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# Trends in Antimicrobial Nonsusceptibility of PCV13-Type Streptococcus pneumoniae Pneumonia in Adults in the United States during 2009–2017

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### Introduction

- The epidemiology of pneumococcal pneumonia in the adult population in the United States constantly evolves
- An important contributor to changing epidemiology is the routine use of 13-valent pneumococcal conjugate vaccine (PCV13) in infants since 2010 and older adults (≥65 years of age) since 2014
- This study evaluated trends in PCV13-type distribution and antimicrobial nonsusceptibility of penicillin G (parenteral, non-meningitis breakpoint) of Streptococcus pneumoniae recovered from adult patients hospitalized with pneumonia in the United States during 2009–2017

### Materials and Methods

#### **Bacterial organisms**

- A total of 7,254 invasive and non-invasive *S. pneumoniae* clinical isolates recovered from adult patients (63.6% and 36.4% from patients aged 18–64 and ≥65 years, respectively) with pneumonia during 2009–2017 were included
- These isolates were part of the SENTRY Antimicrobial Surveillance Program and originated from patients hospitalized in 96 medical centers located in the 9 US Census divisions
- 84.1% (6,104/7,254) of isolates came from lower respiratory tract cultures of which 60.2% (3,676/6,104) came from sputum cultures
- 12.4% (900/7,254) of isolates came from blood cultures

#### Antimicrobial susceptibility testing

 Selected isolates were tested for antimicrobial susceptibility using 96-well frozen-form broth microdilution panels manufactured per the Clinical and Laboratory Standards Institute (CLSI) specifications

### Serotyping

 Serotyping assignment was performed by sequencing the cpsB gene obtained by PCR amplification, followed by Sanger or next-generation sequencing; cpsB sequences were compared to other available sequences via the Basic Local Alignment Search Tool (BLAST) of the National Center for Biotechnology Information (NCBI) or the Pneumococcal Capsule Typing (PneumoCaT)

### Results

#### Serotype distribution

- Distribution of PCV13-type pneumonia declined over the study period from 39.0% in 2009 to 22.7% in 2017 (Figure 1A)
- Distribution of the PPV23-non-PCV13-type (serotypes in the pneumococcal polysaccharide vaccine excluding those in PCV13 vaccine) pneumonia increased from 22.9% in 2009 to 28.2% in 2017 (Figure 1A)

- Distribution of non-vaccine-type (those serotypes not contained in PCV13 or PPV23 vaccines) pneumonia increased consistently from 36.4% in 2009 to 46.8% in 2017 (not shown)
- Distribution of serotype 19A (1 serotype contained in PCV13 vaccine) pneumonia declined consistently over the study period from 17.4% in 2009 to 3.9% in 2017 (Figure 1B)

#### Penicillin nonsusceptibility

- Overall, penicillin nonsusceptibility of S. pneumoniae isolates ranged between 10.6% and 13.9% during 2009–2011; results decreased consistently afterward, reaching 3.8% in 2017 (P=0.0002) (Figure 2)
- The trend for penicillin nonsusceptibility of all S. pneumoniae mirrored that observed for PCV13-type isolates, which peaked in 39.1% in 2011 and then consistently decreased to 14.8% in 2017 (P=0.0023) (Figure 2)
- Penicillin nonsusceptibility results of serotype 19A were highest (75.0%) in 2011–2012 and then consistently decreased to 48.8–49.0% in 2015–2016; results increased to 75.9% in 2017 (Figure 2)
- Penicillin nonsusceptibility for 19A decreased on average 6% per year from 2011 to 2016 (P=0.0015)
- The annual number of 19A isolates from pneumonia decreased progressively over time; since 2014, penicillin nonsusceptibility has been driven by "intermediate" resistance with very few or no isolates being resistant (Table 1)
- Penicillin nonsusceptibility results of PPV23-non-PCV13-type and nonvaccine type isolates remained low across the study period ranging between 0% and 1.4% (Figure 2)

### Conclusions

- Penicillin nonsusceptibility of pneumococcal pneumonia decreased from 13.7% to 3.8% over the study period, driven by changes in serotype distribution and nonsusceptibility within serotypes, particularly serotype
- The reduction in adult serotype 19A pneumonia may have resulted from indirect effects from routine pediatric PCV13 vaccination since 2010 and direct effects from vaccination of adults ≥65 years since 2014
- From 2016 to 2017, the statistically non-significant increase in serotype 19A penicillin nonsusceptibility (all intermediate resistance) may be due to natural fluctuations, as few 19A isolates were identified in these later years
- In addition to PCV13, antibiotic resistance may have decreased because of other factors such as changes in provider prescribing practices,
- Although an increase in non-PCV13 type isolates occurred, these isolates did not exhibit a change in penicillin nonsusceptibility

antibiotic stewardship, and introduction of new clones within a serotype

## Acknowledgements

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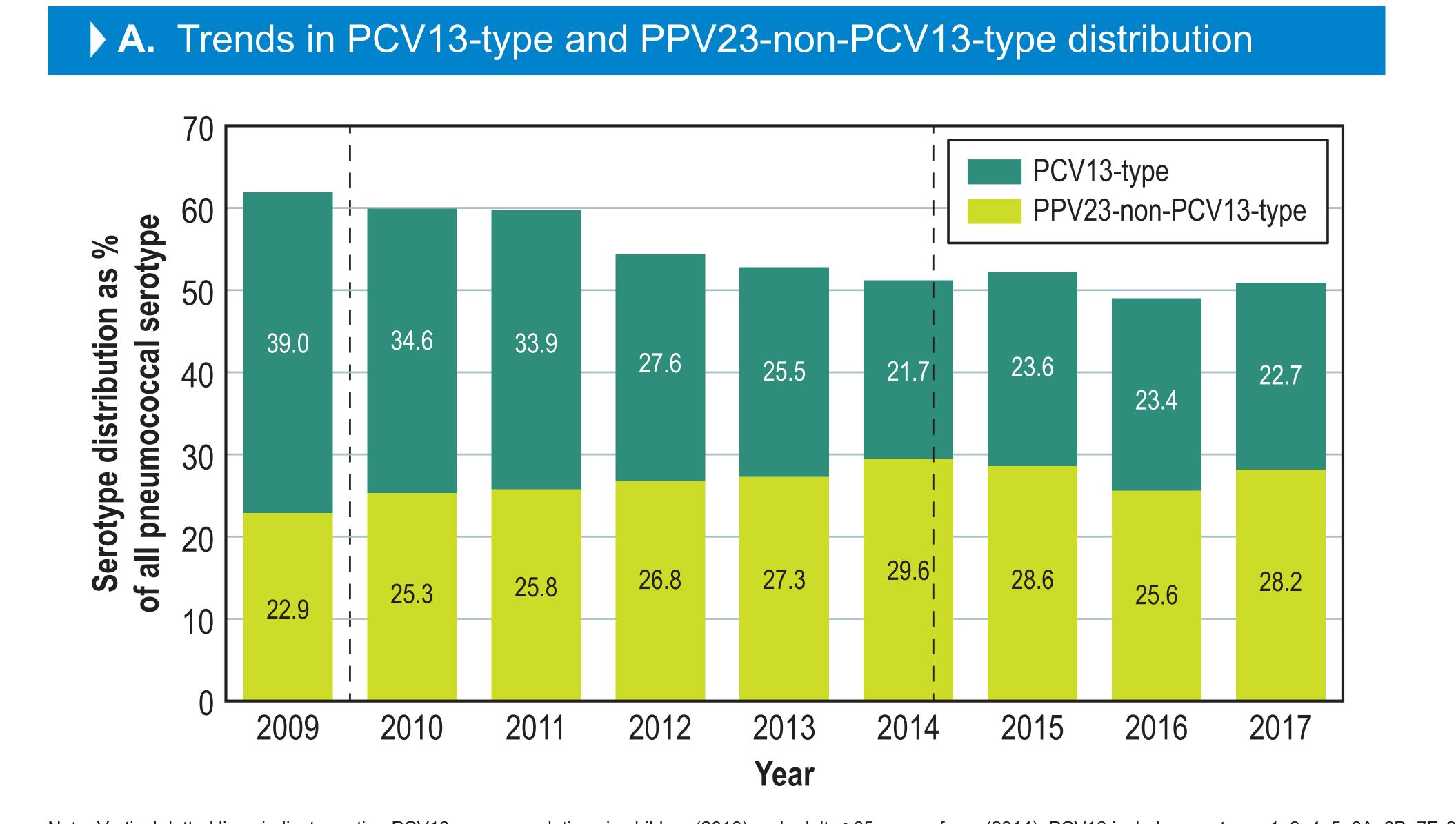
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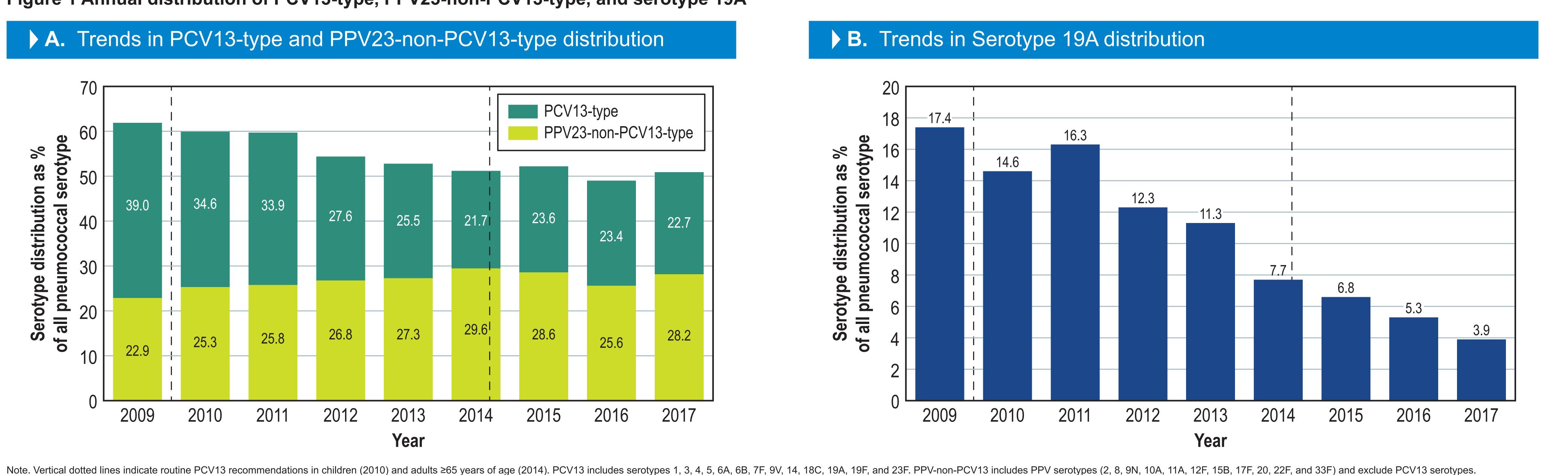
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#### Table 1 Annual count and percentage of serotype 19A by MIC results

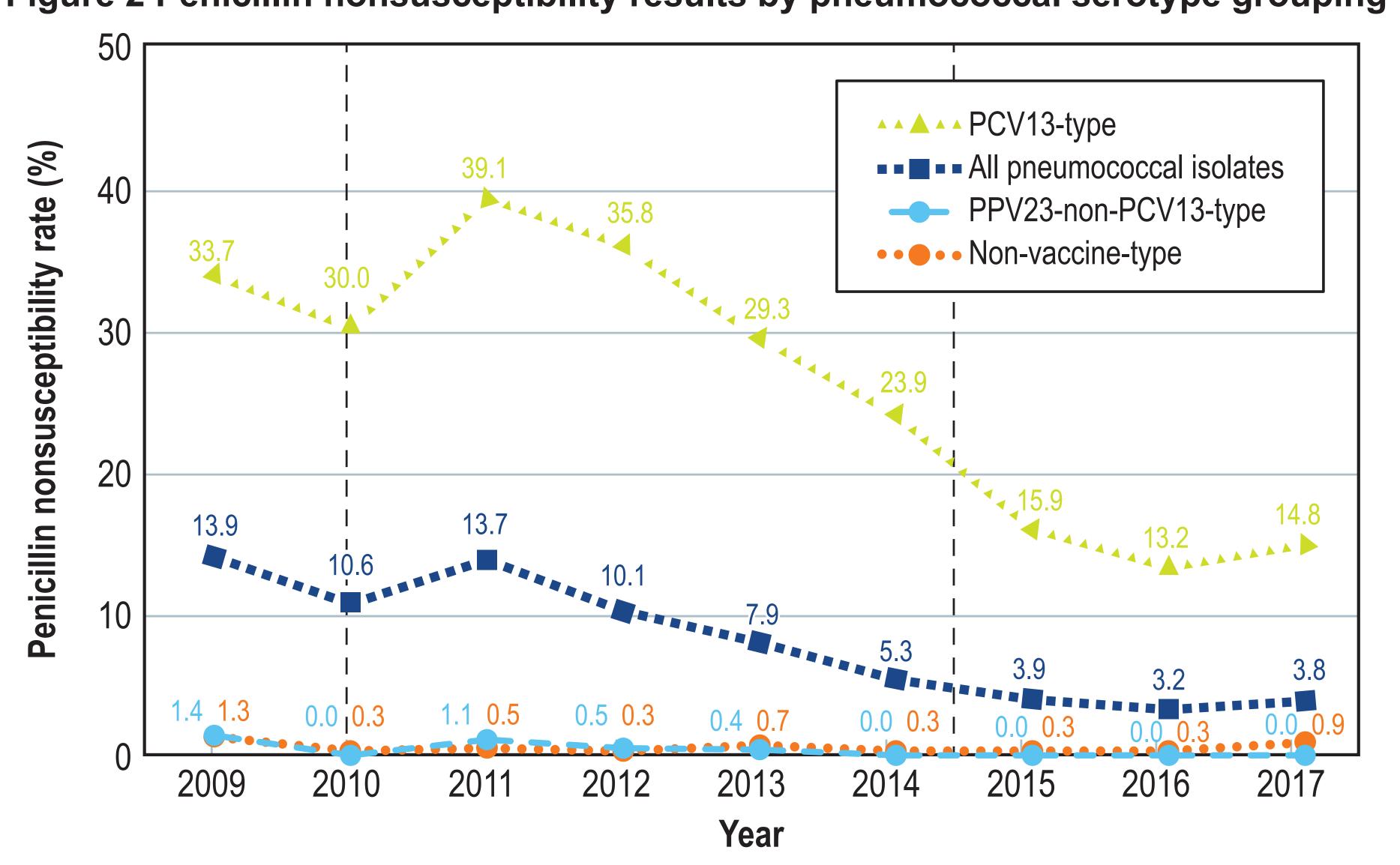
MIC (μg/mL)	Number of 19A isolates per year									Category
	2009	2010	2011	2012	2013	2014	2015	2016	2017	Interpretation
≤0.06	11	17	9	8	20	10	13	5	5	S
0.12-1	26	20	25	9	12	3	3	6	0	
2	1	7	8	6	8	13	9	11	2	
4	58	67	109	60	62	36	24	19	22	I
>4	15	2	17	8	4	2	0	2	0	R
Total	111	113	168	91	106	64	49	43	29	
% penicillin intermediate	52.3	59.3	64.9	65.9	58.5	56.3	49.0	44.2	75.9	
% penicillin resistant	13.5	1.8	10.1	8.8	3.8	3.1	0.0	4.7	0.0	
penicillin nonsusceptible	65.8	65.1	75.0	74.7	62.3	59.4	49.0	48.8	75.9	

#### Figure 1 Annual distribution of PCV13-type, PPV23-non-PCV13-type, and serotype 19A





#### Figure 2 Penicillin nonsusceptibility results by pneumococcal serotype grouping



Note. Vertical dotted lines indicate routine PCV13 recommendations in children (2010) and adults ≥65 years of age (2014). PCV13 includes serotypes 1 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F. PPV23-non-PCV13 includes PPV serotypes (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, and 33F) and exclude PCV13 serotypes.