

OBJECTIVES

Streptococcus pneumoniae remains a leading cause of pneumonia, sepsis and meningitis and disproportionately affects young children and the elderly. In July 2006, vaccination with pneumococcal conjugate vaccine was generally recommended in Germany for all children \leq 24 months. In this study, we present the serotype distribution among adults with IPD, bacteremic pneumococcal pneumonia and IPD with underlying conditions before and after the start of childhood vaccination.

METHODS

The National Reference Center for Streptococci has monitored the epidemiology of invasive pneumococcal disease (IPD) in adults in Germany since 1992. Cases of IPD in adults are reported by a laboratory-based surveillance system, including 265 laboratories throughout Germany. The present analysis includes cases documented between 1992 and 2013. Species confirmation was done by optochin testing and bile solubility testing. All isolates were serotyped using the Neufeld Quellung reaction.

RESULTS

In the first 14 seasons of our surveillance an average of 341 isolates from IPD among adults were received per season. Due to the introduction of a web-based surveillance system (Pneumoweb), these numbers could be increased to about 2000 in the last 5 seasons (Fig. 1).

Before the introduction of childhood vaccination (1992-2006) the most prevalent serotypes among adults with IPD were 14, 3, 7F, 4, 23F, 1 and 9V. In 2012-2013 serotypes 3, 19A, 7F and 22F were most prevalent (Table 1).

Before childhood vaccination 40-45% of IPD cases among adults were caused by PCV7 serotypes. After vaccination this percentage was gradually reduced to 7.8% in 2012-2013 (Fig. 2). This indicates a herd protection effect among adults.

In 2009, higher valent vaccination (PCV10 (April 2009) and PCV13 (December 2009)) was introduced among children. Among adults, a reduction of the percentage of IPD caused by the six extra serotypes from 47.1% in 2010-2011 to 36.0% in 2012-2013 was observed (Fig. 2). The reduction was observed for serotypes 1, 6A, 7F and 19A (Fig. 3). In 2012-2013, the coverage of PPV23 among IPD in adults was 75.7%, coverage of PCV13 was 43.8% (Fig. 4). Serotypes more prevalent in 2012-2013 as compared to the pre-vaccination era were 6C, 10A, 12F, 15A/C, 16F, 23A, 23B (PenR), 24F, 31, 35F and 38 (Table 2).

In 1992-2006 the most prevalent serotypes among bacteremic pneumococcal pneumonia in adults were serotypes 14, 1, 4, 3, 7F and 9V. In 2012-2013 serotypes 3, 19A, 7F, 12F and 22F were most prevalent (Table 3), and the coverages of PCV13 and PPV23 were 48.4% and 77.8% (Fig. 5). Among patients with underlying conditions coverage of PCV13 was 34.7% (PPV23: 70.1%; Fig. 6).

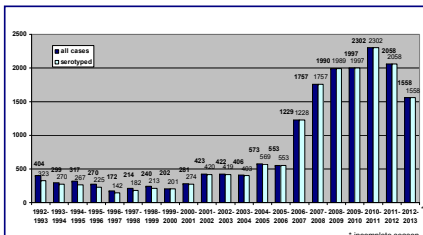


Fig. 1: Number of cases of IPD from adults in Germany and number of serotyped cases per pneumococcal season (July to June in the following year).

Table 1: Prevalence of serotypes among IPD from adults (age \geq 16 y.) in Germany, before (1992-2006) and 6 years (2011-2012) and 7 years (2012-2013) after the introduction of childhood conjugate vaccination (PCV7: 2006, PCV10/PCV13: 2009).

Serotype	1992-2006	%	Serotype	2011-2012	%	Serotype	2012-2013	%
all	4461	100.0	all	2058	100.0	all	1586	100.0
PPV23	3390	67.2	PPV23	1592	77.4	PPV23	1179	75.7
PCV13	3218	72.1	PCV13	1611	78.1	PCV13	853	43.8
PCV10	2661	59.6	PCV10	470	22.8	PCV10	298	18.8
PCV7	1927	43.2	PCV7	153	7.4	PCV7	122	7.8
14	500	11.2	3	258	12.5	3	218	14.0
3	388	8.7	19A	235	11.4	19A	153	9.8
4	367	8.2	7F	211	10.3	7F	126	8.2
9V	341	7.6	22F	127	6.2	22F	112	7.2
1	306	6.9	12F	113	5.6	12F	94	6.0
7F	293	6.6	6C	106	5.2	8	74	4.7
23F	260	5.8	6C	75	3.6	9N	62	4.0
6B	180	4.0	8	70	3.4	11A	56	3.6
8	159	3.6	9M	66	3.2	6C	55	3.5
18F	158	3.5	11A	59	2.9	10A	46	3.0
6A	139	3.1	23B	59	2.9	23B	46	3.0
10A	129	2.9	10A	58	2.8	15A/C	45	3.0
9N	125	2.8	23A	50	2.4	15A	45	2.9
18C	119	2.7	16A	45	2.2	23A	41	2.6
15F	114	2.6	24F	45	2.2	24F	31	2.0
11A	106	2.4	35F	39	1.9	35F	30	1.9
22F	101	2.3	6A	38	1.8	14	29	1.9
10A	79	1.8	1	4	0.2	29	1.8	
24F	46	1.0	15B	28	1.4	35F	24	1.5
20	37	0.8	14	27	1.3	18F	21	1.3
6	35	0.8	31	28	1.3	38	21	1.3
33F	35	0.8	38	24	1.2	35B	21	1.3
23A	30	0.7	16F	23	1.1	31	19	1.2
17F	29	0.7	33F	19	1.1	16F	18	1.2

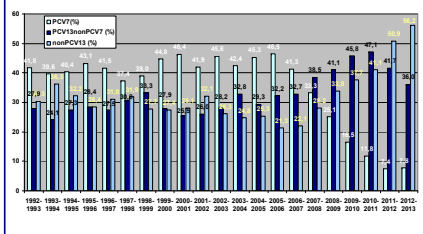


Fig. 2: percentage of PCV7, PCV13-non-PCV7 and non-PCV13 serotypes among cases of IPD from adults in Germany.

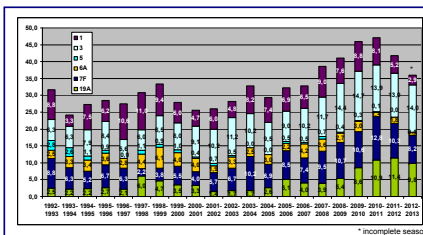


Fig. 3: Percentage cases with serotypes 1, 3, 5, 6A, 7F and 19A among cases of IPD from adults in Germany.

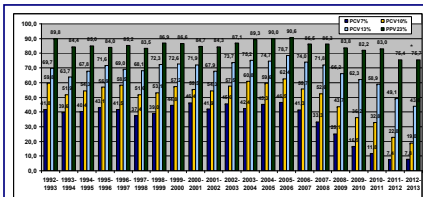


Fig. 4: Theoretical coverage of different vaccine formulations for IPD among adults in Germany per pneumococcal season.

Table 2: Fold increase of serotypes among adults (age \geq 16 y.) with IPD, in 2012-2013 as compared to the last season pre-vaccination (2005-2006).

all serotypes	2006-2006	2012-2013	fold increase	x2.8	change (%)	fold	
all serotypes	79	122	1.5	2.11	86.3	8.1	
PCV7	257	122	0.5	7.21	-83.2	0.2	
non-PCV7	206	126	0.6	1.26	24.5	0.4	
PCV13	683	116	0.17	12.06	-82.3	0.1	
PCV13nonPCV7	178	661	3.7	501	119.1	1.1	
nonPCV13	118	197	1.7	3.92	199.9	1.7	
PPV23	601	1179	2.4	1411	-16.6	0.8	
nonPCV13nonPCV7	78	112	1.4	220	133.0	1.7	
nonPCV23	52	99	1.9	147	128.7	2.5	
6B	26	7	0.3	31	-80.4	0.1	
9V	43	8	0.2	121	-95.4	0.1	
14	75	39	0.5	211	-86.3	0.1	
18C	12	32	1.0	34	-64.5	0.4	
19A	20	21	1.1	29	-62.7	0.4	
23F	38	17	0.4	167	-84.1	0.2	
3	38	45	1.2	127	-89.8	0.4	
5	3	1	0.3	8	-89.2	0.1	
7F	27	18	0.7	123	-92.8	0.1	
8	50	218	4.4	149	82.9	1.6	
6A	12	16	1.3	34	-62.7	0.6	
19A	28	28	1.0	34	-62.7	0.4	
2	0	17	7.4	4.4	49	54.5	1.5
9N	11	62	5.6	31	100.1	2.0	
11A	9	59	6.2	25	120.9	2.2	
12F	3	64	31.3	8	161.2	11.1	
15F	0	0	0	1.6	31.6	1.1	
20	3	13	4.3	8	53.8	1.6	
21	3	3	1.0	6	6.0	1.1	
22F	18	112	6.2	51	120.0	2.2	
23F	16	43	2.7	23	62.5	1.9	
6C	7	95	18.3	33	501.7	6.2	
15C	2	14	7.0	4	100.0	2.0	
15F	1	18	18.0	3	53.8	0.4	
23A	5	41	8.2	24	191.2	2.9	
23B	1	49	49.0	3	153.7	16.3	
24F	3	31	10.3	3	26.8	3.4	
31	2	19	9.5	6	217.2	3.4	
35F	3	24	8.0	6	164.0	2.1	
38	28	21	7.0	8	140.5	2.8	
91	0	3	3.0	0	0	0	

Table 3: Prevalence of serotypes among adults (age \geq 16 y.) with bacteremic pneumonia in Germany, before (1992-2006) and 6 years (2011-2012) and 7 years (2012-2013) after the introduction of childhood conjugate vaccination (PCV7: 2006, PCV10/PCV13: 2009).

Serotype	1992-2006	%	Serotype	2011-2012	%	Serotype	2012-2013	%
all	1463	100.0	all	468	100.0	all	276	100.0
PPV23	1361	90.9	PPV23	387	76.3	PPV23	214	77.8
PCV13	1108	75.3	PCV13	232	49.6	PCV13	133	48.4
PCV10	890	61.3	PCV10	92	19.7	PCV10	64	23.3
PCV7	614	42.3	PCV7	23	4.9	PCV7	25	9.1
14	205	14.1	3	78	16.2	3	38	13.8
3	184	12.6	19A	65	13.9	19A	45	16.3
4	159	10.9	7F	41	8.8	7F	29	9.8
9V	138	9.4	22F	30	6.4	22F	20	7.3
1	114	7.8	12F	28	6.0	12F	19	6.9
9V	108	7.4	12F	25	5.3	6	12	4.4
23F	59	4.1	9N	20	4.3	11	4.0	
8	55	3.8	8	18	3.8	9N	11	4.0
18A	51	3.5	6C	18	3.8	6C	9	3.3
18B	42	2.9	24F	15	3.2	11A	8	2.9
12F	41	2.8	35F	14	3.0	35F	8	2.9
9N	37	2.6	11A	13	2.8	15A	7	2.5
15F	35	2.4	10A	12	2.6	14	5.2	
32	32	2.2	6A	11	2.4	4	6	
6A	31	2.1	23B	8	1.7	19F	6	2.2
18C	30	2.1	35F	6	1.3	35B	6	2.2
18E	17	1.2	15A	6	1.3	25A	5	1.8
8	18	1.2	23A	6	1.3	38	5	1.8
10A	15	1.0	15A	6	1.3	23B	5	1.8
20	13	0.9	33F	6	1.3	10A	4	1.5
24F	11	0.8	15B	6	1.3	24F	4	1.5

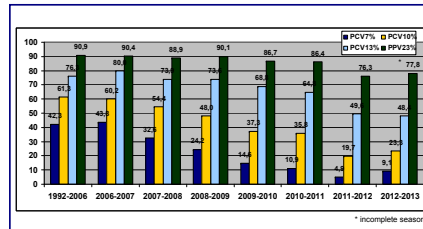


Fig. 5: Theoretical coverage of different vaccine formulations for bacteremic pneumonia among adults in Germany per pneumococcal season.

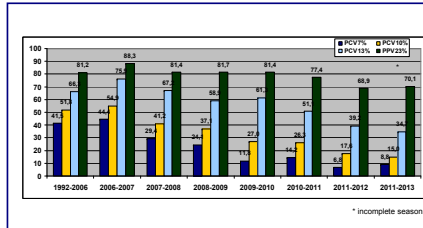


Fig. 6: Theoretical coverage of different vaccine formulations for IPD among adults with underlying disease in Germany per pneumococcal season.

CONCLUSIONS

- Since the general recommendation for childhood pneumococcal conjugate vaccination a clear reduction in IPD has been observed among children.
- In addition, the percentage of IPD among adults caused by PCV7 serotypes was strongly reduced, indicating a herd protection effect.
- Following the introduction of higher valent childhood conjugate vaccines (PCV10 and PCV13) in 2009, a first indication for herd protection to the 'new serotypes' could be observed.
- In the current season (2012-2013) the prevalence of serotypes 1, 6A, 7F and 19A has diminished among adults with IPD.
- Serotype 5 is rare among IPD in German adults.
- Serotypes 6C, 10A, 12F, 15A/C, 16F, 23A, 23B, 24F, 31, 35F and 38 have gained importance among IPD in German adults.
- Serotype 23B is the strongest increasing serotype, and often penicillin resistant.
- The theoretical serotype coverage of PCV13 among adults for IPD and pneumonia is high (43.8% and 48.4% respectively, PPV23: 75.7% and 77.8%).
- Coverage among patients with underlying conditions is lower: PCV13: 34.7%, PPV23: 70.1%.