 19A' are cases due to the additional serotypes contained in PCV13; and 'Other serotypes' are all other culture-positive IPD cases.

IPD became a notifiable disease in 2008. Data presented from 2009 onwards is based on IPD notifications, and data prior to 2009 is from ESR's national laboratory-based surveillance of IPD.

Source: ESR

Pneumococcal serotypes

Of the 447 IPD cases notified in 2015, 430 were referred to ESR for serotyping (ESR, 1 February 2017). Just over 90 percent (22/24) of cases in children aged under 5 years were due to serotypes not covered by PCV10, compared with 71.7 percent (142/198) and 83.6 percent (174/208) of cases in the 5–64 years age group and 65 years and older age group, respectively.

Serotype 19A was the most common of all serotypes (90 cases) in 2015 (ESR, 1 February 2017). Three of these 19A cases were in children aged under 5 years (none of whom had received PCV13), down from 17 cases in this age group in 2014.

Serotype 22F was the most common non-vaccine serotype in 2015, although there was little change in cases of 22F disease between 2014 and 2015 (39 to 40 cases) (ESR, 1 February 2017).

Herd immunity

The addition of PCV to the New Zealand schedule in 2008 has seen significant reductions in IPD due to PCV serotypes in age groups not eligible for routine infant immunisation (Figure 15.2). Between 2006/07 and 2015 the rate of IPD due to all vaccine serotypes in the 65 years and older age group decreased 43 percent, from an average of 28.0 per 100,000 population in 2006/07 to 16.0 per 100,000 in 2015, while in the 5–64 years age group there was a 30 percent decrease over the same time period (5.0 to 3.5 per 100,000) (ESR, 1 February 2017). However the overall rate of IPD in these age groups has only marginally decreased due to non-vaccine serotype replacement disease.

Impact of vaccination on non-invasive pneumococcal disease

While hospitalisations for respiratory infections in children aged 5 years and under have been increasing in New Zealand, hospitalisations for all-cause pneumonia have declined significantly since the implementation of the pneumococcal conjugate vaccine programme in 2008. The largest reductions in all-cause pneumonia hospitalisations between 2006 and 2015 were in Māori (a 12 percent reduction) and Pacific children (a 21 percent reduction) and those living in areas of high deprivation.²⁵ In children aged under 2 years living in Counties Manukau DHB, the introduction of PCV7 was associated with a 70 percent reduction in the risk of pneumonia hospitalisations in Pacific children but there was less impact (a 5 percent risk reduction) for Māori children.²⁶

Antimicrobial resistance

As in other countries, there has been concern at the increase in the prevalence of antimicrobial resistance in *S. pneumoniae* in New Zealand. Introduction of pneumococcal conjugate vaccination has reduced the circulation of resistant pneumococcal serotypes elsewhere.²⁷

In New Zealand, *S. pneumoniae* resistance to betalactams (penicillin and cefotaxime) has shown little change over the last 10 years; the 2015 rate of penicillin resistance (meningitis interpretation) of 21.9 percent was within the range of rates recorded for other years during the last decade (14.1–22.3 percent) (ESR, 1 February 2017). Similarly, the 2015 rate of cefotaxime resistance of 2.6 percent was within the range recorded for other years during the last decade (1.9–5.1 percent).

In 2015 PCV7 serotypes accounted for a smaller proportion (20.2 percent) of the penicillin-resistant isolates than previous years (92.8 percent in 2006/07), and type 19A accounted for a larger proportion (52.1 percent) (ESR, 1 February 2017). The prevalence of penicillin resistance among serotype 19A isolates has increased significantly in recent years from an average of 15.8 percent in 2006/07 to 54.4 percent in 2015.

15.4 Vaccines

15.4.1 Available vaccines

There are two types of pneumococcal vaccine registered (approved for use) and available (marketed) in New Zealand for use against *S. pneumoniae*: protein conjugate pneumococcal vaccine and unconjugated polysaccharide pneumococcal vaccine. In the protein conjugate vaccines, the pneumococcal surface polysaccharide is coupled to a carrier protein. The protein conjugate induces increased production of antibodies, immunological memory and maturation of the antibody response, enabling an effective immune response in children aged under 2 years (see section 1.4.3).

Funded vaccines

PCV10

Each 0.5 mL dose of PCV10 contains:

- 1 µg of pneumococcal polysaccharide serotypes 1, 5, 6B, 7F, 9V, 14 and 23F and 3 µg of serotype 4, conjugated to a total of 9–16 µg of NTHi protein D carrier protein, 3 µg of serotype 18C conjugated to 5–10 µg of tetanus toxoid carrier protein, and 3 µg of serotype 19F conjugated to 3–6 µg of diphtheria toxoid carrier protein, adsorbed onto 0.5 mg of aluminium phosphate
- 4.3 mg of sodium chloride and water for injection.

PCV10 contains no preservative.

PCV13

Each 0.5 mL dose of PCV13 contains:

- 2.2 µg of pneumococcal purified capsular polysaccharides for serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F and 23F, and 4.4 µg of serotype 6B, conjugated to non-toxic diphtheria CRM₁₉₇ protein and adsorbed onto aluminium phosphate (0.565 mg)
- succinic acid, polysorbate 80, aluminium phosphate, phosphate, and sodium chloride in water for injection.

23PPV

Each 0.5 mL dose of 23PPV contains:

- 25 µg of each capsular polysaccharide antigen (serotypes: 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F and 33F)
- sodium chloride, water for injection, and phenol (0.25 percent) added as a preservative.

15.4.2 Efficacy and effectiveness

10-valent pneumococcal conjugate vaccine (PCV10)

IPD

Two key randomised controlled trials have demonstrated the protective efficacy and effectiveness of PCV10 against pneumococcal disease.² The Finnish Invasive Pneumococcal disease (FinIP) study investigated a two- or three-dose infant series plus a toddler booster.²⁸ Vaccine effectiveness against culture-confirmed vaccine-serotype IPD was shown to be 100 percent (95% CI: 83–100) following the 3+1 schedule and 92 percent (95% CI: 58–100) for the 2+1 schedule. Based on national hospital discharge register data, vaccine effectiveness was 71 percent (95% CI: 52–83) for patient file-verified non-laboratory-confirmed IPD.²⁹

In the Clinical Otitis Media and Pneumonia Study (COMPAS) phase III trial in Latin America (Argentina, Colombia and Panama), approximately 24,000 infants received PCV10 or HepB at ages 2, 4 and 6 months with a booster at age 15–18 months.³⁰ The study showed that the vaccine effectiveness of PCV10 was 100 percent (95% CI: 74.3–100) against pneumococcal vaccine-serotype IPD and 65 percent (95% CI: 11.1–86.2) against any IPD.

A matched case-control study conducted in Brazil found that, following the introduction of PCV10 (as a 3+1 schedule) in 2010, the adjusted effectiveness against vaccine-serotype IPD was 83.8 percent (95% CI: 65.9–92.3) for an age-appropriate PCV10 schedule.³¹ The study included 316 cases of IPD and 1,219 neighbourhood age-matched controls. Age-appropriate PCV10 immunisation was up-to-date for 94 (30 percent) cases and 521 (43 percent) of the controls.

Meningitis

A decrease in pneumococcal meningitis morbidity and mortality was observed two years after the introduction of routine PCV10 vaccinations in Brazil in children aged under 2 years, based on data obtained from the Information System on Notifiable Diseases from 2007 to 2012.³²

Overall, the incidence of pneumococcal meningitis decreased by 50 percent from 3.7 per 100,000 population in 2007 to 1.84 per 100,000 in 2012.³² Mortality decreased by 69 percent from 1.3 per 100,000 to 0.4 per 100,000.

During the study period, there were 1,311 cases and 430 deaths attributed to laboratory-confirmed pneumococcal meningitis (serotypes not determined).³² The greatest impact of PCV10 vaccination was seen in the infants aged 6–11 months, with a 73 percent reduction in pneumococcal meningitis incidence (from 7.46 cases per 100,000 in 2007 to 2.02 cases per 100,000 in 2012) and an 85 percent reduction in mortality (from 3.25 deaths per 100,000 in 2007 to 0.49 deaths per 100,000 in 2012).

Pneumonia

The FinIP trial also provided data on the protective effectiveness of PCV10 against hospital-diagnosed pneumonia in Finland. Vaccine effectiveness against all pneumonia episodes was 25.2 percent (95% CI: 2.6–42.6) for the 3+1 PCV10 schedule and 27.6 percent (95% CI: 5.5–44.6) for the 2+1 schedule.² A study in children aged under 4 years showed a significant decrease of 12.65 percent ($p < 0.001$) in all pneumonia hospitalisations in Brazil when comparing the pre-vaccination (2002–2009) and post-PCV10 vaccination introduction periods (2011–2012).³³ No reduction in non-respiratory-cause hospitalisations were observed for the same time period ($p = 0.39$).

Further studies in Brazil have continued to show significant reductions in pneumonia in children aged under 2 years following the introduction of PCV10 to the infant schedule. Active population-based surveillance studies were conducted in Central Brazil (across 17 paediatric hospitals) to investigate pneumonia hospitalisations in children aged under 36 months before and after the introduction of PCV10.³⁴ The relative rate reduction was 13.1 percent (95% CI: –13.4, –12.9) for clinical and 25.4 percent (95% CI: –26.0, –24.7) for x-ray-confirmed pneumonia in children aged 2–23 months.

Otitis media

A secondary outcome of the COMPAS trial in Latin America was to assess the vaccine effectiveness of PCV10 against clinically confirmed acute otitis media (AOM).³⁰ At the end of the study, the intent-to-treat analysis found that vaccine effectiveness against AOM was 19.0 percent (95% CI: 4.4–31.4; $p=0.007$; $n=254$ vaccinated, 308 controls). When the cause of the AOM was investigated further, vaccine effectiveness was calculated as 55.7 percent (95% CI: 21.5–75.0; $n=17$ vaccinated, 38 controls) against pneumococcal AOM and 69.9 percent (29.8–87.1; $n=7$ vaccinated, 23 controls) against vaccine-serotypes. For NTHi confirmed-AOM, vaccine effectiveness was 21.5 percent (95% CI: -43.4, -57.0; $n=19$ vaccinated, 24 controls).

13-valent pneumococcal conjugate vaccine (PCV13)

Individuals at increased risk of IPD

Few studies have investigated the immunogenicity and effectiveness of PCV13 in individuals at increased risk of IPD. Studies using pneumococcal vaccines with similar but fewer antigens have demonstrated vaccine efficacy in individuals with immunocompromising conditions (eg, HIV, sickle cell disease), but the duration of protection against IPD remains unknown.³⁵ High IgG titres have been observed following PCV13 vaccination of children with sickle cell disease,³⁶ HIV infection³⁷ and nephrotic syndrome.³⁸

Oropharyngeal carriage may be a risk factor for IPD in children and adolescents with underlying medical conditions (eg, type 1 diabetes,³⁹ cancer,⁴⁰ cystic fibrosis,⁴¹ asthma⁴²). The broader serotype protection provided by PCV13 may be of benefit for these children when oropharyngeal carriage is considered as a risk factor for pneumococcal disease, although booster doses may be necessary.³⁹

Use of pneumococcal conjugate vaccines in adults

PCV13 induces robust immune responses in adults,^{43, 44, 45, 46} including elderly adults.⁴⁷ The antibody titres vary with serotype and between age groups, particularly for those aged over 65 years.⁴⁶ However, the clinical significance of this variation was not determined.

There is little data on the effectiveness of pneumococcal conjugate vaccines in adults. A large randomised controlled trial was conducted in the Netherlands to investigate the impact of PCV13 vaccination in reducing vaccine-serotype pneumococcal community-acquired pneumonia (CAP), non-bacteraemic and non-invasive pneumococcal CAP, and IPD in adults aged 65 years and older.⁴⁸ PCV13 was effective in preventing vaccine-type pneumococcal CAP (vaccine efficacy 45.6 percent, 95% CI: 21.8–62.5), bacteraemic and non-bacteraemic CAP (vaccine efficacy 45 percent, 95% CI: 14.2–65.3) and vaccine-type IPD (vaccine efficacy 75 percent, 95% CI: 41.4–90.8).

PCV13 is at least as immunogenic as 23PPV in adults. Some studies suggest that 23PPV attenuates the immune response to subsequent doses of PCV13.^{47, 49, 50} This attenuation is not seen if PCV13 is given before 23PPV; PCV13 may augment the response to subsequent 23PPV vaccination.^{47, 49, 50}

23-valent vaccine pneumococcal polysaccharide (23PPV)

The polysaccharide vaccine (23PPV, Pneumovax 23) is made from the purified capsular polysaccharide antigens of 23 serotypes of *S. pneumoniae*. It is available in New Zealand for adults and children from age 2 years. 23PPV includes the 23 serotypes (see Table 15.1) responsible for about 90 percent or more of cases of invasive disease in high-income countries.

23PPV efficacy

Assessment of the efficacy of pneumococcal vaccination depends on whether immune-competent or immunocompromised patients are studied, and whether the end point is pneumococcal pneumonia or bacteraemia.

The problems with the polysaccharide vaccine have been summarised as:

- reduced efficacy in high-risk individuals
- uncertain efficacy against pneumonia
- only suitable for children aged 2 years and older.

Although it is generally accepted that 23PPV is effective at preventing IPD in immune-competent adults, a 2009 meta-analysis concluded that in trials of high quality, there is no evidence of vaccine protection against IPD and that 23PPV may not be protective against either IPD or pneumonia.⁵¹ A subsequent case-control study in patients aged over 60 years concluded that 23PPV provided a significant protective effect against IPD in elderly immune-competent patients.⁵² However, a 2012 review of data from elderly populations concluded that low protection was possible, but differences in study designs prevent definitive conclusions.⁵³

15.4.3 Transport, storage and handling

Transport according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.⁵⁴ Store at +2°C to +8°C. Do not freeze.

15.4.4 Dosage and administration

The dose of PCV10, PCV13 and 23PPV is 0.5 mL, administered by intramuscular injection (see section 2.2.3). 23PPV can also be administered by subcutaneous injection (see section 2.2.3), but there is an increased likelihood of injection site reactions.⁵⁵

Co-administration with other vaccines

PCV10, PCV13 or 23PPV may be administered at the same time as other routine childhood vaccinations, in a separate syringe at a separate injection site (see section 2.2.7 for information about multiple injections at the same visit). The only exception is PCV13 with the quadrivalent meningococcal conjugate vaccine MCV4-D, which should be given at least four weeks after PCV13. This is because when administered concurrently, there is impairment of the immune response to some of the pneumococcal serotypes.^{56, 57}

PCV13 has been associated with increased risk of fever over 39°C and febrile convulsions when co-administered with inactivated influenza vaccine in children aged 6 months to under 5 years. Separation of the vaccines by two days can be offered, but is not essential (see

section 15.6.2). Systemic reactions have been noted in adults aged over 65 years.

Herpes zoster vaccine can be concomitantly delivered with 23PPV (see also section 22.4.4).^{58, 59}

15.5 Recommended immunisation schedule

15.5.1 Usual childhood schedule (PCV10)

PCV10 for children aged under 5 years

PCV10 (Synflorix) vaccine is funded for all children aged under 5 years. Three doses of PCV10 are given as the primary course, with a booster at age 15 months (Table 15.2). Children who started their immunisation course with PCV13 can complete it with PCV10.

Table 15.2: Usual childhood PCV10 (Synflorix) schedule

Age	Vaccine	Comment
6 weeks	PCV10	Primary series
3 months	PCV10	Primary series
5 months	PCV10	Primary series
15 months	PCV10	Booster

Where a previously unimmunised child aged under 5 years presents late for pneumococcal vaccination, the age-appropriate catch-up schedules in Appendix 2 should be followed.

15.5.2 PCV13 and 23PPV for eligible individuals

PCV13 and 23PPV are funded for eligible individuals, **as shown in Tables 15.3, 15.4 and 15.5**. Because the recommended schedule depends on the age of the individual at diagnosis, the tables have been organised into age groups (under 5 years, 5–18 years and 18 years and older).

The PCV13 and 23PPV funding restrictions are as follows. See Tables 15.3–15.5 for the eligible conditions.

PCV13

- One dose of PCV13 is funded for high-risk children aged over 17 months and under 18 years who have previously received four doses of PCV10.
- Up to an additional four doses (as appropriate) of PCV13 are funded for (re-)vaccination of high-risk children aged under 5 years.
- Up to an additional four doses (as appropriate) of PCV13 are funded for (re-)vaccination of eligible individuals aged 5 years and older.

23PPV

- Up to three doses (as appropriate) of 23PPV are funded for individuals with eligible conditions.
- Up to two doses of 23PPV are funded for high-risk children aged under 18 years.

See also section 15.5.3 '(Re-)vaccination'. See sections 4.2 and 4.3 for more information about immunocompromised infants, children and adults, including additional vaccine recommendations and schedule tables for certain conditions.

Table 15.3: High-risk children aged under 5 years: funded PCV13 and 23PPV indications and schedules

PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for children aged under 5 years:

- on immunosuppressive therapy or radiation therapy (vaccinate when there is expected to be a sufficient immune response)
- with primary immune deficiencies
- with HIV infection
- with renal failure or nephrotic syndrome
- who are immune-suppressed following organ transplantation (including HSCT)
- with cochlear implants or intracranial shunts
- with cerebrospinal fluid leaks
- who are receiving corticosteroid therapy for more than 2 weeks, and who are on an equivalent daily dosage of prednisone of 2 mg/kg per day or greater, or children who weigh more than 10 kg on a total daily dosage of 20 mg or greater
- with chronic pulmonary disease (including asthma treated with high-dose corticosteroid therapy)
- who were preterm infants, born before 28 weeks' gestation
- with cardiac disease, with cyanosis or failure
- with diabetes
- with Down syndrome
- who are pre- or post-splenectomy, or with functional asplenia.

Age at diagnosis	Vaccine	Recommended vaccine schedule
<12 months	PCV13	PCV13 ^a at ages 6 weeks, 3, 5 and 15 months or age-appropriate catch-up schedule. <ul style="list-style-type: none"> • If commencing immunisation at ages 7–11 months, give 2 doses of PCV13 at least 4 weeks apart, followed by a booster dose at age 15 months. • For children aged 7–11 months who have completed the primary course with PCV10, give 1 dose of PCV13, followed by the scheduled PCV13 booster at age 15 months.
	23PPV	Following the completion of the PCV course, give 1 dose of 23PPV at age ≥2 years. There must be at least 8 weeks between the last PCV dose and the 23PPV dose. If risk persists, revaccinate once with 23PPV, 5 years after the first 23PPV.

Continued overleaf

Age at diagnosis	Vaccine	Recommended vaccine schedule
12 months to <5 years	PCV13	<p>The PCV13^{a,b} age-appropriate catch-up schedule is as follows.</p> <ul style="list-style-type: none"> • If receiving immunisation for the first time, give 2 doses of PCV13,^b 8 weeks apart. • Children aged >17 months who have completed the primary course of PCV10 but have not received PCV13, give 1 dose of PCV13.^{b,c}
	23PPV	<p>Following the completion of the PCV course, give 1 dose of 23PPV at age ≥ 2 years. There must be at least 8 weeks between the last PCV dose and the 23PPV dose. If risk persists, revaccinate once with 23PPV, 5 years after the 1st 23PPV.</p>

- a PCV13 replaces PCV10 (Synflorix) on the Schedule.
- b If 23PPV has already been given (prior to any doses of PCV13) to children aged under 5 years, wait at least 8 weeks before administering PCV13.
- c There are no safety concerns, regardless of the interval between the last dose of PCV10 and the 1st dose of PCV13.

Table 15.4: Children aged 5 to under 18 years: funded PCV13 and 23PPV indications and schedules

PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for children aged 5 to under 18 years:

- with HIV infection
- who are pre- or post-HSCT^a or chemotherapy^a
- who are pre- or post-splenectomy or with functional asplenia
- who are pre- or post-solid organ transplant
- undergoing renal dialysis
- with complement deficiency (acquired or inherited)
- with cochlear implants
- with primary immunodeficiency.

For catch-up of high-risk children (see Table 15.3) aged 5 to under 18 years:

- 1 dose of PCV13 is funded for high-risk children who have previously received 4 doses of PCV10
- 2 doses of 23PPV are funded for high-risk children.

Age at diagnosis	Vaccine	Recommended vaccine schedule
5 years to <18 years	PCV13	For children who have not previously received PCV13, give 1 dose of PCV13. ^{b,c}
	23PPV	1 dose of 23PPV at least 8 weeks after the PCV13 dose. If risk persists, revaccinate once with 23PPV, 5 years after the 1st 23PPV.

- a PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.
- b If 23PPV has already been given (prior to any doses of PCV13) to children aged under 18 years, wait at least 8 weeks before administering PCV13.
- c There are no safety concerns, regardless of the interval between the last dose of PCV10 and the 1st dose of PCV13.

Table 15.5: Adults aged 18 years and older: funded PCV13 and 23PPV indications and schedules

PCV13 (Prevenar 13) and 23PPV (Pneumovax 23) are funded for (re-)vaccination of patients:

- with HIV infection
- who are pre- or post-HSCT^a or chemotherapy^a
- who are pre- or post-splenectomy or with functional asplenia
- who are pre- or post-solid organ transplant
- undergoing renal dialysis
- with complement deficiency (acquired or inherited)
- with cochlear implants
- with primary immunodeficiency.

Age at diagnosis	Vaccine	Recommended vaccine schedule
≥18 years	PCV13	1 dose of PCV13. ^b
	23PPV	Give a maximum of 3 doses of 23PPV in a lifetime, a minimum of 5 years apart. The 1st 23PPV dose is given at least 8 weeks after PCV13, the 2nd a minimum of 5 years later, and the 3rd dose at age ≥65 years.

- a PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post-HSCT or chemotherapy.
- b If 23PPV has already been given (prior to any doses of PCV13) to adults aged 18 years and older, wait at least 1 year before administering PCV13.

15.5.3 (Re-)vaccination

Up to an additional four doses (as appropriate) of PCV13 are funded for (re-)vaccination of high-risk children aged under 5 years (see Table 15.3) and for (re-)vaccination of children and adults aged 5 years and older:

- with HIV
- who are pre- or post-HSCT or chemotherapy
- who are pre- or post-splenectomy, or with functional asplenia
- who are pre- or post-solid organ transplant
- undergoing renal dialysis
- with complement deficiency (acquired or inherited)
- with cochlear implants
- with primary immune deficiency.

See also sections 4.2 and 4.3.

15.5.4 Recommended but not funded

Two classifications of IPD risk are often identified in the literature: ‘high-risk’ conditions for which there is significant risk of IPD and ‘at-risk’ conditions, which on their own may not significantly increase risk, but when combined together or with lifestyle risk factors can increase an individual’s risk of IPD. This is described as ‘risk stacking’ – the risk of IPD substantially increases with the accumulation of concurrent at-risk conditions.⁶⁰ The risk of pneumococcal infections in those with two or more at-risk conditions may be as high as the risk for those with a recognised high-risk condition.^{61, 62, 63} Therefore, it is not always clear who may benefit from pneumococcal vaccination – the following are some considerations.

Recommendations

PCV13 and 23PPV are recommended but not funded for the following individuals:

- immune-competent adults (aged 18 years and older) at increased risk of pneumococcal disease or its complications because of chronic illness (eg, chronic heart, renal, liver or pulmonary disease, diabetes or alcoholism)
- adults with cerebrospinal fluid leak
- immunocompromised adults at increased risk of pneumococcal disease (eg, those with nephrotic syndrome, multiple myeloma, lymphoma and Hodgkin’s disease)
- individuals of any age who have had one episode of IPD
- smokers.

For those individuals who choose to purchase PCV13 and 23PPV vaccines, providers may follow the age-appropriate schedules in Tables 15.4 and 15.5.

Adults aged 65 years and older with no other risk factors

Give one dose of PCV13 followed at least eight weeks later with 23PPV (not funded).

15.5.5 Pregnancy and breastfeeding

Pneumococcal vaccines are not routinely recommended for pregnant women.

Women of child-bearing age who are eligible for funded PCV13 and 23PPV should be vaccinated before a planned pregnancy or as soon as possible after delivery (see Table 15.5). Administration of these vaccines in pregnancy is unlikely to result in serious adverse effects and may be considered in individuals at the highest increased risk of IPD who were not vaccinated prior to pregnancy but require vaccination prior to delivery.⁶⁴

PCV13 and 23PPV may be given to breastfeeding women.⁶⁴

15.6 Contraindications and precautions

See section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

15.6.1 Contraindications

There are no specific contraindications to pneumococcal polysaccharide or conjugate vaccines apart from a severe reaction to a previous dose or known hypersensitivity to any components of either vaccine.

15.6.2 Precautions

- Systemic reactions (chills, rash and myalgia) may occur when PCV13 and influenza vaccine are administered at the same time. PCV13 has been associated with a slightly higher risk of fever over 39°C and febrile convulsions when co-administered with inactivated influenza vaccine in infants and young children, compared to when administered separately.⁶⁵ Febrile convulsion history is not a contraindication to PCV13 immunisation. If indicated, PCV13 and influenza vaccines may be given to a child aged under 5 years at the same visit.⁶⁴ Parents/guardians should be informed of the small risk of febrile convulsions and separation of vaccines by two days can be offered. If the child has a history of febrile convulsions, separation of the vaccines is recommended.

- 23PPV should not be given to children aged under 2 years due to the reduced immune response associated with polysaccharide vaccines (see section 1.4.3).

15.7 Expected responses and AEFIs

15.7.1 Pneumococcal conjugate vaccines

Pneumococcal conjugate vaccines have excellent safety profiles. A 2016 systematic review found that pneumococcal conjugate vaccines are considered safe for use in children, and serious adverse events are very rarely detected by post-marketing surveillance.⁶⁶

PCV10

Pooled evaluation of data derived from several clinical trials found PCV10 to be very well tolerated and safe with a similar safety profile to other PCVs.⁶⁶ After primary immunisation of infants, mild to moderate irritability and injection site redness were most commonly reported, occurring after 55 percent and 41 percent of all doses, respectively. Fever occurred in 30–35 percent of children, regardless of the dose. Injection site pain increased with age, reported by more than 39 percent of younger children and 58 percent of the older subjects. Severe adverse events were exceptionally rare.

When PCV10 was co-administered with DTaP-containing vaccines, fever of 38°C or higher was reported after about one-third of primary or booster vaccine doses.⁶⁷ Similar results were seen following co-administration of PCV7 and DTaP-containing vaccines.⁶⁷

PCV13

The most commonly reported adverse reactions are injection-site reactions, fever, irritability, decreased appetite, and increased and/or decreased sleep.⁶⁸ An increase in injection site reactions was reported in children older than 12 months compared to rates observed in infants during the primary series with PCV13.

No serious adverse events have been identified for adults, children or associated with underlying disease and immunocompromise.^{69, 70, 71}

15.7.2 Pneumococcal polysaccharide vaccine

Local discomfort, erythema and induration lasting a couple of days are expected responses.⁷² Local and systemic reactions may occur after revaccination of adults, particularly when the second dose is given within five years of the first dose.⁶⁴

15.8 Public health measures

IPD is a notifiable condition, and if confirmed, the laboratory undertaking the testing must notify the local medical officer of health.

Local public health action is not expected in response to individual notifications of this disease.

Antimicrobial prophylaxis is not indicated for close contacts of cases of IPD. For those at high risk of pneumococcal disease where response to vaccination may be poor, antimicrobial prophylaxis may be indicated. Discuss with an appropriate specialist.

For more details on control measures, refer to the 'Invasive pneumococcal disease' chapter of the *Communicable Disease Control Manual 2012*.⁷³

15.9 Variations from the vaccine data sheets

The PCV10 (Synflorix) vaccine data sheet recommends that infants and children who receive a first dose of PCV10 complete the full vaccination course with PCV10. The Ministry of Health recommends that those who started with PCV10 may complete with PCV13 if they are subsequently diagnosed with a PCV13-eligible condition (see section 15.5).

The PCV13 (Prevenar 13) data sheet states that there is no data on the interchangeability of PCV13 with other pneumococcal conjugate vaccines containing a protein carrier different from CRM197. The Ministry of Health recommends that those who started with PCV13 may complete with PCV10 (see section 15.5).

The 23PPV (Pneumovax 23) data sheet states that 23PPV and the herpes zoster vaccine (Zostavax) should not be given concurrently. The Ministry of Health recommends that 23PPV and the herpes zoster vaccine may be given concurrently (see section 22.4.4).^{58, 59}

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