EE358

SYSTEMATIC LITERATURE REVIEW OF COST-EFFECTIVENESS ANALYSES OF ADULT 15- AND 20-VALENT PNEUMOCOCCAL VACCINES

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Background

- Higher-valent pneumococcal conjugate vaccines (PCVs) to prevent pneumococcal disease caused by serotypes contained in PCV13 as well as incremental non-PCV13 serotypes have been implemented for adults in only a few high-income countries.
- Decision makers considering implementation of higher-valent PCVs may benefit from a comprehensive understanding of existing economic evaluations of higher-valent PCVs, including results, conclusions, and key assumptions, such as how vaccine efficacy over time is considered and what data sources have been used.

Objective

- This study aims to review systematically and summarize the findings and assumptions of cost-effectiveness analyses (CEA) of the recently introduced 15- and 20-valent pneumococcal conjugate vaccines (PCV15 and PCV20) in adults.

Methods

- This review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.
- A protocol (CRD42024428846) was developed and registered on the International Prospective Register of Systematic Reviews (PROSPERO).
- We performed a systematic search for CEA studies of PCV15 and/or PCV20 on databases including PubMed, EMBASE, Cost-effectiveness analysis Registry by Tufts Medical Center, EconLit, International HTA Database, and National Immunization Technical Advisory Groups database through October 30, 2023.
- Two reviewers independently screened eligible papers and extracted data. In case of disagreement, it was resolved through discussion with a third reviewer.
- Data extracted included methodology details and assumptions of identified studies such as vaccine efficacy/effectiveness, input sources, and study findings such as incremental cost-effectiveness ratio, conclusions derived, and uncertainties identified.
- Quality assessment was performed using the ECOBIAS tool. Results were synthesized qualitatively to summarize key attributes and conclusions [1].
- Reporting quality was assessed based on the 28-item checklist from the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 statement [2].

Figure 1. PRISMA Diagram

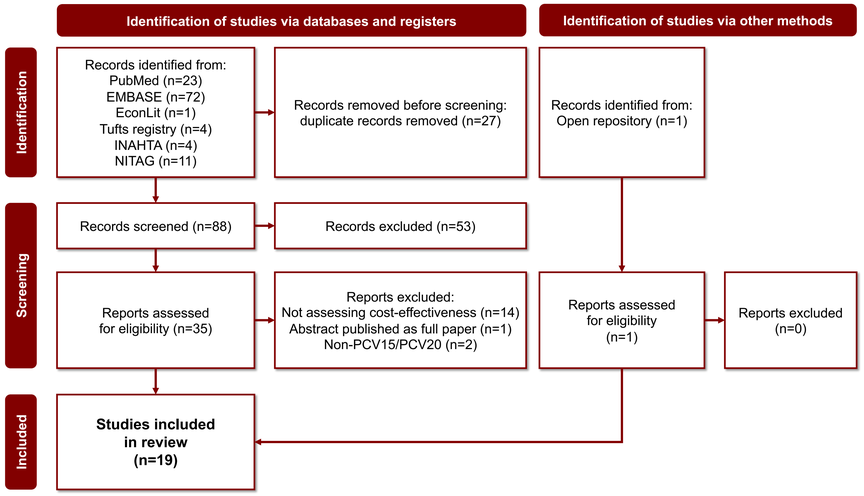

Figure 2. Source for serotype distribution

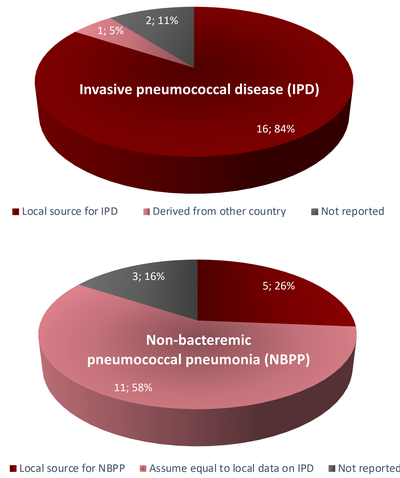

Table 1. Study characteristics, conclusions and key assumptions

Author (Year)	Country	Population[a]	Comparators[b]			Model setup				Effectiveness source		Protect duration[h]		Indirect effects considered	
			PCV	PCV + PPSV	Standard of care	Perspective	Model type	Time horizon	Annual discounting (%)	PCV[f]	PPSV[g]	PCV	PPSV	Pediatric herd effect	Serotype replacement
Cantarero et al (2023)[3]	Spain	Senior (60+)	***PCV20***	PCV15+PPSV23		Healthcare system; Societal	Markov	10 years	3	PCV13 RCT; PCV9 RCT	UK IPD; *UK CAP*	10 (5)	10 (0)	✓	✓
de Boer et al (2023)[4]	Netherland	Senior (65)	PCV15; **PCV20**; PCV21*	PCV15+PPSV23; PCV20+PPSV23	No vaccination; PPSV23; PCV13; PCV13+PPSV23	Societal; Healthcare system	Markov	15 years	4 (cost); 1.5 (effectiveness)	PCV13 RCT	UK IPD; Meta-analysis	15 (4)	5 (2)	✓	✓
Deb et al (2022)[5]	Switzerland	Adult (18+)	**PCV15**		No vaccination	Payer; Societal	Markov	Lifetime	3	PCV13 RCT	NA	15 (5)	N/A	X	X
Dorange et al (2022)[6]*	Sweden	Adult (18+)	***PCV20***		PPSV23; PCV13+PPSV23	Healthcare system; Societal	Hybrid[c]	Lifetime	NR	NR	NR	NR	NR	NR	NR
Gourzoulidis et al (2023)[7]	Greece	Adult (18+)	PCV15; ***PCV20***	PCV15+PPSV23		Public payer (Excluded 3rd party)	Markov	Lifetime	3.5	PCV13 RCT; PCV9 RCT	UK IPD; *UK CAP*	15 (5)	10 (0)	X	X
Hoshi et al (2022)[8]	Japan	Senior (65)	PCV15; ***PCV20***		PPSV23	Payer	Hybrid[d]	Lifetime	2	CDC presentation[22]		15 (5)	15 (0)	X	X
Kuhne et al (2023)[9]	Germany	Adult (18+)	***PCV20***	PCV15+PPSV23	PPSV23; PCV13+PPSV23	Payer; Societal	Hybrid[c]	Lifetime	3	PCV13 RCT; PCV9 RCT	UK IPD; *UK CAP*	15 (5)	10 (0)	✓	X
Mac Mullen et al (2022)[10]*	Argentina	Adult (18+)	***PCV20***	PCV15+PPSV23		Healthcare system	Markov	Lifetime	NR	NR	NR	NR	NR	NR	NR
Malene et al (2023)[11]	Norway	Adult (18+)	***PCV20***		PPSV23	Healthcare system	Markov	Lifetime	Time-dependent[e]	PCV13 RCT; PCV9 RCT	UK IPD; *UK CAP*	15 (5)	10 (0)	✓	X
Marbaix et al (2023)[12]	Belgium	Adult (18+)	***PCV20***	PCV15+PPSV23	No vaccination	Healthcare system	Markov	Lifetime	3	PCV13 RCT; PCV9 RCT	UK IPD; *UK CAP*	15 (5)	10 (0)	✓	X
Mendes et al (2022)[13]	England	Adult (18+)	***PCV20***	PCV15+PPSV23; PCV20+PPSV23	PPSV23	Healthcare system	Markov	Lifetime	3.5	PCV13 RCT; PCV9 RCT	UK IPD; *UK CAP*	15 (5)	10 (0)	✓	X
NACI (2023)[14]	Canada	Adult (50; 65; 75)	PCV15; **PCV20**	PCV15+PPSV23; PCV20+PPSV23	PPSV23	Healthcare system; Societal	Markov	Lifetime	1.5	PCV13 RCT	UK IPD; UK CAP	15 (5)	15 (0)	✓	X
Olsen et al (2022)[15]	Denmark	Adult (18+)	***PCV20***	PCV20+PPSV23	PPSV23	Restricted societal (Excluded Productivity loss)	Markov	Lifetime	Time-dependent[e]	PCV13 RCT; PCV9 RCT	UK IPD; *UK CAP*	15 (5)	10 (0)	✓	X
Polistena et al (2022)[16]	Italy	Senior (65-74)	PCV15; ***PCV20***		PCV13	Healthcare system	Markov	Lifetime	3	PCV13 RCT; PCV9 RCT	NA	15 (5)	N/A	X	X
Restivo et al (2023)[17]	Italy	Adult (18+)	***PCV20***	PCV15+PPSV23; PCV20+PPSV23	No vaccination; PCV13+PPSV23	Societal	Markov	Lifetime	3	PCV13 RCT	UK IPD; Japan CAP	20 (5)	15 (2)	X	X
Smith et al (2021)[18]	USA	Senior (65+)	PCV15; PCV20	PCV15+PPSV23; PCV20+PPSV23	PPSV23; **PCV13+PPSV23**	Healthcare system	Markov	Lifetime	3	Delphi panel estimates		15 (0)	10 (0)	✓	X
Smith et al (2022)[19]	USA	Senior (65)[i]	**PCV20**	PCV15+PPSV23	No vaccination	Healthcare system	Markov	Lifetime	3	Delphi panel estimates		15 (0)	10 (0)	X	X
Wateska et al (2023)[20]	USA	Senior (65)[i]	PCV20; ***PCV21****	PCV15+PPSV23	No vaccination	Healthcare system	Markov	Lifetime	3	Delphi panel estimates		15 (0)	10 (0)	✓	X
Wateska et al (2022)[21]	USA	Adult (50)[i]	**PCV20**	PCV15+PPSV23	PPSV23; PCV13+PPSV23	Healthcare system	Markov	Lifetime	3	Delphi panel estimates		15 (0)	10 (0)	✓	X

Abbreviations: PCV, Pneumococcal conjugate vaccine; PPSV, Pneumococcal polysaccharide vaccine; IPD, Invasive pneumococcal disease; CAP, Community-acquired pneumonia; NA, non applicable; NR, not reported.
Poster presentation; PCV21 is not yet approved but included as a comparator in these studies. Therefore, de Boer et al (2023) did not include it in their cost-effectiveness plane to determine best strategy. **a**. For younger adult from 18 to 59 or 64 (depends on the study), population does not include low-risk population, they only include moderate- or high-risk or underlying medical condition only. **b**. **Red Bold** indicates most favorable strategy among comparators, ***Italic*** indicates dominates other strategies. **c**. probabilistic framework with Markov process **d**. decision tree with Markov model **e**. discount rate was decreased along with model year. **f**. For those studies using PCV9, PCV9 was used to estimate vaccine effectiveness to the high-risk population, CDC Presentation contain the summary of vaccine effectiveness from previous cost-effectiveness analysis of PCVs. **g**. Value in the table indicates source for IPD and source for non-bacteremic pneumonia, respectively. *Italic* indicates that vaccine effectiveness against NBP assumed to be 0. **h**. Number in parenthesis indicates stable period of protection, which means protection waning is applied after this period with certain rate per year (Cantarero, Deb, Gourzoulidis, Kuhne, Malene, Marbaix, Mendes, Olsen, Polistena), linear decline to 0 (Hoshi, de Boer, NACI, Restivo), or estimated from Delphi panel (Smith, Wateska) **i**. Medically underserved minority or not

Results

- Of 120 identified records, 19 studies were included (Figure 1); all concerned high-income countries except one in Argentina[10].
- The majority (16/19) of studies concluded that PCV20 was cost-saving (dominant) or cost-effective. Of the 3 remaining studies, 1 did not include PCV20 (concluded PCV15 is cost-effective vs no vaccination)[5], another conducted prior to approval concluded that neither PCV15 nor PCV20 would be cost-effective compared to the prior US recommendation[18], and the last found PCV20 would be subject to extended dominance by PCV21, a vaccine under regulatory review but not yet approved in any country [20].
- All employed static Markov-type models to compare PCV15 or PCV20 used alone or in combination with 23-valent pneumococcal polysaccharide vaccine (PPSV23) to existing strategies (Table 1).
- Most studies (16/19) used local sources for serotype distribution to calculate vaccine serotype coverage for IPD[3-5,8,9,11-21], whereas for NBPP, the majority (11/19) assumed serotype distribution to be equal to IPD due to the lack of data[4,5,7,11,12,14,15,18-21] (Figure 2).
- Four studies derived vaccine effectiveness and waning from Delphi panel estimates[18-21], whereas others assumed similar serotype-specific efficacy to the adult PCV13 randomized controlled trial (RCT). Waning of protection varied among studies from 10 to 20 years.
- For PPSV against IPD, most studies estimated vaccine effectiveness from UK IPD surveillance. Moreover, 7 studies using UK CAP cohort data for NBP assumed vaccine effectiveness against NBP of PPSV to be zero [3,7,9,11-13,15], but 8 studies assumed 20% to 33.5% at the first year of vaccination[4,8,14,17-21].
- Additionally, 58% (11/19) of studies included indirect effects that attenuate vaccine impact in the adult population such as herd effect from PCV15/20 in children (10/19) or serotype replacement (2/19).
- Most studies were assessed as low risk of bias; two abstracts did not provide sufficient information for assessment [6,10].

Conclusion

- Current evidence indicates that 20-valent PCV is likely to be cost-effective or dominate current adult pneumococcal strategies. Policymakers should consider whether implementing such a program would improve health and lower total long-term costs due to pneumococcus.

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