

OBJECTIVES

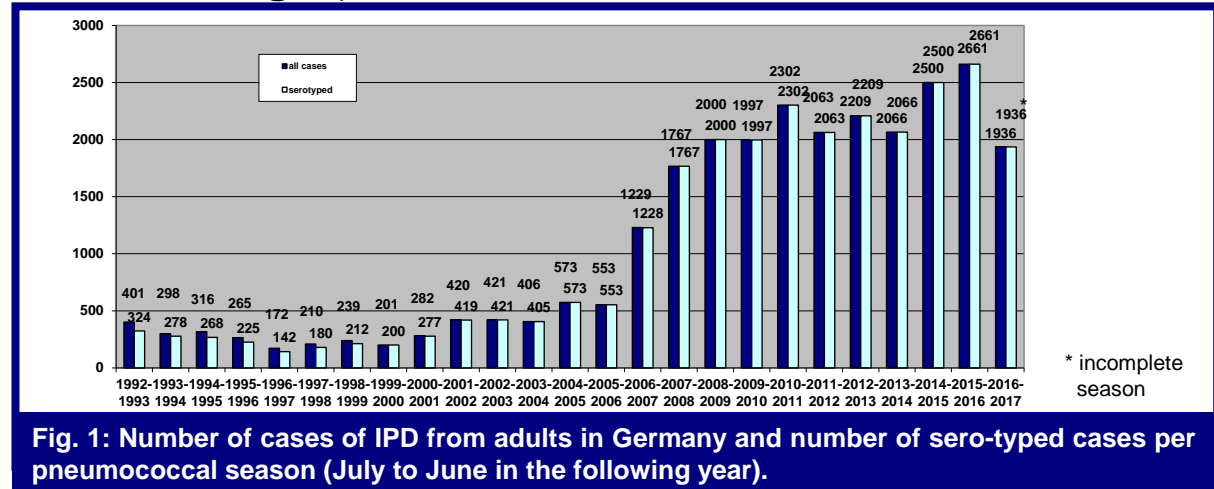
Streptococcus pneumoniae remains a leading cause of pneumonia, sepsis and meningitis and disproportionately affects young children and the elderly. In July 2006, vaccination with pneumococcal conjugate vaccine was generally recommended in Germany for all children ≤ 24 months. PCV13 was licensed for adults in 2011 and uptake in adults has increased since. In this study, we present the burden of disease and serotype distribution among adults with invasive pneumococcal disease (IPD) before and after the start of childhood and adult vaccination.

METHODS

The GNRCS has monitored the epidemiology of IPD in adults in Germany since 1992. Cases of IPD in adults are reported by a laboratory-based surveillance system, including over 300 laboratories throughout Germany. The present analysis includes cases documented between 1992 and 2017. Species confirmation was done by optochin testing and bile solubility testing. All isolates were serotyped using the Neufeld Quellung reaction.

RESULTS

From 2008 to 2014 the amount of IPD isolates sent to the GNRCS has remained stable (2000-2300 per year), but in the last three seasons an increase to 2500-2600 isolates has been observed.: **Fig. 1**).



The majority of reported cases was from adults aged 50 years and older (**Fig. 2**).

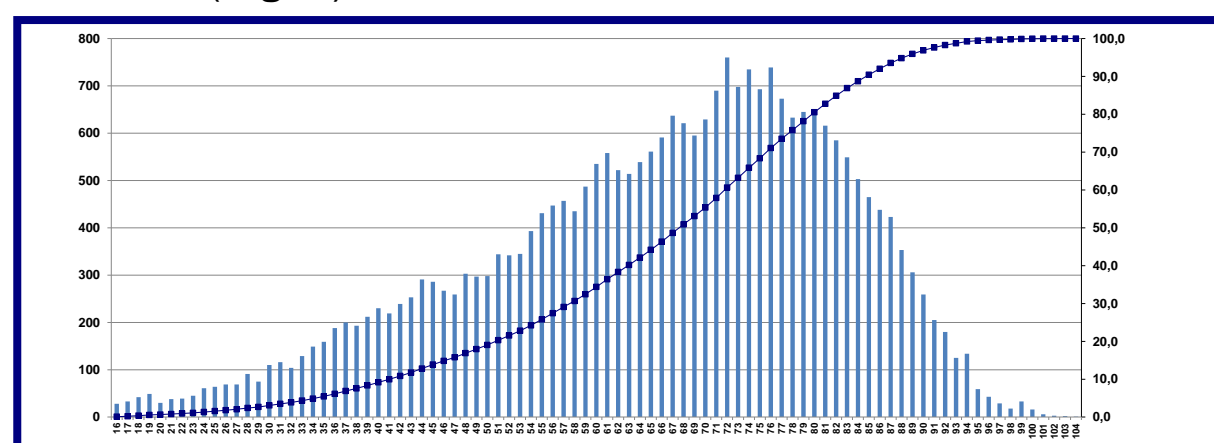


Fig. 2: Age distribution of reported IPD cases among adults (1992-2017, n=27,484).

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 the current season (2016-2017), serotypes 3, 22F, 8, 12F, 9N and 19A were most prevalent (**Table 1**).

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	
	total	%	total	%	total	%	total	%	total	%
all	4477	100.0	2066	100.0	2500	100.0	2661	100.0	1936	100.0
PCV7	3911	87.4	1492	72.2	1799	72.0	1900	71.4	1390	71.8
PCV13	3238	72.3	1250	60.5	1507	60.3	1713	64.0	1338	69.2
PCV10	2581	57.7	973	47.1	1221	48.8	1533	57.6	1357	69.9
PCV7	1943	43.4	720	34.9	107	4.3	94	3.5	103	5.3
14	591	13.2	310	15.0	3	0.1	461	17.3	385	19.9
3	389	8.7	176	8.5	227	9.1	242	9.1	156	8.1
4	368	8.2	161	7.8	199	8.0	218	8.2	8	0.4
7F	307	6.9	145	7.0	8	0.3	211	7.9	123	6.4
9V	296	6.6	109	5.3	136	5.4	153	5.7	91	4.7
23F	285	6.4	99	4.8	19A	7.6	138	5.2	104	5.4
6B	257	5.7	92	4.5	15A	6.0	112	4.2	74	3.8
8	183	4.1	78	3.8	24F	9.8	105	3.9	62	3.2
19F	160	3.6	76	3.7	7F	2.8	79	3.0	60	3.1
6A	153	3.4	75	3.6	11A	0.4	76	2.9	24F	1.2
12F	140	3.1	23B	1.1	16B	0.6	74	2.8	6C	0.3
9N	128	2.9	59	2.9	23B	0.9	66	2.5	45	2.3
18C	120	2.7	54	2.6	23A	0.9	60	2.3	23B	1.2
22F	119	2.7	54	2.6	6C	0.2	56	2.1	35F	1.8
11A	105	2.3	6C	0.3	33F	1.2	51	1.9	20	1.0
24F	103	2.3	33F	1.6	46	1.8	31	1.2	39	2.0
20	101	2.3	35F	1.7	43	1.7	50	1.9	31	1.6
5	80	1.8	35B	1.7	20	0.8	47	1.8	18F	0.9
33F	47	1.0	31	1.5	31	1.2	45	1.7	35B	1.8
23A	38	0.8	25	1.2	15B	0.6	36	1.4	7F	0.4
6C	35	0.8	14	0.7	19F	0.7	35	1.3	33F	1.8
23A	35	0.8	16F	0.8	32	1.3	31	1.2	17F	0.9
23A	32	0.7	19F	0.9	29	1.2	28	1.1	38	2.0
23A	31	0.7	31	1.5	17F	0.7	27	1.0	19B	1.0

Before childhood vaccination 40-45% of IPD cases among adults were caused by PCV7 serotypes. After the start of childhood vaccination this percentage was gradually reduced to 5.3% in July 2016 - March 2017.

In 2009, higher valent vaccines (PCV10 and PCV13) were introduced among children. Among adults, a reduction of the percentage of IPD caused by the six additional serotypes from 47.2% in 2010-2011 to 25.8% in 2015-2016 was observed. First data for the 2016-2017 season (July 2016 - March 2017) indicate a slight increase to 27.6% (**Fig. 3**).

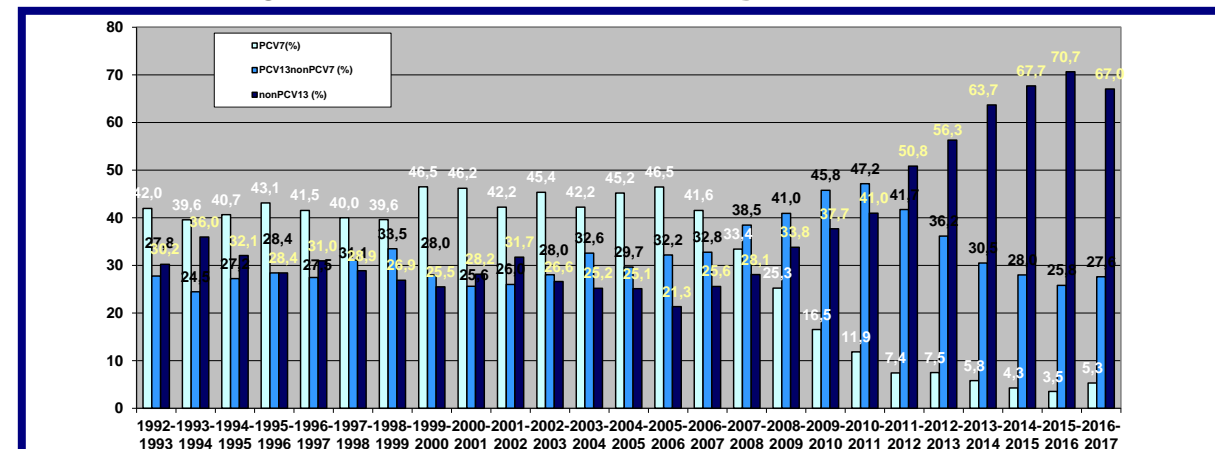


Fig. 3: percentage of PCV7, PCV13-non-PCV7 and non-PCV13 serotypes among cases of IPD from adults in Germany.

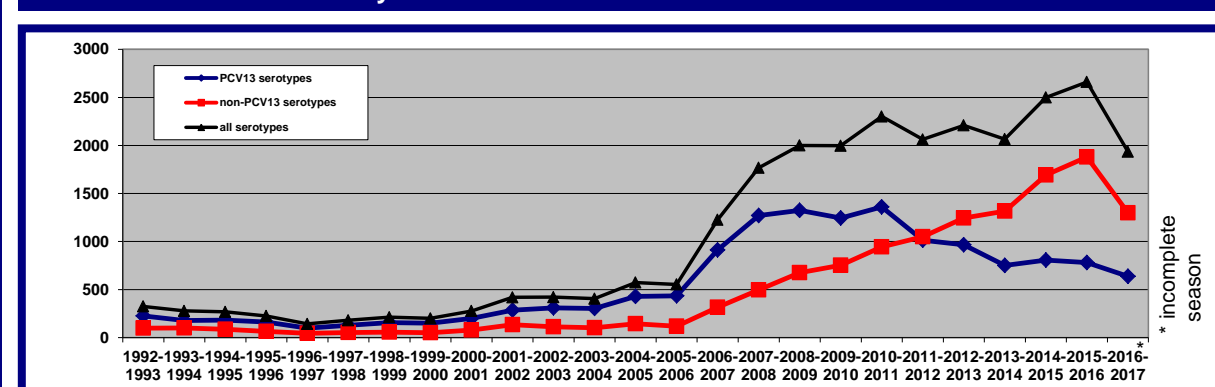


Fig. 5: IPD among adults caused by PCV13 and non-PCV13 serotypes (1992-2017).

The decrease is due to serotypes 1, 6A, 7F and 19A and could be caused by herd- and direct effects in adults. IPD due to serotype 3 has strongly increased since higher-valent vaccine introduction, and is currently the most prevalent serotype, reaching 19.9% in the current season. IPD caused by serotype 19A has remained stable in the last three seasons (**Fig. 4**).

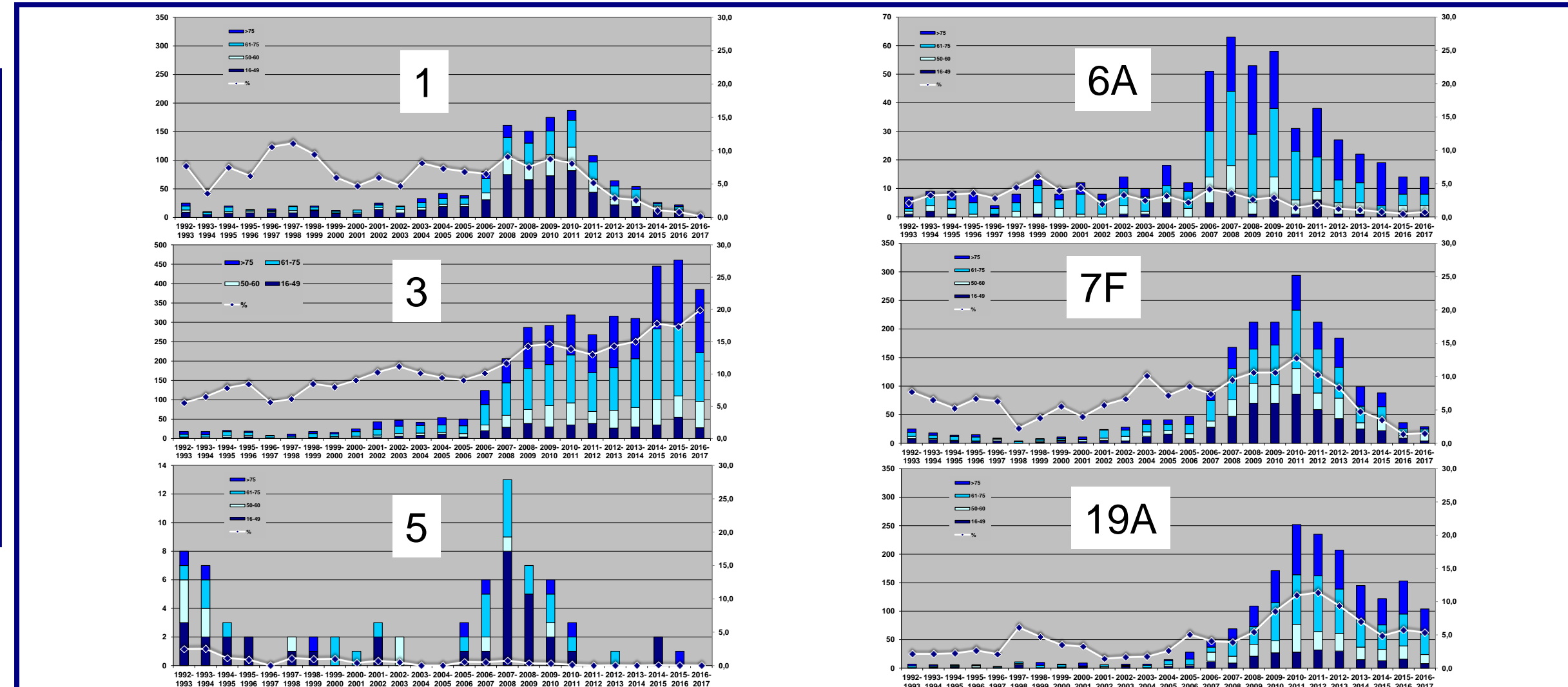


Fig. 4: Case numbers per age group and percentages of IPD caused by serotypes 1, 3, 5, 6A, 7F and 19A among adults in Germany (1992-2017).

Non-PCV13 serotypes have gained in importance since the start of childhood vaccination (**Fig. 5**). Strongest increasing serotypes among IPD in adults are serotypes 10A, 12F, 15A and 23B. Of these, 15A and 23B show the most significant trend and are often penicillin non-susceptible (**Fig. 6**). Over the whole surveillance period, the level of penicillin non-susceptibility has, however, remained low and stable.

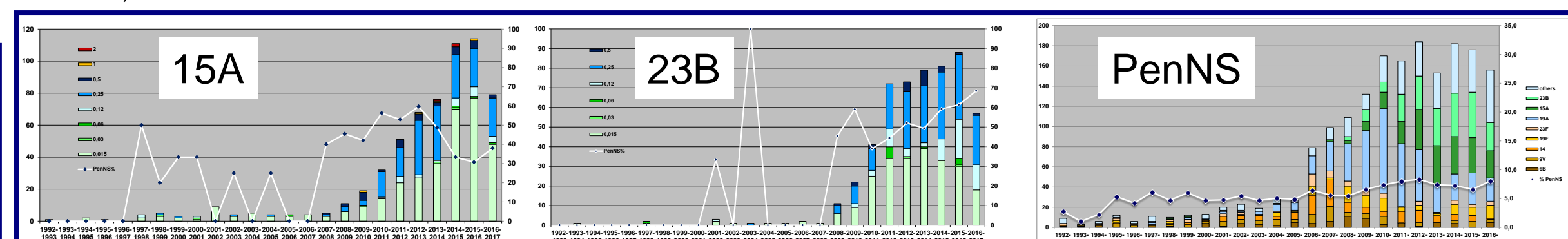


Fig. 6: MIC values of serotype 15A and serotype 23B isolates and penicillin non-susceptible isolates from IPD among adults in Germany (1992-2017).

CONCLUSIONS

- Since the introduction of childhood pneumococcal conjugate vaccination the serotype distribution of IPD among adults has changed substantially.
- PCV7 serotypes have almost disappeared among adult IPD (5.3% in 2016-2017).
- PCV13-non-PCV7 serotypes 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 is not the same for all serotypes, was not observed for serotype 3 and has stabilized for serotype 19A.
- Most prevalent serotypes in IPD among adults in 2016 – 2017 are: 3, 22F, 8, 12F, 9N and 19A.
- Serotypes 15A and 23B show an increasing level of penicillin non-susceptibility.