

EVIDENCE TO RECOMMENDATIONS: PNEUMOCOCCAL VACCINATION FOR ELDERLY ADULTS 60 YEARS OLD AND ABOVE

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HEALTH TECHNOLOGY ASSESSMENT PHILIPPINES

ACKNOWLEDGMENT

University of the Philippines - Foundation for the Advancement of Clinical
Epidemiology (FACE)



Background

Criterion 1. Disease magnitude and severity



Criterion 2. Efficacy/ Effectiveness and Safety

A. *Efficacy/Effectiveness and Immunogenicity*

B. *Safety*

C3. Cost-effectiveness



C4. Affordability and Viability



C5. Household Financial Impact



C6. Ethical, Legal, Social, and Health Systems Impact

Guideline Recommendations

BACKGROUND

*Evidence Considered:
Pneumococcal Vaccines for Adults*

POLICY QUESTIONS



PICO of the current assessment (*elderly only*):

Should PCV-13 or PCV-15 as sequential vaccination with PPSV23 vs. PPSV23 alone for the immunization of **all elderly adults 60 years old and above** against diseases caused by *Streptococcus pneumoniae* be recommended for government financing?

NOTE: A separate recommendation for pneumococcal vaccination in adults 18 to 59 years old shall be released.

POLICY QUESTIONS



Approved PICO (broader scope):

Should PCV-13 or PCV-15 as sequential vaccination with PPSV23 vs. PPSV23 alone for the immunization of **adults 18 year old and above including senior citizens and patients with comorbidities/risk factors** against diseases caused by *Streptococcus pneumoniae* be recommended for government financing?

NOTE: A separate recommendation for pneumococcal vaccination in adults 18 to 59 years old shall be released.

Interventions and Comparator



Pneumococcal Vaccine	PCV13 (Prevenar 13®)	PCV15 (Vaxneuvance®)	PPSV23 (Pneumovax 23®)
Generic Name	Pneumococcal 13-valent conjugate vaccine	Pneumococcal 15-valent conjugate; v114	Pneumococcal polysaccharide vaccine, polyvalent
Presentation	1- and 4-dose vials; liquid	1-dose prefilled glass syringe	1-dose prefilled syringe; liquid
Dose form	Suspension for Injection	Suspension for Injection	Solution For Injection
Dose strength / quantity	One dose (0.5 mL) contains 2.2 mcg of pneumococcal polysaccharide for serotypes 1, 3, 4, 5, 6A, 6B, 9V, 14, 18C, 19A, 19F, 23F; and 4.4 mcg of serotype 7F individually conjugated to CRM ₁₉₇ protein.	One dose (0.5 mL) contains 2 mcg each of polysaccharide serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F, and 4 mcg of serotype 6B individually conjugated by CRM ₁₉₇ protein.	One dose (0.5 ml) contains 25 mcg of each pneumococcal capsular polysaccharide serotype (ST 1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F AND 33F) dissolved in isotonic saline solution containing 0.25% phenol as preservative
Route of administration	for intramuscular use	For intramuscular use	Intramuscular or Subcutaneous use
WHO Prequalification	Pre-qualified	Not Pre-qualified	Not Pre-qualified
PNF Inclusion	Included for all ages	Not yet included	Included for Pedia only (but implemented for seniors already) <i>DOH- Pharmaceutical Division: The basis for the indication in the PNF was the FDA-approved indication specified in the application form and in the attached CPR.</i>

Current Standard of Care



WHO SAGE recommendations (2021)

The **World Health Organization (WHO)** recommends that the introduction of PCV into the national childhood immunization programs should be prioritized over initiating a pneumococcal vaccination program for older adults. Decisions about initiating such a program in adults, using either pneumococcal polysaccharide vaccine (PPSV23) or/and pneumococcal conjugate vaccine (PCV), should take into consideration the local disease burden, cost-effectiveness and other operational considerations.

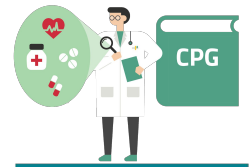
Inclusion in the WHO EML

Pneumococcal vaccine General information	
Section	Indications
Recommendations for all immunization programmes All vaccines should comply with the WHO requirements for biological substances.	Need for immunization against single bacterial diseases

Note: WHO EML listing does not specify the type (whether PPSV or PCV) and valency of pneumococcal vaccines.

Current Standard of Care

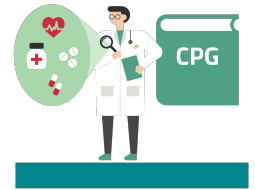
Local guideline recommendations (1 of 4)



Guidelines	Recommendation
DOH Omnibus Health Guidelines for the Elderly (2023)	<p>For elderly ≥ 65 years old</p> <ul style="list-style-type: none">● 20-valent pneumococcal conjugate vaccine (PCV) (given alone) [note: FDA CPR (Dec 2024) was released only after PICO has been set (Aug 2023)]● 15-valent PCV followed by 23-valent pneumococcal polysaccharide vaccine (PPSV)● PCV13 [note: no mention of additional PPSV23]● PPSV23
DOH Omnibus Health Guidelines for Adults (2023)	<p>For Adults with Medical/ Special Conditions or Special Circumstances, specifically those with comorbidities or immunocompromising conditions (i.e., Chronic renal failure congenital or acquired asplenia, Congenital or acquired immunodeficiency (including B-[humoral] or T-lymphocyte deficiency, complement deficiencies, and phagocytic disorders [excluding chronic granulomatous disease]), Generalized malignancy, HIV infection, Hodgkin disease, Iatrogenic immunosuppression (including disease requiring treatment with immunosuppressive drugs such as long-term systemic corticosteroids and radiation therapy), Leukemia, Lymphoma, Multiple myeloma, Nephrotic syndrome, Sickle cell disease and other hemoglobinopathies, Solid organ transplant (excludes persons with a hematopoietic stem cell transplant):</p> <ul style="list-style-type: none">● Option 1: Single-dose PCV20● Option 2: Single-dose PCV15 followed by a single-dose of PPSV23 after ≥ 8 weeks
2023 PHEX Guidelines	<ul style="list-style-type: none">● Among apparently healthy adults ≥ 65 years of age, we <u>recommend</u> the use of PPSV23.● Among apparently healthy adults ≥ 65 years and 18-64 years of age, we <u>suggest</u> the use of PCV 13. [note: no mention of additional PPSV23]● Among apparently healthy adults between 18-64 years of age, there is <u>insufficient evidence</u> to recommend the use of PPSV 23.

Current Standard of Care

Local guideline recommendations (2 of 4)



Guidelines	Recommendation
2018 PSMID Guidelines (1 of 2)	<ul style="list-style-type: none">● For prevention of invasive pneumococcal disease (IPD)<ul style="list-style-type: none">○ PPSV23 and PCV13 can be administered routinely to immunocompetent <u>elderly patients</u>● For prevention of pneumococcal pneumonia<ul style="list-style-type: none">○ PPSV23 can be administered routinely to immunocompetent <u>adults especially the elderly</u>○ PCV13 can be administered routinely to immunocompetent <u>adults</u>● For mortality prevention<ul style="list-style-type: none">○ PPSV23 and PCV13 can be administered routinely to immunocompetent <u>adults especially the elderly</u>

Current Standard of Care

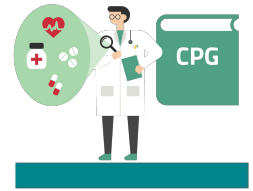
Local guideline recommendations (3 of 4)



Guidelines	Recommendation
2018 PSMID Guidelines (2 of 2)	<p><u>Recommended schedule</u></p> <ul style="list-style-type: none">● PCV13 + PPSV23<ul style="list-style-type: none">○ <i>PCV13 may be given first, followed by PPSV23 at least 1 year after the PCV13 dose. No revaccination with PPSV23 nor PCV13 is needed</i>● PPSV23 (previously vaccinated) + PCV13<ul style="list-style-type: none">○ <i>Adult Filipinos more than 50 years of age who were previously given PPSV23, may be given PCV13 vaccination at least 1 year after.</i>● PPSV23 (previously vaccinated) + PCV13 + PPSV23<ul style="list-style-type: none">○ <i>Adult Filipinos who were previously vaccinated with PPSV23 at less than 50 years old, but who are now 50 years old or more may receive 1 dose of PCV13 at least 1 year after, then another dose of PPSV23 after 1 year of the PCV13 dose</i>● PPSV23 (previously vaccinated) + PPSV23<ul style="list-style-type: none">○ <i>Adult Filipinos more than 50 years of age who were previously given PPSV23, WITHOUT previous PCV13, may opt to be given another dose of PPSV23 after 5 years. No revaccination thereafter.</i>

Current Standard of Care

Local guideline recommendations (4 of 4)



Guidelines	Recommendation
<u>2020 PSMID CPG on Management and Prevention of Adult CAP</u>	<ul style="list-style-type: none">● Pneumococcal polysaccharide vaccine (PPSV) or pneumococcal conjugate vaccine (PCV) are recommended for the prevention of invasive pneumococcal disease in adults 50 years old and older.● Pneumococcal polysaccharide vaccine is recommended for adults to prevent (a) pneumococcal pneumonia, (b) mortality from IPD or pneumonia and (c) pneumonia among high-risk groups and adults 50 years and above.

Current Standard of Care



Other local legislations

- In the Philippines, [Republic Act No. 9994](#) (*Expanded Senior Citizens Act of 2010*) provided legislation that gave **free pneumococcal vaccination to senior citizens**. In 2016, the Expanded Pneumococcal Immunization Program was launched which provides free pneumococcal vaccines nationwide for the elderly. Currently, the Department of Health provides PPV23 to “indigent elderly or senior citizens.”

Research Questions:



C1. Disease Magnitude and Severity

- **RQ.1** What is the magnitude and severity of pneumococcal disease in the Philippines as a public health problem?

C2: Clinical Effectiveness/Efficacy and Safety

- **RQ2.1** Among all elderly adults 60 years old and above, what is the **efficacy and effectiveness** of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination?
- **RQ2.2** Among all elderly adults 60 years old and above, what is the **safety** of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination?

C3. Cost-effectiveness

- **RQ3.** What is the **cost-effectiveness** of PCV13 in sequence to PPSV23, PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination among all elderly adults 60 years old and above?

Research Questions:



C4. Affordability and Viability

- **RQ4.** What is the **budget impact** of PCV13 in sequence to PPSV23, PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination among all elderly adults 60 years old and above?

C5. Household Financial Impact

- **RQ5.** What is the **household financial impact** of pneumococcal disease among all elderly adults 60 years old and above?

C6. Ethical, Legal, Social, Health Systems Impact

- **RQ6.** What are the ethical, legal, social, and health systems implications of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone all elderly adults 60 years old and above?

Guideline Recommendations: What are the current recommendations from **country guidelines** on the use of pneumococcal vaccines (PCV13, PCV15, and PPSV23)?

PICO of the Assessment



HTAC-approved PICO for NLAG

Population	All elderly adults 60 years old and above	
Intervention and Comparator	<p>All PCV available in the market for the prevention of invasive pneumococcal disease, and pneumonia caused by <i>Streptococcus pneumoniae</i>:</p> <ul style="list-style-type: none"> - PCV13 in sequence to PPSV23 - PCV15 in sequence to PPSV23 - Pneumococcal polysaccharide vaccine (PPSV23) alone <i>[currently implemented, despite PNF listing to pedia only]</i> (compared to each other and compared to no vaccination) <p><i>e.g., studies showing relative treatment effect for the following:</i></p> <ul style="list-style-type: none"> - PCV13 + PPSV23 vs PPSV23 alone - PCV15 + PPSV23 vs PPSV23 alone - PCV13 + PPSV23 vs PCV15 + PPSV23 - PPSV23 vs no vaccination - PCV13 + PPSV23 vs no vaccination - PCV15 + PPSV23 vs no vaccination 	
Outcome	<p>CLINICAL:</p> <ul style="list-style-type: none"> ● Efficacy/effectiveness <ul style="list-style-type: none"> ○ Deaths ○ Invasive pneumococcal disease (IPD) and non-bacteremic pneumococcal pneumonia (NBPP) incidence, hospitalizations, and mortality ○ Immunogenicity assessments (OPA titers for the 13 serotypes) ○ Vaccine effectiveness indicated by prevention of VT-CAP, IPD, Nasopharyngeal carriage, including serotype replacement ● Safety <ul style="list-style-type: none"> ○ Local reactions & systemic events ○ Any adverse events ○ Impact to burden of pneumococcal disease and serotype distribution 	<p>ECONOMIC:</p> <ul style="list-style-type: none"> ● Incremental Cost-effectiveness Ratio ● Budget Impact <p>ETHICAL, LEGAL, SOCIAL, HEALTH SYSTEMS:</p> <ul style="list-style-type: none"> ● Ethical (equity), ● legal (global commitment, local laws and policies), ● social (acceptability, equity), and ● health systems (feasibility, impact to practice, human resource needs, infrastructure needs, systems support, acceptability of healthcare workers, serotype surveillance mechanisms, vaccination uptake/ coverage) impact

CRITERION 1. RESPONSIVENESS TO DISEASE MAGNITUDE AND SEVERITY

*Evidence Considered:
Pneumococcal Vaccines for Adults*

Burden of Disease



GLOBAL MORTALITY DATA

Lower Respiratory infections [[Global Burden of Disease Study 2021](#)]

- is the 5th leading cause of death globally in 2021
- consistently part of the top 5 leading cause of death globally since 2000.
- It has an age-standardized death rate of 28.7 per 100,000 cases in 2021.
- ***S pneumoniae*** was responsible for the highest proportions of deaths among LRI cases, with an estimated 505,000 deaths (454,000-555,000) globally

GLOBAL MORBIDITY DATA

Lower Respiratory infections [[Global Burden of Disease Study 2021](#)]

- is the 5th leading cause of disease burden in 2021
- consistently part of the top 5 leading cause of disease burden since 2000.
- ***S pneumoniae*** was responsible for the highest proportions of LRI cases, with an estimated 97.9 million (92.1-104.0) episodes globally.

Burden of Disease

LOCAL DATA ON LRTI



In the Philippines in 2021 [[Non-COVID-19 LRTI Systematic Analysis from the Global Burden of Disease \(GBD\) Study 2021](#)]

AGE Group	MORBIDITY		MORTALITY	
	LRI cases (95% UI)	Incidence Rate (95% UI) cases per 100,000 population	Deaths due to LRI (95% UI)	Mortality Rate (95% UI) deaths per 100 000 population
Across All Age Groups	4,220,000 (4.01 to 4,47 million)	3,725.7 (3540.0 to 3949.1)	51,400 (43,100 to 59,500)	45.4 deaths (38.0 to 52.6)
50–69 years old	1,140,000 (1.04 to 1.24 million)	7,312.9 (6,675.8–7,936.0)	10,837.50 (8,670 to 13,032)	69.5 (55.9 to 84.8)
70 years old	1,080,000 (985,000 to 1.19 million)	29,723.4 (27,225.6 to 32,973.8) [HIGHEST age group]	28,519.13 (21,849 to 33,172) [~55% of the total local deaths due to LRIs]	788.4 (600.7 to 926.2) [HIGHEST age group]

Key findings: The 70 year old age group recorded the **highest LRI-related incidence and mortality rates** among all age groups, and accounted for about half of all LRI-related deaths.

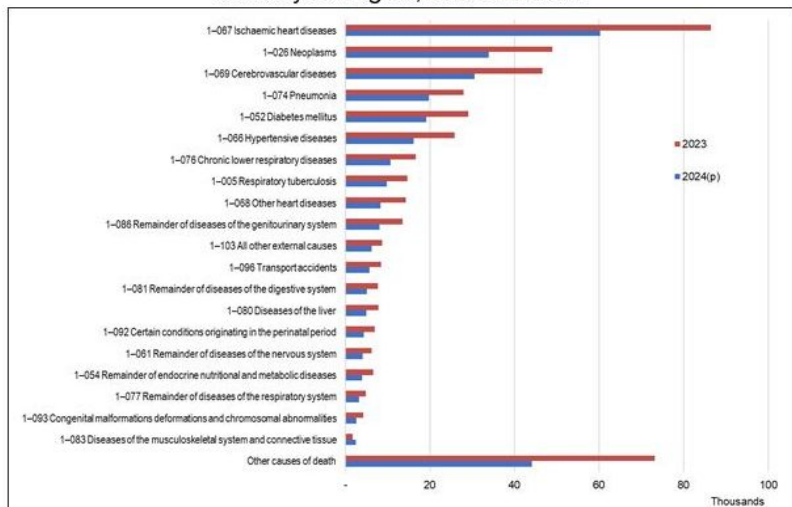
Burden of Disease

LOCAL DATA ON LRTI



PSA, 2024

Figure 1. Top 20 Causes of Mortality, Philippines: January to August, 2023 and 2024



Source: Philippine Statistics Authority (Data on deaths are based on registration at the Office of the City/Municipal Civil Registrars nationwide, and submitted to the Office of the Civil Registrar General; derived from Certificate of Death-Municipal Form No. 103)

In 2023 and 2024, pneumonia was the **4th leading cause of mortality**.

DOH FHSIS Annual Report 2024

Table 1.G.1: Leading Causes of Morbidity, Philippines, 2020 to 2024

Rank				2024 Top 10 Causes of Morbidity	2024		
2020	2021	2022	2023		Count	Rate per 100k population:	% change vs. 2023
1	1	1	1	1. Acute Respiratory Infection (ARI)	2,467,264	2,201.34	30.00% ↑
2	2	2	2	2. Hypertension	1,226,831	1,094.60	42.48% ↑
4	3	3	3	3. Animal Bites	997,421	889.92	64.31% ↑
3	4	4	4	4. Urinary Tract Infection	534,405	476.81	36.18% ↑
7	6	7	5	5. Pneumonia	361,372	322.42	48.57% ↑
5	5	6	6	6. Skin Diseases	342,515	305.60	33.33% ↑
6	7	5	7	7. Acute Lower Respiratory Tract Infection	283,265	252.74	-7.10% □
10	8	9	8	8. Tuberculosis (All Forms)	175,696	156.76	20.83% ↑
9	>10	>10	9	9. Bronchitis	146,792	130.97	62.80% ↑
>10	9	10	10	10. Fever of Unknown Origin	121,774	108.65	40.77% ↑

In 2023,

- acute respiratory infections was the **top cause of morbidity**,
- pneumonia was the **5th leading cause of morbidity**, and
- acute LRTI was the **7th leading cause of morbidity**.

Note: There is no local surveillance specific to the etiology of local pneumonia and LRTI cases.

Invasive Pneumococcal Disease (IPD) cases

- No published data on the local epidemiology of IPD among adults
- The **Antimicrobial Resistance Surveillance Program (ARSP)** is a passive, sentinel, laboratory-based surveillance initiative of the Research Institute for Tropical Medicine (RITM). Due to its passive nature, only a small number of IPD cases are collected each year.
- Epidemiology of IPD in Asian countries: (Hung et al., 2013 [narrative review])
 - Varied incidence:
 - Lowest = 3.7 per 100,000 in Thailand in 2007
 - Highest = 216 per 100,000 in Taiwan in 2006
 - Higher incidence rate (IR) among ≥ 65 years old:
 - Lowest = 26 per 100,000 in Thailand in 2007 (aged ≥ 75 years)
 - Highest = 1,147 per 100,000 in Taiwan in 2006 (aged ≥ 65 years)
 - Varied Case fatality rates (CFR):
 - Lowest = 18% in South Korea in 2002 to 2007
 - Highest = 40% in Taiwan in 2000 to 2008
 - For pneumococcal meningitis, the mortality rate was 50% in a study in Taiwan.

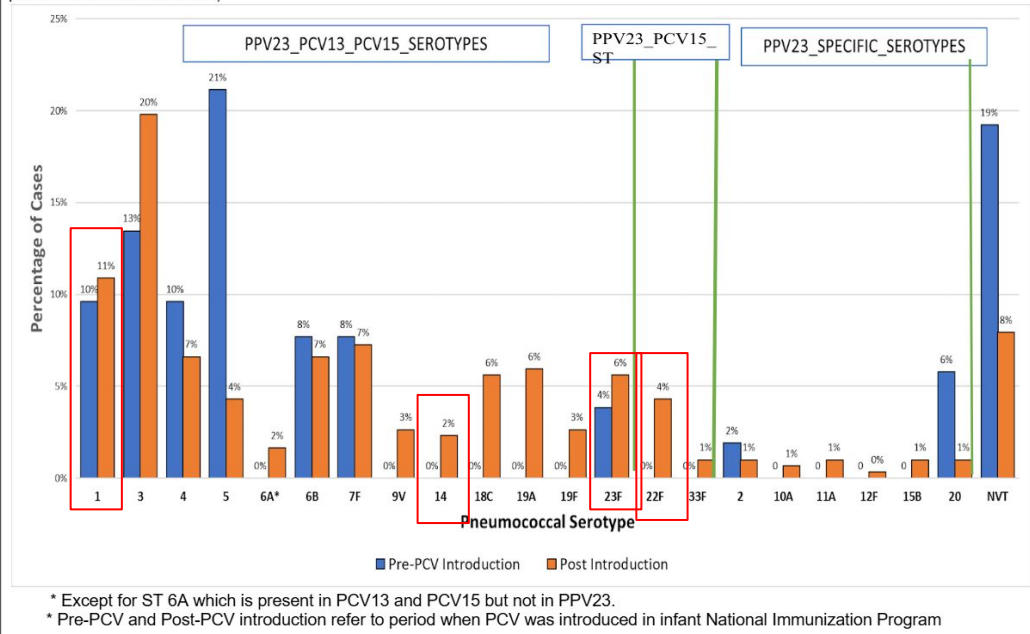
Key findings: No local epidemiology data of IPD among adults. IPD-related incidence and case fatality rates varied widely across Asian countries, with the **highest burden observed among adults ≥ 65 years old**, and mortality rate reaching up to **50% for pneumococcal meningitis in Taiwan**.

Burden of Disease

SEROTYPE CASES



Figure 3. Percentage of Invasive pneumococcal cases per SPN serotypes among 50 years and older (No. of pre-introduction isolates= 52; No. of post-introduction isolates= 303)



PPV23 - being rolled out by DOH to 'indigent elderly or senior citizens' but at low coverage rate (6.99% as of 2023).

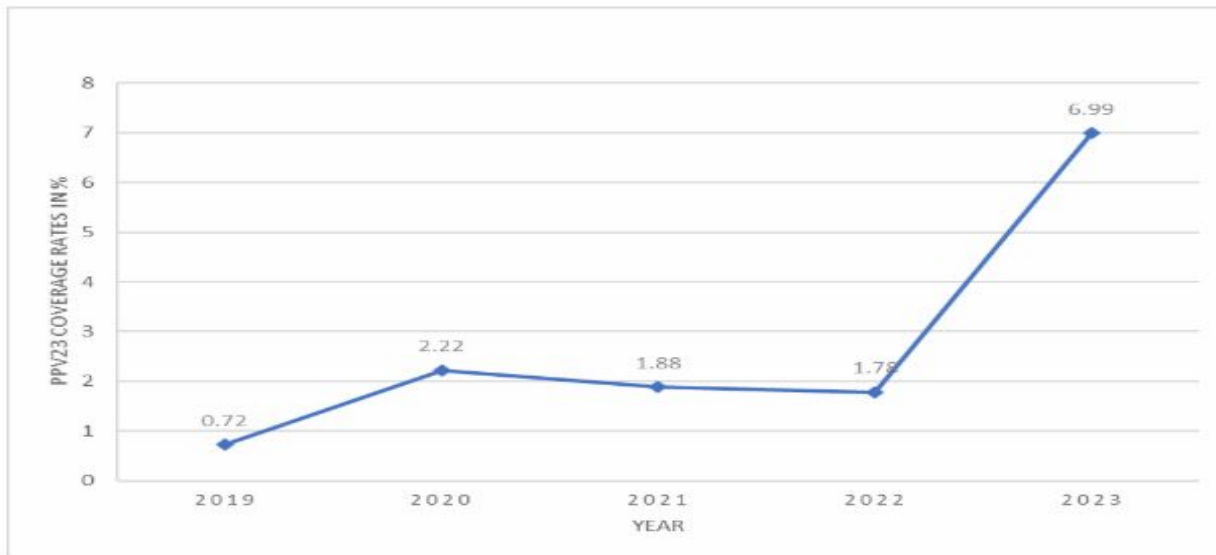
	<5 yo	19 to 49 yo	≥50 yo
most common serotypes (ST) causing IPD post-PCV roll out	3, 18C, 6B, 14, 19A, and 23F	NVT, 1, 3, 4, 5	1, 3, 4, 6B, 7F
Increase in %IPD cases post-PCV roll out	18C, 23F, NVT	4, NVT	1, 3, and 23F
proportion of non-vaccine serotypes (NVT) in IPD patients post-PCV roll out	Increased <i>Denotes a %decrease in cases with serotype being addressed by the vaccine</i>	Increased <i>Denotes a %decrease in cases with serotype being addressed by the vaccine</i>	Decreased <i>Denotes a %increase in cases with serotype being addressed by the vaccine</i>

Key findings: In post-PCV roll out, IPD cases in adults 50 years and older were **mostly caused by serotypes 1, 3, 4, 6B and 7F**, with **increase in IPD cases caused by serotypes 1, 3, and 23F**. There was a **decline in non-vaccine serotypes (NVT) in IPD patients** denoting proportional increase in serotype cases that should already be covered by the vaccines.

Burden of Disease

STATUS OF Pneumococcal Vaccine roll out

Figure 1. PPV23 national annual coverage rates* among elderly from 2019 to 2023



* Denominators used in the coverage rates are the total number of eligible population (60 years old and above)

This upward trend is seen also in all the regions as shown in Figure 2.

Key findings:
Pneumococcal vaccine coverage **generally increased from 2019 to 2022**; however, the **vaccination rate of 6.99% remained low.**

CI: DISEASE MAGNITUDE AND SEVERITY



RQ 1.1. What is the **magnitude and severity** of pneumococcal disease in the Philippines as a public health problem?

HTAC Judgment:

Pneumococcal diseases (PD) caused by *Streptococcus pneumoniae* is one of the leading causes of morbidity and mortality among the elderly population worldwide and in the Philippines. However, there is limited global data and no local data on invasive pneumococcal disease (IPD) and non-bacteremic pneumococcal pneumonia (NBPP). Available evidence on burden is mainly on broader indications such as lower respiratory infections (LRI) and acute respiratory infections (ARI).

Globally in 2021, LRI was the fifth leading cause of mortality and morbidity worldwide. *S. pneumoniae* was responsible for the highest proportion of LRI episodes and deaths, with an estimated 97.9 million episodes (95% UI: 92.1 to 104.0) and 505,000 deaths (95% UI: 454,000 to 555,000) globally across all age groups. [[Global Burden of Disease Study \(GBD\), 2021a](#); [GBD study 2021b](#)]. There is no recent global data available to provide a comprehensive epidemiological profile of invasive pneumococcal disease.

In the Philippines, ARI was the top cause of morbidity in 2024, with pneumonia ranking fifth and acute LRI ranking seventh. Pneumonia was the fourth leading cause of mortality in 2023 and 2024. The age group with the highest incidence and mortality rate of LRI was in elderly adults 70 years and above, followed by 50–69 year olds. However, there is currently no local surveillance to identify the specific etiology of local pneumonia and LRI cases. The available sentinel surveillance does not accurately represent or measure the incidence of IPD cases in the Philippines.

CRITERION 2.

EFFICACY/ EFFECTIVENESS AND SAFETY

*Evidence Considered:
Pneumococcal Vaccines for Adults*

METHODOLOGY

- **Location and selection**

- Database: PubMed and PROSPERO
- Search date: March 30, 2024
- Search terms: (((((PCV13 OR PCV-13 OR "13-valent pneumococcal conjugate vaccine") OR (PCV15 OR PCV-15 OR "15-valent pneumococcal conjugate vaccine")) OR (PPV23 OR PPSV23 OR "23-valent polysaccharide vaccine" OR PPV-23 OR PPSV-23)) AND (efficacy OR effectiveness OR safety)) AND (adults OR elderly)
- Filters: English articles only
- Studies submitted by stakeholders were screened
- Hand-searching of SRs or references from articles for any additional articles was conducted

METHODOLOGY

- **Inclusion criteria**

- Included studies involved adults ≥ 18 years, including those with chronic, immunocompromised, or other high-risk conditions.
NOTE: *The evidence presented will focus only on the elderly population.*
- Interventions were PCV13+PPSV23, PCV15+PPSV23, or PPSV23 alone, with PCV given first in sequential schedules.
- Comparators included placebo or no vaccination, and comparing each other.
- Outcomes were invasive pneumococcal disease (meningitis, bacteremic pneumonia), non-bacteremic pneumococcal pneumonia, nasopharyngeal carriage, immunogenicity (IgG GMCs, OPA GMTs), and safety.
- For immunogenicity studies: IgG geometric mean antibody concentration (GMCs) and opsonophagocytic (OPA) antibody geometric mean titers (GMTs) of serotypes (ST) common to PCV13, PCV15 and PPV23
- Eligible designs were RCTs and observational studies (cohort, case-control, indirect cohort) evaluating direct effects of vaccination in adults.
- Studies that evaluated the direct effects of pneumococcal vaccination on adults

METHODOLOGY

- **Data synthesis**

- Studies were classified by clinical outcomes (vaccine-ST Invasive Pneumococcal Disease, all-ST IPD, vaccine-ST NBPP, all-ST Non-Bacteremic Pneumococcal Pneumonia, Nasopharyngeal Carriage)
- Subgrouped by risk factors (high-risk vs. immunocompromised) and study type
- Odds ratios were computed where applicable, with pooled effects estimated using a random-effects model.
- Heterogeneity was assessed using the I^2 statistic.
- Articles on immunogenicity and safety were summarized.
- As correlates of protection in adults are not established, immunogenicity endpoints varied, using serotype-specific IgG GMCs and OPA assays.

- **Critical appraisal of articles**

- Risk of bias assessment
 - RCTs: Cochrane Collaboration's risk of bias version 2 (ROB-2)
 - Case control/cohort studies: ROBINS-I
- GRADE certainty of evidence- used to rate the overall certainty of evidence (High, moderate, low and very low certain of evidence)

C2: EFFICACY/ EFFECTIVENESS AND SAFETY

Invasive pneumococcal disease (IPD)

Non-bacteremic pneumococcal disease (NBPP)

Nasopharyngeal carriage

Immunogenicity

*Evidence Considered:
Pneumococcal Vaccines for Adults*



A. Overview of evidence: Prevention of Invasive Pneumococcal Disease [IPD] (*bacteremia, meningitis, bacteremic pneumonia*)

	Comparison i.	Comparison ii.	Comparison iii.	Comparison iv.
Intervention	PPSV23 only	PCV13 in sequence to PPSV23 (PCV13+PPSV23)	PCV13+PPSV23	PCV15 in sequence to PPSV23 (PCV15+PPSV23)
Comparator	No vaccination, placebo, other vaccine	No vaccination/placebo	PPSV23 alone	No vaccination, placebo, other vaccine
Included studies	RCT= 1	RCT=0	RCT=0	RCT=0
	1. Ortqvist, 1998			
	Observational=26	Observational=2	Observational=1	Observational=0
Indirect Cohort	Cohort			
1. Andrews, 2004	18. Jackson, 2003	1. Perniciaro, 2021	1. Narsingam, 2022	
2. Singleton, 200	19. Vila-Corcoles, 2006	2. Love, 2021		
3. Wright, 2013	20. Hechter, 2012			
4. Andrews, 2012	21. Ochoa-Gondar, 2014			
5. Rudnick, 2013	22. Tsai, 2015			
6. Gutierrez-Rodriguez, 2014	23. Vila-Corcoles, 2023			
7. Djennad, 2019	24. Kuo, 2016			
8. Shimbashi, 2020	25. Love, 2021			
9. Su, 2021	26. Narsingam, 2022			
10. Perniciaro, 2021				
Matched Case				
11. Dominguez, 2005				
12. Vila-Corcoles, 2009				
13. Vila-Corcoles, 2010				
14. Vila-Corcoles, 2012				
15. Leventer-Roberts, 2015				
16. Kim, 2019				
17. Sun, 2021				

SUMMARY OF EVIDENCE

A. Prevention of IPD

i. PPSV23 alone vs no vaccination

Note: Pooling was not possible due to differences in study designs, as most included studies were observational.

	Summary of studies	Certainty of evidence
Favors PPSV23	15 studies (15 obs)	9 moderate, 3 low, 3 very low
Favors comparator (no vax)	0	
Equivalent	0	
As good as or better	4 studies (1 RCT, 3 obs)	1 low, 3 very low
Inconclusive	7 studies (7 obs)	7 very low

SUMMARY OF EVIDENCE

A. Prevention of IPD

Note: Pooling was not possible due to differences in study designs, as most included studies were observational.

<i>ii. PCV13+PPSV23 vs no vaccination</i>	Summary of studies	Certainty of evidence
Favors PCV13+PPSV23	2 studies (2 obs)	2 very low
Favors comparator (no vaccination)	0	
No significant difference	0	
Inconclusive	0	
<i>iii. PCV13+PPSV23 vs PPSV23 alone</i>	Summary of studies	
Favors PCV13+PPSV23	0	
Favors comparator (PPSV23 alone)	0	
Inconclusive	1 study (1 obs)	1 very low



B. Overview of evidence: Reducing the risk of IPD-related Mortality

	Comparison i.	Comparison ii.	Comparison iii.
Intervention	PPSV23 only	PCV13 in sequence to PPSV23	PCV15 in sequence to PPSV23
Comparator	No vaccination	No vaccination	No vaccination
Included studies	Observational studies= 3	No evidence	No evidence
	<ol style="list-style-type: none"> 1. Soneji, 2011 2. Tsai, 2015 3. Su, 2021 		

SUMMARY OF EVIDENCE

B. Reducing the risk of IPD-related Mortality

i. PPSV23 alone vs no vaccination

Note: Pooling was not possible due to differences in study designs, as most included studies were observational.

	Summary of studies	Certainty of evidence
Favors PPSV23	2 studies (2 obs)	2 very low
Favors comparator (no vaccination)	0	
No significant difference	0	
Inconclusive	1 study (1 obs)	Very low

Note: There were no evidence found for PCV13+PPSV23 and PCV15+PPSV23



C2: EFFICACY/ EFFECTIVENESS AND SAFETY

Invasive pneumococcal disease (IPD)
Non-bacteremic pneumococcal disease (NBPP)
Nasopharyngeal carriage
Immunogenicity

*Evidence Considered:
Pneumococcal Vaccines for Adults*

A. Overview of evidence: Prevention of NBPP

	Comparison i.	Comparison ii.	Comparison iii.	Comparison iv.
Intervention	PPSV23 only	PCV13 in sequence to PPSV23	PCV13+PPSV23	PCV15 in sequence to PPSV23
Comparator	No vaccination, placebo	No vaccination, placebo	PPSV23 alone	No vaccination, placebo, other vaccine
Included studies	RCT=4	RCT=0	RCT=0	RCT=0
	1. Ortqvist, 1998 2. Alfagame, 2005	3. Maruyama, 2010 4. Izumi, 2017		No evidence
	Observational=15	Observational= 1	Observational=1	Observational=0
	1. Chandler, 2022 2. Vila-Corcoles, 2009 3. Suzuki, 2019 4. Nakashima, 2022 5. Kim, 2019 6. Lawrence, 2020 7. Heo, 2022 8. Vila-Corcoles, 2006	9. Ochoa-Gondar, 2014 10. Suzuki, 2017 11. Vila-Corcoles, 2020 12. Vila-Corcoles, 2023 13. Rodriguez-Barradas, 2008 14. Masuda, 2021 15. Vila-Corcoles, 2012	Heo, 2022	Narsingam, 2022

SUMMARY OF EVIDENCE

A. Prevention of NBPP

i. PPSV23 alone vs no vaccination

Note: Pooling was not possible due to differences in study designs, as most included studies were observational.

	Summary of studies	Certainty of evidence
Favors PPSV23	5 studies (1 RCT, 4 Obs)	1 moderate, 2 low, 2 very low
Favors comparator (no vaccination)	0	
Equivalent	0	
As good as or better	2 studies (2 Obs)	1 moderate, 1 very low
Inconclusive	12 studies (3 RCTs, 9 Obs)	1 moderate, 2 low, 9 very low

Note: There were no evidence found for PCV15+PPSV23

SUMMARY OF EVIDENCE

A. Prevention of NBPP

Note: Pooling was not possible due to differences in study designs, as most included studies were observational.

ii. PCV13+PPSV23 vs no vaccination	Summary of studies	Certainty of evidence
Favors PCV13+PPSV23	0	
Favors comparator (no vaccination)	0	
Inconclusive	1 study (1 obs)	Very low
iii. PCV13+PPSV23 vs PPSV23 alone	Summary of studies	Certainty of evidence
Favors PCV13+PPSV23	1 study (1 obs)	Very low
Favors comparator (PPSV23 alone)	0	
No significant difference	0	

B. Overview of evidence: Reducing the risk of NBPP-related Mortality

	Comparison i.	Comparison ii.	Comparison iii.
Intervention	PPSV23 only	PCV13 in sequence to PPSV23	PCV15 in sequence to PPSV23
Comparator	No vaccination, placebo, other vaccine	No vaccination, placebo, other vaccine	No vaccination, placebo, other vaccine
	RCT= 1	RCT=0	RCT=0
	Maruyama, 2010	<i>No evidence</i>	<i>No evidence</i>
	Observational= 3	Observational =0	Observational= 0
	1. Vila-Corcoles, 2006 2. Vila-Corcoles, 2020 3. Vila-Corcoles, 2023	<i>No evidence</i>	<i>No evidence</i>

SUMMARY OF EVIDENCE

B. Reducing the risk of NBPP-related Mortality

i. PPSV23 alone vs no vaccination

Note: Pooling was not possible due to differences in study designs, as most included studies were observational.

	Summary of studies	Certainty of evidence
Favors PPSV23	0	
Favors comparator (no vaccination)	0	
No significant difference	0	
Inconclusive	4 studies (1 RCT, 3 obs)	1 moderate, 3 very low

Note: There were no evidence found for PCV13+PPSV23 and PCV15+PPSV23



C2: EFFICACY/ EFFECTIVENESS AND SAFETY

Invasive pneumococcal disease (IPD)
Non-bacteremic pneumococcal disease (NBPP)

Nasopharyngeal carriage

Immunogenicity

*Evidence Considered:
Pneumococcal Vaccines for Adults*

A. Overview of evidence: Prevention of Nasopharyngeal Carriage

	Comparison i.	Comparison ii.	Comparison iii.
Intervention	PPSV23 only	PCV13 in sequence to PPSV23	PCV15 in sequence to PPSV23
Comparator	No vaccination, placebo, other vaccine	No vaccination, placebo, other vaccine	No vaccination, placebo, other vaccine
Included studies	RCT= 0	RCT=0	RCT=0
	<i>No evidence</i>	<i>No evidence</i>	<i>No evidence</i>
	Observational= 1	Observational =1	Observational= 0
	<u>Branche, 2018</u>	<u>Branche, 2018</u>	<i>No evidence</i>

SUMMARY OF EVIDENCE

B. Prevention of Nasopharyngeal Carriage

i. PPSV23 alone vs no vaccination and ii. PCV13+PPSV23 vs no vaccination

	Summary of studies	Certainty of evidence
Favors PPSV23 or PCV13+PPSV23	1 study (1 obs)*	Low
Favors comparator (no vaccination)	0	
No significant difference	0	
Inconclusive	0	

**both results were from the study of Branche, 2018; noting also that comparing both vaccine regimens with each other showed no significant difference based on $p=0.11$*

Note: There were no evidence found for PCV15+PPSV23

C2: EFFICACY/ EFFECTIVENESS AND SAFETY

Invasive pneumococcal disease (IPD)
Non-bacteremic pneumococcal disease (NBPP)
Nasopharyngeal carriage
Immunogenicity

*Evidence Considered:
Pneumococcal Vaccines for Adults*

SUMMARY OF EVIDENCE

VE on the prevention of:	PPSV23 vs. no vax	PCV13+PPSV23 vs. no vax	PCV13+PPSV23 vs. PPSV23 alone
IPD Incidence	Favors PPSV23: 15 studies (VE: 24-76%) As good as or better: 4 studies Inconclusive: 7 studies	Favors PCV13+PPSV23: 2 studies: (VE: 38-83%)	Inconclusive: 1 study (meningitis)
	VE from Asian countries: 14% to 76%	All western study	All western study
Death due to IPD	Favors PPSV23: 2 studies (VE: 31.5-91%) Inconclusive: 1 study	No evidence	No evidence
	VE from Asian countries: 32.5% to 91%	NA	NA
NBPP incidence	Favors PPSV23: 5 studies (VE: 27.4-77%) As good as or better: 2 studies Inconclusive: 12 studies	Inconclusive: 1 study	Favors PCV13+PPSV23: 1 study (pneumonia) (VE: 12%)
	VE from Japanese studies: 27.4%-77%	Although inc VE from Japanese study: 36.5% (-25, 67.8)	NA
Death due to NBPP	Inconclusive: 4 studies	No evidence	No evidence
	Although inc VE from Japanese study = 91% (-48.4, 99.4)	NA	NA
Nasopharyngeal carriage	Favors PPSV23: 1 study (VE: 76.8%)	Favors PCV13+PPSV23: 1 study (VE: 64.2%)	No evidence
	All western study	All western study	NA

NOTES:

1. Highlighted results = interpretation of majority of studies
2. No studies found reporting effectiveness/efficacy outcomes for PCV15+PPSV23

Evidence Considered:
Diphtheria, Tetanus, and
Pneumococcal Vaccines for Adults

C2: EFFICACY/EFFECTIVENESS



RQ2.1 Among all elderly adults 60 years old and above, what is the **efficacy and effectiveness** of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination?

HTAC Judgment [1 of 4]:

Overall, evidence on clinical effectiveness against invasive pneumococcal disease (IPD), including IPD-related incidence and mortality, as well as non-bacteremic pneumococcal pneumonia (NBPP) and nasopharyngeal carriage in older adults, were only available for PPSV23 alone and PCV13 in sequence to PPSV23 (PCV13+PPSV23), and are mostly from observational studies. Meanwhile, evidence for PCV15 in sequence to PPSV23 (PCV15+PPSV23) is limited to immunogenicity studies.

A. Invasive pneumococcal disease (IPD)

Preventing IPD

i. PPSV23 vs no vaccination

The only RCT found showed a PPSV23 vaccine efficacy of 79% (CI: -0.8% to 98) compared to no vaccination (low certainty of evidence). The 25 observational studies generally showed mixed results. However, majority of these (15 out of 25 studies: 7 indirect cohort, 5 matched case-control, 3 cohort), with moderate to very low certainty evidence, favored PPSV23 alone.

ii. PCV13+PPSV23 vs no vaccination/PPSV23 alone

PCV13+PPSV23 reduced the risk of invasive pneumococcal disease (IPD) compared to no vaccination based on 2 observational studies (1 indirect cohort, 1 cohort) with very low certainty evidence. When PCV13+PPSV23 was compared to PPSV23 alone, one study showed inconclusive results in preventing pneumococcal meningitis.

C2: EFFICACY/EFFECTIVENESS



RQ2.1 Among all elderly adults 60 years old and above, what is the **efficacy and effectiveness** of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination?

HTAC Judgment [2 of 4]:

Reducing the risk of IPD-related Mortality

In terms of reducing IPD mortality, there is generally mixed results on the effect of PPSV23 alone compared to no vaccination among older adults based on 1 impact study and 2 observational studies (1 cohort, 1 indirect cohort) with very low certainty evidence. It can be noted however, that majority of the studies (2 out of 3 studies) favored PPSV23 alone.

B. *Non-bacteremic pneumococcal pneumonia (NBPP)*

Preventing NBPP

i. PPSV23 vs no vaccination

Four RCTs on the vaccine efficacy of PPSV23 alone vs no vaccination showed mixed results (i.e., 3 studies reporting inconclusive results while 1 study showed conclusive favorable results for PPSV23). The 15 observational studies also showed mixed results, with the majority (9 out of 15) also reporting inconclusive results.

ii. PCV13+PPSV23 vs no vaccination/PPSV23 alone

One test-negative study with very low certainty evidence showed inconclusive results on the use of PCV13+PPSV23 compared to no vaccination in terms of effectiveness against NBPP. When PCV13+PPSV23 was compared to PPSV23 alone, one study with very low certainty evidence favored PCV13+PPSV23.

C2: EFFICACY/EFFECTIVENESS



RQ2.1 Among all elderly adults 60 years old and above, what is the **efficacy and effectiveness** of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination?

HTAC Judgment [3 of 4]:

Reducing the risk of NBPP-related Mortality

In terms of reducing the risk of mortality due to NBPP, 1 RCT showed inconclusive results when compared to no vaccination (moderate certainty of evidence). The results of the 3 cohort studies also consistently showed inconclusive results (very low certainty of evidence).

B. Prevention of Nasopharyngeal carriage

In older adults with or without risk factors, 1 cohort study with low certainty evidence showed that both PCV13+PPSV23 and PPSV23 alone are more effective compared to no vaccination in terms of preventing nasopharyngeal carriage.

C2: EFFICACY/EFFECTIVENESS



RQ2.1 Among all elderly adults 60 years old and above, what is the **efficacy and effectiveness** of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination?

HTAC Judgment [4 of 4]:

Immunogenicity

Based on three RCTs, one month after vaccination, the sequential vaccinations of PCV13 followed by PPSV23 elicited significantly higher response compared to PPSV23 alone for the majority of serotypes included in the PCV13 vaccine. One RCT further showed that one year post-vaccination, the sequential regimen continued to have significantly higher IgG titers in majority of the serotypes in the PCV13 vaccine, although there was inconclusive evidence for OPA titers.

Upon comparison of different sequential vaccination strategies, based on one RCT, the PCV15+PPSV23 regimen was found to be non-inferior to PCV13+PPSV23 in terms of immune response against most serotypes present in PCV15. Moreover, PCV15+PPSV23 regimen induced significantly higher responses in serotypes 1, 14, and 23F, as well as serotype 22F, which is present in PCV-15 but not in PCV-13. Except for serotype 1, these other serotypes were not among the most common serotypes in adults ≥ 50 years old in the Philippines based on data from passive surveillance. Local surveillance of pneumococcal STs remains limited and may not be precisely representative of the population, as only limited isolates are serotyped from selected sentinel sites.

CRITERION 2. EFFICACY/EFFECTIVENESS AND SAFETY

*Evidence Considered:
Pneumococcal Vaccines for Adults*

Overview of Available Evidence

Reactogenicity (local and systemic)

A. Older Adults (with or without risk factors)

- a. With and without risk factors
 - i. PCV13 + PPSV23 vs PPSV23 alone
 - 1. Azuma et al, 2023
- b. No risk factors/Generally healthy
 - i. PCV13 + PPSV23 vs PPSV23 alone
 - 1. Juergens et al, 2014
 - ii. PCV13 + PPSV23 vs PCV15 + PPSV23
 - 1. Song et al, 2021

Serious Adverse Events / Deaths

A. Older Adults (with or without risk factors):

- a. With and without risk factors
 - i. PCV13/PPSV23 vs. No vaccination
 - 1. Azuma et al, 2023
 - ii. PCV13 vs. PPSV23
 - 1. Tseng et al, 2018
- b. No risk factors
 - i. PCV13 + PPSV23 vs PPSV23 alone
 - 1. Juergens et al, 2014
 - ii. PCV13 + PPSV23 vs PCV15 + PPSV23
 - 1. Song et al, 2021

A. REACTOGENICITY: Older Adults

	Comparison i.	Comparison ii.
Intervention	PCV13+PPSV23	
Comparator	PPSV23 alone	PCV15+PPSV23
Included studies	a. With or without risk factors 1 RCT - Azuma et al, 2023 b. No risk factors 1 RCT - Juergens et al 2014	No risk factors 1 RCT - Song et al 2021



A. REACTOGENICITY: Older Adults

i. PCV13+PPSV23 alone vs PPSV23 alone [with or without risk factors]

	Author, year	Study type	Country	GRADE COE	Outcome	HTAC Interpretation
1	Azuma et al, 2023	Open label RCT	Japan PCV13/PPSV23 GROUP A - 6 mos apart: n= 43 GROUP B - 1 year apart: n= 40 PPSV23 Group C: n=46	Low	Redness and pain Swelling Systemic reactogenicity reaction	<i>Redness and Pain - Lower rate in the PPSV23 alone arm</i> <i>Swelling - No significant difference</i> Manageable reactogenicity reaction - Low number of events for all groups, resolves in a few days



A. REACTOGENICITY: Older Adults

ii. PCV13+PPSV23 vs PPSV23 alone [no risk factors]

Author, year	Study type	Country	GRADE COE	Results	HTAC interpretation
1 Juergens et al 2014	Open label RCT	South Africa	Very Low	See table below	<p>LOCAL REACTOGENICITY: Generally Lower rate in the PPSV23 alone arm.</p> <p>SYSTEMIC REACTOGENICITY: Generally inconclusive results between the two regimen</p>

Local Reactogenicity (w/in 14 days)	
Event, %	HTAC interpretation
Redness	
Mild	Favors PPSV23 alone
Moderate	Favors PPSV23 alone
Severe	Inconclusive
Pain	
	PCV13+PPSV23 is comparable to or worse than PPSV23 alone
Mild	Favors PPSV23 alone
Moderate	Favors PPSV23 alone
Severe	Favors PPSV23 alone
Swelling	
Mild	Inconclusive
Moderate	Favors PPSV23 alone
Severe	Favors PPSV23 alone
Limitation of arm movement	
	PCV13+PPSV23 is comparable to or worse than PPSV23 alone
Mild	PCV13+PPSV23 is comparable to or worse than PPSV23 alone
Moderate	PCV13+PPSV23 is comparable to or worse than PPSV23 alone
Severe	Favors PPSV23 alone

Systemic Reactogenicity (w/in 14 days)	
Event, %	HTAC interpretation
Fever^b	
any $\geq 38^\circ\text{C}$	Inconclusive
$\geq 38^\circ\text{C}$ to $< 38.5^\circ\text{C}$	Inconclusive
$\geq 38.5^\circ\text{C}$ to $< 39^\circ\text{C}$	Inconclusive
$\geq 39^\circ\text{C}$ but $\leq 40^\circ\text{C}$	Inconclusive
$> 40^\circ\text{C}$	Not estimable
Fatigue	Inconclusive
Headache	Inconclusive
Chills	Inconclusive
Rash	Inconclusive
Vomiting	Inconclusive
Decreased appetite	Inconclusive
	PCV13+PPSV23 comparable to or worse than PPSV23 alone
New generalized muscle pain	Inconclusive
aggravated generalized muscle pain	Inconclusive
New joint pain	Inconclusive
aggravated joint pain	Inconclusive
any systemic event	Inconclusive

A. REACTOGENICITY: Older Adults

iii. PCV13+PPSV23 vs PCV15+PPSV23 [no risk factors]

	Author, year	GRADE COE	Results	HTAC interpretation
1	Song et al 2021	Moderate	<u>PCV13+PPSV23 vs. PCV15+PPSV23 (after a dose of PCV)</u> See next slide	Generally higher injection-site and systemic reactogenic reactions in the PCV15 arm.
	Phase 3 RCT		<u>PCV13+PPSV23 vs. PCV15+PPSV23 (After dose of PPSV23)</u> See next slide.	Generally, the risk of any AE and any vaccine-related injection-site reaction, injection-site pain, and myalgia after a 2nd dose of PPSV23 administered after the PCV15 is comparable to or worse than PPSV23 administered after PCV13 arm.
	Double-blind South Korea		General conclusion	Majority of AE/s following PCV and PPSV23 vaccination were mild in severity

A. REACTOGENICITY: Older Adults

iii. PCV13+PPSV23 vs PCV15+PPSV23 [no risk factors]

	After a dose of PCV (1st dose)	After a dose of PPSV23 (2nd dose)
Any AE	<i>Favors PCV13+PPSV23</i>	PCV15+PPSV23 is comparable to or worse PCV13+PPSV23
Injection-site	<i>Favors PCV13+PPSV23</i>	
Systemic	<i>Favors PCV13+PPSV23</i>	
Any vaccine-related AEs	<i>Favors PCV13+PPSV23</i>	
Injection-site	<i>Favors PCV13+PPSV23</i>	
Systemic	<i>Favors PCV13+PPSV23</i>	
Any solicited AE	<i>Favors PCV13+PPSV23</i>	
Solicited injection-site AEs (Day 1 to Day 5)		
Pain	<i>Favors PCV13+PPSV23</i>	PCV15+PPSV23 is comparable to or worse than PCV13+PPSV23
Swelling	Inconclusive	Inconclusive
Erythema	<i>Favors PCV13+PPSV23</i>	Inconclusive
Solicited systemic AEs (Day 1 to Day 14)		
Fatigue	<i>Favors PCV13+PPSV23</i>	Inconclusive
Myalgia	<i>Favors PCV13+PPSV23</i>	PCV15+PPSV23 is comparable to or worse than PCV13+PPSV23
Headache	Inconclusive	Inconclusive
Arthralgia	Inconclusive	Inconclusive

A. REACTOGENICITY: Older Adults - SUMMARY OF EVIDENCE

Outcome	PCV13+PPSV23 vs PPSV23 alone		PCV13+PPSV23 vs PCV15+PPSV23
	With or without risk factors (k=1) <u>Azuma et al. 2023</u>	No risk factors (k=1) <u>Juergens et al 2014</u>	No risk factors (k=1) <u>Song et al 2021</u>
Local: Redness and Pain	lower in PPSV23 alone		
Local: Swelling	No significant difference		
Local reactions		lower in PPSV23 alone	After dose 1: lower in PCV13
Systemic reactions	NS; Manageable reactogenicity reaction - Low number of events for all groups (<5%), resolves in a few days	Inconclusive	After dose 2: PCV15+PPSV23 is comparable to or worse than PCV13+PPSV23
Certainty of Evidence (GRADE Rating)	Low COE	Very low COE	Moderate COE

COE = *certainty of evidence*



Overview of Available Evidence

Reactogenicity (local and systemic)

A. Older Adults (with or without risk factors)

- a. With and without risk factors
 - i. PCV13 + PPSV23 vs PPSV23 alone
 - 1. Azuma et al, 2023
- b. No risk factors/Generally healthy
 - i. PCV13 + PPSV23 vs PPSV23 alone
 - 1. Juergens et al, 2014
 - ii. PCV13 + PPSV23 vs PCV15 + PPSV23
 - 1. Song et al, 2021

Serious Adverse Events / Deaths

A. Older Adults (with or without risk factors):

- a. With and without risk factors
 - i. PCV13/PPSV23 vs. No vaccination
 - 1. Azuma et al, 2023
 - ii. PCV13 vs. PPSV23
 - 1. Tseng et al, 2018
- b. No risk factors
 - i. PCV13 + PPSV23 vs PPSV23 alone
 - 1. Juergens et al, 2014
 - ii. PCV13 + PPSV23 vs PCV15 + PPSV23
 - 1. Song et al, 2021

A. Serious adverse events: Older Adults

	Comparison i.	Comparison ii.	Comparison iii.
Intervention	PCV13+PPSV23		PCV13
Comparator	PPSV23 alone	PCV15+PPSV23	PPSV23
Included studies	a. With or without risk factors 1 RCT - Azuma et al, 2023 b. No risk factors 1 RCT - Juergens et al 2014	No risk factors 1 RCT - Song et al 2021	With or without risk factors 1 cohort study Tseng et al 2018

A. Serious adverse events and Deaths: Older Adults

i. PCV13+PPSV23 alone vs PPSV23 alone [with or without risk factors]

	Author, year	Study type	Country Interventions	GRADE COE	Results	HTAC interpretation
1	Azuma et al. 2023	Open label RCT	Japan <ul style="list-style-type: none"> Group A - sequential PCV13- PPSV23 (0.5 years interval): n=43 Group B - sequential PCV13–PPSV23 (1.0-y interval): n=40 Group C - PPSV23 alone: n=46 	Low	0 events	No reported events.

i. PCV13+PPSV23 vs PPSV23 alone [no risk factors]

	Author, year	Study type	Country Interventions	GRADE COE
1	Juergens et al 2014	Open label RCT and open extension trial	19 sites in South Africa Dose 1: <ul style="list-style-type: none"> Group 1 and 2 - PCV13 formulations* Group 3 - PPSV23 Dose 2 (after 1 year): <ul style="list-style-type: none"> Group 1 and 2: either PCV13 or PPSV23 	Very Low

*with or w/o aluminum phosphate

Vaccination/ Dose	Outcomes	HTAC interpretation
DOSE 1	Serious AEs (SAEs)	SAEs not related to the study vaccine. Inconclusive when PCV13 formulations were compared to PPSV23
	Death	Higher number of deaths in the PCV arm, but were deemed not related to the study vaccine.
DOSE 2	Serious AEs (SAEs)	SAEs not related to the study vaccine.
	Death	

Evidence Considered:
Pneumococcal Vaccines for Adults

A. Serious adverse events and Deaths: Older Adults

ii. PCV13+PPSV23 vs PCV15+PPSV23 *[no risk factors]*

	Author, year	Study type	Country	GRADE COE	HTAC interpretation
1	Song et al 2021	RCT, double-blind	Multi-site/multicenter (United States [15 sites], the Republic of Korea [2 sites], Spain [3 sites], and Taiwan [2 sites]).	Moderate	<i>Inconclusive.</i>

After Dose of PCV (1st dose)	HTAC interpretation
Any SAE	<i>Inconclusive</i>
Any vaccine-related SAEs	
Death	
After PPSV23 (2nd dose)	HTAC interpretation
Any SAE	<i>Inconclusive</i>
Any vaccine-related SAEs	
Death	

A. Serious adverse events and Deaths: Older Adults

iii. PCV13 vs PPSV23 [with or without risk factors]

	Author, year	Study type	Country	GRADE COE	HTAC interpretation
1	Tseng et al 2018	Obs study	US VAERS from 2014 to 2015	Low	<u>PCV13 vs. PPSV23:</u> The risk of any cardiovascular events (i.e. acute myocardial infarction and Cardiomyopathy; heart failure) after PCV13 is comparable to or worse than PPSV23 arm. The risk for atrial fibrillation had a significantly higher risk in the PCV13 arm, while the risk of having syncope, thrombocytopenia II, and allergic reactions were significantly higher in the PPSV23 arm.

Adverse events groups	HTAC interpretation
Group 1. Cardiovascular events	
Acute myocardial infarction	PCV13 is comparable to or worse than PPSV23
Acute pericarditis	Inconclusive
Atrial fibrillation	Favors PPSV23
Cardiomyopathy; heart failure	PCV13 is comparable to or worse than PPSV23
Group 2. Bell's palsy	Inconclusive
Group 3. Guillain-Barré syndrome	Inconclusive
Group 4. Syncope	Favors PCV13
Group 5. Erythema multiforme	Inconclusive
Group 6. Thrombocytopenia	
Thrombocytopenia I	Inconclusive
Thrombocytopenia II	Favors PCV13
Group 7. Cellulitis and infection	Equivalent
Group 8. Allergic reaction	Favors PCV13
Group 9. Anaphylaxis	Inconclusive

Evidence Considered:
Pneumococcal Vaccines for Adults

A. Serious adverse events and Deaths: Older Adults

Outcome	PCV13+PPSV23 vs PPSV23 alone		PCV15+PPSV23 vs PCV13+PPSV23	PCV13 vs PPSV23
	With or w/o risk factors (k=1) Azuma et al. 2023	No risk factors (k=1) Juergens et al 2014	No risk factors (k=1) Song et al 2021	With or without risk factors (k=1) Tseng et al 2018
Serious AEs	No reported events	After Dose 1 and Dose 2: • SAEs not related to the study vaccine (k=1)	After Dose 1 and Dose 2: • Inconclusive (k=1)	[Adverse events only] Inconclusive: acute pericarditis, bell's palsy, Guillain-Barré syndrome. Erythema multiforme, Thrombocytopenia I, anaphylaxis.
Deaths	No reported events	After Dose 1: 13 deaths in the PCV arm, but were deemed not related to the study vaccine After Dose 2: No deaths reported (k=1)	After Dose 1 and Dose 2: No deaths reported (k=1)	Any cardiovascular events (i.e. acute myocardial infarction and Cardiomyopathy; heart failure) after PCV13 is comparable to or worse than than PPSV23 arm. Risk for atrial fibrillation had a significantly higher risk in the PCV13 arm Risk of having syncope, thrombocytopenia II, and allergic reactions were significantly higher in the PPSV23 arm.
GRADE rating	Low COE	Very Low COE	Moderate COE	Low COE

C2: SAFETY



RQ2.2 Among all elderly adults 60 years old and above, what is the **safety** of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination?

HTAC Judgment [1 of 2]:

Overall, the majority of reported adverse events related to pneumococcal vaccinations were local and systemic reactogenic reactions of mild to moderate severity and transient duration. Evidence on serious adverse events (SAEs) and deaths related to the vaccine also showed a low number of events. Across different outcomes and subpopulations, results were generally **not significantly different** between groups.

A. Local and Systemic Reactogenicity in older adults

Based on two open-label RCTs, PPSV23 alone had significantly lower risk of local injection-site reactions compared to sequential vaccination with PCV13+PPSV23 in older adults with or without risk factors ([Azuma et al, 2023, low COE](#)) and no risk factors ([Juergens et al 2014, very low COE](#)). In terms of systemic reactions, the study on patients with risk factors ([Azuma et al, 2023, low COE](#)) showed low rates of (<5%) in both PPSV23 and PCV13+PPSV23 arm with no significant difference between arms, while the other study on patients with no risk factors ([Juergens et al 2014, very low COE](#)) had inconclusive results.

Based on one Phase III RCT ([Song et al 2021, moderate COE](#)) that examined sequential vaccination of PCV13+PPSV23 and PCV15+PPSV23, 1st dose of PCV13 had significantly lower risk of local and systemic reactions compared to the 1st dose of PCV15, while the 2nd dose of PPSV23 after PCV15 is comparable to or worse than the 2nd dose of PPSV23 after PCV13.

C2: SAFETY



RQ2.2 Among all elderly adults 60 years old and above, what is the **safety** of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination?

HTAC Judgment [2 of 2]:

B. Serious Adverse Events (SAEs) and Deaths in older adults

No SAE and death was reported in one open label RCT [[Azuma et al, 2023](#), *low COE*] that compared PCV13+PPSV23 vs PPSV23 in older adults with or without risk factors. On the other hand, one RCT on older patients with risk factors [[Juergens et al 2014](#), *very low COE*] reported SAEs and deaths, however, these were deemed as **not related to the vaccine**.

One RCT [[Song et al 2021](#), *moderate COE*] compared sequential vaccinations with PCV15+PPSV23 and PCV13+PPSV23 in older patients with no risk factors. **No deaths** were reported in the study and there were **inconclusive results** on the risk of SAEs.

One observational study [[Tseng et al 2018](#), *low COE*] compared single dose vaccines of PCV13 vs PPSV23. Some of the nine pre-identified SAEs examined showed **inconclusive** results (ie., bell's palsy, guillain-barre syndrome, erythema multiforme, thrombocytopenia I and anaphylaxis). The risk of any cardiovascular events (i.e. acute myocardial infarction and cardiomyopathy; heart failure) after PCV13 is **comparable to or worse** than the PPSV23 arm. The risk for atrial fibrillation was **significantly higher in the PCV13 arm**, while the risk of having syncope, thrombocytopenia II, and allergic reactions were **significantly higher in the PPSV23 arm**.

CRITERION 3. COST EFFECTIVENESS

*Evidence Considered:
Pneumococcal Vaccines for Adults*

COST EFFECTIVENESS ANALYSIS

Methodology

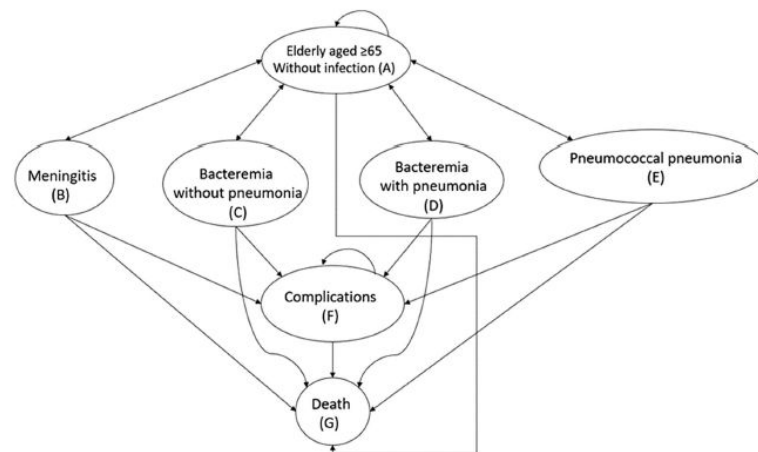
CEA was conducted using the TreeAge Software.

The progression of infections and related health outcomes was projected using a Markov model adapted from Ngamprasertchai et al. (2023) [Thailand]

Input parameters used were either from local evidence or the next best available global evidence. (e.g., near Philippine context)

ICERs comparing the different interventions and comparators were ran under the following analyses:

1. Deterministic Analysis
2. One-Way Sensitivity Analysis
3. Probabilistic Sensitivity Analysis



Schematic depiction of Markov Model for PCV Adult
(Ngamprasertchai et al., 2023)

Evidence Considered:
Pneumococcal Vaccines for Adults

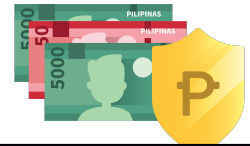
Unadjusted VEs for CEA

	Base Case			
	(using VE of full sequential regimen from the clinical assessment*, not adjusted for local ST coverage)			
	VE against IPD (95% CI)	Reference	VE against NBPP 95% CI)	Reference
PPV23 Alone	76% (54%, 88%)	<i>Tsai, 2015 [Taiwan]</i> <i>Observational</i> <i>Moderate Certainty of Evidence</i>	62% (28%, 81%)	<i>Only 1 RCT by Maruyama 2010 [Japan] had significant results and can be used as base case - Maruyama et al., 2010 [VE= 62% (28, 81)]. Moderate certainty of evidence</i> <i>4 RCTs detected in total. RCTs other than Maruyama had inconclusive results.</i>
PCV13+PPV23 vs. placebo	38% (13%, 55%)	<i>Perniciaro, 2021 [Germany]</i> <i>Observational, Very low Certainty of Evidence</i> <i>No RCTs or Asian studies for sequential.</i>	36.5% (-25%, 67.8%)	<i>Heo et al., 2022 [SoKor]</i> <i>Observational, Very low certainty of evidence</i> <i>VE for all elderly</i>
PCV15+PPV23 vs. placebo				
	Alternate Scenario			
	(using VE of individual vaccines in the regimen, adjusted for local ST coverage)			
	VE against IPD	Reference	VE against NBPP	Reference
PPV23 Alone	79% (-0.8%, 98%)	<i>1 RCT (Ortqvist, 1998, Sweden) [79% (-0.8, 98)] was detected with non-inferior results</i> <i>Low certainty of evidence</i>	32% (-116%, 79%)	<i>Pooled VE from 2 RCTs (Ortqvist, 1998 [Sweden, low certainty of evidence] and Maruyama 2010 [Japan, moderate certainty of evidence])</i>
PCV13+PPV23 vs. placebo	PCV13/15= 75.00% (41.40%, 90.80%)	<i>PCV13 = Bonten, 2015</i>	PCV13/15= 45% (14.2, 65.30%)	<i>PCV13 = Bonten, 2015</i>
PCV15+PPV23 vs. placebo	PPSV23 = 79% (-0.8, 98)	<i>PPV23 = 1 RCT (Ortqvist, 1998, Sweden) [79% (-0.8, 98)] was detected with non-inferior results</i> <i>Low certainty of evidence</i>	PPSV 23 = 32% (-116 to 79)	<i>PPV23 = Pooled VE from 2 RCTs (Ortqvist, 1998 [Sweden, low certainty of evidence] and Maruyama 2010 [Japan, moderate certainty of evidence])</i>

*VEs for the base case were from studies with the best certainty of evidence and Asian studies were preferred.

DETERMINISTIC ANALYSIS

Pneumococcal vaccines vs. No vaccination



	BASE CASE					
Strategy	Cost (PhP) per person	Incremental Cost (PhP)	Effectiveness/QALY per person	Incremental Effectiveness	ICER	NMB
No Vaccine	270.77		7.40			+
PPSV23	718.60	447.83	7.53	0.13	3,444.85	+
PCV13 & PPSV23	1,563.49	1,292.72	7.47	0.07	18,467.43	+
PCV15 & PPSV23	1,841.68	1,570.91	7.47	0.07	22,441.57	+
	ALTERNATE SCENARIO					
Strategy	Cost (PhP) per person	Incremental Cost (PhP)	Effectiveness/QALY per person	Incremental Effectiveness	ICER	NMB
No Vaccine	270.77		7.40			+
PPSV23	735.60	464.83	7.54	0.14	3,320.21	+
PCV13 & PPSV23	1,484.86	1,214.09	7.55	0.15	8,093.93	+
PCV15 & PPSV23	1,765.51	1,494.74	7.54	0.14	10,676.71	+

Threshold Assumption: 2024 [PSA GDP per capita](#) = PHP 234,277 x 0.75 = Php 175,707.75

- All ICERS are below the 2024 GDP per capita, thus all vaccine strategies are cost effective versus no vaccination. Hence, all vaccine strategies are cost-effective at 0.75x GDP vs. no vaccination.

DETERMINISTIC ANALYSIS



BASE CASE: Pneumococcal vaccines compared to each other

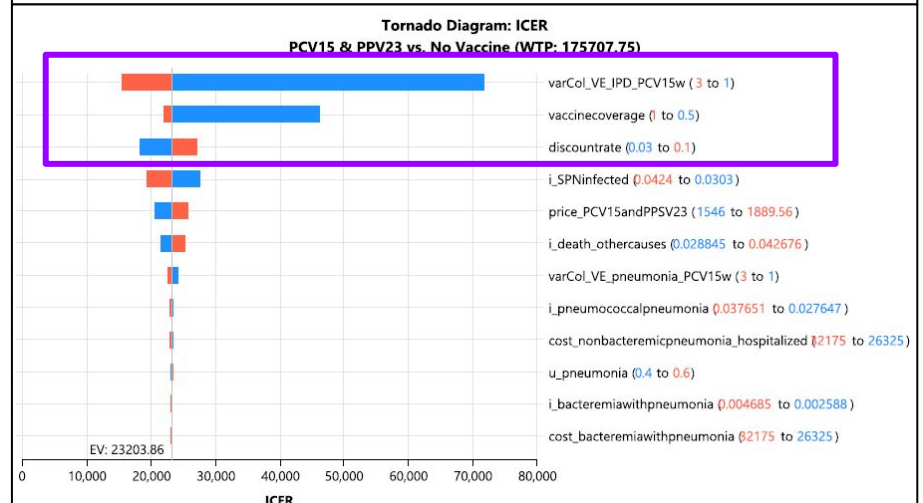
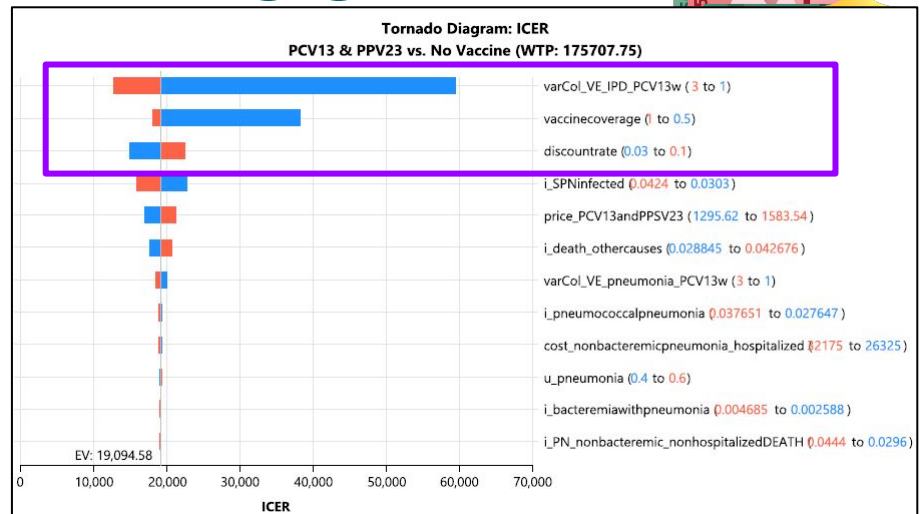
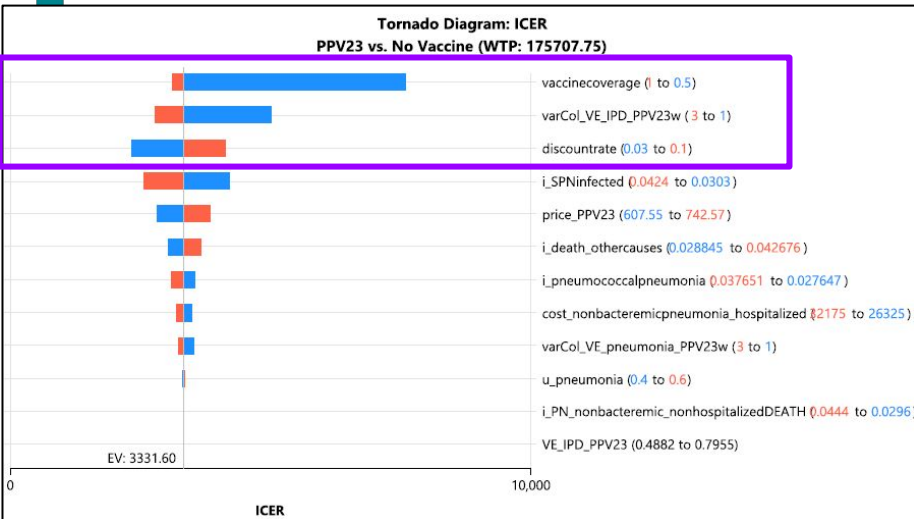
Against each other	Incremental Cost (PhP)	Incremental Effectiveness	ICER	NMB	Interpretation
(PCV13 & PPSV23) vs PPSV23	844.89	-0.06	-14,081.50	-	PCV13 & PPSV23 is less effective and more costly (PPSV23 is cost saving = IC>0, IE<0)
(PCV15& PPSV23) vs PPSV23	1,123.08	-0.06	-18,718.00	-	PCV15 & PPSV23 is less effective and more costly (PPSV23 is cost saving = IC>0, IE<0)
(PCV13 & PPSV23) vs (PCV15&PPSV23)	-278.19	0.00	-	+	Same effectiveness but PCV13 & PPSV23 is cheaper.

Threshold Assumption: 2024 [PSA GDP per capita](#) = PHP 234,277 x 0.75 = Php 175,707.75

- Sequential vaccinations have negative NMB at this threshold vs. PPSV23 (they are less cost-effective than PPSV23 given their lower VE and higher cost).
- PPSV23 is cost-saving compared to sequential PCV+PPV vaccinations.

ONE-WAY SENSITIVITY ANALYSIS

BASE CASE



The most sensitive input parameters for all three regimen vs. no vaccination:

1. Vaccination coverage
2. VE against IPD
3. Discount rate

PROBABILISTIC SENSITIVITY ANALYSIS



BASE CASE

Strategy	Deterministic ICER <i>[Point estimates]</i> <i>(PHP per QALYs gained)</i>	PSA Mean ICER <i>[simulated using random values within the 95% CI range]</i> <i>(PHP per QALYs gained)</i>	Probability of Cost-effectiveness <i>(out of 1000 simulations)</i>
Vs. No Vaccine			
PPSV23	3,444.85	3,358.60	99.9% cost-effective
PCV13 & PPSV23	18,467.43	19,470.85	99.8% cost-effective
PCV15 & PPSV23	22,441.57	23,760.84	99.7% cost-effective
Vs. each other			
(PCV13 & PPSV23) vs PPSV23	-14,081.50	-PhP12,649.55	PCV13&PPSV23 is 100% inferior (IC>0, IE<0)
(PCV15& PPSV23) vs PPSV23	-18,718.00	-PhP16,803.49	PCV15&PPSV23 is 100% inferior (IC>0, IE<0)
(PCV13 & PPSV23) vs (PCV15&PPSV23)	-	-PhP1,572,196.24	PCV13&PPV23 is 49.50% superior compared to PCV15&PPSV23

Vs. No vaccination

- All mean ICERS and >99% of iterations are below the 75% of the 2024 GDP per capita.

Vaccine vs. Vaccine

- Sequential vaccinations were inferior vs. PPSV23 in 100% of iterations given their lower VE and higher cost.
- PCV13+PPSV23 was superior to PCV15+PPSV23 at 49.5% of the iterations

Green = Intervention is superior or cost effective (ICER < 0.75x GDP)

Red = intervention is inferior or not cost effective (ICER > 0.75x GDP)

C3: COST EFFECTIVENESS



RQ3. What is the **cost-effectiveness** of PCV13 in sequence to PPSV23, PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination among all elderly adults 60 years old and above?

HTAC Judgment:

All pneumococcal vaccination strategies were found to be cost-effective compared to no vaccination in both the base case and alternative scenarios, assuming a cost-effectiveness threshold of 0.75x the GDP per capita in 2024. In the probabilistic sensitivity analysis, all vaccine regimens (PPSV23, PCV13+PPSV23, PCV15+PPSV23) were cost-effective in >99% of 1,000 simulations compared to no vaccination.

When compared with each other, PPSV23 alone was cost-saving relative to the sequential PCV+PPSV23 vaccination strategies. Between PCV15+PPSV23 and PCV13+PPSV23, the estimated QALYs gained were equal, but PCV13+PPSV23 was less costly. The ICER results of all pneumococcal vaccine strategies are most sensitive to the vaccination coverage, vaccine effectiveness against IPD cases, and discount rate.

Note: No threshold set in the Philippines yet.

CRITERION 4. AFFORDABILITY AND VIABILITY

*Evidence Considered:
Pneumococcal Vaccines for Adults*

BUDGET IMPACT

Methodology

The following costs were calculated per year over a 5-year time horizon (2025 to 2029):

- A. Cost of vaccination - includes the price per dose, wastage, and storage cost
- B. Cost of treatment - includes the cost of infection and sequelae. The VE for the full regimen from the clinical evidence was used (base case in CEA). Two scenarios were used for the cost of treatment:
 - Scenario 1: Philhealth Case rate cost
 - Scenario 2: Median Hospitalization cost



Cost per Vaccine Regimen		
PPSV23 <i>(DOH procurement data)</i>	₱675.06	Single dose: 5% wastage; 8% storage
PCV13 + PPV23	[CONFIDENTIAL]	
PCV15 + PPV23	[CONFIDENTIAL]	
<i>PCV13 cost per dose (Govt list price from MAH)</i>	[CONFIDENTIAL]	Multi-dose: 10% wastage; 4% storage
<i>PCV15 cost per dose (Govt list price from MAH)</i>	[CONFIDENTIAL]	Single dose: 5% wastage; 8% storage

	BASE CASE <i>(2025 Philhealth Case Rates)</i>	ALTERNATE CASE <i>(Median hospitalization cost from philhealth claims 2018-2024)</i>
COST OF INFECTION	Mean	Median hospitalization cost
Meningitis (ICD Code G00.1, G00.2, G00.9, G03.8, G03.9)	₱50,115.00	₱96,117.34
Bacteremia without pneumonia (ICD Code P36.1, P36.8,P36.9, A40.3, A40.8, A40.9, A41.8, A41.9)	₱62,400.00	₱119,830.15
Bacteremia with pneumonia (ICD Code J10.0, J11.0, J12 to J18, J85.1, or J86)	₱29,250.00	₱26,884.38
Non-bacteremic Pneumococcal pneumonia (ICD10 codes same as bacteremia with pneumonia)-hospitalized	₱29,250.00	₱26,884.38
Nonbacteremic Pneumococcal pneumonia-non hospitalized	₱179.51	<i>no data (use base case)</i>
COST OF SEQUELAE	Mean	Median hospitalization cost
Seizure/Epilepsy (G40.0-G40.9)	₱15,210.00	<i>no data (use base case)</i>
Hearing loss (RVS 69502)	₱45,435.00	<i>no data (use base case)</i>
Neurocognitive impairment (F70-79, F82, F89, F90.8, G24-25, G80-83)	₱18,525.00	<i>no data (use base case)</i>
Behavioural problems (F90-F99)	₱15,210.00	<i>no data (use base case)</i>

BUDGET IMPACT



Year	<u>Projected Population (60 & above)</u>	TARGET POPULATION FOR VACCINATION *
2025	10,986,031	10,436,730
2026	11,402,637	1,354,141
2027	11,834,118	899,825
2028	12,273,775	926,090
2029	12,715,370	946,458
TOTAL		14,563,244



*This assumes that:

- all elderly adults will require vaccination in 2025 regardless of vaccination status from the current DPCB roll out of PPSV23
- 95% vaccine coverage
- No herd immunity, hence, all unvaccinated seniors (remaining 5%) shall be vaccinated in the following year.
- 4% all-cause mortality rate in seniors per year is applied based on 2023 PSA data.

BUDGET IMPACT



BASE COST SCENARIO (philhealth claims cost) *In billions*

Year	No vaccination	PPSV23	PCV13+PPSV23	PCV15+PPSV23
	Treatment Cost	Vaccination Cost + Treatment Cost	Vaccination Cost + Treatment Cost	Vaccination Cost + Treatment Cost
2025	₱4.40	₱8.96	₱18.01	₱20.91
2026	₱4.57	₱2.93	₱4.97	₱5.35
2027	₱4.74	₱2.86	₱4.43	₱4.68
2028	₱4.92	₱3.12	₱4.59	₱4.84
2029	₱5.10	₱3.37	₱4.73	₱5.00
TOTAL	₱23.73 B	₱21.24 B	₱36.73 B	₱40.78 B
<i>Incremental cost vs. no vax</i>		-₱2.50 B	₱13.00 B	₱17.05 B

Note: This scenario was used in the HTAC judgment.

BUDGET IMPACT



ALTERNATE COST SCENARIO (median hospitalization cost) *In billions*

Year	No vaccination	PPSV23	PCV13+PPSV23	PCV15+PPSV23
	Treatment Cost	Vaccination Cost + Treatment Cost	Vaccination Cost + Treatment Cost	Vaccination Cost + Treatment Cost
2025	₱4.08	₱8.81	₱17.79	₱20.69
2026	₱4.23	₱2.78	₱4.75	₱5.13
2027	₱4.39	₱2.69	₱4.20	₱4.45
2028	₱4.56	₱2.93	₱4.35	₱4.61
2029	₱4.72	₱3.17	₱4.49	₱4.75
TOTAL	₱21.99 B	₱20.39 B	₱35.57 B	₱39.62 B
	<i>Incremental cost vs. no vax</i>	-₱1.60 B	₱13.58 B	₱17.64 B

BUDGET IMPACT



2025 Vaccination Cost for 10,436,730 vaccinees		PPSV23	PCV13+PPSV23	PCV15+PPSV23
		₱7.05 billion	₱15.02 billion	₱17.93 billion
NIP Budget for 2025= Php 5,447,897,413.74 (₱ 5.45 billion)	Coverage share of the budget	The whole NIP budget will only cover 77.33%	The whole NIP budget will only cover 36.26%	The whole NIP budget will only cover 30.39%
	Budget increase needed	The NIP budget must be increased 1.29 times	The NIP budget must be increased 2.76 times	The NIP budget must be increased 3.29 times
2025 Budget for PPSV = Php 290,431,040.00 (₱ 290.43 million)	Coverage share of the budget	The PPSV budget will only cover 4.12%	The PPSV budget will only cover 1.93%	The PPSV budget will only cover 1.62%
	Budget increase needed	The PPSV budget must be increased 24.26 times	The PPSV budget must be increased 51.73 times	The PPSV budget must be increased 61.73 times

Note: Cost of vaccination is not affected by the VE and claims/hospitalization cost. Hence, budget impact to the NIP is consistent for all scenarios.

C4: AFFORDABILITY AND VIABILITY



RQ4. What is the **budget impact** of PCV13 in sequence to PPSV23, PCV15 in sequence to PPSV23, or PPSV23 alone compared to each other or no vaccination among all elderly adults 60 years old and above?

HTAC Judgment:

Assuming that the DOH will cover all the eligible target population for five years, pneumococcal vaccination in the elderly population 60 years old and above, including vaccination and treatment costs, ranges from Php 21.24 B to Php 40.78 B. Implementing PPSV23 over a 5-year time horizon will avoid additional expense or incur savings of Php 2.49B compared to no vaccination due to averted cases of pneumococcal infection. On the other hand, implementing PCV13+PPSV23 and PCV15+PPSV23 will incur additional Php 13.00 B and Php 17.05B, respectively.

In terms of vaccination cost, none of the vaccines are considered affordable considering the 2025 PPSV23 budget and even the total NIP budget. The 2025 PPSV23 budget of the NIP will only cover 1.62% (PCV15+PPSV23) to 4.12% (PPSV23 alone) of the vaccination cost. In order to cover the target population, the budget should increase by 24.26x for PPSV23 and 51.73-61.73x for sequential administrations of PCV13+PPSV23 and PCV15+PPSV23 in 2025.

CRITERION 5. HOUSEHOLD FINANCIAL IMPACT



*Evidence Considered:
Pneumococcal Vaccines for Adults*

Household Financial Impact of Pneumococcal Disease



Methodology

- Combined the files from 2018 to 2020 and from 2021 to 2024.
- Filtered per Type of Claims:
 - Excluded: claims that are "denied," "RTH (return to hospital)," and "in process"
 - Filter in: only the claims classified as "PAID" and "APRV4PAYMENT"
- Categorized into:
 - Two age groups: i) 18 to 59 years old and ii) 60 years old and above
 - Eight medical case rate/disease groups:

1	Septicemia (S. pneumoniae specific)	A40.3
2	Septicemia, others/unspecified	A40.8, A40.9, A41.9
3	Meningitis (Pneumococcal)	G00.1
4	Meningitis (Streptococcal)	G00.2
5	Meningitis, others/unspecified	G00.9, G03.8, G03.9
6	Pneumonia (S. pneumoniae), moderate risk	J13.2
7	Pneumonia (S. pneumoniae), high risk	J13.3
8	Pneumonia, others/unspecified	J12.02, J12.03, J12.12, J12.13, J12.22, J12.32, J12.92, J12.93, J14.2, J14.3, J15.42, J15.43, J15.92, J15.93, J18.02, J18.03, J18.12, J18.13

Household Financial Impact of Pneumococcal Disease



Results

A. Per Age Group (2018-2024 Data)

1. **Number of Claims Distribution**
2. **Cost of hospitalization** *-min, max, average, median*
3. **Cost covered by PhilHealth** *-min, max, average, median*
4. **Out-of-Pocket cost** *-min, max, average, median*
5. **Percent Coverage** *-average*
6. **Yearly Trend**

B. Per illness category (2018-2024 Data)

1. **Number of Claims Distribution**
2. **Median Cost of hospitalization**
3. **Median Cost covered by PhilHealth**
4. **Median Out-of-Pocket cost**
5. **Average Percent Coverage**
6. **Trend Per Age group**

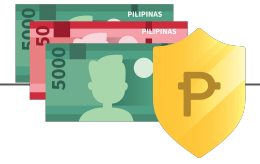
Household Financial Impact of Pneumococcal Disease



A. PER AGE GROUP (2018-2024 data)

	MIN (Php)	MAX (Php)	AVERAGE (Php)	MEDIAN (Php)
18 to 59 years old				
1. Number of Claims	87,624 (44.01% of total claims for adults)			
2. Cost of hospitalization per patient	₱0.00	₱98,763,907.00	₱169,914.39	₱78,726.73
3. Cost covered by PhilHealth per patient	₱2,600.00	₱271,540.00	₱32,415.09	₱32,000.00
4. Out-of-Pocket cost per patient	₱0.00	₱98,724,107.00	₱138,472.10	₱45,648.81
5. Average Coverage			48.75%	
60 years old above				
1. Number of Claims	111,456 (55.99% of total claims for adults)			
2. Cost of hospitalization per patient	₱0.00	₱876,352,867.91	₱263,199.78	₱107,790.96
3. Cost covered by PhilHealth per patient	₱1,692.00	₱351,800.00	₱32,948.60	₱32,000.00
4. Out-of-Pocket cost per patient	₱0.00	₱876,320,867.91	₱231,034.88	₱74,120.60
5. Average Coverage			41.04%	
All Adults ≥ 18 years old				
1. Number of Claims	199,080			
2. Cost of hospitalization per patient	₱0.00	₱876,352,867.91	₱222,140.71	₱93,224.18
3. Cost covered by PhilHealth per patient	₱1,692.00	₱351,800.00	₱32,713.78	₱32,000.00
4. Out-of-Pocket cost per patient	₱0.00	₱876,320,867.91	₱190,293.86	₱59,771.32
5. Average Coverage			44.43%	

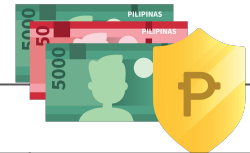
Household Financial Impact of Pneumococcal Disease



A.6. PER AGE GROUP: YEARLY TREND (2018-2024 data)

Admission year	Number of approved/paid claims <small>(%proportion to total claims for the year)</small>	MEDIAN Hospitalization Cost (Php)	MEDIAN Claims Paid (Php)	MEDIAN OOP (Php)	Average Coverage
All Adults > 18 years old					
2018	51,300	₱50,568.88	₱32,000.00	₱18,814.38	60.90%
2019	36,916	₱69,680.85	₱32,000.00	₱37,741.50	51.02%
2020	24,411	₱108,329.92	₱32,000.00	₱75,464.20	40.05%
2021	19,313	₱142,454.00	₱32,000.00	₱109,090.05	32.46%
2022	22,132	₱138,917.91	₱32,000.00	₱105,450.38	32.14%
2023	23,971	₱140,450.88	₱32,000.00	₱107,415.02	31.86%
2024	21,037	₱148,803.54	₱41,600.00	₱108,594.30	36.05%
OVERALL	199,080	₱93,224.18	₱32,000.00	₱59,771.32	44.43%
CONCLUSION	20-50 thousand claims per year Relatively lower number of claims compared to pedia <small>(560,700 claims in 2017-2023)</small>	Increasing cost of hospitalization per year 2018 vs. 2024 cost 194.2% increase	Median claims paid only increased by 30%	Median OOP increases per year	Average Coverage decreases per year

Household Financial Impact of Pneumococcal Disease



A.6. PER AGE GROUP: YEARLY TREND (2018-2024 data)

Admission year	Number of approved/paid claims (%proportion to total claims for the year)	MEDIAN Hospitalization Cost (Php)	MEDIAN Claims Paid (Php)	MEDIAN OOP (Php)	Average Coverage
18 to 59 years old					
2018	21,391 (41.70%)	₱42,339.67	₱32,000.00	₱10,837.17	67.10%
2019	15,118 (40.95%)	₱56,413.44	₱32,000.00	₱24,805.50	56.82%
2020	11,287 (46.24%)	₱91,476.00	₱32,000.00	₱58,719.35	44.16%
2021	9,228 (47.78%)	₱115,598.67	₱32,000.00	₱83,306.01	36.91%
2022	10,430 (47.13%)	₱118,150.84	₱32,000.00	₱84,561.71	35.97%
2023	10,819 (45.13%)	₱117,583.00	₱32,000.00	₱84,741.65	36.03%
2024	9,351 (44.45%)	₱123,763.32	₱41,600.00	₱83,362.32	39.97%
OVERALL	87,624 (44.01%)	₱78,726.73	₱32,000.00	₱45,648.81	48.75%
60 years old above					
2018	29,909 (58.30%)	₱58,434.51	₱32,000.00	₱26,359.15	56.47%
2019	21,798 (59.05%)	₱82,118.77	₱32,000.00	₱49,762.85	47.00%
2020	13,124 (53.76%)	₱128,082.12	₱32,000.00	₱94,716.50	36.52%
2021	10,085 (52.22%)	₱173,386.39	₱32,000.00	₱140,179.86	28.39%
2022	11,702 (52.87%)	₱161,969.94	₱32,000.00	₱128,412.47	28.73%
2023	13,152 (54.87%)	₱165,846.99	₱32,000.00	₱132,692.91	28.43%
2024	11,686 (55.55%)	₱173,740.53	₱41,600.00	₱132,702.83	32.92%
OVERALL	111,456 (55.99%)	₱107,790.96	₱32,000.00	₱74,120.60	41.04%
CONCLUSION	Consistently higher number of claims in the elderly age group	<i>Increasing cost per year, consistently higher in elderly</i>	<i>Median claims paid increases by 30% in 2024; Same for both age group</i>	<i>Median OOP increases per year; consistently higher in elderly</i>	<i>Average Coverage decreases per year; Lower in the elderly</i>

Household Financial Impact of Pneumococcal Disease



B.6. PER ILLNESS CATEGORY: TREND PER AGE GROUP (2018-2024 data)

Illness Category	Number of claims	Proportion of claims	MEDIAN Hospitalization Cost (Php)	MEDIAN Claims Paid (Php)	MEDIAN OOP (Php)	Average Coverage
All Adults 18 years and above						
Septicemia (S. pneumoniae specific)	633	0.32%	₱93,593.46	₱32,000.00	₱59,593.00	45.20%
Septicemia, others/unspecified	17,350	87.15%	₱105,598.13	₱32,000.00	₱71,051.03	42.43%
Meningitis (Pneumococcal)	9	0.00%	₱50,836.50	₱25,700.00	₱25,136.50	47.21%
Meningitis (Streptococcal)	27	0.01%	<i>Highest:</i> ₱170,115.78	₱25,700.00	<i>Highest:</i> ₱144,415.78	<i>33.97%</i>
Meningitis, others/unspecified	6,558	3.29%	₱67,067.31	₱25,700.00	₱40,360.50	47.14%
Pneumonia (S. pneumoniae), moderate risk	677	0.34%	₱29,697.02	<i>Lowest:</i> ₱15,000.00	₱14,592.95	56.02%
Pneumonia (S. pneumoniae), high risk	154	0.08%	₱56,859.29	₱32,000.00	₱24,186.55	56.29%
Pneumonia, others/unspecified	17,518	8.80%	<i>Lowest:</i> ₱24,281.48	<i>Lowest:</i> ₱15,000.00	<i>Lowest:</i> ₱8,385.83	<i>62.69%</i>
TOTAL/OVERALL	199,080	100.00%	₱93,224.18	₱32,000.00	₱59,771.32	44.43%

Household Financial Impact of Pneumococcal Disease



B.6. PER ILLNESS CATEGORY: TREND PER AGE GROUP (2018-2024 data)

Illness Category	Number of claims	Proportion of claims	MEDIAN Hospitalization Cost (Php)	MEDIAN Claims Paid (Php)	MEDIAN OOP (Php)	Average Coverage
18 to 59 years old						
Septicemia (S. pneumoniae specific)	179	0.20%	₱68,295.69	₱32,000.00	₱36,295.69	50.22%
Septicemia, others/unspecified	73,042	83.36%	₱89,880.59	₱32,000.00	₱55,266.84	46.75%
Meningitis (Pneumococcal)	8	0.01%	₱47,685.25	₱25,700.00	₱21,985.25	51.01%
Meningitis (Streptococcal)	21	0.02%	Highest: ₱98,836.18	₱25,700.00	Highest: ₱65,426.18	39.33%
Meningitis, others/unspecified	5,641	6.44%	₱64,219.16	₱25,700.00	₱37,194.90	48.63%
Pneumonia (S. pneumoniae), moderate risk	301	0.34%	₱25,616.00	₱15,000.00	₱10,616.00	59.69%
Pneumonia (S. pneumoniae), high risk	58	0.07%	₱45,345.50	₱32,000.00	₱12,111.03	68.08%
Pneumonia, others/unspecified	8,374	9.56%	Lowest: ₱22,529.88	₱15,000.00	Lowest: ₱6,488.57	65.75%
OVERALL	87,624	100.00%	₱78,726.73	₱32,000.00	₱45,648.81	48.75%
60 years old above						
Septicemia (S. pneumoniae specific)	454	0.41%	₱102,601.87	₱32,000.00	₱67,858.05	43.22%
Septicemia, others/unspecified	100,462	90.14%	₱119,916.06	₱32,000.00	₱85,562.87	39.29%
Meningitis (Pneumococcal)	1	0.00%	₱153,317.00	₱25,700.00	₱127,617.00	16.76%
Meningitis (Streptococcal)	6	0.01%	Highest: ₱232,492.30	₱25,700.00	Highest: ₱202,937.30	15.19%
Meningitis, others/unspecified	917	0.82%	₱95,305.39	₱25,700.00	₱68,468.99	37.96%
Pneumonia (S. pneumoniae), moderate risk	376	0.34%	₱37,533.86	₱15,000.00	₱22,013.18	53.09%
Pneumonia (S. pneumoniae), high risk	96	0.09%	₱69,056.56	₱32,000.00	₱37,056.56	49.17%
Pneumonia, others/unspecified	9144	8.20%	Lowest: ₱26,140.59	₱15,000.00	Lowest: ₱10,474.00	59.88%
TOTAL/OVERALL	111,456	100.00%	₱107,790.96	₱32,000.00	₱74,120.60	41.04%

Household Financial Impact of Pneumococcal Disease



RQ5. What is the household financial impact of pneumococcal disease among adults 18 years old and above including senior citizens and patients with comorbidities/risk factors?

HTAC Judgment Per Age Group: [1 of 2]

Based on PhilHealth data from 2018 to 2024, the median cost of hospitalization due to pneumococcal diseases (i.e. septicemia, meningitis, pneumonia) for adults aged 18 years and above is at ₱93,224.18 per patient. The median claims paid amounts to ₱32,000.00, resulting in a median out-of-pocket cost of ₱59,771.32 per patient.

Notably, older adults aged 60 and above accounted for a greater proportion of paid/approved PhilHealth claims compared to the younger adults 18-59 years old, comprising 55.99% of the total claims paid for adults. Furthermore, the median cost of hospitalization (₱107,790.96) and median out-of-pocket expense (₱74,120.60) were also higher in elderly adults compared to younger adults, whose median costs were ₱78,726.73 and ₱45,648.81, respectively.

It was also observed that the median hospitalization cost due to pneumococcal infections has increased by 194.2% from only ₱50,568.88 in 2018 to ₱148,803.54 in 2024. However, the median claims paid has only increased by 30% from ₱32,000 (2018-2023) to ₱41,600 in 2024.

Household Financial Impact of Pneumococcal Disease



RQ5. What is the household financial impact of pneumococcal disease among adults 18 years old and above including senior citizens and patients with comorbidities/risk factors?

HTAC Judgment Per Illness Category: [2 of 2]

Among the various illness categories, septicemia accounted for the highest number of PhilHealth claims paid, followed by pneumonia. However, it is important to note that the majority of these cases were of 'unspecified' origin, with only a small proportion of claims paid specifically attributed to *Streptococcus pneumoniae*.

The highest median hospitalization costs was recorded for invasive pneumococcal diseases—specifically streptococcal meningitis (₱170,115.78) and septicemia of unspecified origin (₱105,598.13). These conditions also resulted in significantly higher out-of-pocket expenses: ₱144,415.78 for streptococcal meningitis and ₱71,051.03 for septicemia of unspecified origin. In contrast, other conditions such as pneumonia [*unspecified origin and if invasive or non-invasive*] had lower median hospitalization costs (₱24,281.48) and out-of-pocket expenses (₱8,385.83), while moderate risk pneumonia caused by *S. pneumoniae* had a slightly higher costs (₱29,697.29 hospitalization; ₱14,592.95 out-of-pocket).

Overall, both the number of claims paid and the cost of hospitalization were generally higher among elderly patients across all illness categories with the exception for meningitis, which showed a higher number of claims paid and greater hospitalization costs among younger adults.

CRITERION 6. ETHICAL, LEGAL, SOCIAL, AND HEALTH SYSTEMS (ELSHI) IMPLICATIONS

*Evidence Considered:
Pneumococcal Vaccines for Adults*

DATA COLLECTION STRATEGY (1 of 2)

	Study Design	Objective	Participants
Ethical and Social implications	Literature Review (k=8 studies; US, UK, China, Italy)	Ethical and social issues associated with pneumococcal vaccination in adults	N/A
	Focus group discussion (FGD) / Key informant interview (KII) <i>*Part of the guide questions for elderly and adults with high-risk and immunocompromising medical conditions were also related to health system implications</i>		<ul style="list-style-type: none"> • Five (5) elderly participants <ul style="list-style-type: none"> • four elderly individuals aged 68 to 72 years old • One 53-year-old representative from a non-government organization (NGO) working with older persons • Seven (7) Adults with high-risk and immunocompromising medical conditions
Legal implications	Online survey questionnaire / written response	Insights on the use of pneumococcal vaccines for adult immunization (such as procurement issues, vaccination mandates, and compensation on injury or severe side effects)	<ul style="list-style-type: none"> • Staff from the Legal Office of DOH • Staff from the Disease Prevention and Control Bureau (DPCB) of DOH

DATA COLLECTION STRATEGY (2 of 2)

	Study Design	Objective	Participants
Health system implications	Online survey questionnaire	Insight and current understanding: <ul style="list-style-type: none"> • adult pneumococcal disease • general perception in pneumococcal vaccination for adults (awareness, influence, and challenges) • health service delivery • vaccine personal preferences 	<ul style="list-style-type: none"> • Health care providers (private institutions); n=55
	Focus group discussion (FGD)/ Key informant interview (KII) for DOH, regional offices, and RHUs		<ul style="list-style-type: none"> • Five (5) participants <ul style="list-style-type: none"> • four elderly individuals aged 68 to 72 years old • One 53-year-old representative from a non-government organization (NGO) working with older persons • Seven (7) Adults with high-risk and immunocompromising medical conditions • Through civil society organizations (CSOs), target populations (Elderly and adults with comorbidities) were invited • Representatives from the central office of DOH, regional Centers for Health Development (CHD) and City Health Offices (CHOs) or Rural Health Units (RHUs) <ul style="list-style-type: none"> • 9 representatives from 9 CHDs • 9 representatives from 5 city health office (CHO) or rural health unit (RHU) from 2 regions • 2 officials from the two offices of the central DOH • Total of 20 participants from the public health sector
	Direct correspondence with DOH DPCB	Insights on vaccine implementation challenges and experiences	Official correspondence with DOH DPCB



ETHICAL IMPACT



- **Equity issues**

- Primary data gathering [at-risk adults, public health practitioners]:
 - Need to **prioritize indigent and financially incapacitated elderly individuals and adults with comorbidities/risk factors** as a way to address health inequities.
 - **Need to increase overall budget** for immunization programs

- **Accessibility of healthcare services and facilities**

- Primary data gathering [elderly]:
 - **unaware of free vaccinations**
 - vaccines are often **out of stock** or **not readily available**
 - **Distance of health centers** – respondents noted that their peers need to commute or walk long distances, which poses challenge for those with disabilities or mobility issues

- **Accessibility of vaccine information**

- Primary data gathering [private practitioners]: Physicians convince target beneficiaries by informing them of the severity of the disease that can be prevented by the vaccine
- Primary data gathering [DOH offices]:
 - No standardized guidelines on obtaining informed consent for elderly adults who will be receiving immunization
 - Obtaining informed consent is practiced in line with the Medical Professional's Code of Ethics and Patients' Rights.

SOCIAL IMPACT *(1 of 4)*



- **Knowledge on pneumonia/pneumococcal vaccines**

- Literature review:
 - willingness to get vaccinated is associated with level of **awareness and knowledge about vaccine safety, effectiveness, and severity of pneumococcal disease** (Liu 2014 [China]; Di Valerio 2014 [Italy])
- Primary data gathering [elderly & at-risk adults]:
 - Elderly and at-risk adults **understood the general concept of pneumococcal vaccines** as effective preventive measure, but there was **confusion regarding vaccine types**.
 - Participants also understand that **pneumonia is a serious health condition** especially in their group. However, **some still see pneumonia as a “milder illness”** similar to common colds or the flu

- **Preference among vaccine regimens**

- Primary data gathering [elderly & at-risk adults]:
 - Most defer to **expert opinion of medical professionals in choosing vaccine** while one respondent preferred PPSV23-only regimen due to its long-standing use
 - Among at-risk adults, most stated that they would **defer to professionals** but expressed mixed preferences for vaccination regimen

SOCIAL IMPACT *(2 of 4)*



- **Facilitators to pneumococcal vaccination**

- Role of social groups to health awareness and education

- Literature review:

- Social groups such as family and friends, and physicians influence the adults' healthcare decision-making (Zimmerman 2003 [US]; Kalgee 2017 [US]; Liu, 2014 [China])

- Primary data gathering [elderly & at-risk adults]:

- Family → significant role in raising awareness and educating them about importance of receiving these vaccines
- Community groups → social influence as an important sources of information and support for five participants (e.g. local senior citizen associations)
- Healthcare workers → trusted sources of health advice; positive interactions with HCWs contributed to increasing vaccine confidence and willingness

SOCIAL IMPACT *(3 of 4)*



- **Barriers to pneumococcal vaccination**

- *Cost of services*

- Literature review: Vaccination costs as significant deterrent particularly in areas without subsidized programs (Jain 2017 [UK])
- Primary data gathering [elderly]: Out of pocket expenses due to lack of awareness and limited availability of vaccines at health centers

- *Influence of culture, religion, and gender*

- Literature review: Mistrust of modern vaccines (vaccines are harmful) and preference for traditional Chinese medicine (Siu 2021 [China])
- Primary data gathering [elderly]:
 - Belief that pneumonia is caused by extreme heat, cold, and changes in the weather
 - Perceiving pneumonia as natural part of life → choosing not to get vaccinated
 - No religious or gender-related barriers were reported by the respondents

SOCIAL IMPACT *(4 of 4)*



- **Barriers to pneumococcal vaccination [cont]**
 - *Poor health information dissemination*
 - Literature review: Vaccine hesitancy correlates with exposure to negative media and cultural barriers (Gatwood 2021 [US])
 - Primary data gathering [elderly]:
 - Misinformation from social media and peers – Social media, not only as a source of health-related updates, but social media served as platform for spreading vaccine myths and misconceptions contributing to vaccine hesitancy
 - Enhanced health communication through senior citizens associations and media platform to counter misinformation

LEGAL IMPACT *(1 of 2)*



Legal basis for free pneumococcal vaccination for senior citizens in the Philippines

- Primary data gathering [DOH offices]: RA 9994 or Expanded Senior Citizens Act of 2010 and DOH AO-0018 *“Implementing Guidelines on Influenza and Pneumococcal Immunization for Indigent Senior Citizens”*- free pneumococcal vaccination for indigent senior citizens

Policy development:

- Primary data gathering [DOH offices]:
 - The Disease Prevention and Control Bureau (DPCB) manages policy development for the National Immunization Program.
 - Policies, including those involving civic groups and program expansions, are reviewed under the framework of the Universal Health Care (UHC) law.

No specific policy or program for pneumococcal vaccination of younger adults with comorbidities/risk factors.

*Evidence Considered:
Pneumococcal Vaccines for Adults*

LEGAL IMPACT *(2 of 2)*



Vaccine procurement:

- Primary data gathering [DOH offices]:
 - Follows Republic Act 9184 (Government Procurement Act), though a recently passed law is not yet in effect.
 - Universal Health Care (UHC) Act, through Section 34, mandated the Health Technology Assessment (HTA) Council to determine the range of entitlements for government financing of health technologies, including vaccines

WHO Prequalification requirement - DOH DPCB NIP:

"We are requiring procured vaccines to be WHO-prequalified except Pneumococcal polysaccharide polyvalent vaccine (PPSV23) since we are required by law to provide it to senior citizens even though there is no WHO pre-qualified PPSV23 currently. This can be referenced in AO 2019-0041 "Implementing Guidelines in Assuring the Efficacy, Quality, and Safety of Pharmaceutical Products in the Public Health Facilities". In addition, this is also to ensure that products are up to part with global standards and applicable to public health programs."

*Evidence Considered:
Pneumococcal Vaccines for Adults*

HEALTH SYSTEMS IMPACT (1 of 3)



- **Preference of healthcare practitioners**
 - Primary data gathering [private practitioners]:
 - Among the **private practitioners**, most commonly used vaccination strategy was **PCV13 followed by PPSV23**
 - For **public practitioners**, four out of nine **preferred PPSV23** due to its affordability and established use
- **Influence of healthcare practitioners to vaccine uptake**
 - Primary data gathering [private practitioners]: Private practitioners recognize their role as advocates for educating patients and promoting adult immunization
- **Perceived barriers to vaccine acceptance among adult patients**
 - Primary data gathering [private & public health practitioners]:
 - Survey among private practitioners reported high cost (74%), lack of perceived need (51%), safety concerns (44%), and doubts about effectiveness (40%) as major barriers
 - According to public health practitioners, low awareness, long distance, lack of transportation, fear of side effects, cultural beliefs, and inconsistency in vaccine supply and cold chain problems are the main barriers particularly in rural areas

HEALTH SYSTEMS IMPACT (2 of 3)



- **Challenges of the implementation of PPSV23 leading to low coverage among elderly**
 - Direct correspondence [DOH]:
 - *Policy and implementation gaps* – There is a lack of targeted campaigns compared to children or school-based immunization. There is also no centralized digital registry for tracking vaccinated individuals
 - *Procurement and delivery* - procurement and delivery delays
- **Service quality of health centers**
 - Primary data gathering [public health practitioners]: Public health practitioners highlighted the role of barangay health workers in promoting and implementing community health initiatives → encourages elderly to attend routine health check ups
 - Direct correspondence [DOH]:
 - Accuracy and reliability of health record systems – concerns regarding lack of updating of patient vaccination records
 - Review of processes and operational guidelines to improve elderly immunization

HEALTH SYSTEMS IMPACT *(3 of 3)*



- **Need to improve procurement processes**
 - Direct correspondence [DOH]: Evolve to multi-year procurement and improve inventory analysis
- **Need to improve accessibility of services**
 - Primary data gathering [elderly]: Elderly respondents suggested 1) provision of transportation assistance or subsidies for elderly and 2) deploying mobile vaccination units and home-based services
- **Need to improve multimedia communication strategies and awareness campaigns**
 - Primary data gathering [elderly, public health practitioners]: Difficulties of misinformation about pneumococcal vaccines

C6: ELSHI (1 of 3)



RQ6. What are the ethical, legal, social, and health systems implications of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone all elderly adults 60 years old and above?

HTAC Judgment:

Ethical

Equity issues of accessibility and availability of healthcare services and facilities for vaccination were the key issues identified during the focus group discussion (FGD). Respondents support the free pneumococcal vaccination program for senior citizens and adults with comorbidities/risk factors as well as courses of action that will increase vaccine uptake.

Additionally, the lack of a specific guidelines on obtaining informed consent is an ethical issue. The HTA Council highlighted the importance of cascading complete information on potential risks and benefits of vaccination prior to obtaining informed consent when receiving the vaccine among the target population.

Legal

In terms of legal implications, provision of free pneumococcal vaccines for senior citizens is supported by RA 9994 or the Expanded Senior Citizens Act of 2010, and operationalized through the DOH AO 2011-0018 - "Implementing Guidelines on Influenza and Pneumococcal Immunization for Indigent Senior Citizens".

C6: ELSHI (2 of 3)



RQ6. What are the ethical, legal, social, and health systems implications of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone all elderly adults 60 years old and above?

HTAC Judgment:

Social

Based on the primary data gathered, acceptability of pneumococcal vaccination among elderly and at-risk adults is dependent on level of awareness of vaccine safety and benefits, beliefs about pneumonia, influence of social groups (e.g. family, community groups, healthcare workers), cost of services and adequacy of health information dissemination. This is aligned with the literature findings from international studies that social groups influence the adults' healthcare decision-making (Zimmerman 2003 [US]; Kalgee 2017 [US]; Liu, 2014 [China]).

Elderly adult respondents, in particular, have limited knowledge on pneumonia and pneumococcal vaccines. Their social groups help raise awareness and serve as their trusted sources of health advice which contributes to increasing vaccine confidence and willingness. On the other hand, out-of-pocket expenses due to lack of awareness for free vaccination and its limited availability is a key barrier to vaccine uptake. Furthermore, some misconceptions about the cause of pneumonia along with the widespread misinformation in social media and poor health information dissemination contributes to vaccine hesitancy among elderly respondents.

C6: ELSHI (3 of 3)



RQ6. What are the ethical, legal, social, and health systems implications of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone all elderly adults 60 years old and above?

HTAC Judgment:

Health Systems Impact

Based on primary data gathering with public practitioner respondents, there are existing limitations in vaccine supply, cold chain capacity, and human resources, particularly in rural areas. Additionally, direct correspondence with program implementers highlighted that challenges remain in ensuring consistent access due to procurement and delivery delays. They also emphasized the lack of centralized digital registry which is necessary for tracking national immunization coverage.

From the primary data gathering, both public and private practitioner respondents stated that affordability, infrastructure gaps, and low patient awareness contribute to limited vaccine uptake and overall low vaccination coverage. While vaccines are free in some government facilities, indirect costs and inconsistent availability affect access. Private healthcare providers report similar barriers, especially regarding cost and patient hesitancy. Across settings, trust in healthcare providers and localized healthcare information dissemination efforts appear to influence vaccine acceptance, highlighting the complex interplay of systemic and community-level factors in implementing adult immunization programs.

GUIDELINE RECOMMENDATIONS

*Evidence Considered:
Pneumococcal Vaccines for Adults*

INCLUDED GUIDELINES



Scoping of current recommendations on pneumococcal vaccination in adults from the following guidelines.

1	<u>2023 Philippine Periodic Health Examination (PHEX) Guidelines</u>
2	<u>DOH Omnibus Health Guidelines (OHG) for Adults (2023)</u>
3	<u>2020 PSMID CPG on Management and Prevention of Adult CAP</u>
4	<u>Indian CPG / consensus evidence-based recommendation (2019)</u>
5	<u>Advisory Committee on Immunization Practices (ACIP) 2019</u>
6	<u>2016 Saudi Thoracic Society pneumococcal vaccination guidelines (STS, 2016)</u>
7	<u>Australian Immunization Handbook (2021)</u>

GUIDELINES: Elderly Adults (1 of 2)



Guidelines	PPSV23 alone	PCV13	PCV13 followed by PPSV23	PCV15 followed by PPSV23	PCV20 single dose
For healthy persons aged ≥65 years					
DOH OHG for the Elderly (2023)	✓ Recommended	✓ Recommended	No recommendation	✓ Recommended	✓ Recommended
2023 PHEX Guidelines	Not mentioned if alone or in sequence to PCV13	Not mentioned if in sequence to PPSV23	No recommendation	No recommendation	No recommendation
Indian CPG (2019)	✓ Recommended <i>Not mentioned if alone in sequence to PCV13</i>	No recommendation	No recommendation	No recommendation	No recommendation
ACIP, 2019	✓ Recommended	<i>Can be administered based on shared clinical decision-making</i>	✓ Recommended <i>If PCV13 has been given, then give PPSV23 ≥1 year after</i>	No recommendation	No recommendation
For adults aged 65 years or older (immunocompetent with risk factors)					
Indian CPG (2019)	✓ Recommended <i>Not mentioned if alone in sequence to PCV13</i>	No recommendation	<i>Can be administered based on shared clinical decision-making</i>	No recommendation	No recommendation
ACIP, 2019	✓ Recommended	Based on shared clinical decision-making; 1 dose if no previous PCV13 vaccination for those with cochlear implant and CSF leak	✓ Recommended - <u>CSF and cochlear implant</u> : PCV13+PPSV23 (≥8 weeks apart) - <u>Other risk factors</u> : PCV13+PPSV23 (≥1 year apart) <i>Give PPSV23 ≥5 years after any PPSV23 at age <65 years</i>	No recommendation	No recommendation
STS, 2016*	No recommendation	No recommendation	✓ Recommended PCV13+PPSV23 (6-12 months) +PCV13 (5 years after)	No recommendation	No recommendation
For adults aged 65 years or older (immunocompromised)					
Indian CPG (2019)	✓ Recommended <i>Not mentioned if alone in sequence to PCV13</i>	No recommendation	✓ Recommended	No recommendation	No recommendation
ACIP, 2019	No recommendation	✓ Recommended 1 dose if no previous PCV13 vaccination	✓ Recommended PCV13+PPSV23 (≥8 weeks apart) + PPSV23 ≥5 years after any PPSV23 at <65 years	No recommendation	No recommendation
STS, 2016*	No recommendation	No recommendation	✓ Recommended PCV13+PPSV23 (8 weeks apart) +PPSV23 (5 years after)	No recommendation	No recommendation

*Recommendation is for ≥50 years old

GUIDELINES: Elderly Adults (2 of 2)



Guidelines	PPSV23	PCV13	PCV13 followed by 23-valent PPSV	PCV15	PCV15 followed by 23-valent PPSV	PCV20 (single dose or alone)
For healthy and high risk adults aged 50 years and older						
2020 PSMID CPG on Management and Prevention of Adult CAP	Recommended PPSV and PCV for healthy and high risk adults 50 years old and older, however no statement on valency of vaccines. Note: <i>PSMID (2018)</i> recommended sequential administration of the following: <ul style="list-style-type: none"> • PCV13 + PPSV23 • PPSV23 (previously vaccinated at > 50 y.o.) + PPSV23 • PPSV23 (previously vaccinated at >50 y.o.) + PCV13 • PPSV23 (previously vaccinated at <50 y.o.) + PCV13 + PPSV23 					
All non-Indigenous adults at 70 years of age						
Australian Immunization Handbook (2021)	No recommendation	✓ Recommended	No recommendation	✓ Recommended	No recommendation	✓ Recommended
Non-Indigenous adults aged ≥70 years						
Australian Immunization Handbook (2021)	No recommendation	✓ Recommended	No recommendation	✓ Recommended	No recommendation	✓ Recommended

What is the current recommendations from country guidelines on the use of of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone when given to elderly adults 60 years and above?



HTAC Judgment [1 of 2]:

Overall, the HTAC notes that the recommendations across the seven guidelines on pneumococcal vaccines scoped were **varied** depending on age and immune status. In terms of sequential vaccinations, majority of guidelines with recommendation mentioned pneumococcal conjugate vaccines (i.e PCV13, PCV15) as the first dose followed by PPSV23.

A. Older adults

a. Healthy adults aged 65 and older

PPSV23 was recommended by four guidelines – the Department of Health Omnibus Health Guidelines (DOH OHG) for Elderly (2023), Philippine Periodic Health Examination (PHEX) Guidelines (2023), Advisory Committee on Immunization Practices (ACIP, 2019), and Indian Clinical Practice Guidelines (Indian CPG, 2019). Among these, only ACIP explicitly recommended PPSV23 as a single dose regimen. PCV13 is also recommended by the DOH OHG for Elderly (2023) and PHEX (2023) for this population. ACIP (2019) also considers the use of PCV13 based on shared clinical decision-making between physician and patient. In terms of sequential vaccinations, only ACIP (2019) explicitly recommend PCV13+PPSV23 regimen for this population. The DOH OHG (2023) recommended PCV15+PPSV23 but did not explicitly recommend the PCV13+PPSV23 regimen.

b. Immunocompetent older adults with risk factors

Two guidelines - ACIP (2019) and Saudi Thoracic Society (STS) Guidelines (2016) recommended sequential vaccination with PCV13+PPSV23, on the other hand, the Indian CPG (2019) considers this sequential regimen for administration based on shared clinical decision-making. ACIP (2019) also recommended 1-dose PPSV23 for this population, but recommended 1-dose PCV13 specifically for those with cochlear implant and CSF leak and only be administered based on shared clinical decision-making for other risk factors. No recommendations were found for sequential PCV15+PPSV23 vaccination for this population.

What is the current recommendations from country guidelines on the use of of PCV13 in sequence to PPSV23; PCV15 in sequence to PPSV23, or PPSV23 alone when given to elderly adults 60 years and above?



HTAC Judgment [2 of 2]:

c. Immunocompromised older adults

The Indian CPG (2019), ACIP (2019) and STS (2016) recommends the sequential use of PCV13 followed by PPSV23. ACIP (2019) also recommends 1 dose of PCV13 if no previous PCV13 vaccination. No recommendations were found for sequential PCV15+PPSV23 vaccination for this population.

d. General Recommendations for all older adults

Indian CPG (2019) recommended PPSV23 in all adults above 65 years of age. It is unclear however, if it can be given as a single dose or sequential with PCV13. Lastly, PSMID (2020) recommended PPSV and PCV for both healthy and high risk adults 50 years old and older, however there is no statement on valency of vaccines.