

## 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. PCV13 was licenced for adults in 2011 and uptake in adults has increased since. In this study, we present the burden of disease and serotype distribution among children and adults with invasive pneumococcal disease (IPD) before and after the start of childhood and adult vaccination.

## METHODS

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

## RESULTS

Since the start of childhood immunization with PCVs, the number of IPD isolates from children  $<16$  years of age have reduced by almost half. This reduction was observed among all age groups. PCV7 serotypes were strongly reduced, but have not disappeared, and in fact have slightly increased in recent years. PCV13-non-PCV7 serotypes have strongly decreased since 2009-2010 and non-PCV13 serotypes have increased (Fig. 1). Before childhood vaccination (1997-2006) the most prevalent serotypes were 14, 9V, 19F, 6B and 1. In 2015-2016 most prevalent serotypes were 10A, 3, 24F and 12F (Table 1).

Since 2006/2007 the amount of IPD isolates from adults remained stable (2000-2500 per year), with the majority of reported cases from adults aged 50 years and older. A strong reduction in PCV7 and PCV13 serotypes was observed after the start of childhood vaccination, and non PCV13 serotypes have increased. 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 2015-2016 serotypes 3, 8, 12F, 22F, 19A and 9N were most prevalent, followed by 15A, 23A, 10A, 24F and 23B (Table 2).

Serotypes 1, 6A, 7F and 19A have almost disappeared among children, although with different dynamics for each serotype and age group (Fig 3, left). Among adults, serotypes 1, 6A, 7F and 19A have diminished in a similar way (Fig 3, right). Serotype 3 cases are rare among children and no real change is visible. Although most cases were reported in non-vaccinated children. Among adults serotype 3 cases have increased to 16.8% in 2015-2016. Serotype 5 cases are very rare in Germany.

Macrolide resistance levels have strongly decreased with the disappearance of vaccine serotypes. The level of penicillin non-susceptible isolates has remained roughly the same, with vaccine serotypes being replaced by non-vaccine serotypes. Serotypes 15A and 23B are the most prevalent resistant isolates (Fig. 4).

## CONCLUSIONS

- PCV7 serotypes have almost disappeared among childhood and adult IPD.
- PCV13-non-PCV7 serotypes make up for 14.3% of childhood IPD and 25.6% of adult IPD in 2015-2016.
- Most prevalent serotypes in IPD in children are: 10A, 3, 24F, 12F, in adults: 3, 8, 22F, 12F.
- Serotypes 15A and 33F are the most prevalent among macrolide resistant isolates, 15A and 23B among penicillin non-susceptible isolates.

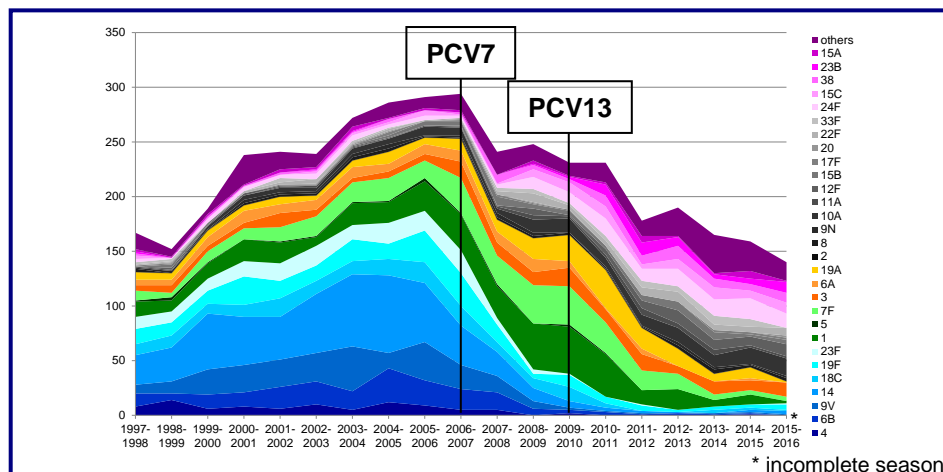


Fig. 1: Number of cases of IPD from children  $<16$  years of age in Germany per pneumococcal season.

Table 1: Prevalence of serotypes among children (age  $<16$  y.) with IPD in Germany, before (1997-2006) and 7, 8, 9 and 10 years (2012-2013, 2013-2014, 2014-2015, 2015-2016) after the introduction of childhood conjugate vaccination (PCV7: 2006, PCV10/PCV13: 2009).

Serotype	average 1997-2006	% total	Serotype	2012-2013	% total	Serotype	2013-2014	% total	Serotype	2014-2015	% total	Serotype	2015-2016	% total
total	221	100.0	total	199	100.0	total	166	100.0	total	159	100.0	total	140	100.0
PCV7	201	91.0	PCV7	118	59.3	PCV7	92	55.4	PCV7	86	54.1	PCV7	80	57.1
PCV13	195	88.2	PCV13	61	30.6	PCV13	38	22.9	PCV13	44	27.7	PCV13	31	22.1
PCV10	174	78.8	PCV10	38	19.1	PCV10	19	11.4	PCV10	23	14.5	PCV10	17	12.1
PCV7	142	64.3	PCV7	5	2.6	PCV7	8	4.8	PCV7	10	6.3	PCV7	11	7.9

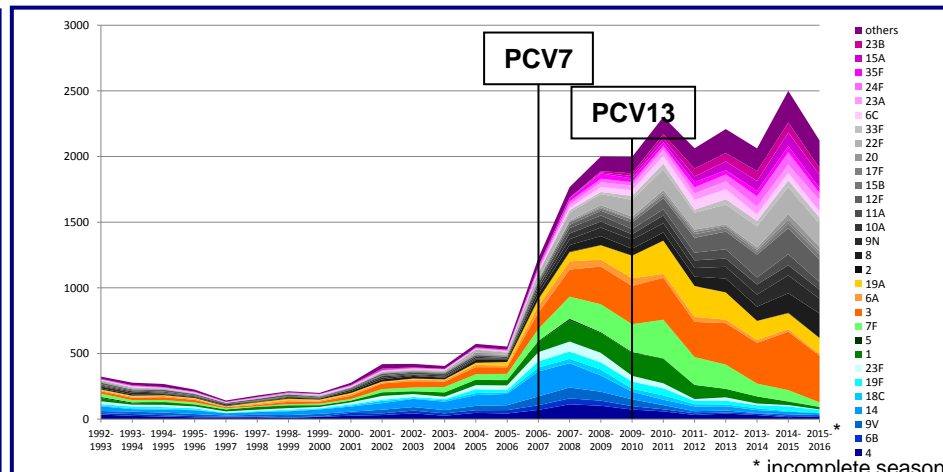


Fig. 2: Number of cases of IPD from adults (16 years of age) in Germany per pneumococcal season.

Table 2: Prevalence of serotypes among adults (age  $\geq 16$  y.) with IPD in Germany, before (1992-2006) and 7, 8, 9 and 10 years (2012-2013, 2013-2014, 2014-2015, 2015-2016) after the introduction of childhood conjugate vaccination (PCV7: 2006, PCV10/PCV13: 2009).

Serotype	all 1992-2006	% total	Serotype	2012-2013	% total	Serotype	2013-2014	% total	Serotype	2014-2015	% total	Serotype	2015-2016	% total
all	4477	100.0	total	2209	100.0	total	2066	100.0	total	2500	100.0	total	2122	100.0
PCV7	3911	87.4	PCV7	1648	74.6	PCV7	1402	72.2	PCV7	1799	72.0	PCV7	1525	71.9
PCV13	3238	72.3	PCV13	965	43.7	PCV13	750	36.3	PCV13	807	32.3	PCV13	618	29.1
PCV10	2581	57.7	PCV10	415	18.8	PCV10	273	13.2	PCV10	221	8.8	PCV10	128	6.0
PCV7	1943	43.4	PCV7	166	7.5	PCV7	120	5.8	PCV7	107	4.3	PCV7	74	3.5

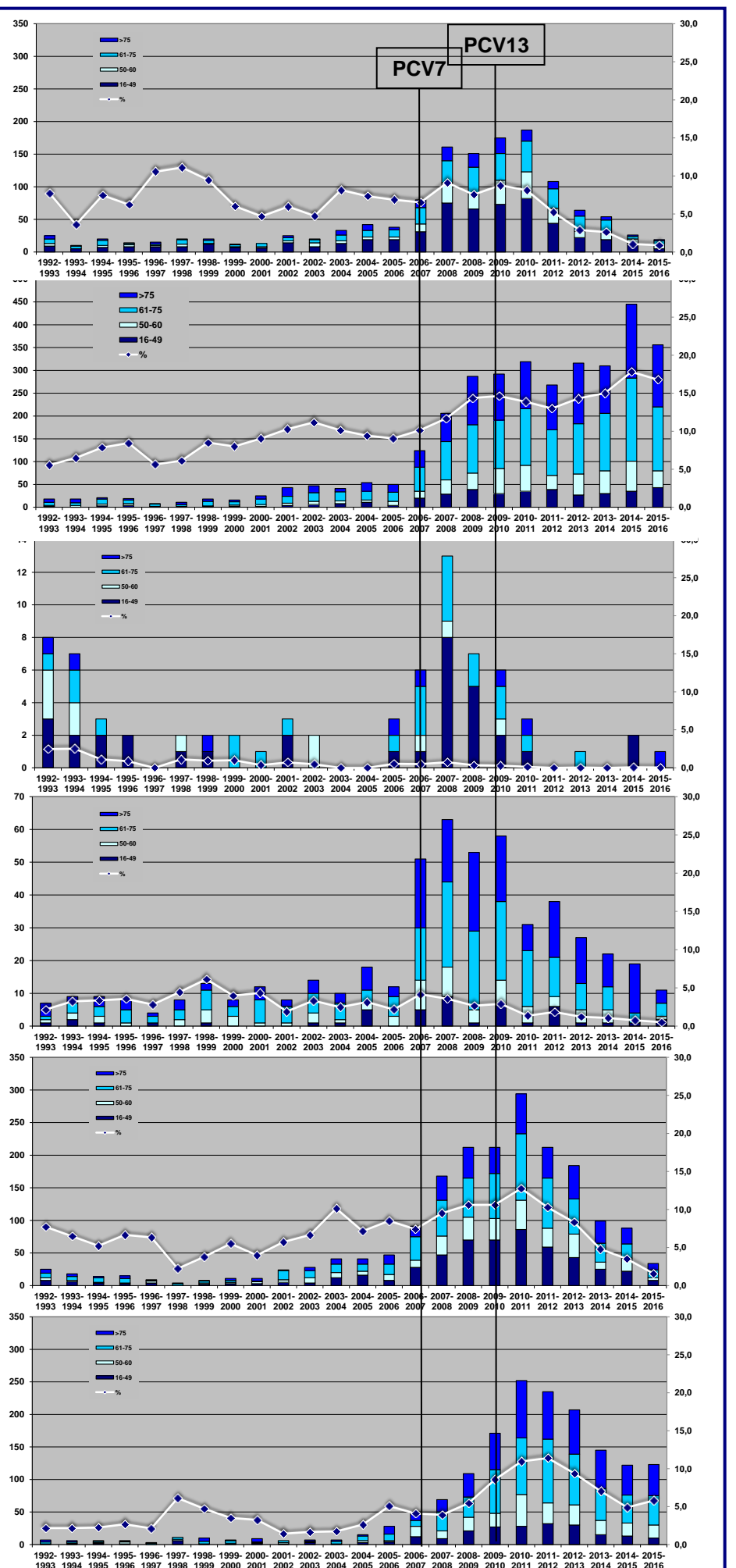
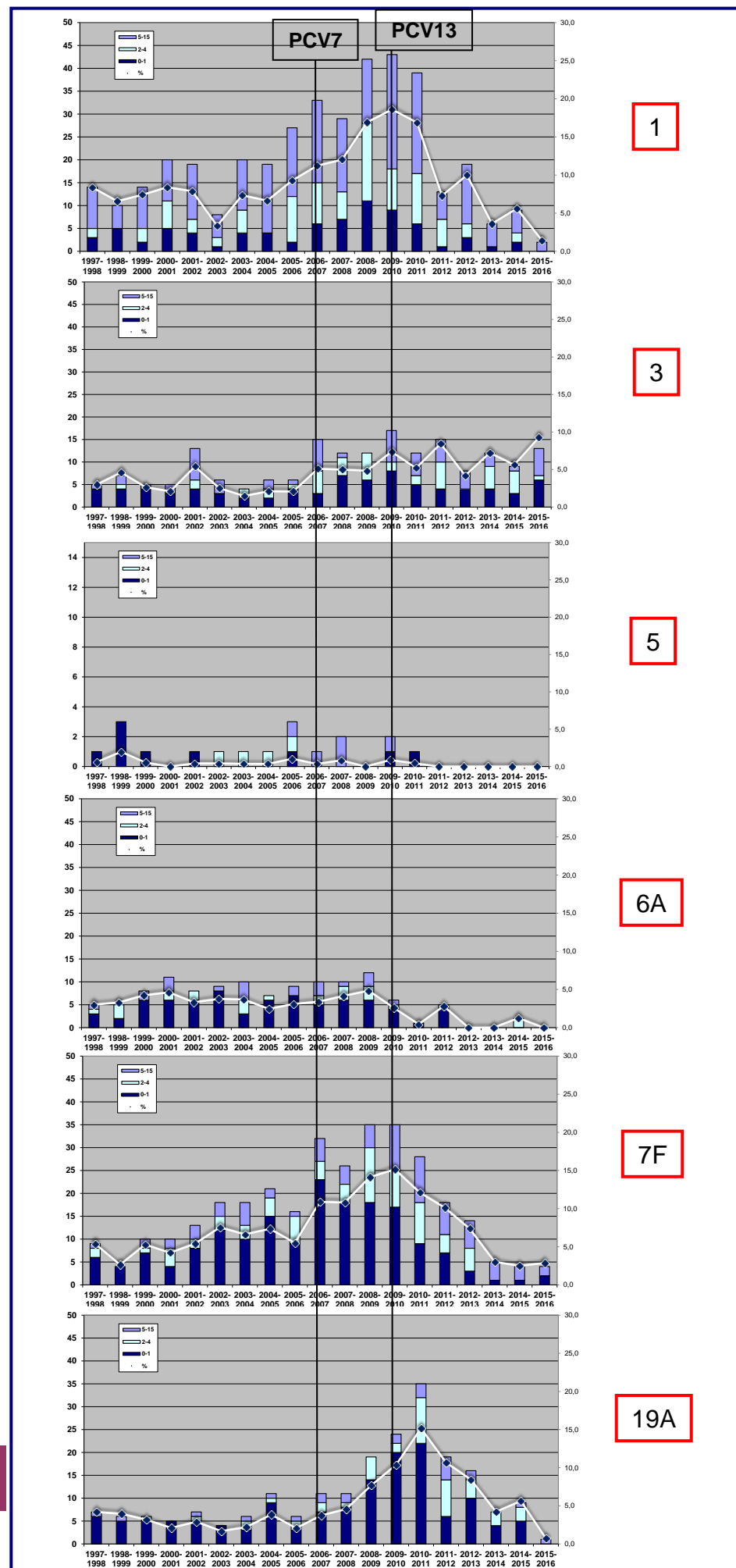


Fig. 3: Case numbers per age group and percentages of IPD caused by serotypes 1, 3, 5, 6A, 7F and 19A among children (left) and adults (right).

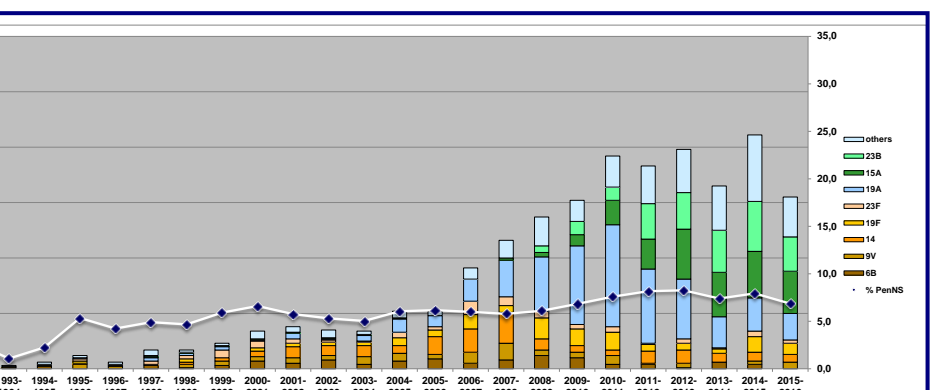
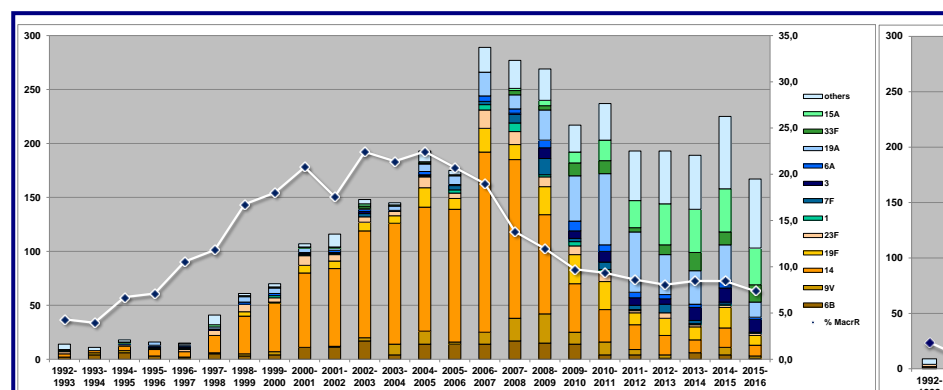


Fig. 4: Macrolide resistant (MIC  $>0.5$   $\mu\text{g/ml}$ ; left) and penicillin non-susceptible (MIC  $>0.06$   $\mu\text{g/ml}$ ; right) serotypes among IPD from children and adults in Germany.