

Title: Cost-effectiveness of PCV20 to Prevent Pneumococcal Disease in the Pediatric Population - A German Societal Perspective Analysis

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Prior presentation: An abstract reporting the results of this study has been submitted to ESPID 2024 (20–24 May), which has been accepted as a poster presentation.

Appendix A: Indirect Effects

The estimates of indirect effects were based on (i) accrual data capturing the ramp-up period until the steady state is reached (i.e. no additional indirect effects would be observed after this state), and (ii) the maximum reduction in pneumococcal disease incidence.

(i) Accrual data

The model assumed that indirect effects on current PCV13 serotypes are in a steady state since PCV13 has been used for more than 10 years. In other words, no additional indirect effects related to PCV13-unique serotypes would be observed with higher-valent vaccines: PCV15 or PCV20. The indirect effects from PCV15 and PCV20, therefore, were only quantified from the newly covered serotypes and assumed to occur gradually over the model time horizon.

The accrual of the indirect effects for PCV15 and PCV20 were informed by IPD surveillance data obtained in the UK (Ladhani et al., 2018[1]) with year 6 of the PCV13 infant program chosen as the steady-state year per Perdrizet et al., 2023[2]. It is noted that Serotype 3 was excluded from the analysis due to its unique immunologic characteristics compared with other PCV13-serotypes and its persistent pneumococcal carriage in pediatrics [3-5], resulting in the use of annual relative change in vaccine-type IPD incidence within the serotype group PCV13 minus PCV7 serotypes (excluding serotype 3 [PCV13-7-ST3]) after the introduction of PCV13. Consequently, the potential decrease in the incidence of the newly covered serotypes in PCV15 and PCV20 was estimated.

(ii) The maximum reduction in pneumococcal disease incidence

The maximum of herd effects against IPD caused by additional serotypes covered by PCV15 and PCV20 was informed by Ladhani et al., 2018[1] and Perdrizet et al., 2023[2].

For hospitalized pneumonia, the effect on children was estimated using an observational study by Levy et al., 2017 that was conducted in France in 2009 – 2015 [6]. The study recorded a 30% decrease in inpatient hospitalizations from emergency room visits following PCV13 implementation in children aged 5-17 years (i.e., post-PCV13 implementation data in 2011 – 2015 compared with the pre-PCV13 period in 2009 – 2010). The model applied adjustment ratios of 70% and 86% to account for differences in serotype distribution pre- PCV13 implementation and the current serotype distribution (i.e. PCV13 serotype coverage was 70% for infants aged <2 and 86% for children 2 to 17 years of age in France [7]). For age groups ≥18 years old, data from a UK-based study for adults was used. The study reported a 15% reduction in the incidence of chest X-ray-confirmed pneumonia cases after the implementation of PCV13 in pediatric vaccination[8]. Likewise, ratios of 67% (18-49 years), 60% (50-65 years), and 56% (≥65 years) were used for adjustment[1]. A similar approach with the same data sources were used to estimate maximum reduction non-hospitalized pneumonia, however, only for children.

For otitis media (OM), it was assumed that indirect effects were only observed in children younger than 5 years old. Maximum decrease in OM incidence was informed by a retrospective cohort study by Lau et al., 2015[9], which included children aged 5 to 9 years in the UK (i.e. comparing OM incidence from before the introduction of PCV13 in 2007 – 2010 with post-PCV13 implementation in 2011 – 2012). To adjust serotype coverage, a ratio adjustment of 71% in 2009, as reported by Ladhani et al., 2018, was used [1].

The model excluded the vaccinated adult population from indirect effects to avoid overestimating indirect effect from the infant vaccination program.

Appendix B: Supplementary tables

Table S1: General population estimates

Age groups	Population size
<12 months	791,254
12–23 months	780,795
24–35 months	789,145
36–47 months	803,334
48–59 months	810,805
5–17 years	9,887,926
18–34 years	16,539,516
35–49 years	15,331,897
50–64 years	19,065,953
≥65 years	18,972,098
Total	83,772,723

Source: German population data from German Federal Statistical Office [10]

Table S2: Number of <12-month-olds in incoming birth cohort

Year in model	Number of infants younger than 12 months in incoming birth cohort
Year 2	747,800
Year 3	752,300
Year 4	750,200
Year 5	747,300
Year 6	743,400
Year 7	738,900
Year 8	734,100
Year 9	729,000
Year 10	723,600

Source: German Federal Statistical Office [10] and German Federal Statistical Office [11]

A birth rate of 1.4 per female was assumed to calculate the number of infants younger than 12 months in incoming birth cohort for per year, based on German Federal Statistical Office [11] estimates.

Table S3: Probability of sequela

Age group	Meningitis [12]	
	Deafness	Non-deafness
All age groups	9.12%	12.48%

Table S4: Age-specific Clinical Outcome Results: Total disease cases and deaths

Age	PCV13 2+1				
	IPD	Hospitalized pneumonia	Non-hospitalized pneumonia	OM	Total deaths due to disease
<12 months	1,177	111,173	182,210	1,098,249	200
12-23 months	1,184	60,995	183,360	1,105,180	112
24-35 months	106	61,494	641,527	1,355,200	59
36-47 months	107	62,070	647,544	1,367,909	60
48-59 months	108	62,670	653,801	292,101	60
5 - 17 years	1,025	132,665	2,434,233	-	1,249
18 - 34 years	2,537	167,228	602,326	-	7,441
35 - 49 years	2,662	175,509	632,155	-	7,807
50 - 64 years	18,734	955,072	1,226,979	-	114,373
65+ years	49,374	5,723,352	2,294,427	-	981,142
Total	77,013	7,512,228	9,498,563	5,218,640	1,112,503

Age	PCV15 2+1				
	IPD	Hospitalized pneumonia	Non-hospitalized pneumonia	OM	Total deaths due to disease
<12 months	1,124	108,506	179,647	1,083,972	194
12-23 months	1,131	59,479	180,736	1,090,433	108
24-35 months	98	59,136	627,168	1,327,219	57
36-47 months	100	59,829	633,389	1,340,573	58
48-59 months	102	60,545	639,840	286,452	58
5 - 17 years	947	128,341	2,377,912	-	1,206
18 - 34 years	2,400	165,368	602,328	-	7,349
35 - 49 years	2,514	173,495	632,157	-	7,707
50 - 64 years	17,674	940,185	1,227,019	-	112,574
65+ years	46,955	5,633,084	2,295,013	-	965,523
Total	73,046	7,387,967	9,395,209	5,128,648	1,094,834

Age	PCV20 3+1				
	IPD	Hospitalized pneumonia	Non-hospitalized pneumonia	OM	Total deaths due to disease
<12 months	771	91,523	163,862	994,998	159
12-23 months	795	50,380	164,995	1,001,950	84
24-35 months	65	48,921	564,945	1,205,969	46
36-47 months	69	50,119	572,054	1,222,117	48
48-59 months	74	51,336	579,341	261,972	49
5 - 17 years	746	116,449	2,223,028	-	1,087
18 - 34 years	1,663	155,368	602,334	-	6,855
35 - 49 years	1,717	162,668	632,165	-	7,173
50 - 64 years	14,192	891,263	1,227,153	-	106,660

65+ years	41,620	5,434,004	2,296,320	-	931,078
Total	61,712	7,052,031	9,026,198	4,687,006	1,053,238

Note: The breakdown results by age groups were mostly consistent with the overall results where more cases avoided related to PCV20 in all included age groups for IPD, hospitalized pneumonia and OM than PCV13, especially in the oldest group of 65+ year-olds. Similarly, PCV20 is estimated to prevent more cases of non-hospitalized pneumonia than PCV13 in children less than 5 years old. The higher valent vaccines showed an increasing number of prevented non-invasive pneumonia. One could observe a shift from severe cases (i.e., hospitalized cases) in the lower valent vaccine strategies to less severe cases (i.e.; non-hospitalized pneumonia) in the higher valent vaccine strategies. Furthermore, better health outcomes from PCV20 were shown by a reduction in deaths due to disease in all age groups, with the greatest reduction observed in those 65 years old and above (50,064 deaths averted).

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