

Dynamics of pneumococcal serotypes and antibiotic resistance in the post childhood vaccination era in Germany

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Background

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 serotype distribution and antibiotic resistance in the eleven years following the start of PCV-vaccination.

Methods

Pneumococcal isolates recovered from children and adults with IPD were serotyped at the German National Reference Center for Streptococci using the Neufeld-Quellung-reaction. Antibiotic resistance was determined using broth microdilution and results were validated using the CLSI breakpoints.

Results

Childhood vaccination has had a profound effect on the distribution of serotypes circulating in Germany, both among vaccinated children (Fig. 1) as well as among non-vaccinated children and adults (herd-protection; Fig. 2).

After the introduction of PCV7, prevalence of the serotypes included in this vaccine was strongly reduced, whereas non-vaccine serotypes (1, 3, 7F, 19A) increased, albeit to a lower level (Figs. 3 and 4).

Higher-valent vaccination resulted in a reduction 1, 7F and 19A among children, but among adults serotypes 3 and 19A persist (Tables 1 and 2).

Vaccination has had a strong effect on antibiotic resistance. Serotypes carrying resistance have disappeared (6B, 9V, 14, 23F, 19A) but other resistant serotypes are on the increase (15A, 23B, 33F; Figs 5 and 6).

Serotypes 15A and 23B are currently the most prevalent penicillin non-susceptible isolates (Fig. 7).

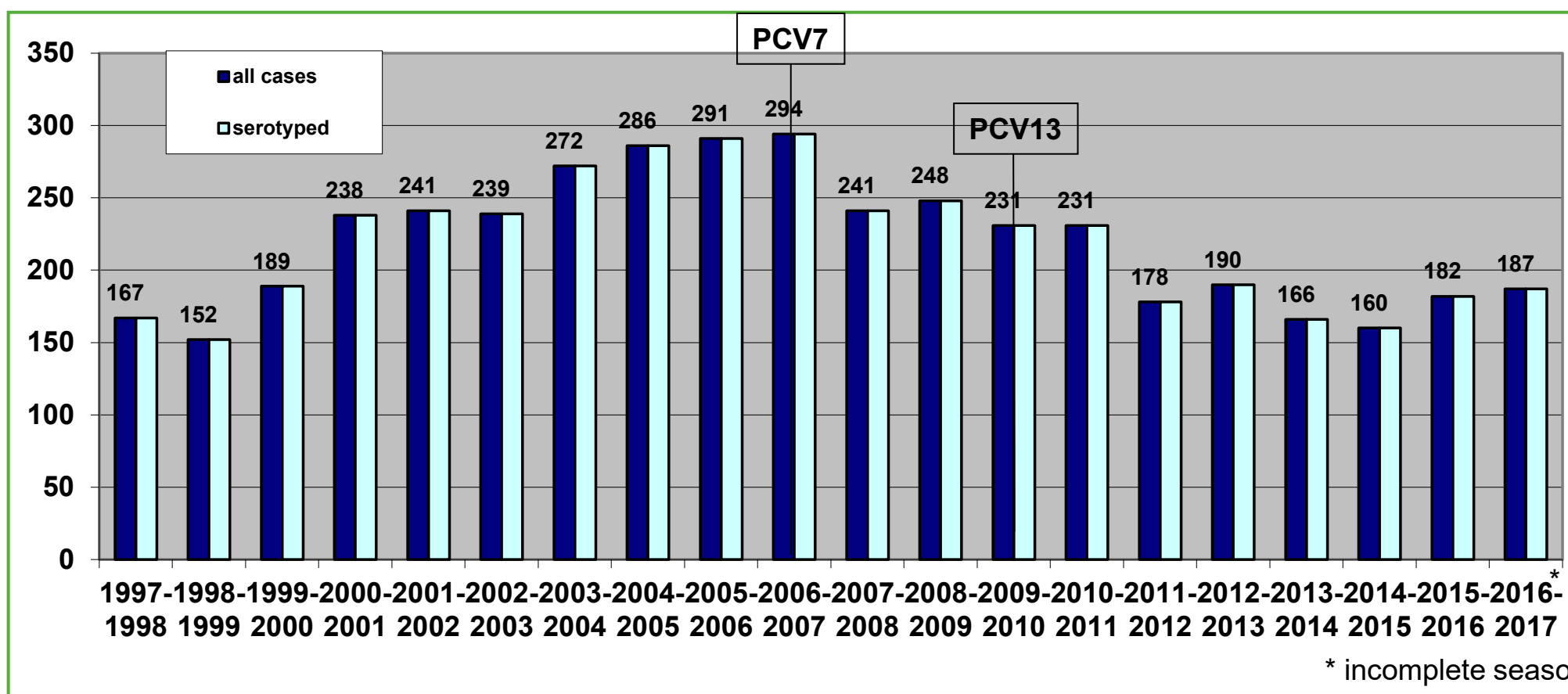


Fig. 1: Number of cases of IPD from children <16 years of age in Germany and number of serotyped cases per pneumococcal season (July to June in the following year).

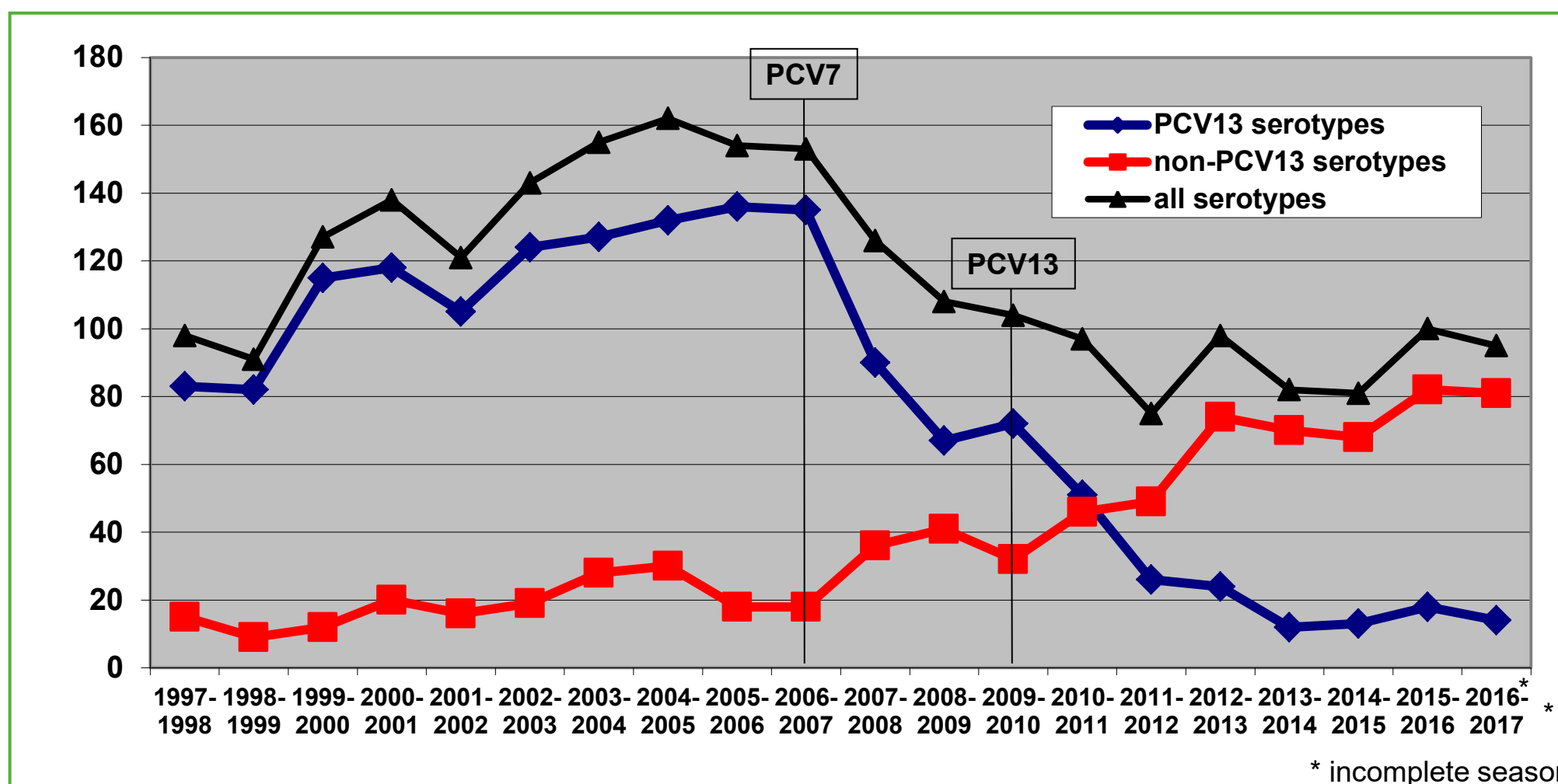


Fig. 3: Number of cases of IPD with PCV13- and non-PCV13 serotypes from children <2 years in Germany per pneumococcal season.

Table 1: 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
	PPV23	201	87.0	PPV23	86	54.1	PPV23	108	59.3	PPV23	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	15C	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	19A	7	3.7
9	4	8	3.5	33F	7	4.4	19F	6	3.3	35F	7	3.7
10	15A	6	2.6	23A	6	3.8	15B	5	2.7	15B	6	3.2
11	19A	6	2.6	23A	6	3.8	7F	5	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	8	4	2.1
15	9A	2	0.9	7F	4	2.5	19A	3	1.6	38	4	2.1
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	6A	2	1.3	1	2	1.1	33F	3	1.6
21	18B	2	0.9	8	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

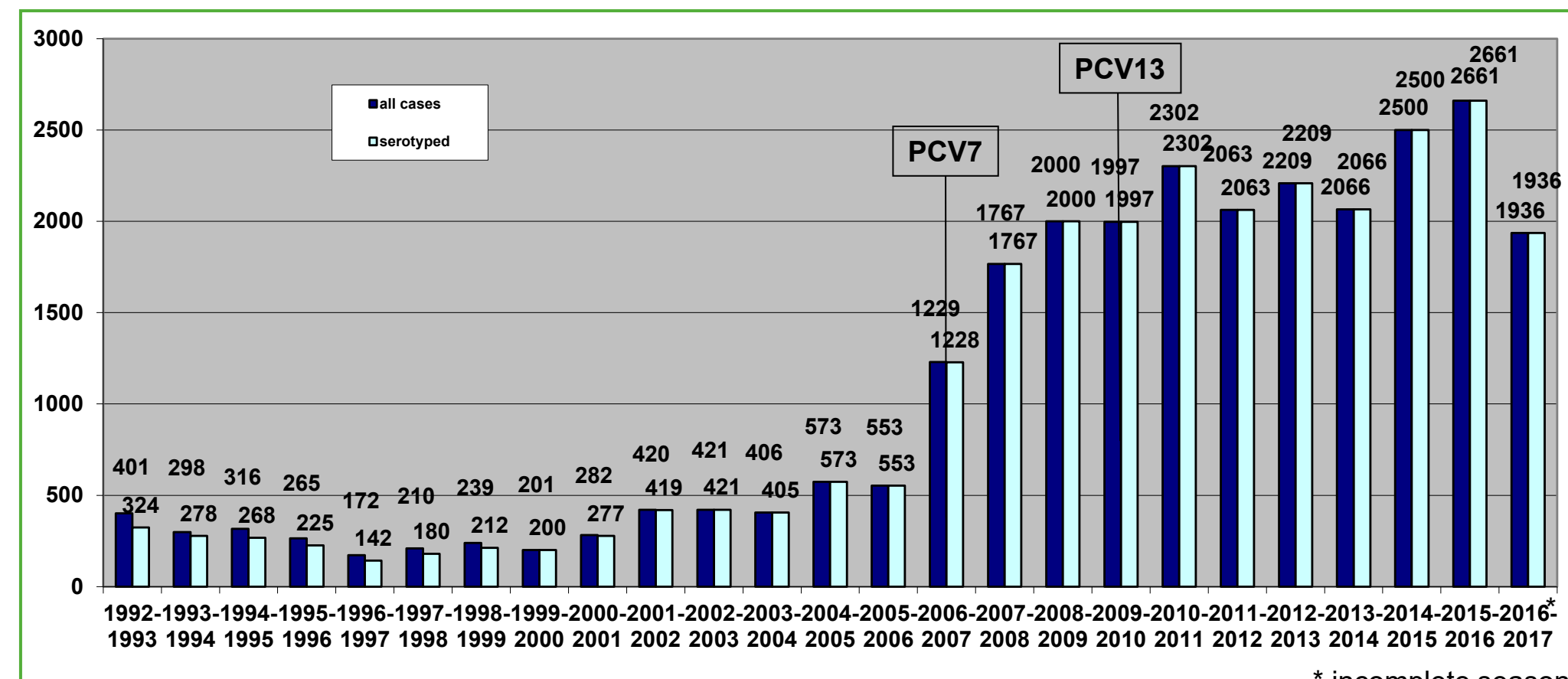


Fig. 2: Number of cases of IPD from adults (≥ 16 y.) in Germany and number of serotyped cases per pneumococcal season (July to June in the following year).

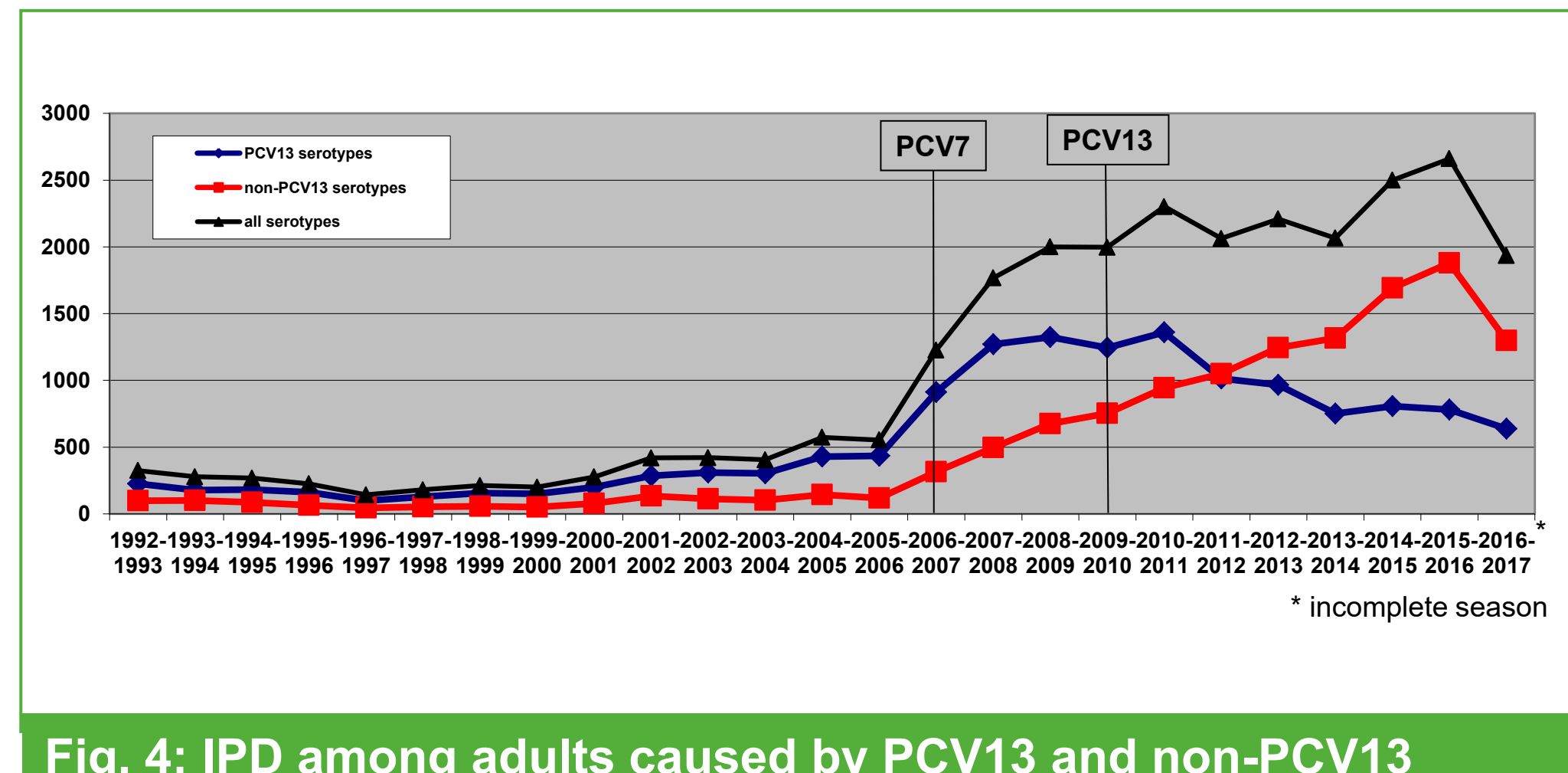


Fig. 4: IPD among adults caused by PCV13 and non-PCV13 serotypes (1992-2017).

Table 2: Table 1: Prevalence of serotypes among adults (age ≥ 16 y.) with IPD in Germany, before (1992-2006) and 8, 9, 10 and 11 years (2013-2014, 2014-2015, 2015-2016, 2016-2017) after the introduction of childhood conjugate vaccination (PCV7: 2006, PCV10/PCV13: 2009).

Serotype	all 1992-2006	%	Serotype	2013-2014	%	Serotype	2014-2015	%	Serotype	2015-2016	%	Serotype	2016-2017	%
all	4477	100.0	total	2066	100.0	total	2500	100.0	total	2651	100.0	total	1938	100.0
PPV23	3911	87.4	PPV23	1492	72.2	PPV23	1799	72.0	PPV23	1900	71.4	PPV23	1390	71.8
PCV13	3238	72.3	PCV13	750	36.3	PCV13	807	32.3	PCV13	781	29.3	PCV13	638	33.0
PCV10	2881	64.4	PCV10	273	13.2	PCV10	221	8.8	PCV10	153	5.7	PCV10	135	7.0
PCV7	1943	43.4	PCV7	120	5.8	PCV7	107	4.3	PCV7	94	3.5	PCV7	103	5.3
14	591	13.2	3	310	15.0	3	445	17.8	3	461	17.3	3	385	19.9
3	389	8.7	12F	176	8.5	22F	207	8.3	8	242	9.1	22F	156	8.1
1	369	8.2	22F	161	7.8	12F	159	6.0	22F	218	8.2	8	153	7.9
7F	296	6.6	19A	145	7.0	8	149	6.0	12F	211	7.9	12F	123	6.4
9V	285	6.4	7F	109	5.3	9N	136	5.4	19A	153	5.7	9N	114	5.9
23F	257	5.7	9A	92	4.5	15A	104	4.2	15A	112	4.2	15A	74	3.8
6B	183	4.1	24F	78	3.8	24F	95	3.8	23A	105	3.9	23A	62	3.2
8	160	3.6	10A	76	3.7	7F	86	3.4	10A	79	3.0	11A	60	3.1
19F	153	3.4	15A	75	3.6	11A	84	3.4	23B	76	2.9	24F	51	2.6
24F	140	3.1	23B	75	3.6	10A	77	3.1	19A	74	2.8	6C	47	2.4
19A	128	2.9	23A	59	2.9	23B	76	3.0	24F	66	2.5	10A	45	2.3
12F	120	2.7	1	54	2.6	23A	63	2.5	6C	60	2.3	23B	45	2.3
9N	119	2.7	11A	54	2.6	6C	57	2.3	33F	56	2.1	33F	42	2.2
18C	105	2.3	6C	50	2.4	33F	50	2.0	38	51	1.9	20	40	2.1
22F	103	2.3	33F	42	2.0	35F	46	1.8	31	50	1.9	16F	39	2.0
11A	101	2.3	35F	42	2.0	43	1.7	35F	50	1.9	31	38	2.0	
10A	80	1.8	35B	34	1.6	35B	42	1.7	20	47	1.8	19F	33	1.7
24F	47	1.0	4	31	1.5	31	40	1.6	16B	45	1.7	35B	30	1.5
20	38	0.8	38	25	1.2	15B	36	1.4	7F	36	1.4	7F	29	1.5
5	35	0.8	14	24	1.2	19F	35	1.4	35B	35	1.3	33F	27	1.4
33F	35	0.8	16F	24	1.2	16F	32	1.3	19C	31	1.2	19F	25	1.3
6C	32	0.7	19F	23	1.1	38	29	1.2	16F	28	1.1	38	24	1.2
23A	31	0.7	31	23	1.1	17F	27	1.1	19F	27	1.0	15B	23	1.2

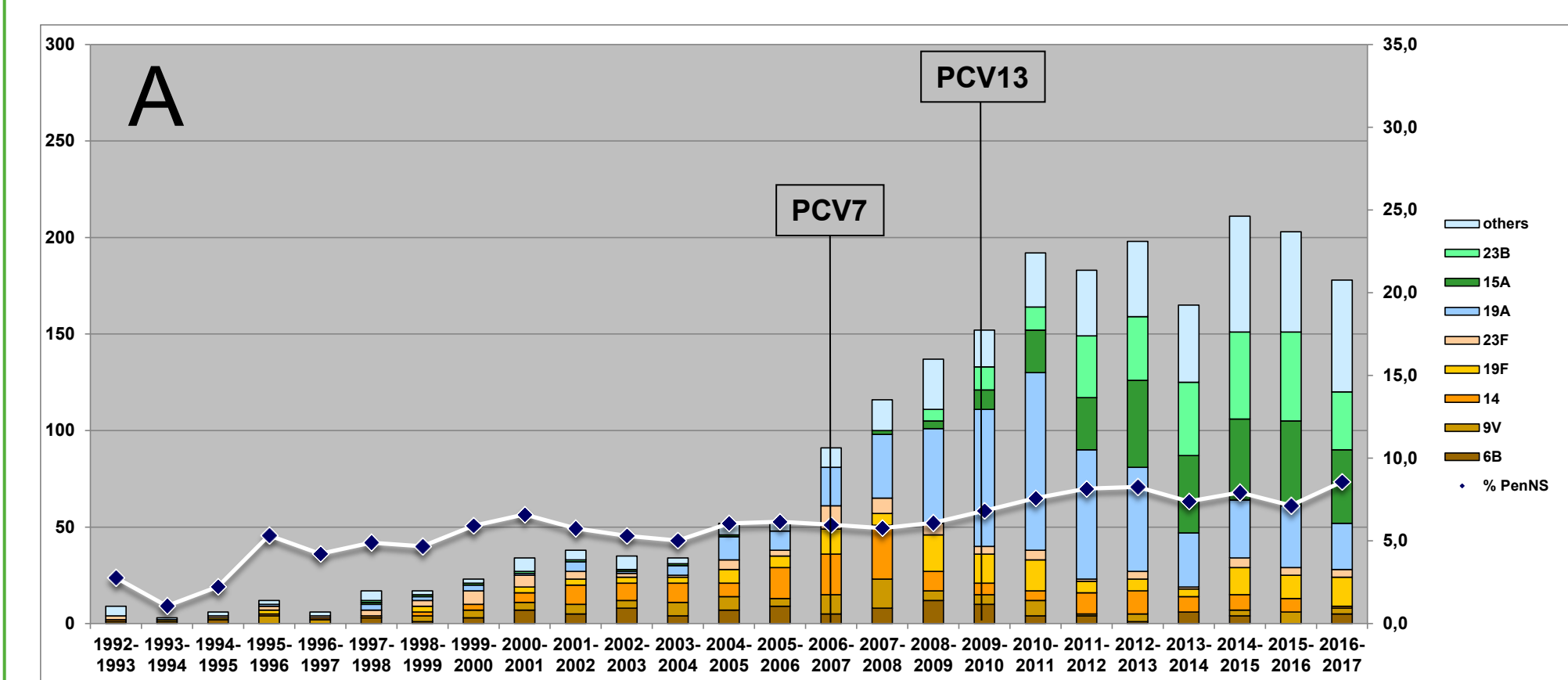


Fig. 5: Serotypes of penicillin non-susceptible isolates from all ages (A), children (B) and adults (C) with IPD in Germany.

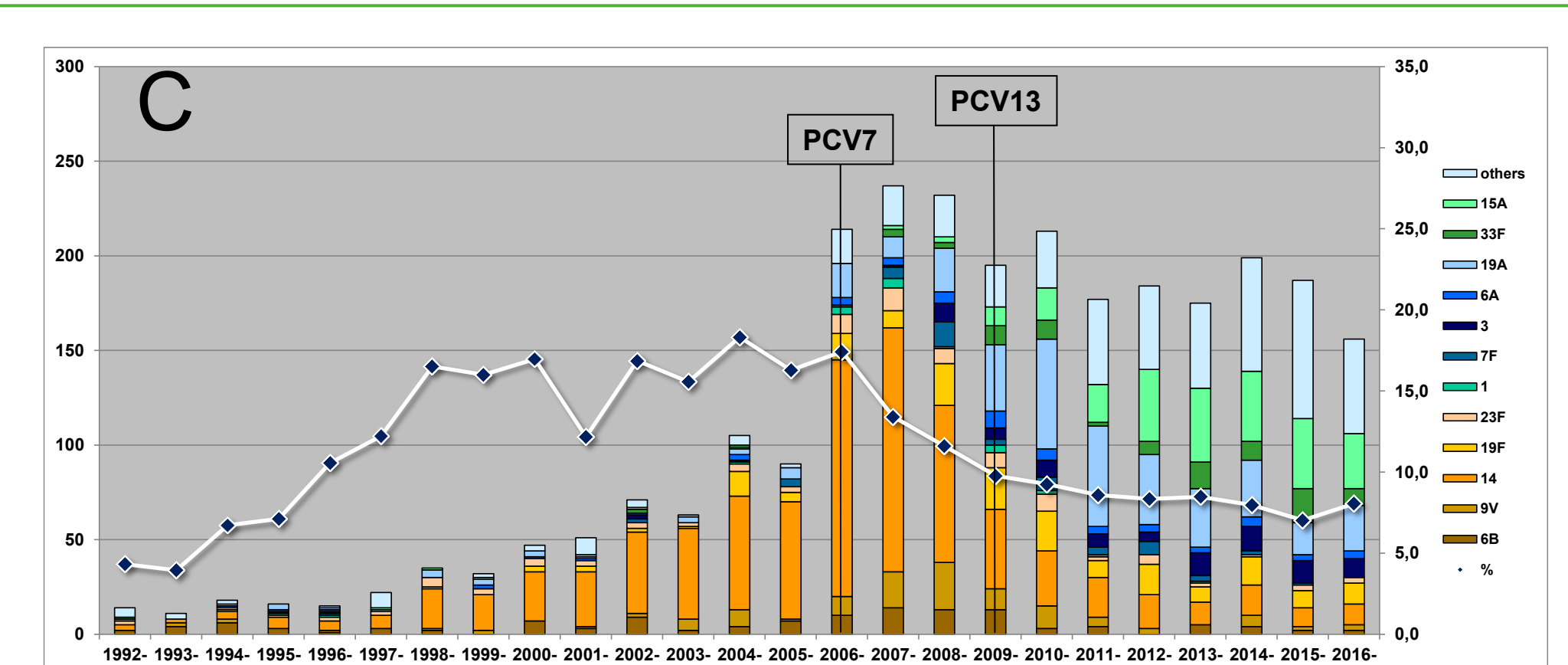
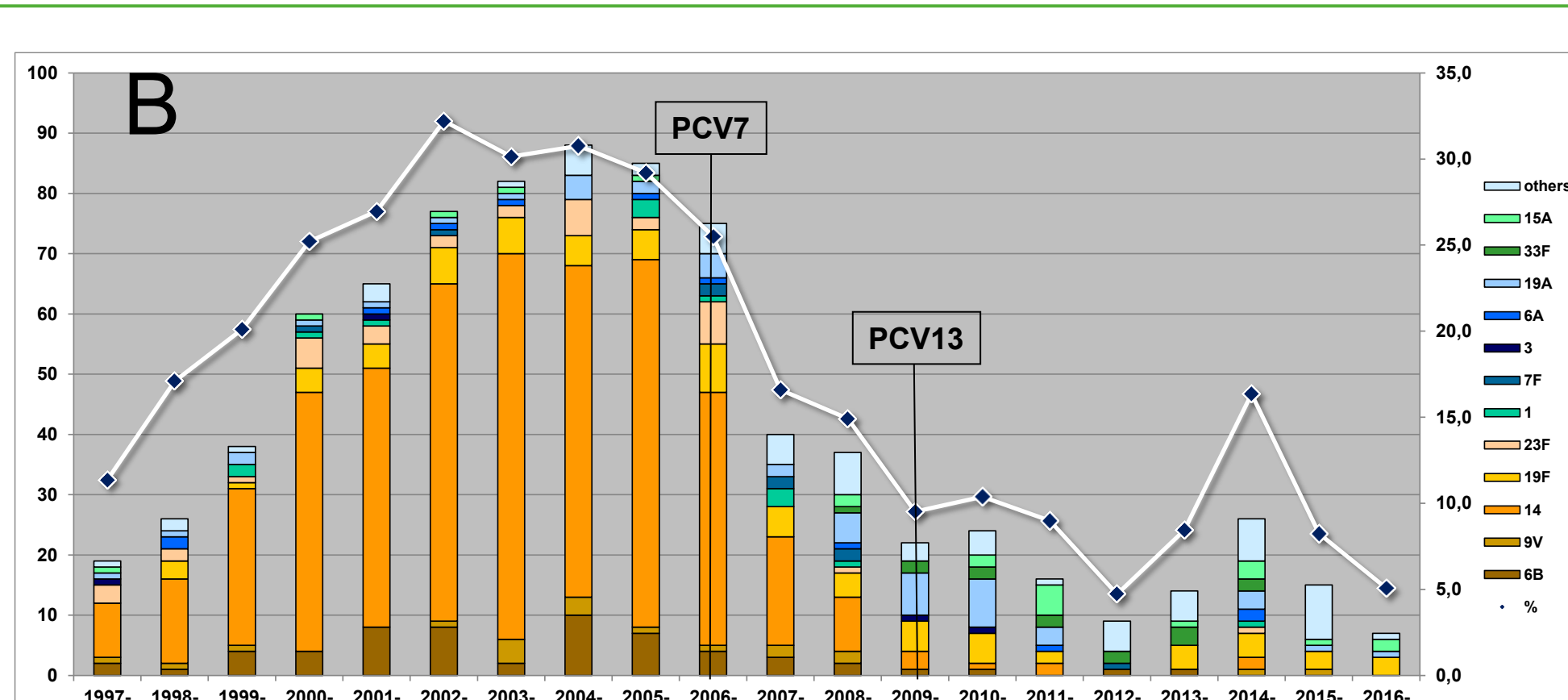
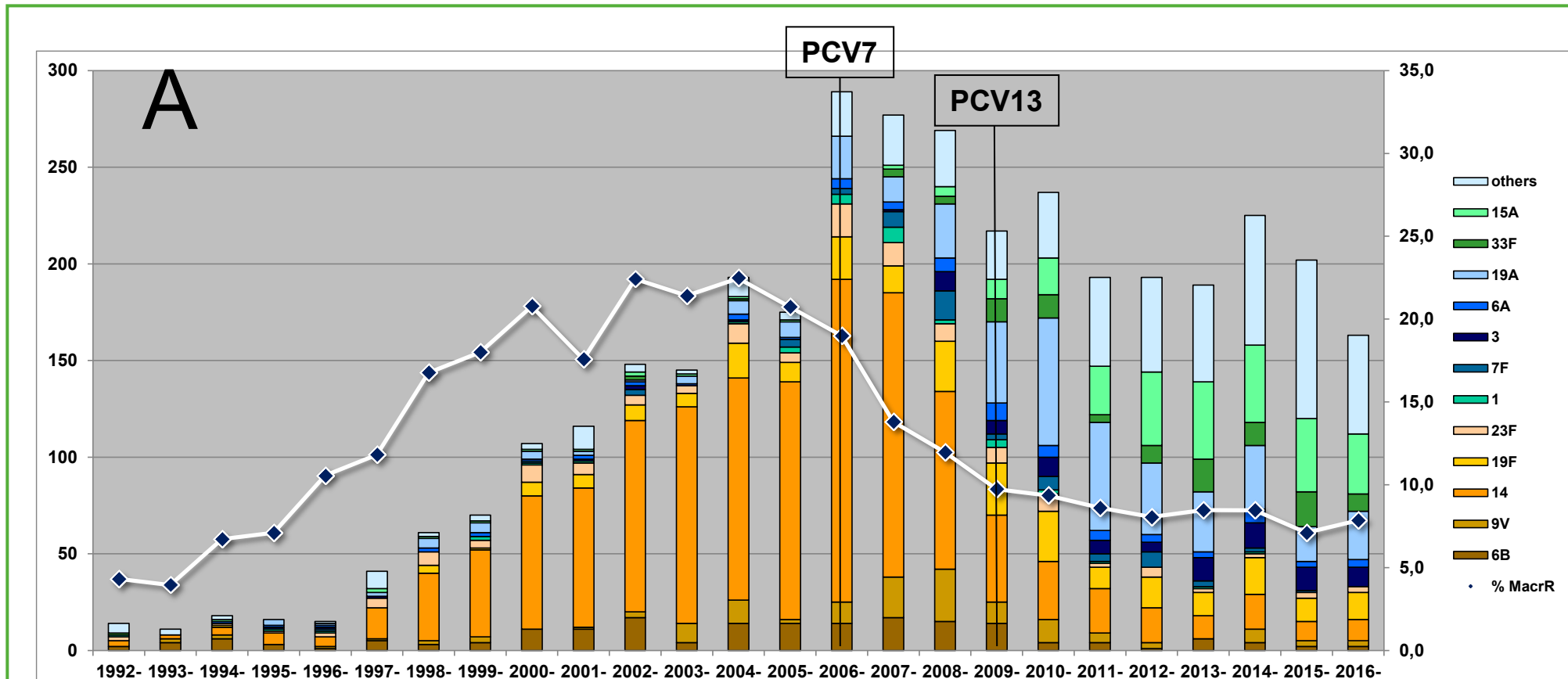
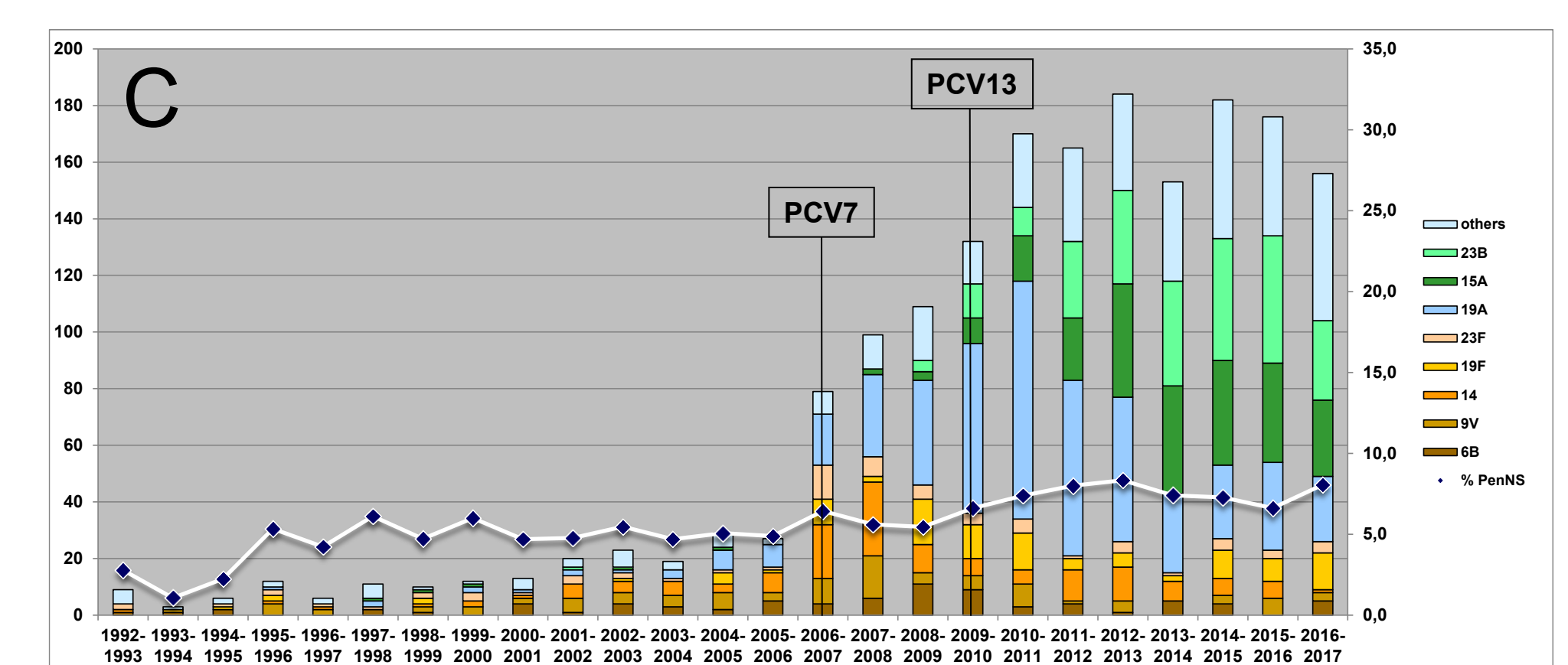
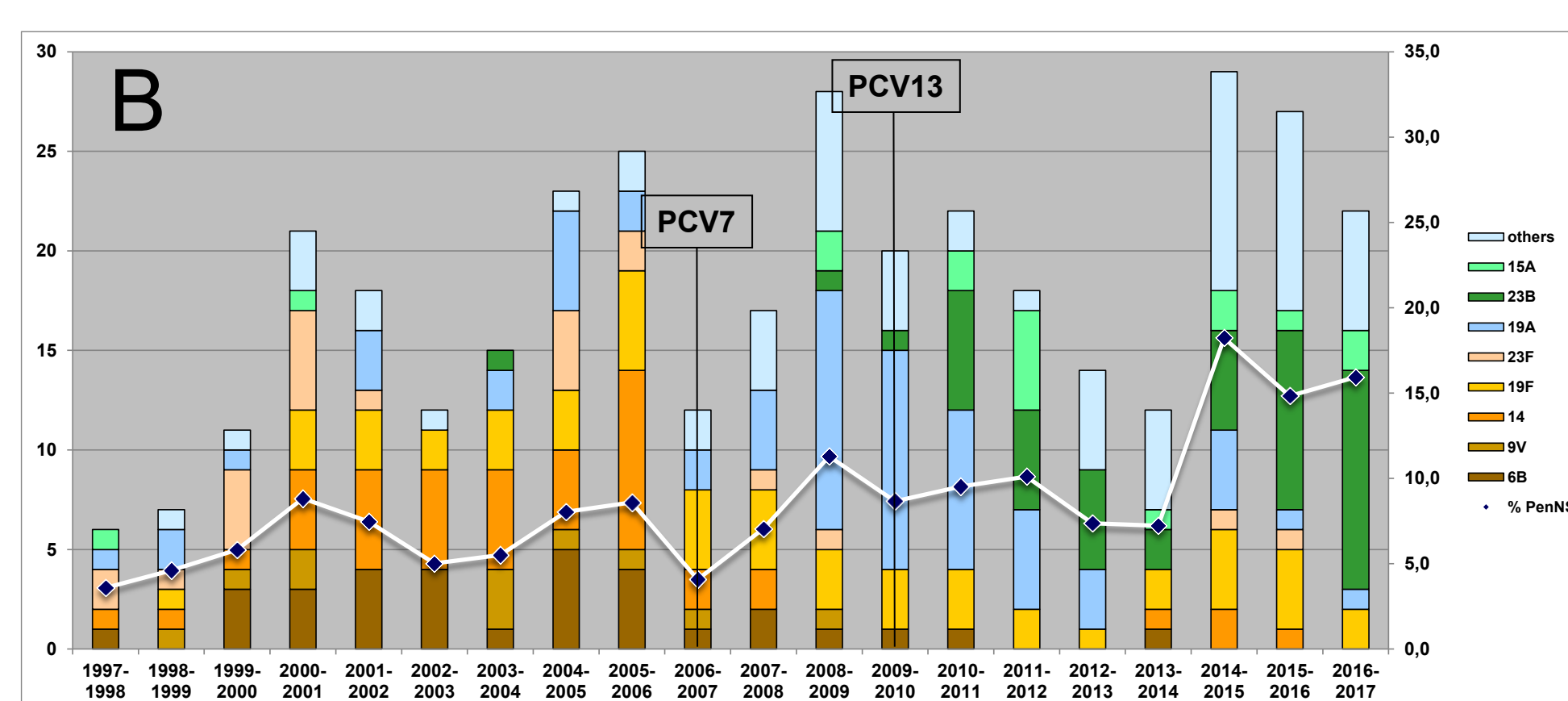


Fig. 6: Serotypes of macrolide resistant isolates from all ages (A), children (B) and adults (C) with IPD in Germany.

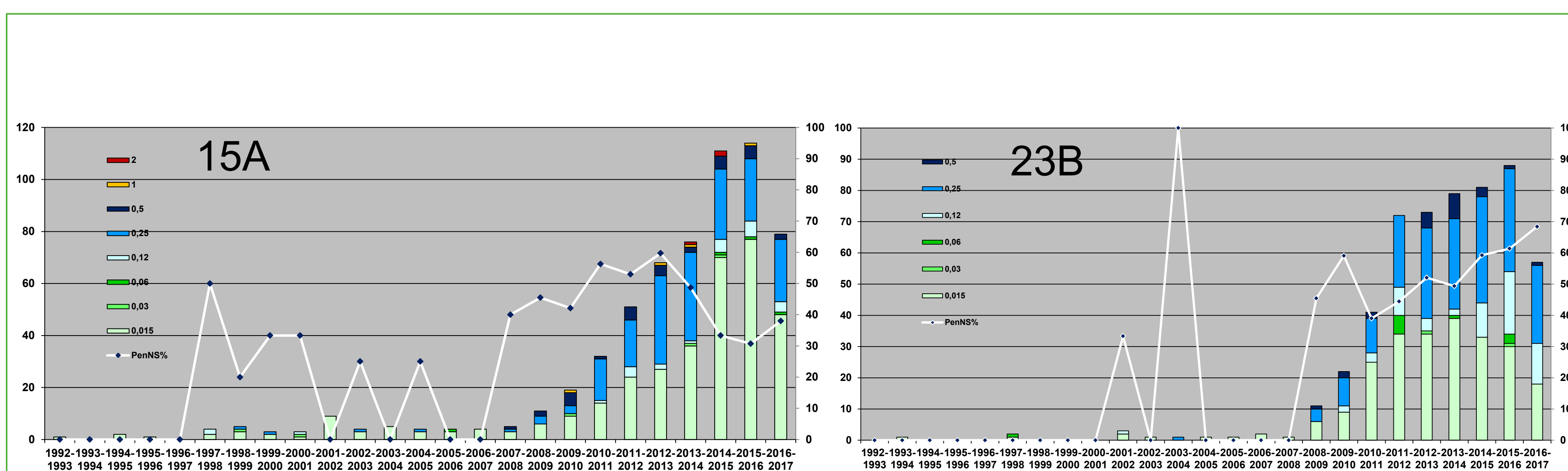


Fig. 7: MIC values of serotype 15A and serotype 23B isolates from IPD among children and adults in Germany (1992-2017).

Discussion

- Since the introduction of childhood pneumococcal conjugate vaccination the serotype distribution of IPD among children and adults has changed substantially.
- PCV7 serotypes have almost disappeared among both children and adults, but PCV13-non-PCV7 serotypes still make up for 27.6% among adult IPD in 2016-2017.
- Although a herd protection effect of PCV7 and PCV13 was observed, the burden of IPD among German adults remains high, underlining the importance of individual vaccination.
- The herd effect among adults is not the same for all serotypes, was not observed for serotype 3 and has stabilized for serotype 19A.
- Currently, serotypes 10A, 15A/B/C, 12F, and 24F are the most prevalent among children <16 years in Germany, and serotypes 3, 22F, 8, 12F, 9N and 19A are most prevalent among adults ≥ 16 years.
- Vaccination has reduced macrolide resistance and serotypes responsible for penicillin and macrolide resistance have changed with serotypes 15A and 23B show an increasing level of penicillin non-susceptibility.