COST-EFFECTIVENESS OF 20- AND 15-VALENT PNEUMOCOCCAL CONJUGATE VACCINES FOR CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS OF ECONOMIC EVALUATIONS

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Background and objective

- Pneumococcal disease, caused by Streptococcus pneumoniae, remains a leading infectious cause of death in children aged <5 years worldwide.[1,2,3]
- Higher-valent pneumococcal conjugate vaccines (PCVs), including PCV15 and PCV20, were approved in 2022-2023 to broaden serotype coverage[2,3] and several studies have evaluated their cost-effectiveness in children.[4,5]
- Prior studies found PCV13 to be highly cost-effective versus no vaccination, while switching from PCV13 to PCV20 yields greater QALY gains and cost savings than switching to PCV15.[6]
- However, existing reviews did not provide pooled results[6] or focused only on earlier PCVs.[7]
- This study aimed to estimate the incremental net benefit (INB) for PCV15 and PCV20 compared with each other, existing pneumococcal vaccination strategies, or no vaccination in children.

Methodology

- Protocol was registered in PROSPERO (CRD420261458306) and findings reported according to PRISMA guideline.[8]
- Cost-effectiveness and cost-utility studies (including conference presentations) comparing PCV15 and/or PCV20 with each other or/and any pneumococcal vaccination strategy, including no vaccination in children ≤18 years were considered.
- PubMed, Embase, Web of Science, and EconLit were searched from May 2022 to March 2026, building on a previous meta-analysis of economic evaluation (MAEE).[7]
- The reference lists of selected articles and conference abstracts from relevant scientific meetings were also searched for additional studies.
- All identified records were deduplicated and screened at the title/abstract and full-text stages.
- The following data were extracted from each study: (i) study characteristics (i.e. author, year, country); (ii) model settings (i.e., model type, time horizon, discount rate, comparators); (iii) key inputs/assumptions (i.e., vaccine price, effectiveness assumptions, population characteristics, willingness to pay [WTP]); and (iv) model outcomes (i.e., incremental costs/effects, ICERs, measures of uncertainty).
- The methodological quality of included studies was assessed using the modified Economic Evaluations Bias (ECOBIAS) checklist.[9]
- Two reviewers independently screened the studies, extracted the data, and assessed the methodological quality. Any disagreements were resolved by consensus or by consultation with a third reviewer.
- The outcome of interest was INB, and data were harmonized using the five scenarios described elsewhere[10] with all monetary values standardized to 2025 US dollars.
- INB represents the monetary value of the incremental health benefits (at a specific WTP) weighing against the incremental costs; a positive INB (>0) indicates that the vaccine strategy is cost-effective against the comparator, whereas a negative INB (<0) indicates it is not.
- INBs were pooled using a DerSimonian–Laird (DL) random-effects model and stratified by vaccine comparison, country income level, perspective, time horizon, and inclusion of herd effects.
- Heterogeneity was assessed using Cochran's Q and I^2 statistics and publication bias was evaluated using funnel plots and Egger's test.
- Prespecified sensitivity analyses were performed by (i) excluding grey literature, (ii) excluding studies with imputed variance, (iii) use of the Hartung-Knapp-Sidik-Jonkman (HK) method for analyses with fewer than five studies, (iv) using WTP thresholds of $50,000 per QALY for U.S. studies, and (v) using WTP threshold of $150,000 per QALY for U.S. studies.
- All analyses were conducted in Stata version 19.0.

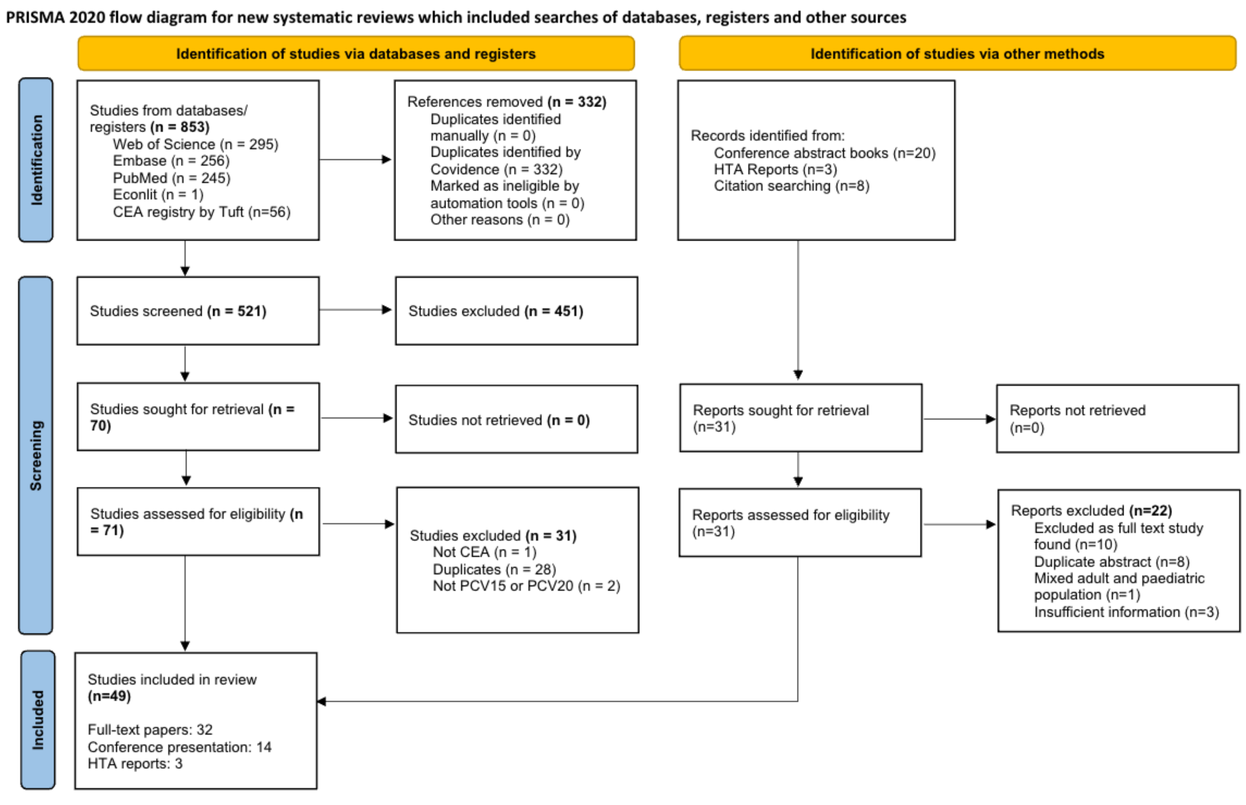

Figure 1: PRISMA flow diagram for study selection

Results

Study characteristics

- A total of 49[4,5,11-57] out of 884 studies were included, comprising 32 full-text publications, 14 conference presentations/posters, and 3 HTA reports **(Figure 1)**.
- By country, the US was the most represented (n=8; 16.33%), followed by Canada, Germany, and Italy with 3 studies each (6.12%)**.**

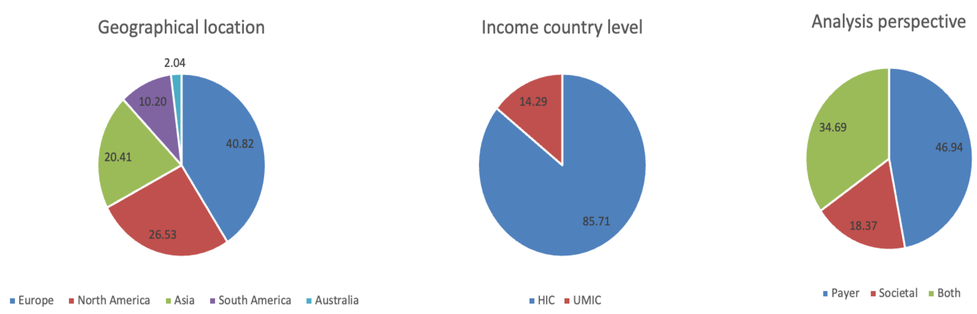

Figure 2: Distribution (%) of studies according to geographical location, income country level and analysis perspective

Meta-analysis findings

- The 49 studies yielded 177 comparisons across 41 unique analysis strata (32 in HICs and 9 in UMICs), of which 19 pooled strata (13 in HICs and 6 in UMICs) were eligible for meta-analysis.

High-income countries

- PCV20 was favored over PCV15 and PCV13 in 7 of 8 pooled strata in HICs, with 6 reaching statistical significance across both payer and societal perspectives at a 10-year time horizon, regardless of modeled herd effects (**Table 1**).
- The single exception was a lifetime societal stratum without population-level herd effects (2 studies)[28,31]; however, the estimate was no longer significant under HK.
- Results remained consistent across all remaining sensitivity analyses.
- In contrast, PCV15 vs PCV13 reached statistical significance in only 1 of 5 pooled strata in HICs, indicating that the incremental value of higher-valent vaccination in these analyses is driven predominantly by PCV20 (**Table 1**).

Upper-middle-income countries

- PCV20 was statistically significantly cost-effective compared to PCV15 from a payer perspective over a 10-year time horizon when herd effects were considered (**Table 1**).
- All remaining comparisons directionally favored PCV20 over PCV15 and PCV13; however, few analyses per stratum limited statistical significance (**Table 1**).
- In a sensitivity analysis applying the HK method, the non-significant finding for PCV20 versus PCV15 (societal perspective, 10-year time horizon, with herd effects) became statistically significant.

Table 1: Pooled incremental net benefits across the strategies

Intervention	Comparator	Perspective	Time horizon	Herd effect†	No. of studies	Pooled INB (95%CI), p-value	Heterogeneity (%)
High income countries							
PCV20	PCV15	HC/Payer	5 years	Yes	2	16.24 (-7.01 to 39.49; p=0.17)	96.02
			10 years	Yes	19	**151.36 (114.84 to 187.88; p<0.001)**	98.63
			10 years	No	7	**7.68 (1.14 to 14.23; p=0.02)**	72.03
		Societal	10 years	Yes	13	**154.51 (85.82 to 223.19; p<0.001)**	95.41
			Lifetime	No	2	**-62.23 (-93.18 to -31.27; p<0.001)**	0.00
	PCV13	HC/Payer	10 years	Yes	16	**617.59 (512.66 to 722.00; p<0.001)**	99.67
			10 years	No	6	**12.27 (1.35 to 23.19; p=0.03)**	89.19
		Societal	10 years	Yes	9	**161.29 (88.28 to 234.30; p<0.001)**	87.84
PCV15	PCV13	HC/Payer	10 years	Yes	3	**101.98 (14.19 to 189.77; p=0.02)**	99.00
			10 years	No	2	-0.46 (-1.60 to 0.67; p=0.42)	0.00
		Societal	10 years	Yes	3	11.45 (-17.78 to 40.69; p=0.44)	86.19
			10 years	No	2	0.002 (-2.41 to 2.42; p>0.99)	0.00
			Lifetime	Yes	3	110.96 (-96.65 to 318.57; p=0.29)	99.99
Upper-middle income countries							
PCV20	PCV15	HC/Payer	10 years	Yes	6	**11.08 (1.93 to 20.22; p=0.02)**	72.51
			10 years	No	2	2.37 (-1.91 to 6.65; p=0.28)	98.84
		Societal	10 years	Yes	3	7.87 (-7.95 to 23.68; p=0.33)	30.64
	PCV13	HC/Payer	10 years	Yes	6	13.94 (-0.13 to 28.02; p=0.05)	73.62
		Societal	10 years	Yes	2	52.08 (-41.91 to 146.07; p=0.28)	84.30
PCV15	PCV13	HC/Payer	10 years	Yes	2	0.10 (-7.12 to 7.32; p=0.98)	22.43

Bold indicates statistically significant results, †Herd effect denotes indirect protection modelled for the general population. Studies using closed single-birth-cohort designs capture indirect effects only within the vaccinated cohort (not at population-level) and are therefore classified as "No"; HC: Healthcare

Limitations

- Limited reporting of variance in primary studies, requiring imputation in our analyses.
- Many model inputs relied on assumptions or expert opinion due to limited data.
- Lack of studies from low-income settings, limiting generalizability of our findings.
- High heterogeneity observed despite stratified analyses (I^2 >95% in several strata).
- As heterogeneous model structures (single-cohort, multi-cohort, population-based) and dosing schedules (2+1, 3+1), might have affected the pooled estimates and contributed to overall heterogeneity; stratification by these factors are planned.

Conclusion

In high-income countries, PCV20 provided significantly greater economic value than PCV15 and PCV13 across most pooled strata, with directionally favorable results in UMICs. Divergent estimates were largely attributable to model structure, particularly single-cohort designs that do not capture population-level indirect effects.

References

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