## Effectiveness of pneumococcal vaccination in older adults in a Real-World setting: a systematic review and meta-analysis of observational studies using test-negative designs



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### Background

- Pneumococcal disease continues to be a major worldwide cause of vaccinepreventable morbidity and mortality, in particular among older adults.
- Pneumococcal vaccination is commonly recommended among older adults above age 65.
- Vaccine effectiveness (VE) of pneumococcal vaccination among older adults in real-world setting is still largely unknown.
- Test-negative design (TND) provides high-quality evidence for estimating VE.

## Objectives

 To understand VE of pneumococcal vaccination in older adults in real-world settings.

### Methods

- Literature search was performed in PubMed:
- Observational studies published between January 2010 and April 2023
- VE of pneumococcal vaccination against pneumococcal disease
- Studies using TND design
- Publication in English
- Independently conducted by two pre-specified investigators.
- Of the 18 articles identified, 7 were included in the meta-analysis (Figure 1).
- Characteristics of individual studies are presented in Table 1.
- Pooled odds ratios (ORs) were estimated using meta-analysis with fixed-effects.
- Results were reported by vaccine type (i.e., 13-valent pneumococcal conjugate vaccine [PCV13] and 23-valent pneumococcal polysaccharide vaccine [PPSV23]).
- Results were further stratified by model type (crude; multivariable-adjusted) and infection type (all; vaccine-serotype).

Figure 1. Flow chart of study selection

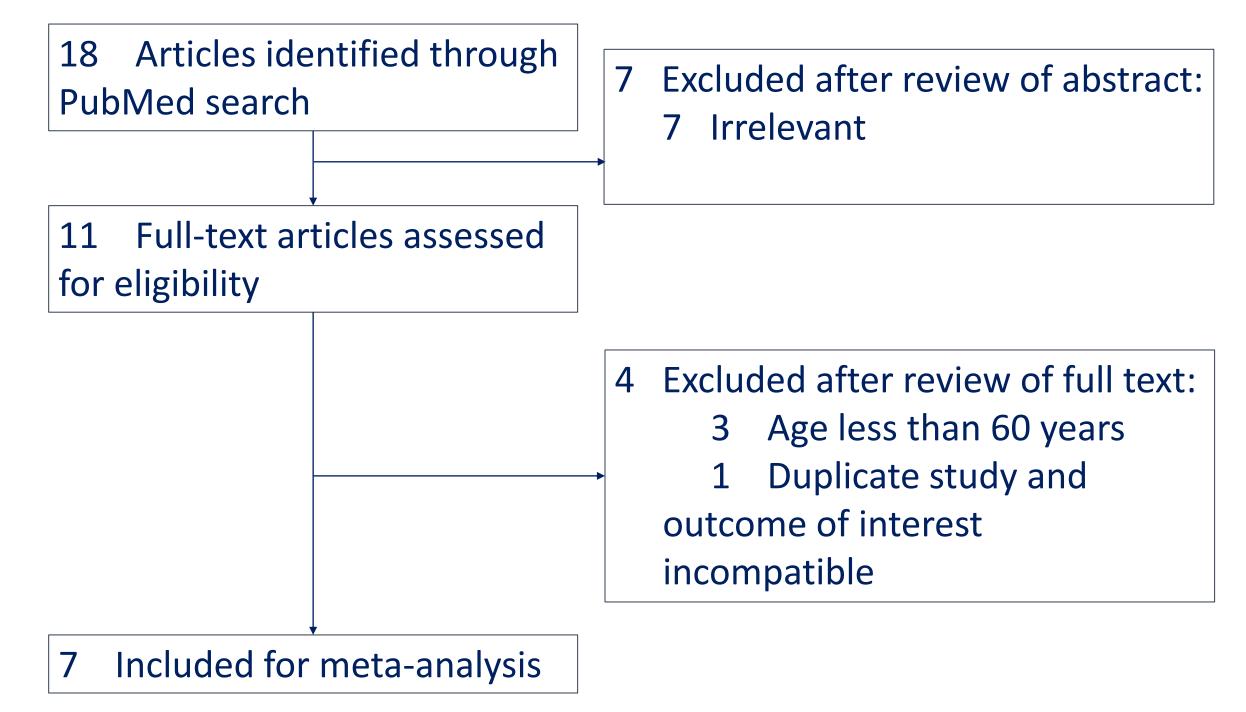


Table 1. Included studies evaluating vaccine effectiveness of pneumococcal vaccination against pneumococcal disease among older adults

Author (year)	Title	Population	Vaccine type
	Effectiveness of Pneumococcal Vaccination Against Pneumococcal Pneumonia Hospitalization in Older Adults: A Prospective, Test-Negative Study	Korea	PCV13, PPSV23
Sun et al (2021)	Effectiveness of 23-Valent Pneumococcal Polysaccharide Vaccine Against Pneumococcal Diseases Among the Elderly Aged 60 Years or Older: A Matched Test Negative Case-Control Study in Shanghai, China	China	PPSV23
Suzuki et al (2017)	Serotype-specific effectiveness of 23-valent pneumococcal polysaccharide vaccine against pneumococcal pneumonia in adults aged 65 years or older: a multicentre, prospective, testnegative design study	Japan	PPSV23
Chandler et al (2022)	23-Valent Pneumococcal Polysaccharide Vaccination Does Not Prevent Community-Acquired Pneumonia Hospitalizations Due to Vaccine-Type Streptococcus pneumoniae	US	PPSV23
Lawrence et al (2020)	Effectiveness of the 23-valent pneumococcal polysaccharide vaccine against vaccine serotype pneumococcal pneumonia in adults: A case-control test-negative design study	UK	PPSV23
McLaughlin et a (2018)	Effectiveness of 13-Valent Pneumococcal Conjugate Vaccine Against Hospitalization for Community-Acquired Pneumonia in Older US Adults: A Test-Negative Design	US	PCV13
Prato et al (2018)	Effectiveness of the 13-valent pneumococcal conjugate vaccine against adult pneumonia in Italy: a case-control study in a 2-year prospective cohort	Italy	PCV13, PPSV23

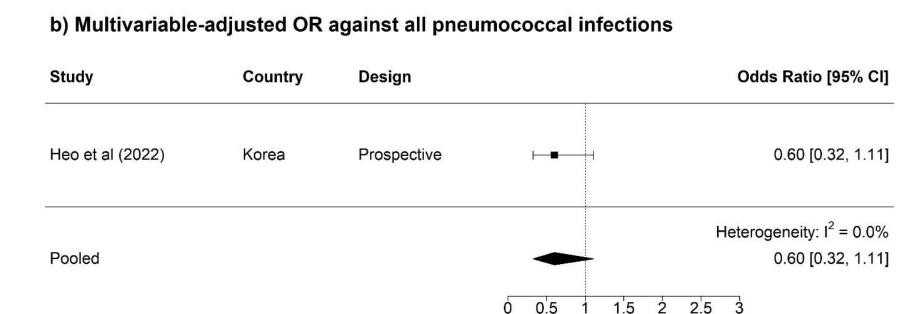
### Results

### **VE of PCV13**

- Three TND studies reported VE of PCV 13
- Pooled multivariable-adjusted OR against vaccine-serotype infections was 0.40 (95% CI: 0.17-0.95) (Figure 2d)
- Only one study reported multivariable adjusted OR of PCV13 against all pneumococcal infection, which did not show a significant effect (Figure 2b)
- Cls were wide and no meaningful statistical comparisons could be made
- The heterogeneity is consistently low in all analysis, partly due to small number of studies

### Figure 2. Pooled odds ratios of VE of PCV13

Korea	Prospective	⊢=					0.57 [	0.32, 1.
723			25				1500151050	powerstrought have
Italy	Prospective	ı—-	•		-1		0.67 [	0.20, 2.
		4	<b>-</b>		į	Heter		y: I <sup>2</sup> = 0. [0.35, 1.
		0 0.5	1 1	.5 2	2.5	3		
-			0 0.5		0 0.5 1 1.5 2 Odds Ratio	0 0.5 1 1.5 2 2.5	0 0.5 1 1.5 2 2.5 3	0 0.5 1 1.5 2 2.5 3



Odds Ratio

c) Crude OR agains	st vaccine-	serotype infecti	ons			
Study	Country	Design			Od	ds Ratio [95% CI]
Heo et al (2022)	Korea	Prospective	<b>⊢</b> ■	T		0.61 [0.19, 2.03]
McLaughlin et al (2018)	US	Retrospective	<b>⊢</b> ■───-1			0.27 [0.08, 0.87]
Prato et al (2018)	Italy	Prospective	F .			0.62 [0.13, 2.84]
Pooled			•		Hetero	ogeneity: I <sup>2</sup> = 0.0% 0.45 [0.21, 0.93]
			0 0.5 1 1	1.5 2	2.5 3	
			Odds	s Ratio		

# d) Multivariable-adjusted OR against vaccine-serotype infections Study Country Design Odds Ratio [95% CI] Heo et al (2022) McLaughlin et al (2018) US Retrospective Heterogeneity: I<sup>2</sup> = 0.0% 0.40 [0.17, 0.95] Odds Ratio

### **VE of PPSV23**

- Six TND studies reported VE of PPSV23
- Pooled multivariable-adjusted
   OR against vaccine-serotype
   infections was 0.80 (95% CI:
   0.66-0.96) (Figure 3d)
- Similar results for pooled multivariable-adjusted OR against all pneumococcal infections, and pooled crude OR against all and vaccine-serotype infections (Figure 3a-c)

### Figure 3. Pooled odds ratios of VE of PPSV23

a) Crude OR agai	inst all pneui	mococcal infect	ions
Study	Country	Design	Odds Ratio [95% CI]
Heo et al (2022)	Korea	Prospective	<b></b> 0.86 [0.62, 1.20]
Sun et al (2021)	China	Retrospective	<b>-</b> ■→ 0.76 [0.59, 0.97]
Suzuki et al (2017)	Japan	Prospective	0.78 [0.59, 1.01]
Prato et al (2018)	Italy	Prospective	1.04 [0.50, 2.17]
Pooled			Heterogeneity: I <sup>2</sup> = 0.0% 0.80 [0.68, 0.93]
			0 0.5 1 1.5 2 2.5
			Odds Ratio

### b) Multivariable-adjusted OR against all pneumococcal infections Odds Ratio [95% CI] Design Heo et al (2022) 0.89 [0.63, 1.26] Sun et al (2021) 0.75 [0.58, 0.97] Retrospective Suzuki et al (2017) 0.73 [0.54, 0.97] Heterogeneity: $I^2 = 0.0\%$ 0.77 [0.65, 0.91] Pooled 0 0.5 1 1.5 2 2.5 Odds Ratio

c) Crude OR again	st vaccine-	serotype infecti	ons	
Study	Country	Design		Odds Ratio [95% CI]
Heo et al (2022)	Korea	Prospective	<b>⊢</b>	0.88 [0.50, 1.57]
Suzuki et al (2017)	Japan	Prospective	⊢■→	0.69 [0.50, 0.96]
Chandler et al (2022)	US	Retrospective	1	1.01 [0.65, 1.57]
Lawrence et al (2020)	UK	Prospective	⊦∎⊢	0.78 [0.61, 1.00]
Pooled			•	Heterogeneity: I <sup>2</sup> = 0.0% 0.79 [0.67, 0.94]
			0 0.5 1 1.5 2 2	5
			Odds Ratio	
d) Multivariable-ad	djusted OR	against vaccine	-serotype infections	
Study	Country	Design		Odds Ratio [95% CI]
Heo et al (2022)	Korea	Prospective		0.94 [0.51, 1.74]
Suzuki et al (2017)	Japan	Prospective	<b>⊢■</b> —-(	0.66 [0.47, 0.94]
Chandler et al (2022)	US	Retrospective	<b>⊢</b>	0.98 [0.63, 1.52]
Lawrence et al (2020)	UK	Prospective	⊢∎⊢	0.80 [0.60, 1.06]
				2

Heterogeneity:  $I^2 = 0.0\%$ 

0 0.5 1 1.5 2 2.5

Odds Ratio

### Conclusions

• The evidence supports the use of both PCV13 and PPSV23 in the prevention of pneumococcal disease in real-world settings.

Pooled