

Reducing pneumococcal risk in people aged 65 years and over

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Disease due to pneumococcus (*Streptococcus pneumoniae*) remains a major source of illness in older people. Conjugated pneumococcal vaccines are used extensively in national paediatric programs, whereas a 23-valent polysaccharide vaccine is mainly used in older people and high-risk groups. Data from the Netherlands have led to licensing of a conjugated pneumococcal vaccine for older people in Australia. This review examines current recommendations on pneumococcal vaccines.

Infections caused by pneumococcus (*Streptococcus pneumoniae*) may involve a normally sterile site, such as blood or joint fluid (known as invasive pneumococcal disease or IPD) but are more commonly local mucosal infections, such as community-acquired nonbacteraemic pneumonia (CAP). Pneumococcal infection remains a major source of illness in older people. Globally, across all age groups, pneumococcus remains the most important pathogen in deaths due to respiratory infections.¹

Data on IPD cases are relatively robust in many countries, but the contribution of pneumococcus to CAP is poorly understood. Assessing data for CAP with any cause and more specifically pneumococcal CAP is challenging as there is often no surveillance mechanism in place, and published studies have used various combinations of diagnostic tests, including blood culture, urinary antigen testing and sputum culture.

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KEY POINTS

- Pneumococcus (*Streptococcus pneumoniae*) remains a major cause of illness in older people and the most important pathogen globally in respiratory infection deaths.
- A conjugated pneumococcal vaccine covering 13 serotypes (13vPCV) is used in the Australian paediatric program, and a polysaccharide vaccine covering 23 serotypes (23vPPV) is mainly used in older people and high-risk groups.
- Both invasive and noninvasive disease rates due to serotypes covered in the childhood 13vPCV program are declining in older adults.
- Data from a clinical trial in the Netherlands led to licensing of 13vPCV for older people in Australia in 2011, but this vaccine is not currently funded under the National Immunisation Program (NIP) for this group.
- Coverage rates for 23vPPV in Australia are suboptimal; all older people presenting for influenza vaccine should have their pneumococcal vaccination status checked and should receive 23vPPV if they have not previously received it.
- Recall and reminder systems should be used to ensure appropriately timed revaccination for those who require it.
- If an older person is to receive both 23vPPV and 13vPCV then 13vPCV should be administered first, followed by 23vPPV eight weeks later.

A review of national databases from 2004 to 2012 and published studies in Australia found the hospitalisation rate with pneumococcal pneumonia in people aged 65 years or over was 274 per 100,000 population, or 20% of all CAP hospitalisations.² GP visits for pneumococcal CAP averaged 455 per 100,000 annually. The hospitalisation rate for IPD in 2012 was 19 per 100,000; thus pneumococcal CAP hospitalisation rates were 15-fold higher than for IPD and the costs to the healthcare system were determined to be about 30-fold higher.²

Trends in the burden of IPD

A conjugated pneumococcal vaccine covering 13 serotypes (13vPCV) is used in the Australian paediatric immunisation program, and a polysaccharide vaccine covering 23 serotypes (23vPPV) is more commonly used in older people and high-risk groups.

The use of pneumococcal vaccines in infants, initially a conjugate pneumococcal vaccine containing seven serotypes (7vPCV) and then conjugate vaccine containing 13 serotypes (13vPCV), has led to a decrease in carriage of the serotypes in these vaccines ('vaccine types') and also to a decrease in vaccine-type disease in older people through herd immunity. For example, an Australian review of IPD trends in non-Indigenous older people showed an ongoing substantial decrease in IPD due to the serotypes in 7vPCV since its introduction in 2004. A similar trend was evident against the additional six serotypes in 13vPCV after only three years of its use, and further decline continues.³ A meta-analysis of the indirect effects of conjugated vaccines found the mean time taken to attain a 90% reduction in vaccine-type IPD was 8.9 years for 7vPCV serotypes and 9.5 years for the additional serotypes in 13vPCV but not 7vPCV.⁴ Conversely, likely as a result of serotype replacement, the proportion of cases of IPD attributable to serotypes in 23vPPV but not 13vPCV is increasing, in Australia from 19% to 27%.³

Trends in the burden of community-acquired pneumonia

Although data on pneumococcal CAP are more limited than those on IPD and somewhat inconsistent, a decline in CAP caused by 13vPCV vaccine types is also expected as a result of the childhood vaccination program. This decrease has already been seen in unvaccinated young adults and older people in some studies.

For example, a cohort study of cases of nonbacteraemic pneumococcal pneumonia in adults in Nottingham, UK, described a 30% reduction in the proportion of cases caused by 13vPCV vaccine types within

three years of the switch from 7vPCV to 13vPCV in the childhood program. This followed an 88% decrease in CAP caused by 7vPCV vaccine types.⁵ In the US, an assessment of the impact of childhood 7vPCV, using the Nationwide Inpatient Sample database, found an annual reduction in pneumonia hospitalisations of 168,000, with most of these hospitalisations in older people.⁶

By ensuring patients aged 65 years and above are made aware of their increased risk of IPD and strongly encouraging vaccination against pneumococcal disease, GPs play a crucial role in helping reduce the pneumococcal burden

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Vaccine effectiveness against community-acquired pneumonia

Published estimates place the burden of hospitalisation due to CAP as at least an order of magnitude greater than that due to IPD.² Thus, the benefit of vaccines against CAP is important in determining approaches to vaccination of older people, even if the burden of disease is decreasing due to immunity to the serotypes in 13vPCV.

Vaccine effectiveness data for 13vPCV against CAP are available from the CAP-ITA study, a randomised controlled trial in people aged 65 years and over in the Netherlands. The study found a vaccine effectiveness of 45% against vaccine-type pneumococcal CAP, 22% against all-type pneumococcal CAP and 5% against all-cause CAP.⁷

Clinical studies and review documents have variously ascribed impacts of 23vPPV against pneumococcal CAP from no effect through to about 50% in many studies. Although the studies have methodological challenges and are difficult to compare, the weight of evidence from the 'better' studies

suggests that the attributable vaccine effectiveness is not zero and is in the range up to 50%. For example, a multicentre Japanese study reported the vaccine effectiveness as 33%.⁸ Protection against all-cause CAP with both vaccine types is similar and low, about 5%.^{9,10}

Which vaccine(s) should we use in older people?

Current recommendations on pneumococcal vaccination in older people, developed by the Australian Technical Advisory Group on Immunisation (ATAGI) and published in the Australian Immunisation Handbook, vary depending on whether they have medical or other conditions that increase their risk of IPD.¹¹ Under ATAGI guidelines, there are two categories of increased IPD risk: A and B (described in Box 1).¹¹ Recommendations according to risk level are as follows.

Adults without conditions associated with increased risk of IPD

- A single dose of 23vPPV is recommended for all non-Indigenous adults at 65 years of age.
- Adults aged over 65 years who did not receive a dose at 65 years of age are recommended to receive a single catch-up dose of 23vPPV as soon as possible.
- Aboriginal and Torres Strait Islander adults without medical conditions that are associated with an increased risk of IPD are recommended to receive:
 - a dose of 23vPPV at the age of 50 years
 - a further dose of 23vPPV five years later.

The minimum interval between any two doses of 23vPPV is five years. Adults are recommended to receive no more than three doses of 23vPPV in their lifetime.

Adults with conditions associated with an increased risk of IPD

- Adults with a newly identified or previously identified medical

1. CONDITIONS ASSOCIATED WITH INCREASED RISK OF INVASIVE PNEUMOCOCCAL DISEASE (IPD)*¹¹

Category A: conditions associated with the highest increased risk of IPD

- Functional or anatomical asplenia, including:
 - sickle cell disease or other haemoglobinopathies
 - congenital or acquired asplenia (e.g. splenectomy), splenic dysfunction
- Immunocompromising conditions, including:
 - congenital or acquired immune deficiency, including symptomatic immunoglobulin (Ig) G subclass or isolated IgA deficiency (note: children who require monthly immunoglobulin infusion are unlikely to benefit from vaccination)
 - immunosuppressive therapy (including corticosteroid therapy 2 mg/kg or more daily of prednisolone or equivalent for more than one week) or radiation therapy, where there is sufficient immune reconstitution for vaccine response to be expected
 - haematological and other malignancies
 - solid organ transplant
 - haemopoietic stem cell transplant
 - HIV infection (including AIDS)
 - chronic renal failure, or relapsing or persistent nephrotic syndrome
- Proven or presumptive cerebrospinal fluid leak
 - cochlear implants
 - intracranial shunts

Category B: conditions associated with an increased risk of IPD

- Chronic cardiac disease
 - particularly cyanotic heart disease or cardiac failure in children
 - excluding hypertension only (in adults)
- Chronic lung disease, including:
 - chronic lung disease in preterm infants
 - cystic fibrosis
 - severe asthma in adults (requiring frequent medical visits and use of multiple medications)
- Diabetes mellitus
- Down syndrome
- Alcoholism
- Chronic liver disease
- Preterm birth at less than 28 weeks' gestation
- Tobacco smoking

* Adapted from The Australian Immunisation Handbook.¹¹

condition(s) associated with the highest increased risk of IPD (category A), except haematopoietic stem cell transplant recipients, are recommended to receive:

- a single dose of 13vPCV at the time of diagnosis
- a dose of 23vPPV at least two months after 13vPCV
- two further doses of 23vPPV at least five years apart.

Stem cell recipients should receive a course of three doses of 13vPCV over six months and then a follow-up dose of 23vPPV 12 months later.

- Adults who have a newly identified or previously identified condition(s) listed in category B (increased risk of IPD) are recommended to receive:
 - a dose of 23vPPV at diagnosis
 - two further doses of 23vPPV at least five years apart (see the case study in Box 2).

PneumoSmart vaccination tool

An online tool that can help identify the recommended pneumococcal vaccination

regimen for individual patients is available at the PneumoSmart website (www.pneumosmart.org.au/clinicians/vaccination-tool). The PneumoSmart vaccination tool also indicates which vaccines are funded under the NIP or PBS.

When would we use conjugated pneumococcal vaccine in older people?

The vaccine 13vPCV was licensed for older people in many countries after a Netherlands study provided evidence that this vaccine gives good protection against vaccine-type IPD and moderate protection against CAP.⁷ It was licensed for people aged over 50 years in Australia in 2011.

The role of 13vPCV in older people and the additional benefit over 23vPPV is contentious. Several countries, including Canada, the UK and Germany, assessed the possible cost versus benefit and decided against using 13vPCV in older people, staying with 23vPPV use. In the US, 13vPCV and 23vPPV are used sequentially in older people. An upcoming

review may clarify the benefit of this approach compared with the use of 23vPPV alone.

Australia is still considering its position. Key issues are the degree of herd immunity provided by the childhood pneumococcal vaccination program and the question whether vaccine-type pneumococcal disease will continue to decline without a conjugate vaccine dose to older people. The Australian and New Zealand Society for Geriatric Medicine recommends that in unvaccinated older people, consideration should be given to first providing a dose of 13vPCV followed by 23vPPV two to six months later.¹² However, 13vPCV is funded only for children up to 5 years of age. Offering 13vPCV to older people with a high risk of serious consequences of CAP may be worthwhile, but they will need to pay privately for it.

Several studies have shown that 23vPPV induces a state of immune tolerance or hyporesponsiveness to subsequent vaccination, where the response to revaccination does not reach the levels

2. CASE STUDY: PNEUMOCOCCAL VACCINATION IN AN OLDER WOMAN WITH ASTHMA

Angie, aged 66 years, has adult-onset asthma with increasing symptoms over time. She has made four visits to the emergency department in the past year with acute exacerbations of her asthma, although she has not required hospital admission. She presents for a review of her asthma medication and influenza vaccination. She states she has never received pneumococcal vaccine and your desktop software has no record of it being given.

Would you offer Angie pneumococcal vaccine and if so, which vaccine should she have?

A substantial proportion of cases of severe disease and deaths in older people with influenza infection are associated with secondary bacterial infection, particularly pneumococcal infection. All Australians aged 65 years and older are entitled to free 23-valent pneumococcal polysaccharide vaccine (23vPPV) at 65 years of age. Angie is at particular risk of a poor outcome of pneumococcal infection because of her asthma and should receive 23vPPV.

Should Angie receive a booster of pneumococcal vaccine and if so, when?

Australian guidelines no longer recommend a routine pneumococcal vaccine booster five years after receipt of the first dose for non-Indigenous adults. Some groups at increased risk of invasive pneumococcal disease are recommended to have either one or two booster doses of vaccine at five-year intervals and are entitled to these vaccines free of charge under the National Immunisation Program.¹⁴ People with severe chronic asthma, such as Angie, are included in those recommended to receive a single booster dose five years after the first dose. Many desktop software systems can program a recall for the next dose.

achieved with primary vaccination.¹³ The clinical significance of this is unknown, but if both 13vPCV and 23vPPV are to be given then 13vPCV should be given first, followed by 23vPPV at least eight weeks later. If 23vPPV has already been

received then administration of 13vPCV should be delayed for 12 months.

Role of general practice

The infant pneumococcal vaccination program in Australia has an average coverage of 93%, but uptake of 23vPPV remains suboptimal, at 54% national coverage in 2009 and less than 50% in 2015-16 based on a NSW Health survey.¹⁴ Serotype replacement is occurring, with an increase in non-vaccine-type pneumococcal disease in Australia. Nevertheless, more effective prevention is possible if coverage rates are increased.

Conclusion

Despite the availability and use of 23vPPV in older people, making an impact on pneumococcal disease rates has been challenging. This is largely because of inadequate coverage, suboptimal effectiveness of this vaccine, serotype replacement and pneumococcal disease due to serotypes not covered in vaccines. In line with many other countries, Australia is reviewing its vaccine policy in older people now that 13vPCV has been licensed in this group. When patients request 13vPCV as well as 23vPPV, or their healthcare provider deems this desirable, then 13vPCV should either be given first or delayed for 12 months if 23vPPV has already been received. MT

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