

Review of evidence to inform the New Zealand National Immunisation Programme, 2026: Pneumococcal – adults and special groups

Prepared by Dr Mary Nowlan on behalf of the Immunisation
Advisory Centre, University of Auckland, for the National
Immunisation Programme at Health New Zealand | Te Whatu
Ora

August 2026

Contents

Acknowledgements	iv
Abbreviations	iv
Executive Summary	vi
Purpose of this review	vi
Burden of pneumococcal disease	vi
Special groups at increased risk of pneumococcal disease	vii
Higher valency pneumococcal vaccines	ix
Summary table of key findings	xi
Recommendations for the New Zealand immunisation programme	xii
Outstanding questions	xii
Introduction	1
Burden of pneumococcal disease in adults	1
Epidemiology in New Zealand	3
Influence of changing vaccination schedules	4
Pneumococcal vaccines for use in adults	8
Other vaccines in clinical development	9
International recommendations for pneumococcal immunisation in adults	10
Review of literature - special groups	17
Risk factors	17
Indirect protection of adults	24
Summary	25
Review of literature - newer pneumococcal vaccines	27
Safety	27
Immunogenicity	28
Vaccine effectiveness and potential impact	30
Summary of evidence	33
Table 10: Burden of disease and pneumococcal vaccination in special groups	33
Table 11: Indirect protection and international recommendations	40
Table 12: Vaccine safety	42
Table 13: Immunogenicity	46
Table 14: Vaccine effectiveness and potential impact	51
Methodology for literature searches	54
Concepts	54
Search details	54
References	55

List of Tables and Figures

Table 1: Number and rate (per 100,000 population) of invasive pneumococcal disease cases notified in 2025, by age and ethnicity (source PHF Science 2026)	5
Table 2 IPD cases, by serotype and ages from 5 years, 2025 (Source PHF Science, provisional data)...	7
Table 3: Comparison of the pneumococcal serotypes contained within high valency vaccines used in adults and groups at high IPD risk	9
Table 4: A summary of some of the international immunisation schedules for pneumococcal vaccinations for older adults and special groups (as of 1 July 2026).	10
Table 5: Extended pneumococcal immunisation programme for adults aged 18 years and over (extracted from the Immunisation Handbook 2026 version 2, table 17.5)	12
Table 6: Comparison of adult clinical risk groups recommended pneumococcal vaccination by country (as of 1 July 2026).....	13
Table 7: Clinical risk groups who should receive pneumococcal immunisation in the UK (Green Book, table 25.2).....	15
Table 8: Frequency of comorbid conditions in adults with community-acquired pneumonia (Source: Torres et al 2013, Thorax open access)	20
Table 9: Post-hoc analysis of subsequent risk of cardiac clinical outcomes after occurrence of pneumonia in two clinical trial cohorts (PARADIGM-HF and PARAGON-HF) (Shen et al, 2021, open access)	23
Table 10: Burden of disease and pneumococcal vaccination in special groups	33
Table 11: Indirect protection and international recommendations	40
Table 12: Vaccine safety	42
Table 13: Immunogenicity	46
Table 14: Vaccine effectiveness and potential impact	51
 Figure 1: Number of invasive pneumococcal disease cases by month and year in New Zealand (Source PHF Science, to 31 July 2026)	3
Figure 2: Invasive pneumococcal serotypes, 2014 - 2025 (PHF Science, IPD annual report 2025)	4
Figure 3: Rates of invasive pneumococcal disease by age group, 2014-2025 (PHF Science, dotted lines indicate years of Schedule changes)	4
Figure 4: Serotype 19A invasive pneumococcal disease by age group, rate per 100,000, 2014-2024 (ESR, IPD annual report 2024)	5
Figure 5: Rate of invasive pneumococcal disease notification, by age and ethnicity, 2025 (data source PHF Science)	6
Figure 6 Rate of invasive pneumococcal disease notifications in adults, by age and ethnicity 2025 (data source PHF Science)	6
Figure 7: Rates of IPD due to serotypes covered by (a) PCV13, and (b) IPD due to serotypes additionally included in PCV20, by age groups per 100,000 population, 2017-2025 (PHF Science, 2026, open access)	8
Figure 8: Pooled risk estimates of risk conditions for adult invasive pneumococcal disease. Summary of the studies that reported incidence rate ratios for the 22 risk domains that were eligible for meta-analysis, stratified by age (Ditzel, 2025 open access)	18
Figure 9: Risk estimates of multimorbidity for adult invasive pneumococcal disease. Forest plot of reported incidence rate ratios stratified by number of comorbidity risk conditions (colour), over different age categories. (Ditzel, 2025, open access)	19

Figure 10: Comparison of rates of hospital admission, outpatient attendance and accident and emergency (A&E) visits for patients with or without community-acquired pneumonia (CAP) hospital diagnosis, stratified by underlying comorbidity and year, in England (Campling, 2020, open access)	21
Figure 11: Adjusted odds ratios for mortality in each clinical risk group for those hospitalised with community-acquired pneumonia compared with those who did not. (Campling, 2020, open access)	22
Figure 12: Model-based opsonophagocytic activity geometric mean ratio in phase 3 clinical trial, participants aged ≥60 years: A) comparing 13 serotypes shared between PCV20 and PCV13; B) additional 7 serotypes shared between PCV20 and 23PPV. (Essink et al 2022, open access)	29

Acknowledgements

I would like to express my gratitude to Professor David Murdoch, Co-leader of The Infection Group at the Department of Pathology and Molecular Medicine, University of Otago Christchurch and Chief Scientist at the Institute for Public Health and Forensic Science (PHF Science), New Zealand, for peer-reviewing this Review of Evidence. I would also like to thank Dr Andrew Anglemyer (PHF Science) for his assistance with collating data.

Abbreviations

ACIP	Advisory Committee on Immunization Practices
AE	adverse events
AEFI	adverse events following immunisation
AF	atrial fibrillation
aHR	adjusted hazard ratio
AMI	acute myocardial infarction
aOR	adjusted odds ratio
ATSI	Aboriginal Torres Strait Islanders – indigenous people of Australia
BMT	bone marrow transplant
95% CI	confidence interval
CAP	community acquired pneumonia
CHD	chronic heart disease
CHF	congestive heart failure
CKD	chronic kidney disease
COPD	chronic obstructive pulmonary disease
CRD	chronic respiratory disease
CSF	cerebrospinal fluid
CV	cardiovascular
CVD	cardiovascular disease
ED	emergency department
ESR	Institute for Environmental and Scientific Research
FDA	Federal Drug Administration (US)
GBS	Guillain-Barré syndrome
GP	general practice / practitioner
GMT / GMC	Geometric mean titre / concentration
GMR	Geometric mean titre ratio
HF	heart failure
HFpEF / HFrEF	heart failure with preserved ejection fraction / with reduced ejection fraction
HR	hazard ratio
HSCT	haematopoietic stem cell transplant
IgG	immunoglobulin G
IPD	Invasive pneumococcal disease
IQR	interquartile range
IR	incidence risk

IRR	Incidence risk ratio
LRTI	lower respiratory tract infection
MAAE	medically attended adverse events
MELAA	Middle Eastern, Latin American and African ethnicity
mRNA-CV	messenger RNA COVID-19 vaccine
MSD	Merck Sharp and Dohm
NIP	National Immunisation Programme
NOCI	new-onset chronic illness
NP	nasopharyngeal
NPC	nasopharyngeal carriage
NZ	Aotearoa New Zealand
OPA	opsonophagocytic activity
PD	pneumococcal disease
PCV7, 13, 20 or 21	Pneumococcal conjugate vaccine, 7-valent, 10-valent, 13-valent, 20-valent or 21-valent
23PPV	Pneumococcal polysaccharide vaccine 23-valent
PHF Science	New Zealand Institute of Public Health and Forensic Science
PLHIV	people living with HIV
RCT	Randomised controlled trial
RTI	respiratory tract infection
SAE	severe adverse events
SD	standard deviation
Spn	<i>Streptococcus pneumoniae</i>
SRMA	systematic review meta-analysis
TIA	transient ischaemic attack
UK	United Kingdom
US	United States of America
US CDC	Centers for Disease Prevention and Control (US)
UTI	urinary tract infection
VAERS	Vaccine adverse event reporting system (US)
WHO	World Health Organization

Executive Summary

Purpose of this review

This review of evidence aims to assess the benefits of the vaccination of adults with underlying health conditions against pneumococcal disease. It has two main focuses:

- to consider whether there are additional indications or age groups with high burdens of disease, for which pneumococcal vaccination is not routinely recommended or is not funded as part of an extended immunisation programme for special groups in New Zealand
- to evaluate the use of higher valency pneumococcal conjugate vaccines in adults and their potential to replace 23-valent pneumococcal polysaccharide vaccine (23PPV) and the 13-valent pneumococcal conjugate vaccine (PCV13).

It draws on literature published between January 2019 and June 2026 and examines epidemiology, systematic reviews, disease burden and vaccine effectiveness, published clinical trial data on vaccine safety and immunogenicity, and international experience. This information will support the National Immunisation Programme and updates to the Immunisation Handbook in New Zealand. Due to resource constraints, this is a rapid review, not a systematic review, and the quality of the evidence has not been formally graded. Cost-benefit analyses are beyond the scope of this review. It was commissioned as part of a contract for services between the Immunisation Advisory Centre at the University of Auckland and Health New Zealand | Te Whatu Ora to address certain questions about pneumococcal vaccination in adults with the potential introduction of higher valency pneumococcal conjugate vaccines (PCVs). The opinions and interpretations of the literature presented are solely those of the author.

Burden of pneumococcal disease

Key findings

- The burden pneumococcal disease in New Zealand is shaped by age, multimorbidity, ethnic and socioeconomic inequities, and evolving serotype patterns.
- Young children and oldest adults are the most affected, particularly those of Māori and Pacific ethnicity.
- Non-invasive pneumococcal pneumonia is not notifiable but likely to contribute significantly to the burden of pneumococcal infections.

Pneumococcal disease remains a significant public health issue in New Zealand, with the burden concentrated in specific age and population groups despite vaccination efforts. Pneumococcal infections range from mild infections, such as otitis media and sinusitis, to localised non-invasive pneumonia, and severe invasive infection (invasive pneumococcal disease) in normally sterile body cavities resulting in bacteraemic pneumonia, sepsis and meningitis. Overall, the burden of pneumococcal disease in New Zealand is shaped by age, multimorbidity, inequities affecting Māori and Pacific populations, and evolving serotype patterns. Although not clearly documented, IPD is likely to be the tip of the iceberg for pneumococcal disease burden in adults. While vaccination has reduced disease incidence, particularly in young children, persistent adult burden and disparities highlight the need for broader, risk-based vaccination strategies and improved prevention measures.

Highest burden in older adults and young children, with strong role of comorbidities

In New Zealand, invasive pneumococcal disease (IPD) occurs most frequently in adults aged 65 years and over, who accounted for the largest number of cases in 2025, with similar incidence rates to infants aged under 2 years. The rate of IPD in adults aged over 75 years exceeds that in young children for whom vaccination is available. Risk increases markedly with age, immunosenescence and the presence of comorbidities, particularly when multiple conditions and risk factors coexist (“risk stacking”), which can elevate risk to levels comparable to traditional high-risk groups.

In older adults, an underestimated, vaccine-preventable cause of hospitalisation due to pneumococcal infections is non-bacteraemic pneumococcal pneumonia (also known as community-acquired pneumococcal pneumonia).

Significant ethnic inequities in disease burden

Māori and Pacific peoples experience disproportionately high rates of IPD across all age groups. In 2025, IPD incidence in Māori and Pacific adults aged 50 years and older was 3–5 times higher than in non-Māori/non-Pacific populations. These disparities widen as IPD incidence increases in older age groups: Māori and Pacific adults aged 75 years and over are four- and five-times greater risk of IPD. These inequities are linked to a higher prevalence of comorbidities in younger ages, socioeconomic deprivation, and increased exposure to transmission risks (e.g., multigenerational households).

Changing epidemiology and ongoing serotype-related challenges

Although pneumococcal vaccination has reduced the overall disease burden, New Zealand has experienced shifts in disease patterns due to vaccine schedule changes and serotype replacement. A rise in serotype 19A followed the recent use of PCV10, particularly affecting infants and later older adults via transmission. While reintroduction of PCV13 reduced disease in children, adult disease persists. A substantial proportion of adult IPD cases are caused by serotypes covered by higher-valency vaccines (e.g., 23PPV, PCV20 and PCV21), indicating ongoing gaps in protection.

Persistent transmission despite indirect (herd) protection

Childhood immunisation provides some indirect protection to adults, but this is incomplete and varies due to serotype replacement and transmission dynamics. Evidence suggests that indirect effects may be plateauing in some settings, with continued disease in susceptible adults being driven by specific serotypes and possible transmission from both young children and young adults.

Special groups at increased risk of pneumococcal disease

Key findings

- Adult groups currently funded pneumococcal vaccinations remain at highest risk of IPD.
- Multimorbidity substantially increases the burden of pneumococcal disease.
- The burden is substantial in adults with chronic illness before the age of 65 years.
- Community-acquired (non-invasive) pneumococcal pneumonia increases the risk for adverse cardiovascular outcomes and those with underlying cardiovascular disease are at high risk of IPD.
- Severe outcomes are also seen in those with chronic diseases not currently indicated for funded pneumococcal vaccines.

Individuals with immunocompromising conditions remain at the highest risk of IPD and pneumococcal immunisation programmes typically target these recognised immunocompromised cohorts. Growing evidence shows that the health burden is also driven by individuals aged under 65, living with non-immunocompromising chronic diseases not eligible for pneumococcal vaccination. Risk increases further when multiple comorbidities are present.

Bidirectional impact

The relationship between pneumonia and chronic conditions is highly bidirectional: an acute respiratory infection acts as a systemic catalyst to induce organ damage and inflammation; while preexisting chronic diseases simultaneously accelerate infection severity, double bacteraemia rates and multiply the odds of severe outcomes. Patients with chronic respiratory disease, liver disease and cardiovascular disease experience particularly severe outcomes, including greater risk of hospitalisation, bacteraemia, heart failure and death.

Role for pneumococcal vaccination

Pneumococcal vaccination can help to prevent pneumococcal infections and their downstream complications in these ‘at increased risk’ groups. Beyond reducing the risk of pneumonia and invasive disease, vaccination has been associated with lower rates of cardiovascular events, including acute myocardial infarction, stroke and all-cause mortality in older adults. Evidence also suggests vaccination may reduce hospitalisations in patients with COPD and cardiovascular disease. These broader benefits support the use of pneumococcal vaccination as an important preventive strategy in individuals with chronic health conditions, particularly those with multimorbidity who are at elevated risk of severe disease and long-term complications.

Pneumococcal pneumonia and IPD cases could also be reduced by encouraging greater uptake of vaccines against viral respiratory infections such as influenza, respiratory syncytial virus and COVID-19, particularly in adults with multiple comorbidities, and close contacts within multi-generational homes or residential care facilities.

Risk factors

From the literature, there appears to be three tiers of risk factors for IPD.

1. **High risk** due to moderate to severe immunocompromise: unable to prevent invasive infections or conditions where infections can more readily access normally sterile compartments, including primary immunodeficiencies and HIV infection, asplenia, haematological malignancies, cerebrospinal fluid leakage, kidney disease requiring dialysis, transplant recipients, Down syndrome/Trisomy 21 (including adults).
2. **Increased risk** due to underlying chronic medical conditions that facilitate opportunistic infections or in whom infections can progress to become invasive: such as congestive heart failure, chronic respiratory diseases like cystic fibrosis, bronchiectasis and COPD, moderate immunosuppression, chronic liver disease, diabetes mellitus, neurological diseases and vascular diseases like cerebrovascular and ischaemic heart diseases. These are amplified by increasing age. The risk of IPD increases with two or more underlying conditions to match the risk for tier 1. The absolute risk is greatest with increasing age over 65 years, particularly with increased frailty, but for those with multiple comorbidities aged under 65 years, the relative risk is greater.

3. **Potential risk** due to pneumococcal coinfections following respiratory virus infection. Preventing viral infections such as influenza, respiratory syncytial virus (RSV), COVID-19 can help to reduce the risk of pneumonia and cardiovascular events, which in turn, lower the risk of IPD, heart failure and hospitalisation that can lead to increased frailty. Risk groups include individuals with a chronic medical condition, but also those with obesity, a risk for exacerbation of respiratory disease such as asthma, with certain lifestyle factors (eg smoking, alcoholism), and environmental factors, such as housing conditions, occupational risks, pollution or passive smoking. Multiple coexisting factors increase the risk.

Generally, tier 1 conditions are eligible for pneumococcal vaccination in New Zealand, alongside seasonal influenza and COVID-19 vaccines, but eligibility differs between PCV13 and 23PPV and adults or children. Tier 2 conditions are unable to access funded pneumococcal vaccination and are likely to benefit from protection against more opportunistic serotypes. Tier 1 and tier 2 are generally funded seasonal influenza vaccine and all adults over 30 years are eligible for variant-matched COVID-19 vaccines. Although an RSV vaccine is available, it is not yet funded.

Higher valency pneumococcal vaccines

The evidence for the use of new, higher valency pneumococcal vaccines was considered. These vaccines are not yet approved for use in New Zealand and there is limited real-world use of them internationally. Much of the data presented is from pivotal clinical trials in which efficacy is inferred by immunogenicity data.

Vaccine safety

Key findings

- Across clinical trials and post-licensure surveillance, PCV20 (Prevenar® 20, Pfizer) and PCV21 (Capvaxive®, MSD) demonstrate favourable and consistent safety profiles across age groups.
- Safety profiles of PCV20 and PCV21 are comparable with those of PCV13 and 23PPV

Common adverse events include mild to moderate injection-site pain and systemic symptoms (e.g. myalgia, fatigue). Older adults generally reported fewer adverse events than younger adults. Fever is uncommon and was reported by less than 1–2% of recipients. No serious adverse events reported during clinical trials have been considered vaccine related. Real-world passive safety surveillance reports to the US Vaccine Adverse Events Reporting System (VAERS) were consistent with trial findings; a possible Guillain–Barré syndrome signal is under investigation, but rates remain low and within expected background levels.

Higher-valency PCVs with modified carrier proteins have shown similar safety profiles to the licensed pneumococcal vaccines during early-stage clinical development in adults.

Immunogenicity

Key findings

- PCV20 and PCV21 elicit robust, functional immune responses across all included serotypes, meeting non-inferiority criteria compared with existing vaccines.
- PCV20: non-inferior to PCV13 for shared serotypes and to 23PPV for most additional serotypes; strong opsonophagocytic (OPA) antibody responses seen across age groups

- PCV21: non-inferior to PCV20 for shared serotypes and superior for most unique serotypes, suggesting broader protection
- Responses are maintained across age groups and in adults with chronic conditions (clinical trials excluded immunocompromise)
- Limitations of immunogenicity data include the absence of defined immune correlates of protection for each serotype and reliance on immunobridging rather than clinical endpoints.

During clinical trials, immunogenicity is assessed by measuring serotype-specific antibody responses (functional antibody opsonophagocytic activity and serum immunoglobulin G titres) and compared with antibody titres from pivotal clinical trials of older PCV vaccines (PCV7 and PCV13) to demonstrate non-inferiority and infer efficacy.

PCV20

Across multiple phase 3 clinical trials, PCV20 demonstrated a broad, functional immune response to all 20 pneumococcal serotypes and was consistently non-inferior to PCV13 for shared serotypes. Only serotype 8 missed the non-inferiority criteria compared with 23PPV in older adults, but the immune response was considered robust with at least a four-fold rise in functional antibody titres in most participants.

The immune response to PCV20 in non-immunocompromised adults at increased risk of pneumococcal disease was like that seen in healthy groups; however, the clinical trials excluded individuals who were immunocompromised who are a significant risk group for IPD. No impact on immunogenicity was seen for either vaccine when PCV20 is coadministered with mRNA COVID-19 vaccines.

PCV21

When compared with PCV20 or 23PPV, PCV21 induced robust antibody responses to shared and unique serotypes in a range of adult age groups. It is likely to provide broader protection against serotypes currently covered by PCV13 and 23PPV.

Vaccine effectiveness and potential impact

Key findings

- Real-world effectiveness data is limited for these vaccines
- PCV20 shows moderate effectiveness against IPD and pneumococcal pneumonia in older adults, including immunocompromised groups. Greater effect seen against all-cause pneumonia and lower respiratory tract infections.

Limited real-world evidence for PCV20 shows moderate vaccine effectiveness of around 25% against IPD and around 23% against pneumococcal pneumonia, with larger population impact for broader outcomes such as all-cause pneumonia. A large retrospective cohort study in adults aged 65 years and over found absolute reductions are small for IPD but substantial for pneumonia and lower respiratory tract infections, particularly in high-risk groups. For example, larger effects were shown in higher-risk groups, with 1.3–2.4 times higher absolute rate reductions in those with immunocompromise or chronic conditions. One study in individuals with inflammatory bowel disease on immunosuppressive treatment reported PCV20 to be associated with a 50% reduction in pneumonia and severe outcomes, though confounding is likely.

A modelling study in the UK suggested that targeted vaccination of high-risk groups could be more efficient in older adults than a universal age-based vaccination programme. PCV20 given to new aged-care residents was projected to have a greater impact than 23PPV given as a universal age-based strategy from 65 years.

At the time of writing, no real-world effectiveness evidence was available for PCV21.

Conclusions

Pneumococcal disease in adults is driven by age, multimorbidity and inequity. Newer conjugate vaccines (particularly PCV20 and PCV21) offer broad protection with good safety and immunogenicity profiles. Early real-world evidence indicates meaningful reductions in disease, especially for common outcomes like pneumonia. Current, but limited evidence, suggests that targeted vaccination strategies for high-risk groups, such as in aged-care facility residents, are likely to deliver the greatest health impact and efficiency for immunisation programmes.

Summary table of key findings

Outcome	Key findings	Implications
Burden of pneumococcal disease		
	High IPD risk over age 65 years and particularly aged over 75 years; strong additive effect from multimorbidity; marked ethnic inequities	Supports targeting high-risk groups, including age-care residents, and addressing access inequities
	Accumulated risk at a younger age for adults with heart and other organ failure, vascular disease, chronic respiratory disease.	Increased benefits of pneumococcal vaccination in those with multiple comorbidities, including ages <65 years.
	Three tiers of risk have emerged: high risk, increased risk and potential risk with viral coinfections.	Further study of pneumococcal risk in adults is required. Encourage greater uptake of respiratory viral vaccines, like influenza, across all risk groups
	Non-invasive pneumococcal pneumonia is an underestimated health burden in adults.	Much of the public health benefit of adult pneumococcal vaccination is likely to come through preventing non-bacteraemic pneumococcal pneumonia
Higher valency pneumococcal vaccines		
Safety	PCV20 and PCV21 are well tolerated; mostly mild–moderate AEs; no vaccine-associated SAE.	No major safety barriers to programme expansion
Immunogenicity	Robust responses; PCV20 non-inferior to PCV13; PCV21 broader coverage for adults	Supports transitioning to higher-valency PCVs
Effectiveness	Moderate VE (~25% against IPD); strong impact on pneumonia; higher benefit in high-risk groups	Population benefit driven by common pneumococcal disease outcomes rather than IPD alone
Programme impact	Targeted strategies could be more efficient (fewer need to be vaccinated for impact); PCV20 benefit greater than 23PPV	Incorporate risk-based or hybrid strategies

Recommendations for the New Zealand immunisation programme

Recommendation	Details
Adopt a higher-valency PCV (e.g. PCV20 or PCV21) for adult programmes	Likely to provide broader coverage and greater impact than 23PPV.
Prioritise high-risk populations	- Focus on individuals with multimorbidity and residents of aged-care facilities, as well as current immunocompromised groups. - Employ targeted strategies where efficiency (number needed to be vaccinated) is substantially improved.
Address inequities in access and uptake	- Improve vaccine delivery for older Māori and Pacific populations and those with chronic diseases. - Integrate vaccination into routine care settings (e.g. dialysis units, specialist clinics). - Simplify vaccination schedules as much as possible. - Align with international trends toward single-dose PCV strategies to improve uptake.
Continue surveillance and evaluation	- Monitor serotype replacement and long-term effectiveness. - Include pneumonia hospitalisations in evaluation of impact. - Evaluate the incidence of pneumococcal disease in adults aged under 65 years
Support integrated respiratory disease prevention strategies.	- Promote uptake of influenza, COVID-19 and RSV vaccines to reduce co-infection risk in those at risk of complications and more widely to reduce community and household transmission of these viruses. - Assess the potential impact of pneumococcal vaccination on non-invasive pneumococcal infections, such as community-acquired pneumonia and all-cause pneumonia hospitalisations. - Offer vaccination to those with heart failure, vascular diseases like ischaemic heart disease and cerebrovascular disease, chronic respiratory disease and chronic liver disease.
Coadminister pneumococcal vaccine with other vaccines	If routinely offered at age 65 years and over, co-administer with other funded vaccines offered at that age, such as zoster, influenza and Tdap vaccines.

Outstanding questions

Real-world evidence on safety and effectiveness of PCV20 (Prevenar 20) and PCV21 (Capvaxive) is just emerging. Any impacts of immunisation on IPD rates will be slow to emerge through epidemiological surveillance.

This review was unable to determine whether vaccination should be offered for all adults aged 65 years and over or to continue to target the high-risk groups already funded PCV13/23PPV vaccinations. However, evidence suggests expansion of eligibility to additional adult groups and to elderly adults. These include adults with multimorbidity, regardless of age, with congestive heart failure, ischaemic heart disease, chronic liver disease or chronic respiratory disease, as well as residents of aged-care facilities and other frail adults. Monitoring pneumococcal pneumonia hospitalisations would be a useful to assess the potential vaccine impact in adults but more challenging than IPD notifications to obtain.

Surveillance of predominant serotypes would determine whether either PCV20 or PCV21 provides better protection to high-risk groups and older adults, particularly when the PCV20 programme is underway in infants. PCV21 has a similar serotype coverage to 23PPV, providing additional protection against serotypes not covered by PCV20, particularly against less invasive, opportunistic serotypes more likely to cause disease in adults with weakened immune responses.

Review of evidence: Pneumococcal – adults and special groups

Prepared by: Dr Mary Nowlan, Senior Advisor
Immunisation Advisory Centre, University of Auckland, New Zealand

Prepared for: Directorate of Protection – Immunisation, Health
New Zealand | Te Whatu Ora

August 2026

Introduction

This review of evidence aims to assess the benefits of vaccination against pneumococcal disease in adults with underlying health conditions. It has two main focuses:

- to consider whether there are indications or age groups for which pneumococcal vaccination is not routinely recommended or funded as part of an extended immunisation programme for special groups
- to evaluate the use of higher valency pneumococcal conjugate vaccines in adults and their potential to replace pneumococcal polysaccharide vaccine (23PPV) and the 13-valent pneumococcal conjugate vaccine (PCV13).

It draws on literature published between January 2019 and June 2026 and examines epidemiology, systematic reviews, disease burden and vaccine effectiveness, published clinical trial data on vaccine safety and immunogenicity, and international experience. This information will support the National Immunisation Programme and updates to the Immunisation Handbook in New Zealand. Due to resource constraints, this is not a systematic review and the quality of the evidence has not been formally graded. Cost-benefit analyses are beyond the scope of this review. It was commissioned as part of a contract for services between the Immunisation Advisory Centre at the University of Auckland and Health New Zealand | Te Whatu Ora to address certain questions about pneumococcal vaccination with the potential rollout of higher valency pneumococcal conjugate vaccines (PCVs) in adults. The opinions and interpretations of the literature presented are solely those of the author.

Key questions considered for this review are:

- Would broadening the eligibility for pneumococcal vaccination benefit those with underlying chronic diseases, such as vascular diseases and respiratory diseases?
- Should pneumococcal vaccination be offered to adults with multiple comorbidities that individually are currently not eligible for funded vaccine under the extended pneumococcal immunisation schedule?
- Do PCV20 or PCV21 provide additional benefits over the current pneumococcal vaccines (PCV13 and 23PPV) for adults at high risk of invasive pneumococcal disease?
- Will introducing PCV20 to the childhood Schedule provide any indirect protection to adults?
- Should PCV20 or PCV21 be used in a universal age-based programme, such as those aged over 65 or 75 years?
- Would PCV21 provide better serotype coverage than PCV20 in adult groups?

Burden of pneumococcal disease in adults

Age and comorbidities are important factors for increasing the risk of invasive pneumococcal disease (IPD) and community-acquired pneumonia (CAP). Infections with the most invasive serotypes are more commonly seen in younger people with few comorbidities, whereas the low invasive types are more opportunistic, infecting those with multiple comorbidities and older age.¹

A previous review of evidence² found two classifications of risk in both children and adults in the literature, namely:

- high-risk conditions, for which there is a significant risk from pneumococcal infection and IPD
- ‘at-risk’ conditions, which on their own may not significantly increase risk, but when combined with or without life-style risk factors can increase an individual’s likelihood of developing IPD.

Patients with comorbidities affecting the respiratory system and the immune system are particularly at high risk of IPD and death. Chronic respiratory disease, particularly chronic obstructive pulmonary disease (COPD), cystic fibrosis and lung cancer, is associated with impaired respiratory immunity and increased infection risk. In the New Zealand context, bronchiectasis is an important cause of chronic respiratory disease, with high rates starting in childhood. Compromised immunity is a significant risk factor in opportunistic infections like pneumococcus.

Other, non-immunocompromising conditions can increase the risk of community-acquired pneumonia (CAP or non-bacteraemic pneumococcal pneumonia), and in some cases can progress further to become invasive bacteraemic pneumonia. The incidence of pneumococcal-associated disease is likely to be underestimated due to CAP, which unlike IPD is not notifiable unless it progresses to be invasive. Non-immunocompromising risk factors include chronic liver disease, diabetes and cardiovascular disease and previous pneumonia.^{2, 3}

Pneumococcal disease in older adults

As individuals age, waning immune responsiveness and comorbidities increase the risk for pneumococcal disease. Infections in older patients with multiple comorbidities are likely to be less-invasive opportunistic serotypes.¹

The concept of ‘risk stacking’ is highly relevant in older adults as the prevalence of comorbidities increases. For example, the high incidence of cardiovascular disease, chronic liver disease, diabetes and lung disease in those aged over 65 years adds to the IPD risk in older people. Almost half of the IPD cases in the over 65-year age group reported in the UK had at least one risk factor, the most common being cardiovascular disease.⁴

Pneumococcal disease in other adults

Younger adults with multiple comorbidities and lifestyle or environmental factors can also be at increased risk of IPD. The risk of life-threatening pneumococcal infections in children and adults with two or more comorbidities is as high as in those with a recognised high-risk condition, and those with three or more risk conditions were at substantially higher risk than those with a ‘high-risk’ condition.⁴ As reported in our previous review,² the risk of IPD for adults aged 50 – 64 years with a single non-immunocompromising medical condition was found to be twice that of the general population.^{5, 6} The US-based study found that for adults aged 18 – 49 years, the rate of all-cause pneumonia doubled in those with one underlying condition and was six times higher in those with three or more conditions.^{5, 6} In adults aged 50 – 59 years, the rate ratio increased from 1.7 to over 5 with three or more conditions.⁵

Multiple risk factors are particularly applicable for Māori or Pacific peoples, in whom underlying conditions such as obesity, cardiovascular disease or diabetes generally present at a younger age than for European and Asian adults. Other factors increasing the risk of pneumococcal disease are living with poverty and in crowded, multigenerational houses with young children who bring respiratory viruses to the household.

See **Review of literature - special groups** section below for further details and more recent evidence around risk groups.

Summary

Age, comorbidity burden and pneumococcal serotype characteristics are major determinants of risk for invasive pneumococcal disease and community-acquired pneumonia. Highly invasive serotypes are more commonly associated with younger, otherwise healthy individuals, whereas opportunistic serotypes predominate in older adults and those with multimorbidity.

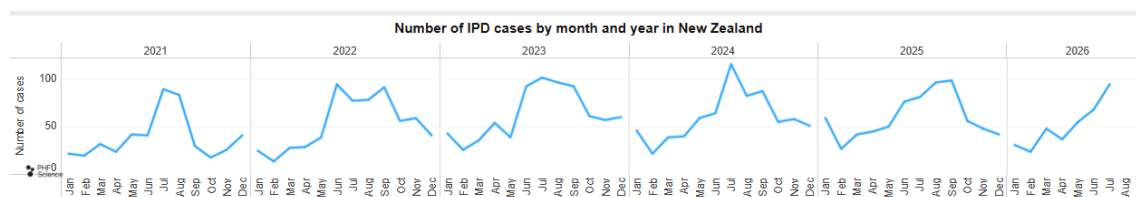
Risk from pneumococcal disease increases substantially in those with chronic respiratory, cardiovascular, metabolic and immunocompromising conditions. Risk rises further with accumulating comorbidities, often equalling or exceeding that of traditionally defined high-risk groups. Immunosenescence and multimorbidity drive a disproportionate disease burden in older adults, while younger adults with multiple conditions also experience markedly increased risk and associated health inequities. Although immunocompromising conditions confer the greatest relative risk, cumulative multiple comorbidities amplify susceptibility and reduce the independent effect of age alone. Despite this, age remains an important risk factor for adverse outcomes when combined with frailty and multimorbidity. These findings supporting vaccination strategies based on overall risk burden rather than age alone.

Epidemiology in New Zealand

This section considers the incidence and burden of invasive pneumococcal disease and pneumococcal infections in Aotearoa New Zealand (NZ) over recent years. IPD is a notifiable disease, cases are reported to EpiSurv and analysed by the Institute of Public Health and Forensic Science (PHF Science).

A seasonal pattern is common with peaks in IPD incidence coinciding with winter / early spring months, associated with increases in influenza and other seasonal respiratory viruses. See Figure 1.

Figure 1: Number of invasive pneumococcal disease cases by month and year in New Zealand (Source PHF Science, to 31 July 2026)



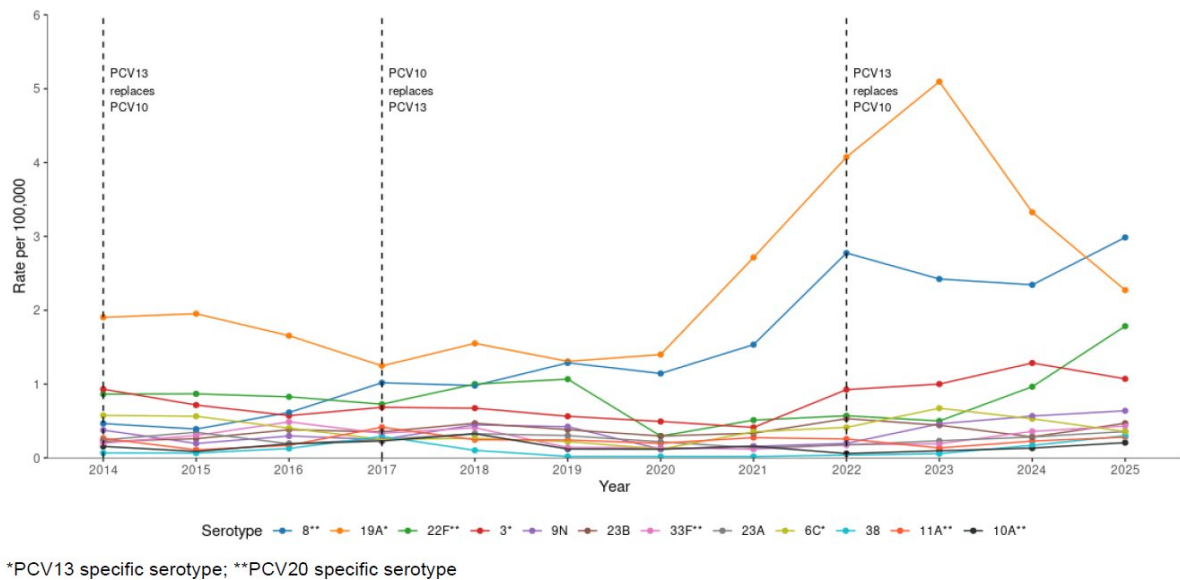
From 1 January to 31 July 2026, out of 357 IPD notifications, 19 (5%) were aged under 5 years, 172 cases (48%) were aged 5 – 64 years and 166 cases (46%) were aged 65 years and over. Half of these were of Māori or Pacific ethnicity (104 and 75/341 with known ethnicity).

For the latest published data see the [Invasive Pneumococcal Disease dashboard](#) and for monthly and annual reports see [PHF Science Digital library](#).

Influence of changing vaccination schedules

Pneumococcal conjugate vaccines have been highly effective at reducing IPD incidence overall. But unlike trends in countries that continually used PCV13, the predominance of serotype 19A pneumococcal disease in New Zealand highlighted the risks of inadequate serotype coverage (see Figure 2).

Figure 2: Invasive pneumococcal serotypes, 2014 - 2025 (PHF Science, IPD annual report 2025)



Uniquely, the New Zealand National Immunisation Schedule (childhood Schedule) has twice switched between PCV10 and PCV13 since 2011. Following further changes – firstly from a three-dose primary schedule with PCV13 to PCV10 in 2017, and then to a two-dose primary PCV10 schedule in 2020 – New Zealand experienced a marked rise in IPD in infants aged under 2 years (as shown in Figure 3).^{7,8} Cases in older adults subsequently continued to increase from 2023, particularly in adults age 75 years and over.

Figure 3: Rates of invasive pneumococcal disease by age group, 2014-2025 (PHF Science, dotted lines indicate years of Schedule changes)

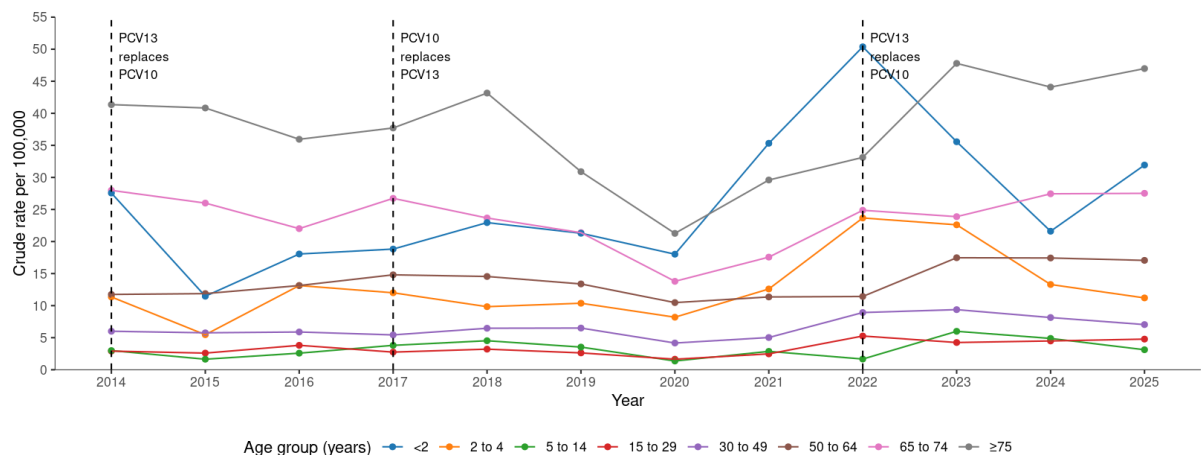


Figure 4: Serotype 19A invasive pneumococcal disease by age group, rate per 100,000, 2014-2024 (ESR, IPD annual report 2024)

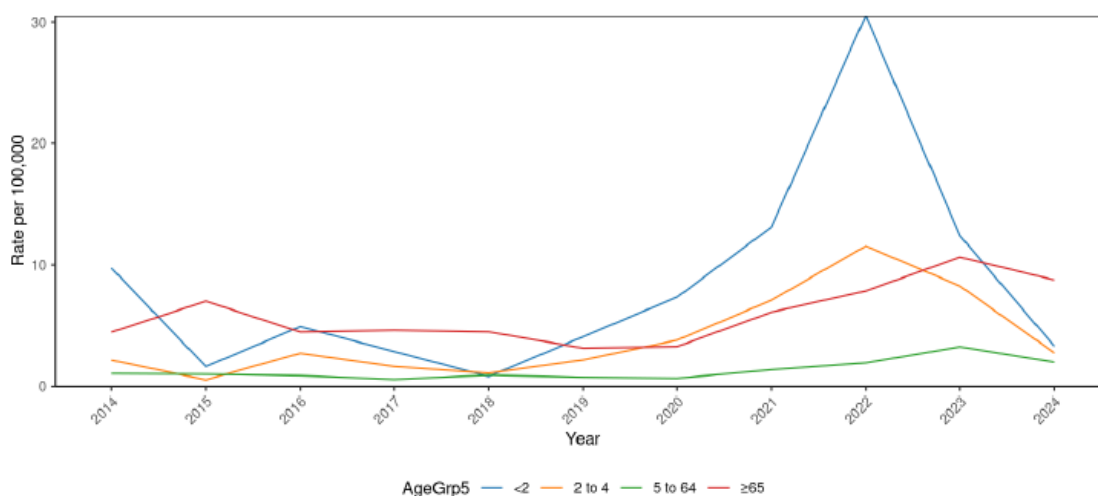


Figure 4 shows that the spike in cases in infants during 2022 (blue line) was echoed by an increase in serotype 19A IPD in adults aged ≥65 years from 2023 (red line), likely due to higher nasopharyngeal carriage and transmission from young children. Although a rapid decline was seen in the vaccinated infant cohort in 19A IPD following PCV13 reintroduction in late 2022 (from a peak of 70% in 2022 to 19% in 2024), the continued increase during 2023 in older adults (to 33%) underscored the importance of continual monitoring and appropriate vaccine selection for sustained population protection. By 2025, the proportion of 19A in adults aged ≥65 years had fallen to 16%.⁹

Invasive pneumococcal disease incidence in 2025

During 2025, the bulk of the IPD cases were in adults aged over 65 years (326 / 720 cases), but the incidence rates were similar between infants and older adults (31.9 vs 36.2 per 100,000 population; see Table 1). The rate of IPD in adults aged ≥65 years has been increasing since 2020. Some of these data were supplied by PHF Science directly and are to be considered as provisional. Where indicated, data was also published in the finalised 2025 IPD report published on 30 July 2026.⁹

Table 1: Number and rate (per 100,000 population) of invasive pneumococcal disease cases notified in 2025, by age and ethnicity (source PHF Science 2026)

Ethnicity	Age group														Total by ethnicity	
	<2 years		2–4 years		5–14 years		15-29 years		30–49 years		50–64 years		≥65 years			
	No.	rate	No.	rate	No.	rate	No.	rate	No.	rate	No.	rate	No.	rate	No.	rate
Asian	6	24.8	7	19.3	4	3.2	3	1.5	7	1.8	3	2.5	14	18.4	44	4.5
European/ Other	4	8.3	4	5.5	9	3.0	16	3.2	41	5.4	67	10.3	207	28.5	348	11.4
Māori	22	63.8	5	9.7	4	2.2	21	9.0	39	17.4	62	47.8	65	93.7	218	23.6
Pacific People	6	50.3	4	22.4	4	6.1	9	8.8	17	16.9	29	57.0	38	136.4	107	28.4
Total by age	38	31.9	20	11.2	21	3.1	49	4.8	104	7.0	162	17.1	326	36.2	717	13.5

Across all ethnicities, the rates continue to increase between those aged 65 – 74 and in those aged 75 years and over (27.5 to 45.7 per 100,000) and were much higher than for adults aged 30 – 49 and 50 – 64 years (7.0 and 17.1 per 100,000 population; data provided by PHF Science).

People of Māori and Pacific ethnicity are disproportionately affected by IPD (see Figure 5), across all age groups. Rates of IPD are notably high in the under 2-year-old children and rise markedly from age 50 years. The incidence of IPD in Māori and Pacific adults aged 50 – 64 years and 65 years and over were three to five times higher than for European/Other/MELAA adults. With a high incidence of IPD in older adults, the discrepancy by ethnicity is even greater in those aged over 75 years (see Figure 6). Compared with European and other ethnicities, the IPD rates were also five times higher in elderly adults of Pacific ethnicities and four times higher for Māori.

Figure 5: Rate of invasive pneumococcal disease notification, by age and ethnicity, 2025 (data source PHF Science)

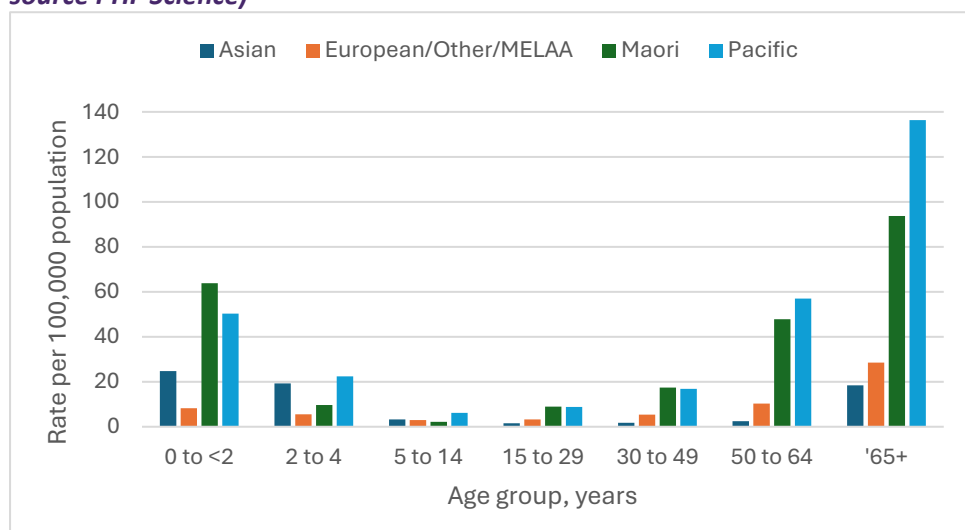
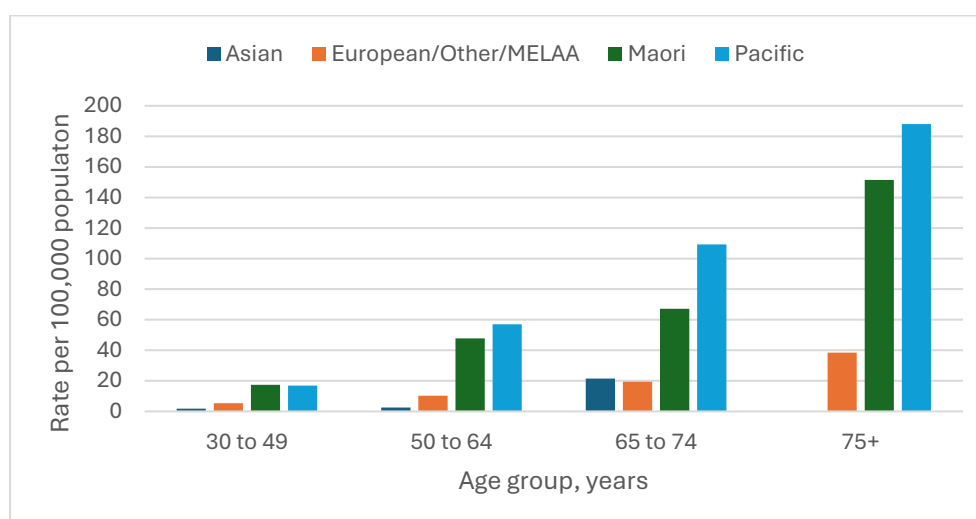


Figure 6 Rate of invasive pneumococcal disease notifications in adults, by age and ethnicity 2025 (data source PHF Science)



Predominant serotypes

Table 2 shows the serotypes of isolates collected from IPD cases by age group from age 5 years (noting that it does not include cases aged under 5 years). In these age groups, 19 cases isolates were not serotyped and there was one non-typeable case. The table shows a large proportion of cases in 2025 would have been covered by PCV20: 264/336 (78.5%) aged 5-64 years and 215/326 (66%) ages ≥65 years. For those aged 65 and over, an additional 73 cases (22%) had PCV21-specific serotypes.

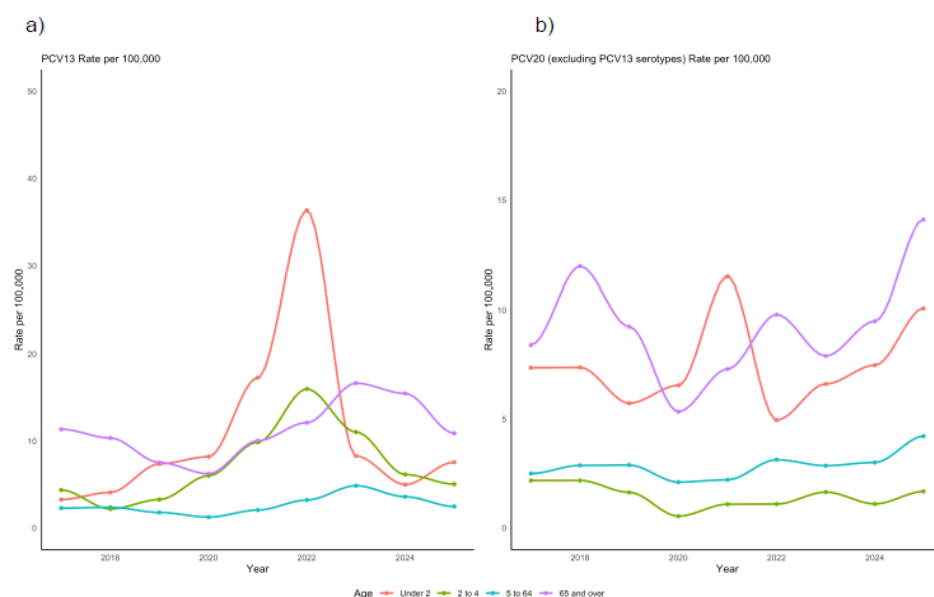
Figure 7 shows how the rates of PCV13-type IPD have changed with time since 2017 and the additional types included in PCV20. See Table 3 for serotypes covered by each vaccine. PCV20 serotypes have increased in both young children and older adults.

Table 2 IPD cases, by serotype and ages from 5 years, 2025 (Source PHF Science, provisional data)

§ cross protection from 15B/C in vaccine # Non-PCV included 1 non-typeable case and 19 cases for which serotypes were not available.

Serotypes	Ages 5 to 64 years	Ages ≥65 years
PCV7	7	8
PCV10	3	0
PCV13	82	81
19A	56	49
3	25	31
6A	1	1
PCV15	47	64
22F	40	51
33F	7	13
PCV20	125	62
8	112	41
10A	4	6
11A	4	10
12F	3	0
15B	2	5
PCV21	37	73
9N	14	18
15A	0	4
15BC [§]	1	0
15C [§]	1	6
16F	3	6
17F	3	3
23A	4	14
23B	10	13
31	0	3
35B	1	9
Non-PCV[#]	35	38
Total	336	326

Figure 7: Rates of IPD due to serotypes covered by (a) PCV13, and (b) IPD due to serotypes additionally included in PCV20, by age groups per 100,000 population, 2017-2025 (PHF Science, 2026, open access)



Summary

Generally, the pneumococcal immunisation programme in New Zealand has successfully reduced the incidence of invasive pneumococcal disease and other pneumococcal infections in children with indirect protection given to older adults. Following a surge in serotype 19A disease that coincided with the use of PCV10 on a reduced schedule, the schedule was urgently switched back to PCV13 in late 2022. Direct protection against the predominant serotype 19A was rapidly restored for those aged under 1 year, but cases of 19A IPD continued to increase in older age groups, particularly adults aged 65 years and over. Adults are also at high risk of IPD caused by PCV20 and PCV21 serotypes. Routine vaccination of all infants with PCV20 could eventually provide indirect protection to older age groups, but that would still leave a reasonable proportion of cases, particularly in older adults, that could be covered by PCV21.

Pneumococcal vaccines for use in adults

An extended immunisation programme is available to children aged over 5 years and adults in New Zealand who have certain underlying conditions that increase their risk for IPD. See **Table 5** for the adult indications for funded pneumococcal immunisation. Two vaccines are used currently, 13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent polysaccharide pneumococcal vaccine (23PPV). Adults aged over 65 years are not routinely funded pneumococcal vaccination but are recommended 23PPV as it is more affordable and has broader serotype coverage.

There are two types of pneumococcal vaccine.

- Pneumococcal conjugate vaccines (PCV)**
 contain pneumococcal polysaccharides conjugated to a carrier protein
 - PCV13 – Prevenar® 13 (Pfizer)
 - PCV15 – Vaxneuvance® (MSD) (not approved for use in NZ)
 - PCV20 – Prevenar® 20 (Pfizer) (not approved for use in NZ)
 - PCV21 – Capvaxive (MSD) (not approved for use in NZ)

Other higher valency pneumococcal conjugate vaccines are in development for use in adults, (eg two PCV24 vaccines and PCV31).

- Pneumococcal polysaccharide vaccine (PPV) – 23PPV; Pneumovax 23 (MSD)**
 contains only pneumococcal polysaccharides, limitation is that multiple doses result in hyporesponsiveness, thereby limiting the duration of protection.

For the serotypes covered by each vaccine, see Table 3.

Table 3. Comparison of the pneumococcal serotypes contained within high valency vaccines used in adults and groups at high IPD risk

Serotype	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B/C	2	9N	15A	16F	17F	20	23B	24F	31	35B
Vaccine																														
23PPV	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓		✓	✓		✓	✓		
PCV13	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓																	
PCV20	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓										
PCV21		✓				✓	✓							✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

PCV21 (Capvaxive, MSD; designated V116 in clinical trials) is specifically designed to offer broad protection to adults. It has eight unique serotypes associated with adult pneumonia and IPD that are not present in any of the current PCV vaccines and partially included in 23PPV.

Note that Sanofi and SK Science are also developing a 21-valent PCV (designated GBP410 in phase 3 clinical trials across Australia, Europe, South Korea and the US) for use in children.¹⁰

Other vaccines in clinical development

One 24-valent PCV (designated Pn-MAPS24v; Affinivax, acquired by GSK) has been designed using a Multiple Antigen Presenting System (MAPS) platform to induce robust T and B cell responses.¹¹ It contains 24 polysaccharides: all 13 in PCV13 and 10 in 23PPV (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 22F, and 33F) plus 20B. Each serotype is biotinylated and complexed with a unique fusion protein. The fusion protein consists of rhizavadin fused to two pneumococcal protein segments derived from genetically conserved surface protein genes (sp1500 and sp0785, associated with virulence of serotype 3). The fusion of the two proteins confers protection against colonisation and generates antibodies that opsonise and kill pneumococcal strains.¹²

Another 24-valent PCV (designated VAX-24; Vaxcyte) utilises a cell-free protein synthesis platform to insert non-native amino acids (para-azidomethyl-L-phenylalanine) into eCRM to form a proprietary modified CRM – the carrier protein used in Prevenar (PCV7, 13 and 20) vaccines. These serve as polysaccharide conjugation sites for each polysaccharide, activated with a small-molecule linker

(dibenzocyclooctyne). This process is known as ‘click chemistry’. The concept is designed to maximise exposure of T cell epitopes, to reduce carrier protein to polysaccharide ratio and to enhance manufacturing consistency. This enables PCV development with increased serotype coverage while minimising suppression by the carrier protein.¹³ This vaccine contains serotypes 1, 2, 3, 4, 5, 6A, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20B, 22F, 23F, and 33F (combination from PCV20 and 23PPV, plus 20B).

Vaxcyte is also utilising the same platform as for VAX-24 to develop a 31-valent PCV31 (designated VAX-31; Vaxcyte), with eCRM for polysaccharide conjugation to maximise exposure of T cell epitopes. Subtypes in PCV31 account for around 95% of IPD in adults in the US – including an additional 11 serotypes not in PCV20 and 12 not in PCV21. PCV31 includes capsular polysaccharide antigens of serotypes 1, 2, 3, 4, 5, 6A, 6B, 7C, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15A, 15B, 16F, 17F, 18C, 19A, 19F, 20C, 22F, 23A, 23B, 23F, 31, 33F, and 35B.¹⁴

International recommendations for pneumococcal immunisation in adults

Presented is a summary of the pneumococcal vaccine recommendations in adults in a selection of other countries. See Table 4 for a summary of vaccines available by country.

Table 4: A summary of some of the international immunisation schedules for pneumococcal vaccinations for older adults and special groups (as of 1 July 2026).

Country	Routine schedule	Available vaccines	Comments
New Zealand	age 65 years and over	PCV13 and 23PPV	none funded, available for private purchase
	special groups	PCV13 and 23PPV	discrepancies between vaccine eligibility, and between adults and children aged 5-<18 years
Australia	age ≥ 65 years	PCV21	funded from 1 July 2026
	aged ≥25, ATSI	PCV21	
	special groups	PCV20 PCV21	aged <18 years aged >18 years, from 1 July 2026
Canada	age 65 years and over	PCV20 or PCV21	regardless of previous PCV vaccination status, 1 year apart. PCV15/23PPV if PCV20 or PCV21 are unavailable some provinces provide PCV20 or PCV21 only for those who have not received 23PPV.
	special groups	PCV20 PCV20 or PCV21 (or complete doses with PCV20 if partially vaccinated)	ages 2 to- <18 years ages ≥18 years
UK	age 65 years and over	23PPV or PCV20 (when available)	single dose
	special groups	PCV13	single dose PCV20, no additional dose required at age 65
US	age ≥50 years and over	PCV15+23PPV, PCV20 or PCV21	single dose for all PCV naive
	special groups aged >19 - 49	PCV15+23PPV, PCV20 or PCV21	aged 19-49 years who previously received PCV13, complete series with PCV20 or PCV21 if previously received PCV13+23PPV – review when aged 50 years.

ATSI - Aboriginal and Torres Strait Islander people

Sources:

- <https://www.tewhaturora.govt.nz/for-health-professionals/clinical-guidance/immunisation-handbook/17-pneumococcal-disease>
- <https://immunisationhandbook.health.gov.au/contents/vaccine-preventable-diseases/pneumococcal-disease>
- <https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-16-pneumococcal-vaccine.html>
- <https://www.gov.uk/government/publications/pneumococcal-the-green-book-chapter-25>
- <https://www.cdc.gov/acip-recs/hcp/vaccine-specific/pneumococcal.html>

General strategies

International policies are converging towards higher-valency PCVs and simplified schedules, but implementation varies. The US is expanding age-based recommendations and simplifying regimens, whereas Canada, Korea and the UK maintain more cautious, risk-based approaches with optional sequential strategies. European guidance aligns with simplification but prioritises improving coverage and addressing heterogeneity across programmes.^{4, 15-21}

1. Age-based vs risk-based strategies

The US has transitioned to broad age-based vaccination, from aged ≥65 years to age ≥50 years.¹⁸ Whereas Canada, UK and Korea have put greater emphasis on risk-based approaches.^{4, 20, 21} Europe has mixed age and risk-based approaches but supports simplification.¹⁹ In July 2026, Australia also introduced PCV21 based on an age-based approach from age ≥25 years for Indigenous (Aboriginal and Torres Strait Islander peoples) and from age 65 for non-Indigenous peoples.

2. Vaccine strategy

US and Europe prefer single-dose PCV20 or PCV21 approaches.^{18, 19} Canada and Korea retain sequential schedules as options.^{20, 21}

3. Adoption of newer vaccines

The US has rapidly adopted the use of PCV20 and PCV21.^{17, 18} PCV21 does not contain serotype 4 that is prevalent in certain populations in Alaska, Colorado, Navajo Nation, New Mexico, and Oregon. PCV20 or PCV15/23PPV is likely to provide greater coverage for these groups. (Note, serotype distribution is unknown in some states without IPD surveillance¹⁸). Europe supports PCV20 uptake.¹⁹ Canada/Korea are transitioning more gradually transition^{20, 21} The UK is focussed on delivery optimisation over product transition alone⁴

4. Focus on multimorbidity

UK and Europe: Strong emphasis on risk accumulation and under-vaccinated groups.^{4, 19} US: Increasingly simplified for population-level implementation, e.g. from age 50 years for all.¹⁸

Vaccine recommendations for adult special groups, from age 18 years

This section reviews the international recommendations around the underlying medical conditions associated with a high risk for pneumococcal infections and for invasive disease in adults. See Table 5 for details of the New Zealand extended pneumococcal immunisation schedule in adults.

Table 5: Extended pneumococcal immunisation programme for adults aged 18 years and over (extracted from the Immunisation Handbook 2026 version 2, table 17.5)

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, intracranial shunts^b or cerebrospinal fluid leaks^b
- with primary immunodeficiency

a. PCV13 is funded pre- or post-HSCT or chemotherapy. 23PPV is only funded post HSCT or chemotherapy.

b. Only PCV13 is funded for these indications; 23PPV is recommended but not funded.

The following highlights the current (as of July 2026) recommendations in a selection of countries for the range special groups that are considered at medical, lifestyle or environmental risk of pneumococcal disease to update our previous review of evidence.² See also hyperlinks to sources given below. A direct comparison with the adult schedule in New Zealand with Australia (for PCV21 from 1 July 2026), Canada, UK and US schedules is given in Table 6.

Table 6: Comparison of adult clinical risk groups recommended pneumococcal vaccination by country (as of 1 July 2026)

Risk group / condition	New Zealand (funded)	Australia (funded)	Canada (recommended)	United Kingdom (funded)	United States (recommended)
Previous episode of IPD	No (addition in 2027)	Yes	Not specified	Yes	Not specified
Asplenia / splenic dysfunction, incl. haemoglobinopathies	No only pre/post splenectomy	Yes	Yes	Yes	Yes
Primary immunodeficiency	Yes	Yes	Yes	Yes	Yes
Complement deficiency	Yes	Not specified	Yes	Yes	Yes
Haematological malignancy	Limited, if on chemotherapy	Yes	Yes	Yes	Yes
Solid organ transplant	Yes	Yes	Yes	Yes	Yes
Stem cell transplant (HSCT)	Yes	Yes	Yes	Yes	Yes
HIV infection	Yes	Yes	Yes	Yes	Yes
Immunosuppressive therapy	No	No	Yes	Yes	Yes
Non-haematological malignancy (chemo/radiotherapy)	Yes, 23PPV post-chemotherapy	No	Yes	Yes	Yes
CSF leak / cochlear implant / intercranial shunts	Yes (limitations)	Yes	Yes	Yes (excluding shunts)	Yes
Chronic respiratory disease: bronchiectasis COPD, severe asthma, interstitial lung disease	No	Yes (limitations ^d)	Yes	Yes	Yes
Chronic kidney disease	Yes (on dialysis)	Yes	Yes	Yes	Yes
Chronic heart disease ^a	No	No	Yes	Yes	Yes
Chronic liver disease ^b	No	Yes	No	Yes	Yes
Diabetes mellitus	No	No	Yes	Yes	Yes
Smoking	No	No	Yes	Yes	Yes
Alcohol/substance use	No	No	Yes	Yes	Yes
settings or communities with high IPD risk	No	ATSI ^d people from age 25y	Yes ^e	-	-
homeless	No	No	Yes		
occupational risk	No	No	Yes	Yes	

- CHD – including ischaemic heart disease under medical follow-up, chronic heart failure, hypertension with cardiac complications
- CLD – includes cirrhosis, biliary atresia, chronic hepatitis
- Excluding severe asthma and interstitial and fibrotic lung disease
- ATSI - Aboriginal and Torres Strait Islander peoples
- Settings with high IPD risk – eg residential care

Australia

<https://immunisationhandbook.health.gov.au/resources/tables/table-risk-conditions-for-pneumococcal-vaccination-and-eligibility-for-nip-funding>

From 1 July 2026, the National Immunisation Programme in Australia replaced PCV13, 15 or 20 and 23PPV in adult groups with PCV21. Anyone eligible for extended pneumococcal vaccination aged under 18 years will receive PCV20.

Canada

<https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-16-pneumococcal-vaccine.html#a3>

The following are the recommended groups for PCV15, PCV20 or PCV21 vaccination in Canada. Spacing of one year is recommended between previous 23PPV and PCV20 or PCV21 doses, but this may be reduced to eight weeks prior to planned immunosuppression or when diagnosed with a disease leading to immunodeficiency. Minimum interval between PCVs is eight weeks.

Immunocompromising conditions

- congenital immunodeficiencies involving any part of the immune system
- immunocompromising conditions or immunosuppressive therapy, within the last two years, including use of long-term corticosteroids, chemotherapy, radiation therapy and immunosuppressive biologics
- HIV infection
- haematopoietic stem cell transplant (HSCT) recipients
- active malignant neoplasms, including leukaemia and lymphoma
- candidates and recipients of solid organ or islet transplants
- chronic kidney disease, particularly those individuals with stage four and five chronic kidney disease, and those with nephrotic syndrome, on dialysis or with renal transplant
- functional or anatomic asplenia (congenital or acquired) or splenic dysfunction, including Sickle cell disease and other haemoglobinopathies.

In addition to the predominantly immunocompromised groups funded in NZ, Canadian recommendations include individuals with these medical conditions:

- chronic heart disease, including ischaemic heart disease under medical follow-up, chronic heart failure, hypertension with cardiac complications
- diabetes mellitus, particularly if aged over 50 years
- chronic lung disease, including COPD, bronchiectasis, interstitial lung fibrosis, cystic fibrosis, asthma requiring medical care in preceding 12 months.
- chronic neurologic conditions that may impair clearance of oral secretions
- chronic cerebrospinal fluid (CSF) leak.

Canada also considers social, behavioural and environmental risk factors, such as:

- individuals who are unhoused
- communities or setting with high IPD rates, (e.g. residential care)
- smoking, particularly if aged over 50
- substance abuse (alcohol, cocaine, injectable drugs)
- occupational risk – long term exposure to metal fumes (i.e. welders).

United Kingdom

<https://www.gov.uk/government/publications/pneumococcal-the-green-book-chapter-25>

<https://www.gov.uk/government/collections/pneumococcal-vaccination-programme>

Table 7 lists the risk groups recommended and funded additional pneumococcal vaccination in the UK.

Table 7: Clinical risk groups who should receive pneumococcal immunisation in the UK (Green Book, table 25.2)

Clinical risk group	Examples (decision based on clinical judgement)
Asplenia or dysfunction of the spleen	This also includes individuals with coeliac disease who are diagnosed with splenic dysfunction and all haemoglobinopathies including homozygous sickle cell disease
Chronic respiratory disease (chronic respiratory disease refers to chronic lower respiratory tract disease)	This includes chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema; and such conditions as bronchiectasis, cystic fibrosis, interstitial lung fibrosis, pneumoconiosis and bronchopulmonary dysplasia (BPD). Individuals in whom respiratory function may be compromised due to neurological or neuromuscular disease (such as cerebral palsy). Asthma is not an indication, unless so severe as to require continuous or frequently repeated use of systemic steroids (as defined in Immunosuppression below).
Chronic heart disease	This includes those requiring regular medication and/or follow-up for ischaemic heart disease, congenital heart disease, hypertension with cardiac complications, and chronic heart failure.
Chronic kidney disease	Nephrotic syndrome, chronic kidney disease at stages 4 and 5 and those on kidney dialysis or with kidney transplantation.
Chronic liver disease	This includes cirrhosis, biliary atresia and chronic hepatitis.
Diabetes	Diabetes mellitus requiring insulin or anti-diabetic medication. This does not include diabetes that is only diet controlled.
Immunosuppression	Due to disease or treatment, including patients undergoing chemotherapy leading to immunosuppression, bone marrow transplant, asplenia or splenic dysfunction, complement disorder, HIV infection at all stages, multiple myeloma or genetic disorders affecting the immune system (such as IRAK-4, NEMO). Individuals on or likely to be on systemic steroids for more than a month at a dose equivalent to prednisolone at 20mg or more per day (any age), or for children under 20kg, a dose of 1mg or more per kg per day.
Individuals with cochlear implants	It is important that immunisation does not delay the cochlear implantation.
Individuals with cerebrospinal fluid leaks	This includes leakage of cerebrospinal fluid such as following trauma or major skull surgery (does not include CSF shunts).
Occupational risk	Please see page 10.

Pneumococcal vaccination is considered for individuals at risk of frequent or continuous exposure to metal fumes (such as welders), accounting for the exposure control measures in place. In these situations, vaccination should not replace the need for measures to prevent or reduce exposure.

United States

https://www.cdc.gov/pneumococcal/hcp/vaccine-recommendations/risk-indications.html#cdc_generic_section_6-risk-conditions

(A decision-making tool is also available as an app [PneumoRecs VaxAdvisor](#))

Indications for pneumococcal vaccination for both children and adults:

- cerebrospinal fluid leak
- chronic liver disease
- cochlear implant
- an immunocompromising condition
- diabetes mellitus.

Immunocompromising conditions in both children and adults:

- congenital or acquired asplenia, or splenic dysfunction
- congenital or acquired immunodeficiency (including lymphocyte and complement deficiencies and phagocytic disorders)
- diseases or conditions treated with immunosuppressive drugs or radiation therapy (including haematological malignancy and solid organ transplant)
- HIV infection
- Sickle cell disease or other haemoglobinopathy.

Indication for pneumococcal vaccination of adults, specifically:

- chronic heart disease, includes congestive heart failure and cardiomyopathies, excludes hypertension
- chronic lung disease, includes chronic obstructive pulmonary disease, emphysema, and asthma
- chronic renal failure or nephrotic syndrome
- alcoholism or cigarette smoking.

Review of literature - special groups

Generally, the groups at greatest risk of invasive pneumococcal disease are those already eligible for funded pneumococcal vaccination.²² However, as mentioned previously, other conditions and comorbidities also increase the risk of invasive disease and other pneumococcal infections, such as non-invasive pneumococcal pneumonia, and form a significant burden on health services. Pneumococcal vaccines are not funded in New Zealand for adults with health conditions such as diabetes, chronic respiratory disease, chronic heart disease and heart failure, and chronic liver disease, including those with more than one underlying condition, regardless of age.

This section considers the recent evidence around the role these comorbidities play in the pneumococcal burden. Focus is on non-immunocompromising conditions, such as heart, lung and liver diseases, and the bi-directional relationship between community-acquired pneumonia (CAP) and chronic comorbidities. It highlights the role pneumococcal vaccination can play in reducing severe outcomes.

See Table 10 for details of the studies presented below.

Risk factors

As mentioned above, there are recognised high-risk conditions for which pneumococcal vaccination is generally funded, such as HIV infection, organ transplantation, asplenia and haematological malignancies.²² Other conditions, which on their own, are not as strongly associated with risk for invasive pneumococcal disease, but in conjunction with older age and multiple chronic conditions, increase risk from pneumococcal infection that can lead to hospitalisation and progress to invasive disease.

An expert review⁴ suggested that the increased likelihood of pneumococcal infections in individuals with multiple risk factors be taken into consideration when making pneumococcal vaccine recommendations. The UK has noted an increase in cases of pneumococcal septic arthritis in older adults and those with comorbidities that are associated with non-vaccine serotypes and 23PPV/non-PCV13 serotypes.⁴ Although 23PPV was offered to certain groups, access and coverage was suboptimal.

Furthermore, viral-bacterial coinfections are common.⁴ In addition to offering pneumococcal vaccination to those with underlying conditions, prevention of preceding viral infections with influenza, respiratory syncytial virus and COVID-19 vaccines can help to reduce the incidence of pneumococcal infections and adverse outcomes of respiratory illness.

Invasive pneumococcal disease

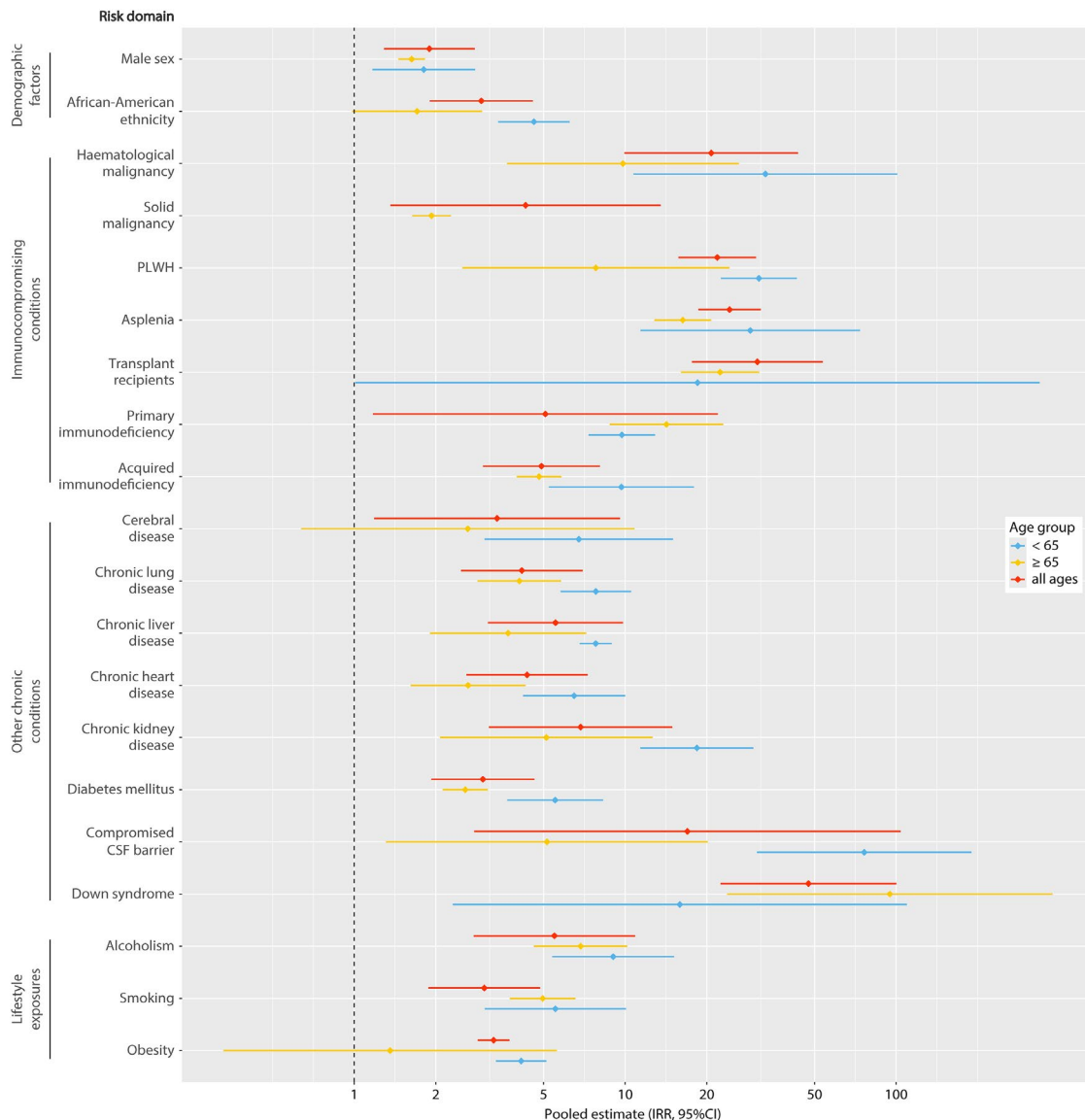
Ditzel et al (2025) conducted a systematic review that identified more than 50 different conditions that increase the risk for IPD in adults.²² Twenty-two conditions were used as domains for a meta-analysis (see Figure 8). The conditions with the highest incidence rate ratio (IRR) were predominantly immunocompromising, for example:

- transplant = 30.8 (95% CI 17.6 – 53.6)
- asplenia = 24.3 (18.6 – 31.7)

- HIV infection = 21.9 (15.7 – 30.4)
- haematological malignancy = 19.6 (11.1 – 34.7)
- chronic kidney disease, age <65y = 18.4 (11.4 – 29.7) versus ages ≥65y = 5.2 (2.1 – 12.6)
- compromised cerebrospinal fluid barrier = 17.0 (2.8 – 103.9)
- Down syndrome = 47.5 (22.5 – 100.2)

The conditions with the most pronounced risk were in line with the current US recommendations for pneumococcal vaccination.

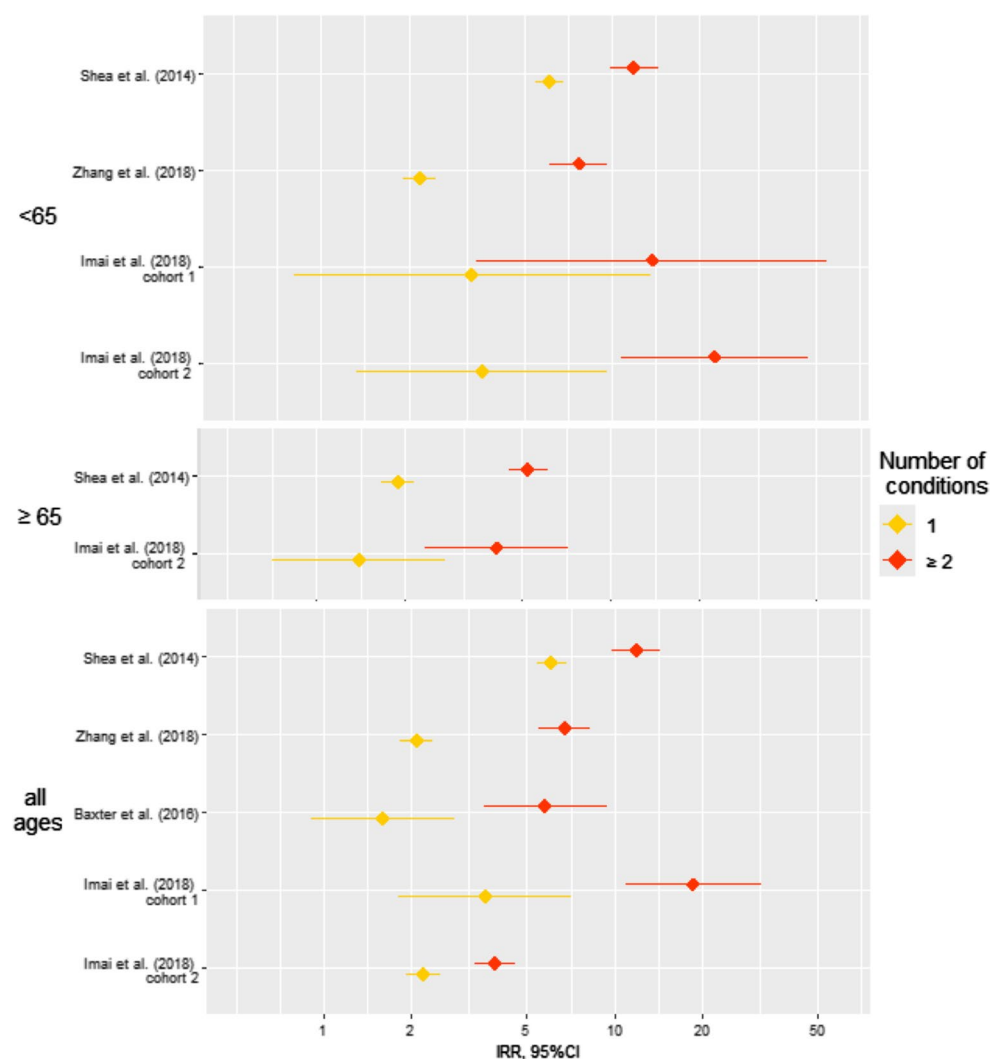
Figure 8: Pooled risk estimates of risk conditions for adult invasive pneumococcal disease. Summary of the studies that reported incidence rate ratios for the 22 risk domains that were eligible for meta-analysis, stratified by age (Ditzel, 2025 open access)



Abbreviations: IPD - invasive pneumococcal disease; PLWH - people living with human immunodeficiency virus; CSF - cerebrospinal fluid; IRR - incidence rate ratio

However, several of the reviewed studies suggested a cumulative risk with multimorbidity (see Figure 9).²² After adjusting for underlying conditions, the direct risk associated with age alone was reduced. Risk associated with given conditions was higher in those aged below 65 years than for the older populations, such as diabetes, chronic liver disease, chronic kidney disease, and for those of African American ethnicity. Secondary immunodeficiency, including immunosuppressive treatment, had a comparable relative risk to chronic lung disease, chronic liver disease, chronic heart disease or alcoholism.²² It was noted that within the studies included in this systematic review there was a high degree of bias and heterogeneity.

Figure 9: Risk estimates of multimorbidity for adult invasive pneumococcal disease. Forest plot of reported incidence rate ratios stratified by number of comorbidity risk conditions (colour), over different age categories. (Ditzel, 2025, open access)



Conclusion

Although immunocompromising conditions are most significantly associated with IPD, chronic disease and multiple comorbidities increase the risk of pneumococcal disease in adults under 65 years.

Community-acquired pneumococcal pneumonia

Community-acquired pneumococcal pneumonia (CAP) is a significant health burden, particularly in older adults and those with underlying health conditions. Community-acquired pneumococcal pneumonia can progress to invasive bacteraemic pneumonia in an estimated 25% of pneumonia cases.²³ The risk of pneumonia increases with coexisting comorbidities and with age.²⁴

As presented in an earlier review of evidence,² a 2013 literature review identified several comorbid conditions associated with an increased risk of CAP in European adults.³ Table 8 gives the frequency of these comorbid conditions in patients with CAP across several of the reviewed studies.

Table 8: Frequency of comorbid conditions in adults with community-acquired pneumonia (Source: Torres et al 2013, Thorax open access)

Comorbid condition	Number of cohorts with data*	Patients with condition (%)
Previous pneumonia	10	3.2–33.8
Chronic respiratory disease	25	9.7–68
COPD	21	9.4–62
Asthma	9	3–50.0
Chronic heart disease	23	10–47.2
Heart failure	27	1.0–46
Diabetes mellitus	48	4.9–33.0
Cerebrovascular disease/stroke	26	3.2–33
Dementia	12	1.1–33.6
Cancer	33	4.3–18.0
Chronic liver disease	36	0.3–20
Chronic renal disease	39	0.5–26.7

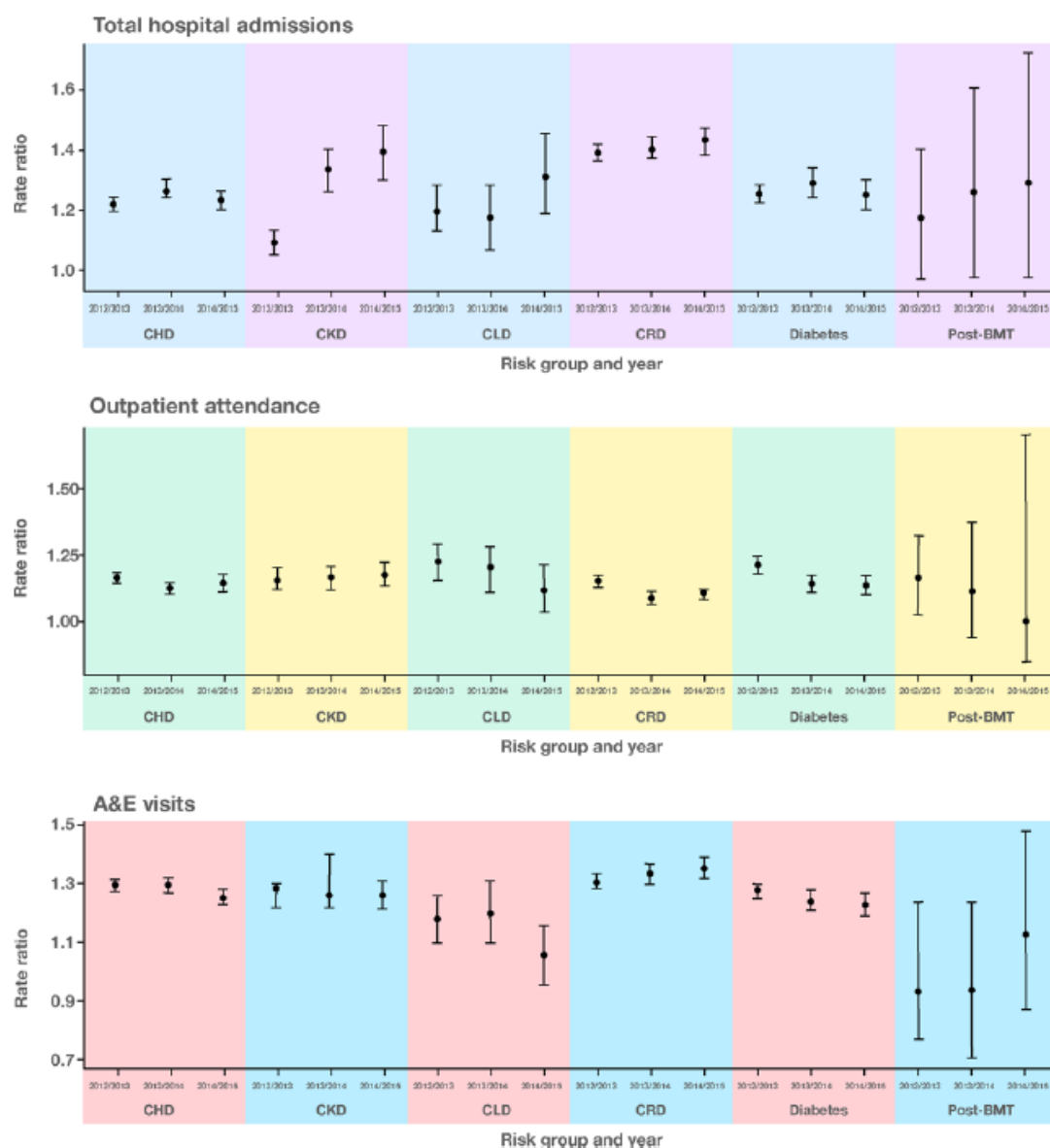
*For studies that only reported data separately for each cohort, all cohorts were included; for studies that reported data for the overall study population, the summary data were used.
COPD, chronic obstructive pulmonary disease.

Large-scale retrospective data reflects a growing volume of chronically unwell, at-risk patients. A French cohort study in 2018 found that 10% of adults (mean age 66.1 years, with over half aged over 65 years) in a general health database covering 40 million people were considered at risk of pneumococcal disease. If these four million adults, 18% had at least two comorbidities, 90% had chronic medical conditions and 14% had an immunocompromising comorbidity: 72% with diabetes, 17% with chronic respiratory disease, 8% with chronic liver failure and, predominantly representing the older age group, 12% had heart failure.²⁵

Bidirectional exacerbation: pneumonia and comorbidities

The relationship between pneumonia and chronic comorbidities is heavily bidirectional. An acute episode of community-acquired pneumonia or invasive pneumococcal disease acts as a severe systemic catalyst, destabilising underlying chronic conditions. Conversely, those conditions simultaneously increase the severity of infection.

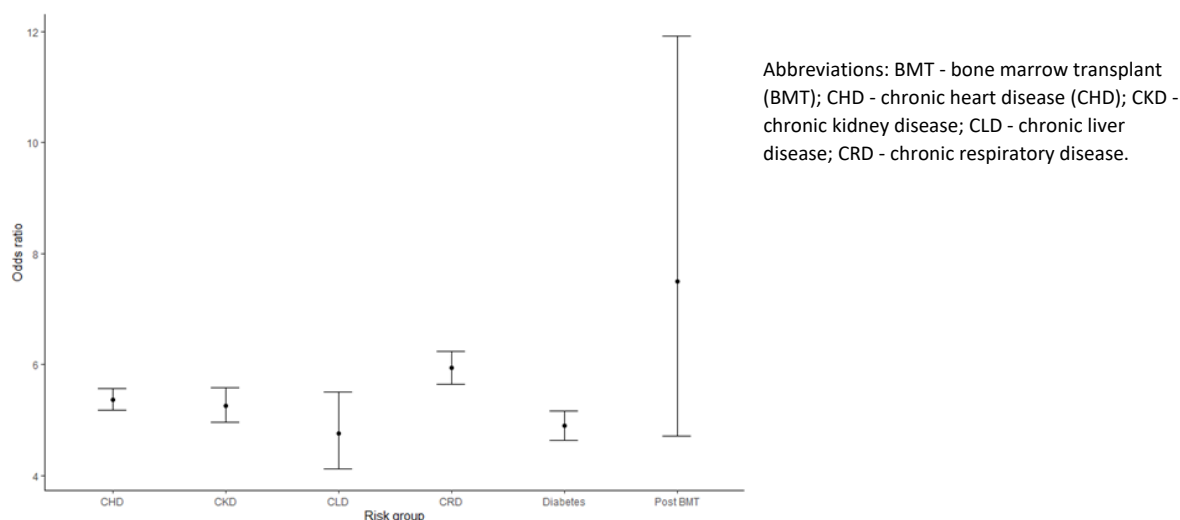
Figure 10: Comparison of rates of hospital admission, outpatient attendance and accident and emergency (A&E) visits for patients with or without community-acquired pneumonia (CAP) hospital diagnosis, stratified by underlying comorbidity and year, in England (Campling, 2020, open access)



Prevention of CAP in individuals with underlying comorbidities helps to reduce the burden on the patient and the healthcare system. A retrospective cohort study in England found that an episode of hospitalised CAP in patients with underlying comorbidities significantly increased the burden on the patient and healthcare for at least three years, when compared with individuals with the same comorbidities not hospitalised for CAP.²⁶ Six comorbidities were examined: bone marrow transplant, chronic heart disease, chronic kidney disease, chronic liver disease and chronic respiratory disease. Patients with immunocompromise were not included. Figure 10 shows the rates of hospital utilisation by comorbidity and year after initial diagnosis of hospitalised CAP and compared with those without CAP.

Figure 11 shows the odds of death by comorbidity after initial hospitalisation for CAP.²⁶ Patients with chronic respiratory disease had almost six times the odds of in-hospital mortality.

Figure 11: Adjusted odds ratios for mortality in each clinical risk group for those hospitalised with community-acquired pneumonia compared with those who did not. (Campling, 2020, open access)



Chronic liver disease

Data (published in a letter) from the CAPNETZ cohort study in Germany underscored that patients with chronic liver disease (CLD) present with hospitalised CAP ($n=289$; median age 64 years) at a significantly younger median age than those without CLD ($n=5,449$, median age 73 years).²⁷ Despite their younger age and fewer baseline cardiovascular comorbidities, patients hospitalised with CAP with CLD had double the incidence of concurrent bacteraemia (19.6% vs. 8.9%; $p < 0.001$); higher 30-day mortality (11.3% vs. 7.1%; odds ratio = 1.67; 95% CI 1.12 – 2.49; $p = 0.054$) and prolonged hospital stays than those without CLD.²⁷

Socioeconomic and health deprivation

A retrospective clinical record review in Christchurch Hospital identified hotspots of adults hospitalised with CAP in Christchurch, New Zealand, that were associated with geographical areas of high socioeconomic deprivation and health equity.²⁸ Of the 924 cases in the study, 40/370 cases sampled had *S. pneumoniae* infection. The mean age of the cases was 70 years (± 18 years), but the mean age of cases identifying as Māori was 12 years younger than age of cases with NZ European ethnicity. Compared with the least deprived quintile, rate ratios were highest for the two most deprived quintiles: RR 1.5 (95% CI 1.3 – 1.8) and 1.6 (1.3 – 2.0). This risk increased when stratified by health deprivation (RR 2.3; 1.8 – 3.0). Of the cases, 75% had at least one and 17% had more than three underlying comorbidities; most common being chronic cardiovascular disease and chronic respiratory disease. Geographically, most areas had rates below 5 per 1,000, but in two areas rates were 51 and 22 per 1,000. Rates remained high in these areas after removing cases in age-care residences and age distribution did not closely mirror the CAP hotspots. Socioeconomic deprivation was an important but not the only factor in the CAP clusters. This data highlights a role for targeted preventative interventions in identifiable hotspots.²⁸

Conclusions

Community-acquired pneumococcal pneumonia (CAP) disproportionately affects people with chronic health conditions, including respiratory, cardiovascular, liver and kidney disease, diabetes and immunocompromising conditions. These conditions increase the risk and severity of CAP, while pneumonia can worsen underlying disease, increase healthcare utilisation, and elevate mortality.

The evidence highlights particularly poor outcomes in patients with chronic respiratory, liver and heart disease, emphasising the importance of prevention of pneumococcal infections in at-risk populations. Socioeconomic disparities compound risk factors associated with age and chronic disease.

Cardiovascular disease

The risk of IPD is increased in cardiac patients, particularly in those with congestive heart failure. Additionally, pneumococcal pneumonia is associated with onset of cardiac complications – including acute myocardial infarction, arrhythmia or new or worsening heart failure, and long-term cardiovascular disease.²⁹

Pneumococci interact with the cardiovascular system through virulence factors, resulting in pneumolysin-induced cardiac toxicity, platelet activation and myocardial invasion, and induce long-term proinflammatory and prothrombotic mechanisms. Some capsular serotypes have a greater propensity to invade and persist within cardiac myocytes.²⁹

Post-hoc analysis of two clinical trials (PARADIGM-HF and PARAGON-HF) found that pneumonia in ambulatory patients with heart failure was linked to a three- to five-fold increase in mortality risk, which peaks acutely but remains elevated beyond three months post pneumonia (see Table 9).²⁴ The patients with pneumonia also had more comorbidities, including COPD, diabetes and atrial fibrillation, than those without pneumonia incidence.

Table 9: Post-hoc analysis of subsequent risk of cardiac clinical outcomes after occurrence of pneumonia in two clinical trial cohorts (PARADIGM-HF and PARAGON-HF) (Shen et al, 2021, open access)

	Unadjusted HR* (95% CI)	p Value	Adjusted HR*† (95% CI)	p Value
PARADIGM-HF				
All-cause death	5.19 (4.47–6.03)	<0.001	4.34 (3.73–5.05)	<0.001
CV death	4.40 (3.68–5.26)	<0.001	3.62 (3.02–4.34)	<0.001
HF hospitalization	2.95 (2.30–3.78)	<0.001	2.39 (1.86–3.07)	<0.001
CV death or HF hospitalization	3.34 (2.79–3.99)	<0.001	2.72 (2.27–3.26)	<0.001
PARAGON-HF				
All-cause death	4.53 (3.73–5.50)	<0.001	3.76 (3.09–4.58)	<0.001
CV death	3.65 (2.79–4.79)	<0.001	3.03 (2.31–3.98)	<0.001
HF hospitalization	2.19 (1.70–2.84)	<0.001	1.98 (1.52–2.58)	<0.001
CV death or HF hospitalization	2.45 (1.97–3.05)	<0.001	2.22 (1.77–2.77)	<0.001

*Hazard ratios were estimated with stratification by geographic region. †Adjusted variables included randomized treatment, age, sex, left ventricular ejection fraction, NYHA functional class, systolic blood pressure, HF duration, previous HF hospitalization, history of myocardial infarction, hypertension, diabetes, and atrial fibrillation, eGFR, and log-transformed NT-proBNP.

Heart disease increases the risk of pneumonia, which in turn, can exacerbate underlying heart disease. CAP can also significantly accelerate the development of heart failure. A greater risk for heart disease was observed in younger adults who had survived an episode of pneumonia but may not typically be seen as being at risk for heart failure. Over a median 10-year follow-up in Canada, 11.9% of adults with no prior history of heart failure developed the condition post-pneumonia compared to 7.4% of matched controls (adjusted hazard ratio [aHR] 1.6; 95% CI 1.44 – 1.81; $p < 0.001$).³⁰ This relative risk was highest in patients under the age of 65 years (aHR = 1.98) and in

those who experienced pneumococcal bacteraemia (aHR = 2.4).³⁰ Although older adults had the highest absolute risk, the relative risk was greater in younger adults.

Protective effects of pneumococcal vaccination against cardiovascular disease

The benefits of pneumococcal vaccination extend beyond preventing pneumococcal disease by offering broader protection against cardiovascular and other health impacts.

A systematic review and meta-analysis showed 23PPV decreased the overall risk of cardiovascular events (relative risk [RR] 0.91; 95% CI 0.84 – 0.99; 15 studies), acute myocardial infarction (AMI; RR 0.88; 0.79 – 0.98; 12 studies) and all-cause mortality (RR 0.71; 0.60 – 0.84) in adults aged over 65 years.³¹

Lower odds of AMI (adjusted odds ratio [aOR] 0.70; 95% CI 0.62 – 0.80) and stroke (aOR 0.71; 0.77 – 0.86) were observed in older adults (mean age 80 years) vaccinated with 23PPV in Japan. This protection was greatest within 6 months of vaccination (aOR 0.55 against AMI) but waned by two years.³² It was noted that the greater protection was observed in these adults at an older age than in other studies, which may be due to confounding from healthy lifestyle and user biases. A high proportion of the AMI and stroke cases had comorbidities, including CHF, cardiac arrhythmias, valvular disease, peripheral vascular disorders, hypertension, COPD, diabetes or renal failure. Adjustment for influenza vaccine uptake did not change the results.³²

In a small, prospective, observational study (published as a letter), PCV13 vaccination was shown to reduce the risk of hospitalisation in 121 COPD patients with non-exacerbating COPD plus cardiovascular disease (CVD).³³ Statistically fewer vaccinated COPD patients with CVD were hospitalised than those who were unvaccinated (16% vs 50%, $p = 0.007$). No difference was observed in those with COPD without CVD. COPD exacerbations were predominantly associated with bacterial infections, but only 15% were pneumococcal, such that the effect of PCV13 was non-significant in those with exacerbated COPD.³³

Conclusion

Heart disease increases the risk of pneumonia, which in turn, can exacerbate underlying heart disease. CAP can also significantly accelerate the development of heart failure, including in adults not previously considered to be at increased cardiovascular disease risk. As well as reducing the risk for pneumonia, pneumococcal vaccination can reduce the heart disease burden by preventing pneumococcal infections acting as systemic catalyst for AMI and strokes.

Indirect protection of adults

As detailed in Table 10, the nasopharyngeal (NP) carriage and transmission of pneumococcal serotypes can influence the disease burden in different age groups. It is commonly stated that vaccination of children provides indirect protection to older age groups. Nasopharyngeal carriage dynamics are a key determinant of pneumococcal transmission and age-specific disease burden, underpinning the indirect (herd) effects of paediatric PCV programmes. A targeted review found, generally, that infant PCV programmes reduce adult carriage of vaccine-type serotypes, though effects are heterogeneous and offset by serotype replacement, leaving a persistent burden from non-vaccine types.³⁴

Modelling from Israel demonstrated that declines in IPD among adults were primarily driven by reduced carriage in older vaccinated children (aged ≥ 36 months), with limited contribution from infant protection, reflecting a stronger impact from the toddler booster dose on transmission; catch-up vaccination in children aged 1–5 years was therefore identified as a strategy to accelerate indirect protection.³⁵ However, evidence from Germany suggests these indirect effects may have plateaued, with persistent and, in some cases, increasing adult IPD due to specific serotypes (notably serotypes 3, 4, 19F and 19A), despite sustained declines in infant disease.³⁶

Emerging data from the UK indicate that young adults may act as an independent reservoir, exhibiting higher carriage of certain PCV13 serotypes than vaccinated children and mirroring serotype patterns seen in older adults. Thereby, highlighting gaps in indirect protection and important considerations for vaccination policy across the life course.³⁷

Conclusions

While paediatric pneumococcal conjugate vaccine (PCV) programmes provide indirect protection through reduced vaccine-type carriage and transmission, these effects are variable, limited by serotype replacement, and may be plateauing in some settings in which there is persistent adult disease and evidence that young adults may be contributing to ongoing transmission to susceptible adults. These findings support a life-course vaccination approach alongside prevention of viral co-infections to reduce pneumococcal disease and adverse outcomes.

Summary

Individuals with immunocompromising conditions remain at the highest risk of invasive pneumococcal disease (IPD) and pneumococcal vaccination programmes typically target immunocompromised cohorts. Growing evidence shows that adults aged under 65 years with chronic conditions, such as diabetes, chronic respiratory disease, chronic heart disease, chronic liver disease and chronic kidney disease, also experience a substantially increased burden of pneumococcal disease. Risk increases further when multimorbidity is present. The health burden is particularly driven by individuals aged under 65 living with non-immunocompromising chronic diseases not eligible for pneumococcal vaccination.

The relationship between pneumonia and these chronic conditions is highly bidirectional: an acute respiratory infection acts as a systemic catalyst to induce organ damage and inflammation; while preexisting chronic diseases simultaneously accelerate infection severity, double bacteraemia rates, and multiply the odds of severe outcomes. Patients with chronic respiratory, liver and cardiovascular diseases can experience particularly severe outcomes, including a greater risk of hospitalisation, bacteraemia, heart failure and death.

Pneumococcal vaccination can help to prevent pneumococcal infections and their downstream complications in these 'at-risk' groups. Beyond reducing the risk of pneumonia and invasive disease, vaccination has been associated with lower rates of cardiovascular events, including acute myocardial infarction, stroke and all-cause mortality in older adults. Evidence also suggests vaccination may reduce hospitalisations of patients with COPD and cardiac disease. These broader benefits support the use of pneumococcal vaccination as an important preventive strategy in individuals with chronic health conditions, particularly those with multimorbidity who are at elevated risk of severe disease and long-term complications.

There appears to be three tiers of risk factors for IPD and other severe pneumococcal infection outcomes:

1. **High risk** due to moderate to severe immunocompromise: unable to prevent invasive infections or in whom infections can more readily access normally sterile compartments, such as primary immunodeficiencies and HIV infection, asplenia, haematological malignancies, cerebrospinal fluid leakage, kidney disease requiring dialysis, transplant recipients, Down syndrome/Trisomy 21 (including adults).
2. **Increased risk** with underlying chronic medical conditions that facilitate opportunistic infections or in whom infections can progress to become invasive: such as congestive heart failure, chronic respiratory diseases like cystic fibrosis and COPD, immunosuppression, chronic liver disease, diabetes mellitus, vascular diseases like cerebrovascular and ischaemic heart disease, and neurological diseases, plus increasing age. Having two or more underlying conditions places an individual at the same level of IPD risk as those in tier 1. The absolute risk is greatest with increasing age over 65 years, particularly with increased frailty, but for those with multiple comorbidities and under 65 years, the relative risk is greater.
3. **Potential risk** due to pneumococcal coinfections following a respiratory virus infection: preventing viral infections such as influenza, respiratory syncytial virus (RSV), COVID-19 can help to reduce the risk of pneumonia and cardiovascular events, which in turn, lower the risk of IPD, heart failure and hospitalisation that can lead to increased frailty. This includes individuals with obesity, a risk for exacerbation of respiratory conditions such as asthma, those with certain lifestyle factors (e.g., smoking, alcoholism), and environmental factors, such as housing conditions, occupation and pollution or passive smoking. Multiple coexisting factors increase the risk.

Generally, tier 1 conditions are eligible for pneumococcal vaccination in New Zealand, alongside seasonal influenza and COVID-19 vaccines, but eligibility differs between PCV13 and 23PPV and adults or children. Those with tier 2 and 3 conditions are unable to access funded pneumococcal vaccination in NZ, but most are eligible for influenza and COVID-19 vaccination. Although one RSV vaccine (Arexvy® GSK) is available to adults aged from 50 years, it is not yet funded.

Although nasopharyngeal carriage and transmission underpin indirect (herd) protection from paediatric vaccination programmes, some countries have noted a plateau and persistent adult infections, despite reductions in younger age groups. These findings support a life-course vaccination approach alongside prevention of viral co-infections to reduce pneumococcal disease and adverse outcomes.

Review of literature - newer pneumococcal vaccines

The following summarises published literature about the use of higher valency pneumococcal vaccines in adult groups, including those with underlying health conditions that increase their risk for invasive pneumococcal disease and adults aged over 65 years. See Table 12, Table 13 and Table 14 for details of the studies presented.

Safety

Most of the safety data are from clinical trials since these vaccines have only recently received regulatory approval and real-world experience is limited at the time of writing. See Table 12 for further study details.

20-valent pneumococcal conjugate vaccine

Evidence from clinical trials indicates that PCV20 (Prevenar 20) has a comparable safety and tolerability profile to PCV13 and 23PPV in adults aged 18 years and over, including pneumococcal-naïve individuals and those with prior vaccination.³⁸⁻⁴³ Across phase 2 and 3 randomised controlled trials (RCT), local and systemic adverse events were typically mild to moderate, most commonly injection-site pain and myalgia (ranged from <15% to 70% in younger age groups and <10% – 40% for over 65 year groups). Lower reactogenicity is observed in older adults and fever was infrequent (<1% – 2% in PCV20 and PCV13 groups). Serious adverse events were rare and not considered vaccine related. Co-administration with mRNA COVID-19 vaccine was also well tolerated and did not increase adverse event rates.⁴⁴

Real-world evidence from post-licensure surveillance in adults aged ≥19 years, reported to the US Vaccine Adverse Events Reporting System (VAERS), showed that the safety profile of PCV20 is consistent with findings from clinical trials. Injection-site reactions were commonly reported, with overall rates of serious adverse events remaining low.⁴⁵ A signal for Guillain–Barré syndrome has been identified and is under investigation, although reported rates remain low and within expected background levels.

21-valent pneumococcal conjugate vaccine

As for PCV20, PCV21 has a comparable safety profile to PCV13 and 23PPV.^{46, 47} In phase 3 RCTs, adverse events were common with up to 80% of participants reporting at least one adverse event, but these were generally mild to moderate and transient. Injection-site pain, fatigue, and headache most frequently reported with similar incidence and intensity between vaccine groups. As seen with other vaccines, higher reactogenicity was observed in younger adults. No vaccine-related serious adverse events or deaths were identified.^{46, 47} Safety profiles were consistent across age groups and aligned with findings from other pneumococcal conjugate vaccine studies. Real-world evidence remains limited at the time of writing.

Pneumococcal vaccines with modified conjugates – higher valency vaccines in development

Overall, safety profiles of newer PCVs in development – two 24-valent and a 31-valent vaccine – were consistent across age groups, including older adults, and aligned with expectations for

conjugate vaccines. These vaccines are designed to improve immunogenicity and T cell response to pneumococcal polysaccharides, which often increases reactogenicity.

Clinical trial data indicate that these vaccines have safety and tolerability profiles comparable to existing PCVs across adult populations. The currently published literature is from phase 1 and 2 dose-finding and first-in-human studies. Phase 1–2 and phase 2 RCT of PCV24 candidates (Affinivax and Vaxcyte) and PCV31 (Vaxcyte) demonstrated that adverse events were generally mild to moderate, transient, and like comparator vaccines, PCV13 or PCV20.¹²⁻¹⁴ Injection-site pain, tenderness, fatigue, myalgia, and headache were commonly reported. While reactogenicity increased at higher doses in some groups, severe adverse events were uncommon, and no vaccine-related serious adverse events or consistent safety concerns were identified over follow-up periods of up to 6 months.

Summary

Together, clinical trial data and real-world evidence support a favourable and consistent safety profile for PCV20 and PCV21 across adult populations. Younger adults reported more local and systemic reactions than older groups, as is commonly reported for other vaccines. Safety of the PCV vaccines with modified carrier proteins appear to be comparable to the currently licensed higher valency vaccines.

Immunogenicity

Regulatory approval of PCV20 (and other new pneumococcal vaccines) is based on immunogenicity and non-inferiority against a predecessor or comparator, because IPD is a rare disease, phase 3 efficacy studies are impractical. Much of the immunogenicity data for PCV20 considers ‘non-inferiority’ to the serotypes in common with the licensed PCV13 vaccine. No serotype-specific immunological correlates of protection have been established for pneumococcal conjugate vaccines.

WHO defines primary analysis endpoints of clinical trial data for non-inferiority between pneumococcal vaccines to be the percentage of subjects with IgG ≥ 0.35 $\mu\text{g/ml}$ and serotype-specific IgG geometric mean concentration ratios (GMR) between vaccine of interest and a licensed comparator.⁴⁸ If one or more serotype fails to meet both sets of criteria, the regulatory approval authority for each country (ie Medsafe in New Zealand) should take into consideration the disease burden associated with those serotypes. Based on efficacy and effectiveness from studies of the PCV7 vaccine, non-inferiority of the additional serotypes in the new vaccines (PCV20 or PCV21) is assumed by comparing the proportions of participants that reached IgG ≥ 0.35 $\mu\text{g/ml}$ for each new serotype against any serotype that achieves the lowest percentage of IgG ≥ 0.35 $\mu\text{g/ml}$ in the licensed comparator (PCV13) group. Functional antibody titres are assessed using opsonophagocytic activity (OPA) assays. This data is obtained from a subset of trial participants, but again, since no serotype-specific correlates of protection are defined, geometric mean titre ratios (GMR) are used to compare new and licensed vaccines.⁴⁸

The measure of immunogenicity used to confirm non-inferiority does not necessarily indicated long-term protection. A UK study using an indirect cohort method in infants given PCV13 found that serotype-specific correlates of protection may be higher or lower than 0.35 $\mu\text{g/ml}$, and that vaccine effectiveness may be lower than predicted by the clinical trial immunogenicity data.⁴⁹ Therefore, caution is required when predicting vaccine efficacy from immunogenicity data from clinical trials.

Clinical trials can only demonstrate non-inferiority or equivalence between the vaccine formulations in a selected group of healthy participants.

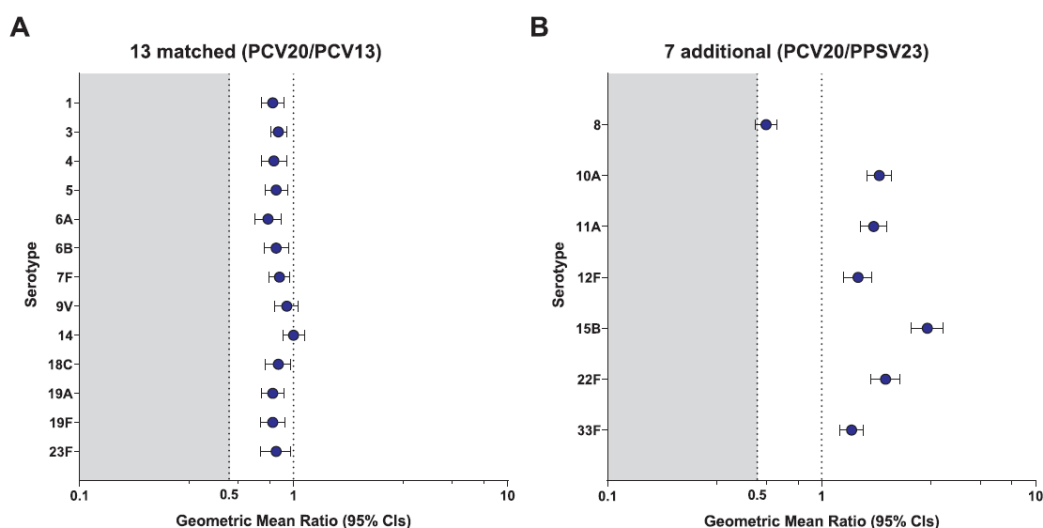
See Table 13 for further study details.

Phase 3 clinical trials – PCV20

A pivotal phase 3 clinical trial, conducted in the US and Sweden, found robust functional (opsonophagocytic activity, OPA) antibody responses across all 20 serotypes in PCV20 across different age groups (18 – 49 years, 50 – 59 years and ≥ 60 years) compared with PCV13 (see Figure 12).³⁸ The PCV20 OPA geometric mean titres (GMT) were slightly lower for the PCV13-matched serotypes than PCV13. Serotype 8 did not quite meet non-inferiority for PCV20 compared with 23PPV in the ≥ 60 age group, but the PCV20 response was higher for the other six shared serotypes.³⁸ When compared by immunobridging, the OPA response to PCV20 for all 20 serotypes in the younger age groups were non-inferior to those aged 60 – 64 years.

Figure 12: Model-based opsonophagocytic activity geometric mean ratio in phase 3 clinical trial, participants aged ≥ 60 years: A) comparing 13 serotypes shared between PCV20 and PCV13; B) additional 7 serotypes shared between PCV20 and 23PPV. (Essink et al 2022, open access)

Non-inferiority declared if lower bound of the two-sided 95% confidence interval (95% CI) for GMR was >0.5 (two-fold criterion).



Further phase 3 clinical studies, conducted in India,⁴¹ Japan, South Korea and Taiwan,⁴² found consistent and similarly robust immune responses.

PCV20 was shown to be a valid alternative to 23PPV revaccination in individuals with prior pneumococcal vaccination history. A US and Swedish phase 3 study investigated PCV20 in older adults who had previously received 23PPV, PCV13 or both and compared with controls who received, respectively, PCV13, 23PPV or PCV20 only.⁴³ Robust immune responses were seen against the PCV20 serotypes, regardless of prior vaccination. Baseline OPA GMTs were highest for those who had previously received both PCV13 and 23PPV, and lowest for those who had received 23PPV only.

Post-hoc analysis of two clinical trials^{38, 40} found that immune responses to PCV20 serotypes were robust and non-inferior to PCV13 in adults with a higher risk of pneumococcal disease (e.g., diabetes, chronic pulmonary disease, but excluding immunocompromised groups).⁵⁰

Coadministration of PCV20 and mRNA-COVID-19 vaccine (Comirnaty) does not result in clinically significant interference of the immune response to either vaccine in adults aged ≥ 65 years. The observed GMR for the PCV20 serotypes were 2.5 – 24.5 in the coadministered group and 2.3 – 30.6 in the PCV20 alone group.⁴⁴

Summary

Across multiple phase 3 clinical trials, PCV20 demonstrated a broad, functional immune response to 20 pneumococcal serotypes and is consistently non-inferior to PCV13 for shared serotypes. Only serotype 8 missed the non-inferiority criteria compared with 23PPV in older adults, but the immune response was considered robust with ≥ 4 -fold rise in functional antibody titres in most participants. The immune response to PCV20 in non-immunocompromised adults at increased risk of pneumococcal disease was like that seen in healthy groups; however, the clinical trials excluded individuals who were immunocompromised who are a significant risk group for IPD. No impact on immunogenicity was seen for either vaccine when PCV20 is coadministered with COVID-19 vaccine.

Phase 3 clinical trials - PCV21

Fewer clinical trials have been published for PCV21 than PCV20. A pivotal clinical trial (STRIDE-3) conducted in 11 countries investigated immunogenicity in two cohorts stratified by age comparing PCV21 with PCV20.⁴⁶ Cohort 1 with age groups ranging from 50 to over 85 years and cohort 2 aged from 18 – 49 years. In cohort 1, PCV21 non-inferiority in comparison to PCV20 was confirmed for all 10 shared serotypes and superiority was met for 10 out of 11 of the unique serotypes in PCV21. Non-inferiority was not met for serotype 6C, although robust immune responses were observed for similar proportion of participants with a ≥ 4 -fold increase in OPA antibody titres for both PCV21 and PCV20. Immunobridging criteria were met for 21 serotypes in cohort 2 compared with 50 – 64 years age group in cohort 1.⁴⁶

A phase 3 study (STRIDE-9) in Japan in 450 pneumococcal naïve adults showed PCV21 was non-inferior to 23PPV for 12 common serotypes and for cross-reactive 15B. PCV21 induced numerically higher GMTs than 23PPV against the remaining eight unique serotypes and cross-reactive 6C.⁴⁷

Summary

When compared with PCV20 or 23PPV, PCV21 induced robust antibody responses to shared and unique serotypes in a range of adult age groups. It is likely to provide broader protection against serotypes currently covered by PCV13 and 23PPV.

Vaccine effectiveness and potential impact

Data is limited on the real-world effectiveness of the higher valency PCVs currently in use. Regulatory approval was granted based on immunogenicity and immunobridging from previous PCVs (ie PCV7 and PCV13) for the shared serotypes and antibody responses to the extra serotypes.

Studies are underway. For example, a Merck/MSD-sponsored test-negative case-control study is evaluating PCV21 (Capvaxive, MSD) against pneumococcal pneumonia in older adults in US and Canada ([HMA-EMA real-world data catalogue](#), EU PAS1000000640) but is not due to analyse data until 2029. A phase 4 study is being conducted in Czechia, Israel and Spain investigating vaccine effectiveness of PCV20 (Prevenar 20) against vaccine-type IPD in adults aged 65 and over, using surveillance data (EU PAS1000000007) for which data analysis was due to commence this year.

Details of published retrospective studies for PCV20 are summarised below and detailed in Table 14. No studies were found to date about the effectiveness of PCV21 in adults or high-risk groups.

Real-world effectiveness

A large retrospective cohort study in the US (2022–2024; ~16.5 million adults aged ≥65 years in Medicare) found that PCV20 vaccination was associated with moderate protection against a range of pneumococcal and respiratory outcomes, although serotype-specific effectiveness could not be assessed and there was some residual confounding around healthcare usage. Adjusted vaccine effectiveness was 25.6% (95% CI 17.4 – 33.0) against IPD, 23.3% (16.3 – 29.8) against pneumococcal pneumonia, 15.2% (14.5 – 15.9) against all-cause pneumonia, and 7.4% (6.9 – 7.8) against lower respiratory tract infection (LRTI). During the first year, this corresponded to reductions of 12.0 (8.0 – 16.0) IPD cases and 12.8 (8.2 – 17.4) pneumococcal pneumonia cases per 100,000, and much larger reductions for broader outcomes (758 fewer cases all-cause pneumonia and 636 LRTI cases per 100,000).⁵¹ Noting that those who had received PCV20 prior to the study were excluded, and follow-up was excluded if they received 23PPV within 2 years, PCV13 within 5 years and PCV15 prior to the study date.⁵¹

Effects were stronger in higher-risk groups, with 1.3–2.4 times higher absolute rate reductions in those with immunocompromise or chronic conditions. For example, in immunocompromised adults, there were 30 fewer IPD cases and around 1,864 fewer all-cause pneumonia cases per 100,000 with adjusted vaccine effectiveness of 25.0% (13 – 35.3) and 16.5% (15.5 – 17.6), respectively. Overall, PCV20 was associated with reductions in pneumococcal disease and a substantial public health impact through prevention of pneumonia and LRTI in older adults.⁵¹

PCV20 vaccination was associated with a lower risk of bacterial pneumonia and other respiratory and severe clinical outcomes in individuals with inflammatory bowel disease (IBD) receiving immunosuppressive medications in the US. The retrospective analysis included 12,796 individuals after propensity matching. It compared those vaccinated with PCV20 with unvaccinated controls (mean age vaccinated group 55.8 ± 17.1 years and controls 55.2 ± 16.3 years).⁵² Relative risk (RR) reductions were observed for pneumonia (RR 0.54, 95% CI 0.47 – 0.63), acute respiratory failure (0.42, 0.35 – 0.50), hospital admission (0.57, 0.53 – 0.62), ICU admission (0.47, 0.40 – 0.57), and all-cause mortality (0.32, 0.25 – 0.40); no effect seen for meningitis (RR 1.00, 0.42 – 2.40). Protective effects against pneumonia were consistent across age groups, including ages 18 – 39 years (RR 0.50, 0.29 – 0.84) and 40 – 64 years (0.55, 0.43 – 0.70).⁵² Note, this study did not adjust for prior pneumococcal or other vaccinations, socioeconomic factors, and potential healthy user bias. The authors did not believe that vaccination alone accounted for the marked reduction in outcomes but is a low-risk intervention used as part of a care bundle for individuals with IBD.⁵²

Modelling impact

Surveillance data from England (2022–23) found that IPD was associated with high mortality in adults aged over 80 years. Adults living in care homes had a substantially higher risk than the general population aged over 65 years.⁵³ A modelling study compared a planned programme of vaccinating all adults from age 65 years with PCV20 with vaccination only of new care-home residents. The modelling suggested that vaccinating all adults at age 65 would prevent some cases and deaths, but is relatively inefficient (for example, ~3,700 people need vaccination [NNV] with 23PPV to prevent one IPD case and NNV ~19,455 people to prevent one death). Targeting new care-home residents prevents more outcomes per dose (NNV ~687 per case and ~1,095 per death). It was estimated that

PCV20 could have a greater impact than 23PPV, with lower NNVs (e.g. NNV ~384 per case and ~774 per death in care-home residents). However, effectiveness of PCV20 is not yet established in any age group.⁵³

Summary

PCV20 has the potential to make a meaningful population impact on IPD and respiratory outcomes in adults. Based on limited data, vaccine effectiveness in older adults was around 25% against IPD and pneumococcal pneumonia. The risk reduction was around double in immunocompromised groups. It is unclear whether PCV20 will have a greater overall impact than 23PPV. One study suggested that targeting high-risk groups (e.g. new aged-care home residents) may provide greater benefit than universal age-based vaccination.

No data was available around the real-world effectiveness and potential impact of PCV21 in older adults and special groups.

Summary of evidence

Table 10: Burden of disease and pneumococcal vaccination in special groups

Outcomes	Ref	Participants / study design	Results	Findings
Burden in adults with comorbidities				
Review of risk groups	4	Review of evidence for adults at increased risk of IPD, UK Estimated 12.7% English population had ≥1 risk factor	• PLWHIV IRR 14.6% vs general population, 4.5-fold higher rate despite antiretroviral treatment. • Risk stacking: ≥2 comorbidities significantly higher risk of PD than single high-risk condition – not formally recognised in UK vaccination guidelines. • Consensus statement HSCT revaccination recommendations – 3 primary doses from 3-6 months post HSCT and booster at 18 months with either PCV13 or 23PPV. • Overall, large gap in uptake for risk groups with PCV13 and 23PPV. Eg. Dialysis – preferred place for vaccination in dialysis units rather than GP due to frequency of visits. But few accessing vaccination. Despite this, funding only available to support vaccination programmes in primary care settings.	
systematic review, high risk conditions	22	Systematic review of 58 reports and 46 included for meta-analysis. • More than 50 different risk conditions for adults IPD were identified, 22 used for domains for meta-analysis. • High level of bias and heterogeneity.	Highest IRRs immunocompromising conditions: • Transplant = 30.8 (17.6-53.6) • Asplenia = 24.3 (18.6-31.7) • PLHIV = 21.9 (15.7-30.4) • Haematological malignancy = 19.6 (11.1-34.7) • CKD <65y = 18.4 (11.4-29.7) vs CKD ≥65y = 5.2 (2.1-12.6) • Compromised CSF barrier = 17.0 (2.8-103.9) • Down syndrome = 47.5 (22.5-100.2) Several studies suggested cumulative risk with multimorbidity. After adjusting for underlying conditions, age posed a small direct risk. • Below age 65y, risk associated with a given condition was higher than in the older population eg diabetes, chronic liver disease, African American ethnicity. Secondary immunodeficiency, including adults on immunosuppressive medication, mediated a relative risk size comparable to chronic lung, liver, or heart disease or alcoholism.	Most pronounced conditions with largest risk were in line with current US recommendations for pneumococcal vaccination.

continued next page

Outcomes	Ref	Participants / study design	Results	Findings
Proportion of adults at risk of pneumococcal disease	25	Annual cross-sectional study on retrospective data, France 2014-2018 to assess number of adults eligible for pneumococcal vaccination. Total sample of 40 million adults beneficiaries in scheme.	In 2018, identified over 4 million patients at-risk of pneumococcal disease • Mean age 66.1 years (55.1% aged ≥ 65 years), 18% ≥ 2 comorbidities. • 14% immunocompromised (youngest ages, mean age 57.2 years $\pm$ 15.5) Of these, ~3.6 million (90%) had chronic medical conditions (mean age 67.4 years $\pm$ 14.3): • 72% diabetes • 17% chronic respiratory disease • 12% heart failure (oldest age group at mean of 76.8 $\pm$ 13.1 years) • 8% chronic liver failure. In all cases, the numbers of those at risk had increased between 2014 and 2018.	This study assessed the annual size of the population at risk for pneumococcal disease in France in 2018. Approximately 10% of adults were considered at increased risk of pneumococcal disease, with 90% of these adults with chronic medical conditions and 14% immunocompromised.
Risk and complications of community-acquired pneumococcal pneumonia				
Hospitalisation, NZ	28	Retrospective clinical record review, adult CAP admissions at Christchurch Hospital, NZ. Socioeconomic status using Geocoding of residential addresses. total of 2066 recorded CAP admissions, 1194 excluded (<18y, out of region, no primary diagnosis, recently hospitalised).	924 hospitalisations included (81% NZE, 9% Māori, 5% pacific, 25% other). 76% ≥ 1 and 17% ≥ 3 major comorbidities; most common chronic cardiovascular (47%) and 34% chronic respiratory disease. Of 40% with sputum samples taken, <i>H. influenzae</i> 22% and <i>S. pneumoniae</i> 11% of CAP. 13% coinfection with virus. Ages (mean 70 $\pm$ 18y) • <50 = 127 case (14%) • 50-64 = 158 (17%) • 65-79 = 318 (34%) • ≥ 80 = 324 (35%) CAP hotspots, not equally distributed across SES quintiles ($P < 0.0001$) rates compared with quintile 1 (least deprived vs most deprived), rate ratio • Highest quintiles 1.5 (1.3-1.8) and 1.6 (1.3-2.0); stratified by health deprivation RR 2.3 (1.8-3.0) and income 1.4 (1.1-1.8) • Māori and Pacific vs NZ European – younger and higher proportion in highest deprivation. • Geographically – most areas had rates <5 per 1000 but 2 areas rates 51 and 22 per 1000, removing age-care residents did not alter upper outliers and were not distorting results. • Māori and Pacific ethnicity correlated with deprivation – possible that deprivation not ethnicity is predominant risk factor • Average age of CAP in Māori 12 years younger than NZE.	Study identified CAP hotspots in Christchurch associated with socioeconomic disparities in health equity. Although age was a risk factor, the CAP hotspots did not closely mirror age distribution across the city. Socioeconomic deprivation was an important but not the only factor in the CAP clusters. These data highlight a role for targeted preventative interventions in these hotspots.

Outcomes	Ref	Participants / study design	Results	Findings
Chronic liver disease	27	CAPNETZ study, CAP 2001-2017, Germany – identifying patients CLD Total cohort of 11,832 with episodes of CAP, 5449 hospitalised with information on presence or absence of CLD. (Letter)	In this cohort, 289 patients (5.3%) with CAP had CLD. These patients were significantly younger than those without. Median age 64 years (50-73) vs 73 (64-80 years) $p<0.001$ CLD patients with CAP had lower incidence of cardiac disease, CVD, diabetes – likely due to younger age. Chronic respiratory diseases were more common in this group. CAP survival was lower despite younger age • 30d mortality CLD vs non-CLD = 11.3% vs 7.1%; OR 1.67 (1.12-2.49) $p=0.014$ • 180d mortality = 19% vs 15.5%; OR 1.38 (1.0 – 1.92, $p=0.054$ • Age ≥ 65 y, CVD, CHF, CLD independently associated with 30d mortality. • CLD = 2nd highest in hospitalised CAP (OR 2.35 (1.55-3.66)) Higher median hospital stay with CLD, even with other severe comorbidities – 12d (IQR 8-16) vs 10 (8-14) $p<0.001$ CAP cases with bacteraemia CLD vs without = 19.6% vs 8.9%, $p<0.001$	Hospitalisation and mortality rates of those with CAP and CLD are higher than for those without CLD., even in those with other severe morbidities. Patients with CLD are hospitalised with CAP at a younger age than those without, despite having fewer other comorbidities, except chronic respiratory disease. Patients with CLD and CAP have double the incidence of bacteraemia than those with CAP without CLD.
continued next page				
Underlying comorbidities	26	Retrospective cohort study of 2.2 million patients aged ≥ 18 years, England, hospital burden of CAP over 3 years. ICD10 codes. Examine impact of a episode of hospitalised CAP in those with ≥ 1 of six underlying comorbidities: CHD, CKD, CLD, CRD, diabetes, post-HSCT with inpatient admission in 2012/2013. Patients with CAP 2013/2014 followed 3 years and propensity-score matched to those with same comorbidities not hospitalised with CAP at any point in 3 years. Counter-balanced severity with healthcare utilisation during baseline year (2012/13)	After selecting hospital CAP in 2013/14 and 1:1 matched controls number in each group: CHD = 36,386, CKD = 12,190, CLD 2,222, CRD 20,764, diabetes = 16,382, post-BMT = 2,711 Relative risk (RR) of hospital admission after CAP ranged from: (see Figure 10) Statistically significant increase in health-care resource utilisation observed. Increase maintained for ≥ 2 years. Patients with comorbidities hospitalised for CAP had substantially higher odds of in-hospital mortality vs those without comorbidity. OR (95% CI), each $p < 0.0001$ (see Figure 11) • BMT = 7.5 (4.7-11.9) • CLD = 4.76 (4.12-5.51) • CRD = 5.94 (5.65-6.24) Limitations – accuracy of CAP diagnosis – some pneumonia result of other conditions. Unable to distinguish between community vs hospital acquired pneumonia (did exclude all cases onset >48h after admission) The study only included 6 comorbidities and did not include those with immunosuppression or functional asplenia.	This study demonstrates the importance of prevention of CAP in patients with comorbidities. Admission to hospital for CAP can impact patient and healthcare system for 3 years after initial diagnosis. Risk of admission and mortality is significantly increased for 3 years after initial CAP hospitalisation in those with comorbidities

Outcomes	Ref	Participants / study design	Results	Findings
Cardiovascular events	29	Review of cardiac complications associated with Spn CAP	Pneumococcal CAP is associated with cardiac complications – including AMI, new/worsening arrhythmia, new/worsening heart failure. Most common among older adults and nursing home residents. Increase risk for long-term CVD. Theories include involvement of major Spn protein virulence factor – pneumolysin in cardiac toxicity and platelet-driven neutrophil activation. Pneumococcal adhesins have also been suggested to facilitate the trans-endothelial passage of the bacterium from circulation into the heart tissue. Some capsular serotypes appear to have a greater propensity to invade the myocardium and to persist in the cardiac cells and monocytes. Some studies suggest the presence of persistent antigenemia following pneumococcal infections predispose to systemic proinflammatory/prothrombotic phenotype. Close interaction between influenza and pneumococcal pneumonia.	
continued next page				
Pneumonia in patients with heart disease	24	Post-hoc analysis, incidence of pneumonia in PARADIGM-HF trial which included 8,399 ambulatory patients aged ≥ 18 y with reduced ejection fraction heart failure (HFrEF) on contemporary therapy and compared with 3,796 patients aged ≥ 50 y with preserved ejection fraction (HFpEF) in the PARAGON-HF trial. (North America, Europe, Latin America, Asia-Pacific) Comparator groups for pneumonia were another type of infection – urinary tract infection.	PARADIGM-HF trial: - mean age 63.6 (± 11.4) without pneumonia / 66.9 ± 11.6 without pneumonia ($p < 0.0001$) 528 (6.3%) developed pneumonia - incidence rate: 29 (95% CI 27-32) per 1000 patient-years - patients with pneumonia had more comorbidity (COPD 25.6% vs 12.0%), diabetes (42.6% vs 34.1%), AF (45.6% vs 36.2%) - post-first pneumonia = 3–5-fold elevation in risk of subsequent outcomes. PARAGON-HF: - mean age 72.4y (± 8.4) without pneumonia / 75.6y ± 8.0 without pneumonia ($p < 0.0001$) 510 (10.6%) with pneumonia - IR = 39 (36-42) per 1000 patient-years - patients with pneumonia also had more comorbidity, including COPD (26.2% vs. 12.5%), diabetes (48.6% vs. 42.3%) and AF (61.4% vs. 51.5%). No difference for current smoking. Patients who had pneumonia had HF for longer, but no difference in frequency of previous HF hospitalisations. Urinary tract infection – many variables associated with pneumonia also increased risk of UTI – older age, longer duration symptomatic HF, more comorbidities (sex differed). Unadjusted HRs for the analysed outcomes ranged from 1.31 to 2.23, compared with 2.19 to 5.19 associated with pneumonia.	The incidence of investigator-reported pneumonia was high in patients with HF, especially HFpEF. An episode of pneumonia was associated with an approximately 4-fold elevation in risk of death. The risk was greatest around the time of the pneumonia episode but remained elevated beyond 3 months. Encourage more greater use of pneumococcal and influenza vaccination in patients with heart failure.

Outcomes	Ref	Participants / study design	Results	Findings
continued next page				
Risk of heart failure post CAP	30	Prospective controlled study, Canada 2000-2002. 4988 adults with CAP, no history of heart failure, matched by age, sex and setting of treatment with adults aged ≤65y without pneumonia (controls) or prevalent heart failure (n=23). Av age 55 years, 53.1% male, 63% outpatients. (Excluded immunocompromised and other high-risk groups) Adjusted for comorbidity index	- Over median of 9.9 years (IQR range 5.9-10.6), 11.9% with pneumonia had heart failure vs 7.4% controls (aHR = 1.6 (1.44-1.81), p<0.001) - within 90 days of pneumonia discharge 1.4% vs 0.6%, aHR = 1.61 (1.44-1.81, p<0.001) - within 1 year of discharge 3.3% vs 1.4%, aHR = 1.86 (1.5-2.32; p<0.001). - Those aged <65 years had lowest absolute increase but greatest relative risk of heart failure: 4.8% vs 2.2%, aHR = 1.98 (1.5-2.53) - Those aged >65y had highest absolute increase but lowest relative risk: 24.8% 18.9%, aHR = 1.55 (1.36-1.77) - Pneumococcal bacteraemia – significant risk of heart failure – 13.3% vs 7.4%, aHR = 2.4 (1.08-5.3); non-pneumococcal bacteraemia – no increased risk in heart failure vs controls (aHR = 0.89; 0.32-2.4) - No increase in risk of stroke or fractures shown (heart failure risk not a reflection of increased frailty).	Community acquired pneumonia increases risk of heart failure. Risk is extended to younger adults who survive an episode of pneumonia but may not typically be seen as higher risk for heart failure. Consider use of pneumococcal vaccination in patients at high risk of pneumonia and CV disease. Subsequent shortness of breath or wheeze may not be related to another RTI but new onset heart disease.
Use of 23PPV and/or PCV13 in special groups				
23PPV protection against cardiovascular disease	31	SRMA, 1946-2019, 18 studies included total 716,108 participants.	23PPV vaccination decreases risks of any cardiovascular event (AMI, CHF, cerebrovascular (eg stroke/TIA events) in all age groups, but significant ≥65 not younger: - Any CV event: RR =0.91 (95% CI 0.84-0.99; 15 studies) - AMI: 0.88 (0.79-0.98; 12 studies) - Cerebrovascular (4 studies) – no significant difference 0.96 (0.83-1.10) - All-cause mortality – all age groups 0.78 (0.68-0.88) vs ≥65 years 0.71 (0.60-0.84) Possible confounding for healthier controls in those aged 18-64y, as unlikely to received 23PPV under 65 if healthy. Low numbers and lack of specific-event reporting, unable to assess impact of 23PPV on new or worsening CHF or arrhythmias.	Polysaccharide pneumococcal vaccination decreased the risk of some cardiovascular diseases particularly for those aged ≥65 years.
continued next page				

Outcomes	Ref	Participants / study design	Results	Findings
Vaccine effectiveness 23PPV against CVD	32	Population-based nested case-control study (VENUS), Japan. 383,781 individuals, 5,356 with acute myocardial infarction (AMI) and 25,730 with stroke matched with 26,753 and 128,397 event-free controls, respectively. 23PPV vaccinated compared with unvaccinated.	follow-up median 2.5 years (IQR 2.2-2.5) Mean age of index date = AMI 79.3 (SD 7.6) stroke 79.4 (7.4 years) 23PPV vaccinated had lower odds of AMI or Stroke • AMI aOR= 0.70 (0.62-0.80) • Stroke aOR = 0.81 (0.77-0.86) More recent 23PPV (within 6 months) further lowered odds. No difference if vaccinated ≥ 720 days prior to event/matched index data • < 6m AMI aOR = 0.55 (0.42-0.72); stroke 0.83 (0.74-0.93) • >720 days AMI = 1.11 (0.84-1.47); stroke 0.90 (0.78-1.03) AMI and stroke cases had higher percentage of comorbidities (CHF, cardiac arrhythmias, valvular disease, peripheral vascular disorders, hypertension, COPD, diabetes, renal failure. • No difference in the number of months with outpatient visit over prior 6 months • Adjustment for influenza vaccination did not change results	23PPV vaccination decreased the risk of AMI and stroke in older adults, including those with underlying cardiovascular comorbidities. Noted that this study had a higher age (~80 years) and greater protection was reported than other studies. Although there was potential confounding lifestyle and healthy-user biases, sensitivity analyses suggest 23PPV had a role in reducing CV events.
Impact of PCV13 on COPD and CVD	33	Sub analysis of prospective observational study, 121 COPD patients followed for 18 months with/out CVD (ischaemic heart disease, HF, arrhythmia, cerebrovascular accidents). (letter to editor)	71/121 patients (59%) classified as having CVD with COPD (COPD/+CVD) compared with COPD/-CVD group. • 50% of non-vaccinated vs 16.1% of vaccinated COPD/+CVD patients were hospitalised (p = 0.007) • Not statistically different for COPD/-CVD vaccinated and unvaccinated (23% vs 13%, p=0.413) In COPD/+CVD group, exacerbator (based on number of hospital admissions during study period for COPD, excluding CAP) and non-exacerbator phenotypes identified: • PCV13 vaccination reduced risk in non-exacerbating patients (OR 0.05, P=0.013) • 43.3% of the non-vaccinated COPD/+CVD non-exacerbator phenotype patients were admitted to hospital at least once compared to only 3.8% of the vaccinated ones. • Not significant for exacerbator type p=068 • Not significant for COPD/-CVD group.	PCV13 vaccination reduced risk of hospitalisation in patients with non-exacerbating COPD plus cardiovascular disease. COPD exacerbations were predominantly associated with bacterial infections, only 15% pneumococcal. Limitations – small sample size – observed effects did not fit logistic regression adequately.

continued next page

Outcomes	Ref	Participants / study design	Results	Findings
----------	-----	-----------------------------	---------	----------

Abbreviations: AF – atrial fibrillation; aHR – adjusted hazard ratio; AMI – acute myocardial infarction; aOR – adjusted odds ratio; BMT – bone marrow transplant; CAP – community-acquired pneumonia; CHD – chronic heart disease; CHF – congestive heart failure; CKD – chronic kidney disease; CLD – chronic lung disease; COPD – chronic obstructive pulmonary disease; CRD – chronic respiratory disease; CSF – cerebrospinal fluid; CV – cardiovascular; CVD – cardiovascular disease; GP – general practice; HF – heart failure; HFpEF – heart failure with preserved ejection fraction; HFrEF – heart failure with reduced ejection fraction; HR – hazard ratio; HSCT – haematopoietic stem cell transplant; IPD – invasive pneumococcal disease; IQR – interquartile range; IR – incidence risk; IRR – incidence rate ratio; PD – pneumococcal disease; PLHIV – people living with HIV; 23PPV – 23-valent pneumococcal polysaccharide vaccine; PCV – pneumococcal conjugate vaccine; RR – risk ratio; RTI – respiratory tract infection; Spn – *Streptococcus pneumoniae*; SRMA – systematic review meta-analysis; TIA – transient ischaemic attack; UTI – urinary tract infection; UK – United Kingdom; US – United States of America

Table 11: Indirect protection and international recommendations

Outcomes	Ref	Participants / study design	Results	Findings
Transmission and indirect protection				
Indirect protection from children	34	Targeted literature review March 2023.	Impact of infant PCV programme on NPC in adults – most studies showed a decrease, two show increased non-vaccine types. indirect effects have been shown with established paediatric vaccination programmes in young, adults with underlying conditions and older adults. Dependent on serotype replacement and variable magnitude of indirect effect. Burden due to non-vaccine serotypes remains high in adults.	
Preschool age, indirect protection	35	Surveillance data, Israel. 2009-2016. PCV7 catch up in children under 24 months, replaced with PCV13 in 2010. NP swabs taken from first 4 Jewish and 4 Bedouin children aged under 5 years who visited ED. Recorded number of PCV doses received. Data only based on Jewish children (n=4,464) due to the way IPD data was collected in the regions. Modelled indirect effects.	Among 4,464 Jewish children, prevalence of PCV7 serotypes in NP swabs declined from 21% in 2009 to 2.6% in 2016, apparent in all ages under 5. Most rapid declines in 12-23 and 24-35 months, slower in <12m and 36-59 months. A decline in IPD due to PCV7 serotypes in adults (age 18-39, 40-64 and 65) was most strongly associated with increase in direct effect from 36-54, 30-59 and 30-54 months. Statistical support from 6-59 months but weaker significance if included <12m infants. Strong evidence that direct protection among older children (from 36 months) related to decline in IPD in adults but direct protection against carriage for under 12 months was not as important for indirect protection. Declines in carriage ≥24 months and under 6 months were most strongly associated with declines in adult IPD (PCV7 serotypes).	With the building of pneumococcal immunity in children and reducing carriage in preschool-aged children, rather than infants, maintain indirect benefits of PCVs to adults. The first two doses in infancy have a weak effect on colonisation but the toddler booster dose provides strong protection against carriage and subsequent transmission. These finding suggest that catch-up campaigns in children aged 1-5 years could accelerate indirect benefits of PCVs.
Limited indirect protection	36	IPD cases in Germany. 23PPV routinely recommended age ≥60y but low uptake	- IPD in infants declined from 11.09 to 5.94 per 100,000 between 2003/6 to 2017/18. - Adults cases ≥60y rose from 1.64 to 10.08. PCV13-IPD = 31% of cases - due to ST3 (21% of cases for age group) - Coverage for PCV15 and PCV20 in children would increase to 8.5% and 28%, respectively, but in adults increase by 10.4% and 21.9%.	Seems herd protection from infant programme has reached its limit in Germany (serotype 4, 19F and 19A IPD have persisted in adults) and no herd protection from serotype 3.

continued next page

Review of Evidence, 2026: Pneumococcal – adults and special groups

Outcomes	Ref	Participants / study design	Results	Findings
Adults as a reservoir	37	Nasal wash samples from adults age 18-44 years without close contact young children (Liverpool, UK) in 2011-2019. NPC from NP swabs was compared in adults 18-44y with vaccinated young children aged 13-48 months (Thames Valley), and national IPD data 214-2019. Serotype-specific case-carrier ratio – estimate no. of carriers / serotype-specific IPD cases.	98 isolates from 97 carriers from 1631 adults (standardise carriage prevalence 6.4%) Carriers ranged from 18-58 years. Only 1 carried ≥1 serotype. - Higher proportion PCV13 serotypes in young adults than children (22.2% vs 4.3%) - Different serotype distribution in young adults vs children. Abundant serotypes in young adults – 3, 8, 37 – likely circulating in adults and older children. - Invasiveness was generally higher in young adults. Serotype invasiveness was highly correlated (R=0.9) in young adults. - Serotype 37 was not reported in IPD cases for same period	Particular serotypes may be circulating in young adults. These were similar to the predicted serotype distribution in older adults. Such that young adults may be a reservoir for pneumococcus in the community and older adults.
International recommendations				
Comparison between countries	4	Review of evidence for UK programme (2023)	- Uptake of 23PPV is low in high-risk groups, national strategies required to urgently optimise vaccine access and coverage. - Lack of international consensus around risk groups - Noted an increase in pneumococcal septic arthritis in older adults and underlying comorbidities due to non-vaccine and 23PPV/non-PCV13 serotypes	
Older adults and at-risk groups	19	Review of programmes (2022-2024)	- Single dose of PCV20 for older adult and high-risk groups - Additional dose of PCV20 for those previously vaccinated with PCV13/23PPV or incomplete schedule. - Most European countries recommended PCV20 for adults aged ≥65 years, some from age ≥60 years. - For high-risk groups, most countries recommend PCV20 as an option from age 18 years, some only from 50 years.	
Abbreviations: ED – emergency department; IPD – invasive pneumococcal disease; NP – nasopharyngeal; NPC – nasopharyngeal carriage; PCV – pneumococcal conjugate vaccine; PCV20, PCV15, PCV13 – 20-valent, 15-valent, 13-valent pneumococcal conjugate vaccine; 23PPV – 23-valent pneumococcal polysaccharide vaccine; UK – United Kingdom				

Table 12: Vaccine safety

Outcomes	Ref	Participants / study design	Results	Findings
PCV20				
Pivotal trial safety, immunogenicity and tolerability	38	Phase 3 RCT three age groups (18-49, 50-49, ≥60y). US and Sweden. Randomised 1:1 to 1 dose PCV20 or PCV13. Those aged ≥60 received saline or 23PPV. (NCT03760146, Pfizer)	- Out of 3009 randomised participants aged ≥60 y, 2997 received first vaccination (66.2% aged 60-64y, 31.4% aged 65-79y and 2.3% aged ≥80y). 432/445 (97%) aged 50-59 and 423/448 (94%) aged 18-49 completed the study. - Fever (≤7d) – 0.9-1.5% PCV20 and 0.8%-1.8% PCV13 - Muscle pain most frequent reaction, highest in younger group (60-70% vs <40% older) - SAE up to 6 months f/u – infrequent and similar between vaccines in each age group – none considered vaccine related.	Severity and frequency of local and systemic reactions were similar for PCV20 and PCV13. No safety concerns identified.
Safety, tolerability	39	Phase 2 RCT 444 adults aged 60-64y in US. Randomised 1:1 to PCV20 plus 1 month later saline or PCV13 + 23PPV 1 month later. (NCT03313037, Pfizer).	- Local and systemic reactions were similar between groups. No vaccine-related SAE - Local pain at injection site (57.7% PCV20 vs 53.6% PCV13 and muscles pain (43.2% and 36.5%) most frequent reactions – mild to mod in severity, lasting 1-2 days. - No SAE were considered vaccine related. No deaths occurred.	PCV20 was well tolerated in adults aged 60-64 years and consistent with other PCVs.
Immunogenicity and safety	40	phase 3, RCT, 1708 pneumococcal naïve adults aged 18-49y randomised 2:2:2:1 to three lots of PCV20 vs PCV13. (NCT03828617, Pfizer)	Three lots of PCV20 tested against PCV13	Safety profile similar to PCV13.
Safety and immunogenicity, India	41	phase 3 RCT in Indian adults aged ≥18 years given PCV20 Groups aged 18-49 and ≥50 y, 200 per group. First 50 of each group enrolled in immunogenicity study. (NCT05875727, Pfizer)	38% reported local reactions, 23% system events within 7 days of vaccination. - Injection site pain (43.5% 18-49y and 32% aged ≥50y) - Systemic: muscle pain (14.5% and 9%), fatigue (12% both), headache (11.5% and 12%). Fever 3% and 1.5%. - No SAE or deaths reported.	PCV20 was well tolerated with acceptable safety profile in Indian adults. Findings consistent with other studies.

continued next page

Review of Evidence, 2026: Pneumococcal – adults and special groups

Outcomes	Ref	Participants / study design	Results	Findings
safety and immunogenicity, SE Asia, ≥60	42	phase 3 Japan, S Korea, Taiwan. 1421 age ≥60 years (stratified 60-64y and ≥65y) Randomised 1:1 to receive PCV20 plus saline after 1 month or PCV13 plus 23PPV. (NCT04875533, Pfizer)	1421 included in safety population. 44.5% age 60-64y; 50.6% aged 65-74y and 5.2% aged ≥75y - Similar local reactions to PCV13 and to previous studies. - Two SAE considered potentially vaccine related in one participant following PCV13 (pyrexia and urticaria). No SAE to PCV20.	Safety profile of PCV20 was consistent in this study to other studies and PCV13. No safety concerns raised.
prior pneumococcal vaccination age ≥65	43	Phase 3 RCT in US and Sweden. Three cohorts of adults (n=875) aged ≥65 years (median age 68-69 years) Randomised 2:1 to PCV20 or PCV13. - History of 23PPV only = 1 dose PCV20 or PCV13 - History PCV13 only – given 1 dose PCV20 or 23PPV - History of both – given PCV20 only	- Similar rates of local and systemic reactions and AE after PCV20 across cohorts and similar to PCV13 and 23PPV in control groups. - Reactions were mild to moderate. Most frequent – pain at injection site and muscle pain. - Fever was infrequent: 2 participants (0.8%) PCV20 with prior 23PPV; 2 participants (1.6%) after 23PPV with prior PCV13. - No SAE were considered vaccine related and were consistent with medical events in the age group.	PCV20 safety and tolerability profile was similar between adults aged ≥65 years with different pneumococcal vaccination histories and to PCV13 and 23PPV in control groups.
PCV20 coadministered with Comirnaty, age ≥65 years.	44	phase 3 RCT in US. 570 adults aged ≥65 years randomised 1:1:1 to coadministered PCV20 plus mRNA-CV (Comirnaty), to PCV20/saline or mRNA-CV/saline. (NCT04887948, Pfizer)	Most frequent were mild to moderate local reaction - injection site pain in 60-73%, lower in PCV20 only group, median duration 2.5-3days - systemic events – fatigue across all groups, fever uncommon (1 case (0.5%) coadministered, 2 cases (1.1%) mRNA-CV only) - Addition of PCV20 didn't appear to increase rate of AE – coadministered similar to mRNA-CV alone. (Coadministered for any related AE 4 [2.1% (0.6-5.4)] vs 0 for PCV20-only and 1 [0.5% (0-3.0)] mRNA-CV only Incidence of AE and SAE were low. No AE led to discontinuation and no SAE were considered vaccination related.	Overall safety profile of PCV20 coadministered with mRNA-CV was like that of mRNA-CV. Coadministration was well tolerated.

continued next page

Outcomes	Ref	Participants / study design	Results	Findings
Post licensure VAERS	45	US VAERS aged ≥19 years, Oct 2021-Dec 2023	Ages 19-64y (n = 798) - Injection-site reactions 29%, pain 17%, erythema 15% fever 15% Age ≥65y (n=1178) - Injection-site reaction 35%, pain 15%, pain in extremity 14%, erythema 13% GBS – data mining alert for serious reports 11 clinical verified / 20 reports, 7/11 vaccine recipients aged ≥65y - Of 11 cases, median time 14 days to onset, 5 received another vaccine on same visit. - Reporting rate – 0.5 cases per million distributed.; 0.9 cases per 100,000 person-years. - US CDC and FDA investigating signal further. Previous studies found no increase in risk associated with PCV13.	VAERS report findings were similar to PCV13 in adults aged ≥19 years. Rates of GBS were comparable to the background rates for this age group but not known how many doses were distributed to the population at higher risk of GBS.
PCV21				
Safety and immunogenicity, with/out chronic medical conditions, PCV21 vs PCV20	46	phase 3 V116/ PCV21 (STRIDE-3), 11 countries or territories. Stratified by age - cohort 1 50-64, 65-74, 75-84, ≥85y) randomised 1:1 for PCV21 or PCV20 (n=1179 vs 1177) - cohort 2 ages 18-49 years 2:1 PCV21 vs PCV20 (n=200 vs 100) - Prespecified conditions did not include immunocompromise (chronic organ diseases, diabetes, smoking, alcohol disorder) (NCT05425732, MSD)	- Cohort 1: 58.2% PCV21 vs 66.2% PCV20 reported ≥1 AE - Cohort 2: 82% PCV21 vs 79% PCV20 ≥1 AE - Most common – injection-site pain a, fatigue, headache; generally similar between vaccine groups. - No SAE or deaths were considered vaccine related.	PCV21 was generally well tolerated with a similar safety profile to PCV20. The safety results were consistent with other numerous PCV studies in adults. Incidence of adverse events were higher in younger adults, as also seen with other PCVs. Study excluded those with previous pneumococcal vaccination and those with immunocompromising conditions.
≥65 y, Japan	47	phase 3 V116/PCV21 (STRIDE-9), 450 pneumococcal vaccine-naïve ≥65y, Japanese adults. Randomised 1:1 PCV21 or 23PPV (NCT05633992, MSD)	40% in each group reported ≥1 AE, mild to moderate intensity, ≤3 days - Comparable AE between cohorts. - No SAE or deaths associated with the vaccine.	PCV21 has a comparable safety profile to 23PPV and is generally well tolerated in pneumococcal vaccine-naïve Japanese adults aged ≥65 years. Findings were consistent to other PCV21 RCT.

continued next page

Review of Evidence, 2026: Pneumococcal – adults and special groups

Outcomes	Ref	Participants / study design	Results	Findings
higher valency				
PCV24 (Astellas/Affinivax)	12	Phase 2 RCT, dose finding – adults 18-64 and 65-85 years. Randomised PCV24 (designated ASP3372, since renamed AFX3772, Astellas Pharma/Affinivax) or PCV13. A non-randomised group aged 65-85y who received PCV13 also given 23PPV.	Both age cohorts – most frequent local reaction pain and tenderness within 2-3 days and systemic – headache, fatigue and myalgia with either vaccine.	PCV24 was well tolerated in both age groups and had a comparable reactogenicity profile to PCV13.
PCV24 (Vaxcyte), older adults	13	Phase 2 RCT dose finding VAX-24 vs PCV20 (Prevenar 20) 200 adults aged ≥65 years.(NCT05297578.)	43.4% – 68.6% of VAX-24 groups reported ≥1 solicited AE 37.3-62.7% - ≥local AE and 28.3-44% ≥ systemic AE. Large overlapping CI with PCV20. - Most were mild to moderate in intensity - No severe solicited AE in PCV20 group. - Severe solicited AE in VAX-24 groups – ranged from 3.8% to 7.8%, included erythema, fatigue, muscle pain, headache, joint pain, local pain. - No MAAE, NOCI or SAE considered vaccine related or apparent pattern in 6 months post vaccination.	Safety profile was comparable across the three doses of VAX24 and PCV20. Findings supported the use of 2.2µg VAX-24 into phase 3 trials.
PCV31 (Vaxcyte), over 50 years.	14	phase 1-2 dose finding RCT, pneumococcal naïve adults aged ≥50y given PCV31 (VAX-31; Vaxcyte) or PCV20. Safety followed for 6 months. Total 1015 randomised to 3 dose groups plus PCV20 group; mean age 59.8 SD 6.7	- Overall, safety profile was consistent between groups. - Participants reported ≥1 AE: 76% (95% CI 70-81%) low dose, 78% (72-83%) mid dose, 83% (78-87) high dose PCV31 and 71% (65-77) PCV20 - Most started day 1 and median duration 2 days (IQR 1-4) 2% reported grade 3 solicited AE across all groups: local pain, swelling, redness, fever, headache, fatigue, myalgia. Similar between PCV31 and PCV20 - No SAE or NOCI associated with vaccines. - Five participants had 8 probably vaccine-related medically attended AE in low and med dose PCV31 groups only.	Despite potentially enhance immunogenicity, safety profile was consistent with an experimental PCV24 (VAX24) and PCV20.

Abbreviations: AE – adverse events; CDC – Centers for Disease Control and Prevention; FDA – Federal Drug Administration; GBS – Guillain-Barré syndrome; MAAE – medically attended adverse events; mRNA-CV – messenger RNA COVID-19 vaccine; MSD – Merck Sharp and Dohm; NOCI – new onset chronic illness; PCV – pneumococcal conjugate vaccine; 23PPV – 23-valent pneumococcal polysaccharide vaccine; RCT – randomised controlled trial; SAE – serious adverse events; SD – standard deviation; US – United States; US CDC - Centers for Disease Prevention and Control (US); VAERS – Vaccine adverse events reporting system;

Table 13: Immunogenicity

Outcomes	Ref	Participants / study design	Results	Findings
PCV20				
Pivotal trial safety, immunogenicity and tolerability	38	phase 3 RCT three age groups: 18-49 y (n=423 completed study), 50-59 y (n=432), ≥60y (n=2835). US and Sweden. Randomised 1 dose PCV20 or PCV13. Those aged ≥60 received saline or 23PPV OPA compared in ≥60 group. Younger participants PCV20 response immunobridged to age 60-64 y response. (NCT03760146, Pfizer)	Primary immunogenicity objectives were met (at 1 month) – PCV20 non-inferior to 13 matched PCv13 serotypes and 6 additional 23PPV serotypes (age≥60 y). • OPA GMT slightly lower for PCV20 for PCV13-matched serotypes. • Serotype 8 did not meet non-inferiority PCV20 vs 23PPV OPA GMR = 0.55 (0.49-0.62), but higher for remaining 6 shared serotypes. • Secondary objective – OPA response in younger age groups non-inferior to 60-64y-grou for all 20 serotypes. Highest in younger group.	PCV20 elicited robust, functional antibody response to all 20 serotypes in adults. Non-inferior response to 13 shared serotypes with PCV13 and for 6/7 shared serotypes with 23PPV.
immunogenicity and safety	40	phase 3, RCT, 1708 pneumococcal naïve adults aged 18-49y randomised 2:2:2:1 to three lots of PCV20 vs PCV13. (NCT03828617, Pfizer)	• No difference between lots • Non-inferiority criteria met	Three lots of PCV20 induced a consistent and robust immune response to all 20 vaccine serotypes in young adults.
safety and immunogenicity, India	41	phase 3 RCT in Indian adults aged ≥18 years given PCV20 Groups aged 18-49 and ≥50 y, 200 per group. First 50 of each group enrolled in immunogenicity study. (NCT05875727, Pfizer)	• OPA GMT increased from baseline to 1 month post PCV20 vaccination to all 20 serotypes. • GMFR ranged from 5.9 to 49.8 for PCV13-matched serotypes and from 5.4 to 15.7 for additional 7 serotypes. • Prevacination GMTs were higher for young participants. • % participants with OPD ≥LLOQ ranged from 88.9% - 100% for PCV13 serotypes and 98.9% - 100% for additional 7 serotypes.	PCV20 elicited robust immune response in Indian adults aged ≥18 years. Findings were consistent with previous RCT in adults.
safety and immunogenicity, SE Asia, ≥60	42	phase 3 Japan, S Korea, Taiwan. 1421 age ≥60 years (stratified 60-64y and ≥65y) Randomised 1:1 to receive PCV20 plus saline after 1 month or PCV13 plus 23PPV. (NCT04875533, Pfizer)	• PCV20 was non-inferior to PCV13 for all 13 shared serotypes and to 23PPV for 6/7 additional serotypes. • Non-inferiority missed for serotype 8 although it induced a robust immune response. • 80.5% participants had a ≥4-fold increase in OPA titres from baseline to 1 month post PCV20 for serotype 8. (ranged from 61.1% to 86.9% for additional 7 serotypes).	PCV20 elicited a robust immune response in East Asian adults aged ≥60 years in Japan, South Korea and Taiwan to all vaccine serotypes. Findings were consistent with previous RCT in adults.

continued next page

Review of Evidence, 2026: Pneumococcal – adults and special groups

Outcomes	Ref	Participants / study design	Results	Findings
prior pneumococcal vaccination age ≥65	43	Phase 3 RCT in US and Sweden. Three cohorts, adults (n=875) aged ≥65 years (median age 68-69 years) Randomised 2:1 to PCV20 or PCV13. - History of 23PPV only - 1 dose PCV20 or PCV13 - History PCV13 only – given 1 dose PCV20 or 23PPV - History of both – given PCV20 only	PCV13 serotypes - baseline OPA GMT higher for those with prior PCV13/23PPV, then PCV13, lowest with 23PPV only. 1 month post PCV20 – OPA GMT numerically higher for prior PCV13 only, lowest prior 23PPV only. GMFR highest with prior PCV13. for additional 7 serotypes - OPA GMT were numerically highest for PCV13/23PPV, followed by 23PPV and then PCV13. - GMFR highest for PCV13 (naïve to these serotypes)	Robust immune responses were observed against 20 vaccine serotypes, regardless of previous pneumococcal vaccination. Data suggested that PCV20 would be a preferred choice as an alternative to 23PPV revaccination, if indicated.
Immunogenicity in adults at risk 18 - 64	50	Post hoc analysis two phase 3 RCT. Total 4369 participants aged 18-64 years. Study 1 ³⁸ three cohorts – 18-49, 50-59, ≥60y, randomised 1:1 age ≥60 and 3:1 younger to PCV20 or PCV13. ≥60y given 23PPV 1 month later. (NCT03760146) study 2 ⁴⁰ adults 18-49y, 3 lots PCV20 ≥1 medical risk factor or smoker (incl diabetes, chronic pulmonary disease, excluding immunocompromised)	- Median age lower in the PCV20 groups 30% had ≥1 risk factor - OPA GMR PCV20 comparable to PCV13 for 13 matched serotypes - OPA GMR higher for PCV20 than 23PPV, except serotype 8 (as seen in original study). Other immunogenicity measures showed response to all PCV20 serotypes.	Robust immune responses were shown against all 20 serotypes in adults with higher risk of pneumococcal disease (excluded immunocompromised).
PCV20 coadministered with Comirnaty, age ≥65 years.	44	phase 3 RCT in US. 570 adults aged ≥65 years randomised 1:1:1 to coadministered PCV20 plus mRNA-CV (Comirnaty; designated BNT162b2), to PCV20/saline or mRNA-CV/saline. (NCT04887948, Pfizer)	- Observed SARS-CoV-2 GMFR at 1 month post vaccination were similar between coadministered and mRNA-CV only groups (35.5 and 39.0, respectively) - PCV20 elicited robust response 1 month when coadministered with mRNA-CV for all 20 pneumococcal serotypes. - Similar response to PCV20-alone. - Observed GMFR: 2.5 – 24.5 coadministered and 2.3-30.6 PCV20 alone. - OPA ≥4-fold rise: 24.6-67.9% coadministered vs 22.7% - 71.0% alone. - Post hoc analysis (model-based OPA GMR, lower bound GMR >0.5) = 2-fold non-inferiority margin would have been met for all 20 serotypes between groups.	Coadministration of PCV20 and mRNA-CV dose not result in clinically significant interference of the immune response to either vaccine.

continued next page

Outcomes	Ref	Participants / study design	Results	Findings
PCV21				
Safety and immunogenicity, with/out chronic medical conditions, PCV21 vs PCV20	46	phase 3 V116/ PCV21 (STRIDE-3), 11 countries or territories. Stratified by age - cohort 1 50-64, 65-74, 75-84, ≥85y) randomised 1:1 for PCV21 or PCV20 (n=1179 vs 1177) - cohort 2 ages 18-49 years 2:1 PCV21 vs PCV20 (n=200 vs 100) - immunobridging for 21 serotypes for adults aged 18-49 to 50-64 years (OPA GMT lower bound 95% CI > 0.5 for non-inferiority) Prespecified conditions did not include immunocompromise (chronic organ diseases, diabetes, smoking, alcohol disorder) (NCT05425732, MSD)	cohort 1 - PCV21 met non-inferiority to PCV20 for all 10 shared serotypes (p<0.0001 for each serotype) - Superiority was met for 10/11 unique serotypes in PCV21 - Lower bound 95% CI ≥2.0 for all except serotype 15 C (1.77) - Immune response similar to PCV20 for 15B serotype (cross-reaction from 15C) - Serotype 6C did not meet acceptable response; similar proportion of individuals with ≥4-fold OPA Ab rise to 6C before and after vaccination was similar between PCV21 and PCV20 groups. (6A cross-protects against 6C). cohort 2 (immunobridging) - Met the predefined criterion for all 21 serotypes in PCV21 for those aged 18-49 vs age 50-64y. (lower bound 95% CI OPA GMR >0.5).	PCV21 is non-inferior to PCV20 for serotypes in common and superior for unique serotypes, except 6C. Robust responses were seen against 6C but non-inferiority was not met.
≥65y, Japan	47	phase 3 V116/PCV21 (STRIDE-9), 450 pneumococcal vaccine-naïve ≥65y, Japanese adults. Randomised 1:1 PCV21 or 23PPV (NCT05633992, MSD)	- Immunogenicity endpoint – OPA GMT day 30 - PCV21 was non inferior to 23PPV for 12 common serotypes and for cross-reactive serotypes 15B. - PCV21 was superior for unique 15C - GMT for PCV21 was numerically higher than 23PPV for remaining 8 unique serotypes and cross-reactive serotype 6C	PCV21 has potential to broaden serotype protection against pneumococcal disease in older adults in Japan.

continued next page

Outcomes	Ref	Participants / study design	Results	Findings	
higher valency vaccines					
PCV24 (Astellas/Affinivax)	12	Phase 1 / 2 RCT, first in human dose finding – adults 18-64 and 65-85 years. Randomised PCV24 (designated ASP3372, since renamed AFX3772, Astellas Pharma/Affinivax) or PCV13 Immunogenicity measures day 30 post vaccination. Group 1 (phase 1): Pneumo-naïve, age 18-49, n=40 per treatment arm (dose 2µg, 5µg or PCV13) Group 2 (phase 2): pneumo-naïve age 65-85y 132/treatment arm (dose 2µg, 5µg or PCV13) Group 3 (phase 2): previously vaccinated PCV13, aged 65-85y, n=99, given 23PPV.	Group 1 (age 18-84) - OPA titres increased for all 24 serotypes day 1-30. - OPA GMT comparable for shared PCV13 serotypes and greater for PCV24-only serotypes. - IgG responses were robust and comparable for shared PCV13 types; statistically higher against serotype 3 for PCV24 (2 and 5µg) and higher for unique serotypes. Group 2 (age 65+, naïve) - OPA GMT comparable for most shared serotypes and significantly greater for unique serotypes. - OPA GMTs were significantly greater for serotype 3 than PCV13. Group 3 (age 65+ prior PCV13, given 23PPV) - Baseline OPA GMT were significantly lower for PCV13-naïve than PCV13-experienced. - Day 30 OPA GMT were greater for PCV13-naïve PCV24 recipients than PCV13-23PPV recipients. - Day 30 OPA GMT following PCV24 were significantly greater than 23PPV for most serotypes including 10/11 serotypes not found in PCV13.	These groups had preexisting antibody to sp1500+sp0785 fusion protein. Specific IgG increased for all PCV24 participants - aged 18-64 years GMFR increased by 5-6-fold - ages 65-85 GMFR increased by 9-13-fold. - No increases in PCV13 only groups. Th17 cell induction - Group 1: day 30 5µg group significantly more fusion protein specific Th17 and higher IL-17 production than PCV13 group. No difference for lower doses. - Group 2: no significant difference at day 7 but at day 30 fusion-protein specific Th17, IL-17 and IL-22 were significantly greater in 5µg group vs PCV13 but not for lower doses.	Robust immunogenicity was shown for this PCV24 candidate with functional antibody response comparable or higher than serotypes shared with PCV13 or 23PPV. Further larger studies are required since baseline levels varied in these groups. No clinical significance has been determined yet for fusion-protein-specific antibody and Th17 responses.

continued next page

Review of Evidence, 2026: Pneumococcal – adults and special groups

Outcomes	Ref	Participants / study design	Results	Findings
PCV24 (Vaxcyte), older adults	13	Phase 2 RCT dose finding VAX-24 vs PCV20 (Prevenar 20) 200 adults aged ≥65 years. (NCT05297578.) Exploratory immunogenicity comparisons.	- All study vaccines induced a robust OPA response. 2.2µg doses elicited similar GMTs to PCV20 for all 20 shared serotypes. - GMT point estimates were higher for VAX-24 for 16/20 shared serotypes and OPA GMT were significantly higher for non-PCV20 serotypes. Dose response effect was seen. - Likewise, similar proportions of participants had ≥4-fold increase in OPA titres at 1 month for shared serotypes. And higher for VAX-24 only serotypes.	VAX-24 elicited a robust immune response in older adults against 24 serotypes. At a dose of 2.2 µg met non-inferiority criteria compared with PCV20.
PCV31 (Vaxcyte), over 50 years.	14	phase 1-2 dose finding RCT, pneumococcal naïve adults aged ≥50y given PCV31 (VAX-31; Vaxcyte) or PCV20. Safety followed for 6 months. Total 1015 randomised to 3 dose groups plus PCV20 group; mean age 59.8 SD 6.7	- Immunogenicity results were similar across age subgroups with lower responses with increasing age. - OPA GMT for high doses were on average approx. 23% higher than those of PCV20 across 20 shared serotypes, mid dose with similar polysaccharide content to PCV20 was only 8% higher overall and numerically lower for 6 serotypes (including ST3). - High dose elicited highest response against ST3.	VAX-31 elicited a robust immune response across all 31 serotypes. A mid and high doses, it met non-inferiority criteria against shared PCV20 serotypes. Low dose was non-inferior for 18/20 serotypes. For 11 additional serotypes, VAX-31 met predetermined OPA superiority for all doses.

Abbreviations: GMT – geometric mean titre; GMFR – geometric mean titre fold rise; GMR – geometric titre ratio; LLOQ – lower level of quantification; OPA – opsonophagocytic activity; PCV – pneumococcal vaccine (13, 20 or 21 valent); 23PPV – 23-valent polysaccharide vaccine; ST3 – serotype 3.

Table 14: Vaccine effectiveness and potential impact

Outcomes	Ref	Participants / study design	Results	Findings	
PCV20					
Real-world effectiveness	51	Retrospective Medicare databased cohort study, adults ≥65y, US. July 2022-June 2024, Excluded if had PCV20 prior to study, follow-up excluded if received 23PPV within 2 yrs, PCV13 within 5 years or PCV15 prior to study date. (Pfizer funded) Unable to report on serotype specific vaccine effectiveness as serotypes were not available. Residual confounding for health-care use was likely in younger, lower risk groups but not in immunocompromised or older adults.	16.5 million individuals included in study out of 56.9 million in database aged >65 y on 28 Jan 2022 (rounded numbers): • 2.01 million PCV20 vaccinated and 16.0 million unvaccinated. • Of included, 459,708 (2.8%) contributed to PCV20 follow-up only, 14.5 million (87.8%) contributed to unvaccinated follow-up only and 1.55 million (9.4%) contributed to both. Adjusted vaccine effectiveness: • IPD: 25.6% (95% CI 17.4–33.0) • All pneumococcal pneumonia: 23.3% (16.3–29.8) • All-cause pneumonia: 15.2% (14.5–15.9) • LRTI: 7.4% (6.9–7.8)	During 1 st year follow-up, adjusted absolute rate reduction associated with PCV20: overall cases averted per 100,000 • IPD: 12.0 (95% CI 8.0–16.0) • All pneumococcal pneumonia: 12.8 (8.2–17.4) • All-cause pneumonia: 758.0 (664.2–851.7) • LRTI: 636.1 (503.8–768.4) This study included subgroups not included in licensure trials such as immunocompromised and adults aged over 85 years. For immunocompromised groups: • IPD: aVE 25.0% (13.0–35.3) cases averted: 30 (18.9-45.1) • All pneumococcal pneumonia: aVE 23.6% (12.6–33.2) cases averted: 27.7 (13.5–42.2) • All-cause pneumonia: aVE 16.5% (15.5–17.6) cases averted: 1864 (1537–2191) • LRTI: aVE 9.0% (8.1–9.8) cases averted: 1519.9 (1112.5–1927.3)	PCV20 was associated with a lower risk of pneumococcal infection and pneumonias among adults age ≥65 years in the US. Within a year, substantial public health impact was evident due to reductions in all-cause pneumonia and LRTI.
				Absolute rate reduction estimates in groups with immunocompromise or chronic medical conditions were 1.3 to 2.4 times higher than lower risk adults.	

continued next page

Outcomes	Ref	Participants / study design	Results	Findings
Real-world effectiveness, IBD	52	Retrospective analysis, US. Main outcome, bacterial pneumonia from 30d post vaccination. Crohn disease or ulcerative colitis with ≥ 1 IBD therapy. Controls, unvaccinated.	- After propensity score matching (for demographics and pneumonia risk factors), 12,796 included in analysis. - Mean age 55.8 ± 17.1 years controls and 55.2 ± 16.3 vaccinated. - Common comorbidities included hypertension, asthma and diabetes; also included chronic kidney disease, rheumatoid arthritis and HIV infection. Most common IBD therapies: prednisone (69%), methylprednisolone (52%), budesonide (34%), adalimumab (15%), infliximab (14%) and azathioprine (13%) (several other meds used) PCV20 group vs control, relative risk (RR) - Pneumonia – 0.54 (0.47-0.63) - Acute respiratory failure – 0.42 (0.35-0.50) - Hospital admission – 0.57 (0.53-0.62) - ICU admission – 0.47 (0.40-0.57) - All-cause mortality – 0.32 (0.25-0.40) - Meningitis (0.2% both groups) – not lower risk – 1.00 (0.42-2.40) - Pneumonia by age: 18-39 y (0.50; 0.29-0.84); 40-64 (0.55, 0.43-0.70)	Patients with IBD who received PCV20 had lower risk of pneumonia and improved clinical outcomes. It is effective in individuals on a range of immunosuppressive therapies and immunocompromising conditions. Study did not control for prior pneumococcal vaccinations, other concomitant vaccinations, socioeconomic status or healthy user bias. Authors did not believe that vaccination alone accounted for marked reduction in outcomes but is a low-risk intervention used as part of a care bundle.

continued next page

Review of Evidence, 2026: Pneumococcal – adults and special groups

Outcomes	Ref	Participants / study design	Results	Findings
Vaccination in age-care, 23PPV or PCV20, vs all over 65 years.	53	Observational surveillance, 2022-23 England. IPD and care home data ≥65y Rate of IPD cases 18.0 per 100,000 ages 65-79 and 37.5 per 100,000 in those aged 80+ (with double CFR 34%). Overall rate 8.13/100K Limitation VE of PCV20 has not been confirmed. (estimate based on PCV13) No PCV data against death. combine VE – VE against IPD and VE against 30-day mortality (18% for 23PPV). For PCV conducted sensitivity analyses assuming VE against death of 18%, 20%, 25% and 30%.	- Adults aged 65–69 years, accounted for only 2.9% of new care home residents. Estimated 121,587 new care-home residents annually. 2,574 IPD cases / 10.63 million adults aged ≥65 (603,109 were aged 65 y) 69.4% were due to 23PPV-serotypes (1787) and 60.8% (1566) due to PCV20-serotypes - Assumed 4.4 times increase in risk of IPD in care homes – 492 cases 23PPV-type IPD over lifetime of new residents in 2022/23 Assuming VE 36% IPD and 18% death for 23PPV: 23PPV offered to all the 65 y/os could have prevented 163/452 (36%) of cases and 31/66 (47%) of 23PPV-deaths over 5 years. - NNV 3700 to prevent 1 case and 19,455 to prevent 1 death. Vaccinate only new care home residents (121,587 people) with 23PPV - Prevent 177 cases (35%) of 492 expected lifetime cases and 111 (48%) of 233 deaths expected without vaccination - NNV 687 /case and 1095 / death Vaccinate all adults aged 65 with PCV20 (assuming 75% VE against PCV20-IPD and 18% death) - Prevent 303 / 404 cases (75%) and 43/54 deaths (80%) - NNV 1990 /case and 14026 / death Vaccinated only new care home resident with PCV20: - Prevent 317 / 422 cases (75%) and 157/197 deaths (80%) - NNV 384 and 774	Pneumococcal vaccination of new care-home residents could prevent more IPD cases and more deaths in care homes for older adults than provided by current programme in the general population (eligible for PCV20 from age 65 years). This would require 20% more doses. PCV20 likely to have a greater impact than 23PPV.

Abbreviations: aVE – adjusted vaccine effectiveness; CFR – case-fatality rate; IPD – invasive pneumococcal disease; NNV – number need to vaccinate; PCV – pneumococcal vaccine (13, 20 or 21 valent); 23PPV – 23-valent polysaccharide vaccine; VE – vaccine efficacy;

Methodology for literature searches

Published literature in online medical databases, with additional references added as review progressed using PubMed and Google Scholar. Most searches were conducted between January 2026 – May 2026. Additional literature was included in July 2026. Systematic reviews were included, and where necessary for clarification, cited papers in these were reviewed for further details. Grey literature, letters to journal editors, conference proceedings and reports were also included. Total library 347 references (includes over 50 references related to infant vaccination with PCV20 for a separate review).

Concepts

Pneumococcal disease	Vaccine	adult	immunisation	PCV20	PCV	Immunogenicity	Safety
IPD	vaccin*		immuni?ation	20-valent	polysaccharide	antibody response	adverse events
Pneumococc?	safety		immunity	21-valent	valent	OPA	
Streptococcus pneumoniae	efficacy				conjugate*	IgG	
pneumonia	immunogenicity						
	effectiveness						

Search details

2019 – 2026 (first search conducted 12 Jan 2026, additional search 29 April 2026)

Medline OVID

#	Searches	Results	Type	Runtime	Actions	Annotations
1	*Pneumococcal Vaccines/ and *Vaccines, Conjugate/	542	Advanced	0.16	Display Results More ▾	
2	limit 1 to (english language and yr=2019 -Current*)	128	Advanced	0.44	Display Results More ▾	
3	*Adult/	502	Advanced	0.02	Display Results More ▾	
4	2 and 3	0	Advanced	0.04	Save More ▾	
5	*Pneumococcal Vaccines/	6103	Advanced	0.00	Display Results More ▾	
6	3 and 5	0	Advanced	0.01	Save More ▾	
7	limit 5 to (english language and yr=2019 -Current*)	1345	Advanced	0.21	Display Results More ▾	
8	3 and 7	0	Advanced	0.01	Save More ▾	
9	adult_m_dtl.	232814	Advanced	0.02	Display Results More ▾	
10	7 and 9	65	Advanced	0.03	Display Results More ▾	

#10 – manually selected 39 related to PCV20, excluded cost-effectiveness studies

11	PCV20.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	337
12	limit 11 to (english language and humans and yr=2019 -Current*)	231
13	9 and 12	22

Selected a further 2

14	PCV21.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	62
15	limit 14 to (english language and humans and yr=2019 -Current*)	44

Manually selected 33, removed 14 duplicates. Included some cost-effectiveness studies if they seemed closely relevant to topics of interest.

Scopus

Advanced query 

Search within Article title, Abstract, Keywords 	Search documents * pcv20 20 valent pneumococcal conjugate vaccine 
--	--

AND 

Search within Article title, Abstract, Keywords 	Search documents adult 
--	---

Limit – English, 2019-2026 = 131 articles, manually selected 39, removed 8 duplicates

As above for PCV21 / adult; limit 2023 [none before, 2019] - 2026 = 50 articles, manually selected 15, removed 9 duplicates

Additional literature search – pneumococcal disease in special groups (to July 2026)

*Pneumococcal Infections/ or pneumococcal disease.mp. AND high-risk.m_titl. – 72 found, selected 23

*Pneumococcal Infections/ or pneumococcal disease.mp. AND Cardiovascular Diseases/ = 14, selected 9

*Pneumococcal Infections/ or pneumococcal disease.mp. AND *Comorbidity/ = 7, selected 3

*Pneumococcal Vaccines/ and adult.mp. or Adult/ and *Cardiovascular Diseases/ = 7, selected 4

*Pneumococcal Vaccines/ and adult.mp. or Adult/ and immunocompetent.mp. = 32, selected 4

*Pneumococcal Vaccines/ and chronic liver disease.mp. = 19, selected

In total, manually selected 28 after removing 4 duplicates

Pneumonia, Bacterial/ or Pneumonia/ or Pneumonia, Pneumococcal/ or Community-Acquired Pneumonia/ and chronic liver disease.mp. = 36, selected 19

References

1. Ahl J, Littorin N, Forsgren A, et al. High incidence of septic shock caused by *Streptococcus pneumoniae* serotype 3--a retrospective epidemiological study. BMC Infect Dis. 2013;13:492. doi: 10.1186/1471-2334-13-492
2. Nowlan M, The Immunisation Advisory Centre. Antigen literature review for the New Zealand National Immunisation Schedule, 2016: Pneumococcal disease – in high-risk groups. University of Auckland; 2016 1 November 2016
<https://immune.org.nz/publications/antigen-literature-review-for-the-new-zealand-national-immunisation-schedule-2016-pneumococcal-disease-in-high-risk-groups>
3. Torres A, Peetermans WE, Viegi G, et al. Risk factors for community-acquired pneumonia in adults in Europe: a literature review. Thorax. 2013;68(11):1057–65. doi: 10.1136/thoraxjnl-2013-204282
4. Campling J, Vyse A, Liu HH, et al. A review of evidence for pneumococcal vaccination in adults at increased risk of pneumococcal disease: risk group definitions and optimization of vaccination coverage in the United Kingdom. Expert Rev Vaccines. 2023;22(1):785–800. doi: 10.1080/14760584.2023.2256394

5. Pelton SI, Shea KM, Weycker D, et al. Rethinking risk for pneumococcal disease in adults: the role of risk stacking. *Open Forum Infect Dis.* 2015;2(1):ofv020. doi: 10.1093/ofid/ofv020
6. Shea KM, Edelsberg J, Weycker D, et al. Rates of pneumococcal disease in adults with chronic medical conditions. *Open Forum Infect Dis.* 2014;1(1):ofu024. doi: 10.1093/ofid/ofu024
7. Anglemeyer A, McNeill A, DuBray K, et al. Invasive pneumococcal disease: Concerning trends in serotype 19A notifications in New Zealand. *Clin Infect Dis.* 2022;74(10):1859–61. doi: 10.1093/cid/ciab766
8. Institute for Environmental and Scientific Research. Invasive pneumococcal disease annual report 2024. Porirua, New Zealand; 2025 May 2025 <https://www.phfscience.nz/digital-library/invasive-pneumococcal-disease-annual-report-2024/>
9. PHF Science. Invasive pneumococcal disease annual report 2025. Porirua: New Zealand Institute for Public Health and Forensic Science 2026 30 July 2026. Report No.: FW26018 <https://www.phfscience.nz/digital-library/invasive-pneumococcal-disease-annual-report-2025/>
10. SK bioscience-Sanofi's 21-valent pneumococcal conjugate vaccine candidate for phase 3 studies IND amendment review completed by U.S. FDA [press release]. Republic of Korea: SK bioscience, 17 Jan 2025 2025. 'Available from': https://www.skbioscience.com/en/news/news_01_01?mode=2&id=288&page=5
11. Malley R, Lu YJ, Sebastian S, et al. Multiple antigen presenting system (MAPS): state of the art and potential applications. *Expert Rev Vaccines.* 2024;23(1):196–204. doi: 10.1080/14760584.2023.2299384
12. Chichili GR, Smulders R, Santos V, et al. Phase 1/2 study of a novel 24-valent pneumococcal vaccine in healthy adults aged 18 to 64 years and in older adults aged 65 to 85 years. *Vaccine.* 2022;40(31):4190–8. doi: 10.1016/j.vaccine.2022.05.079
13. Wassil J, Sisti M, Fairman J, et al. A phase 2, randomized, blinded, dose-finding, controlled clinical trial to evaluate the safety, tolerability, and immunogenicity of a 24-valent pneumococcal conjugate vaccine (VAX-24) in healthy adults 65 years and older. *Vaccine.* 2024;42(25):126124. doi: 10.1016/j.vaccine.2024.07.025
14. Wassil J, Fairman J, Fierro CA, et al. Safety, tolerability, and immunogenicity of a 31-valent pneumococcal conjugate vaccine (VAX-31) in healthy adults aged 50 years and older from the USA: a phase 1/2, double-blinded, active-controlled, parallel-group, dose-finding randomised clinical trial. *Lancet Infect Dis.* 2026. doi: 10.1016/S1473-3099(26)00059-9
15. Kobayashi M, Farrar JL, Gierke R, et al. Use of 15-valent pneumococcal conjugate vaccine and 20-valent pneumococcal conjugate vaccine among U.S. adults: Updated recommendations of the Advisory Committee on Immunization Practices - United States, 2022. *MMWR - Morbidity & Mortality Weekly Report.* 2022;71(4):109–17. doi: 10.15585/mmwr.mm7104a1
16. Kobayashi M, Pilishvili T, Farrar JL, et al. Pneumococcal vaccine for adults aged ≥19 Years: Recommendations of the Advisory Committee on Immunization Practices, United States, 2023. *MMWR Recomm Rep.* 2023;72(3):1–39. doi: 10.15585/mmwr.rr7203a1
17. Kobayashi M, Leidner AJ, Gierke R, et al. Use of 21-valent pneumococcal conjugate vaccine among U.S. adults: Recommendations of the Advisory Committee on Immunization Practices - United States, 2024. *MMWR - Morbidity & Mortality Weekly Report.* 2024;73(36):793–8. doi: 10.15585/mmwr.mm7336a3
18. Kobayashi M, Leidner AJ, Gierke R, et al. Expanded recommendations for use of pneumococcal conjugate vaccines among adults aged ≥50 Years: Recommendations of the Advisory Committee on Immunization Practices - United States, 2024. *MMWR - Morbidity & Mortality Weekly Report.* 2025;74(1):1–8. doi: 10.15585/mmwr.mm7401a1
19. Sotgiu G, Puci M, Bartoletti M, et al. Recommendations on PCV20 vaccine in adults and at-risk populations. *Eur Respir Rev.* 2025;34(178). doi: 10.1183/16000617.0016-2025

20. Song JY, Kwon KT, Park WB, et al. Pneumococcal vaccination in Korean adults: 2025 recommendations by the Korean Society of Infectious Diseases. *Infect Chemother.* 2025;57(3):335–9. doi: 10.3947/ic.2025.0042
21. Wierzbowski A, Pless R, Hildebrand KJ. Summary of the NACI statement on public health level recommendations on the use of pneumococcal vaccines in adults, including the use of 15-valent and 20-valent conjugate vaccines. *Can Commun Dis Rep.* 2023;49(23):81–6. doi: 10.14745/ccdr.v49i23a08
22. Ditzel K, Giardina F, Ten Oever J, et al. Risk conditions for invasive pneumococcal disease in adults: a systematic review and meta-analysis. *eClinicalMedicine.* 2025;89:103522. doi: 10.1016/j.eclinm.2025.103522
23. Said MA, Johnson HL, Nonyane BA, et al. Estimating the burden of pneumococcal pneumonia among adults: a systematic review and meta-analysis of diagnostic techniques. *PLoS ONE.* 2013;8(4):e60273. doi: 10.1371/journal.pone.0060273
24. Shen L, Jhund PS, Anand IS, et al. Incidence and outcomes of pneumonia in patients with heart failure. *J Am Coll Cardiol.* 2021;77(16):1961–73. doi: 10.1016/j.jacc.2021.03.001
25. Wyplosz B, Fernandes J, Goussiaume G, et al. Adults at risk of pneumococcal disease in France. *Infect Dis Now.* 2021;51(8):661–6. doi: 10.1016/j.idnow.2021.07.006
26. Campling J, Jones D, Chalmers J, et al. Clinical and financial burden of hospitalised community-acquired pneumonia in patients with selected underlying comorbidities in England. *BMJ Open Respir Res.* 2020;7(1):10. doi: 10.1136/bmjresp-2020-000703
27. Bellinghausen C, Pletz MW, Rupp J, et al. Chronic liver disease negatively affects outcome in hospitalised patients with community-acquired pneumonia. *Gut.* 2021;70(1):221–2. doi: 10.1136/gutjnl-2020-320876
28. Crequer N, McCall C, Swanson A, et al. Clustering of community-acquired pneumonia in hospitalised adults in the Christchurch Region: association with socio-economic deprivation. *N Z Med J.* 2025;138(1617):85–99. doi: 10.26635/6965.6905
29. Feldman C, Normark S, Henriques-Normark B, et al. Pathogenesis and prevention of risk of cardiovascular events in patients with pneumococcal community-acquired pneumonia. *J Intern Med.* 2019;285(6):635–52. doi: 10.1111/joim.12875
30. Eurich DT, Marrie TJ, Minhas-Sandhu JK, et al. Risk of heart failure after community acquired pneumonia: prospective controlled study with 10 years of follow-up. *BMJ.* 2017;356:j413. doi: 10.1136/bmj.j413
31. Marra F, Zhang A, Gillman E, et al. The protective effect of pneumococcal vaccination on cardiovascular disease in adults: A systematic review and meta-analysis. *Int J Infect Dis.* 2020;99:204–13. doi: 10.1016/j.ijid.2020.07.038
32. Narii N, Kitamura T, Komukai S, et al. Association of pneumococcal vaccination with cardiovascular diseases in older adults: The vaccine effectiveness, networking, and universal safety (VENUS) study. *Vaccine.* 2023;41(13):2307–13. doi: 10.1016/j.vaccine.2023.02.077
33. Figueira Goncalves JM, Garcia Bello MA, Bethencourt Martin N, et al. Impact of 13-valent pneumococcal conjugate polysaccharide vaccination on severe exacerbations in patients with chronic obstructive pulmonary disease and established cardiovascular disease. *Eur J Intern Med.* 2019;63:e14–e6. doi: 10.1016/j.ejim.2019.03.010
34. Flem E, Mouawad C, Palmu AA, et al. Indirect protection in adults ≥ 18 years of age from pediatric pneumococcal vaccination: a review. *Expert Rev Vaccines.* 2024;23(1):997–1010. doi: 10.1080/14760584.2024.2416229
35. Weinberger DM, Pitzer VE, Regev-Yochay G, et al. Association between the decline in pneumococcal disease in unimmunized adults and vaccine-derived protection against colonization in toddlers and preschool-aged children. *Am J Epidemiol.* 2018;188(1):160–8. doi: 10.1093/aje/kwy219

36. van der Linden M, Imohl M, Perniciaro S. Limited indirect effects of an infant pneumococcal vaccination program in an aging population. *PLoS ONE*. 2019;14(8):e0220453. doi: 10.1371/journal.pone.0220453
37. El Safadi D, Hitchins L, Howard A, et al. Pneumococcal carriage and disease in adults in England, 2011-2019: The importance of adults as a reservoir for pneumococcus in communities. *J Infect Dis*. 2025;231(1):e17–e27. doi: 10.1093/infdis/jiae351
38. Essink B, Sabharwal C, Cannon K, et al. Pivotal phase 3 randomized clinical trial of the safety, tolerability, and immunogenicity of 20-valent pneumococcal conjugate vaccine in adults aged ≥ 18 years. *Clin Infect Dis*. 2022;75(3):390–8. doi: 10.1093/cid/ciab990
39. Hurley D, Griffin C, Young M, et al. Safety, tolerability, and immunogenicity of a 20-valent pneumococcal conjugate vaccine (PCV20) in adults 60 to 64 years of age. *Clin Infect Dis*. 2021;73(7):e1489–e97. doi: 10.1093/cid/ciaa1045
40. Klein NP, Peyrani P, Yacisin K, et al. A phase 3, randomized, double-blind study to evaluate the immunogenicity and safety of 3 lots of 20-valent pneumococcal conjugate vaccine in pneumococcal vaccine-naïve adults 18 through 49 years of age. *Vaccine*. 2021;39(38):5428–35. doi: 10.1016/j.vaccine.2021.07.004
41. Giriappa B, Choraria N, Ponce P, et al. Immunogenicity and safety of 20-valent pneumococcal conjugate vaccine in pneumococcal vaccine-naïve adults ≥ 18 years of age in India: A phase 3 single-arm trial. *Hum Vaccin Immunother*. 2026;22(1):2605847. doi: 10.1080/21645515.2025.2605847
42. Haranaka M, Young Song J, Huang KC, et al. A phase 3 randomized trial of the safety and immunogenicity of 20-valent pneumococcal conjugate vaccine in adults ≥ 60 years of age in Japan, South Korea, and Taiwan. *Vaccine*. 2024;42(5):1071–7. doi: 10.1016/j.vaccine.2024.01.004
43. Cannon K, Elder C, Young M, et al. A trial to evaluate the safety and immunogenicity of a 20-valent pneumococcal conjugate vaccine in populations of adults ≥ 65 years of age with different prior pneumococcal vaccination. *Vaccine*. 2021;39(51):7494–502. doi: 10.1016/j.vaccine.2021.10.032
44. Fitz-Patrick D, Young M, Yacisin K, et al. Randomized trial to evaluate the safety, tolerability, and immunogenicity of a booster (third dose) of BNT162b2 COVID-19 vaccine coadministered with 20-valent pneumococcal conjugate vaccine in adults ≥ 65 years old. *Vaccine*. 2023;41(28):4190–8. doi: 10.1016/j.vaccine.2023.05.002
45. Oliveira M, Marquez P, Ennulat C, et al. Post-licensure safety surveillance of 20-valent pneumococcal conjugate vaccine (PCV20) among US adults in the vaccine adverse event reporting system (VAERS). *Drug Saf*. 2025;48(3):279–86. doi: 10.1007/s40264-024-01498-2
46. Platt HL, Bruno C, Buntinx E, et al. Safety, tolerability, and immunogenicity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3): a randomised, double-blind, active comparator controlled, international phase 3 trial. *The Lancet Infectious Diseases*. 2024;24(10):1141–50. doi: 10.1016/S1473-3099(24)00344-X
47. Kishino H, Inoue S, Matsuoka O, et al. A phase 3 randomized trial (STRIDE-9) to evaluate the safety, tolerability, and immunogenicity of V116, a population-specific pneumococcal conjugate vaccine, in pneumococcal vaccine-naïve Japanese adults ≥ 65 years of age. *Vaccine*. 2025;62:127456. doi: 10.1016/j.vaccine.2025.127456
48. World Health Organization. Recommendations to assure the quality, safety and efficacy of pneumococcal conjugate vaccines, Annex 3, TRS No 977. 2013 19 October 2013 <https://www.who.int/publications/m/item/pneumococcal-conjugate-vaccines-annex3-trs-977>
49. Andrews NJ, Waight PA, Burbidge P, et al. Serotype-specific effectiveness and correlates of protection for the 13-valent pneumococcal conjugate vaccine: a postlicensure indirect cohort study. *Lancet Infect Dis*. 2014;14(9):839–46. doi: 10.1016/S1473-3099(14)70822-9

50. Sabharwal C, Sundaraiyer V, Peng Y, et al. Immunogenicity of a 20-valent pneumococcal conjugate vaccine in adults 18 to 64 years old with medical conditions and other factors that increase risk of pneumococcal disease. *Hum Vaccin Immunother.* 2022;18(6):2126253. doi: 10.1080/21645515.2022.2126253
51. Miles AC, Vojcic J, Peyrani P, et al. Real-world effectiveness of 20-valent pneumococcal conjugate vaccine against all-cause outcomes among Medicare beneficiaries aged 65 years and older in the USA: a retrospective cohort study. *Lancet Infect Dis.* 2026. doi: 10.1016/S1473-3099(26)00115-5
52. Mohamed MFH, Gupta SR, Beran A, et al. Pneumococcal vaccine is associated with improved outcomes in inflammatory bowel disease: Insights from a propensity-matched study in the United States. *Dig Dis Sci.* 2026. doi: 10.1007/s10620-025-09653-0
53. Abdullahi F, Patel T, Stoker K, et al. Pneumococcal vaccination for new residents entering older adult care homes in England: national observational surveillance study. *Lancet Healthy Longev.* 2025;6(6):100726. doi: 10.1016/j.lanhl.2025.100726