Invasive pneumococcal disease in children under 16 years of age: Incomplete rebound in incidence after the maximum effect of PCV13 in 2012-13 in Germany

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BACKGROUND

The infant pneumococcal conjugate vaccine (PCV) program in Germany began with a recommendation from the Standing Vaccination Committee (STIKO) of the Robert Koch Institute for high-risk children only in 2001, which was then expanded to all children in 2006.

The original recommendation was for three primary doses, administered during the third, fourth, and fifth months of life, and one booster dose administered between twelve and fifteen months of age.

The recommendation was reduced in 2015 to two primary doses (at the third and fifth months of life) and one booster dose.

OBJECTIVE

The objective of this study was the identification a potential nadir of the impact of the PCV program on invasive pneumococcal disease (IPD) in children under 16 in Germany.

METHODS

We used nationwide, active surveillance of IPD based on two independent data sources, one from pediatric hospitals and wards, and one from microbiological laboratories, and applied a capture-recapture correction (CRC) for underreporting.

Annual IPD incidence rates by age group, serotype, site of infection, and relative incidence reduction were compared to those from the prevaccination period (1997 to 2001) at the identified nadir and for the most recent season. We calculated vaccine coverage at 24 months of age using health insurance claims data.

RESULTS

Since 2009, nearly all (96-97%) of children had received at least two doses of PCV. The maximum impact of the PCV program on overall IPD incidence was achieved in 2012/13 (-48% [95%CI: -55% to –39%]).

Non-PCV13 serotypes accounted for 84.1% of the IPD cases in 2015/2016. The most frequent non-PCV serotypes in IPD in 2016/17 were 10A, 24F, 15C, 12F, 38, 22F, 23B, and 15B.

The impact at nadir was highest in children 0-1 years of age both in meningitis and non-meningitis cases, whereas the impact for other age groups was higher for meningitis cases. The rebound mainly pertained to non-meningitis cases.

CONCLUSIONS

- It appears that the maximum impact of pneumococcal conjugate vaccination has been attained
- Signs of a rebound in IPD incidence are apparent
- Sustained surveillance for IPD in children is warranted to assess whether these trends will continue

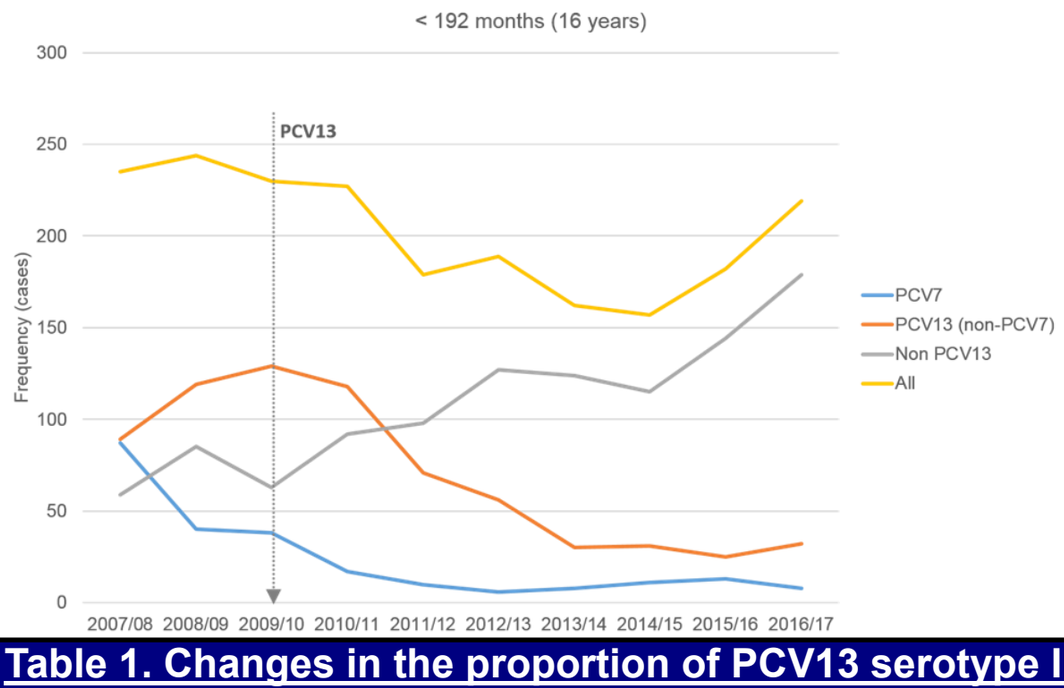

Figure 1: Distribution of serotypes for all IPD cases in children in Germany < 16 years (192 months), from 2007/08 to 2016/17. Vaccine serotypes declined sharply, though the overall number of cases was largely affected by serotype replacement .

Table 1. Changes in the proportion of PCV13 serotype IPD by age group. The proportion of the PCV13 serotypes in meningitis cases, non-meningitis IPD, and all IPD cases measured for three time periods: before the introduction of PCV13, after PCV13 implementation, and the most recent pneumococcal season.

age	**0 - <24 months**					
period	**non-meningitis**	p-value compared to period before	**meningitis**	p-value compared to period before	**overall**	p-value compared to period before
2000/01-2009/10	82.6%		79.9%		81.7%	
2010/11-2016/17	34.4%	<.0001	25.7%	<.0001	31.7%	<.0001
2016/17	14.5%	0.0046	7.7%	0.1462	12.8%	0.0029
age	**24 - <60 months**					
period	**non-meningitis**	p-value compared to period before	**meningitis**	p-value compared to period before	**overall**	p-value compared to period before
2000/01-2009/10	85.7%		78.4%		83.9%	
2010/11-2016/17	47.7%	<.0001	21.2%	<.0001	41.0%	<.0001
2016/17	44.4%	0.8659	7.7%	0.2427	34.7%	0.7445
age	**60 - <192 months**					
period	**non-meningitis**	p-value compared to period before	**meningitis**	p-value compared to period before	**overall**	p-value compared to period before
2000/01-2009/10	84.4%		62.2%		77.2%	
2010/11-2016/17	69.7%	0.0004	30.2%	<.0001	56.2%	<.0001
2016/17	15.6%	<.0001	14.3%	0.2522	15.1%	<.0001
age	**0 - <192 months**					
period	**non-meningitis**	p-value compared to period before	**meningitis**	p-value compared to period before	**overall**	p-value compared to period before
2000/01-2009/10	83.9%		75.8%		81.4%	
2010/11-2016/17	47.2%	<.0001	25.9%	<.0001	40.7%	<.0001
2016/17	21.9%	<.0001	10.0%	0.0369	18.5%	<.0001

Table 2: IPD incidence per 100,000 and IPD incidence reduction calculated from hospital and microbiological laboratory surveillance with CRC for underreporting. Incidence estimates and reduction percentages calculated with reference to the incidence rate in 2008/09, by age group and year, with 95% confidence intervals (95% CI).

Age	IPD incidence pre PCV10/13 (95% CI)	IPD incidence transition year: PCV7 to PCV10/13 (95%CI)	IPD incidence 5 y post 2008/09 (95%CI)	IPD incidence 6 y post 2008/09 (95%CI)	IPD incidence 7 y post 2008/09 (95%CI)	IPD incidence 8 y post 2008/09 (95%CI)	IPD Incidence change in % (95%CI)
	2008/09	**2009/10**	**2013/14**	**2014/15**	**2015/16**	**2016/17**	**2008/09 – 2016/17**
<2 y	12.9 (9.0-16.7)	13.1 (8.3-17.8)	7.6 (5.1-10.2)	11.0 (9.4-12.9)	15.8 (13.9-18.0)	13.7 (12.0 to 15.8)	+7 (-13 to +31)
2-4 y	6.4 (4.7-8.1)	5.9 (3.2-8.5)	3.4 (2.1-4.7)	2.0 (1.5-2.7)	1.4 (1.0-2.0)	3.2 (2.6 to 4.1)	-49 (-62 to -32)
<5 y	9.0 (7.2-10.9)	9.0 (6.2-11.8)	5.3 (3.8-6.8)	6.2 (5.4-7.1)	7.0 (6.2-8.0)	8.0 (7.1 to 8.9)	-12 (-25 to +3)
5-15y	1.7 (0.9-2.4)	2.1 (1.1-3.1)	0.7 (0.4-1.0)	0.8 (0.6-1.0)	0.9 (0.7-1.2)	1.9 (1.6 to 2.2)	12 (-11 to +41)
< 16	3.8 (3.5-4.1)	4.2 (3.1-9.8)	2.0 (1.4-2.6)	2.3 (2.0-2.6)	2.9 (2.6-3.2)	3.6 (3.3 to 4.0)	-4 (-16 to +10)