

RESEARCH PAPER



Pneumococcal serotype distribution: A snapshot of recent data in pediatric and adult populations around the world

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ABSTRACT

S. pneumoniae infection remains a serious public health concern despite the availability of vaccines covering up to 23 of more than 94 known serotypes. The purpose of the present study was to monitor recent serotype distribution data. PubMed, EMBASE, Cochrane Reviews and Ingenta databases were searched. Serotype data covering invasive pneumococcal disease (IPD) and non-IPD were extracted from articles published from March 2014 to March 2015. Fifty-nine studies presented pneumococcal serotype prevalence by specific age categories. Most prevalent serotypes not covered by pneumococcal conjugate vaccines (PCV) were as follows: 15B, 22F, 15A, 23A among children under the age of 7 y with IPD; among adults with IPD: 22F, 11A, 10A, 38 in the 65 y and older age group; 12F, 9N, 8 in the 50–64 year-old age group and 12F, 8, 6C, 16F in the 15–59 age group. Geographic variations in serotype distribution highlight the importance of monitoring evolving pneumococcal serotype prevalence after pneumococcal vaccine implementation.

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Introduction

Infection with *Streptococcus pneumoniae* in children and adults may manifest as invasive pneumococcal disease (IPD) (e.g. meningitis, septicemia, bacteremia and bacteremic pneumonia) or non-IPD (e.g. otitis media and non-bacteremic pneumonia).¹ Currently, more than 94 different pneumococcal serotypes have been identified and are classified on the basis of unique polysaccharides expressed in the capsule.²

In 1983, a 23-valent pneumococcal polysaccharide vaccine (PPV23) was indicated for pediatric populations at high risk for pneumococcal disease and for older adults. In 2000, a pneumococcal conjugate vaccine (PCV) which included serotypes 4, 6B, 9V, 14, 18C, 19F and 23F (7-valent; PCV7) was first licensed in the USA and indicated for the prevention of pneumococcal disease in pediatric populations.¹ In an attempt to expand coverage against additional pneumococcal serotypes, 2 other PCVs were introduced in 2009.³ The 10-valent vaccine contains all 7 serotypes in PCV7 as well as serotypes 1, 5, and 7F. The 13-valent vaccine (PCV13) contains all 10 serotypes in PCV10 and additionally contains 3, 6A, and 19A.¹

Individual serotype prevalence can change over time in different geographic regions or age groups.⁴ Furthermore, while the implementation of PCVs has resulted in a substantial reduction of the incidence of IPD related to the decrease in vaccine-type (VT) IPD, there has been an observed increase in non-VT IPD.² This highlights the need to monitor serotype data after pneumococcal vaccines (i.e., PCV10, PCV13) are adopted in different countries to observe changes in serotype prevalence and identify newly emerging serotypes. During recent years, after adoption of

PCV13 in both pediatric and adult populations in multiple countries, an increasing number of studies from around the world have been conducted, which demonstrate the changing patterns of pneumococcal serotype distributions. It seems important to summarize the most recent serotype data available from surveillance networks and individual studies to monitor the current picture. The objective of this scoping literature review was to summarize pneumococcal serotype distribution as reported in the literature between March 2014 and March 2015 and identify any notable trends.

Results

From among 180 studies selected based on inclusion criteria and subsequently included in this scoping review, approximately 90 of them presented pneumococcal serotype prevalence stratified by different age categories, chosen for correspondence to the target age groups of either conjugate or polysaccharide vaccines. After reviewing the various age groups reported to identify the best organization of the serotype data, 31 studies were excluded because they did not conform to the age groups of interest for this scoping literature review. We present the most recent data from the 59 studies, which reported serotype distribution among subjects in the following age groups of interest: under the age of 7 y (51 studies, Table 1), adults aged older than 65 y (12 studies, Table 2), 50 to 64 y (4 studies, Table 3) and 15 to 59 y (8 studies, Table 4). The latter 2 age groups overlap because otherwise would have required omitting 2 studies.^{5,6} The results are tabulated by geographic region

Table 1. Strains of *S. pneumoniae* among children under the age of 7 years.

Source	Country (year)	Study population (N)	PCV7 ^a	PCV10-specific [1, 5, 7F]	PCV13-specific [3, 6A, 19A]	PPV23-specific serotypes ^b	NV serotypes
IPD in Africa Eastern Mediterranean Region							
Ben-Shimol et al. 2014 ⁷	Israel (2012–13)	Children <5 y with IPD (155)	12 (7.7)–[NS]	37 (23.9)–[NS] ^c	—	—	106 (68.4)–[NS] ^d
Ben-Shimol et al. 2015 ⁸	Israel (2012–13)	Children <5 y with IPD (NS)	7.0% [6B, 14]	11.1% [5]	14.4% [19A]	12F: 26.2% • 15B/C: 8% • 33F: 5.3% 10A: 2.1%	15A: 2.7% • 10B: 2.1% • other: 21.1%
von Gottberg et al. 2014 ⁹	South Africa (2012)	IPD children < 2 y (373)	77 (20.6)–[19F]	34 (9.1)–[5]	57 (15.3)–[19A]	8: 9.7% • 15B: 6.4% • 12F: 3.8% 9N: 2.4%	7C: 2.1% • 13: 0.8% • 34: 1.6% -other: 28.2%
Ba et al. 2014 ¹⁰	Senegal (2007–08)	NP carriage and IPD among children <2 y (132)	49 (37.1)–[6B, 19F]	4 (3.0)–[1]	18 (13.6)–[6A]	11A: 5.3% • 15B: 3.8% • 10A: 20: 3.0%	23B: 1.5% • 9A: 9L: 18B: 18F: 19B: 23A: 0.8% • NT: 20.5%
Ndlangisa et al. 2014 ¹¹	South Africa (2007)	Children < 5 y with IPD (1084)	637 (58.8)–[14]	58 (5.4)–[1]	233 (21.5)–[6A]	8: 12F: 22F: 0.8% • Other: 2.3%	157 (14.5)–[NS] ^d
IPD in Asia Pacific Region							
Wei et al. 2015 ¹²	Taiwan (2013)	Children ≤ 5 y old with IPD (134)	27 (20.1)–[14]	0 (0)–[NA]	73 (54.5)–[19A]	—	34 (25.4)–[NS] ^d
Chiba et al. 2014 ¹³	Japan (2012)	Children <4 y old with IPD (144)	18 (12.5)–[NS]	—	—	—	126 (87.5)–[NS] ^e
Cho et al. 2014 ¹⁴	South Korea (2006–10)	Children <5 y old with IPD (110)	47 (42.7)–[NS]	1 (0.9)–[NS]	37 (33.6)–[NS]	—	25 (22.7)–[NS] ^d
IPD in Europe							
Skoczynska et al. 2014 ⁵	Poland (2011–13)	Children 0–4 y old with IPD (145)	81 (55.9)–[14]	7 (4.8)–[1]	27 (18.6)–[19A]	15B/C: 6.9% • 10A: 11A: 2.8% 22F: 1.4% • 8: 0.7%	10 (6.9)–[NS]
Lepoutre et al. 2015 ¹⁵	France (2012)	Children < 2 y old with IPD (201)	13 (6.5)–[19F]	14 (7.0)–[7F]	16 (8.0)–[19A]	12F: 9.5% • 15B: 7.0% • 22F: 5.0%	24F: 19.9% • 15A: 6.5% • 15C: 2.0%
Aguilar et al. 2014 ¹⁶	Portugal (2008–12)	Children <5 y old with IPD (283)	75 (26.5)–[14]	58 (20.5)–[7F]	78 (27.6)–[19A]	—	6C: 0.5% • other: 28.4%
Del Amo et al. 2014 ¹⁷	Spain (2007–11)	Children ≤ 6 y old hospitalized with IPD (159)	22 (13.8)–[19F]	89 (56.0)–[1]	46 (28.9)–[19A]	22F: 1.9% • 10A: 1.3% • 8: 15B: 0.6%	72 (25.4)–[NS]
Navarro-Torne et al. 2015 ¹⁸	Europe (26 countries –2010)	Children < 5 y old with IPD (570)	107 (18.8)–[NS]	329 (57.7)–[NS] ^c	—	—	6C: 24B: 28: 38: 0.6%
Navarro-Torne et al. 2014 ¹⁹	Europe (21 countries –2010)	Children < 5 y old with IPD (NS)	19.2%–[NS]	26.9%–[NS]	27.0%–[NS]	—	134 (23.5)–[NS] ^d
del Amo et al. 2014 ²⁰	Spain (2007–9)	Children ≤ 5 y old hospitalized with IPD (141)	18 (12.8)–[14]	62 (44.0)–[1]	53 (37.6)–[19A]	10A: 15B/C: 22F: 0.7%	26.9%–[NS] ^d
IPD in Latin America							
Echániz-Avilés et al. 2015 ²¹	Mexico (2012)	Children ≤ 5 y old hospitalized with IPD (105)	22 (21.0)–[19F]	5 (4.8)–[1]	47 (44.8)–[19A]	—	23B: 1.4% • 15A/F: 24B: other: 0.7%
Abate et al. 2014 ²²	Argentina (1993–2011)	Children 0–11 months old hospitalized with IPD (96)	45 (46.9)–[14]	27 (28.1)–[5]	12 (12.5)–[19A]	8: 3.1% Others (totaling 5.2%): 2, 7C, 11, 12, 15B, 16A, 18A, 18B, 20, 35F, 42	31 (29.5)–[NS] ^c
Parra et al. 2014 ²³	Colombia (2009–10)	Children <2 y old with IPD (950)	252 (26.5)–[14]	100 (10.5)–[1]	100 (10.5)–[3]	12F: 1.6% • 8: 1.1% • 9N: 0.9% 11A: 22F: 0.7% • 17F: 0.6% • 10A: 0.5%	10F: 28A: 2.1% 16F: 1.2% • 6C: 23A: 0.7% 13: 15A: 18A: 34: 0.6% • 15C: 23B: 25A: 28A: 35B: 0.4% • other: 38.8%
						15B: 0.3% • 33F: .02% • 20: 0.1%	

Table 1. (Continued)

Source	Country (year)	Study population (N)	n (%) - [most prevalent serotype]					
			PCV7 ^a	PCV10-specific [1, 5, 7F]	PCV13-specific [3, 6A, 19A]	PPV23-specific serotypes ^b	NV serotypes	
Kandasamy et al. 2015 ³⁶	Nepal (2012)	NPC among healthy children between 6 weeks and 2 y old (304)	63 (20.7)–[14]	1 (0.3)–[5]	29 (9.5)–[6A]	15B: 3.9% • 10A: 2.3% • 17F: 2.0% 8; 9N; 20; 22F: 1.0% 11A; 12F; 33F: 0.3%	11D; 35A: 2.3% • 34; 35B; 35F: 2.0% 6C; 13; 35C; 23A; 33B: 1.6% 7C; 16F; 39; 1.3% • 7B; 15A; 15C; 21; 45 1.0% • 25 serotypes: <1% Other NS/NT: 19.4%	
Khoshdel et al. 2014 ³⁷	Iran (2010–11)	NPC among healthy children <5 y old (107)	38 (35.5)–[23F]	—	—	—	—	
Farida et al. 2014 ³⁸	Indonesia (2010)	NPC among healthy children between 6 and 60 months of age (111)	40 (36.0)–[6A/B] ^c	0 (0)–[NA]	0 (0)–[NA]	11A; 15B/C: 9.9%	23A: 4.5% • 15A: 1.8% Others/NT: 37.8%	
Hanieh et al. 2014 ³⁹	Nepal (2009)	NPC among healthy children between 1.5 and 24 months of age (1100)	187 (17.0)–[6A/B] ^c	7 (0.6)–[1, 5]	17 (1.5)–[19A]	15B/C: 3.6% • 9N/L: 1.3% • 33F: 1.0% 17F: 20: 0.8% • 22F: 0.7%	34: 2.4% • 11: 2.3% • 35B: 1.4% • 23A: 1.1% • 15A/F: 1.0% • 17 serotypes: <1% Other NS/NT: 8.8%	
non-IPD in Europe								
Luminos et al. 2014 ⁴⁰	Romania (2011–13)	NPC among healthy children ≤ 5 y old (453)	199 (43.9)–[19F]	2 (0.4)–[NS]	89 (19.6)–[6A]	—	163 (66.0)–[NS] ^e	
Mayanskiy et al. 2014 ⁴¹	Russia (2009–13)	Noninvasive SP isolates from children at hospital, median age 3.5 y (835)	486 (58.2)–[19F]	13 (1.6)–[7F]	152 (18.2)–[3]	15B: 3.5% • 11A: 3.1% • 9N: 1.4%	23A: 2.0% • 15C: 1.6% • 37: 1.3%	
Dunais et al. 2015 ⁴²	France (2012)	NPC among healthy children between 3 and 40 months of age (168)	0 (0)–[NA]	0 (0)–[NA]	11 (6.5)–[19A]	10A: 1.1% • 17F: 0.7% • 8: 0.5% 22F; 33F: 0.4% • 12F: 0.2% • 20: 0.1%	35F: 0.8% • 34: 0.7% • 16F: 0.2% 15A; 23B: 0.4% • 5 serotypes: 0.2%	
Mameli et al. 2015 ⁴³	Italy (2011)	NPC among healthy children aged between 3 months 5 y (124)	2 (1.6)–[14]	0 (0)–[NA]	6 (4.8)–[3, 6A, 19A]	11A: 11.3% • 10A: 8.1% • 22F: 3.2% 12F: 1.6% • 8; 17F: 0.8%	9 serotypes: 0.1% 23A/B: 11.3% • 35B: 10.7% • 15A: 9.5% 6C: 5.4% • Other NS/NT: 20.2% 15A: 23.4% • 6C; 35F: 7.3% • 23A: 5.6% 21; 24F; 29; 3.2% • 16A; 23B; 28F: 2.4%	
van der Linden et al. 2015 ⁴⁴	Germany (2010–11)	NPC among children with AOM aged between 2 months and 5 y (107)	11 (10.3)–[19F]	2 (1.9)–[7F]	53 (49.5)–[3]	22F: 4.7%	33: 1.6% • 5 serotypes: <1% Other NS/NT: 1.6%	
Grivea et al. 2014 ⁴⁵	Greece (2010–11)	NPC among healthy children aged between 2 and 5 y (341)	6 (1.8)–[19F]	10 (2.9)–[7F]	64 (18.8)–[19A]	15B/C: 10.6% • 11A: 7.6% • 10A: 4.4% 22F: 2.6% • 33F: 0.9% • 20: 0.3%	23B; 35B 3.6% • 6C: 1.8% Other NS/NT: 24.3% 23B: 12.6% • 21; 16F: 7.6% • 15A: 7.0% 6C: 6.7% • 23A: 2.3% • 24F; 31: 1.2% 7C; 33A; 35F: 0.9% • 4 serotypes: 0.3%	

Pasinato et al. 2014 ⁴⁶	Italy (2010–11)	NPC among children aged between 6 and 59 months (1728)	436 (25.2)–[19F]	272 (15.7)–[5]	157 (9.1)–[19A]	33F: 1.0% • 22F: 0.8% • 20: 0.2% 8: 0.1%	23B: 1.9% • 21: 1.2% • 23A: 1.0% 16F: 35B: 29: <1% Other NS/NT: 5.6%
Gladstone et al. 2015 ⁴⁷	UK (2010–11)	NPC among ≤ 4 y old (99)	1 (1.0)–[68]	2 (2.0)–[1, 7F]	8 (8.1)–[19A]	33F: 8.1% • 11A: 15B: 7.1%	21: 12.1% • 6C: 9.1% • 35F: 9.1% 23B: 8.1% • 15A: 6.1% • 16F: 4.0%
Del Amo et al. 2014 ¹⁷	Spain (2007–11)	SP carriage among healthy children ≤ 6 y old (209)	30 (14.4)–[19F]	2 (1.0)–[1]	39 (18.7)–[19A]	10A: 4.8% • 11A: 15B: 4.3% • 22F: 3.8% 17F: 2.4% • 33F: 1.0% • 9N: 12F: 0.5%	23A: 4.0% • 35B: 3.0% 6C: 9.1% • 23B: 8.1% • 23A: 4.3% 34: 15A: 2.9% • 16F: 2.1; 35B: 2.4% 15C: 3.1; 1.9% • 29: 1.4% • 35F: 1.0%
Alfayate-Migueléiz et al. 2014 ⁴⁸	Spain (2009–10)	NPC among children aged between 1 and 4 y (343)	46 (13.4)–[14, 23F]	0 (0)–[NA]	81 (23.6)–[6A]	11A: 6.1% • 15B: 4.7% • 22F: 2.3% 33F: 2.0% • 17F: 1.2%	7 serotypes: 0.5% 15A: 23B: 7.3% • NT: 5.0% • 6C: 4.7% 23A: 35B: 4.1% • 15C: 2.6% • 35F: 1.7%
del Amo et al. 2014 ²⁰	Spain (2007–9)	NPC among healthy children ≤ 5 y old (224)	56 (25.0)–[6A/B] ^b	19 (8.5)–[5]	35 (15.6)–[19A]	15B/C: 4.0% • 10A: 22F: 2.2% • 20: 1.8% 11A/D: 17F: 1.3% • 33F: 0.9% • 2: 0.4%	24F: 1.2% • 9 serotypes: <1% Other NS: 2.3% 23A: 4.5% • 6C: 4.0% • 23B: 3.6% 35B: 2.2% • 15A/F: 2.1: 1.8%
non-IPD in Latin America							
Grijalva et al. 2014 ⁴⁹	Peru (2009–11)	NPC among Andean children <3 y old with ARI (681)	147 (21.6)–[19F]	5 (0.7)–[1, 7F]	40 (5.9)–[19A]	11A: 4.7% • 10A: 4.0% • 15B: 1.6% 22F: 1.0% • 17F: 20: 33F: 0.7% 8: 0.3% • 9N: 12F: 0.1%	13: 34: 1.3% • 16F: 3.1% • 13: 2.6% 6C: 4.3% • 23B: 3.1% • 13: 2.6% 11A/D: 2.5% • 15A: 2.1% • 15C: 1.9% 35B: 1.8% • 15A/F: 1.5% • 7C: 35F: 1.3%
non-IPD in North America							
Martin et al. 2014 ⁵⁰	US (2012–13)	NPC among children with AOM aged between 6 and 23 months (113)	2 (1.8)–[19F, 23F]	0 (0)–[NA]	14 (12.4)–[19A]	15B: 10.6% • 11A: 8.0% • 10A: 2.7% 17F: 2.7% • 2 serotypes: <1%	35B: 8.8% • 15C: 7.1% • 15A: 4.4% 40: 3.5% • 16F: 2.2; 33: 35F: 2.7%
Ricketson et al. 2014 ⁵¹	Canada (2011–12)	NPC among healthy children < 5 y of age (183)	5 (2.7)–[19F]	0 (0)–[NA]	13 (7.1)–[19A]	11A: 13.1% • 22F: 9.3% • 15B: 7.7% 33F: 2.2% • 9N: 10A: 1.6% • 8: 0.5%	19B: 25A: 34: 37: 44: 0.9% Other NS: 21.3% 35F: 11.5% • 23B: 7.7% • 15C: 23A: 6.0% 15A: 35B: 5.5% • 6C: 4.9% • 21: 2.7% 7C: 1.1% • 6 serotypes: 0.5%

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Table 1. (Continued)

Source	Country (year)	Study population (N)	n (%) - [most prevalent serotype]				
			PCV7 ^a	PCV10-specific [1, 5, 7F]	PCV13-specific [3, 6A, 19A]	PPV23-specific serotypes ^b	NV serotypes
Gounder et al. 2014 ⁵²	US (2011–12)	NPC among Alaskan children < 5 y of age (938)	10 (1.1)–[19F]	1 (0.1)–[7F]	83 (8.9)–[19A]	11A: 8.2% • 15B: 6.6% • 33F: 5.7% 22F: 2.9% • 10A: 2.7% 9N; 17F: 1.5% • 8: 1.2%	16F: 8.3% • 35B: 8.2% • 6C: 7.7% 23B: 6.7% • 21: 5.3% • 15A: 4.3% 35F: 3.4% • 23A: 2.7% • 31: 2.0% 7C: 1.8% • 34: 1.3% • 37: 1.1% NT: 6.4%
Loughlin et al. 2014 ⁵³	US (2010–11)	NPC among children < 5 y of age (1080)	64 (6.1)–[NS]	89 (8.5)–[NS] ^c	178 (22.3)–[19A]	22F: 7.4% • 15B: 5.1% • 11A: 3.6%	927 (88.3)–[NS] ^d 6C: 8.1% • 23B: 7.9% • 15A: 5.9%
Keck et al. 2014 ⁵⁴	US (2008–09)	NPC among Alaskan children < 5 y of age (798)	13 (1.6)–[19F]	43 (5.4)–[7F]	10A: 2.7% • 33F: 2.8% • 9N: 1.0% 17F: 0.8% • 8: 12F: 0.1%	16F: 4.8% • 23A: 3.6% • 35F: 3.5% 35B: 1.9% • 15C: 1.6% • 22A: 1.1% 3 serotypes: <1% • Other NS: 5.9%	

AOM: acute otitis media; ARI: acute respiratory infection; HIV: human immunodeficiency virus; IPD: invasive pneumococcal disease; OM: otitis media; NA: not applicable; NPC: nasopharyngeal carriage; NS: not specified; NT: non-type-able; NV: non-vaccine; SP: *S. pneumoniae*.

^aPCV7 serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F;

^bPPV23-specific serotypes: 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F;

^cPCV13 serotypes not found in PCV7;

^dnon-PCV13 serotypes;

^enon-PCV7 serotypes;

^fincludes serotype 6A;

^gPCV10 serotypes;

^hnon-PCV10 serotypes

Table 2. Strains of *S. pneumoniae* among adults aged 65 y and older.

Source	Country (year)	Study population (N)	PCV7 ^a	PCV10-specific [1, 5, 7F]	n (%)—[most prevalent serotype]				NV serotypes	
					PCV13-specific[3, 6A, 19A]	PPV23- specific ^b	PPV23 serotypes			
IPD in Europe										
Harboe et al. 2014 ⁵⁵	Denmark (2011–13)	Adults with IPD aged ≥ 65 y (1439)	97 (6.7)–[4]	265 (18.4)–[1]	224 (15.6)–[3]	549 (38.2)	[NS]	304 (21.1)–[NS]		
Skoczynska et al. 2014 ⁶	Poland (2011–13)	Adults with IPD aged ≥ 65 y (373)	116 (31.3)–[14]	21 (5.7)–[1]	110 (29.6)–[3]	57 (15.3)	9N: 3.8% • 22F: 3.0% • 11A: 2.1% 10A: 1.9% • 12F: 1.9% • 8: 1.6% 15B/ C: 1.1%	67 (18.1)–[NS]		
Guevara et al. 2014 ⁵⁶	Spain (2010–13)	Adults with IPD aged ≥ 65 y (114)	12 (10.5)–[NS]	47 (41.2)–[NS] ^c	210 (28.3)–[19A]	214 (28.9)	12F: 5.9% • 22F: 5.8% • 8: 3.8% Other NS: 9.6%	55 (48.2)–[NS] ^c		
Verhaegen et al. 2014 ⁵⁷	Belgium (2009–11)	Adults with IPD aged ≥ 65 y (742)	59 (8.0)–[NS]	146 (19.7)–[7F]				141 (19.0)–[NS]		
Navarro-Torres et al. 2015 ¹⁸	Europe (26 countries–2010)	Adults with IPD aged ≥ 65 y (1108)	191 (17.2)–[NS]	385 (34.7)–[NS] ^c				532 (48.0)–[NS] ^d		
Ochoa-Gondar et al. 2015 ⁵⁸	Spain (2006–09)	Adults with IPD aged ≥ 65 y (96)	14 (14.6)–[14]	17 (17.7)–[7F]	29 (30.2)–[19A]	13 (13.5)	9N: 4.2% • 8: 12F: 2.1% • 10A: 15A: 17F: 22F: 33F: 1.0%	38: 5.2% • 16/16F: 23B: 31: 3.1%		
								11/11F: 23A: 24F: 2.1% 10B: 15A: 35F: 37: 1.0%		
IPD in Latin America										
García Gabarrot et al. 2014 ⁵	Uruguay (2011–12)	Adults with IPD aged ≥ 60 y (150)	14 (9.3)–[NS]	52 (34.7)–[NS] ^c		84 (56) ^d	[NS]			
IPD in North America										
Moore et al. 2015 ²⁴	US (2011–13)	IPD cases among adults aged ≥ 65 y (3618)	45 (1.2)–[19F]	95 (2.6)–[7F]	423 (11.7)–[3]	–	22F: 5.9% • 11A: 1.6% ^e	6C: 2.7% • 23A: 2.0% 35B: 1.8% • 16F: 1.6% ^e 723 (58.6)–[NS] ^f		
Worham et al. 2014 ⁵⁹	US (2009)	Adults with IPD aged ≥ 65 y (1233)	510 (41.4)–[NS] ^f							
non-IPD in Asia, North America, and Europe										
Kim et al. 2014 ⁶⁰	South Korea (2013)	Adults with IPD or pneumococcal pneumonia aged ≥ 65 y (114)	14 (12.3)–[19F]	1 (0.9)–[7F]	34 (29.8)–[3]	32 (28.1)	11A/D/F: 14.0% • 20: 22F: 3.5%	34: 6.1% • 15A/F: 35B: 4.4% • 6D: 13: 2.6% • 6C: 7B/7C: 11E: 16F: 23A: 23B: 0.9% • Other NS: 3.5%		
Richter et al. 2014 ⁶¹	US (2012–13)	Adults with IPD or non-IPD aged ≥ 65 y (346)	–	–	≥ 73 (21.1)–[3] ^f	–	15B: 2.6% • 10A: 33F: 1.8% • 8: 0.9% 11A: 22F: 6.0% ^g	6C: 6.0% • 15A: 23A: 5.0% ^f		
Domenech et al. 2014 ⁶²	Spain (2009–12)	SP strains causing acute exacerbations among COPD patients aged 70.2 ± 8.7 y (197)	23 (11.7)–[19F]	5 (2.5)–[7F]	30 (15.2)–[3]	48 (24.2)	11A: 6.1% • 10A: 4.0% 17F: 22F: 33F: 3.0% 9N: 12F: 1.5% • 15B: 1.0%	15A: 9.6% • 6C: 5.6% 23A: 23B: 4.5% 16F: 35B: 3.5% • 31: 24F: 2.5%		

COPD: chronic obstructive pulmonary disease; IPD: invasive pneumococcal disease; NA: not applicable; NPC: nasopharyngeal carriage; NS: not specified; NV: non-vaccine; SP: *S. pneumoniae*^aPCV7 serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F;^bPPV23-specific serotypes: 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F;^cPCV13 serotypes not found in PCV7;^dnon-PCV13 serotypes;^ePCV13-serotypes and the 5 most common among non-PCV serotypes reported;^fPCV13-serotypes;^gserotype-specific data for the 8 most common serotypes by age group were reported.

Table 3. Strains of *S. pneumoniae* among adults aged between 50 and 64 years.

Source	Country (year)	Study population (N)	n (%)—[most prevalent serotype]					
			PCV7 ^a	PCV10-specific [1, 5, 7F]	PCV13-specific [3, 6A, 19A]	PPV23- specific ^b	PPV23 serotypes	NV serotypes
IPD in Europe and North America								
Skoczynska et al. 2014 ⁶	Poland (2011–13)	Adults with IPD aged between 55 and 64 y (249)	78 (31.3)—[4]	19 (7.6)—[1]	74 (29.7)—[3]	43 (17.3)	8; 9N: 4.4% • 11A: 2.8% 12F; 15B/C: 2.0% • 22F: 1.6%	32 (12.9)—[NS]
Moore et al. 2015 ²⁴	US (2011–13)	Adults with IPD aged between 50 and 64 y (2994)	24 (0.8)—[19F]	73 (2.4)—[7F]	201 (6.7)—[3]	258 (8.6) ^c	22F: 3.7% • 9N; 12F: 1.7% 33F: 1.5% ^c	6C: 1.5% • 16F: 1.3% ^c
Verhaegen et al. 2014 ⁵⁷	Belgium (2009–11)	Adults with IPD aged between 50 and 64 y (370)	22 (5.9)—[NS]	114 (30.8)—[7F]	73 (19.7)—[19A]	100 (27)	12F: 10.3% • 8; 22F: 3.5% ^d	48 (13.0)—[NS] ^d
Wortham et al. 2014 ⁵⁹	US (2009)	Adults with IPD aged between 50 and 64 y (1067)	523 (49.0)—[NS] ^e	—	—	—	—	544 (51.0)—[NS] ^f

IPD: invasive pneumococcal disease; NA: not applicable; NS: not specified; NV: non-vaccine; SP: *S. pneumoniae*

^aPCV7 serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F;

^bPPV23-specific serotypes: 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F;

^cPCV serotypes and the 5 most common non-PCV serotypes were reported;

^donly the serotypes accounting for at least 4% of isolates overall were reported;

^ePCV13-serotypes;

^fnon-PCV13-serotypes.

and disease type (IPD or non-IPD) in reverse chronological order (newest to oldest). Of specific interest for the purposes of this article is the prevalence of non-PCV serotypes; prevalence data for PCV7, PCV10 and PCV13 serotypes are grouped, and non-PCV-serotype prevalence data are provided by serotype as available.

Serotype distribution reporting varied widely among studies; many concentrated only on conjugate vaccine coverage and provided no information about other serotypes while others provided data of exquisite granularity.

Pneumococcal serotype distribution among children aged under the age of 7 y

There were 21 studies^{6–26} providing serotype distribution data among children under the age of 7 y with IPD and 30^{17,20,27–54} providing data on nasopharyngeal carriage, otitis media or other non-IPD conditions. Two studies from Spain contained both IPD and non-IPD data (Table 1).^{17,20}

Conjugate vaccine serotypes (i.e., serotypes included in PCV13) causing IPD among children were highly prevalent (> 60% of serotypes) in 11 reports,^{6,11,12,14,16–22} including 6 of 7 European studies,^{6,16–20} while the highest prevalence from North American studies was 46%.²⁵ In contrast, conjugate vaccine serotypes causing non-IPD conditions among children were more than 50% prevalent in only 5 of 30 studies (Table 1).^{31,33,40,41,44}

Prevalence of serotypes uniquely covered by PPV23 was reported in a total of 33 papers. Most often ranking in the top 3 among those serotypes in PPV23 but not in PCV13 for IPD-related pneumococcal illness were serotypes 15B (or 15B/C) reported in 9 papers^{6,8–10,15,17,20,24,26} at up to 11.8% prevalent,²⁶ 5 papers reporting serotype 22F ($\leq 11.3\%$)^{15,17,20,24,26} and 4 papers each reporting serotype 12F ($\leq 26.2\%$),^{8,9,15,23} 8 ($\leq 9.7\%$)^{6,9,22,23} or 10A ($\leq 3\%$).^{6,10,17,20} For non-IPD related carriage or illness, the top 3 serotypes uniquely covered by PPV23 were 15B-15B/C (19 papers; $\leq 22.6\%$),^{17,20,28,33–36,38,39,41,42,45,47–}

^{52,54} 11A (17 papers; $\leq 13.1\%$),^{17,28,31,34,35,38,41–43,47–49,51,52,54} 10A (8 papers; $\leq 8.1\%$)^{17,20,34,36,43,45,49,50} and 22F (8 papers; $\leq 6.5\%$).^{20,35,43,44,46,48,51,54}

Prevalence of serotypes not covered by any pneumococcal vaccines (i.e., PCV13 or PPV23) was reported in a total of 34 papers. Most often ranking in the top 3 among non-vaccine serotypes in IPD-related pneumococcal illness were serotypes 15A reported in 4 papers at up to 6.5% prevalent,^{8,15,17,23} serotype 23A (3 studies; $\leq 10.6\%$),^{10,23,26} 6C (5 studies; $\leq 7.2\%$)^{15,17,23,24,26} or 23B (6 studies; $\leq 5.6\%$).^{10,17,20,23,24,26} For non-IPD related carriage or illness, the most common serotypes were 15A (22 papers; $\leq 23.4\%$),^{17,20,28,29,31,33–36,38,39,41–43,45,47–52,54} 23A (21 papers; $\leq 6.0\%$),^{17,20,28,31,33–36,38,39,41–43,45–49,51,52,54} 35B (18 papers; $\leq 10.7\%$)^{17,20,29,31,34–36,39,42,44,46–52,54} and 6C (17 papers; $\leq 9.1\%$).^{17,20,28,31,34–36,42–45,47–49,51,52,54} A total of 21 papers included serotypes 16F, 23B or 35F at up to 12.6% prevalence.^{17,20,28,29,31,34–36,41–52,54} Serotype 24F appears to be more frequent in Europe among both IPD (1.3–19.9%)^{15,17} and non-IPD (1.2–5.6%),^{43,45,48} cases.

Pneumococcal serotype distribution among adults aged 65 y and older

There were 9 studies reporting serotype distribution data among adults aged 65 y and older with IPD^{5,6,18,24,55–59} and another 3 with similar data on non-IPD conditions (Table 2).^{60–62} Conjugate vaccine serotypes (i.e., serotypes included in PCV13) causing IPD among older adults were highly prevalent (> 60% of serotypes) in only 2 studies, one Polish⁶ and one Spanish.⁵⁸ Conjugate vaccine serotypes were generally less prevalent among non-IPD conditions, the highest prevalence reported being 43% in a South Korean study.⁶⁰

Prevalence of serotypes uniquely covered by PPV23 was reported in 7 studies. Among the most prevalent serotypes, 5 studies reported 22F ($\leq 6.0\%$)^{6,24,57,60,61} and 4 studies reported 11A (\leq

Table 4. Strains of *S. pneumoniae* among adults aged between 15 and 59 years.

Source	Country (year)	Study population (N)	n (%)—[most prevalent serotype]					
			PCV7 ^a	PCV10-specific [1, 5, 7F]	PCV13-specific [3, 6A, 19A]	PPV23-specific ^b	PPV23 serotypes	NV serotypes
IPD								
Moore et al. 2015 ²⁴	US (2011–13)	Adults with IPD aged between 18 and 49 y (1990)	23 (1.2)—[4]	62 (3.1)—[7F]	102 (5.1)—[3]	125 (6.3)	22F: 4.1% ● 12F: 1.9% ● 8: 1.7%	6C: 1.0% ● Other NS: 79.2% ^c
Skoczynska et al. 2014 ⁶	Poland (2011–13)	Adults with IPD aged between 15 and 54 y (315)	119 (37.8)—[4, 14]	26 (8.3)—[1]	71 (22.5)—[3]	62 (19.7)	8: 3.8% ● 9N; 12F: 3.5% 10A; 15B/C: 2.5% ● 11A; 22F: 1.9%	32 (10.2)—[NS]
von Gottberg et al. 2014 ⁹	South Africa (2012)	Adults with IPD aged between 25 and 44 y (1260)	256 (20.3)—[4]	199 (15.8)—[1]	251 (19.9)—[19A]	320 (25.4)	12F: 9.2% ● 8: 4.7% ● 9N: 3.1% 22F: 2.4% ● 10A; 15B: 2.1% ● 17F: 1.8%	16F: 3.1% ● 13: 2.5% ● 7C: 1.9% 34: 1.3% ● Other: 9.7%
Garcia Gabarrot et al. 2014 ⁵	Uruguay (2011–12)	Adults with IPD aged between 15 and 59 y (126)	10 (7.9)—[NS]	47 (37.3)—[NS] ^d	—	—	—	69 (54.8)—[NS] ^e
Verhaegen et al. 2014 ⁵⁷	Belgium (2009–11)	Adults with IPD aged between 18 and 49 y (220)	13 (5.9)—[NS]	102 (46.4)—[1]	22 (10.0)—[19A]	—	12F: 7.3% ● 8: 4.5% ● 22F: 2.3% ^f	≥ 26 (11.8)—[NS] ^f
Van Mens et al. 2014 ⁶⁴	Netherlands (2008–10)	Adults with IPD aged between 20 and 45 y (148)	34 (23.0)—[NS]	—	—	—	—	114 (77.0)—[NS]
Wortham et al. 2014 ⁵⁹	US (2009)	Adults with IPD aged between 18 and 49 y (978)	536 (54.8)—[NS] ^g	—	—	—	—	442 (45.2)—[NS] ^e
non-IPD								
Hammitt et al. 2014 ³⁰	Kenya (2012)	NPC among adults aged 18–49 y (116)	10 (8.6)—[NS] ^h	—	—	—	—	106 (91.4)—[NS] ⁱ

IPD: invasive pneumococcal disease; NA: not applicable; NS: not specified; NV: non-vaccine; SP: *S. pneumoniae*

^aPCV7 serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F;

^bPPV23-specific serotypes: 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F;

^cPCV serotypes and the 5 most common non-PCV serotypes were reported;

^dPCV13 serotypes not found in PCV7;

^eNon-PCV serotypes;

^fOnly the serotypes accounting for at least 4% of isolates overall were reported;

^gPCV13-serotypes;

^hPCV10 serotypes;

ⁱNon-PCV10 serotypes.

14.0%).^{24,61–63} Further, among the 4 studies reporting IPD-related pneumococcal illness,^{6,24,57,58} serotypes 8 (range: 1.6–3.8%) and 12F (1.9–5.9%) were reported in all of them and 9N (3.8% and 4.2%)^{6,58} and 10A (1.9% and 1.0%)^{6,58} were reported in 2 studies. For non-IPD related carriage or illness, the most prevalent serotype was 11A in all 3 studies.^{60–62} Prevalence of serotypes 15B (1.0–2.6%) and 10A (1.8–4.0%) were also noteworthy.^{60,62}

Prevalence of serotypes not covered by any pneumococcal vaccines was reported in only 2 IPD studies, which reported serotypes 38 (5.2%)⁵⁸ and 6C (2.7%)²⁴ to be the most prevalent. Three non-IPD related carriage or illness studies, reported serotypes 15A (9.6%),⁶² 34 (6.1%)⁶⁰ and 6C (6.0%)⁶¹ to be the most prevalent.

Pneumococcal serotype distribution among adults aged 50–64 y

There were 4 studies reporting serotype distribution data among adults aged between 50 and 64 y with all reporting on IPD (Table 3).^{6,24,57,59} Prevalence of conjugate vaccine serotypes ranged from 9.9% to 68.6%.

Prevalence of serotypes uniquely covered by PPV23 was reported in 3 studies with serotypes 12F, 9N, 8 and 22F being the most prevalent.^{6,24,57} Collective prevalence of serotypes not covered by any pneumococcal vaccines ranged from 2.8% to 13.0%.

Pneumococcal serotype distribution among adults aged 15–59 y

There were 7 studies reporting serotype distribution data among adults aged between 15 and 59 y with IPD^{5,6,9,24,57,59,64} and a single study from Kenya reporting pneumococcal carriage with serotype data limited to prevalence of PCV10 and non-PCV10 serotypes (Table 4).³⁰ Conjugate vaccine serotypes causing IPD were highly prevalent (> 60% of serotypes) in 2 studies.^{6,57} Prevalence of serotypes uniquely covered by PPV23 was reported in 4 studies^{6,9,24,57} 2 of which reported 12F to be most prevalent. Other prevalent serotypes of note were 8 (4 studies; ≤ 4.7%),^{6,9,24,57} 22F (4 studies; ≤ 4.1%)^{6,9,24,57} and 9N (3 studies; ≤ 3.5%).^{6,9,24} Prevalence of serotypes not covered by any pneumococcal vaccines was reported in 2 IPD studies. Serotypes 6C and 16F were the most prevalent among

non-vaccine serotypes in a US and South African study, respectively.^{9,24}

Discussion

The majority of the 49 published studies identified in this literature review reporting serotype distribution data among pediatric populations were conducted in countries where pediatric PCVs were incorporated into the national immunization program. Despite the availability of PCV, among the 21 studies assessing IPD among children, serotypes included in PCV accounted for >60% of the total serotypes in 11 reports.^{6,11,12,14,16-22} Serotype 19A was among the most commonly identified in all of the geographic regions included in this review. In addition, serotypes 1 and 14 were prominent in Europe and Latin America and serotypes 6B, 14 and 19F were important in Africa-East Mediterranean, demonstrating geographic variations in the prevalence of PCV serotypes among pediatric IPD cases. In contrast, from the 30 studies assessing carriage unrelated to IPD among children, only 5 studies reported PCV serotypes accounting for more than 50% of the total serotypes.^{31,33,40,41,44} It would appear from the current snapshot that the introduction of PCV has had a greater impact in reducing nasopharyngeal carriage of PCV-specific serotypes among children without IPD than on IPD itself; further pneumococcal surveillance in coming years may show an additional impact on IPD cases caused by PCV serotypes in pediatric populations.

PCV serotypes were responsible for >60% of total serotypes in IPD cases in few studies among adults aged 65 y and older^{6,58} and 15–59 y.^{6,57} Overall, serotypes 1, 4, 14 and 19A were among the most prevalent PCV serotypes among adults with IPD, while serotype 3 is the most common PCV serotype among adult IPD cases in North America. While the current picture suggests that the availability of PCVs may have had a great effect in targeting PCV-specific serotypes among adult IPD cases, the introduction of PCV7 previously led to an overall reduction in the incidence of all-type IPD ranging from 80% in the US to 30–40% in Europe among children aged less than 5 y.⁶⁵

Globally, several non-PCV IPD serotypes covered by PPV23 were identified; 11A appears to be very prominent among both pediatric and adult non-IPD cases. Although serotypes 15B/C also appear to be common among pediatric non-IPD cases, it is possible that 15B itself may actually be less prevalent. A number of non-vaccine serotypes (i.e., beyond those included in PPV23 and 6A) were reported, both among children and adults. Further understanding of the serotype distribution and dynamics of serotype replacement would be gained from monitoring the most prevalent non-vaccine serotypes in future studies.

There are limitations to be considered in interpreting the results presented in this scoping literature review. It was intended to provide a cross-sectional view of the most recently published data available, which may include studies that were conducted before March 2014 but only published during the selected period (i.e., March 2014–March 2015) for this review. There were no restrictions on sample size as an inclusion criterion for this report, resulting in variations in the denominators used to calculate serotype prevalence. Many studies did not

provide complete serotype distribution data, so it was not possible to report serotype prevalence by vaccine groups (e.g., PCV7, PCV10 not PCV7, PCV13 not PCV7, PPV23 not PCV13), which is useful in making meaningful comparisons across studies. Studies that did not report serotype prevalence according to age categories (e.g., pediatric and adult populations combined) were not further discussed in this analysis, possibly resulting in additional bias.

Another limitation is that the majority of studies reported pneumococcal serotype distribution related to IPD. Nasopharyngeal pneumococcal carriage, the initial step in the development of pneumococcal disease in adults, is sparsely reported. There are also scarce data on non-invasive disease (i.e., non-bacteremic pneumococcal pneumonia both in children and in adults and acute otitis media in children) in the published literature, which is important because the impact of pneumococcal vaccines on non-invasive diseases is indicative of their value to general public health.⁶⁶ There were only 3 studies assessing acute otitis media, which identified serotypes 3 and 25A among the most common.^{27,44,50} In addition, adult populations are not as commonly surveyed as pediatric populations although it is important to understand the impact of PCV introduction and emerging pneumococcal serotypes in adults, especially in the high-risk age group of 65 y and older.

Despite the decline in prevalence of PCV serotypes after PCV implementation, they still circulate and remain a significant source of burden for pediatric IPD, especially in Europe and Latin America, and for adult IPD, in particular in the 15–64-year age group; but the latter is likely due to PCVs' not being routinely used for this age group. Other possible explanations include that although PCVs are included in the national immunization programs in many jurisdictions, an effect may only be observed over a long time period if vaccine uptake rate is far from optimal. The emergence of serotypes 11A and 15B/C appears to be a consequence of the replacement of PPV23 with PCV which do not include these 2 serotypes. Geographic variations in serotype distribution highlight the importance of monitoring the evolving pneumococcal serotype prevalence after pneumococcal vaccine implementation. Ongoing national surveillance is essential to identify newly emerging serotypes despite implementation of new pneumococcal vaccines which inevitably replace the serotypes targeted by vaccines. This permits evidence-based serotype selection in the design of future pneumococcal vaccines.

Materials and methods

Study design and searches

An extensive literature search was conducted to extract serotype distribution data covering invasive pneumococcal disease (IPD) and non-IPD by region from March 2014 to March 2015. This time frame was chosen because it would provide the most recent data, which is the necessary first step for annual monitoring and identification of trends in pneumococcal serotype prevalence. The PubMed database was searched from February 2014 to March 19, 2015. The search was conducted a month earlier to ensure all relevant publications from the start of March 2014 had been captured. Similarly, the EMBASE,

Cochrane Reviews and Ingenta databases were searched from January 2014 until March 19, 2015. The search terms used in all database searches were as follows: (pneumococ* OR streptococcus pneumoniae) AND (serotype OR serogroup).

Available abstracts from the following infectious diseases conferences were also searched: European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), ID Week, International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD), International Congress on Infectious Disease (ICID) and Infectious Diseases Society of America (IDSA). The websites for Centers for Disease Control and Prevention (CDC) and the World Health Organizations (WHO) were also searched. The exclusion criteria were randomized controlled trials, case reports, commentaries, editorials, news and letters.

Data extraction and analysis

The data extracted included author and year of publication, country, study period, study characteristics, total population, age groups, PCV immunization program status and distribution of serotypes reported. The serotype prevalence was calculated wherever possible and stratified by geographic region, age groups and type of pneumococcal disease (i.e., IPD versus non-IPD). When the prevalence data were presented only graphically, they were extracted using WebPlot Digitizer (<http://arohatgi.info/WebPlotDigitizer/app/>). The overall and top-ranking serotypes covered by PCV7, PCV10, and PCV13 are extracted and summarized in this review paper. Since the 23-valent polysaccharide vaccine (PPV23) is also indicated for children aged 2 y or older with high risk, we also summarized the serotypes within PPV23 but not in PCV13 and those serotypes not included in any pneumococcal vaccines used among children aged less than 7 y.

Instead of pooling serotype distribution data, serotype prevalence was ranked in terms of how often (i.e., number of citations) a given serotype appeared among the top 3 within each study. All available serotype distribution data were collected but only data from the most recent year or span of years is summarized in this review. Although it was noted whether or not PCV was part of the immunization schedule at the time data were collected, classifying the data presented here by immunization status has not been done because there was generally little to no information available as to uptake and no consistent classification was feasible.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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