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REVIEW

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Global distribution and characteristics of pneumococcal serotypes in adults

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ABSTRACT

The introduction of pneumococcal conjugate vaccines (PCVs) into pediatric national immunization programs (NIP) has significantly reduced invasive pneumococcal diseases and pneumococcal pneumonia caused by PCV serotypes in adults due to herd immunity. However, diseases caused by PCV13 serotypes persist, mainly serotype 3, known for its severity. With the reduction in PCV13 serotypes, diseases caused by non-PCV13 serotypes increased. Residual and emerging serotypes vary regionally; serotype 8 in Europe and South Africa, and serotype 4 in the US and Canada. PCV20 and PCV21 were recently developed, which can prevent residual and emerging pneumococcal diseases where herd immunity is well-established. In countries that have not introduced PCV into pediatric NIP, the pneumococcal disease burden due to PCV serotypes is still marked. Given that serotype distribution varies by region and evolves over time, this review aimed to discuss serotype distribution and disease severity in adults across countries to support future pneumococcal vaccine strategies.

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Introduction

Streptococcus pneumoniae is one of the major pathogens of human diseases. It causes both invasive pneumococcal disease (IPD), such as bacteremia and meningitis, and non-invasive pneumococcal disease (NIPD), such as non-bacteremic pneumonia.[1] The global pneumococcal disease burden is the most marked in children aged <5 years and adults aged ≥65 years.[1–3] IPD is associated with a higher mortality rate than NIPD, while the incidence of non-bacteremic pneumonia exceeds that of IPD in adults.[4,5] Therefore, epidemiological evidence regarding both IPD and non-bacteremic pneumonia is important when considering the disease burden loaded on society.

To combat pneumococcal diseases, vaccines have been developed and implemented worldwide for both children and adults. The capsular polysaccharides of pneumococcus induce virulence, and more than 90 different capsular types have been reported.[6] These serotypes comprise the basis of pneumococcal vaccines. In 1944, the first pneumococcal vaccine containing polysaccharides was developed and tested in a clinical trial.[7] However, with the discovery of penicillin, interest in vaccines to prevent pneumococcal diseases declined. Despite this, penicillin could not prevent deaths caused by pneumococcal diseases, which led to renewed efforts in pneumococcal vaccine development. Eventually, a vaccine containing 23 capsular polysaccharides (a 23-valent pneumococcal polysaccharide vaccine: PPSV23) was developed and introduced in 1983.[7] PPSV23 covers 23 serotypes: serotype 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F. Polysaccharide vaccines primarily induce a B-cell-mediated immune response without T-cell involvement. Therefore, it was found that PPSV23 failed to immunize infants and toddlers, who are also at high risk for pneumococcal disease. To address this issue, pneumococcal conjugate vaccines (PCVs), which elicit a T-cell-dependent immune response, were developed, promoted by the success of *Haemophilus influenzae* type b vaccine.[7] The first PCV, a 7-valent pneumococcal conjugate vaccine (PCV7), including serotype 4, 6 B, 9 V, 14, 18C, 19F, and 23F, was introduced in 2000 and demonstrated high-level effectiveness in children.[8] Subsequently, two kinds of higher-valency PCVs were implemented: a 10-valent pneumococcal conjugate vaccine (PCV10) in 2009, covering PCV7 plus 1, 5, and 7F, and 13-valent pneumococcal conjugate vaccine (PCV13) in 2010, covering PCV10 plus 3, 6A, and 19A. PCV7, PCV10, and PCV13 have been introduced into national immunization program (NIP) for children, which has directly reduced the incidence of vaccine-covered pneumococcal diseases and nasopharyngeal carriage among vaccinated children, and indirectly reduced the incidence of pneumococcal diseases among adults and children who have not received pneumococcal vaccination due to the prevention of transmission, resulting in herd immunity and serotype replacement.[9–11] In contrast, PPSV does not reduce nasopharyngeal carriage of *S. pneumoniae*; therefore, it cannot confer herd immunity. With the reduction of pneumococcal diseases caused by PCV-covered serotypes, pneumococcal diseases caused by residual or emerging serotypes remain and are still major causes of morbidity and mortality,

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especially among older adults. Although PPSV23 has been introduced into NIP for adults in several countries, pneumococcal diseases caused by PPSV23 non-PCV13 serotypes continue to circulate and cause diseases in adults.[12,13] Thus, it may be necessary to reconsider the optimal pneumococcal vaccination strategy for adults, including conjugate vaccines.

Currently, higher-valency PCVs are also available: the 15-valent pneumococcal conjugate vaccine (PCV15) and 20-valent pneumococcal conjugate vaccine (PCV20). PCV15 includes PCV13 plus 22F and 33F, and PCV20 includes PCV15 plus 8, 10A, 11A, 12F, and 15B. PCV15 and PCV20 have replaced PCV13 in pediatric NIP, and have been added to options for adults in several countries.[14–17] Additionally, a 21-valent pneumococcal conjugate vaccine (PCV21) that covers residual serotypes among adults was recently developed and approved by the U.S. Food and Drug Administration and has become an option for adult pneumococcal vaccines in the US.[18] PCV21 targets only adults and includes serotypes 3, 6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F, 9N, 17F, 20, 15A, 15C, 16F, 23A, 23B, 24F, 31, and 35B.

Many studies have evaluated the incidence and distribution of pneumococcal serotypes in children and adults in individual countries or regions. The resulting epidemiological data are essential when selecting pneumococcal serotypes to include in newly developed pneumococcal vaccines and determining the pneumococcal vaccination policy in each country or region. Since the introduction of PCV into pediatric NIP, the incidence of pneumococcal diseases caused by vaccine-covered serotypes in adults has declined due to herd immunity[9,10,19] However, with respect to individual serotypes, persistent and emerging serotypes among adults vary by country. This could be due to country-specific differences in sampling, vaccination strategies, and population dynamics.[20] In addition to serotype distribution, the severity of pneumococcal diseases caused by each serotype is important when deciding on target pneumococcal serotypes for both vaccine development and implementation.

Herein, we discuss the serotype distribution of pneumococcal diseases in adults, including IPD and pneumococcal pneumonia, among both high-income and non-high-income countries based on the World Bank classification,[21] and the severity of diseases caused by individual serotypes, aiming to better understand the epidemiology of pneumococcal diseases in adults and develop and implement future pneumococcal vaccines. As the serotype distribution, surveillance systems, and laboratory methods used to confirm pneumococcal cases differ among countries, we focused on describing and discussing the local epidemiology of adults of each country. Countries were selected based on the availability of post-vaccine introduction data for adults where pneumococcal vaccines have been introduced into pediatric NIP or commonly used for children. For countries where pneumococcal vaccine has not been introduced into pediatric NIP or not commonly used, data covering the period after 2010 for adults were considered. Additionally, countries were selected based on the availability of data detailing the number and proportion of individual pneumococcal serotypes in adults with IPD or pneumococcal pneumonia, facilitating the calculation of vaccine coverage rates if not directly provided. The characteristics of each country, the current use of pneumococcal vaccines for children and adults, and the latest PCV coverage in children are summarized in Supplementary Table S1. Since the data utilized in this article were collected only from previously published studies, an additional ethical review was not necessary.

Pneumococcal serotype distributions in high-income countries among adults

Since the introduction of PCV10 or PCV13 into pediatric NIP of high-income countries, the incidence and proportion of pneumococcal diseases caused by PCV10 or PCV13 serotypes have declined across all age groups due to direct vaccination and indirect herd immunity.[9,10,19] However, serotype replacement has occurred to different extents across countries and geographical areas.[20] Additionally, serotypes emerging since the introduction of PCV differ depending on the country and geographical area.

North America

In the US, PCV7 and PCV13 were introduced into pediatric NIP in 2000 and 2010, respectively, with a 3 + 1 dosing schedule. PPSV23 was introduced for older adults in 1984, and PCV13 has been recommended for use in adults aged 19–64 years who are immunocompromised.[22] One study evaluated the serotype distribution before and after the introduction of PCV7 across all age groups, using *S. pneumoniae* clinical isolates collected from medical centers in the US. After its introduction, IPD cases caused by PCV7 serotypes decreased from 70.1% in 1999–2000 to 1.9% in 2010–2011 of total IPD cases among children aged ≤5 years, and IPD cases caused by PCV7 serotypes decreased from 48.0% in 1999–2000 to 4.7% in 2010–2011 of total IPD cases among other age groups. These results provide evidence of the direct and indirect effects of PCV7.[23] Another study evaluated the IPD incidence among adults aged ≥20 years following the introduction of PCV13 into pediatric NIP. The study was conducted through Active Bacterial Core surveillance (ABCs), an active, laboratory- and population-based system establish by the Centers for Disease Control and Prevention's Emerging Infections Program, using isolates of *S. pneumonia*. It found that, after PCV13 introduction to pediatric NIP, the incidence of IPD in 2013–2014 in adults decreased; IPD cases caused by PCV13 serotypes declined by 57 and 70% in adults aged 19–64 years with risks of pneumococcal diseases and adults aged ≥65 years, respectively. In contrast, IPD cases caused by PPSV23 non-PCV13 serotypes increased in adults aged 19–64 years with risks, but no changes were observed in those aged ≥65 years. IPD cases caused by non-vaccine type (NVT) serotypes did not change on comparing age groups. The decline in 19A contributed to the reduction in IPD cases caused by PCV13.[24] However, since 2014, no further reduction in IPD cases caused by PCV13 serotypes has been noted among adults.[25,26] In 2017–2018, the proportions of IPD caused by PCV13 plus serotype 6C, PPSV23 non PCV13 serotypes, and NVT serotypes were 30, 44, and 27% of total IPD cases, respectively, in adults aged 50–64 years, and 27, 36, and 37% in adults aged ≥65 years (Table 1). Serotype 3 accounted for 60% of IPD cases caused

Table 1. Prevalent serotype and proportion of vaccine-covered serotypes among adults in high-income countries in North America.

County	Type	Year	Population	Prevalent serotypes	Vaccine coverage	Reference
Canada	IPD	2022	Aged 15–49	4 (21.8%), 12F (10.5%), 3 (9.3%), 9 V (7.6%)	PCV13: 51.8% PCV15: 57.0% PCV20: 78.3% PPSV23 non-PCV20: 10.8% NVT*: 10.9%	33
			Aged 50–64	4 (14.9%), 3 (14.6%),9 V (6.6%), 8 (6.5%)	PCV13: 46.8% PCV15:52.6% PCV20: 70.5% PPSV23 non-PCV20: 11.1% NVT*: 18.5%	
			Aged ≥65	3 (13.3%), 22F (9.9%), 9N (6.7%), 4 (5.6%)	PCV13: 32.2% PCV15:44.2% PCV20: 58.5% PPSV23 non-PCV20: 11.0% NVT*: 30.6%	
Canada	Pneumonia	2015	Aged ≥16	3 (2.8%†), 19A (1.5%†), 7F (0.9%†)	PCV13: 6.3%† PPSV23 non-PCV13: 1.7%† NVT: 1.0%†	36
United States	IPD	2017–2018	Aged 50–64	NA	PCV13 plus 6C: 30% PPSV23 non-PCV13: 44% NVT: 27%	27
			Aged ≥65	NA	PCV13 plus 6C: 27% PPSV23 non-PCV13: 36% NVT: 37%	
United States	IPD	2018–2019	Aged 16–64‡	NA	PCV13: 30% PCV15 non-PCV13: 13% PCV20 non-PCV13: 28% PPSV23 non PCV13: 43%	14
			Aged ≥65	NA	PCV13: 27% PCV15 non-PCV13: 15% PCV20 non-PCV13: 27% PPSV23 non PCV13: 35%	
United States	IPD	2018–2020	Aged 16–64‡	NA	PCV20: 58% PCV21: 81%	18,28
			Aged ≥65	NA	PCV20: 54% PCV21: 85%	
United States	Pneumonia	2018–2020	Aged ≥18	3 (1.6%§), 22F (1.1%§), 19A (0.8%§), 35B (0.7%§)	PCV15: 5.8%§ PCV20: 6.7%§ PCV21: 9.3%§	32
			Aged 18–49	3 (1.1%§), 19A (0.9%§), 22F (0.8%§), 35B (0.8%§)	PCV15: 4.0%§ PCV20: 4.7%§ PCV21: 8.0%§	
			Aged 50–64	3 (2.2%§), 22F (1.7%§), 19F (0.9%§), 9N (0.9%§)	PCV15: 7.3%§ PCV20: 8.4%§ PCV21: 11.3%§	
			Aged ≥65	3 (1.4%§), 22F (0.7%§), 23A (0.7%§)	PCV15: 5.8%§ PCV20: 6.9%§ PCV21: 8.7%§	

The country names are arranged in alphabetical order. Some of the data listed were recalculated from the data published in each article. PCV13 serotypes includes serotype 4, 6B, 9 V, 14, 18C, 19F, 23F, 1, 5, 7F, 3, 6A, and 19A; PCV15 serotypes includes PCV13 serotypes plus 22F and 33F serotypes; PCV20 serotypes includes PCV15 serotypes plus 8, 10A, 11A, 12F, and 15B; PCV21 serotypes includes 3, 6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F, 9N, 17F, 20, 15A, 15C, 16F, 23A, 23B, 24F, 31, and 35B; and PPSV23 serotypes includes serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9 V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F.

*NVT here includes all serotypes not included in PCV13, PCV15, PCV20 or PPV23.

†The proportion shown is the percentage of cases in which each serotype was detected among all community-acquired pneumonia cases tested for *Streptococcus pneumoniae*.

‡Adults aged 16–64 years with a risk of pneumococcal disease.

§The proportion shown is the percentage of cases in which each serotype was detected among the total community-acquired pneumonia cases.

Abbreviations: IPD, invasive pneumococcal disease; NA, not applicable; PCV13, a 13-valent pneumococcal conjugate vaccine; PCV15, a 15-valent pneumococcal conjugate vaccine; PCV20, a 20-valent pneumococcal conjugate vaccine; PCV21, a 21-valent pneumococcal conjugate vaccine; PPSV23, a 23-valent pneumococcal polysaccharide vaccine; NVT, non-vaccine type.

by PCV13 serotypes in adults aged ≥65 years, while serotypes 19A and 19F accounted for 10 and 9% of them, respectively.[27] In 2018–2022, the proportions of IPD cases caused by PCV20 and PCV21 serotypes were 58 and 81% of total IPD cases in adults aged 16–64 years with a risk of pneumococcal disease, and 54 and 85% of total IPD cases in adults aged ≥65 years, respectively. The above two study findings were also obtained through the ABCs system and included pneumococcal isolates of IPD cases.[18,28] Several studies utilizing the ABCs data from Western regions of the US reported an increase in IPD cases caused by serotype 4 in adults who were unhoused or showed drug/alcohol abuse.[29,30] A similar trend was observed in the serotype distribution associated with pneumococcal pneumonia; one multicenter prospective study conducted in 2013–2016, which enrolled adults aged ≥18 years hospitalized with radiographically confirmed community-acquired pneumonia (CAP) across 10 US cities, revealed that PCV13 and PCV20 serotypes were associated with 4.6 and 7.8% of total radiologically-confirmed CAP cases in adults, respectively. The most common serotypes were 19A (1.3%), 3 (1.1%), and 22F (1.1%)

of total CAP cases.[31] Another prospective surveillance study evaluated the serotype distribution among adults aged ≥18 years hospitalized with CAP at three hospitals in Tennessee and Georgia between 2018 and 2020. Among the 2,917 adults hospitalized with CAP, 352 tested positive for *S. pneumoniae*, including 51 cases of IPD. Among total 2,917 CAP patients, PCV15, PCV20, and PCV21 serotypes were detected in 5.8, 6.7, and 9.3%, respectively. Among 1,107 CAP patients aged ≥65 years, PCV15, PCV20, and PCV21 serotypes were detected in 5.8, 6.9, and 8.7% of CAP patients, respectively. The most common serotypes were 3 (1.6% of total CAP cases), 22F (1.1%), 19A (0.8%), and 35B (0.7%).[32]

In Canada, PCV7, PCV10, and PCV13 were introduced into the pediatric NIP between 2002 and 2011. The vaccination schedule for PCV13 varies by region, typically following a 2 + 1 dosing schedule, while some areas adopt a 3 + 1 schedule.[33] PPSV23 has been available for use in adults since 1989 and can be administered at physician offices, pharmacies, and public health clinics.[34] One study evaluated the pneumococcal serotype distribution in IPD cases involving adults aged ≥65 years between 2010 and 2016, using national surveillance data conducted by the Public Health Agency of Canada. The national IPD serotype surveillance relies on a passive laboratory-based system, utilizing all invasive isolates collected from provincial and territorial public health laboratories. The study showed that the proportion of IPD cases caused by PCV13 non-PCV7 serotypes declined significantly from 39.5 to 18.6% of the total. In contrast, the proportion of PPSV23 and NVT serotypes increased from 26.3 to 36.2% and from 25.1 to 38.4%, respectively. The decline in serotypes 7F and 19A led to a reduction in IPD cases caused by PCV13 serotypes, and the number of IPD cases caused by serotype 3 remained constant throughout the study period.[35] Another study assessed the serotype distribution in adults aged ≥16 years hospitalized with CAP across five Canadian provinces between 2010 and 2015. This study was part of the Serious Outcomes Surveillance Network of the Canadian Immunization Research Network, which has been actively monitoring CAP and IPD in hospitalized adults since December 2010. The number of CAP cases caused by serotypes 7F and 19A declined over time, but the number of CAP cases caused by serotype 3 increased during the study period.[36] The national IPD surveillance revealed the pneumococcal serotype distribution from 2016 to 2022. The most common serotypes in 2022 were 4, 12F, 3, and 9 V in adults aged 16–49 years, 4, 3, 9 V, and 8 in those aged 50–64 years, and 3, 22F, 9N, and 4 in those aged ≥65 years. PCV13, PCV15, and PCV20 accounted for 51.8, 57.0, and 78.3% in adults aged 16–49 years, 46.8, 52.8, and 70.5% in those aged 50–64 years, and 32.2, 44.2, and 58.5% in those aged ≥65 years, respectively.[33,37] One prospective, active, population-based surveillance of IPD cases in adults aged ≥18 years in the Calgary area found that serotype 4 was becoming more common among unhoused adults in Canada, similar to the US.[38,39] Currently, high-valency PCVs are available in these two countries. In the US, the Advisory Committee on Immunization Practices (ACIP) decided to recommend PCV15 and PCV20 in 2021 for adults aged ≥65 years and those aged 19–64 years with underlying medical conditions[40]; in 2024, ACIP recommended single-dose PCV21 as an option for adults aged ≥18 years for whom PCV is recommended; and PCV15 and PCV20 replaced PCV13 for pediatric NIP.[15,18] In Canada, PCV21 was authorized for use in adults aged ≥18 years in 2024. Since November 2024, PCV20 or PCV21 has been recommended for all adults aged ≥65 years and for those aged 18–64 years with IPD-related risk factors.[41,42] It is necessary to monitor the serotype distribution since the introduction of PCV15, PCV20, and PCV21 can alter this distribution among both children and adults.

The United Kingdom

In European countries, an increase in the incidence of IPD cases caused by non-PCV serotypes has been reported from 2006 to 2019, following the introduction of PCVs in children,[43–49] whereas it has remained stable in the US.[25,50] PCV7 was introduced into pediatric NIP in 2006 with a 2 + 1 dosing schedule and rapidly achieved a coverage rate exceeding 90% in the UK. PCV13 replaced PCV7 in 2010 maintaining the same dosing schedule. In 2020, the UK implemented a reduced 1 + 1 dosing schedule based on the evidence from clinical trial and modeling studies.[51] All adults aged ≥65 years and individuals aged ≥2 years with clinical risks for pneumococcal diseases have been recommended to receive PPSV23 since 2003.[52] National surveillance of IPD, covering the entire population of England and Wales from 2000 to 2010, showed that IPD cases caused by PCV7 serotypes declined in all age groups, following the introduction of PCV7.[53] The national surveillance of IPD also showed that PCV13 introduction in 2010 led to a reduction in IPD cases caused by additional PCV13 serotypes across all age groups within four years post-introduction, which was due to the reduction of serotypes 1, 3, 6A, 7F, and 19A.[54] However, the national surveillance of IPD showed that in 2016–2017, the incidence of IPD cases involving adults aged ≥15 years increased due to the rise in IPD cases caused by non-PCV13 serotypes, especially serotype 8, 12F, and 9N, and PCV13 serotypes, including serotype 3 and 19A. The most common serotype in adults aged ≥65 years in 2016–2017 was serotype 8 (15.7%), followed by 3 (11.5%), and 12F (9.3%) (Table 2).[43] In January 2020, the UK implemented a reduced 1 + 1 PCV13 pediatric NIP program. The national surveillance of IPD reported that the annual number of IPD cases between 2020 and 2023 was lower than that in 2019–2020, possibly due to the restrictions imposed by the COVID-19 pandemic. In 2022–2023, the proportion of IPD cases caused by PCV13 serotypes increased from 19.7% in 2019–2020 to 30.4% in 2022–23 among individuals aged ≥15 years, mainly due to serotype 3. The most common serotypes were 3 (18%), 8 (17%), 22F (8%), and 9N (6%).[51] Regarding the distribution of serotypes responsible for pneumococcal pneumonia, one team conducted a prospective study of pneumococcal pneumonia in adults aged ≥16 years hospitalized with CAP at four university hospitals in the UK.[55,56] In that study, PCV13, PCV15, PCV20, and PPSV23 non-PCV13 serotypes accounted for 31.0, 35.0, 55.6, and 32.3% of adult patients hospitalized with pneumococcal pneumonia in 2018–2022, respectively. The most common serotype was 3 (21.9%), followed by 8 (15.7%).[55] Another study evaluated the serotype distribution in adults aged ≥18 years with CAP or lower

Table 2. Prevalent serotype and proportion of vaccine-covered serotypes among adults in high-income countries in Europe and Israel.

County	Type	Year	Population	Prevalent serotypes	Vaccine coverage	Reference
Austria	IPD	2015–2016	Aged ≥50	3 (28.7%), 19A (7.4%), 22F (6.1%), 8 (5.5%)	PCV10: 16.8% Non-PCV10: 83.2%	[45]
Denmark	IPD	2017–2019	Aged ≥65	8 (23.6%), 3 (9.6%), 22F (9.6%), 9N (7.2%), 12F (6.8%)	PCV10: 3% PCV13: 14% PCV15: 26% PCV20: 63%	[66]
Finland	IPD	2017–2019	Aged ≥65	19A (22.0%), 3 (15.2%), 6C (11.2%), 22F (9.6%)	PCV10: 9% PCV13: 48% PCV15: 58% PCV20: 67%	[66]
France	IPD	2015–2017	Aged ≥65	3 (14.3%), 22F (8.1%), 19A (7.4%), 8 (6.9%)	PCV13 plus 6C: 26.7%	[60]
Germany	IPD	2017–2018	aged ≥60	3 (20.9%), 8 (9.8%), 22F (7.6%), 9N (7.0%), 19A (5.2%)	PCV13: 31.4% PCV15: 41.0% PCV20: 64.0% PPSV23: 73.6%	[62]
Greece	Pneumonia	2017–2019	Adult 19–64	3 (7.1%*)	PCV13: 10%* PCV15: 12%* PCV20: 13%* PPSV23: 14%*	[71]
			Aged ≥65	3 (2.7%*), 19A (1.2%*)	PCV13: 6%* PCV15: 6%* PCV20: 8%* PPSV23: 10%*	
Ireland	IPD	2015–2016	Aged ≥65	19A (9.7%), 3 (8.6%), 12F (8.6%), 8 (8.0%), 33F (8.0%)	PCV13: 23.4% PCV15: 38.9% PCV20: 50.3% PPSV23: 69.7% PCV21: 82.9%	[65]
Israel	IPD	2014–2015	Aged ≥18	12F, 16F, 8, 19A, 3†	PCV7: 7% PCV13: 26% PPSV23 non-PCV13: 40% Non-PPSV23: 34%	[73]
Israel	Pneumonia	2014–2015	aged ≥50	3 (2.4%*), 23F (1.2%*), 19A (0.6%*)	PCV13: 7.6%*	[74]
Italy	IPD	2017	All age	8 (22.1%), 3 (14.4%), 22F (5.9%), 12F (5.7%)	PCV13: 18.3% PPSV23: 48.1%	[46]
Italy	Pneumococcal cases	2010–2016	Aged ≥14	3 (13.3%), 8 (9.4%), 19A (7.3%)	PCV13: 45.0%	[47]
Norway	IPD	2017–2019	Aged ≥65	22F (16.7%), 3 (13.8%), 9N (8.3%), 8 (6.7%)	PCV10: 4% PCV13: 20% PCV15: 40% PCV20: 57%	[66]
Spain	IPD	2019	Aged 18–64	8 (30.3%), 3 (12.2%), 12F (6.3%), 9N (6.3%)	PCV13: 24% PPSV23 non-PCV13: 58% NVT: 18%	[44]
			Aged ≥65	8 (18.7%), 3 (13.2%), 22F (5.3%), 12F (4.6%)	PCV13: 25% PPSV23 non-PCV13: 45% NVT: 30%	
Spain	Pneumonia	2017–2019	Aged ≥18	3 (14.8%), 8 (9.4%), 11A (8.3%)	PCV13: 32% PCV15: 39% PCV20: 65%	[58]
			Aged 18–64	3, 8, 7F, 12F in adults aged 18–49† 3, 8, 11A in adults aged 50–64†	PCV13: 42% PCV15: 48% PCV20: 72% PPSV23: 77%	
			Aged ≥65	3, 11A, 22F, 19A in adults aged 65–74† 3, 19A, 11A, 31, 8 in adults aged ≥ 75†	PCV13: 38% PCV15: 44% PCV20: 61% PPSV23: 64%	
Sweden	IPD	2017–2019	Aged ≥65	3 (15.6%), 19A (9.7%), 8 (8.1%), 15A (5.8%)	PCV10: 4% PCV13: 31% PCV15: 41% PCV20: 59%	[66]
Sweden	Pneumonia	2016–2018	Aged ≥18	3 (5.0%*), 8 (1.9%*), 11A (1.9%*), 19A (1.9%*)	PCV13: 10.8%* PCV15: 12.5%* PCV20: 17.0%*	[68]
			Aged 18–64	3 (5.3%*), 8 (4.1%*), 19A (3.6%*), 11A (2.4%*)	PCV13: 12.4%* PCV15: 13.6%* PCV20: 20.7%*	
			Aged ≥65	3 (4.9%*), 11A (1.7%*), 22F (1.7%*), 5 (1.4%*)	PCV13: 10.0%* PCV15: 12.0%* PCV20: 15.2%*	
United Kingdom	IPD	2016–2017	Aged 5–64	8 (27.2%), 12F (17.9%), 3 (7.0%)	PCV13: 17.1%	[43]
			Aged ≥65	8 (15.7%), 3 (11.5%), 12F (9.3%)	PCV13: 21.6%	

(*Continued*)

Table 2. (Continued).

County	Type	Year	Population	Prevalent serotypes	Vaccine coverage	Reference
United Kingdom	IPD	2022–2023	Aged ≥15	3 (18%), 8 (17%), 22F (8%), 9N (6%)	PCV13: 30.4%	[51]
United Kingdom	Pneumonia	2018–2022	Aged ≥16	3 (21.9%), 8 (15.7%)	PCV13: 31.0% PCV15: 35.0% PCV20: 55.6% PPSV23 non-PCV13: 32.3%	[55]
United Kingdom	Pneumonia and LRTI	2021–2022	Aged ≥18	8 (3.2%§), 7F (1.0%§), 3 (1.0%§)	PCV13 plus 6C: 4.2%§ PCV15 plus 6C: 4.7%§ PCV20 plus 6C/15C: 8.6%§ PPSV23 plus 15C: 9.3%§	[57]
			Aged 18–64	8 (3.1%§), 23F/B (1.0%§), 14 (0.7%§)	PCV13 plus 6C: 3.5%§ PCV15 plus 6C: 3.8%§ PCV20 plus 6C/15C: 6.7%§ PPSV23 plus 15C: 7.5%§	
			Aged ≥65	8 (3.3%§), 7F (1.3%§), 3 (1.3%§)	PCV13 plus 6C: 4.6%§ PCV15 plus 6C: 5.2%§ PCV20 plus 6C/15C: 9.7%§ PPSV23 plus 15C: 10.4%§	

The country names are arranged in alphabetical order. Some of the data listed were recalculated from the data published in each article. PCV7 serotypes includes serotype 4, 6 B, 9 V, 14, 18C, 19F, and 23; PCV10 serotypes includes PCV7 serotypes plus 1, 5, and 7F; PCV13 serotypes includes PCV10 serotypes plus 3, 6A, and 19A; PCV15 serotypes includes PCV13 serotypes plus 22F and 33F serotypes; PCV20 serotypes includes PCV15 serotypes plus 8, 10A, 11A, 12F, and 15B; PCV21 serotypes includes 3, 6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F, 9N, 17F, 20, 15A, 15C, 16F, 23A, 23B, 24F, 31, and 35B; and PPSV23 serotypes includes serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9 V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F.

*The proportion shown is the percentage of cases in which each serotype was detected in the total community-acquired pneumonia cases.

†The proportion is not available.

§The proportion shown is the percentage of cases in which each serotype was detected in patients with respiratory infections who were tested for *Streptococcus pneumoniae*.

Abbreviations: IPD, invasive pneumococcal disease; PCV7, a 7-valent pneumococcal conjugate vaccine; PCV10, a 10-valent pneumococcal conjugate vaccine; PCV13, a 13-valent pneumococcal conjugate vaccine; PCV15, a 15-valent pneumococcal conjugate vaccine; PCV20, a 20-valent pneumococcal conjugate vaccine; PCV21, a 21-valent pneumococcal conjugate vaccine; PPSV23, a 23-valent pneumococcal polysaccharide vaccine; NVT, non-vaccine type.

respiratory tract infections who were hospitalized at two hospitals in Bristol, UK, between 2021 and 2022. Of 2,445 patients with respiratory infections who tested for *S. pneumoniae*, PCV13 plus serotype 6C, PCV15 plus serotype 6C, PCV20 plus serotype 6C/15C, and PPSV23 plus serotype 15C were detected in 4.2, 4.7, 8.6, and 9.3% of the 2,445 cases, respectively. The most common serotypes were 8 (3.2% of 2,445 cases), 7F (1.0%), and 3 (1.0%).[57] In the UK, after the introduction of PCV13, IPD cases caused by serotype 3 decreased; however, numbers started increasing among adults from four years post-introduction. Serotype 8 emerged in both IPD and pneumonia patients.

Spain and Italy

Similar to the UK, serotype 8 emerged in other European countries, especially Spain and Italy (Table 2). In Spain, the Ministry of Health makes general recommendations for vaccine policies, but 19 individual regions can implement their own vaccination policies according to local epidemiology and cost-effectiveness. In 2015, the Ministry of Health introduced PCV13 for pediatric NIP using a 2 + 1 schedule.[44] Since 2004, the Ministry of Health has recommended PPSV23 for immunocompetent adults aged ≥65 years. A prospective, national, observational study that included all IPD isolates reported by hospitals evaluated the nationwide serotype distribution of IPD cases between 2009 and 2019. After the introduction of PCV13 for pediatric NIP, IPD cases caused by PCV13 serotype decreased from 66% in 2009 (pre-PCV period) to 24% in 2019 (post-PCV period) in adults aged 18–64 years and 65% in 2009 to 25% in 2019 in adults aged ≥65 years. IPD cases caused by PPSV23 non-PCV13 serotypes increased from 22% in 2009 to 58% in 2019 in adults aged 18–64 years, and 17% in 2009 to 45% in 2019 in adults aged ≥65 years, being primarily due to the emergence of serotype 8 (from 5.2 to 30.3% in adults aged 18–64 years and from 5.8 to 18.7% in adults aged ≥65 years). In 2019, the most common serotypes were 8 (30.3% in adults aged 18–64 years and 18.7% in adults aged ≥65 years) and 3 (12.2% in adults aged 18–64 years and 13.2% in adults aged ≥65 years).[44] One study evaluated the serotype distribution in adult pneumococcal pneumonia patients aged ≥18 years who attended at a university hospital in Southern Barcelona are of Spain between 2011 and 2019. This study utilized the pneumococcal isolates from blood or respiratory samples in patients with radiology-confirmed pneumonia. It revealed that serotype 3 was the most common between 2011 and 2019, and the prevalence of serotypes 8 and 11A increased significantly from 2011–2013 to 2017–2019 among adults aged ≥18 years with pneumococcal pneumonia. In 2017–2019, the most common serotypes were 3, 8, and 11A. PCV13, PCV15,

PCV20, and PPSV23 serotypes accounted for 42, 48, 72, and 77% of total cases in adults aged 18–64 years, respectively. PCV13, PCV15, PCV20, and PPSV23 accounted for 38, 44, 61, and 64% in adults aged ≥65 years, respectively.[58]

In Italy, PCV7 was introduced into pediatric NIP between 2006 and 2010. PCV13 was licensed and replaced PCV7 for pediatric NIP in 2010 following a 3 + 1 dosing schedule.[46,59] According to IPD surveillance by the Ministry of Health, the proportion of IPD cases caused by PCV13 serotypes decreased, and IPD cases caused by PPSV23 serotypes increased from 2007 to 2017. PCV13 and PPCV23 serotypes accounted for 18.3 and 48.1% of total cases, respectively, in 2017. The number of IPD cases caused by serotypes 3, 8, 12F, and 22F increased from 2007 to 2017, and the proportion of IPD cases caused by serotypes 3, 8, 12F, and 22F in 2017 was 14.4, 22.1, 5.7, and 5.9%, respectively.[46] One study investigated the distribution of serotypes before and after the introduction of PCV13 responsible for pneumococcal diseases in individuals aged ≥14 years who were hospitalized with a diagnosis of pneumococcal infection to three Italian regions where PPSV23 vaccination rate was very low (<10%). The proportion of IPD cases caused by PCV13 serotypes decreased from 62.3 to 45.0% after the introduction of PCV13, and the most common serotypes after the introduction were 3 (13.3%), 8 (9.4%), and 19A (7.3%). Serotypes that increased after the introduction were 8, 23A, and 33.[47]

Other European countries and Israel

In France, PCV7 was licensed in 2001 but not covered by health insurance, which resulted in low vaccine coverage rates (<10% until December 2002).[60,61] In 2006, PCV7 became covered and was recommended for all children aged <2 years, and PCV13 replaced PCV13 in 2010, adopting a 2 + 1 dosing schedule, which resulted in a high vaccination coverage rate among children.[60] A previous study investigated the incidence of IPD between 2001 and 2017, using population-based, prospective surveillance data on IPD from both children and adults across metropolitan France, covering 97% of the French population. PCV7 introduction did not lead to a significant reduction in the incidence of total IPD cases; however, PCV13 introduction in 2010 was followed by a significant decrease in the incidence of total IPD cases. The incidence of IPD cases caused by PCV7 or PCV13 serotypes decreased significantly after PCV7 or PCV13 implementation in both children and adults. However, the incidence of IPD cases caused by serotype 3 did not decrease from 2001 to 2017. PCV13 serotypes plus 6C and 3 accounted for 26.7 and 14.3%, respectively, of the total cases in 2015–2017 in adults aged ≥65 years. In 2015–2017, the most common serotypes in adults aged ≥65 years were 3 (14.3%), 22F (8.1%), 19A (7.4%), and 8 (6.9%).[60]

Germany has recommended PCV for all children aged <2 years since 2006, initially following a 3 + 1 dosing schedule, which was changed to a 2 + 1 dosing in 2015.[62] PCV10 was introduced in April 2009, and PCV13 has been in use since December 2009, with costs fully reimbursed by health insurance. The German National Reference Center for Streptococci has conducted IPD surveillance since 1992. Among adults, the proportion of IPD cases caused by PCV7 serotypes decreased from 40 to 45% in 1992–2006 to 5.8% in 2013–2014 and remained between 3.5 and 5.2% since 2014. The proportion of IPD cases caused by PCV13 non-PCV7 serotypes decreased from 47% in 2010–2011 to 28% in 2014–2015 and remained constant thereafter. In 2017–2018, PCV13, PCV15, PCV20, and PPSV23 accounted for 31.4, 41.0, 64.0, and 73.6% of all IPD cases, respectively, in adults aged ≥60 years. The most common serotype in 2017–2018 was 3 (20.9%), followed by 8 (9.8%), 22F (7.6%), 9N (7.0%), and 19A (5.2%).[62,63] One prospective multicenter study evaluated the proportion of PCV13 serotypes in adults aged ≥18 years with radiographically confirmed CAP from 2012 to 2017. This study utilized urine samples for serotyping, employing the serotype-specific multiplex urinary antigen detection assay, which enabled the detection of PCV13 serotypes. During the observation period, PCV13 serotypes accounted for 7.4% of patients with all causes of CAP, half of which were serotype 3.[64]

In Ireland, PCV7 was introduced into pediatric NIP in 2008 with a 2 + 1 dosing schedule and subsequently replaced by PCV13 in 2010. Adults aged ≥65 years are recommended to receive PPSV23. One study assessed the incidence of IPD in adults aged ≥65 years between 2007 and 2016, using national IPD surveillance data. From 2007–2008 to 2015–2016, there was a 94% reduction in IPD cases caused by PCV7 serotypes; however, there was no decline in additional PCV13 serotypes over the same period in comparison with 2009–2010. The incidence of IPD caused by PPSV23 non-PCV13 and NVT serotypes increased from 2009–2010 to 2015–2016. In 2015–2016, the most common serotypes were 19A (9.7%), 3 (8.6%), 12F (8.6%), 8 (8.0%), and 33F (8.0%). PCV13, PCV15, PCV20, PPSV23, and PCV21 serotypes accounted for 23.4, 38.9, 50.3, 69.7, and 82.9%, respectively.[65]

Even though Nordic countries have similar healthcare systems and demographics, the serotype distribution of IPD cases in adults aged ≥65 years varies among them. One study, utilizing public IPD surveillance data from Denmark, Finland, Norway, and Sweden, investigated the incidence and serotype distribution of IPD cases in adults aged ≥65 years between 2010 and 2019 in these countries. The incidence of IPD cases caused by PCV13 serotypes declined from 2010 to 2019 in all four countries, but that of IPD cases caused by PPSV23 non-PCV13 serotypes increased during the same period in Denmark, Finland, and Norway. The proportions of vaccine-covered serotypes in 2017–2019 were as follows: PCV10 serotypes accounted for 3, 9, 4, and 4% in Denmark, Finland, Norway, and Sweden, respectively; PCV13 accounted for 14, 48, 20, and 31% in Denmark, Finland, Norway, and Sweden, respectively; PCV15 accounted for 26, 58, 40, 41% in Denmark, Finland, Norway, and Sweden, respectively; and PCV20 accounted for 63, 67, 57, and 59% in Denmark, Finland, Norway, and Sweden, respectively. The most common serotypes were 8, 3, 22F, and 9N in Denmark; 19A, 3, 6C, and 22F in Finland; 22F, 3, 9N, and 8 in Norway; and 3, 19A, 8, and 15A in Sweden.[66] The proportion of PCV13 serotypes was higher in Finland and Sweden, possibly because of the difference in PCV included in pediatric NIP.[67] PCV7 with a 2 + 1 dosing schedule was introduced in 2006, 2007,

and 2009 into pediatric NIP in Norway, Denmark, and Sweden, respectively, whereas Finland introduced PCV10 in 2010. PCV13 replaced PCV7 in Denmark and Norway in 2010 and 2011, respectively. In contrast, Sweden introduced PCV10 and PCV13 with a 2 + 1 dosing schedule in 2010, and switched to PCV10-only use in 2019. The difference in the type of PCV may have influenced the serotype distribution. In Sweden, one prospective, population-based, single-site study assessed the serotype distribution among hospitalized patients aged ≥18 years with radiologically confirmed CAP who were admitted to a university hospital from 2016 to 2018. The most common serotypes in adults aged ≥18 years were 3 (5.0% of total CAP cases), 8 (1.9%), 11A (1.9%), and 19A (1.9%). PCV13, PCV15, and PCV20 serotypes were detected in 12.4, 13.6, and 20.7% of the total CAP cases, respectively, in adults aged 18–64 years; and PCV13, PCV15, and PCV20 serotypes were detected in 10.0, 12.0, and 15.2% of the total CAP cases, respectively, in adults aged ≥65 years.[68]

Other European countries reported a similar reduction in IPD cases caused by PCV13 following the introduction of PCVs in children. In Greece, PCV7 became available in 2004 and was incorporated into pediatric NIP in 2006 with a 3 + 1 dosing schedule.[69,70] PCV13 was introduced into pediatric NIP in 2010. A prospective multicenter study conducted between 2017 and 2019 evaluated the serotype distribution among adults aged ≥19 years with pneumococcal pneumonia who were hospitalized with clinically and radiographically confirmed CAP in all hospitals in two cities in Greece. A total of 53.8% of pneumococcal pneumonia was caused by PCV13 serotypes. The most common serotypes were 3 (4.1% of 482 CAP) and 19A (1.2% of 482 CAP). In adults aged ≥65 years, PCV13, PCV15, PCV20, and PPSV23 accounted for 5.8, 6.4, 8.2, and 9.5% of total 328 CAP, respectively.[71] In Israel, PCV7 was introduced into pediatric NIP in 2009 with a 2 + 1 dosing schedule and replaced by PCV13 in 2010. National active surveillance of all adult IPD, initiated in 2009, has been employed to evaluate the serotype distribution in adult aged ≥18 years. At four years after PCV7 introduction and 2.5 years after PCV13 introduction, the incidence of adult IPD caused by PCV7 and PCV13 serotypes decreased, especially in younger adults, with an increase in the incidence of IPD cases caused by NVT serotypes.[72] Subsequently, the incidence of IPD cases caused by PCV7 and PCV13 serotypes decreased by 79.4 and 70.1% in 2014–2015, respectively. However, the decrease in serotypes 3, 19A, and 7F was slow. In contrast, the incidence of non-PCV13 serotypes has been increasing, specifically 12F, 9N, 10A, 16F, 24F, 15 B, 17F, 15, and 6C. Serotype 8 was also detected and the third most common serotypes in 2014–2015.[73] A similar trend was observed regarding the serotype distribution of pneumococcal pneumonia. One study, conducted between 2014 and 2015, evaluated the serotype distribution among adults aged ≥50 years with radiographically confirmed CAP who presented to three hospitals in Israel. Among the 498 CAP cases, 80 were positive for *S. pneumoniae*. The most common serotype was 3, followed by 23F and 19A.[74]

In contrast, Austria introduced PCV10 with a 2 + 1 dosing schedule in 2012. National IPD surveillance revealed that compared with the incidence in 2009–2011, IPD cases caused by PCV10 serotypes were reduced by 58 and 65% among individuals <5 and ≥50 years, respectively, in 2013–2017, while no vaccine effects were observed among those aged 5–49 years. Regarding adults aged ≥50 years, non-PCV10 serotypes constituted 83.2% of all serotyped IPD cases in 2015–2016, and serotype 3 was the most common (28.7%), followed by 19A (7.4%), 22F (6.1%), and 8 (5.5%). The proportion of IPD cases by serotype 8 increased significantly, and the proportion of IPD cases by serotype 19A increased in 2015–2016 among adults aged ≥50 years.[45]

Asia

In Asian countries, emerging serotypes after PCV13 introduction differed from those in North America and European countries; serotypes 4 and 8 did not emerge (Table 3). In Japan, PCV7 became available for children in 2010, PCV7 was incorporated into pediatric NIP with a 3 + 1 dosing schedule in April 2013, and PCV13 replaced PCV7 in November 2013. PPSV23 was introduced into NIP for adults aged ≥65 years in 2014.[75] A national surveillance program for IPD has been conducted since 2013. Regarding the introduction of PCV13 into NIP for children, the proportion of IPD cases by PCV13 serotypes decreased within the three years following its introduction. The proportion of PPSV23 non-PCV13 serotypes remained unchanged in both adults aged 15–64 and ≥65 years. Serotypes 3 and 19A decreased among adults aged ≥65 years, although serotype 3 remained the most common. In adults aged ≥65 years between 2018 and 2019, the proportions of PCV13, PCV15, PCV20, and PPSV23 were 30, 38, 56, and 57% of the total, respectively, and the most common serotypes were 3, 35 B, and 23A. Serotypes 4 and 8 accounted for less than 1% of IPD cases in 2018–2019.[77] A similar trend was observed in the serotype distribution of adult pneumococcal pneumonia. One multicenter study evaluated the serotype distribution among individuals aged ≥15 years with radiographically confirmed pneumococcal CAP between 2011 and 2020. Regarding the introduction of PCV13 into pediatric NIP, the proportion of IPD cases caused by PCV13 serotypes decreased within the four years following its introduction; however, no reduction in the proportion of IPD cases caused by PCV13 serotypes was subsequently observed. The decrease in serotypes 3 and 19F contributed to the decline in PCV13, but serotype 3 was the most common in 2018–2020. In 2018–2020, PCV13, PCV15, PCV20, PCV21, and PPSV23 accounted for 38.5, 43.3, 59.6, 67.3, and 56.8% of the total, respectively, in individuals aged ≥15 years. No pneumococcal pneumonia was caused by serotype 4 or 8 in 2018–2020.[78] Currently, PCV15 and PCV20 are available for both children and adults, and have been incorporated into pediatric NIP since 2024 in Japan.[17,78] For adults, PCV15 and PCV20 are optional and not included in NIP, the same as PCV13.

South Korea introduced PCV10 and PCV13 with 3 + 1 dosing schedule into pediatric NIP in 2014, and PPSV23 has been applied for older adults since 2013. One study evaluated the serotypes of IPD cases collected from patients of all age groups at a tertiary-care hospital in Korea between 2008 and 2014. The proportion of PCV13 serotypes was 50.9 and 52.8%

Table 3. Prevalent serotype and proportion of vaccine-covered serotypes among adults in high-income countries in Asia and Oceania.

County	Type	Year	Population	Prevalent serotypes	Vaccine coverage	Reference
Australia	IPD	2017	Non-indigenous aged 50–64	3 (13%)	PCV7: 11% PCV13: 35% PPSV23 non PCV13: 40% NVT: 25%	83
			Non-indigenous aged ≥ 65	3 (16%)	PCV7: 10% PCV13: 33% PPSV23 non PCV13: 30% NVT: 39%	
		2016–2017	Indigenous aged 25–49	8 (NA), 3 (4%)	PCV7: 15% PCV13: 27% PPSV23 non PCV13: 47% NVT: 27%	
			Indigenous aged ≥ 50	3 (12%)	PCV7: 8% PCV13: 29% PPSV23 non PCV13: 28% NVT: 43%	
Australia	IPD	2018–2022	Aged ≥18	3 (15.8%), 22F (8.7%), 9N (8.5%), 19F (7.7%), 19A (5.9%)	PCV13: 34.5% PCV15: 43.6% PCV20: 57.6% PPSV23: 57.4% PCV21: 68.2%	84
			Aged ≥65	3 (16.6%), 19F (9.4%), 22F (8.9%), 9N (7.5%), 6C (7.0%)	PCV13: 35.3% PCV15: 44.5% PCV20: 54.3% PPSV23: 54.1% PCV21: 65.1%	
Japan	IPD	2018–2019	Aged ≥65	3 (10%), 19A (7%), 12F (7%)	PCV13: 30% PCV15: 38% PCV20: 56% PPSV23: 57%	76
Japan	Pneumonia	2018–2019	Adults ≥15	3 (11.5%), 6B (10.6%), 19A (8.7%), 11A (8.7%)	PCV13: 38.5% PCV15: 43.3% PCV20: 59.6% PPSV23: 56.8% PCV21: 67%	77
			Adults ≥65	NA	PCV13: 38.0% PCV15: 43.0% PCV20: 54.4% PPSV23 non- PCV13: 16.5%	
New Zealand	IPD	2022–2023	All	19A (34.7%), 8 (21.4%), 3 (8.0%)	PCV10: 3.5%	87
			Aged 5–64	19A, 8, 3*	NA	
			Aged ≥65	19A, 8, 3*	NA	
South Korea	IPD	2017–2019	Aged 19–50	19A (11.1%), 12F (9.5%), 23A (7.9%)	PCV13: 19.0% PCV15: 27.0% PCV20: 55.6% PCV21: 71.4% PPSV23: 60.3%	80
			Aged 51–64	3 (13.9%), 23A (8.9%), 22F (8.9%)	PCV13: 30.7% PCV15: 39.6% PCV20: 53.5% PCV21: 71.3% PPSV23: 55.4%	
			Aged ≥65	3 (16.1%), 34 (9.9%), 11A (7.8%)	PCV13: 34.4% PCV15: 40.1% PCV20: 59.9% PCV21: 73.4% PPSV23: 60.9%	
Taiwan	IPD	2017–2020	Aged ≥20	23A (14.8%), 15A (13.1%), 3 (10.5%), 19A (10.1%), 14 (8.0%)	PCV13: 44.7% PCV15: 45.6% PCV20: 52.7% PPSV23: 49.4% PCV21: 58.6%	81
			Aged 20–49	23A (17.2%), 3 (12.1%), 19A (12.1%), 14 (6.9%), 6A (6.9%), 34 (6.9%)	PCV13: 53.4% PCV15: 53.4% PCV20: 60.3% PPSV23: 55.2% PCV21: 60.3%	

(*Continued*)

Table 3. (Continued).

County	Type	Year	Population	Prevalent serotypes	Vaccine coverage	Reference
			Aged 50–64	15A (19.0%), 23A (12.7%), 29 (10.1%), 19A (8.9%), 15B (8.9%)	PCV13: 31.6% PCV15: 32.9% PCV20: 43.0% PPSV23: 41.8% PCV21: 59.5%	
			Aged ≥65	23A (15.0%), 15A (13.0%), 3 (12.0%), 14 (11.0%), 19A (10.0%)	PCV13: 50.0% PCV15: 51.0% PCV20: 56.0% PPSV23: 52.0% PCV21: 57.0%	

The country names are arranged in alphabetical order. Some of the data listed were recalculated from the data published in each article. PCV7 serotypes includes serotype 4, 6 B, 9 V, 14, 18C, 19F, and 23; PCV10 serotypes includes PCV7 serotypes plus 1, 5, and 7F; PCV13 serotypes includes PCV10 serotypes plus 3, 6A, and 19A; PCV15 serotypes includes PCV13 serotypes plus 22F and 33F serotypes; PCV20 serotypes includes PCV15 serotypes plus 8, 10A, 11A, 12F, and 15B; PCV21 serotypes includes 3, 6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F, 9N, 17F, 20, 15A, 15C, 16F, 23A, 23B, 24F, 31, and 35B; and PPSV23 serotypes includes serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9 V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F.

*The proportion is not available.

Abbreviations: IPD, invasive pneumococcal disease; NA, not applicable; PCV7, a 7-valent pneumococcal conjugate vaccine; PCV10, a 10-valent pneumococcal conjugate vaccine; PCV13, a 13-valent pneumococcal conjugate vaccine; PCV15, a 15-valent pneumococcal conjugate vaccine; PCV20, a 20-valent pneumococcal conjugate vaccine; PCV21, a 21-valent pneumococcal conjugate vaccine; PPSV23, a 23-valent pneumococcal polysaccharide vaccine; NVT, non-vaccine type.

in individuals aged 6–64 and ≥65 years, respectively. The most common serotype was 3 (13.9–14.2%).[79] Another study evaluated the serotype distribution of pneumococcal isolates causing IPD across all age groups, collected from 16 hospitals in Korea between 2017 and 2019. In 2017–2019, after its introduction, the proportion of PCV13 serotypes declined to 30–40% in individuals aged ≥6 years. In adults aged ≥65 years, PCV13, PCV15, PCV20, PCV21, and PPSV23 accounted for 34.4, 40.1, 59.9, 73.4, and 60.9%, respectively, of the total, and the most common serotype was 3 (16.1%), followed by 34 (9.9%), 11A (7.8%), 10A (7.3%), 35B (6.8%), and 19A (6.3%). IPD cases caused by serotype 4 or 8 were not reported in 2017–2019.[80] In Taiwan, PCV7 was introduced into a funded vaccination program for children in 2009, and PCV13 was incorporated with a 2 + 1 dosing schedule in 2012. PPSV23 was funded for adults aged ≥75 years in 2007–2008, and currently, PCV13 and PPSV23 are funded for a single dose for adults aged ≥65 years.[81] According to the national surveillance of IPD cases in adults aged ≥20 years between 2017 and 2020, the most common serotypes were 23A (14.8%), 15A (13.1%), 3 (10.5%), 19A (10.1%), and 14 (8.0%). The proportions of IPD cases caused by serotype 4 or 8 were 0.8 and 1.3%, respectively. PCV13, PCV15, PCV20, PPSV23, and PCV21 serotypes accounted for 44.7, 45.6, 52.7, 49.4 and 58.6%, respectively, in adults aged ≥20 years. The serotype distribution pattern was similar to that among adults aged ≥65 years.[81]

Oceania

Australia and New Zealand introduced different PCVs for pediatric NIP. Australia introduced PCV7 into pediatric NIP in 2005 with a 3 + 0 dosing schedule, and PCV13 replaced PCV7 in 2011. A study evaluated the serotype distribution of IPD cases among individuals not identified as Indigenous across all Australian jurisdictions, except the Northern Territory, between 2002 and 2014, using data from the National Notifiable Disease Surveillance System (NNDSS). The study found that the incidence of PCV serotypes has declined in both children and adults following the introduction of PCVs. Conversely, the incidence of IPD cases by NVT serotypes has increased since the introduction of PCV7 in adults.[82] Another study utilizing NNDSS data assessed serotype-specific IPD incidence in both indigenous adults aged ≥25 years and non-indigenous adults aged ≥50 years between 2002 and 2017. In non-indigenous adults aged ≥50 years, IPD cases caused by PCV7 and PCV13 serotypes declined after the introduction of PCV7 and PCV13 for children. However, IPD cases caused by serotype 3 increased from 2002 to 2017, with serotype 3 being the most common. This trend differed among indigenous adults. In such adults aged 15–49 years, the total number of IPD cases did not significantly change after PCV introduction for children, and the total number of IPD cases increased among indigenous adults aged ≥50 years, possibly due to the different impact on total IPD cases. The proportion of PCV7 serotypes in IPD cases before the introduction of PCV7 was smaller than that in non-indigenous adults, and the subsequent increase in NVT serotypes was larger. In 2017, PCV13 and PPCV23 non-PCV13 accounted for 33 to 35% and 30 to 40%, respectively, in non-indigenous adults aged ≥50 years. PCV13 serotypes accounted for 27 to 29% in indigenous adults aged ≥25 years in 2016–2017. Serotype 3 was the most common serotype in non-indigenous and indigenous adults aged ≥50 years, while serotype 8 was the most common serotype in indigenous adults aged 25–49 years.[73] Another study evaluated the current serotype distribution of pneumococcal isolates from IPD cases across all ages in Victoria, Australia, between 2018 and 2022, as part of state laboratory-based surveillance. Between 2018 and 2022, in adults aged ≥18 years, the most common serotype was 3 (15.8%), followed by 22F (8.7%), 9N (8.5%), and 19F (7.7%); and PCV13, PCV15, PCV20, PPSV23, and PCV21 accounted for 34.5, 43.6, 57.6, 57.4, and 68.2%.[84]

In New Zealand, PCV7 was introduced into pediatric NIP in 2008 with a 3 + 1 dosing schedule. PCV10 was used between 2011 and 2014, with a switch to PCV13 in 2014. PCV10 was introduced again in 2017 based on possible cross-protection between 19F and 19A, and the dosing schedule was changed to 2 + 1 in 2020. Children with high-risk

underlying medical conditions were eligible for PCV13 with a 3 + 1 dosing schedule. However, a study evaluating IPD incidence across all age groups from 2017 to 2020 revealed that, after switching to PCV10 for pediatric immunization, the number of IPD cases caused by serotype 19A increased, especially in children.[85] Therefore, New Zealand switched to PCV13 with a 2 + 1 dosing schedule in December 2022.[86] The latest data from national laboratory-based surveillance of pneumococcal isolates from IPD cases show that 19A was the most common serotype, followed by 8 and 3, in individuals aged 5–64 years and those aged ≥65 years in 2022–2023.[87]

In summary, although pediatric PCV immunization programs are well-established and indirect effects have been observed among adults in high-income countries, pneumococcal diseases caused by PCV13 serotypes persist among adults. Serotype 3 is one of the most common serotypes, and serotype 4 has reemerged in the Western US and Canada in specific populations. Serotype 8 has emerged in European countries, especially in the UK, Spain, and Italy, but not in North America or Asian countries. In countries where PCV10 was introduced during the observation period, such as Finland, Austria, and New Zealand, serotype 19A ranked as the most or second most prevalent serotype; these data do not support PCV10's cross-protection against serotype 19A. In many countries, serotypes covered by newly developed high-valency PCVs accounted for more than half of distributed serotypes, and they can provide additional protection against pneumococcal diseases in adults in these countries. As a consequence of the introduction of PCV15 and PCV20 for children and adults and PCV21 for adults, the serotype distribution in both children and adults is expected to change. Therefore, ongoing evaluation of the latest serotype distribution is important.

Pneumococcal serotype distributions in non-high-income countries among adults

Immunization programs for pneumococcal diseases differ among non-high-income countries. Serotype replacement occurred in countries where PCV was included in pediatric NIP, while pneumococcal diseases caused by PCV serotypes remained dominant in countries where PCV had not been included in pediatric NIP (Table 4).

In countries where pneumococcal vaccines were not included in pediatric NIP or the rate of vaccine coverage was low regardless of their introduction into pediatric NIP, pneumococcal diseases caused by PCV-covered serotypes remained a marked burden. Since PCVs and PPSV23 are available but not included in NIP of China, the vaccine coverage rate has remained low due to high costs.[88,89] A multicenter observational study evaluated pneumococcal isolates from IPD cases in both children and adults treated at 27 tertiary hospitals in China between 2012–2015. The study showed that the most common serotypes in adults aged ≥18 years were 3 (21.7%), 19F (11.8%), and 19A (10.5%). PCV10 and PCV13 serotypes accounted for 38.1 and 69.9% of the total, respectively, in adults aged 18–64 years. In those aged ≥65 years, PCV10, PCV13, PCV15, PCV20, and PPSV23 serotypes accounted for 23.1, 71.8, 71.8, 76.9, and 82.1%, respectively. Among children ≤4 years, the proportion of PCV10 and PCV13 serotypes were 55.3 to 61.7%, and 89.5%, respectively.[90] Another multicenter study conducted in 2018–2022 evaluated the distribution of serotypes causing IPD or pneumococcal pneumonia across all age groups hospitalized at five hospitals in China. They found that in adults aged ≥50 years, the most common serotypes were 3 (15.8%), 19F (12.9%), and 19A (11.9%); and PCV10, PCV13, PCV15, and PCV20 accounted for 24.8, 57.4, 57.4, 57.4, and 58.4%, respectively.[91] These results indicate that the burden of PCV13 serotypes in both children and adults in China is large. In the Philippines, PCV13 was introduced into pediatric NIP in 2015, but vaccine coverage remains low (30–60% in 2015–2019).[92] One study evaluated the serotype distribution in IPD cases across all age groups, using laboratory-based surveillance conducted at 24 sites representing 16 of 17 regions in the country between 2012 and 2018. In adults aged ≥65 years, the most common serotypes were 3 (10.2%), 4 (9.1%), and 1 (9.1%), all of which were included in PCV13. PCV7, PCV10, PCV13, and PPPSV23 serotypes accounted for 29.1, 50.9, 69.1, and 89.1%, respectively. PCV serotypes accounted for a high proportion of children aged ≤5 years as well; PCV7, PCV10, and PCV13 accounted for 54.9, 66.4, and 70.8% of children aged ≤5 years, respectively.[92] India introduced PCV13 with a 2 + 1 dosing schedule in 2017 in a phased manner into pediatric NIP.[93] One systematic review estimated the proportion of IPD cases caused by PCV serotypes in children aged ≤5 years, revealing that PCV10 and PCV13 serotypes accounted for 67.3 to 78.4% of all IPD cases before the introduction of PCVs in children in 2017.[94] PCV13 and PPSV23 for adults aged ≥65 years and those aged 18–64 years with risks of pneumococcal diseases have been recommended by the Geriatric Society of India and Expert Group of the Association of Physicians of India.[95] A prospective study evaluated the serotype distribution of IPD cases in adults aged ≥18 years who attended inpatient and outpatient services at a tertiary care center in South India between 2007 to 2017. The study showed that PCV10, PCV13, and PPSV23 serotypes accounted for 44.5, 58.6, and 67.4% of the total, respectively. The most common serotypes were 1, 3, 5, and 19F, which were included in PCV13.[96] In both adults and children, the burden of vaccine-covered serotypes before the introduction of PCV in children was considerable in India.

In 2008, Turkey introduced PCV7 with a 3 + 1 dosing schedule for children but replaced it with PCV13 in 2011.[97] PCV13 can be received free of charge at immunization centers, resulting in a 97% childhood vaccination rate.[98] One study evaluated the serotype distribution of pneumococcal diseases, including pneumonia, bacteremia, meningitis, pleuritis and peritonitis, in adults aged ≥18 years across 21 centers in Turkey between 2015 and 2018. The most common serotypes were 19F (13.0%), 3 (11.9%), and 1 (9.7%) in adults aged 18–64 years, and 3 (18.4%), 19F (9.9%), and 1 (8.5%) in those aged ≥65 years. PCV13, PCV15, PCV 20, and PPSV23 serotypes accounted for 62.8, 65.1, 71.0, and 74.3% of the total, respectively, in adults aged 18–64 years, and 66.0, 69.5, 80.1, and 78.7% of the total, respectively, in those aged ≥65 years. Even

Table 4. Prevalent serotype and proportion of vaccine-covered serotypes among adults in non-high-income countries.

County	Type	Year	Population	Prevalent serotypes	Vaccine coverage	Reference
Asia						
China	IPD/Pneumonia	2018–2022	Aged ≥50	3 (15.8%), 19F (12.9%), 19A (11.9%)	PCV10: 24.8% PCV13: 57.4% PCV15: 57.4% PCV20: 58.4% PPSV23: 57.4% PCV21: 50.5%	88
India	IPD	2007–2017	Aged ≥19	1 (11.4%), 3 (8.2%), 5 (6.0%), 19F (6.0%), 8 (5.0%)	PCV10: 44.5% PCV13: 58.7% PPSV23: 67.4%	89
			Aged 19–65	1 (12.4%), 3 (6.9%), 5 (6.4%), 19F (5.5%), 8 (4.6%)	PCV10: 44.8% PCV13: 56.9% PPSV23: 66.5%	
			Aged ≥66	3 (16.1%), 19F (8.9%), 14 (8.9%), 7F (7.1%)	PCV10: 42.9% PCV13: 69.6% PPSV23: 73.2%	
Philippines	IPD	2012–2018	Aged ≥65	3 (10.2%), 4 (9.1%), 1 (9.1%)	PCV7: 29.1% PCV10: 50.9% PCV13: 69.1% PPPSV23: 89.1%	90
Turkey	Pneumococcal diseases	2015–2018	Aged ≥18	3 (14.1%), 19F (12.0%), 1 (9.3%), 23F (5.6%)	PCV13: 63.9% PCV15: 66.6% PCV20: 74.1% PPSV23: 75.9%	91
			Aged 18–64	19F (13.0%), 3 (11.9%), 1 (9.7%)	PCV13: 62.8% PCV15: 65.1% PCV20: 71.0% PPSV23: 74.3%	
			Aged ≥65	3 (18.4%), 19F (9.9%), 1 (8.5%)	PCV13: 66.0% PCV15: 69.5% PCV20: 80.1% PPSV23: 78.7%	
Africa						
South Africa	IPD	2017–2019	Aged 45–64	8 (15.1%), 12F (8.8%), 3 (8.4%), 19A (7.0%)	PCV13: 30.3% PCV15: 34.3% PCV20: 63.7% PPSV23: 70.1% PCV21: 70.6%	92
			Aged ≥65	8 (17.8%), 3 (11.2%), 19A (8.6%), 22F (5.4%)	PCV13: 33.3% PCV15: 38.9% PCV20: 69.4% PPSV23: 71.6% PCV21: 74.3%	
South America						
Brazil	IPD	2014–2015	Aged 18–64	NA	PCV10: 25.6%	93
		2014–2015	Aged ≥65	NA	PCV10: 20.4%	
Colombia	IPD	2015–2017	Aged ≥18	3 (12.5%), 19A (10.0%), 1 (8.8%)	PCV10: 22.5% PCV13: 51.3% PPSV23: 58.8% NVT: 35.0%	94

Some of the data listed were recalculated from the data published in each article. PCV7 serotypes includes serotype 4, 6 B, 9 V, 14, 18C, 19F, and 23; PCV10 serotypes includes PCV7 serotypes plus 1, 5, and 7F; PCV13 serotypes includes PCV10 serotypes plus 3, 6A, and 19A; PCV15 serotypes includes PCV13 serotypes plus 22F and 33F serotypes; PCV20 serotypes includes PCV15 serotypes plus 8, 10A, 11A, 12F, and 15B; PCV21 serotypes includes 3, 6A, 7F, 19A, 22F, 33F, 8, 10A, 11A, 12F, 9N, 17F, 20, 15A, 15C, 16F, 23A, 23B, 24F, 31, and 35B; and PPSV23 serotypes includes serotypes 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9 V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F.

Abbreviations: IPD, invasive pneumococcal disease; NA, not applicable; PCV7, a 7-valent pneumococcal conjugate vaccine; PCV10, a 10-valent pneumococcal conjugate vaccine; PCV13, a 13-valent pneumococcal conjugate vaccine; PCV15, a 15-valent pneumococcal conjugate vaccine; PCV20, a 20-valent pneumococcal conjugate vaccine; PCV21, a 21-valent pneumococcal conjugate vaccine; PPSV23, a 23-valent pneumococcal polysaccharide vaccine.

four years after the introduction of PCV13 for children, the proportion of PCV13 was approximately 60% in cases of adult pneumococcal pneumonia.[98]

In Latin America, since 1993, there has been a surveillance system called the Regional Immunization System or Sistema Regional de Vacunas in Spanish (SIREVA), which involves a national laboratory conducting surveillance of bacterial pneumonia, sepsis/bacteremia, and meningitis and is organized by PAHO.[99] The SIREVA II project was launched in 2005 by PAHO.[100] PCV has been included in pediatric NIP, and IPD cases caused by PCV serotypes have declined in Latin America.[101] In Brazil, PCV10 with a 3 + 1 dosing schedule was introduced into pediatric NIP in 2010[102] and has been offered freely in primary health care units.[103] One study evaluated the serotype distribution of IPD cases across all age groups before and after the introduction of PCV10, using national laboratory-based surveillance data collected between 2005 and 2015. The proportion of PCV10 serotypes in total IPD cases declined from 41.7% in 2005–2009 to 19.1% in 2014–2015 and from 40.0% in 2005–2009 to 21.1% in 2014–2015, in adults with meningitis aged 18–64 and ≥65 years, respectively. For non-meningitis cases, it declined from 57.4 to 30.0% and 43.6 to

20.3% over the same period in adults aged 18–64 and ≥65 years, respectively. IPD cases by non-PCV10 serotypes increased over the study period, driven mainly by serotypes 3, 6C, and 19A, which are not covered by PCV10.[102] Mexico introduced PCV7 in 2006 initially for children living in the poor regions with a 3 + 0 dosing schedule, and universal vaccination for children in 2008 with a 2 + 1 dosing schedule. In 2011, PCV13 was gradually introduced into pediatric NIP with a 2 + 1 dosing schedule. PPSV23 was incorporated into NIP for adults aged ≥65 years in 2006.[104] One study investigated the serotype distribution of pneumococcal isolates from IPD and NIPD cases across all age groups using laboratory-based surveillance data from 2000 to 2014, evaluating changes before and after PCV7 introduction for children. The proportion of IPD cases caused by PCV7 serotype decreased. Serotype 3 was the most common serotype in adults aged ≥50 years in the post-PCV7 period, and a high proportion of IPD cases caused by serotype 19A was observed in all age groups.[104] Colombia introduced PCV10 with a 2 + 1 dosing schedule into pediatric NIP in 2012.[105] PCV10 vaccination was free for children, leading to high vaccination coverage. PPSV23 has not been universally included in NIP, except in the capital city, where PPSV23 has been funded by municipal immunization program for citizens aged ≥60 years.[106] One study reported the serotype distribution of IPD cases in adults aged ≥18 years hospitalized at five tertiary hospital in Bogotá in Colombia between 2011 and 2017. From 2011 to 2017, a decrease in IPD cases caused by PCV10 serotypes was observed over the study period, with an increase in additional PCV13 serotypes, including 3, 6A, and 19A. From 2015 to 2017, in adults aged ≥18 years, the most common serotypes were 3 (12.5%) and 19A (10.0%); and the proportions of IPD cases caused by PCV10, PCV 13, PPSV 23, and NVT serotypes were 22.5, 51.3, 58.8, and 35.0%, respectively.[106] Another study evaluated the serotype distribution of IPD cases across all age groups from 82 hospitals in Bogotá in Colombia, using a laboratory-based surveillance data. The study showed that the number of IPD cases caused by serotypes 19A and 3 increased in all age groups since the introduction of PCV10 in children.[107] In countries which introduced PCV10 as a pneumococcal vaccine for children, serotype 19A and 3 have emerged since the introduction.

South Africa introduced PCV7 into its immunization program in 2009, and PCV7 was replaced by PCV13 with a 2 + 1 dosing schedule in 2011.[108] National laboratory-based surveillance for IPD across all age groups in South Africa began in 1999. One study evaluated effects of PCV in the prevention of PCV13 serotypes, using the national surveillance data between 2005 to 2019. In adults, IPD cases caused by PCV7 serotypes and additional PCV13 serotypes declined over the study period. In contrast, IPD cases caused by NVT serotypes have increased, especially for adults aged ≥65 years. In adults aged ≥65 years, the reduction in overall IPD cases was smaller than that in younger groups due to the large increase in IPD cases caused by non-PCV13 serotypes, especially serotype 8. In 2017–2019, the most common serotypes were 8 (15.1%), 12F (8.8%), 3 (8.4%), and 19A (7.0%) in adults aged 45–64 years, and 8 (17.8%), 3 (11.2%), and 19A (8.6%) in adults aged ≥65 years. PCV13, PCV15, PCV20, PPSV23, and PCV21 accounted for 30.3, 34.3, 63.7, 70.1, and 70.6%, respectively, in adults aged 45–64 years; and PCV13, PCV15, PCV20, PPSV23, and PCV21 accounted for 33.3, 38.9, 69.4, 71.6, and 74.3%, respectively, in adults aged ≥65 years in 2017–2019.[108] Similar to European countries, IPD cases caused by serotype 8 emerged in South Africa following the introduction of PCV13 for children.

To summarize, in countries where PCV was not included in pediatric NIP, the proportion of IPD cases by PCV serotype was high in both children and adults. Serotypes 3 and 19A have emerged, especially in countries where PCV10 is used. In countries without immunization programs or free access to pneumococcal vaccines, the initial step is to include pneumococcal vaccines in NIP and increase vaccine coverage among target populations, even though this may be not easy to achieve. Epidemiological studies of pneumococcal disease in adults have been limited in these countries, and it is necessary to develop surveillance systems to implement in future pneumococcal vaccination strategies.

Clinical characteristics of pneumococcal serotypes in adults

PCV7 was developed to include pneumococcal serotypes that cover approximately 80% of serotypes causing IPD in children.[109,110] After its introduction, higher-valency PCVs were developed and introduced throughout the world. Selecting appropriate serotypes to include in vaccination strategies is important to prevent diseases effectively. In addition to the latest information on serotype distribution, evidence of which serotypes are associated with more severe disease is important.

Serotype 3 has a thick capsular membrane, and its colonies have a mucoid appearance on blood agar. This facilitates high-level virulence and prevents phagocytosis.[111] Serotype 3 has been shown to elicit lower antibody levels in response to PCV13 and PCV20 compared with other serotypes. Moreover, these antibody levels decline more rapidly over time,[112,113] further complicating efforts to reduce the disease burden. Based on clinical presentation, serotype 3 was reported to be associated with high mortality among adults,[106,114–120] meningitis,[121] shock,[122] pneumonia with complications, including renal and respiratory failure,[123] empyema,[124] and necrotizing pneumonia.[125] One study reported that IPD caused by serotype 3 was independently associated with major adverse cardiovascular events (MACE).[126] Additionally, serotype 3 was associated with lower quality-adjusted life years (QALY) among patients aged ≥65 years.[127]

Another study evaluated disease severity among patients with CAP, and it showed that compared with patients with non-PCV13 CAP, those with PCV13 serotype CAP exhibited higher 30-day mortality (adjusted odds ratio: 1.70).[55] Among other PCV13 serotypes, 19A, 19F, and 6A have been reported to be associated with higher mortality in several studies.[106,114,119–121,128,129] Serotype 19A was associated with shock[130] and empyema.[124] Serotype 19F was associated with meningitis[121] and higher QALY loss in patients aged >65 years.[127]

Among unique PPSV23 serotypes, serotype 8 has primarily emerged in Europe, as mentioned above. Serotype 8 has been reported to be associated with a high case fatality rate in

patients with meningitis and invasive disease.[115,129,131,132] Serotype 9N has been reported to be associated with high mortality[114,115,128] and MACE.[126] Serotype 11A was associated with higher mortality in patients with IPD.[116,121] Since the introduction of PCV13 into pediatric NIP, the incidence of pneumococcal disease due to non-PCV13 serotypes has been increasing, and some non-PCV13 serotypes have been reported to be associated with severe diseases. Therefore, it is necessary to monitor these serotypes.

Development and implementation of pneumococcal vaccine from perspective of pneumococcal serotypes

Knowledge on the global serotype distribution in adults and severity of each pneumococcal serotype raises several issues regarding pneumococcal vaccine development and vaccination strategies.

Serotype 3 has been persistent among adult pneumococcal diseases even in countries with well-established nationwide PCV13 immunization programs for children, which indicates that there has been insufficient herd protection against serotype 3 among adults. The possible reasons are as follows: immunogenicity data showed that antibody levels and opsonophagocytic titers against serotype 3 were lower than those generated by other serotypes[113,133,134]; low levels of immunogenicity could lead to low mucosal immunity and low-level effectiveness against nasopharyngeal carriage[135,136] Furthermore, several studies estimated that higher titers of antibodies were required to protect against IPD caused by serotype 3.[137,138] In addition, pneumococcal diseases caused by serotype 3 may be more severe than those due to other serotypes. Thus, direct vaccination using a pneumococcal vaccine that is effective against serotype 3 should be considered. Clinical trials comparing PCV15 with PCV13 reported that PCV15 led to higher antibody levels for serotype 3 than PCV13.[139,140] PCV15 may be an optional pneumococcal vaccine, especially in countries where pneumococcal disease caused by serotype 3 has constituted a burden.

Although vaccination policies differ depending on the country, several countries have introduced PPSV23 into NIP for older people and adults at risk. However, the incidence or proportion of pneumococcal diseases caused by serotypes included in PPSV23 has not declined, possibly because of the limitations of the direct effectiveness of PPSV23 or low vaccination coverage among target populations. By reviewing the latest serotype distribution, the introduction of high-valency PCV may reduce the incidence of pneumococcal diseases among adults. However, increasing the valency of pneumococcal vaccines has consistently been associated with reduced antibody levels[141] due to antigen competition. This competition imposes a limitation on the number of antigens that can be included in a single vaccine formulation, highlighting the inherent challenges in current vaccine development strategies. Furthermore, the introduction of high-valency PCVs may lead to serotype replacement by pneumococcal serotypes that are currently uncommon or of limited clinical significance. To address the constraints of serotype inclusion and potential for future serotype replacement, the development of new-generation pneumococcal vaccines is required, such as protein-based and whole-cell pneumococcal vaccines, which are capable of providing serotype-unspecific protection.[142,143] The proportion of vaccine-covered serotypes is comparable among countries with similar pediatric pneumococcal vaccination strategies; however, remaining or emerging serotypes differ. In the Western US and Canada, serotype 4 has emerged, especially among the unhoused individuals or those showing drug/alcohol abuse. Unhoused individuals reportedly face a higher pneumococcal disease risk due to limited access to vaccinations, close contact with others in shelters, and an increased rate of substance abuse.[144,145] Moreover, drug abuse is associated with a high risk of causing human immunodeficiency virus (HIV) infection, and certain substances, such as crack cocaine, have been reported to suppress the immune response. Additionally, the use of injectable drugs in unsanitary environments or through improper injection techniques can result in tissue damage, causing localized inflammation and increasing the risk of bacterial infections.[146–149] Serotype 4 is not covered by PCV21; therefore, it is necessary to use pneumococcal vaccines, including serotype 4, depending on the target populations in these countries. Serotype 8 has emerged in European countries, especially in the UK, Spain, and Italy, and South Africa, and pneumococcal disease caused by serotype 8 can be invasive. In countries where serotype 8 has emerged, direct vaccination with pneumococcal vaccines including serotype 8 should be considered. The incidence of pneumococcal diseases caused by serotype 19A has been increasing in countries where PCV10 has been introduced. It may be more favorable to introduce higher-valency PCVs such as PCV13, if possible.

Pneumococcal vaccine is essential for addressing the burdens of pneumococcal disease. However, several challenges require attention. First, it is necessary to increase vaccination uptake among adults, particularly older adults and individuals with a high pneumococcal disease risk. Efforts should prioritize raising awareness and improving accessibility, especially for high-risk groups of people and vulnerable populations. The following interventions have been reported as effective to increase vaccine uptake: invitations and reminders via telephone, letters, and e-mails; reminders targeting at healthcare staff; educational programs about vaccination; and combining multiple interventions, which has proven to be the most effective strategy across diverse populations.[150] These approaches can be valuable tools to enhance vaccine coverage. From the perspectives of policymakers and healthcare systems, addressing systemic barriers to vaccination, such as cost, logistical challenges, and disparities in healthcare access, is crucial. It is essential to recognize that availability and accessibility are distinct concepts. Additionally, strengthening pneumococcal disease surveillance systems to monitor vaccine uptake and the disease burden in real-time is essential. Improved data collection will facilitate more precise interventions and enhance epidemiological insights.

Conclusion

Even though PCV has been successfully introduced into NIP for children and reduced pneumococcal diseases caused by PCV serotypes, the burden of PCV13 serotypes, especially serotype 3, remains. The proportion of pneumococcal diseases

caused by non-PCV13 serotypes has increased along with a reduction in pneumococcal diseases caused by PCV13 serotypes, and direct vaccination of adults with novel PCV has the potential to prevent residual pneumococcal diseases in adults. However, residual and emerging serotypes differ across countries. Therefore, pneumococcal vaccination strategies should be determined based on local epidemiological data.

The incidence of IPD cases by vaccine-covered serotypes and the serotype distribution in adults differs by country and has been changing over time, even within countries. To determine the optimal pneumococcal vaccination strategy for adults, the latest epidemiological information on the local serotype distribution in adult pneumococcal diseases is essential. Thus, ongoing surveillance to investigate the incidence and proportion of pneumococcal diseases by serotype should be maintained, and the development of surveillance is an urgent issue in countries where surveillance systems have yet to be established.

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Abbreviations

PCV13	13-valent pneumococcal conjugate vaccine
PCV15	15-valent pneumococcal conjugate vaccine
PCV20	20-valent pneumococcal conjugate vaccine
PCV21	21-valent pneumococcal conjugate vaccine
PPSV23	23-valent pneumococcal polysaccharide vaccine
PCV7	7-valent pneumococcal conjugate vaccine
PCV10	10-valent pneumococcal conjugate vaccine
ABCs	Active Bacterial Core surveillance
ACIP	Advisory Committee on Immunization Practices
CAP	community-acquired pneumonia
HIV	human immunodeficiency virus
IPD	nvasive pneumococcal disease
MACE	major adverse cardiovascular events
NIP	national immunization program
NIPD	noninvasive pneumococcal disease
NNDSS	National Notifiable Disease Surveillance System
NVT	non-vaccine type
PCV	pneumococcal conjugate vaccine
QALY	quality-adjusted life years

References

1. Drijkoningen JJ, Rohde GG. Pneumococcal infection in adults: burden of disease. Clin Microbiol Infect. 2014;20(Suppl 5):45–51. doi:10.1111/1469-0691.12461.
2. O'Brien KL, Wolfson LJ, Watt JP, Henkle E, Deloria-Knoll M, McCall N, Lee E, Mulholland K, Levine OS, Cherian T, et al. Burden of disease caused by Streptococcus pneumoniae in children younger than 5 years: global estimates. Lancet. 2009;374 (9693):893–902. doi:10.1016/S0140-6736(09)61204-6.
3. World Health Organization. Pneumococcal disease. [accessed 2024 Oct 28]. https://www.who.int/teams/health-product-policy-and-standards/standards-and-specifications/norms-and-standards/vaccine-standardization/pneumococcal-disease.
4. Said MA, Johnson HL, Nonyane BA, Deloria-Knoll M, O'Brien KL, Hill PC, Team AAPBS. 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.
5. Ferreira-Coimbra J, Sarda C, Rello J. Burden of community-acquired pneumonia and unmet clinical needs. Adv Ther. 2020;37(4):1302–1318. doi:10.1007/s12325-020-01248-7.
6. Daniels CC, Rogers PD, Shelton CM. A review of pneumococcal vaccines: current polysaccharide vaccine recommendations and future protein antigens. J Pediatr Pharmacol Ther. 2016;21 (1):27–35. doi:10.5863/1551-6776-21.1.27.
7. Musher DM, Anderson R, Feldman C. The remarkable history of pneumococcal vaccination: an ongoing challenge. Pneumonia (Nathan). 2022;14(1):5. doi:10.1186/s41479-022-00097-y.
8. Whitney CG, Farley MM, Hadler J, Harrison LH, Bennett NM, Lynfield R, Reingold A, Cieslak PR, Pilishvili T, Jackson D, et al. Decline in invasive pneumococcal disease after the introduction of protein–polysaccharide conjugate vaccine. N Engl J Med. 2003;348 (18):1737–1746. doi:10.1056/NEJMoa022823.
9. Shiri T, Datta S, Madan J, Tsertsvadze A, Royle P, Keeling MJ, McCarthy ND, Petrou S. Indirect effects of childhood pneumococcal conjugate vaccination on invasive pneumococcal disease: a systematic review and meta-analysis. Lancet Glob Health. 2017;5 (1):e51–e59. doi:10.1016/S2214-109X(16)30306-0.
10. Tsaban G, Ben-Shimol S. Indirect (herd) protection, following pneumococcal conjugated vaccines introduction: a systematic review of the literature. Vaccine. 2017;35(22):2882–2891. doi:10.1016/j.vaccine.2017.04.032.
11. Pletz MW, Maus U, Krug N, Welte T, Lode H. Pneumococcal vaccines: mechanism of action, impact on epidemiology and adaption of the species. Int J Antimicrob Agents. 2008;32(3):199–206. doi:10.1016/j.ijantimicag.2008.01.021.
12. Grant LR, Slack MPE, Theilacker C, Vojicic J, Dion S, Reinert RR, Jodar L, Gessner BD. Distribution of serotypes causing invasive pneumococcal disease in older adults from high-income countries and impact of pediatric and adult vaccination policies. Vaccine. 2023;41(38):5662–5669. doi:10.1016/j.vaccine.2023.08.001.
13. Lansbury L, Lim B, McKeever TM, Lawrence H, Lim WS. Non-invasive pneumococcal pneumonia due to vaccine serotypes: a systematic review and meta-analysis. EClinicalMedicine. 2022;44:101271. doi:10.1016/j.eclinm.2022.101271.
14. Kobayashi M, Farrar JL, Gierke R, Britton A, Childs L, Leidner AJ, Campos-Outcalt D, Morgan RL, Long SS, Talbot HK, 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

Morb Mortal Wkly Rep. 2022;71(4):109–117. doi:10.15585/mmwr.mm7104a1.
15. Jennifer L, Farrar RG, Kristin L, Diepreye A, Lindsay Z, Adam L, Sarah S, Kobayashi M. Use of 20-valent pneumococcal conjugate vaccine among U.S. Children: updated recommendations of the advisory committee on immunization practices — United States, 2023. [accessed 2024 Oct 28]. https://stacks.cdc.gov/view/cdc/133252.
16. Centers for Disease Control and Prevention. Recommended vaccines for children. [accessed 2024 Oct 28]. https://www.cdc.gov/pneumococcal/vaccines/children.html.
17. Joint committee of the Japanese respiratory society, the Japanese association for infectious diseases, and the Japanese society for vaccinology. Approach to pneumococcal vaccination for adults 65 years and older. [accessed 2024 Oct 28]. https://www.kansensho.or.jp/uploads/files/guidelines/o65haienV/o65haienV_240930.pdf.
18. Kobayashi MLA, Gierke R, Farrar JL, Morgan RL, Campos-Outcalt D, Schechter R, Poehling KA, Long SS, Loehr J, Cohen AL, 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 Morb Mortal Wkly Rep. 2024;73(36):793–798. doi:10.15585/mmwr.mm7336a2.
19. Izurieta P, Bahety P, Adegbola R, Clarke C, Hoet B. Public health impact of pneumococcal conjugate vaccine infant immunization programs: assessment of invasive pneumococcal disease burden and serotype distribution. Expert Rev Vaccines. 2018;17(6):479–493. doi:10.1080/14760584.2018.1413354.
20. Lewnard JA, Hanage WP. Making sense of differences in pneumococcal serotype replacement. Lancet Infect Dis. 2019;19(6):e213–e220. doi:10.1016/S1473-3099(18)30660-1.
21. The World Bank. World bank country and lending groups. [accessed 2025 Jan 3]. https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups.
22. Centers for Disease Control and Prevention. Use of 61-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the advisory committee on immunization practices (ACIP). MMWR Morb Mortal Wkly Rep. 2012;13(1):232–235. doi:10.1111/ajt.12073.
23. Richter SS, Heilmann KP, Dohrn CL, Riahi F, Diekema DJ, Doern GV. Pneumococcal serotypes before and after introduction of conjugate vaccines, United States, 1999–20111. Emerg Infect Dis. 2013;19(7):1074–1083. doi:10.3201/eid1907.121830.
24. Ahmed SS, Pondo T, Xing W, McGee L, Farley M, Schaffner W, Thomas A, Reingold A, Harrison LH, Lynfield R, et al. Early impact of 13-valent pneumococcal conjugate vaccine use on invasive pneumococcal disease among adults with and without underlying medical conditions—United States. Clin Infect Dis. 2020 June 10. 70(12):2484–2492. doi:10.1093/cid/ciz739.
25. Gierke R. Current epidemiology of pneumococcal disease, United States- 2019 updates. Presented at the Advisory Committee of Immunization Practices meeting; 2021.June 25; [accessed 2024 Oct 28]; Atlanta (GA). https://stacks.cdc.gov/view/cdc/109108.
26. Matanock A, Lee G, Gierke R, Kobayashi M, Leidner A, Pilishvili T. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged ≥65 years: updated recommendations of the advisory committee on immunization practices. MMWR Morb Mortal Wkly Rep. 2019;68(46):1069–1075. doi:10.15585/mmwr.mm6846a5.
27. Gierke R. Current epidemiology of pneumococcal disease and pneumococcal vaccine coverage among adults, United States. Presented at the Advisory Committee of Immunization Practices meeting; 2021. Feb 25; [accessed 2024 Oct 28]; Atlanta (GA). https://stacks.cdc.gov/view/cdc/107067/cdc_107067_DS1.pdf.
28. Gierke R. Current epidemiology of pneumococcal disease among adults, United States. Presented at the Advisory Committee of Immunization Practices meeting; 2024. Feb 24; [Accessed 2024 Oct 28]; Atlanta (GA). https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-02-28-29/02-Pneumococcal-Gierke-508.pdf.
29. Beall B, Walker H, Tran T, Li Z, Varghese J, McGee L, Li Y, Metcalf BJ, Gierke R, Mosites E, et al. Upsurge of conjugate vaccine serotype 4 invasive pneumococcal disease clusters among adults experiencing homelessness in California, Colorado, and New Mexico. J Infect Dis. 2021;223(7):1241–1249. doi:10.1093/infdis/jiaa501.
30. Metcalf BJ, Chochua S, Walker H, Tran T, Li Z, Varghese J, Snippes Vagnone PM, Lynfield R, McGee L, Li Y, et al. Invasive pneumococcal strain distributions and isolate clusters associated with persons experiencing homelessness during 2018. Clin Infect Dis. 2021;72(12):e948–e956. doi:10.1093/cid/ciaa1680.
31. Isturiz R, Grant L, Gray S, Alexander-Parrish R, Jiang Q, Jodar L, Peyrani P, Ford KD, Pride MW, Self WH, et al. Expanded analysis of 20 pneumococcal serotypes associated with radiographically confirmed community-acquired pneumonia in hospitalized US adults. Clin Infect Dis. 2021;73(7):1216–1222. doi:10.1093/cid/ciab375.
32. Self WH, Johnson KD, Resser JJ, Whitney CG, Baughman A, Kio M, Grijalva CG, Traenkner J, Johnson J, Miller KF, et al. Prevalence, clinical severity, and serotype distribution of pneumococcal pneumonia among adults hospitalized with community-acquired pneumonia in Tennessee and Georgia, 2018–2022. Clin Infect Dis. 2024;79(4):838–847. doi:10.1093/cid/ciae316.
33. Griffith A, Golden AR, Lefebvre B, McGeer A, Tyrrell GJ, Zhanel GG, Kus JV, Hoang L, Minion J, Van Caeseele P, et al. Invasive pneumococcal disease surveillance in Canada, 2021–2022. Can Commun Dis Rep. 2024;50(5):121–134. doi:10.14745/ccdr.v50i05a02.
34. Public Health Agency of Canada. National Advisory Committee on Immunization (NACI). Update on the use of pneumococcal vaccines in adults 65 years of age and older —a public health perspective. [accessed 2025 Jan 3]. https://www.canada.ca/en/public-health/services/publications/healthy-living/update-on-the-use-of-pneumococcal-vaccines-in-adult.html.
35. Demczuk WHB, Martin I, Desai S, Griffith A, Caron-Poulin L, Lefebvre B, McGeer A, Tyrrell GJ, Zhanel GG, Gubbay J, et al. Serotype distribution of invasive Streptococcus pneumoniae in adults 65 years of age and over after the introduction of childhood 13-valent pneumococcal conjugate vaccination programs in Canada, 2010–2016. Vaccine. 2018;36(31):4701–4707. doi:10.1016/j.vaccine.2018.06.018.
36. LeBlanc JJ, ElSherif M, Ye L, MacKinnon-Cameron D, Ambrose A, Hatchette TF, Lang ALS, Gillis HD, Martin I, Demczuk W, et al. Streptococcus pneumoniae serotype 3 is masking PCV13-mediated herd immunity in Canadian adults hospitalized with community acquired pneumonia: a study from the serious outcomes surveillance (SOS) network of the Canadian immunization research network (CIRN). Vaccine. 2019;37(36):5466–5473. doi:10.1016/j.vaccine.2019.05.003.
37. Golden A, Griffith A, Demczuk W, Lefebvre B, McGeer A, Tyrrell G, Zhanel G, Kus J, Hoang L, Minion J, et al. Invasive pneumococcal disease surveillance in Canada, 2020. Can Commun Dis Rep. 2022;48(9):396–406. doi:10.14745/ccdr.v48i09a04.
38. Lemay JA, Ricketson LJ, Zwicker L, Kellner JD. Homelessness in adults with invasive pneumococcal disease (IPD) in Calgary, Canada. Open Forum Infect Dis. 2019;6(10). doi:10.1093/ofid/ofz362.
39. Kellner JD, Ricketson LJ, Demczuk WHB, Martin I, Tyrrell GJ, Vanderkooi OG. Whole-genome analysis of streptococcus pneumoniae serotype 4 causing outbreak of invasive pneumococcal disease, Alberta, Canada. Emerg Infect Dis. 2021;27(7):1867–1875. doi:10.3201/eid2707.204403.
40. Kobayashi MPT, Farrar JL. Pneumococcal vaccine for adults aged ≥19 years: recommendations of the advisory committee on immunization practices, United States, 2023. MMWR Recomm Rep. 2023;72:1–39.

41. Government of Canada. Pneumococcal vaccines: Canadian immunization guide. [accessed 2025 Feb 7]. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-16-pneumococcal-vaccine.html.
42. Public Health Argency of Canada. Summary of national advisory committee on immunization (NACI) statement of November 15, 2024. [accessed 2025 Feb 7]. https://www.canada.ca/content/dam/phac-aspc/documents/services/publications/vaccines-immunization/national-advisory-committee-immunization-summary-recommendations-use-pneumococcal-vaccines-adults-pneu-c-21/naci-summary-2024-11-15.pdf.
43. Ladhani SN, Collins S, Djennad A, Sheppard CL, Borrow R, Fry NK, Andrews NJ, Miller E, Ramsay ME. Rapid increase in non-vaccine serotypes causing invasive pneumococcal disease in England and Wales, 2000–17: a prospective national observational cohort study. Lancet Infect Dis. 2018;18(4):441–451. doi:10.1016/S1473-3099(18)30052-5.
44. de Miguel S, Domenech M, González-Camacho F, Sempere J, Vicioso D, Sanz JC, de Miguel S, Comas LG, Ardanuy C, Fenoll A, et al. Nationwide trends of invasive pneumococcal disease in Spain from 2009 Through 2019 in children and adults during the pneumococcal conjugate vaccine era. Clin Infect Dis. 2021;73(11):e3778–e3787. doi:10.1093/cid/ciaa1483.
45. Richter L, Schmid D, Kanitz EE, Zwazl I, Pöllabauer E, Jasinska J, Burgmann H, Kundi M, Wiedermann U. Invasive pneumococcal diseases in children and adults before and after introduction of the 10-valent pneumococcal conjugate vaccine into the Austrian national immunization program. PLOS ONE. 2019;14(1):e0210081. doi:10.1371/journal.pone.0210081.
46. Monali R, De Vita E, Mariottini F, Privitera G, Lopalco PL, Tavoschi L. Impact of vaccination on invasive pneumococcal disease in Italy 2007–2017: surveillance challenges and epidemiological changes. Epidemiol Infect. 2020;148:e187. doi:10.1017/S0950268820001077.
47. Nieddu F, Moriondo M, De Vitis E, Ricci S, Indolfi G, Resti M, Vocale C, Landini MP, Sartor A, Azzari C, et al. PCV13 serotype decrease in Italian adolescents and adults in the post-PCV13 era: herd protection from children or secular trend? Vaccine. 2017;35(11):1544–1550. doi:10.1016/j.vaccine.2017.01.064.
48. Hanquet G, Krizova P, Valentiner-Branth P, Ladhani SN, Nuorti JP, Lepoutre A, Mereckiene J, Knol M, Winje BA, Ciruela P, et al. Effect of childhood pneumococcal conjugate vaccination on invasive disease in older adults of 10 European countries: implications for adult vaccination. Thorax. 2019;74(5):473–482. doi:10.1136/thoraxjnl-2018-211767.
49. Hanquet G, Krizova P, Dalby T, Ladhani SN, Nuorti JP, Danis K, Mereckiene J, Knol MJ, Winje BA, Ciruela P, et al. Serotype replacement after introduction of 10-valent and 13-valent pneumococcal conjugate vaccines in 10 Countries, Europe. Emerg Infect Dis. 2022;28(1):137–138. doi:10.3201/eid2801.210734.
50. Moore MR, Link-Gelles R, Schaffner W, Lynfield R, Lexau C, Bennett NM, Petit S, Zansky SM, Harrison LH, Reingold A, et al. Effect of use of 13-valent pneumococcal conjugate vaccine in children on invasive pneumococcal disease in children and adults in the USA: analysis of multisite, population-based surveillance. Lancet Infect Dis. 2015;15(3):301–309. doi:10.1016/S1473-3099(14)71081-3.
51. Bertran M, D'Aeth JC, Abdullahi F, Eletu S, Andrews NJ, Ramsay ME, Litt DJ, Ladhani SN. Invasive pneumococcal disease 3 years after introduction of a reduced 1 + 1 infant 13-valent pneumococcal conjugate vaccine immunisation schedule in England: a prospective national observational surveillance study. Lancet Infect Dis. 2024 May. 24(5):546–556. doi:10.1016/S1473-3099(23)00706-5.
52. UK Health Security Agency. Immunisation against infectious disease– the green book; 2013 (updated 2020). [Accessed 2024 Oct 28]. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/857267/GB_Chapter_25_pneumococcal_January_2020.pdf.
53. Miller E, Andrews NJ, Waight PA, Slack MP, George RC. Herd immunity and serotype replacement 4 years after seven-valent pneumococcal conjugate vaccination in England and Wales: an observational cohort study. Lancet Infect Dis. 2011;11(10):760–768. doi:10.1016/S1473-3099(11)70090-1.
54. Waight PA, Andrews NJ, Ladhani SN, Sheppard CL, Slack MP, Miller E. Effect of the 13-valent pneumococcal conjugate vaccine on invasive pneumococcal disease in England and Wales 4 years after its introduction: an observational cohort study. Lancet Infect Dis. 2015;15(5):535–543. doi:10.1016/S1473-3099(15)70044-7.
55. Lansbury L, Lawrence H, McKeever TM, French N, Aston S, Hill AT, Pick H, Baskaran V, Edwards-Pritchard RC, Bendall L, et al. Pneumococcal serotypes and risk factors in adult community acquired pneumonia 2018–20: a multicentre UK cohort study. Lancet Reg Health Eur. 2024;37:100812. doi:10.1016/j.lanepe.2023.100812.
56. Pick H, Daniel P, Rodrigo C, Bewick T, Ashton D, Lawrence H, Baskaran V, Edwards-Pritchard RC, Sheppard C, Eletu SD, et al. Pneumococcal serotype trends, surveillance and risk factors in UK adult pneumonia, 2013–18. Thorax. 2020;75(1):38–49. doi:10.1136/thoraxjnl-2019-213725.
57. Hyams C, Lahuerta M, Theilacker C, King J, Adegbite D, McGuinness S, Grimes C, Campling J, Southern J, Pride MW, et al. Surveillance of pneumococcal serotypes in adults hospitalised with acute lower respiratory tract infection in Bristol, UK. Vaccine. 2024;42(7):1599–1607. doi:10.1016/j.vaccine.2024.02.007.
58. Fernández-Delgado L, Càmara J, González-Díaz A, Grau I, Shoji H, Tubau F, Martí S, Domínguez MÁ, Carratalà J, Yuste J, et al. Serotypes in adult pneumococcal pneumonia in Spain in the era of conjugate vaccines. Microorganisms. 2021;9(11):2245. doi:10.3390/microorganisms9112245.
59. Ansaldi F, de Florentis D, Canepa P, Bandettini R, Diana MC, Martini M, Durando P, Icardi G. Epidemiological changes after PCV7 implementation in Italy: perspective for new vaccines. Hum Vaccin. 2011 Jan. 7(sup1):211–216. doi:10.4161/hv.7.0.14602.
60. Ouldali N, Varon E, Levy C, Angoulvant F, Georges S, Ploy MC, Kempf M, Cremniter J, Cohen R, Bruhl DL, et al. Invasive pneumococcal disease incidence in children and adults in France during the pneumococcal conjugate vaccine era: an interrupted time-series analysis of data from a 17-year national prospective surveillance study. Lancet Infect Dis. 2021;21(1):137–147. doi:10.1016/S1473-3099(20)30165-1.
61. Cohen R, Levy C, de La Rocque F, Gelbert N, Wollner A, Fritzell B, Bonnet E, Tetelboum R, Varon E. Impact of pneumococcal conjugate vaccine and of reduction of antibiotic use on nasopharyngeal carriage of nonsusceptible pneumococci in children with acute otitis media. Pediatr Infect Dis J. 2006;25(11):1001–1007. doi:10.1097/01.inf.0000243163.85163.a8.
62. van der Linden M, Imöhl M, Perniciaro S, Melo-Cristino J. 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.
63. Ellingson MK, Weinberger DM, van der Linden M, Perniciaro S. Potential impact of higher-valency pneumococcal conjugate vaccines among adults in different localities in Germany. J Infect Dis. 2024;229(6):1669–1673. doi:10.1093/infdis/jiad538.
64. Forstner C, Kolditz M, Kesselmeier M, Ewig S, Rohde G, Barten-Neiner G, Rupp J, Witzenrath M, Welte T, Pletz MW, et al. Pneumococcal conjugate serotype distribution and predominating role of serotype 3 in German adults with community-acquired pneumonia. Vaccine. 2020;38(5):1129–1136. doi:10.1016/j.vaccine.2019.11.026.
65. Corcoran M, Vickers I, Mereckiene J, Murchan S, Cotter S, Fitzgerald M, Mcelligott M, Cafferkey M, O'FLANAGAN D, Cunney R, et al. The epidemiology of invasive pneumococcal disease in older adults in the post-pcv era. Has there been a herd effect? Epidemiol Infect. 2017;145(11):2390–2399. doi:10.1017/S0950268817001194.

66. Palmborg A, Skovdal M, Molden T, Ahman H, Chen L, Banefelt J, Melo-Cristino J. Invasive pneumococcal disease among the elderly in the later era of paediatric pneumococcal conjugate vaccination—a longitudinal study over 10 years based on public surveillance data in the Nordics. PLOS ONE. 2023;18(6):e0287378. doi:10.1371/journal.pone.0287378.
67. Naucler P, Galanis I, Morfeldt E, Darenberg J, Örtqvist Å, Henriques-Normark B. Comparison of the impact of pneumococcal conjugate vaccine 10 or pneumococcal conjugate vaccine 13 on invasive pneumococcal disease in equivalent populations. Clin Infect Dis. 2017;65(11):1780–1790.e1. doi:10.1093/cid/cix685.
68. Hansen K, Rünow E, Torisson G, Theilacker C, Palmborg A, Pan K, Jiang Q, Southern J, Beavon R, Gessner BD, et al. Radiographically confirmed community-acquired pneumonia in hospitalized adults due to pneumococcal vaccine serotypes in Sweden, 2016–2018—The ECAPS study. Front Public Health. 2023;11:1086648. doi:10.3389/fpubh.2023.1086648.
69. Grivea IN, Priftis KN, Giotas A, Kotzia D, Tsantouli AG, Douros K, Michoula AN, Syrogiannopoulos GA. Dynamics of pneumococcal carriage among day-care center attendees during the transition from the 7-valent to the higher-valent pneumococcal conjugate vaccines in Greece. Vaccine. 2014;32(48):6513–6520. doi:10.1016/j.vaccine.2014.09.016.
70. Isaacman DJ, McIntosh ED, Reinert RR. Burden of invasive pneumococcal disease and serotype distribution among streptococcus pneumoniae isolates in young children in Europe: impact of the 7-valent pneumococcal conjugate vaccine and considerations for future conjugate vaccines. Int J Infect Dis. 2010;14(3):e197–209. doi:10.1016/j.ijid.2009.05.010.
71. Liapikou A, Konstantinidis A, Kossyvaki V, Skiadas J, Menegas D, Méndez C, Beavon R, Begier E, Gessner BD, Milionis H, et al. Pneumococcal serotypes in adults hospitalized with community-acquired pneumonia in Greece using urinary antigen detection tests: the EGNATIA study, November 2017 – April 2019. Hum Vaccin Immunother. 2022;18(5):2079923. doi:10.1080/21645515.2022.2079923.
72. Regev-Yochay G, Katzir M, Strahilevitz J, Rahav G, Finn T, Miron D, Maor Y, Chazan B, Schindler Y, Dagan R, et al. The herd effects of infant PCV7/PCV13 sequential implementation on adult invasive pneumococcal disease, six years post implementation; a nationwide study in Israel. Vaccine. 2017;35(18):2449–2456. doi:10.1016/j.vaccine.2017.03.031.
73. Regev-Yochay G, Chowers M, Chazan B, Gonzalez E, Gray S, Zhang Z, Pride M. Distribution of 13-valent pneumococcal conjugate vaccine serotype streptococcus pneumoniae in adults 50 years and older presenting with community-acquired pneumonia in Israel. Hum Vaccin Immunother. 2018;14(10):2527–2532. doi:10.1080/21645515.2018.1475811.
74. Regev-Yochay G, Paran Y, Bishara J, Oren I, Chowers M, Tziba Y, Istomin V, Weinberger M, Miron D, Temper V, et al. Early impact of PCV7/PCV13 sequential introduction to the national pediatric immunization plan, on adult invasive pneumococcal disease: a nationwide surveillance study. Vaccine. 2015;33(9):1135–1142. doi:10.1016/j.vaccine.2015.01.030.
75. National Institute of Infectious Diseases. Fact sheet of the 23-valent pneumococcal polysaccharide vaccine 2018. [Accessed 2024 Oct 28]. https://www.mhlw.go.jp/file/05-Shingikai-10601000-Daijinkanboukouseikagakuka-Kouseikagakuka/0000184910_1.pdf.
76. Tamura K, Chang B, Shimbashi R, Watanabe H, Tanabe Y, Kuronuma K, Oshima K, Maruyama T, Fujita J, Abe S, et al. Dynamic changes in clinical characteristics and serotype distribution of invasive pneumococcal disease among adults in Japan after introduction of the pediatric 13-valent pneumococcal conjugate vaccine in 2013–2019. Vaccine. 2022;40(24):3338–3344. doi:10.1016/j.vaccine.2022.04.062.
77. Maeda H, Gopal Dhoubhadel B, Sando E, Suzuki M, Furumoto A, Asoh N, Yaegashi M, Aoshima M, Ishida M, Hamaguchi S, et al. Long-term impact of pneumococcal conjugate vaccines for children on adult pneumococcal pneumonia in Japan: two multicenter observational studies from 2011 to 2020. Vaccine. 2022;40(37):5504–5512. doi:10.1016/j.vaccine.2022.07.041.
78. Ministry of Health, Labour and Welfare. Materials at the 57th meeting of the subcommittee on immunization and vaccine of the health science council (held on July 31, 2024). 2024. [accessed 2024 Oct 28]. https://www.mhlw.go.jp/content/10900000/001281992.pdf.
79. Kim SH, Bae IK, Park D, Lee K, Kim NY, Song SA, Kim HR, Jeon GW, Urm S-H, Shin JH, et al. Serotype distribution and antimicrobial resistance of streptococcus pneumoniae isolates causing invasive and noninvasive pneumococcal diseases in Korea from 2008 to 2014. Biomed Res Int. 2016;2016:1–7. doi:10.1155/2016/6950482.
80. Kim GR, Kim EY, Kim SH, Lee HK, Lee J, Shin JH, Kim YR, Song SA, Jeong J, Uh Y, et al. Serotype distribution and antimicrobial resistance of Streptococcus pneumoniae causing invasive pneumococcal disease in Korea between 2017 and 2019 after introduction of the 13-valent pneumococcal conjugate vaccine. Ann Lab Med. 2023;43(1):45–54. doi:10.3343/alm.2023.43.1.45.
81. Chien YC, Lee YL, Liu PY, Lu MC, Shao PL, Lu PL, Cheng S-H, Lin C-Y, Wu T-S, Yen M-Y, et al. National surveillance of antimicrobial susceptibilities to dalbavancin, telavancin, tedizolid, eravacycline, omadacycline and other comparator antibiotics and serotype distribution of invasive Streptococcus pneumoniae isolates in adults: results from the surveillance of multicenter antimicrobial resistance in Taiwan (SMART) programme in 2017-2020. J Glob Antimicrob Resist. 2021;26:308–316. doi:10.1016/j.jgar.2021.07.005.
82. Jayasinghe S, Menzies R, Chiu C, Toms C, Blyth CC, Krause V, McIntyre P. Long-term impact of a "3 + 0" schedule for 7- and 13-valent pneumococcal conjugate vaccines on invasive pneumococcal disease in Australia, 2002–2014. Clin Infect Dis. 2017;64(2):175–183. doi:10.1093/cid/ciw720.
83. Menzies R, Stein AN, Booy R, Van Buynder PG, Litt J, Cripps AW. The impact of the changing pneumococcal national immunisation program among older australians. Vaccine. 2021;39(4):720–728. doi:10.1016/j.vaccine.2020.12.025.
84. Higgs C, Kumar LS, Stevens K, Strachan J, Sherry NL, Horan K, Zhang J, Stinear TP, Howden BP, Gorrie CL, et al. Population structure, serotype distribution and antibiotic resistance of Streptococcus pneumoniae causing invasive disease in Victoria, Australia. Microb Genom. 2023;9(7). doi:10.1099/mgen.0.001070.
85. Anglemyer A, McNeill A, DuBray K, Sonder GJB, Walls T. Invasive pneumococcal disease: concerning trends in serotype 19A notifications in New Zealand. Clin Infect Dis. 2022;74(10):1859–1861. doi:10.1093/cid/ciab766.
86. Healthify. Pneumococcal vaccine. [accessed 2024 Oct 28]. https://www.healthnavig ator.org.nz/medicines/p/pneumococcal-vaccine/.
87. Infectious diseases intelligence and surveillance. Invasive pneumococcal disease biannual report July 2022 to June 2023. [accessed 2024 Oct 28]. https://www.esr.cri.nz/digital-library/invasive-pneumococcal-disease-biannual-report-july-2022-to-june-2023/.
88. Men W, Dong Q, Shi W, Yao K. Serotype distribution and antimicrobial resistance patterns of invasive pneumococcal disease isolates from children in mainland China—a systematic review. Braz J Microbiol. 2020 June. 51(2):665–672. doi:10.1007/s42770-019-00198-9.
89. Wang J, Q-S W, Lu J, Y-H N, Zhou F. Low vaccination coverage of pneumococcal conjugate vaccines (PCVs) in Shanghai, China: a database analysis based on birth cohorts from 2012 to 2020. Vaccine. 2021;39(42):6189–6194. doi:10.1016/j.vaccine.2021.09.011.
90. Li MC, Wang Y, Zhang H, Liu Y, Chen XJ, Yang HW, Ma P, Wang D-C, Zhang B-C, Dong A-Y, et al. Serotype distribution and clinical characteristics associated with streptococcus pneumoniae among Chinese children and adults with invasive pneumococcal disease: a multicenter observational study. Hum Vaccin Immunother. 2021;17(1):146–156. doi:10.1080/21645515.2020.1757996.

91. Miao C, Yan Z, Chen C, Kuang L, Ao K, Li Y, Li J, Huang X, Zhu X, Zhao Y, et al. Serotype, antibiotic susceptibility and whole-genome characterization of Streptococcus pneumoniae in all age groups living in Southwest China during 2018–2022. Front Microbiol. 2024;15:1342839. doi:10.3389/fmicb.2024.1342839.
92. Sia SB, Lagrada ML, Gayeta JM, Masim MAL, Abad JP, Magbanua MA, Ablola FB. Serotype distribution and antimicrobial resistance of Streptococcus pneumoniae in the Philippines, 2012–2018. West Pac Surveill Response J. 2021;12(4):1–8. doi:10.5365/wpsar.2021.12.4.834.
93. Manoharan A, Jayaraman R. Pneumococcal vaccines. Indian J Med Microbiol. 2018;36(4):465–474. doi:10.4103/ijmm.IJMM_18_442.
94. Singh J, Sundaresan S, Manoharan A, Shet A. Serotype distribution and antimicrobial susceptibility pattern in children ≤5 years with invasive pneumococcal disease in India – a systematic review. Vaccine. 2017;35(35):4501–4509. doi:10.1016/j.vaccine.2017.06.079.
95. GERIATRIC SOCIETY OF INDIA. Indian recommendations for vaccination in older adults. [accessed 2024 Oct 28]. http//www.geriatricindia.com/publications.html.com.
96. Jayaraman R, Varghese R, Kumar JL, Neeravi A, Shanmugasundaram D, Ralph R. Invasive pneumococcal disease in Indian adults: 11 years' experience. J Microbiol Immunol Infect. 2019;52(5):736–742. doi:10.1016/j.jmii.2018.03.004.
97. Çelik M, Abdullayeva M, Alp-Çavuş S. Nasopharyngeal carriage and serotype distribution of Streptococcus pneumoniae in elderly: a cross-sectional study in Turkey. Infect Dis Clin Microbiol. 2022;4(2):99–106. doi:10.36519/idcm.2022.120.
98. Hascelik G, Soyletir G, Gulay Z, Sancak B, Yaman A, Gurler N, Aydemir SS, Bayramoglu G, Aydin F, Cekin Y, et al. Serotype distribution of Streptococcus pneumoniae and pneumococcal vaccine coverage in adults in Turkey between 2015 and 2018. Ann Med. 2023;55(1):266–275. doi:10.1080/07853890.2022.2160877.
99. Pan-American Health Organization (PAHO). Surveillance of bacterial pneumonia and meningitis in children aged under 5 years field guide. 2010. [accessed 2024 Oct 28]. https://iris.paho.org/handle/10665.2/49153.
100. Agudelo CI, Castañeda-Orjuela C, Brandileone M, Echániz-Aviles G, Almeida SCG, Carnalla-Barajas MN. The direct effect of pneumococcal conjugate vaccines on invasive pneumococcal disease in children in the Latin American and Caribbean region (SIREVA 2006–17): a multicentre, retrospective observational study. The Lancet Infect Dis. 2021;21(3):405–417.
101. Bardach A, Ruvinsky S, Palermo MC, Alconada T, Sandoval MM, Brizuela ME, Wierzbicki ER, Cantos J, Gagetti P, Ciapponi A, et al. Invasive pneumococcal disease in Latin America and the Caribbean: serotype distribution, disease burden, and impact of vaccination. A systematic review and meta-analysis. PLOS ONE. 2024;19(6):e0304978. doi:10.1371/journal.pone.0304978.
102. Brandileone MC, Almeida SCG, Minamisava R, Andrade AL. Distribution of invasive Streptococcus pneumoniae serotypes before and 5 years after the introduction of 10-valent pneumococcal conjugate vaccine in Brazil. Vaccine. 2018;36(19):2559–2566. doi:10.1016/j.vaccine.2018.04.010.
103. Andrade AL, Minamisava R, Policena G, Cristo EB, Domingues CM, de Cunto Brandileone MC, Almeida SCG, Toscano CM, Bierrenbach AL. Evaluating the impact of PCV-10 on invasive pneumococcal disease in Brazil: a time-series analysis. Hum Vaccin Immunother. 2016;12(2):285–292. doi:10.1080/21645515.2015.1117713.
104. Carnalla-Barajas MN, Soto-Noguerón A, Sánchez-Alemán MA, Solórzano-Santos F, Velazquez-Meza ME, Echániz-Aviles G, Márquez-Díaz F, Martínez-Medina L, Olvera-Herrera ME, Miranda-Novales MG. Changing trends in serotypes of S. pneumoniae isolates causing invasive and non-invasive diseases in unvaccinated population in Mexico (2000-2014). Int J Infect Dis. 2017;58:1–7. doi:10.1016/j.ijid.2017.02.005.
105. Camacho-Moreno G, Leal AL, Patino-Nino J, Vasquez-Hoyos P, Gutierrez I, Beltran S, Álvarez-Olmos MI, Mariño A-C, Londoño-Ruiz JP, Barrero R, et al. Serotype distribution, clinical characteristics, and antimicrobial resistance of pediatric invasive pneumococcal disease in Colombia during PCV10 mass vaccination (2017–2022). Front Med. 2024;11:1380125. doi:10.3389/fmed.2024.1380125.
106. Castro ALL, Camacho-Moreno G, Montanez-Ayala A, Varon-Vega F, Alvarez-Rodriguez JC, Valderrama-Beltran S, Ariza BE, Pancha O, Santana AY, Flórez NS, et al. Invasive Pneumococcal Disease Characterization in Adults and Subgroups aged <60 years and >/= 60 years in Bogota, Colombia. IJID Reg. 2022;3:293–299. doi:10.1016/j.ijregi.2022.04.007.
107. Severiche-Bueno DF, Severiche-Bueno DF, Bastidas A, Caceres EL, Silva E, Lozada J, Gomez S, Vargas H, Viasus D, Reyes LF, et al. Burden of invasive pneumococcal disease (IPD) over a 10-year period in Bogotá, Colombia. Int J Infect Dis. 2021;105:32–39. doi:10.1016/j.ijid.2021.02.031.
108. von Gottberg A, Kleynhans J, de Gouveia L, Tempia S, Meiring S, Quan V, von Gottberg A, de Gouveia L, du Plessis M, von Mollendorf C, et al. Long-term effect of pneumococcal conjugate vaccines on invasive pneumococcal disease incidence among people of all ages from national, active, laboratory-based surveillance in South Africa, 2005-19: a cohort observational study. Lancet Glob Health. 2024;12(9):e1470–e1484. doi:10.1016/S2214-109X(24)00263-8.
109. Black S, Shinefield H, Fireman B, Lewis E, Ray P, Hansen JR, Elvin L, Ensor KM, Hackell J, Siber G, et al. Efficacy, safety and immunogenicity of heptavalent pneumococcal conjugate vaccine in children. Northern California kaiser permanente vaccine study center group. Pediatr Infect Dis J. 2000;19(3):187–195. doi:10.1097/00006454-200003000-00003.
110. Hausdorff WP, Bryant J, Paradiso PR, Siber GR. Which pneumococcal serogroups cause the most invasive disease: implications for conjugate vaccine formulation and use, part I. Clin Infect Dis. 2000;30(1):100–121. doi:10.1086/313608.
111. Luck JN, Tettelin H, Orihuela CJ. Sugar-coated killer: serotype 3 pneumococcal disease. Front Cell Infect Microbiol. 2020;10:613287.
112. Essink B, Sabharwal C, Cannon K, Frenck R, Lal H, Xu X, Sundaraiyer V, Peng Y, Moyer L, Pride MW, 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):390–398. doi:10.1093/cid/ciab990.
113. van Deursen AMM, van Houten MA, Webber C, Patton M, Scott DA, Patterson S. Immunogenicity of the 13-valent pneumococcal conjugate vaccine in older adults with and without comorbidities in the community-acquired pneumonia immunization trial in adults (CAPiTA). Clin Infect Dis. 2017;65(5):787–795.
114. Weinberger DM, Harboe ZB, Sanders EA, Ndiritu M, Klugman KP, Rückinger S, Dagan R, Adegbola R, Cutts F, Johnson H, et al. Association of serotype with risk of death due to pneumococcal pneumonia: a meta-analysis. Clin Infect Dis. 2010;51(6):692–699. doi:10.1086/655828.
115. Amin-Chowdhury Z, Collins S, Sheppard C, Litt D, Fry NK, Andrews N, Ladhani SN. Characteristics of invasive pneumococcal disease caused by emerging serotypes after the introduction of the 13-valent pneumococcal conjugate vaccine in England: a prospective observational cohort study, 2014–2018. Clin Infect Dis. 2020 Nov 5. 71(8):e235–e243. doi:10.1093/cid/ciaa043.
116. Houseman C, Chapman KE, Manley P, Gorton R, Wilson D, Hughes GJ. Decreasing case fatality rate following invasive pneumococcal disease, North East England, 2006–2016. Epidemiol Infect. 2019;147:e175. doi:10.1017/S0950268819000657.
117. Luján M, Gallego M, Belmonte Y, Fontanals D, Vallès J, Lisboa T, Rello J. Influence of pneumococcal serotype group on outcome in adults with bacteraemic pneumonia. Eur Respir J. 2010;36(5):1073–1079. doi:10.1183/09031936.00176309.

118. Savrasova L, Krumina A, Cupeca H, Zeltina I, Villerusha A, Grope I, Viksna L, Dimina E, Balasegaram S. Invasive pneumococcal disease in Latvia in PCV10 vaccination Era, 2012–2018. Front Pediatr. 2021;9:532489. doi:10.3389/fped.2021.532489.
119. Meichtry J, Born R, Küffer M, Zwahlen M, Albrich WC, Brugger SD, Mühlemann K, Hilty M. Serotype epidemiology of invasive pneumococcal disease in Swiss adults: a nationwide population-based study. Vaccine. 2014;32(40):5185–5191. doi:10.1016/j.vaccine.2014.07.060.
120. Hughes GJ, Wright LB, Chapman KE, Wilson D, Gorton R. Serotype-specific differences in short- and longer-term mortality following invasive pneumococcal disease. Epidemiol Infect. 2016;144(12):2654–2669. doi:10.1017/S0950268816000856.
121. Grabenstein JD, Musey LK. Differences in serious clinical outcomes of infection caused by specific pneumococcal serotypes among adults. Vaccine. 2014;32(21):2399–2405. doi:10.1016/j.vaccine.2014.02.096.
122. Garcia-Vidal C, Ardanuy C, Tubau F, Viasus D, Dorca J, Liñares J, Gudiol F, Carratala J. Pneumococcal pneumonia presenting with septic shock: host- and pathogen-related factors and outcomes. Thorax. 2010;65(1):77–81. doi:10.1136/thx.2009.123612.
123. Torres A, Menéndez R, España PP, Fernández-Villar JA, Marimón JM, Cilloniz C, Méndez R, Egurrola M, Botana-Rial M, Ercibengoa M, et al. The evolution and distribution of pneumococcal serotypes in adults hospitalized with community-acquired pneumonia in Spain using a serotype-specific urinary antigen detection test: the CAPA study, 2011–2018. Clin Infect Dis. 2021;73(6):1075–1085. doi:10.1093/cid/ciab307.
124. Bewick T, Sheppard C, Greenwood S, Slack M, Trotter C, George R, Lim WS. Serotypes associated with the development of pneumococcal para-pneumonic effusion in adults. Eur Respir J. 2013;42(3):733–741. doi:10.1183/09031936.00144712.
125. Pande A, Nasir S, Rueda AM, Matejowsky R, Ramos J, Doshi S, Kulkarni P, Musher DM. The incidence of necrotizing changes in adults with pneumococcal pneumonia. Clin Infect Dis. 2012;54(1):10–16. doi:10.1093/cid/cir749.
126. Africano HF, Serrano-Mayorga CC, Ramirez-Valbuena PC, Bustos IG, Bastidas A, Vargas HA, Gómez S, Rodriguez A, Orihuela CJ, Reyes LF, et al. Major Adverse Cardiovascular Events During Invasive Pneumococcal Disease are Serotype Dependent. Clin Infect Dis. 2021;72(11):e711–e719. doi:10.1093/cid/ciaa1427.
127. van Hoek AJ, Andrews N, Waight PA, George R, Miller E, van Hoek AJ. Effect of serotype on focus and mortality of invasive pneumococcal disease: coverage of different vaccines and insight into non-vaccine serotypes. PLOS ONE. 2012;7(7):e39150. doi:10.1371/journal.pone.0039150.
128. Cohen C, Naidoo N, Meiring S, de Gouveia L, von Mollendorf C, Walaza S, Naicker P, Madhi SA, Feldman C, Klugman KP, et al. Streptococcus pneumoniae serotypes and mortality in adults and adolescents in South Africa: analysis of national surveillance data, 2003 - 2008. PLOS ONE. 2015;10(10):e0140185. doi:10.1371/journal.pone.0140185.
129. De Miguel S, Latasa P, Yuste J, García L, Ordobás M, Ramos B, Pérez M, Ortiz MA, Sanz JC. Age-dependent serotype-associated case-fatality rate in invasive pneumococcal disease in the autonomous community of madrid between 2007 and 2020. Microorganisms. 2021;9(11):2286. doi:10.3390/microorganisms9112286.
130. Burgos J, Falcó V, Borrego A, Sordé R, Larrosa MN, Martinez X, Planes AM, Sánchez A, Palomar M, Rello J, et al. Impact of the emergence of non-vaccine pneumococcal serotypes on the clinical presentation and outcome of adults with invasive pneumococcal pneumonia. Clin Microbiol Infect. 2013;19(4):385–391. doi:10.1111/j.1469-0691.2012.03895.x.
131. Oligbu G, Collins S, Djennad A, Sheppard CL, Fry NK, Andrews NJ, Borrow R, Ramsay ME, Ladhani SN. Effect of pneumococcal conjugate vaccines on pneumococcal meningitis, England and Wales, July 1, 2000-June 30, 2016. Emerg Infect Dis. 2019;25(9):1708–1718. doi:10.3201/eid2509.180747.
132. Sa-Leao R, Pinto F, Aguiar S, Nunes S, Carrico JA, Frazao N, Gonçalves-Sousa N, Melo-Cristino J, de Lencastre H, Ramirez M, et al. Analysis of invasiveness of pneumococcal serotypes and clones circulating in Portugal before widespread use of conjugate vaccines reveals heterogeneous behavior of clones expressing the same serotype. J Clin Microbiol. 2011;49(4):1369–1375. doi:10.1128/JCM.01763-10.
133. Yeh SH, Gurtman A, Hurley DC, Block SL, Schwartz RH, Patterson S, Jansen KU, Love J, Gruber WC, Emini EA, et al. Immunogenicity and safety of 13-valent pneumococcal conjugate vaccine in infants and toddlers. Pediatrics. 2010;126(3):e493–505. doi:10.1542/peds.2009-3027.
134. Feng S, McLellan J, Pidduck N, Roberts N, Higgins JPT, Choi Y, Izu A, Jit M, Madhi SA, Mulholland K, et al. Immunogenicity and seroefficacy of 10-valent and 13-valent pneumococcal conjugate vaccines: a systematic review and network meta-analysis of individual participant data. EClinicalMedicine. 2023;61:102073. doi:10.1016/j.eclinm.2023.102073.
135. Pichichero M, Kaur R, Scott DA, Gruber WC, Trammel J, Almudevar A, Center KJ. Effectiveness of 13-valent pneumococcal conjugate vaccination for protection against acute otitis media caused by Streptococcus pneumoniae in healthy young children: a prospective observational study. Lancet Child Adolesc Health. 2018;2(8):561–568. doi:10.1016/S2352-4642(18)30168-8.
136. Dagan R, Patterson S, Juergens C, Greenberg D, Givon-Lavi N, Porat N, Gurtman A, Gruber WC, Scott DA. Comparative immunogenicity and efficacy of 13-valent and 7-valent pneumococcal conjugate vaccines in reducing nasopharyngeal colonization: a randomized double-blind trial. Clin Infect Dis. 2013;57(7):952–962. doi:10.1093/cid/cit428.
137. Choi EH, Zhang F, Lu YJ, Malley R, Burns DL. Capsular polysaccharide (CPS) release by serotype 3 pneumococcal strains reduces the protective effect of anti-type 3 CPS antibodies. Clin Vaccine Immunol. 2016;23(2):162–167. doi:10.1128/CVI.00591-15.
138. Andrews NJ, Waight PA, Burbidge P, Pearce E, Roalfe L, Zancolli M, Slack M, Ladhani SN, Miller E, Goldblatt D, 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):839–846. doi:10.1016/S1473-3099(14)70822-9.
139. Platt HL, Cardona JF, Haranaka M, Schwartz HI, Narejos Perez S, Dowell A, Chang C-J, Dagan R, Tamms GM, Sterling T, et al. A phase 3 trial of safety, tolerability, and immunogenicity of V114, 15-valent pneumococcal conjugate vaccine, compared with 13-valent pneumococcal conjugate vaccine in adults 50 years of age and older (PNEU-AGE). Vaccine. 2022;40(1):162–172. doi:10.1016/j.vaccine.2021.08.049.
140. Platt HL, Greenberg D, Tapiero B, Clifford RA, Klein NP, Hurley DC. A phase II trial of safety, tolerability and immunogenicity of V114, a 15-valent pneumococcal conjugate vaccine, compared with 13-valent pneumococcal conjugate vaccine in healthy infants. Pediatr Infect Dis J. 2020;39(8):763–70.
141. Schlingmann B, Castiglia KR, Stobart CC, Moore ML. Polyvalent vaccines: high-maintenance heroes. PLOS Pathog. 2018;14(4):e1006904.
142. Morais V, Texeira E, Suarez N. Next-generation whole-cell pneumococcal vaccine. Vaccines (Basel). 2019;7(4):151. doi:10.3390/vaccines7040151.
143. Moffitt KL, Malley R. Next generation pneumococcal vaccines. Curr Opin Immunol. 2011;23(3):407–413. doi:10.1016/j.coi.2011.04.002.
144. Beall B, Chochua S, Li Z, Tran T, Varghese J, McGee L, Li Y, Metcalf BJ. Invasive pneumococcal disease clusters disproportionally impact persons experiencing homelessness, injecting drug users, and the Western United States. J Infect Dis. 2022;226(2):332–341. doi:10.1093/infdis/jiac058.

145. McCosker LK, El-Heneidy A, Seale H, Ware RS, Downes MJ. Strategies to improve vaccination rates in people who are homeless: a systematic review. Vaccine. 2022;40(23):3109–3126. doi:10.1016/j.vaccine.2022.04.022.
146. Harboe ZB, Larsen MV, Ladelund S, Kronborg G, Konradsen HB, Gerstoft J, Larsen CS, Pedersen C, Pedersen G, Obel N, et al. Incidence and risk factors for invasive pneumococcal disease in hiv-infected and non-hiv-infected individuals before and after the introduction of combination antiretroviral therapy: persistent high risk among hiv-infected injecting drug users. Clin Infect Dis. 2014;59(8):1168–1176. doi:10.1093/cid/ciu558.
147. McKee G, Choi A, Madill C, Marriott J, Kibsey P, Hoyano D. Outbreak of invasive streptococcus pneumoniae among an inner-city population in Victoria, British Columbia, 2016–2017. Can Commun Dis Rep. 2018;44(12):317–323. doi:10.14745/ccdr.v44i12a02.
148. Schillberg E, Isaac M, Deng X, Peirano G, Wylie JL, Van Caeseele P, Pillai DR, Sinnock H, Mahmud SM. Outbreak of invasive Streptococcus pneumoniae serotype 12F among a marginalized inner-city population in Winnipeg, Canada, 2009-2011. Clin Infect Dis. 2014;59(5):651–657. doi:10.1093/cid/ciu366.
149. Dworkin MS, Ward JW, Hanson DL, Jones JL, Kaplan JE. Pneumococcal disease among human immunodeficiency virus-infected persons: incidence, risk factors, and impact of vaccination. Clin Infect Dis. 2001;32(5):794–800. doi:10.1086/319218.
150. National Institute for Health and Care Excellence (NICE). Vaccine uptake in the general population. [accessed 2025 Jan 3]. https://www.nice.org.uk/guidance/ng218/evidence/b-barriers-to-and-facilitators-for-vaccine-uptake-pdf-11072221743.