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Effectiveness of Pneumococcal Vaccines in Preventing Acute Otitis Media in Children — A Targeted Literature Review

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Background

- Acute otitis media (AOM), defined as the presence of middle ear fluid with ≥1 sign or symptom of acute middle ear inflammation (eg, otalgia, otorrhoea, fever, or irritability), is a common pediatric infectious disease
- Globally, the incidence of AOM is estimated to be 14,775 per 100,000 population, with the highest incidence rates in children <5 years (Dong, 2025)
- Clinical presentations of AOM vary from simple AOM to more severe types, such as recurrent AOM (rAOM) and AOM-related complications, which may require hospitalization or surgery
- *Streptococcus pneumoniae* is one of the most common pathogens causing AOM
- Previous systematic literature reviews (SLRs) have shown that pneumococcal conjugate vaccines (PCVs) are effective in reducing risks of AOM and related complications (de Sévaux 2020, Marra 2022, and Wannarong 2023)
- The current study updated the previous reviews on the effects of pneumococcal vaccines on AOM-related outcomes

Objectives

To synthesize the evidence on the effectiveness of pneumococcal vaccines in preventing AOM and related outcomes in children ≤5 years based on the recent published studies and reviews

Methods

- 3 recently published SLRs were identified from the literature (de Sévaux 2020, Marra 2022, and Wannarong 2023)
  - Synthesized direct effects of pneumococcal vaccines on AOM-related outcomes
  - Included randomized controlled trials (RCTs) and observational studies
  - Covered studies published up to June 2020 based on the earliest SLR
- A targeted literature review (TLR) was conducted on February 19, 2025, using MEDLINE and Embase to identify records published from January 2020 onward, supplementing the previously published SLRs
  - Original studies since 2020 were selected using the following criteria:
    - Population: Children ≤5 years
    - Intervention: PCV or 23-valent pneumococcal polysaccharide vaccine (PPSV23) in routine childhood immunization
    - Outcomes: All-cause AOM, pneumococcal AOM, rAOM, AOM-related surgeries or complications, and severe AOM
    - Study design: Clinical trials or observational studies
    - Other criteria: Published as full-text articles in English

Outcome definitions

- Primary outcomes: vaccine effectiveness (VE) against all-cause AOM or pneumococcal AOM (ie, AOM caused by *S. pneumoniae*)
  - Defined as a relative reduction in risk of all-cause or pneumococcal AOM comparing pneumococcal vaccine to no vaccination or pre-vaccination
- Secondary outcomes: VE against rAOM, OM-related surgical procedures, AOM-related complications, or severe AOM
- Data extraction and evidence synthesis
  - Study characteristics (authors, year published), study design, pneumococcal vaccines, as well as outcome definitions and values were extracted from:
    - Original studies identified from the TLR
    - SLRs: Data were extracted from published tables
  - VEs and their statistical significance (if reported) were extracted directly from the studies or derived based on published information (eg, pre- and post-PCV incidence rates)
  - Medians and ranges of VE estimates were summarized by pneumococcal vaccine and study design (ie, RCTs and observational studies) for each outcome among children ≤5 years

Results

Overview of identified studies

- A total of 63 studies were included in this review (**Table 1**)
  - 4 studies from the TLR, all of which were observational studies
    - 3 studies were conducted in Israel, and 1 in Sweden
    - 3 studies were retrospective and 1 prospective
    - 3 studies compared PCV13 (two primary doses in the first year plus a booster in the second year, ie, 2+1) vs the pre-PCV period, and 1 compared PCV13, PCV10, and PCV7 (all in the 2+1 schedule) vs. the pre-PCV period
  - 59 non-duplicate studies from the 3 published SLRs, including both RCTs and observational studies
    - de Sévaux et al. 2020: An SLR of RCTs published up to June 2020, including all-cause and pneumococcal AOM and rAOM
    - Marra et al. 2022: An SLR of observational studies up to January 2021, including AOM, tympanostomy tube insertion, myringotomy, and tympanic membrane perforation (TMP)
    - Wannarong et al. 2023: An SLR of RCTs and observational studies up to October 2022, including rAOM, tympanostomy tube insertion, mastoiditis, TMP, and severe AOM

Table 1. Summary of included studies by data source, outcome and PCV type

	Primary outcomes		Secondary outcomes			
	All-cause AOM	Pneumococcal AOM	rAOM	Surgery	Complications	Severe AOM
TLR						
RCTs (n=0)	–	–	–	–	–	–
Observational studies (n=4)	n=2 -PCV13 (2) -PCV10 (1) -PCV7 (1)	n=1 -PCV13 (1) -PCV7 (1)	n=2 -PCV13 (2)	n=1 -PCV13 (1)	n=1 -PCV13 (1)	n=1 -PCV13 (1) -PCV10 (1) -PCV7 (1)
SLRs						
RCTs (n=15)	n=9 -PCV10 (4) -PCV7 (5)	n=8 -PCV10 (2) -PCV7 (6)	n=6 -PCV11 (1) -PCV7 (5)	n=8 -PCV10 (1) -PCV7 (7)	n=7 -PCV7 (1)	n=2 -PCV10 (1) -PCV7 (1)
Observational studies (n=45)	n=37 -PCV13 (10) -PCV10 (15) -PCV7 (23)	–	n=6 -PCV7 (2)	n=8 -PCV13 (4) -PCV10 (2) -PCV7 (8)	n=3 -PCV13 (1) -PCV7 (3)	n=3 -PCV13 (2) -PCV10 (1) -PCV7 (2)

PCV, pneumococcal conjugate vaccine; AOM, acute otitis media; rAOM, recurrent AOM; TLR, targeted literature review; RCT, randomized controlled trial; SLR, systematic literature review.
Notes: N indicates the number of publications. The numbers in parentheses indicate the number of publications for each PCV type. One publication may include one or more PCV types.

Primary outcomes

- All-cause AOM (**Figure 1**)
  - 2 observational studies from the TLR estimated VE against all-cause AOM (Marom 2021 and Edmondson-Jones 2021)
    - VE estimates ranged from 4% to 25% for PCV13, 7% to 10% for PCV10, and 3% to 12% for PCV7
    - VE estimates adjusted for demographics and/or comorbidities were smaller than unadjusted VE estimates and were mostly non-significant
  - 2 SLRs summarized the outcome
    - Median (range) of VE estimates were 15% (6–34%) for PCV10/11 and 3% (-5–7%) for PCV7 based on the SLR of RCTs (de Sévaux 2020)
    - Median (range) of VE estimates were 32% (2–68%) for PCV13, 23% (4–84% excluding the outlier) for PCV10, and 20% (0–63%) for PCV7 based on the SLR of observational studies (Marra 2022)
- Pneumococcal AOM (**Figure 2**)
  - Only 1 observational study from the TLR estimated VE against pneumococcal AOM (Ben-Shimol 2020)
    - VE estimates against overall, vaccine-type (VT) and non-vaccine type (NVT) pneumococcal AOM were 86%, 97%, and 33%, respectively, for PCV13 (all significant)
    - Corresponding VE estimates for PCV7 were smaller: 36%, 62%, and -8%, respectively (significance not reported)
  - The outcome was only reported in 1 SLR of RCTs (de Sévaux 2020)
    - Median VE estimates against overall, VT and NVT pneumococcal AOM were 55%, 69%, and 21% for PCV10/11
    - Median VE estimates against overall, VT and NVT pneumococcal AOM were 25%, 61%, and -30% for PCV7

Figure 1. Point estimates of VE against all-cause AOM

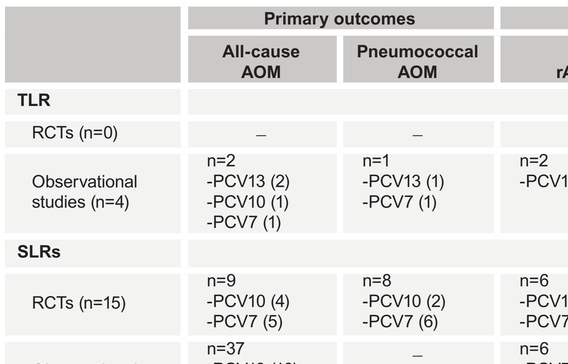
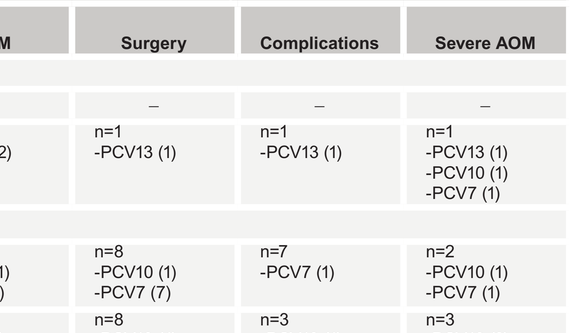


Figure 2. Point estimates of VE against pneumococcal AOM

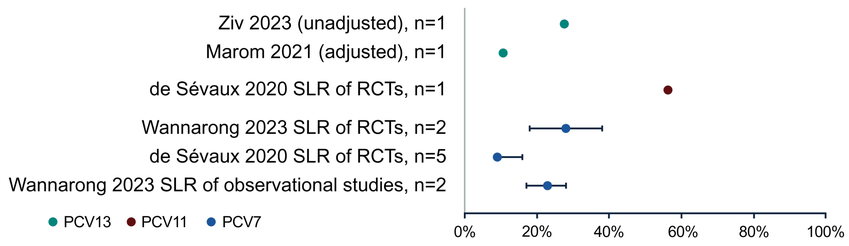


VE, vaccine effectiveness; AOM, acute otitis media; SLR, systematic literature review; RCT, randomized controlled trial; VT, Vaccine serotypes; NVT, Non-vaccine serotypes;
Notes: Median, maximum and minimum point estimates of VE from each study were presented in the graph. N is the number of VE estimates; one study may have >1 VE estimate (eg, for different age groups).
VE was defined as a relative reduction in risk of all-cause or pneumococcal AOM comparing pneumococcal vaccines to no vaccination or pre-vaccination.
* VE estimates were adjusted for demographics and/or comorbidities.
** The range was presented after excluding an outlier of -96%.

Secondary outcomes

- rAOM (**Figure 3**)
  - All studies defined rAOM as ≥3 episodes in a 6-month period or ≥4 episodes in a 12-month period
  - 2 observational studies from the TLR estimated VE against rAOM for PCV13
    - One study estimated an unadjusted VE of 28% (p=0.03) (Ziv 2023)
    - The other study estimated an adjusted VE of 11% (p<0.001) (Marom 2021)
  - 2 SLRs summarized the outcome for PCV10/11 and PCV7
    - One SLR of RCTs reported a VE estimate of 56% for PCV11 based on only 1 observation and a median VE estimate of 9% (range: 9–16%) for PCV7 (de Sévaux 2020)
    - The other SLR of RCTs reported a median VE estimate of 28% (range: 18–38%) for PCV7 (Wannarong 2023)
    - The SLR of observational studies showed similar findings to the second SLR of RCTs, with median (range) being 23% (17–28%) (Wannarong 2023)

Figure 3. Point estimates of VE against rAOM



VE, vaccine effectiveness; rAOM, recurrent acute otitis media; SLR, systematic literature review; RCT, randomized controlled trial; PCV, pneumococcal conjugate vaccine; AOM, acute otitis media.
Median, maximum and minimum point estimates of VE from each study were presented in the graph. N is the number of VE estimates; one study may have >1 VE estimate (eg, for different age groups).
VE was defined as a relative reduction in risk of rAOM among children who had ≥1 AOM comparing pneumococcal vaccines to no vaccination or pre-vaccination.

- Surgery (**Table 2**)
  - Only 1 observational study from the TLR estimated the outcome
    - The study defined surgery as the placement of ventilation tubes, adenoidectomies, mastoidectomy, and intracranial surgery
    - VE estimate was -1% and insignificant for PCV13
  - 2 SLRs summarized surgery outcomes
    - Surgery included tympanostomy tube insertion and myringotomy
    - SLR of RCTs reported a VE estimate of 13% for PCV10 based on only 1 observation and a median VE estimate of 23% (range: 7–51%) for PCV7 (Wannarong 2023)
    - One SLR of observational studies reported wide ranges of VE estimates (from negative to positive) for all three PCV types (Marra 2022), while the other study reported median (range) of 23% (16–79%) similar estimates for PCV7 compared to the results from the SLR of RCTs (Wannarong 2023)
- Complications (**Table 2**)
  - Only 1 observational study from the TLR estimated VE against long-term complications (Ziv 2023)
    - Complications were defined as hearing loss, speech disturbance, mastoiditis, and tympanic membrane perforation (TMP)
    - VE was -97% for PCV13, indicating an increase in the risk of surgery, but it was non-significant
  - 2 SLRs summarized this outcome (Wannarong 2023 and Marra 2022)
    - Complications were defined as TMP and/or mastoiditis
    - 3 observational studies and 1 RCT included in the two SLRs suggested positive effects for PCV13 (22%) and PCV7 (median VE ranging from 16% to 65%)
- Severe AOM (**Table 2**)
  - Only 1 observational study from the TLR estimated VE against severe AOM (Edmondson-Jones 2021)
    - Severe AOM was defined as ≥3 diagnoses of AOM in a 6-month period or ≥4 AOM diagnoses in a 12-month period, or hospitalization due to AOM
    - Median (range) of VE estimates was 6% (-9–32%) for PCV13, 19% (14–50%) for PCV10, 4% (-18–35%) for PCV7
    - VE estimates for each PCV varied by age group
  - 1 SLR summarized this outcome for RCTs and observational studies, respectively (Wannarong 2023)
    - Severe AOM was defined as moderate-to-severe otalgia or otalgia for ≥48 hours or fever ≥39°C
    - It reported VE estimates in RCTs of 34% for PCV10 and 5% for PCV7, each based on 1 observation only
    - The median VE estimates in observational studies were 24% for PCV13, 27% for PCV10, and 51% for PCV7

Table 2. Point estimates of VE against other secondary outcomes

	PCV type					
	PCV13		PCV10/11		PCV7	
Outcomes	Source	Median (Range)	Source	Median (Range)	Source	Median (Range)
Surgery	***TLR observational studies*** Ziv 2023 (unajdusted), n=1	-1%	***TLR observational studies***	–	***TLR observational studies***	–
	SLR RCTs	–	***SLR RCTs*** *Wannarong 2023 SLR of RCTs, n=1*	13%	***SLR RCTs*** *Wannarong 2023 SLR of RCTs, n=7*	28% (7-51%)
	SLR observational studies Marra 2022 SLR of observational studies, n=14	5% (-56-49%)	***SLR observational studies*** Marra 2022 SLR of observational studies, n=3	15% (-6-18%)	***SLR observational studies*** *Wannarong 2023 SLR of* observational studies, n=3 Marra 2022 SLR of observational studies, n=17	23% (16-79%) -3% (-56-30%)
Complications	***TLR observational studies*** Ziv 2023 (unajdusted), n=1	-97%	***TLR observational studies***	–	***TLR observational studies***	–
	SLR RCTs	–	***SLR RCTs***	–	***SLR RCTs*** *Wannarong 2023 SLR of RCTs, n=1*	65% (7-51%)
	SLR observational studies *Wannarong* 2023 SLR of observational studies, n=1	22%	***SLR observational studies***	–	***SLR observational studies*** *Wannarong 2023 SLR of* observational studies, n=2 Marra 2022 SLR of observational studies, n=1	16% (10-21%) 47%
Severe AOM	***TLR observational studies*** Edmondson-Jones 2021 (unajdusted), n=3	6% (-9-32%)	***TLR observational studies*** Edmondson-Jones 2021 (unajdusted), n=3	19% (14-50%)	***TLR observational studies*** Edmondson-Jones 2021 (unajdusted), n=6	4% (-18-35%)
	SLR RCTs	–	***SLR RCTs*** *Wannarong 2023 SLR of* observational studies, n=1	34%	***SLR RCTs*** *Wannarong 2023 SLR of RCTs, n=1*	5%
	SLR observational studies *Wannarong* 2023 SLR of observational studies, n=2	24% (9-39%)	***SLR observational studies*** *Wannarong 2023 SLR of* observational studies, n=1	27%	***SLR observational studies*** *Wannarong 2023 SLR of* observational studies, n=2	51% (39-62%)

VE, vaccine effectiveness; PCV, pneumococcal conjugate vaccine; TLR, targeted literature review; SLR, systematic literature review; RCT, randomized controlled trial; AOM, acute otitis media.
Notes: N is the number of VE estimates; one study may have >1 VE estimate (eg, for different age groups).
VE was defined as a relative reduction in an outcome comparing pneumococcal vaccines to no vaccination or pre-vaccination.

Summary of findings

Primary outcomes

- Observational studies generally suggested PCVs reduced risk of all-cause AOM. However, there was substantial variability in VE estimates for each PCV
- VE against overall and VT pneumococcal AOM were more pronounced compared to all-cause AOM for all PCVs
- VE against pneumococcal AOM was numerically larger for PCV13 compared to PCV10/11 and PCV7 based on limited evidence

Secondary outcomes

- Compared to primary outcomes, VE against secondary outcomes generally showed more variability and uncertainty
- rAOM: Original observational studies and RCTs demonstrated significant VE for PCV13 and PCV11; SLR of RCTs and observational studies also showed positive PCV7 effects against rAOM
- Surgery: There was substantial uncertainty about VE against surgery for all PCV types, ranging from considerable negative to positive effects
- Complications: The limited number of studies suggested positive VE against TMP and mastoiditis for PCV13 and PCV7. However, PCV13 was not effective in preventing long-term complications
- Severe AOM: SLR of RCTs and observational studies generally suggested positive VE for PCVs, while the original observational study indicated VE might vary by age

Limitations

- The findings focused on the comparisons between a pneumococcal vaccine and no vaccination or pre-vaccination and did not include direct comparisons of pneumococcal vaccines
- The review is qualitative in nature due to substantial heterogeneity across studies. Cautions need to be taken when pooling the results, as differences in methodology may substantially impact the findings
- Some observational studies were descriptive in nature; therefore, the direct effect estimates may be biased by confounders (eg, other interventions occurring at the same time). In such cases, the direct effects of PCVs on AOM may be overestimated
- This review did not identify any empirical studies for newer vaccines, such as PCV15 and PCV20
- Evidence from RCTs on the primary outcomes of PCV13 is also lacking

Conclusions

- The existing literature suggests that PCVs are effective in preventing AOM among children ≤5 years, particularly pneumococcal AOM, compared to no vaccination or pre-vaccination
- PCVs also appear effective in reducing the risk of rAOM among children with a history of ≥1 AOM
- Evidence on other outcomes—including surgery, complications, and severe AOM—is mixed or limited
- Overall, there is substantial variability in VE estimates for the same outcome for each PCV, largely due to heterogeneity in data source and methodology
- Future studies are indicated to address the evidence gap for higher-valency PCVs

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