

Effects of 7 years of immunization with higher-valent pneumococcal conjugate vaccines among children in Germany

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BACKGROUND AND AIMS

A general recommendation for vaccination with pneumococcal conjugate vaccine (PCV) was issued for children ≤ 2 years in Germany in 2006. In 2009, two higher-valent PCVs (PCV10, PCV13) were licensed in Germany. Here, we present data on invasive pneumococcal disease (IPD) -cases sent in for serotyping in the eleven years following the start of PCV-vaccination.

METHODS

Pneumococcal isolates recovered from children with IPD were serotyped at the GNRCS using the Neufeld-Quellung-reaction.

RESULTS

IPD cases among children have reduced from about 300 before vaccination to about 200 in the current season (2016-2017; **Fig. 1**). Reductions were seen in all three age groups (**Fig. 2**). In 2015-2016, 100 IPD isolates recovered from children < 2 years were sent in, of which only 18 had PCV13 serotypes. This represents a reduction of 35% compared to 2005/2006 (before vaccination introduction) and a reduction of 20% since the introduction of higher-valent vaccines (**Fig 3**). Among the PCV13-non-PCV7 serotypes, reductions were observed for serotypes 1 (-100%), 6A (-100%), 7F (-89%) and 19A (-75%). Serotype 3 showed no reduction, serotype 5 remains very rare in Germany (**Fig. 4**). Among the remaining 18 PCV13 cases in children < 2 years reported in 2015/2016, nine children were not vaccinated (**Table 1**). Among the non-vaccine serotypes, 10A, 12F, 15A/B/C, 24F and 38 were most prevalent (**Table 2**).

Compared to 2009/2010, among children 2-4 years and 5-16 years reductions were observed for serotype 1 (-100% and -92%) and serotype 7F (-100%, -50%), whereas cases of serotypes 5, 6A and 19A were rare in these age groups. Serotype 3 cases have decreased among 2-4 year old children from 2 to 1 and from 7 to 6 cases in 5-15 year olds (**Fig. 4**).

Serotypes of penicillin non-susceptible and macrolide resistant isolates have changed after the start of childhood vaccination. Macrolide resistance levels have dropped substantially (**Fig. 5**).

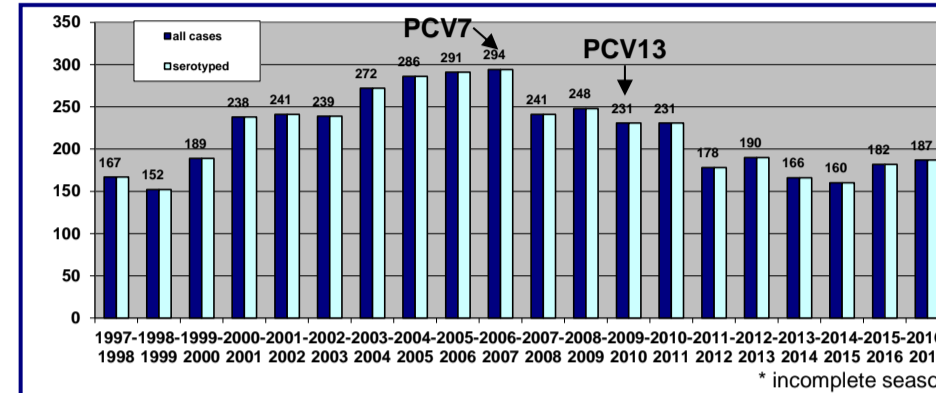


Fig. 1: Number of cases of IPD from children < 16 years of age in Germany and number of serotyped cases per pneumococcal season (July to June in the following year).

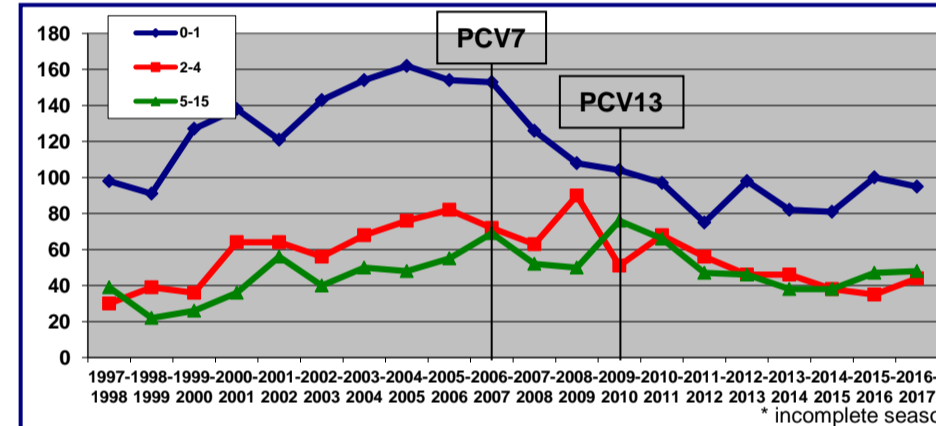


Fig. 2: Number of cases of IPD from children in Germany per pneumococcal season in three age groups: 0-1 year (blue), 2-4 years (red), 5-15 years (green).

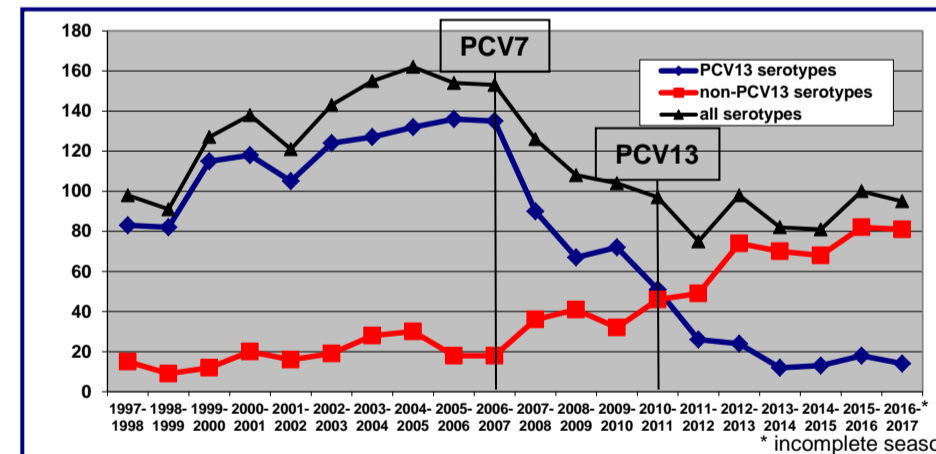


Fig. 3: Number of cases of IPD with PCV13- and non-PCV13 serotypes from children < 2 years in Germany per pneumococcal season.

Table 2: Serotype ranking among IPD in children in Germany.

Rank	Serotype	average 1997-2006	%	Serotype	2014-2015	%	Serotype	2015-2016	%	Serotype	2016-2017	%
	total	231	100.0	total	159	100.0	total	182	100.0	total	187	100.0
	PCV23	201	87.0	PCV23	86	54.1	PCV23	108	59.3	PCV23	102	54.5
	PCV13	195	84.4	PCV13	44	27.7	PCV13	38	20.9	PCV13	39	20.9
	PCV10	174	75.3	PCV10	23	14.5	PCV10	20	11.0	PCV10	9	4.8
	PCV7	142	61.5	PCV7	10	6.3	PCV7	13	7.1	PCV7	7	3.7
1	14	49	21.2	24F	19	11.9	10A	24	13.2	3	22	11.8
2	9V	23	10.0	10A	15	9.4	3	15	8.2	10A	17	9.1
3	19F	17	7.4	19A	10	6.3	12F	15	8.2	23B	17	9.1
4	6B	17	7.4	1	9	5.7	24F	14	7.7	22F	15	8.0
5	1	17	7.4	3	9	5.7	15C	13	7.1	24F	13	7.0
6	23F	14	6.1	12F	8	5.0	23B	12	6.6	16C	12	6.4
7	7F	13	5.6	15A	7	4.4	38	10	5.5	12F	8	4.3
8	18C	13	5.6	15C	7	4.4	22F	10	5.5	18A	7	3.7
9	4	9	3.9	35F	7	4.4	19F	6	3.3	35F	7	3.7
10	6A	8	3.5	38	6	3.8	15B	6	3.3	15A	6	3.2
11	19A	6	2.6	23A	6	3.8	7F	6	2.7	15B	5	2.7
12	3	6	2.6	22F	5	3.1	8	5	2.7	35B	5	2.7
13	10A	4	1.7	23B	5	3.1	9N	4	2.2	19F	4	2.1
14	24F	4	1.7	35F	5	3.1	14	3	1.6	38	4	2.1
15	9A	2	0.9	3	2	1.3	20	2	1.1	9N	3	1.6
16	9N	2	0.9	35B	4	2.5	23A	3	1.6	11A	4	2.1
17	15A	2	0.9	19F	3	1.9	35B	3	1.6	23A	4	2.1
18	8	2	0.9	14	2	1.3	6C	3	1.6	12A	3	1.6
19	15B	2	0.9	18C	2	1.3	18C	2	1.1	17F	3	1.6
20	15C	2	0.9	2	2	1.3	2	2	1.1	35F	3	1.6
21	18B	2	0.9	3	2	1.3	20	2	1.1	9N	3	1.6
22	22F	2	0.9	21	2	1.3	21	2	1.1	20	2	1.1
23	5	1	0.4	34	2	1.3	31	2	1.1	16F	2	1.1
24	38	1	0.4	11A	2	1.3	11A	2	1.1	6C	2	1.1

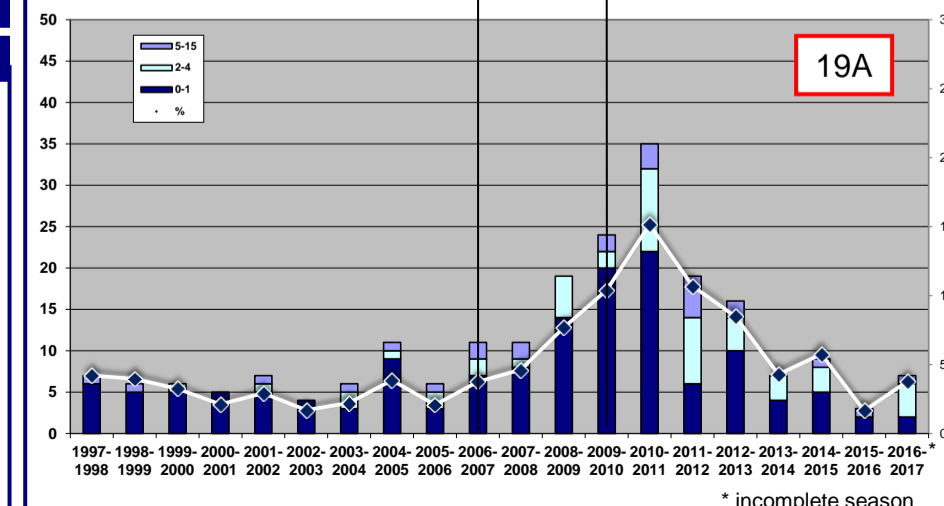
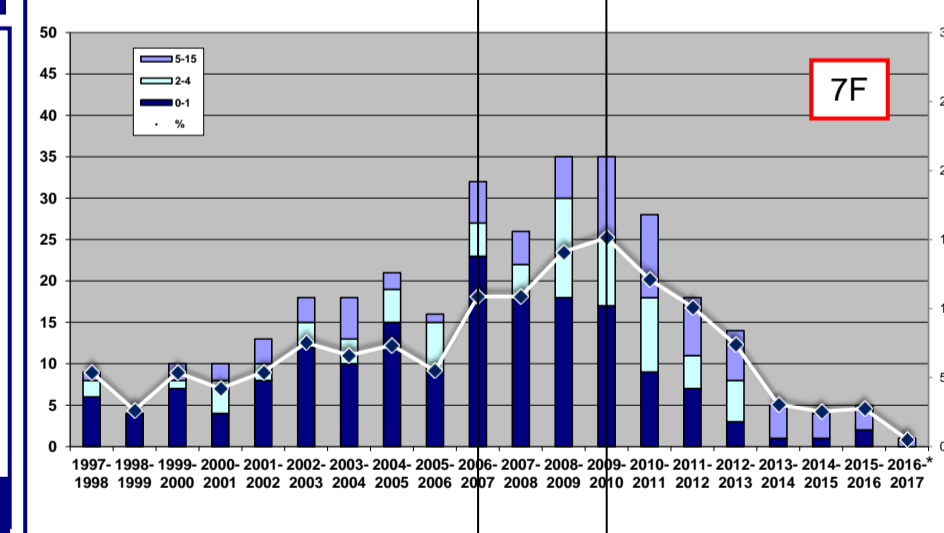
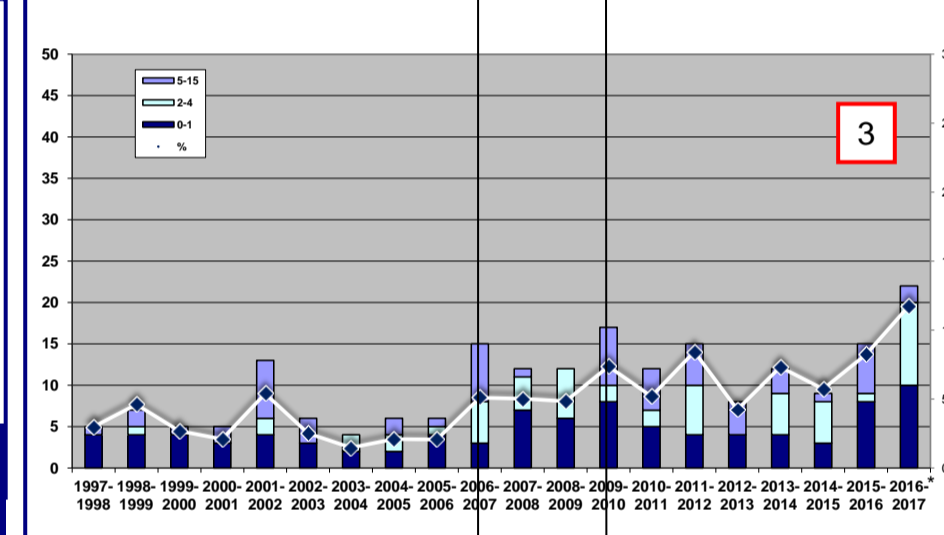
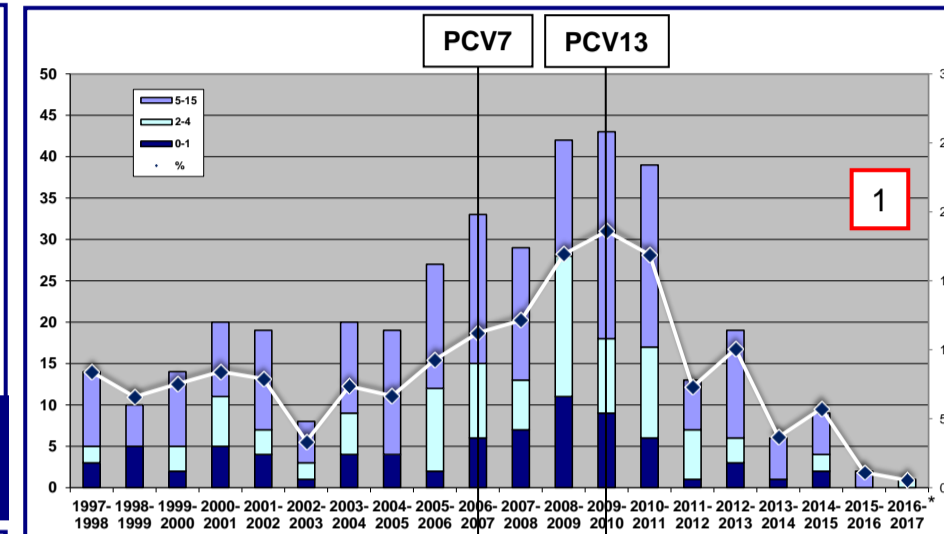


Fig. 4: Number of cases of IPD from children in Germany with serotypes 1, 3, 7F and 19A per pneumococcal season (July to June in the following year).

Table 1: Vaccination status of children < 2 years of age with IPD caused by a PCV13 serotype.

Year	Isolate	Diagnosis	Age (mo)	Serotype	Vaccination status	Conclusion
2015-2016	68872	meningitis	1	3	not vaccinated	not vaccinated
	70842		14	3	not vaccinated	not vaccinated
	72140		3	3	not vaccinated	not vaccinated
	68822	pneumonia, pleuritis, pleuraempyema	7	3	PCV13	vaccinated acc. to age
	71385	pneumonia	23	3	PCV13	vaccinated acc. to age
	72462	sepsis	22	3	PCV13	vaccinated acc. to age (2+1 schedule)
	68364		1	3	unknown	unknown
	70152	otitis media, mastoiditis	3	3	unknown	unknown
	71968		5	7F	not vaccinated	not vaccinated
	68589		5	7F	PCV13	one dose 4 days before onset
	68712	pneumonia	20	14	not vaccinated	not vaccinated
	72184	otitis media, pneumonia	21	19A	PCV13	vaccinated acc. to age
	72752	pneumonia	13	19A	PCV13	vaccinated acc. to age (no booster)
	70435		0	19F	not vaccinated	not vaccinated
	70582		1	19F	not vaccinated	not vaccinated
68680		8	19F	not vaccinated	not vaccinated	
71710		13	19F	unknown	unknown	
72292		5	19F	unknown	unknown	
2016-2017	73271	sepsis	1	3	not vaccinated	not vaccinated
	74071	pneumonia	19	3	not vaccinated	not vaccinated
	74172		21	3	not vaccinated	not vaccinated
	75360	sepsis	2	3	not vaccinated	not vaccinated
	76295		0	3	not vaccinated	not vaccinated
	74260	HUS	19	3	PCV13	vaccinated acc. to age
	76510	sepsis, pneumonia	8	3	PCV13	vaccinated acc. to age
	73416	sepsis	2	3	unknown	unknown
	73602	meningitis	3	3	unknown	unknown
	73976	sepsis, pneumonia	6	3	PCV13	one dose 7 days before onset of disease
74003		15	6B	not vaccinated	not vaccinated	
75596		15	19A	not vaccinated	not vaccinated	
76694		16	19A	unknown	unknown	
74224	mastoiditis	16	19F	not vaccinated	not vaccinated	

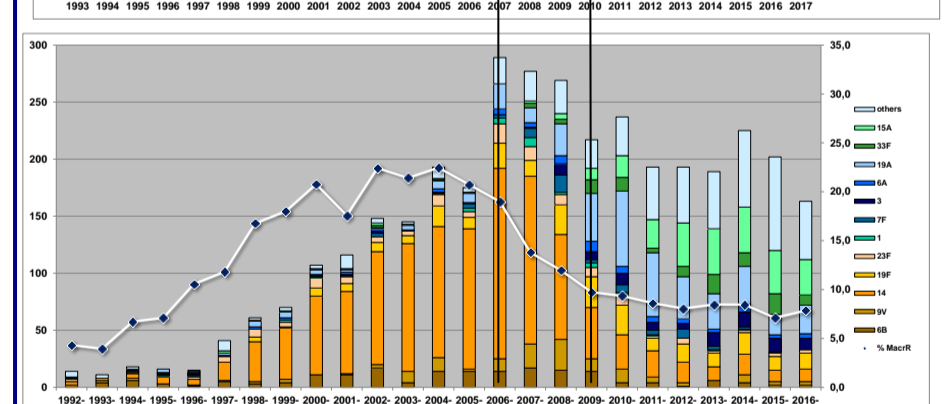
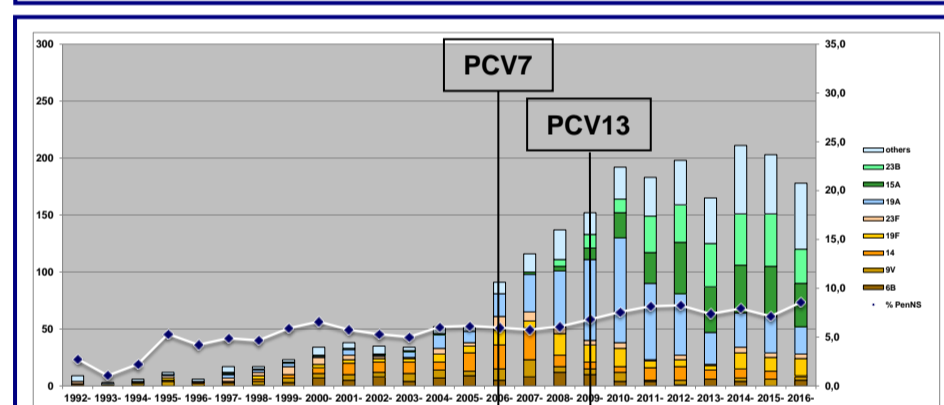


Fig. 5: Serotypes of penicillin non-susceptible and macrolide resistant isolates from children and adults with IPD in Germany.

CONCLUSIONS

- More than seven years after the introduction of higher-valent vaccines, PCV13 serotypes have almost disappeared among children.
- More than half of the remaining vaccine type IPD cases occur in non-vaccinated children ($< 2y$).
- Currently, serotypes 10A, 15A/B/C, 12F, and 24F are the most prevalent serotypes among children < 16 years in Germany.
- Serotypes responsible for penicillin and macrolide resistance have changed.