Invasive Pneumococcal Disease in Germany and Possible Impact of new Pneumococcal Conjugate Vaccine Formulations

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BACKGROUND

Streptococcus pneumoniae remains a leading cause of infectious disease among children and older adults. In July 2006, vaccination with pneumococcal conjugate vaccine (PCV) was generally recommended in Germany for all children ≤24 months of age. Apart from a strong direct effect, pneumococcal conjugate vaccination has shown herd protection among non-vaccinated children and adults. For adults ≥60 years of age, a recommendation for vaccination with pneumococcal polysaccharide vaccine (PPV23) has been in place since 1998.

METHODS

The GNRCS has monitored the epidemiology of invasive pneumococcal disease (IPD) in Germany in children since 1997 and adults since 1992. All isolates were serotyped using the Neufeld-Quellung-reaction.

RESULTS

Pneumococcal vaccines have been developed as early as 1911, first as whole cell vaccines, then as polysaccharide vaccines. Interest in vaccine development was lost with the discovery of penicillin, but regained with the emergence of penicillin resistant pneumococci. However, neither the use of antibiotics, nor polysaccharide vaccines induced any change in the epidemiology and mortality of IPD. Only with the introduction of conjugate vaccines, which are effective in children under the age of two, dramatic changes in the epidemiology of pneumococcal diseases were observed, in all ages groups (**Fig. 1**).

Currently, only one 23-valent polysaccharide vaccine (PPV23) is available, whereas six different conjugate vaccines have been developed, of which five are still marketed. With the exception of serotype 6A, the serotype composition of each of the different PCVs represents a subset of the 23 serotypes included in PPV23 (**Fig. 2**).

Childhood PCV-vaccination in Germany has changed the serotype distribution both among children as well as among adults. The prevalence of PCV13 vaccine serotypes among children <18 years reduced from 84% in the pre-PCV period to 20% in 2019-2020, among adults ≥18 years and ≥60 years from 72% to 30%. The percentage of PCV13 serotypes in IPD among adults has remained stable ≈30% for 7 seasons. However, serotype coverage showed slight differences during the SARS-CoV-2 pandemic, especially among children. (**Tabs. 1, 2, 3**).

New PCV-formulations containing 15 and 20 serotypes have been approved for adults over 18 years of age. PCV15 would have increased serotype coverage among children from 18.5% to 25.3% in 2018-2019, and from 31.8% to 34.6% in 2021-2022. PCV20 would have covered 55.6% and 58.9%, respectively. Relative coverage increase was lower in 2021-2022, due to effects induced by the SARS-CoV-2 pandemic. For adults ≥18 years coverage increase for PCV15 (compared to PCV13) would have been 8.6% in 2018-2019, and 5.2% in 2021-2022, for PCV20 35.1% and 26.8%, respectively. For adults ≥60 years the coverage increase was 9.1% and 5.4% for PCV15 in 2018-2019 and 2021-2022, respectively, for PCV20, 33.4% and 25.9%, respectively (**Figs. 3, 4, 5**).

In 2021-2022, the difference in coverage between PCV20 and PPV23 was 7.1% for adults ≥18 years and 6.6% for adults ≥60 years of age. This difference was mainly caused by serotype 9N (**Tabs 2, 3**).

CONCLUSIONS

- Pneumococcal conjugate vaccines have drastically changed the epidemiology of invasive pneumococcal disease
- The herd protection effect of PCV7/PCV13 on the serotype distribution of IPD among adults in Germany has reached its limit, with PCV13 serotypes remaining at a prevalence of about 30%.
- PCV15 would increase serotype coverage (compared to PCV13) among children by 3% to 7%, among adults ≥18 years or ≥60 years by 5% to 9%.
- PCV20 would increase serotype coverage (compared to PCV13) among children by 27% to 37%, among adults ≥18 years or ≥60 years by 26% to 35%.
- For adults ≥60 years, the current coverage of PCV20 and PPV23 is very similar: 59.2% vs. 65.7%. The small difference is mainly caused by serotype 9N.

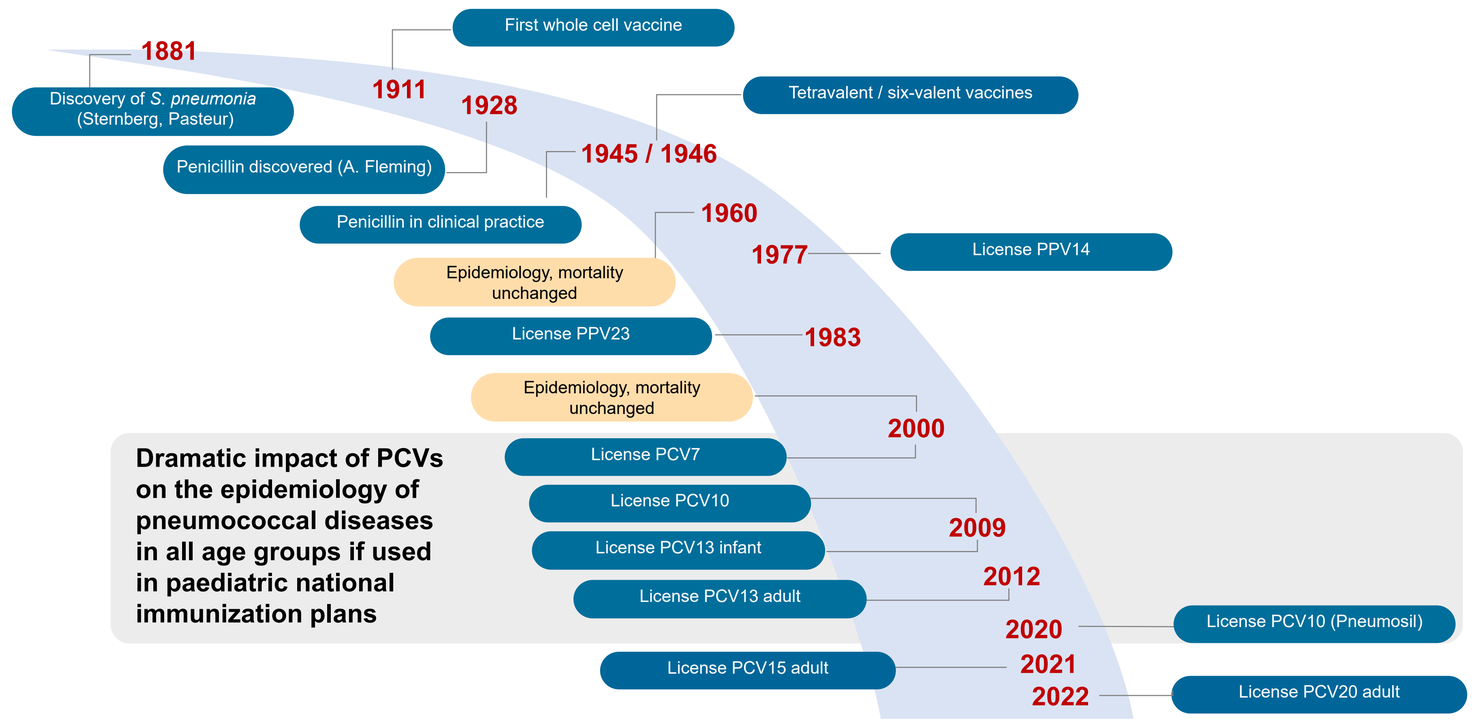
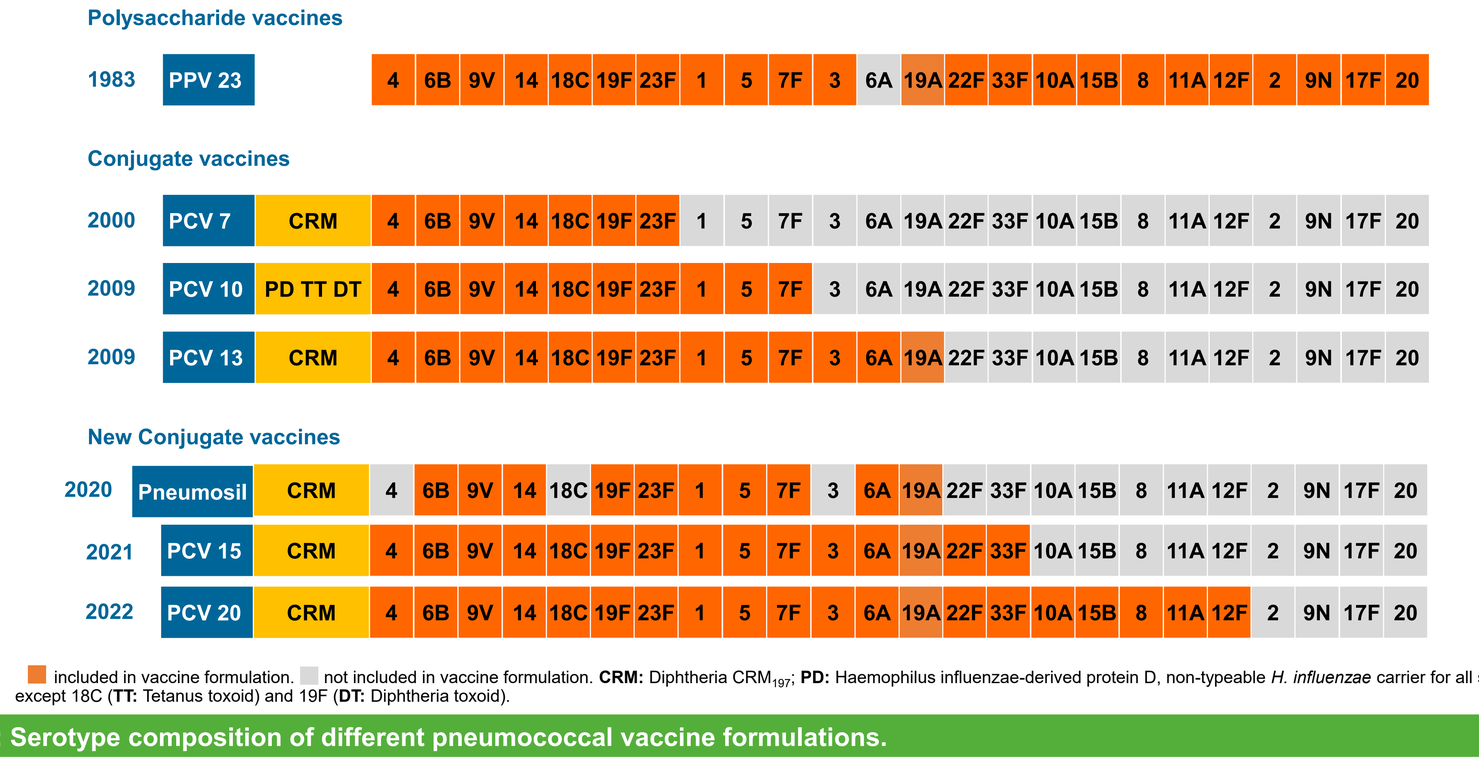


Fig. 1: History of pneumococcal vaccination.



included in vaccine formulation. not included in vaccine formulation. **CRM:** Diphtheria CRM_{197}; **PD:** Haemophilus influenzae-derived protein D, non-typeable *H. influenzae* carrier for all serotypes except 18C (**TT:** Tetanus toxoid) and 19F (**DT:** Diphtheria toxoid).

Fig. 2: Serotype composition of different pneumococcal vaccine formulations.

	Serotype	1997-2006	%	Serotype	2018-2019	%	Serotype	2019-2020	%	Serotype	2020-2021	%	Serotype	2021-2022	%
	total	2171	100,0	total	178	100,0	total	187	100,0	total	70	100,0	total	107	100,0
	PCV20	1949	89,8	PPV23	108	60,7	PPV23	105	56,1	PPV23	29	41,4	PPV23	69	64,5
	PPV23	1904	87,7	PCV20	99	55,6	PCV20	100	53,5	PCV20	29	41,4	PCV20	63	58,9
	PCV15	1856	85,5	PCV15	45	25,3	PCV15	57	30,5	PCV15	12	17,1	PCV15	37	34,6
	PCV13	1827	84,2	PCV13	33	18,5	PCV13	44	23,5	PCV13	9	12,9	PCV13	34	31,8
	PCV10	1623	74,8	PCV10	10	5,6	PCV10	9	4,8	PCV10	1	1,4	PCV10	7	6,5
	PCV7	1297	59,7	PCV7	10	5,6	PCV7	8	4,3	PCV7	1	1,4	PCV7	7	6,5
1	14	545	25,1	10A	21	11,8	3	27	14,4	15C	10	14,3	3	19	17,8
2	1	174	8,0	23B	17	9,6	24F	21	11,2	23B	10	14,3	15C	12	11,2
3	6B	163	7,5	15B	12	6,7	10A	12	6,4	24F	8	11,4	19A	8	7,5
4	19F	157	7,2	3	11	6,2	23B	11	5,9	10A	7	10,0	10A	8	7,5
5	23F	143	6,6	19A	11	6,2	15C	10	5,3	19A	6	8,6	8	7	6,5
6	7F	139	6,4	15C	10	5,6	19A	8	4,3	11A	4	5,7	19F	6	5,6
7	18C	126	5,8	22F	9	5,1	8	8	4,3	8	3	4,3	15B	6	5,6
8	9V	87	4,0	12F	9	5,1	12F	8	4,3	23A	3	4,3	24F	4	3,7
9	6A	77	3,5	19F	7	3,9	15B	8	4,3	3	2	2,9	35F	4	3,7
10	4	76	3,5	8	7	3,9	22F	7	3,7	22F	2	2,9	12F	3	2,8
11	3	65	3,0	24F	7	3,9	11A	7	3,7	12F	2	2,9	16F	3	2,8
12	19A	62	2,9	9N	6	3,4	35F	7	3,7	6B	1	1,4	23B	3	2,8
13	10A	36	1,7	38	6	3,4	33F	6	3,2	33F	1	1,4	35B	3	2,8
14	24F	32	1,5	11A	5	2,8	38	6	3,2	15B	1	1,4	22F	2	1,9
15	15B	22	1,0	27	4	2,2	19F	5	2,7	7B	1	1,4	11A	2	1,9
16	9N	22	1,0	33F	3	1,7	15A	4	2,1	7C	1	1,4	9N	2	1,9
17	9A	19	0,9	17F	3	1,7	21	4	2,1	15A	1	1,4	17F	2	1,9
18	15A	18	0,8	21	3	1,7	27	4	2,1	16F	1	1,4	20	2	1,9
19	38	18	0,8	23A	3	1,7	35B	3	1,6	25F	1	1,4	15A	2	1,9
20	8	17	0,8	35B	3	1,7	6B	2	1,1	28A	1	1,4	38	2	1,9
21	22F	16	0,7	23F	2	1,1	9N	2	1,1	28F	1	1,4	18C	1	0,9
22	5	13	0,6	10B	2	1,1	20	2	1,1	35B	1	1,4	33F	1	0,9
23	33F	13	0,6	15A	2	1,1	10B	2	1,1	35D	1	1,4	10F	1	0,9
24	15C	12	0,6	28F	2	1,1	16F	2	1,1	NT	1	1,4	21	1	0,9

Tab. 1: Serotype distribution among IPD isolates from children <18 years of age in Germany. Single serotype prevalences are ranked.

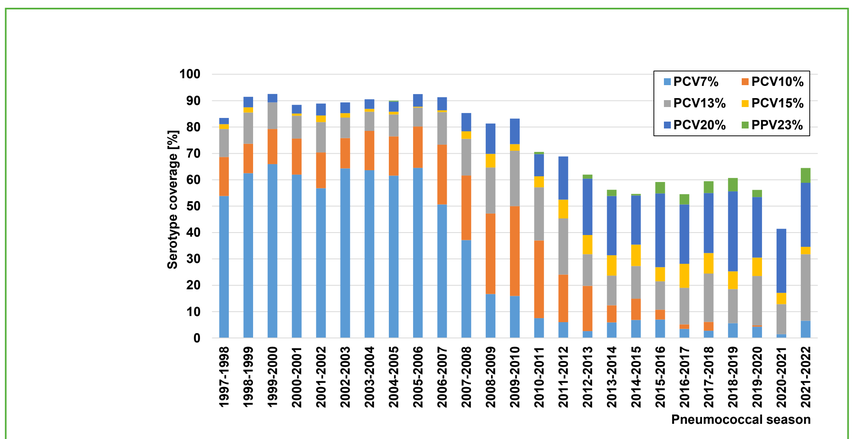


Fig. 3: Serotype coverage of different vaccine formulations among IPD isolates from children <18 years of age in Germany.

	Serotype	all 1992-2006	%	Serotype	2018-2019	%	Serotype	2019-2020	%	Serotype	2020-2021	%	Serotype	2021-2022	%
	total	4441	100,0	total	3183	100,0	total	2388	100,0	total	1001	100,0	total	1345	100,0
	PPV23	3883	87,4	PPV23	2365	74,3	PPV23	1702	71,3	PPV23	696	69,5	PPV23	919	68,3
	PCV20	3835	86,4	PCV20	2076	65,2	PCV20	1528	64,0	PCV20	607	60,6	PCV20	823	61,2
	PCV15	3358	75,6	PCV15	1231	38,7	PCV15	922	38,6	PCV15	367	36,7	PCV15	533	39,6
	PCV13	3220	72,5	PCV13	959	30,1	PCV13	706	29,6	PCV13	307	30,7	PCV13	463	34,4
	PCV10	2565	57,8	PCV10	187	5,9	PCV10	149	6,2	PCV10	69	6,9	PCV10	84	6,2
	PCV7	1938	43,6	PCV7	171	5,4	PCV7	142	5,9	PCV7	66	6,6	PCV7	80	5,9
1	14	590	13,3	3	643	20,2	3	447	18,7	3	198	19,8	3	300	22,3
2	3	388	8,7	8	446	14,0	8	344	14,4	8	156	15,6	8	166	12,3
3	4	366	8,2	22F	231	7,3	22F	181	7,6	9N	65	6,5	19A	74	5,5
4	1	298	6,7	9N	203	6,4	9N	124	5,2	22F	46	4,6	9N	68	5,1
5	7F	294	6,6	12F	157	4,9	12F	111	4,6	23B	39	3,9	22F	62	4,6
6	9V	287	6,5	19A	118	3,7	19A	96	4,0	19A	37	3,7	11A	51	3,8
7	23F	258	5,8	23B	99	3,1	23A	78	3,3	35F	37	3,7	23B	50	3,7
8	6B	180	4,1	11A	98	3,1	23B	78	3,3	23A	35	3,5	4	49	3,6
9	8	158	3,6	10A	91	2,9	4	70	2,9	4	33	3,3	35F	46	3,4
10	19F	152	3,4	23A	86	2,7	15A	68	2,8	11A	33	3,3	15A	43	3,2
11	6A	140	3,2	15A	81	2,5	24F	67	2,8	15A	29	2,9	23A	38	2,8
12	19A	127	2,9	35F	78	2,5	11A	66	2,8	10A	27	2,7	10A	37	2,8
13	12F	120	2,7	4	67	2,1	10A	59	2,5	16F	24	2,4	35B	32	2,4
14	9N	118	2,7	24F	62	1,9	35F	48	2,0	35B	23	2,3	6C	31	2,3
15	18C	105	2,4	6C	59	1,9	6C	47	2,0	24F	19	1,9	24F	26	1,9
16	22F	103	2,3	20	58	1,8	20	37	1,5	33F	14	1,4	15B	24	1,8
17	11A	98	2,2	38	56	1,8	15C	37	1,5	20	14	1,4	16F	22	1,6
18	10A	77	1,7	16F	54	1,7	33F	35	1,5	6C	14	1,4	31	22	1,6
19	24F	47	1,1	15B	53	1,7	38	35	1,5	15C	14	1,4	7C	20	1,5
20	20	38	0,9	35B	45	1,4	16F	34	1,4	19F	13	1,3	20	17	1,3
21	5	35	0,8	19F	43	1,4	35B	34	1,4	17F	13	1,3	19F	16	1,2
22	33F	35	0,8	33F	41	1,3	19F	30	1,3	12F	12	1,2	17F	16	1,2
23	6C	31	0,7	17F	39	1,2	17F	27	1,1	15B	12	1,2	12F	12	0,9
24	23A	31	0,7	15C	37	1,2	15B	26	1,1	7C	9	0,9	15C	11	0,8

Tab. 2: Serotype distribution among IPD isolates from adults ≥18 years of age in Germany. Single serotype prevalences are ranked.

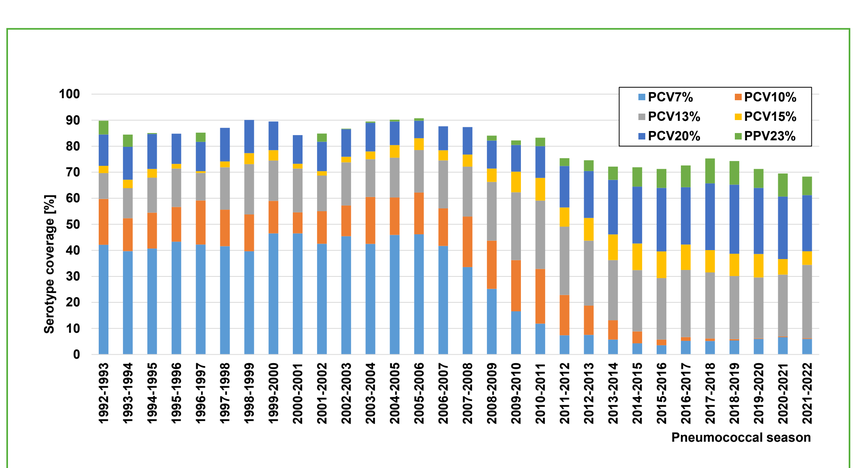


Fig. 4: Serotype coverage of different vaccine formulations among IPD isolates from adults ≥18 years of age in Germany.

	Serotype	all 1992-2006	%	Serotype	2018-2019	%	Serotype	2019-2020	%	Serotype	2020-2021	%	Serotype	2021-2022	%
	total	2786	100,0	total	2343	100,0	total	1723	100,0	total	696	100,0	total	955	100,0
	PPV23	2423	87,0	PPV23	1709	72,9	PPV23	1173	68,1	PPV23	469	67,4	PPV23	627	65,7
	PCV20	2405	86,3	PCV20	1500	64,0	PCV20	1056	61,3	PCV20	407	58,5	PCV20	565	59,2
	PCV15	2120	76,1	PCV15	929	39,7	PCV15	667	38,7	PCV15	260	37,4	PCV15	370	38,7
	PCV13	2035	73,0	PCV13	718	30,6	PCV13	494	28,7	PCV13	216	31,0	PCV13	318	33,3
	PCV10	1556	55,9	PCV10	110	4,7	PCV10	77	4,5	PCV10	34	4,9	PCV10	43	4,5
	PCV7	1246	44,7	PCV7	101	4,3	PCV7	73	4,2	PCV7	32	4,6	PCV7	42	4,4
1	14	397	14,2	3	515	22,0	3	334	19,4	3	150	21,6	3	220	23,0
2	3	291	10,4	8	282	12,0	8	207	12,0	8	90	12,9	8	98	10,3
3	4	210	7,5	22F	179	7,6	22F	146	8,5	9N	44	6,3	19A	50	5,2
4	23F	188	6,7	9N	154	6,6	9N	87	5,0	22F	33	4,7	9N	47	4,9
5	9V	186	6,7	12F	100	4,3	19A	70	4,1	23A	32	4,6	22F	46	4,8
6	7F	167	6,0	19A	86	3,7	23A	64	3,7	19A	29	4,2	23B	39	4,1
7	1	130	4,7	11A	76	3,2	12F	62	3,6	23B	29	4,2	11A	38	4,0
8	6B	120	4,3	10A	74	3,2	23B	59	3,4	35F	27	3,9	15A	37	3,9
9	6A	102	3,7	23A	69	2,9	15A	58	3,4	11A	24	3,4	23A	37	3,9
10	8	95	3,4	23B	69	2,9	11A	51	3,0	15A	18	2,6	35F	37	3,9
11	19F	91	3,3	15A	65	2,8	24F	51	3,0	16F	18	2,6	6C	26	2,7
12	19A	86	3,1	35F	61	2,6	10A	45	2,6	35B	17	2,4	10A	25	2,6
13	9N	80	2,9	24F	53	2,3	35F	40	2,3	10A	16	2,3	35B	25	2,6
14	12F	65	2,3	6C	50	2,1	6C	37	2,1	24F	12	1,7	24F	24	2,5
15	22F	64	2,3	38	48	2,0	38	33	1,9	33F	11	1,6	15B	23	2,4
16	11A	59	2,1	16F	42	1,8	15C	32	1,9	20	11	1,6	4	19	2,0
17	18C	54	1,9	15B	39	1,7	4	29	1,7	6C	11	1,6	7C	17	1,8
18	10A	47	1,7	35B	38	1,6	16F	28	1,6	17F	10	1,4	16F	15	1,6
19	24F	33	1,2	19F	34	1,5	33F	27	1,6	4	9	1,3	31	15	1,6
20	6C	25	0,9	20	34	1,5	20	27	1,6	19F	9	1,3	19F	12	1,3
21	33F	21	0,8	33F	32	1,4	35B	25	1,5	15B	9	1,3	12F	11	1,2
22	20	21	0,8	4	28	1,2	15B	24	1,4	15C	9	1,3	17F	11	1,2
23	23A	21	0,8	17F	28	1,2	19F	21	1,2	12F	8	1,1	20	9	0,9
24	15B	19	0,7	31	26	1,1	31	20	1,2	7B	7	1,0	7B	9	0,9

Tab. 3: Serotype distribution among IPD isolates from adults ≥60 years of age in Germany. Single serotype prevalences are ranked.

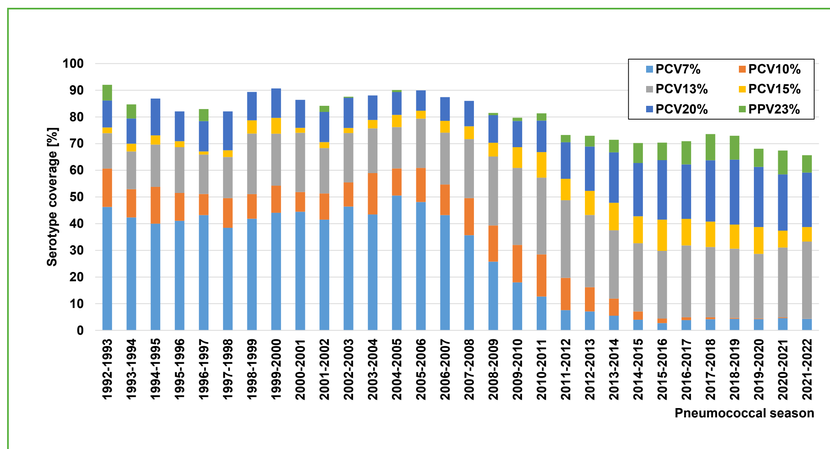


Fig. 5: Serotype coverage of different vaccine formulations among IPD isolates from adults ≥60 years of age in Germany.