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Serotype Distributions and Susceptibility Profiles of *Streptococcus pneumoniae* Associated With Noninvasive Infections in Adult Patients in the United States (2009–2012)

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ABSTRACT

Background: There is limited knowledge of serotypes causing noninvasive pneumococcal infections in adults. This study reports serotype distribution and susceptibility profiles of *S. pneumoniae* causing infections and recovered from non-sterile sites in adult patients in the USA (2009-2012).

Methods: 2,927 *S. pneumoniae* isolated from adult patients (≥18 years of age) seen/hospitalized in 50 centers located in the nine USA Census regions. Isolates were recovered mostly (87.0%; 2,547/2,927) from lower respiratory tract specimens. Serotyping was performed by *cpsB* sequencing, and multiplex PCR. Serotypes 6A/6B, and 7A/7F were differentiated by Quellung. Susceptibility testing applied CLSI methods (M07-A9) and interpretations (M100-S24).

Results: Prevalence of PCV7 serotypes remained stable over the four-year study period (4.6 – 5.5%; *P*=0.953), mostly represented by 19F (64.6% of PCV7). Overall, PCV13 serotypes were identified in 32.7% of samples, declining from 33.7 – 35.5% in 2009 – 2011 to 28.2% in 2012 (*P*=0.007), with a significant decrease in serotypes 7F (*P*=0.013) and 6A (*P*=0.01). Percentages of 19A remained constant (15.8 – 17.1%) during 2009-2011, dropping to 12.2% in 2012 (*P*=0.089). PPSV23-nonPCV13 showed similar overall percentage rates; however, serogroup 15B/15C increased from 2.7 to 6.3%; *P*=0.010. The proportion of non-vaccine serotypes increased gradually during the study period (*P*=0.044), particularly for serotype 35B (from 3.6% in 2009 to 8.2% in 2012; *P*=0.001). Overall, susceptibility rates for penicillin (up to 83.8%; MIC, ≤2 µg/ml) and clindamycin (up to 81.1%) increased over the period when tested against PCV7 and 19F serotypes; while serotype 19A demonstrated decreasing susceptibility rates for penicillin (from 33.2 to 25.3%).

Conclusion: The proportion of PCV7 serotypes associated with adult infections appears stable. Although still elevated (28.2% in 2012), the percentages of PCV13 decreased, driven by serotypes 19A, 6A and 7F, which suggests the impact of indirect effect. Proportions of serotypes 35B and 15B/15C appear to be increasing. Continued surveillance is needed to truly assess the burden of PCV13 serotypes in this older USA population.

INTRODUCTION

In 2000, 7-valent pneumococcal conjugate vaccine (PCV7) was introduced into the infant immunization program in the United States, and a marked decline in the incidence of invasive pneumococcal disease (IPD) was documented among children <5 years old.[1,2] Further evidence also demonstrated reduction of IPD among the adult population following introduction of PCV7, which has been attributed to a reduction of nasopharyngeal colonization in vaccinated children (indirect or herd effects).[3] The decline in IPD among children <5 years old was accompanied by a sustained decline in hospitalizations for pneumonia among children <2 years old through 2009, as well as among the adult population.[4]

In 2010, 13-valent pneumococcal conjugate vaccine (PCV13) replaced PCV7 in the United States, and emerging data for PCV13 have been consistent with earlier reports for PCV7. These emerging data have indicated rapid and significant reductions in the incidence of IPD among children <5 years old, especially in reducing diseases caused by serotypes 19A and 7F.[5] In addition, these emerging reports described clear evidence of indirect effects of PCV13 use in children and in all adult age groups.[6] Moreover, studies demonstrated significantly reduced hospital admissions caused by IPD and non-IPD in children <5 years old, as well as in some adult age groups, 2 years after introduction of PCV13 in the United States.[7]

The diagnostic assays available for the detection and determination of pneumococcal serotypes in noninvasive community-acquired pneumonia are limited. As a result, information about the serotypes causing non-IPD and the dynamics associated with serotypes and infection/colonization are also limited. Studies using recently developed serotype-specific urinary antigen detection technologies have suggested potential differences in serotype distributions between pneumococci-causing IPD and pneumonia.[8,9] This study was conducted to determine the serotype distribution of *Streptococcus pneumoniae* recovered from non-sterile sites (predominately sputum or lower respiratory tract) among patients ≥18 years of age and to evaluate the serotype distribution over the years 2009–2012.

MATERIALS AND METHODS

Clinical Isolates

A total of 2927 *S pneumoniae* clinical isolates received during the 2009–2012 surveyed years as part of the SENTRY Antimicrobial Surveillance Program were included in the study. These isolates were recovered from adult patients (≥18 years of age) seen/hospitalized in 50 medical centers located in the 9 US census regions. Only medical sites contributing *S pneumoniae* for ≥3 consecutive surveyed years were included. Isolates were recovered primarily (87.0%; 2547/2927) from lower respiratory tract cultures (mostly sputum; 54.7%), and each year, approximately one third of the isolates were contributed by each of the 3 age groups evaluated (18–49, 50–64, and ≥65 years). Most US census regions contributed between 7.6%–13.2% of isolates; however, the New England and East North Central regions contributed 15.3% and 20.0%, respectively, and West South Central contributed only 4.0% of isolates.

Bacterial identification was performed by the participating microbiology laboratory and confirmed by the central monitoring laboratory (JMI Laboratories, North Liberty, IA). Confirmation of bacterial identification was performed by colony morphology and biochemical algorithms. When the bacterial identification was questionable using phenotypic methods or an untypeable serotyping result was obtained by the applied methodology, isolates were subjected to a polymerase chain reaction (PCR) assay for further identification.

Antimicrobial Susceptibility Testing

Isolates were tested for susceptibility by broth microdilution methods according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI; M07-A9).[11] Validation of the minimal inhibitory concentration (MIC) values was performed by concurrent testing of quality control strain *S pneumoniae* American Type Culture Collection (ATCC) 49619. In addition, the inoculum density was monitored by colony counts to ensure an adequate number of cells for each testing event. MIC interpretations were based on the CLSI M100-S24.[12]

Pneumococcal Serotyping

Isolates were subjected to PCR assays for amplification of the *cpsB* gene, amplicons were sequenced on both strands, and the nucleotide sequences were analyzed using the Lasergene software package (DNASTAR, Madison, WI).[10] Sequences were compared with others available via PubMed (http://www.ncbi.nlm.nih.gov/blast/). Because of sequence homology among certain serotypes, those showing nucleotide sequence similarity >99% were grouped (eg, 9V/9A, 7F/7A, 11A/11D, 15A/15F, 22F/22A, 15B/15C). All isolates determined to be serogroup 6 by sequencing analysis were subjected to multiplex PCR assays for confirmation and discrimination between 6A/6B and 6C/6D. Isolates determined to be serogroup 6A/6B and 7F/7A were serotyped by the capsular swelling method using commercially available antisera according to manufacturer's instructions (Statens Serum Institut, Copenhagen, Denmark).

RESULTS

- The percentage of PCV7 serotypes remained stable over time (approximately 5%; *P*=0.953), and 19F accounted for the majority of PCV7 serotypes (64.6%; 95/147; **Table 1**).
- Overall, PCV13 serotypes declined (*P*=0.007). A decrease in the prevalence of 7F (*P*=0.013) and 6A (*P*=0.010) was noted, whereas 19A (*P*=0.089) was less frequently detected in 2012 compared with 2009–2011 **(Table 1)**.
- When the PCV7 and PCV13 serotypes were analyzed by age group, PCV7 serotypes were more commonly isolated from patients ≥65 years of age (38.8%) compared with patients aged <65 years (29.9%–31.3%; **Table 2**).
- The PCV13 serotypes were identified in similar overall proportions across the age groups (32.8%–33.9%). A decline in the proportion of PCV13 serotypes over time (from 37.4% in 2009 to 30.0% in 2012) was observed in patients ≥65 years of age **(Table 2)**.
- Serotypes contained within the 23-valent pneumococcal polysaccharide vaccine (PPSV23) but not present in PCV13 (PPSV23-nonPCV13) did not change in prevalence over the 4 years. Among PPSV23-nonPCV13 serotypes, serogroup 15B/15C increased in occurrence over time (*P*=0.010; **Table 1**). However, the frequency of the PPSV23-nonPCV13 serotypes decreased steadily among the 18–49 population age group from 39.6% in 2009 to 29.4% in 2012 (*P*=0.035; **Table 2**).
- Overall, the proportion of nonvaccine serotypes increased gradually during the study period (*P*=0.044; **Table 1**). An increase in the occurrence of serotype 35B was noticeable, from 3.6% in 2009 to 8.2% in 2012 (*P*=0.001). Other serotypes, such as 6C/6D and 23A, also demonstrated a slight increase in proportion over the last 3 years of the study (2010–2012; **Table 1**).
- Isolates clustering within the nontypeable group remained overall stable during the period **(Table 1)**. However, the prevalence of these isolates shifted between the age groups evaluated; in 2009, 53.8% of nontypeable isolates were obtained from adults 50–64 years of age, but by 2012, this rate had fallen to 13.3% (*P*=0.012). By contrast, the percentage of the nontypeable isolates recovered from patients ≥65 years of age increased from 7.7%–60.0% over the same period (*P*=0.009; **Table 2**).

Table 1. Distribution of Serogroups/Types of Noninvasive *S pneumoniae* Collected During 2009–2012 in the United States

Serogroup/Type*	n (%) by Year 2009	2010	2011	2012	All Years
PCV7	25 (4.6)	38 (5.5)	47 (5.0)	37 (5.0)	147 (5.0)
19F	15 (2.7)	24 (3.5)	31 (3.3)	25 (3.4)	95 (3.2)
18 (18A/18B/18C/18F)	3 (0.5)	2 (0.3)	0 (0.0)	2 (0.3)	7 (0.2)
9V/9A	3 (0.5)	0 (0.0)	6 (0.6)	2 (0.3)	11 (0.4)
6B	2 (0.4)	2 (0.3)	4 (0.4)	2 (0.3)	10 (0.3)
23F	2 (0.4)	4 (0.6)	2 (0.2)	3 (0.4)	11 (0.4)
14	0 (0.0)	4 (0.6)	1 (0.1)	2 (0.3)	7 (0.2)
4	0 (0.0)	2 (0.3)	3 (0.3)	1 (0.1)	6 (0.2)
PCV13†	195 (35.5)	232 (33.7)	319 (33.8)	210 (28.2)	956 (32.7)
19A	88 (16.0)	109 (15.8)	161 (17.1)	91 (12.2)	449 (15.3)
3	50 (9.1)	60 (8.7)	84 (8.9)	64 (8.6)	258 (8.8)
7F†	21 (3.8)	22 (3.2)	24 (2.5)	13 (1.7)	80 (2.7)
6A†	11 (2.0)	3 (0.4)	3 (0.3)	5 (0.7)	22 (0.8)
1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
5	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
PPSV23-nonPCV13	134 (24.4)	172 (25.0)	229 (24.3)	197 (26.4)	732 (25.0)
11A/11D	34 (6.2)	41 (6.0)	49 (5.2)	44 (5.9)	168 (5.7)
22A/22F	31 (5.6)	36 (5.2)	49 (5.2)	35 (4.7)	151 (5.2)
15B/15C†	15 (2.7)	36 (5.2)	47 (5.0)	47 (6.3)	145 (5.0)
17F	14 (2.6)	11 (1.6)	15 (1.6)	11 (1.5)	51 (1.7)
10A	13 (2.4)	6 (0.9)	20 (2.1)	11 (1.5)	50 (1.7)
9N/9L	12 (2.2)	22 (3.2)	26 (2.8)	21 (2.8)	81 (2.8)
33F/33A/37	7 (1.3)	8 (1.2)	14 (1.5)	12 (1.6)	41 (1.4)
8	4 (0.7)	4 (0.6)	5 (0.5)	6 (0.8)	19 (0.6)
20	2 (0.4)	6 (0.9)	3 (0.3)	9 (1.2)	20 (0.7)
12F/12A/44/46	2 (0.4)	2 (0.3)	1 (0.1)	1 (0.1)	6 (0.2)
Nonvaccine†	207 (37.7)	271 (39.4)	374 (39.6)	324 (43.4)	1176 (40.2)
6C/6D	45 (8.2)	40 (5.8)	64 (6.8)	54 (7.2)	203 (6.9)
23A	31 (5.6)	32 (4.7)	54 (5.7)	46 (6.2)	163 (5.6)
15A/15F	30 (5.5)	40 (5.8)	44 (4.7)	34 (4.6)	148 (5.1)
23B	22 (4.0)	22 (3.2)	37 (3.9)	43 (5.8)	124 (4.2)
35B†	20 (3.6)	45 (6.5)	75 (7.9)	61 (8.2)	201 (6.9)
16F	15 (2.7)	23 (3.3)	22 (2.3)	16 (2.1)	76 (2.6)
31	13 (2.4)	18 (2.6)	23 (2.4)	20 (2.7)	74 (2.5)
35F/47F	10 (1.8)	10 (1.5)	11 (1.2)	8 (1.1)	39 (1.3)
34	6 (1.1)	17 (2.5)	12 (1.3)	11 (1.5)	46 (1.6)
7C/7B/40	5 (0.9)	12 (1.7)	10 (1.1)	7 (0.9)	34 (1.2)
13	3 (0.5)	4 (0.6)	3 (0.3)	8 (1.1)	18 (0.6)
21	3 (0.5)	2 (0.3)	6 (0.6)	7 (0.9)	18 (0.6)
38/25F/25A	1 (0.2)	2 (0.3)	9 (1.0)	5 (0.7)	17 (0.6)
Other	3 (0.5)	4 (0.6)	4 (0.4)	4 (0.5)	15 (0.5)
Nontypeable	13 (2.4)	13 (1.9)	22 (2.3)	15 (2.0)	63 (2.2)
All	549 (100.0)	688 (100.0)	944 (100.0)	746 (100.0)	2927 (100.0)

PCV7=7-valent pneumococcal conjugate vaccine; PCV13=13-valent pneumococcal conjugate vaccine; PPSV23=23-valent pneumococcal polysaccharide vaccine.
*Differences in serotype prevalence rates over time were assessed by calculating the *P* values by the chi-square test for trends using Epi Info™, version 7.1.1.14.
†*P* value <0.05, which was considered statistically significant.

- All isolates were susceptible to vancomycin and linezolid (data not shown), and the overall penicillin (parenteral susceptible breakpoint [non-meningitis]; ≤2 µg/mL) and ceftriaxone nonsusceptibility rates were 10.3%–15.0% and 7.7%–10.9%, respectively **(Table 3)**.
- When the penicillin susceptibility was analyzed by the oral breakpoint (susceptible breakpoint; ≤0.06 µg/mL), overall nonsusceptibility rates were between 38.3%–46.3%, and high rates were noted for PCV7 (19F), PCV13 (19A), and nonvaccine (6C/6D, 23A, 15A/15F, 23B, and 35B) serotypes. PPSV23-nonPCV13 serotypes showed lower nonsusceptibility rates for oral penicillin, except for 15B/15C.

Table 2. Distribution of Vaccine Types of Noninvasive *S pneumoniae* According to Subject Age Group During 2009–2012 in the United States

Vaccine Type* by Age Group, y	n (%) by Year 2009	2010	2011	2012	All Years
PCV7	25 (4.6)	38 (5.5)	47 (5.0)	37 (5.0)	147 (5.0)
18–49	7 (28.0)	9 (23.7)	16 (34.0)	14 (37.8)	46 (31.3)
50–64	11 (44.0)	10 (26.3)	16 (34.0)	7 (18.9)	44 (29.9)
≥65	7 (28.0)	19 (50.0)	15 (31.9)	16 (43.2)	57 (38.8)
PCV13	195 (35.5)	232 (33.7)	319 (33.8)	210 (28.2)	956 (32.7)
18–49	64 (32.8)	74 (31.9)	118 (37.0)	68 (32.4)	324 (33.9)
50–64	58 (29.7)	82 (35.3)	99 (31.0)	79 (37.6)	318 (33.3)
≥65	73 (37.4)	76 (32.8)	102 (32.0)	63 (30.0)	314 (32.8)
PPSV23-nonPCV13	134 (24.4)	172 (25.0)	229 (24.3)	197 (26.4)	732 (25.0)
18–49†	53 (39.6)	65 (37.8)	75 (32.8)	59 (29.4)	252 (34.4)
50–64	45 (33.6)	49 (28.5)	77 (33.6)	75 (38.1)	246 (33.6)
≥65	36 (26.9)	58 (33.7)	77 (33.6)	63 (32.0)	234 (32.0)
Nonvaccine	207 (37.7)	271 (39.4)	374 (39.6)	324 (43.4)	1176 (40.2)
18–49	63 (30.4)	99 (36.5)	119 (31.9)	106 (32.7)	387 (32.9)
50–64	68 (32.9)	88 (32.5)	128 (34.2)	109 (33.6)	393 (33.4)
≥65	76 (36.7)	84 (31.0)	127 (34.0)	109 (33.6)	396 (33.7)
Nontypeable	13 (2.4)	13 (1.9)	22 (2.3)	15 (2.0)	63 (2.2)
18–49	5 (38.5)	3 (23.1)	8 (36.4)	4 (26.7)	20 (31.7)
50–64†	7 (53.8)	6 (46.2)	7 (31.8)	2 (13.3)	22 (34.9)
≥65†	1 (7.7)	4 (30.8)	7 (31.8)	9 (60.0)	21 (33.3)
All	549 (100.0)	688 (100.0)	944 (100.0)	746 (100.0)	2927 (100.0)

PCV7=7-valent pneumococcal conjugate vaccine; PCV13=13-valent pneumococcal conjugate vaccine; PPSV23=23-valent pneumococcal polysaccharide vaccine.
*Differences in serotype prevalence rates over time were assessed by calculating the *P* values by the chi-square test for trends using Epi Info™, version 7.1.1.14.
†Calculated *P* value <0.05, which was considered statistically significant.

Table 3. Nonsusceptible Rates of Most Common Serogroups/Types Observed Among Noninvasive *S pneumoniae* Collected During 2009–2012 in the United States

Percent of Nonsusceptibility* by Year

Serogroup/Type	Penicillin 2009	Penicillin 2010	Penicillin 2011	Penicillin 2012	Ceftriaxone 2009	Ceftriaxone 2010	Ceftriaxone 2011	Ceftriaxone 2012
PCV7	32.0 (52.0)	28.9 (52.6)	19.1 (55.3)	16.2 (51.4)	28.0	21.1	17.0	21.6
19F	26.7 (46.7)	33.3 (50.0)	25.8 (45.2)	20.0 (60.0)	20.0	25.0	22.6	20.0
Additional PCV13	34.9 (52.3)	33.6 (50.0)	42.6 (58.6)	35.7 (51.9)	26.7	22.8	29.2	31.4
19A	66.8 (89.8)	61.5 (86.2)	78.9 (96.3)	74.7 (91.2)	50.0	41.3	52.2	63.7
3	0.0 (0.0)	0.0 (0.0)	0.0 (2.4)	0.0 (6.2)	0.0	0.0	0.0	0.0
7F	0.0 (9.5)	0.0 (0.0)	0.0 (8.3)	0.0 (0.0)	0.0	0.0	0.0	0.0
PPSV23-nonPCV13	0.7 (10.4)	0.0 (8.1)	1.3 (15.7)	0.5 (13.2)	2.2	0.0	1.7	1.5
11A/11D	0.0 (8.8)	0.0 (2.4)	0.0 (8.2)	2.3 (6.8)	2.9	0.0	2.0	2.3
22A/22F	0.0 (6.5)	0.0 (0.0)	4.1 (14.3)	0.0 (2.9)	3.2	0.0	2.0	2.9
15B/15C	0.0 (33.3)	0.0 (33.3)	2.1 (44.7)	0.0 (36.2)	0.0	0.0	2.1	0.0
17F	0.0 (7.1)	0.0 (0.0)	0.0 (0.0)	0.0 (9.1)	0.0	0.0	0.0	9.1
10A	7.7 (15.4)	0.0 (0.0)	0.0 (5.0)	0.0 (0.0)	7.7	0.0	0.0	0.0
9N/9L	0.0 (0.0)	0.0 (4.5)	0.0 (7.7)	0.0 (4.8)	0.0	0.0	0.0	0.0
33F/33A/37	0.0 (0.0)	0.0 (0.0)	0.0 (7.1)	0.0 (8.3)	0.0	0.0	7.1	0.0
Nonvaccine	1.9 (44.0)	0.4 (47.6)	0.5 (55.0)	0.3 (52.8)	1.9	0.0	1.6	0.9
6C/6D	0.0 (60.0)	0.0 (42.5)	0.0 (59.4)	0.0 (55.6)	0.0	0.0	3.1	0.0
23A	0.0 (45.2)	0.0 (75.0)	0.0 (70.4)	0.0 (71.7)	0.0	0.0	0.0	0.0
15A/15F	0.0 (76.7)	0.0 (97.5)	0.0 (90.9)	0.0 (88.2)	0.0	0.0	0.0	0.0
23B	0.0 (27.3)	0.0 (27.3)	2.7 (32.4)	0.0 (44.2)	0.0	0.0	2.7	0.0
35B	5.0 (80.0)	2.2 (91.1)	1.4 (95.9)	1.6 (91.8)	5.0	0.0	2.7	4.9
16F	6.7 (13.3)	0.0 (0.0)	0.0 (9.1)	0.0 (6.2)	6.7	0.0	4.5	0.0
31	7.7 (7.7)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	7.7	0.0	0.0	0.0
35F/47F	0.0 (0.0)	0.0 (10.0)	0.0 (0.0)	0.0 (0.0)	0.0	0.0	0.0	0.0
34	0.0 (0.0)	0.0 (0.0)	0.0 (8.3)	0.0 (9.1)	0.0	0.0	0.0	0.0
7C/7B/40	0.0 (20.0)	0.0 (0.0)	0.0 (10.0)	0.0 (0.0)	0.0	0.0	0.0	0.0
Nontypeable	0.0 (23.1)	7.7 (61.5)	0.0 (40.9)	0.0 (13.3)	0.0	0.0	0.0	0.0
All	13.3 (38.3)	11.6 (38.8)	15.0 (46.3)	10.3 (41.3)	10.7	7.7	10.9	9.7

Serogroup/Type	Clindamycin 2009	Clindamycin 2010	Clindamycin 2011	Clindamycin 2012	Erythromycin 2009	Erythromycin 2010	Erythromycin 2011	Erythromycin 2012
PCV7	32.0	31.6	23.4	18.9	52.0	52.6	59.6	48.6
19F	40.0	37.5	29.0	24.0	46.7	50.0	41.9	40.0
Additional PCV13	34.9	33.2	44.8	38.1	45.6	49.6	60.2	52.4
19A	64.8	56.9	73.3	70.3	73.9	80.7	91.9	86.8
3	6.0	5.0	15.5	12.5	6.0	8.3	14.3	14.1
7F	0.0	0.0	0.0	7.7	4.8	0.0	8.3	7.7
PPSV23-nonPCV13	1.5	3.5	5.7	3.6	26.1	22.1	34.1	32.5
11A/11D	0.0	0.0	2.0	4.5	35.3	19.5	34.7	27.3
22A/22F	6.5	2.8	12.2	5.7	17.9	16.7	36.7	20.0
15B/15C	0.0	5.6	6.4	2.1	46.7	38.9	61.7	53.2
17F	0.0	0.0	0.0	0.0	28.6	18.2	20.0	9.1
10A	0.0	0.0	0.0	9.1	7.7	0.0	10.0	9.1
9N/9L	0.0	13.6	3.8	4.8	0.0	18.2	3.8	9.5
33F/33A/37	0.0	0.0	14.3	0.0	71.4	50.0	57.1	91.7
Nonvaccine	15.5	18.1	16.9	14.5	33.3	37.6	42.9	37.0
6C/6D	2.2	2.5	3.1	5.6	53.3	40.0	56.2	50.0
23A	6.5	15.6	16.7	13.0	9.7	25.0	18.5	26.1
15A/15F	80.0	92.5	95.5	88.2	86.7	95.0	97.7	94.1
23B	0.0	4.5	5.4	9.3	13.6	4.5	27.0	11.6
35B	5.0	4.4	4.1	1.6	40.0	60.0	62.2	54.1
16F	0.0	0.0	9.1	6.2	0.0	13.0	9.1	6.2
31	15.4	0.0	0.0	5.0	23.1	27.8	26.1	25.0
35F/47F	0.0	0.0	0.0	0.0	0.0	10.0	27.3	12.5
34	0.0	11.8	0.0	0.0	0.0	11.8	8.3	18.2
7C/7B/40	20.0	0.0	0.0	0.0	20.0	0.0	0.0	0.0
Nontypeable	15.4	30.8	13.6	0.0	23.1	53.8	40.9	33.3
All	18.9	19.8	23.5	18.0	35.7	38.1	46.6	40.1

PCV7=7-valent pneumococcal conjugate vaccine; PCV13=13-valent pneumococcal conjugate vaccine; PPSV23=23-valent pneumococcal polysaccharide vaccine.
*Percentage of nonsusceptible isolates according to the susceptible parenteral (≤2 µg/mL; for non-meningitis) and oral (≤0.06 µg/mL; between parentheses) penicillin breakpoints, ceftriaxone (≤1 µg/mL), clindamycin (≤0.25 µg/mL), and erythromycin (≤0.25 µg/mL) published in the CLSI M100-S24 document.

CONCLUSIONS

- **This 4-year longitudinal study indicates a stable (4.6%–5.5%) but persistent presence of PCV7 serotypes (mainly 19F) causing non-IPD among adults in the United States. Of note, approximately 30% of PCV7 strains were isolated from the 18–49 (31.3%) and 50–64 (29.9%) age groups, but these serotypes were slightly more common in patients ≥65 years of age (38.8%).**
- **The overall prevalence of PCV13 serotypes showed signs of decline. The prevalence of serotype 19A remained elevated overall (15.3%), and this was the predominant serotype detected during each year. However, a decrease in 19A prevalence (12.2%) was noted in 2012 compared with previous years (15.8%–17.1%). Serotypes 7F and 6A decreased in prevalence over time, and no change was observed for other PCV13 serotypes.**
- **The results shown here suggest the presence of an indirect effect of PCV13. However, continued surveillance is needed to assess the herd effects of PCV13 in this older population and to more fully understand the emergence of any nonvaccine and nontypeable serotypes.**

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