SEROTYPE DISTRIBUTION OF *Streptococcus Pneumoniae* RECOVERED FROM ADULTS IN THE UNITED STATES AND SELECTED EUROPEAN COUNTRIES (2009-2013)

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INTRODUCTION

- *Streptococcus pneumoniae* is an important pathogen responsible for community-acquired pneumonia (CAP), bacteraemia, meningitis and otitis media, and continues to be a major cause of morbidity and mortality worldwide.
- Following the introduction of the seven-valent and 13-valent pneumococcal conjugate vaccines (PCV7, PCV13) in National Immunization Programs (NIPs) globally, a decline in the incidence of invasive pneumococcal disease (IPD) and non-IPD has been documented among children <5 years of age (see **Table 1** for NIP within countries included in this study).
- Widespread use of these vaccines has been associated with declines in pneumococcal infections (herd effects) in the older, non-vaccinated, population as a result of a reduction in transmission of vaccine-type pneumococci.
- It is important to continually evaluate serotypes in IPD and non-IPD among the adult population.
- This study was conducted to determine the prevalence and serotype distribution of *S. pneumoniae* in clinical isolates associated with non-invasive lower respiratory tract infections (recovered mostly from sputum or lower respiratory tract secretions) among adult patients in the US and selected European countries from 2009 through 2013.

METHODS

Clinical isolates

- A total of 5,303 *S. pneumoniae* isolates (4,323, US; 423, France; 164, Germany; 180, Ireland; 213, United Kingdom [UK]) were included.
- Isolates were recovered from patients ≥18 years of age between 2009 - 2013.
- Most (80.3%) *S. pneumoniae* isolates originated from lower respiratory tract specimen cultures - only 6.7% of isolates were cultured from invasive sources.
- Isolates were collected and submitted to a central monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA), as part of the SENTRY Antimicrobial Surveillance Program following specific guidelines.
- Bacterial identification was performed by the participating microbiology laboratory and confirmed by the central monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA).
- 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 PCR assay for further identification.

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 analysed using the Lasergene software package (DNASTAR, Madison, Wisconsin, USA).
- Sequences were compared to others available via Pubmed (http://www.ncbi.nlm.nih.gov/blast/). Due to sequence homology among certain serotypes, those showing nucleotide sequence similarity greater than 99% were grouped (e.g. 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

PCV7 Serotypes

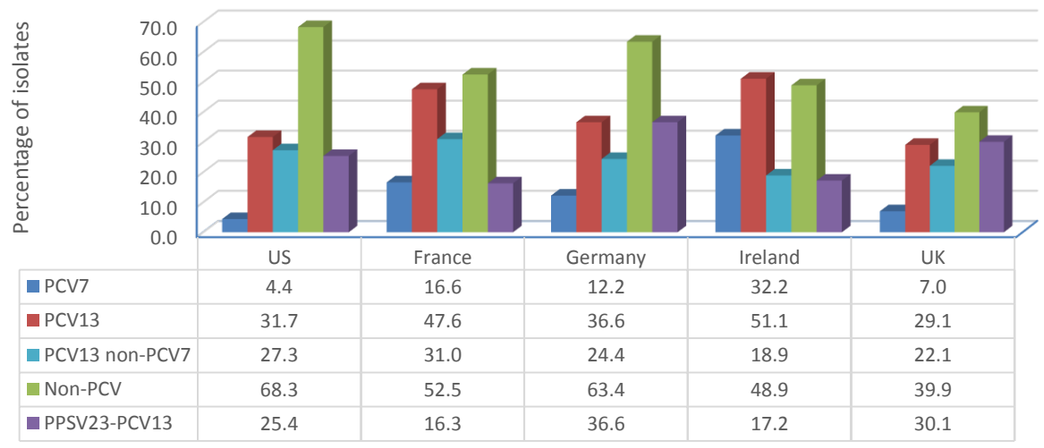
- Between 2009-2013, PCV7 serotypes were most prevalent in adults in Ireland (32.2%), where PCV7 use in infants did not begin until 2008 (**Figure 1** and **Table 1**).
- PCV7 serotypes were lowest among respiratory isolates in adults in the US, as PCV7 implementation in US infants occurred 6 to 8 years earlier than in France, Germany, Ireland and the UK (**Figure 2A**).

PCV13 Serotypes

- In each of the respective countries, PCV13 was incorporated into the infant NIPs in 2009/2010 (**Table 1**). The percent of isolates associated with PCV13 serotypes decreased by 17%, 25%, 24%, 24% and 6.2% in France, Germany, Ireland, the UK and the US, respectively (2010-2013 vs 2009-2010) (**Figure 2B**).
- Serotypes 19A (16.1%), 3 (9.1%) 7F (5.1%) and 6A (1.1%) were detected in the US during 2009-2010, and decreased to 12.4%, 8.1%, 1.3% and 0.6%, respectively, in the second period (**Table 2**).
- While the overall prevalence of PCV13 serotypes decreased in Europe (from 54.8% to 30.9%), primarily due to decreases of 3 and 6A, serotype 19A increased in France, Germany and Ireland (**Tables 1** and **Table 2**).

Non-PCV13 serotypes

- The prevalence of non-PCV13 serotypes increased among all countries investigated (2010-2013 vs 2009-2010) (**Figure 2C**).
- The prevalence of serotypes unique to PPSV23 increased between the respective time periods in each country examined, with the exception of France (19.0% vs 14.8%; **Figure 2D**).



	US	France	Germany	Ireland	UK
PCV7	4.4	16.6	12.2	32.2	7.0
PCV13	31.7	47.6	36.6	51.1	29.1
PCV13 non-PCV7	27.3	31.0	24.4	18.9	22.1
Non-PCV	68.3	52.5	63.4	48.9	39.9
PPSV23-PCV13	25.4	16.3	36.6	17.2	30.1

Figure 1: Relative overall percentages of *S. pneumoniae* vaccine serotypes observed in the USA and European countries collected during 2009-2013 in the SENTRY Antimicrobial Surveillance Program.

Table 1: Summary of pneumococcal vaccine recommendations .

France	Infants • PCV7 introduced into NIP in 2006 (2 + 1); replaced by PCV13 in 2010. Vaccine coverage ~94 %. Other ages • PCV13 recommended for at risk (≥2 years of age) since 2013 • PPV23 recommended for at risk (≥5 years of age) since 2013
Germany	Infants • PCV7 introduced into NIP in 2006 (3+1); replaced by PCV10/PCV13 in 2009; current uptake is >90%, of which 96% is PCV13. Other ages • PCV13 for some at-risk age groups since 2014 • PPV23 recommended for at-risk adults since 1982. Recommended for those ≥ 60 years since 1998.
Ireland	Infants • PCV7 introduced into NIP in 2008 (2 + 1); replaced by PCV13 in 2010. Vaccine coverage ~91 % Other ages • PCV13/PPV23 for some medium and high-risk age groups since 2013 • PPV23 for those ≥65 years since 2013
United Kingdom	Infants • PCV7 introduced into NIP in 2006 (2 + 1); replaced by PCV13 in 2010. Vaccine uptake ~90%. Other ages • PPV23 for at risk ≥ 2 years since 1992 and all ≥65 years since 2003.
United States	Infants • PCV7 introduced into NIP in 2000 (3 + 1); replaced by PCV13 in 2010. Vaccine uptake ~90%. Other ages • PPV23 for those ≥65 years since 1983; PCV13 followed by PPV23 for those ≥65 years since 2014.

CONCLUSIONS

- The prevalence of PCV7 serotypes associated with non-invasive lower respiratory tract infections in adults in the US and Europe declined. However, PCV7 serotypes remained elevated in France (12.0%), Germany (12.6%) and Ireland (21.9%).
- The higher prevalence of PCV7 serotypes observed in respiratory isolates in adults in Ireland may be due to a later implementation of the paediatric NIP (2008), compared to the other investigated countries.
- Prevalence of PCV13 serotypes also decreased during the study period in all evaluated countries, which can be attributed presumably to herd effects from paediatric NIPs. However, the prevalence of PCV13 serotypes remained high in Ireland (42.2%) and France (38.9%).
- Despite PPV23 use in adults, the prevalence of the serotypes contained in PPV23 and not PCV13 generally increased after the introduction of PCV13 into the infant NIP. Other studies have shown an increase in the serotypes unique to PPV23 for IPD in adults in the UK following PCV13 use in infants.
- Continued surveillance is needed to monitor the impact of PCV13 on the distribution of *S. pneumoniae* serotypes among older US and European adults as paediatric immunisation programmes mature.

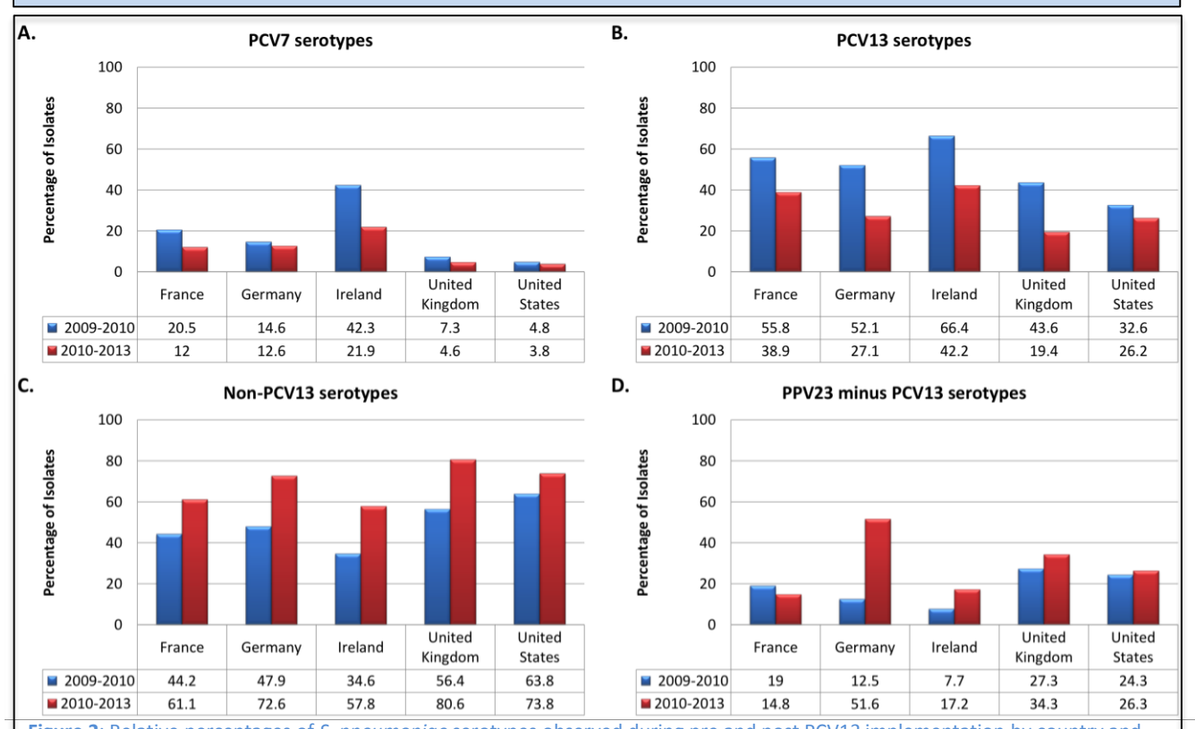


Figure 2: Relative percentages of *S. pneumoniae* serotypes observed during pre and post PCV13 implementation by country and sampling year.

Table 2: Serotype distribution of PCV7 and PCV13 isolates detected between sampling periods in the US and European countries.

Serogroup/type	Number of isolates (%) by region			
	US		Europe	
	2009-2010	2012-2013	2009-2010	2012-2013
PCV7	72 (4.8)	64 (3.8)	72 (20.9)	44 (11.7)
19F	43 (2.9)	43 (2.5)	21 (6.1)	18 (4.8)
18(18A/18B/18C/18F)	5 (0.3)	2 (0.1)	3 (0.9)	3 (0.8)
9V/9A	3 (0.2)	5 (0.3)	12 (3.5)	6 (1.6)
6B	6 (0.4)	4 (0.2)	11 (3.2)	7 (1.9)
23F	7 (0.5)	4 (0.2)	10 (2.9)	1 (0.3)
14	5 (0.3)	2 (0.1)	13 (3.8)	4 (1.1)
4	3 (0.2)	4 (0.2)	2 (0.6)	5 (1.3)
PCV13	540 (36.2)	443 (26.2)	189 (54.8)	116 (30.9)
19A	240 (16.1)	210 (12.4)	31 (9.0)	33 (8.8)
3	136 (9.1)	136 (8.1)	48 (13.9)	23 (6.1)
7F	76 (5.1)	22 (1.3)	14 (4.1)	12 (3.2)
6A	16 (1.1)	10 (0.6)	16 (4.6)	4 (1.1)
1	0 (0.0)	1 (<0.1)	6 (1.7)	0 (0.0)
5	0 (0.0)	0 (0.0)	2 (0.6)	0 (0.0)

Table 3: Serotype distribution of specific PCV7 and PCV13 isolates detected between sampling periods in European countries.

Serogroup/type	Number of isolates (%) by European country							
	France		Germany		Ireland		United Kingdom	
	2009-2010	2012-2013	2009-2010	2012-2013	2009-2010	2012-2013	2009-2010	2012-2013
PCV7								
19F	9 (23.1)	9 (69.2)	3 (42.9)	3 (25.0)	8 (36.4)	4 (28.6)	1 (25.0)	2 (40.0)
18(18A/18B/18C/18F)	1 (2.6)	0 (0.0)	1 (14.3)	2 (16.7)	1 (4.5)	0 (0.0)	0 (0.0)	1 (20.0)
9V/9A	8 (20.5)	2 (15.4)	1 (14.3)	0 (0.0)	2 (9.1)	2 (14.3)	1 (25.0)	2 (40.0)
6B	6 (15.4)	2 (15.4)	0 (0.0)	0 (0.0)	4 (18.2)	5 (35.7)	1 (25.0)	0 (0.0)
23F	5 (12.8)	0 (0.0)	2 (28.6)	0 (0.0)	2 (9.1)	1 (7.1)	1 (25.0)	0 (0.0)
14	8 (20.5)	0 (0.0)	0 (0.0)	2 (16.7)	5 (22.7)	2 (14.3)	0 (0.0)	0 (0.0)
4	2 (5.1)	0 (0.0)	0 (0.0)	5 (41.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
PCV13								
19A	18 (26.9)	18 (62.1)	3 (16.7)	4 (28.6)	3 (25.0)	9 (69.2)	7 (35.0)	2 (12.5)
3	29 (43.3)	8 (27.6)	12 (66.7)	8 (57.1)	1 (8.3)	0 (0.0)	6 (30.0)	7 (43.8)
7F	7 (10.4)	2 (6.9)	2 (11.1)	1 (7.1)	2 (16.7)	3 (23.1)	3 (15.0)	6 (37.5)
6A	8 (11.9)	1 (3.4)	0 (0.0)	1 (7.1)	6 (50.0)	1 (7.7)	2 (10.0)	1 (6.3)
1	3 (4.5)	0 (0.0)	1 (5.6)	0 (0.0)	0 (0.0)	0 (0.0)	2 (10.0)	0 (0.0)
5	2 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

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