HTAC Deliberation for the Preliminary Recommendation on PCV for the Pediatric Population

Evidence considered

DOST

Background and context of PCV assessment and implementation

Context — PCVs included in the PNF

The Philippine National Formulary

Search by Generic name

PNEUMOCOCCAL CONJUGATE VACCINE

Found 1 record

PNEUMOCOCCAL CONJUGATE VACCINE

ATC: J07AL02

Anatomical: Anti-Infectives for systemic use
Therapeutic: Vaccines
Pharmacological: Bacterial Vaccines
Chemical Class: Pneumococcal Vaccines

Technical Specification: (PNF Primary Care | Reserved AMs)

IM > 10-valent (2 mL) Suspension for IM injection in 3 mL Multidose vial (IM) ***(Rx)***

IM > 13-valent 0.5 mL single dose, Suspension for IM injection in 0.5 mL Pre-filled syringe (IM) ***(Rx)***

IM > 13-valent Suspension for IM injection in 2 mL Multidose vial (IM) ***(Rx)***

Indicated for the following minimum serotypes: 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F

Indications:

Immunization of infants and children against Streptococcus pneumoniae infection and invasive diseases caused by serotypes included in the vaccine

Dose:

Contraindication:

Hypersensitivity to any component of the vaccine

Dose Adjustment:

DOST

Context — Procurement history of PCV

	2020	2021	2022	2023
Brand procured	**PCV13 Pfizer**	**PCV10 GSK**	**PCV10 GSK**	**PCV10 GSK**
Number of doses procured	**7,800,000**	**6,500,000**	**2,000,000**	**3,500,000**
Winning bid price (price per dose)	**Php 3,271,632,000 (Php 419.44)** *Ref. DOH DPCB*	**Php 2,243,995,000 (Php 345.23)** *Ref. DOH DPCB*	**Php 631,360,000 (Php 315.68)** *Ref. DOH DPCB*	**Php 972,265,000 (Php 277.79)** *Ref. DOH Website, 2024*

Context — 2020 Recommendation

The HTA Council **recommends the multi-dose vial preparation of pneumococcal conjugate vaccines (PCV)** indicated for the following minimum serotypes: **1, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.** Both PCV10 and PCV13 which are currently authorized by the Philippine FDA on the publication date of this evidence summary represent good value for money, with the potential of reducing pneumococcal diseases in the country. To ensure equity, affordability, and universal vaccine coverage which can only be ensured by obtaining lower vaccine prices, a competitive tendering process is important.

Recommendation letter to OSEC (2020)

PICO

Population	Participants involving healthy children (i.e., children with no pre-existing disease/infection) under 5 years old
Intervention	PCV10-GSK, PCV13, PCV10-SII or PCV15 with at least three doses, with or without co-administration of other vaccines
Comparator	Other vaccines, other PCV brands, placebo, or no vaccination
Outcome	<u>CLINICAL</u> Efficacy: - Invasive pneumococcal disease - Clinical pneumonia - Acute otitis media - Nasopharyngeal carriage - Immunogenicity Safety <u>ECONOMIC</u> - Incremental cost-effectiveness ratio - Budget impact analysis - Household financial impact <u>ELSHI</u> Ethical impact Legal impact Social impact Health systems impact - Impact to burden of pneumococcal disease and serotype distribution - Incidence of AMR- resistant pneumococcus

PCV Products Comparison

	PCV10GSK (Synflorix®)	PCV13 (Prevenar 13®)	PCV10SII (Pneumosil®)	PCV15(Vaxneuvance®)
Generic Names	Pneumococcal nontypeable H. influenzae protein D conjugate vaccine (PHiD CV)	Pneumococcal 13-valent conjugate vaccine	Pneumococcal Polysaccharide conjugate vaccine (10-valent); SIIPL-PCV	Pneumococcal 15-valent conjugate, v114
PHL FDA-approved indications for children	Prevention of IPD, pneumonia, and AOM in the contained serotypes and cross-reactive response against ST19A for children 6 wks to 5 y.o.	Prevention of IPD, pneumonia, and AOM in the contained serotypes for individuals 6 weeks of age and above	Prevention of IPD, pneumonia, and AOM in the contained serotypes in infants and toddlers fro 6 wks up to 2 y.o.	Prevention of IPD, pneumonia, and AOM in the contained serotypes for infants, children and adolescents from 6 wks to 17 y.o.
Dosage Formulation/Strength	1 dose (0.5 mL) contains 1 mcg of Pneumococcal polysaccharide for ST 1, 5, 6B, 7F, 9V, 14, and 23F, and 3 mcgs ST4, 18C and 19 F	1 dose (0.5 mL) contains 2.2 mcg of Pneumococcal polysaccharide for ST 1,3,4, 5, 6A, 6B, 9V, 14, 18C, 19A, 19F, 23F; and 4.4. mcg of ST7F	1 dose (0.5 mL) contains 2 mcg of Pneumococcal polysaccharide for ST 1, 5, 9V, 14, 19A, 19F, 23F, 7F, 6A 2 mcg each; and 4 mcg of ST6B	1 dose (0.5 mL) contains 2 mcg each of polysaccharide ST 1,3,4, 5, 6A, 7F, 9V, 14, 18C,19A, 19F, 22F, 23F, 33F, and 4 mcg of ST6B
Presentation	1-, 2- and, and 4-dose vials; liquid	1- and 4-dose vials; liquid	1- and 5-dose vials; liquid	1-dose prefilled glass syringe
Dose Quantity, Route of Administration	0.5 mL, Intramuscular (IM)	0.5 mL, Intramuscular (IM)	0.5 mL, Intramuscular (IM)	0.5 mL, Intramuscular (IM)
Dose Measurement needed	For MDV, Yes	For MDV, Yes	For MDV, Yes	No
Vaccine vial monitor presence and type	Yes, Type 30	Yes, Type 30	Yes, Type 30	None
Open vial Handling and storage	For MDV. may be kept for use up to 28 days if stored at 2-8° C	For MDV. may be kept for use up to 28 days if stored at 2-8° C	For MDV. may be kept for use up to 28 days if stored at 2-8° C	N/A, Single use
Shelf-life (from date of manufacture)	48 mos, 2-8° C: (1-and 2- dose) 36 mos, 2-8° C: (4- dose)	36 mos, 2-8° C	36 mos, 2-8° C	18 mos, 2-8° C

PCV Products Comparison

	PCV10GSK (Synflorix®)	PCV13 (Prevenar 13®)	PCV10SII (Pneumosil®)	PCV15(Vaxneuvance®)
Cold chain volume per dose	1-dose: 11 .50 cm3 2-dose: 4.80 cm3 4-dose: 2.40 cm3	1-dose: 12.0 cm3 4-dose: 3.5 cm3	1-dose: 14 .06 cm3 5-dose: 3.51 cm3	N/A
Vaccination schedule (based on manufacturer recommendation)	3p +1 OR 2p +1 1st dose: may be given as early as 6 wks of age Booster dose: from 9 mos onwards Interval: 3 primary doses with an interval of at least 1 month between doses and a booster dose at least 6 mos after the last primary dose 2p+1: 2 primary doses given 2 months apart and a booster dose at least 6 mos after the last primary dose	3p +1 OR 2p +1 2 mos, 4 mos, 6 mos, 12-15 mos Can be given as early as 6 wks Interval: 4-8 wks apart with 4th dose given at least 2 mos after the 3rd dose	3p +0 OR 3p +1 6 wks, 10 wks, 14 wks with or w/o booster dose at 9-10 mos or 12-15 mos of age Interval: At least 4 weeks apart with 4th dose given at least 6 mos after the last primary dose	2p +1 OR 3p +1 3-dose regimen: 1st dose-given as early as 6-12 wks 2nd dose- 8 wks later 3rd dose- given approx. 11-15 mos of age 4 dose regimen: 1st dose-given as early as 6-12 wks w/ interval of 4-8 wks between doses in the primary series followed by a 4th dose given approx. 11-15 mos of age and at least 2 mos after the 3rd dose
Co-administration	Can be given concomitantly with any of the following monovalent or combination vaccines: Diphtheria-tetanus-acellular-pertussis vaccine (DTPa), Hepatitis B Vaccine, Inactivated polio vaccine (IPV), H influenzae Type b (Hib), DP whole cells Pertussis vaccine (DTPw), MMR Varicella vaccine, Meningococcal serogroup C conjugate vaccine, Meningococcal serogroups A, C , W-15 and Y conjugate vaccine, OPV, Rotavirus vaccine	Can be given concomitantly with any of the following vaccine antigens, either as monovalent or combination vaccines: *Diphtheria, tetanus, acellular or whole -cell pertussis, Inactivated poliomyelitis vaccine, H influenzae Type b (Hib), Hepatitis A, Hepatitis B, Meningococcal serogroup C , MMR, Varicella vaccine, Rotavirus vaccine*	Can be given concomitantly with any of the following vaccine antigens, either as monovalent or combination vaccines: *Diphtheria, tetanus, whole -cell pertussis, Inactivated or oral poliomyelitis vaccine, H influenzae Type b (Hib), Yellow fever, Measles Vaccine, Rubella vaccine, Rotavirus vaccine*	Can be given concomitantly with any of the following vaccine antigens, either as monovalent or combination vaccines: *Diphtheria, tetanus, pertussis, poliomyelitis vaccine, H influenzae Type b (Hib), Hepatitis A, Hepatitis B, MMR, Varicella vaccine, Rotavirus vaccine*

- DPCB FSCMD and NIP requirement for procurement of vaccine product for the program:
    a. Vaccine vial monitors (VVM)
    b. WHO-prequalification
  - Above requirements not specified in AO or department issuance; reflected in the purchaser's specifications in the procurement documents
  - Multi-dose vial preparations are not required for the NIP.

	PCV13 (Prevenar)	PCV10 GSK (Synflorix)	PCV 10 SII (Pneumosil)	PCV 15 (Vaxneuvance)
Vaccine vial monitor (VVM)	Yes, Type 30*	Yes, Type 30*	Yes, Type 30*	No
WHO prequalification	Yes	Yes	Yes	No

***VVM Type 30:** refers to the vial with high stability used in vaccines*

Price of PCV Vaccines

	Cost (Php)				
	Price per dose	Wastage cost	Storage cost	Total cost per dose	Total cost for 3 doses
PCV10^{GSK}	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
PCV10^{SII}	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
PCV13	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED
PCV15	REDACTED	REDACTED	REDACTED	REDACTED	REDACTED

Total vaccine costs= Total cost for 3 doses of PCV product per person vaccinated x the number to be vaccinated (vaccine coverage rate x population of cohort in 2023)

SAGE Recommendations:

Choice of PCV Product (2019)

- Both **PCV10GSK and PCV13 have substantial impacts** against pneumonia, vaccine-type IPD and NP carriage. There is at present insufficient evidence of a difference in the net impact of the 2 products on overall disease burden. PCV13 may have an additional benefit in settings where disease attributable to serotype 19A or serotype 6C is significant. The choice of product to be used in a country **should be based on programmatic characteristics, vaccine supply, vaccine price, the local and regional prevalence of vaccine serotypes and antimicrobial resistance patterns**.

Dosing Schedule Impact (2019)

- *SAGE therefore recommends administration of PCV in either a 2p+1 or a 3p+0 schedule starting as early as 6 weeks of age and a minimum interval of 4 weeks and a maximum of 8 weeks in the primary series for the 2p+1 schedule, with a booster dose 9–18 months thereafter.*

C1: Responsiveness to Magnitude and Severity

Burden of the Disease *(Wahl et al., 2018)*

Global Data (2015):

- About 3.7 million cases of severe pneumococcal disease in children < 5 y.o.
- Significant portion in developing countries in Africa and Asia
- An estimated 294,000 deaths among < 5 y.o.

Local Data (2015):

- Pneumonia is one of the top 10 leading causes of morbidity and mortality across all age groups
- Estimated deaths among children < 5 y.o.:
  - *3,182* deaths due to *pneumococcal pneumonia*
  - *357* deaths due to *pneumococcal meningitis*

Serotypes in PCV products

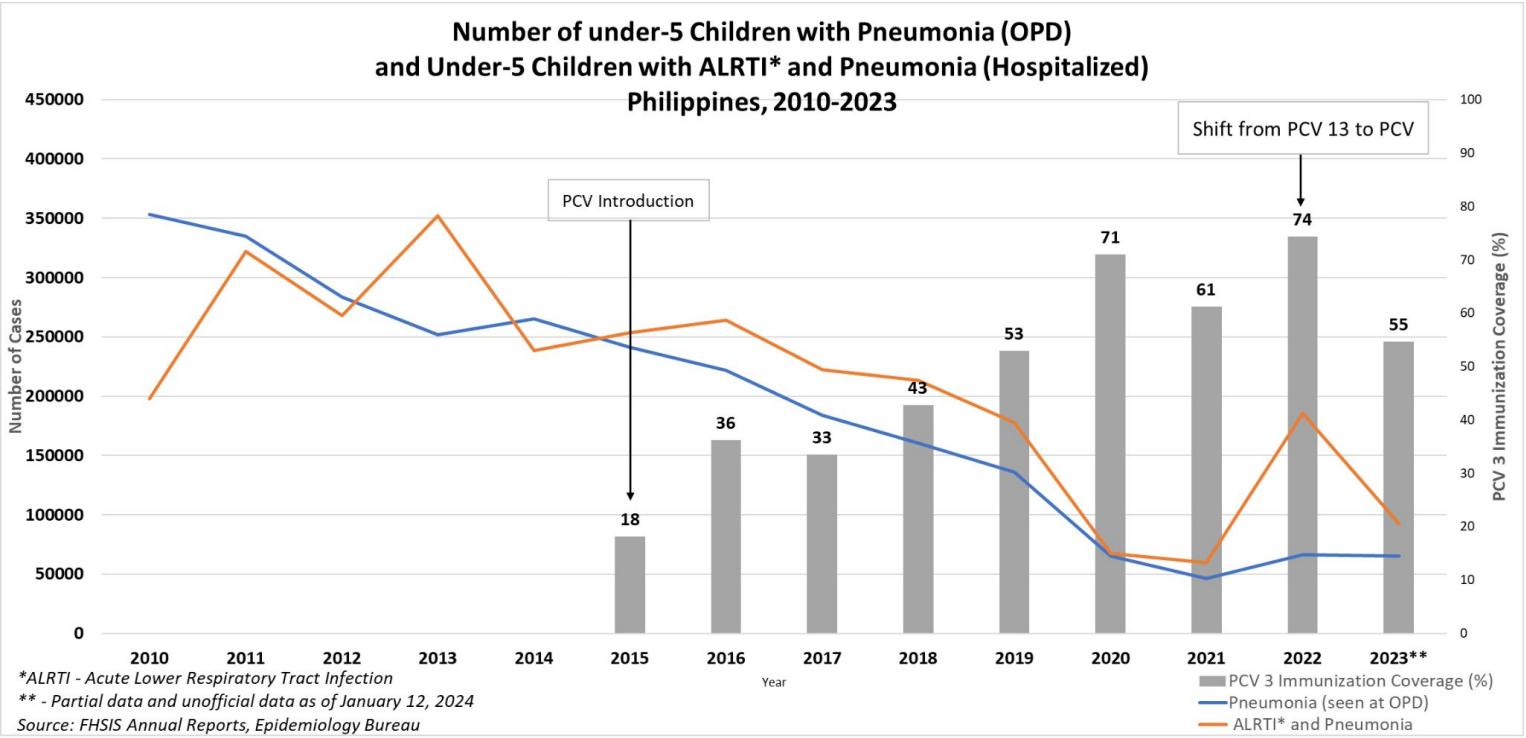
Vaccine	Serotypes (% prevalence) Top 10 most prevalent														
	18C (10%)	19A (7%)	6B (7%)	3 (6%)	23F (6%)	14 (6%)	1 (5%)	5 (4%)	7F (4%)	9V (4%)	4 (3%)	19F (2%)	6A (2%)	22F (1%)	33F (1%)
PCV7	■		■		■	■				■	■	■			
PCV10GSK	■	■	■		■	■	■	■	■	■	■	■			
PCV10SII		■	■		■	■	■	■	■	■		■	■		
PCV13	■	■	■	■	■	■	■	■	■	■	■	■	■		
PCV15	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■

*Shaded boxes indicate serotypes included in the corresponding PCV product
*cross reactivity

PCV use and pneumococcal serotypes (ST) in the country

Most common serotypes	**Pre-PCV vaccination period**	**Post-PCV vaccination period**
	5, 14, 1, 6B and 6A	ST18C and 19A
Biggest decrease in prevalence from pre- to post-PCV period	• 5 (78%)→Present in all • 6A (74%)→Present in PCV10SII, 13&15 • 1 and 14 (50%)→Present in all	
Biggest increase in prevalence from pre- to post-PCV period	• 19A (7x)→Present in PCV10SII, 13&15 with cross-reactivity for PCV10GSK • 3 (6x)→Present in PCV13 &15 • 9A (4x)→Non-vaccine ST (not included in Top10 STs)	
Increase in proportion of non-vaccine serotypes (NVT) from pre-PCV to post-PCV periods	• 27% to 37%	
Limitations	• Relatively small number of isolates reported (passive nature of the surveillance) • Lack of a clinical case definition for the surveillance • Variability in specimen collection, storage and reporting *Note: These are the same limitations of the evidence used during the previous assessment*	

Burden of the Disease: *Philippines*

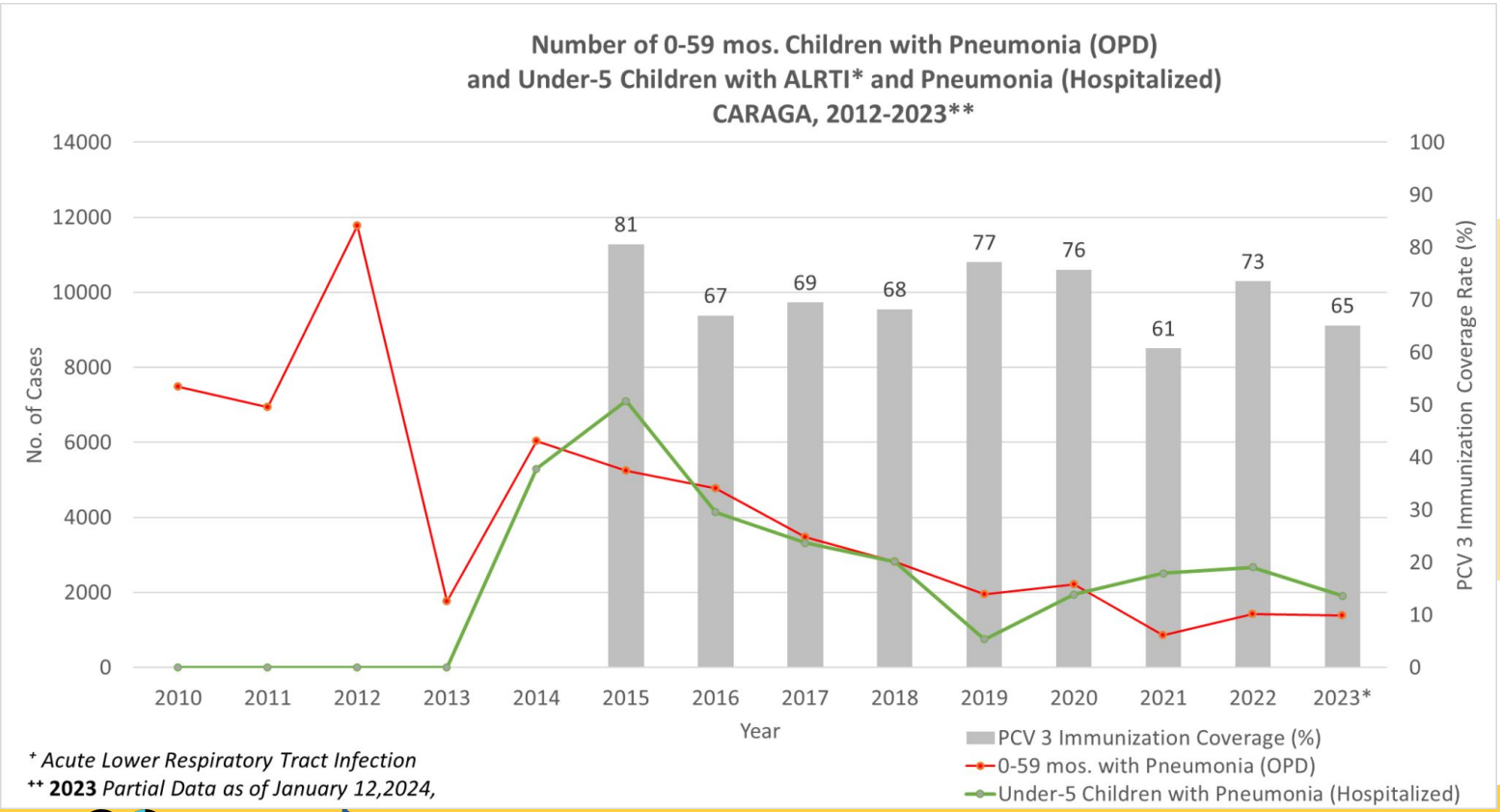


253,588 cases of **hospitalized <u>all-cause</u> pneumonia** and **acute lower respiratory tract infection** (ALRTI) in children <5 y.o. (2015)

There was a spike of hospitalized pneumonia and ALRTI in 2022 but in general, there was a decreasing trend of outpatient pneumonia, hospitalized pneumonia and ALRTI cases from 2017 to 2023.

Note: No data specific for pneumococcal pneumonia

Burden of the Disease: *CARAGA Region [high PCV coverage area]*



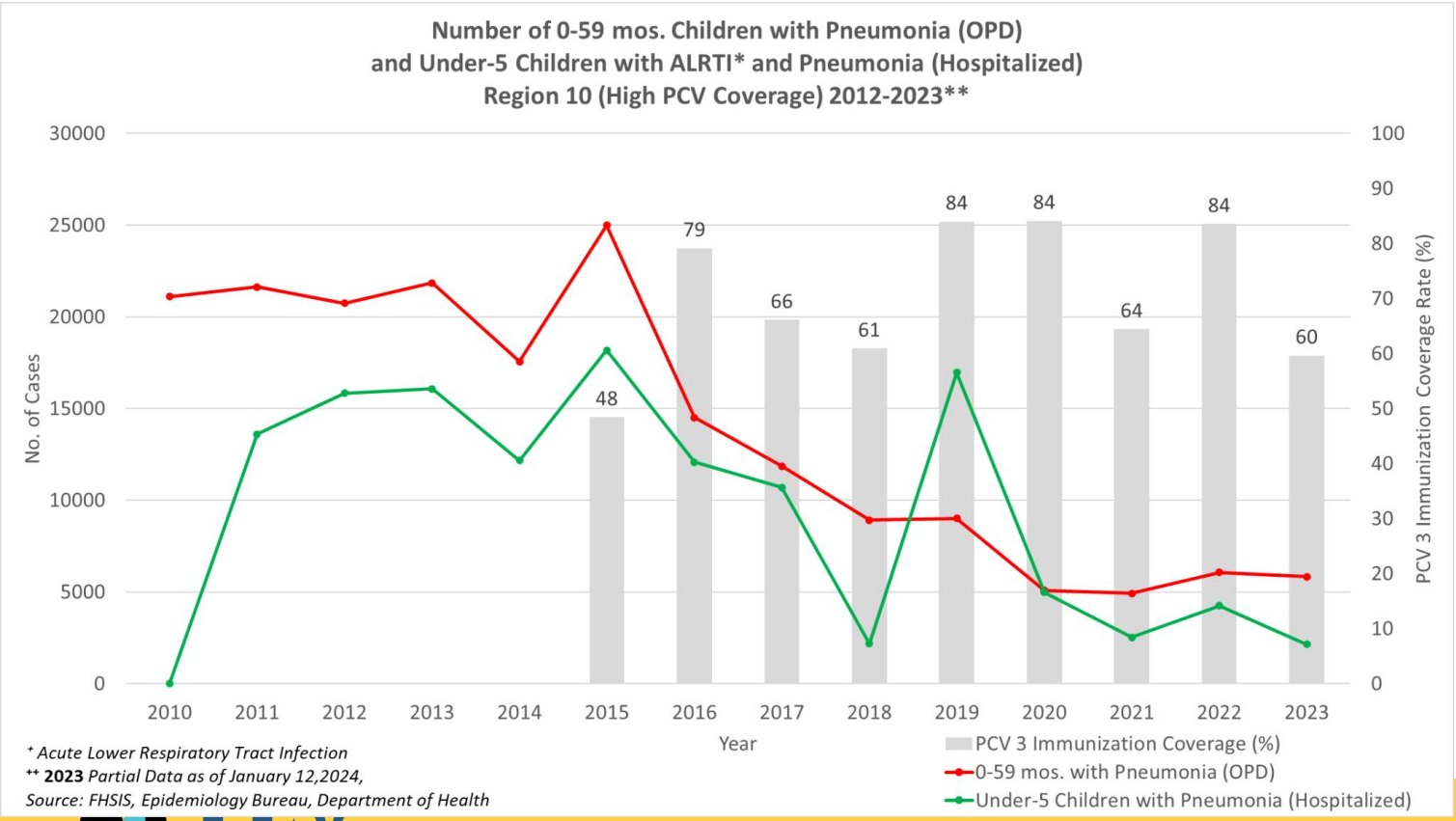
* *Acute Lower Respiratory Tract Infection*
** **2023** *Partial Data as of January 12,2024,*

Decreasing trend of outpatient pneumonia cases from 2017 to 2023, and for hospitalized pneumonia and ALRTI (2017 to 2019) with a gradual increase in 2019 towards 2023.

DOST

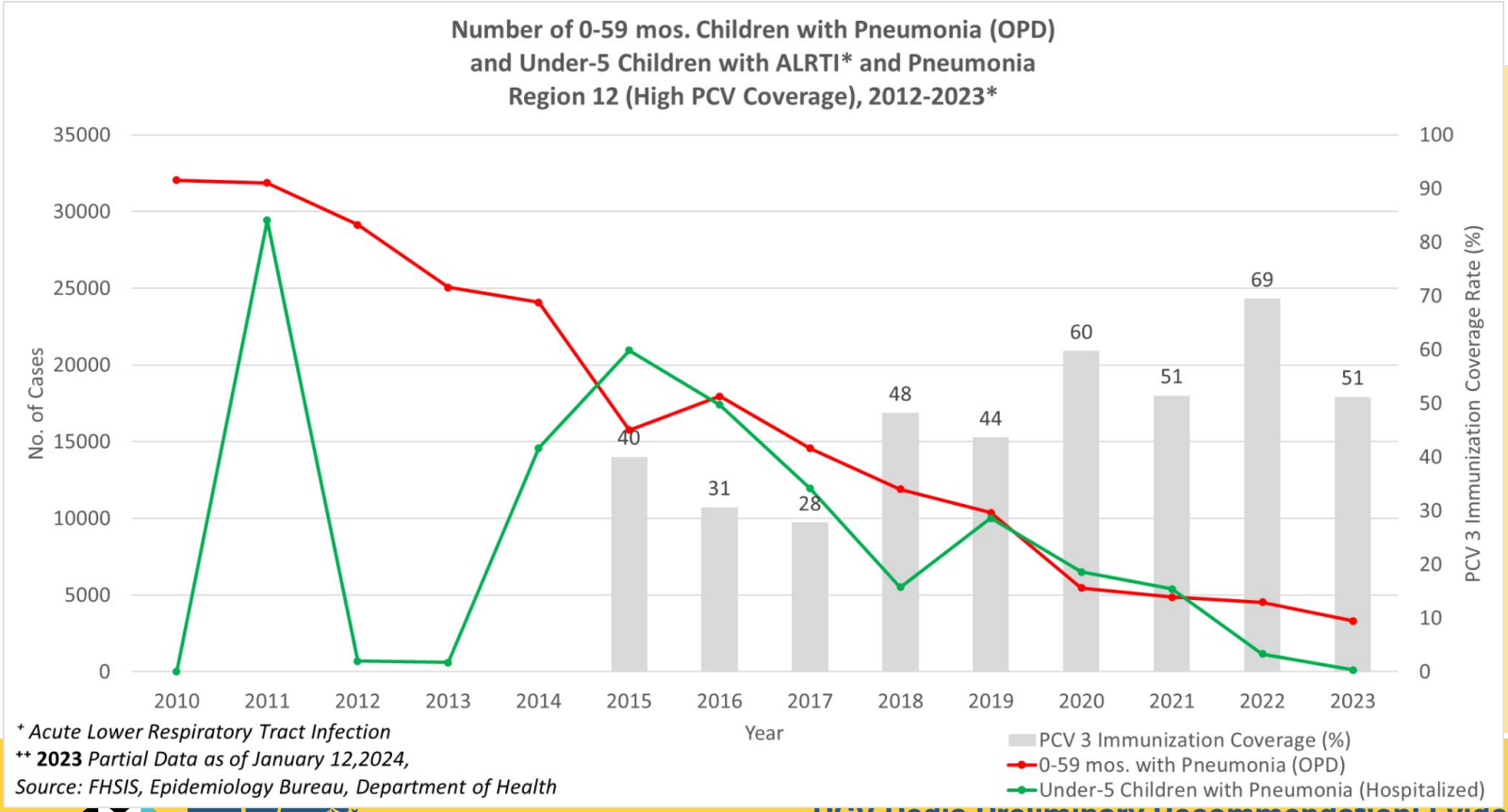
PCV Pedia Preliminary Recommendation: Evidence Considered

Burden of the Disease: *Region 10 (high PCV coverage area)*



Decreasing trend of outpatient pneumonia from 2017 to 2023 while cases of hospitalized pneumonia and ALRTI dropped in 2018 but reached a sharp increase the following year before it declined towards 2023.

Burden of the Disease: *Region 12 (high PCV coverage area)*

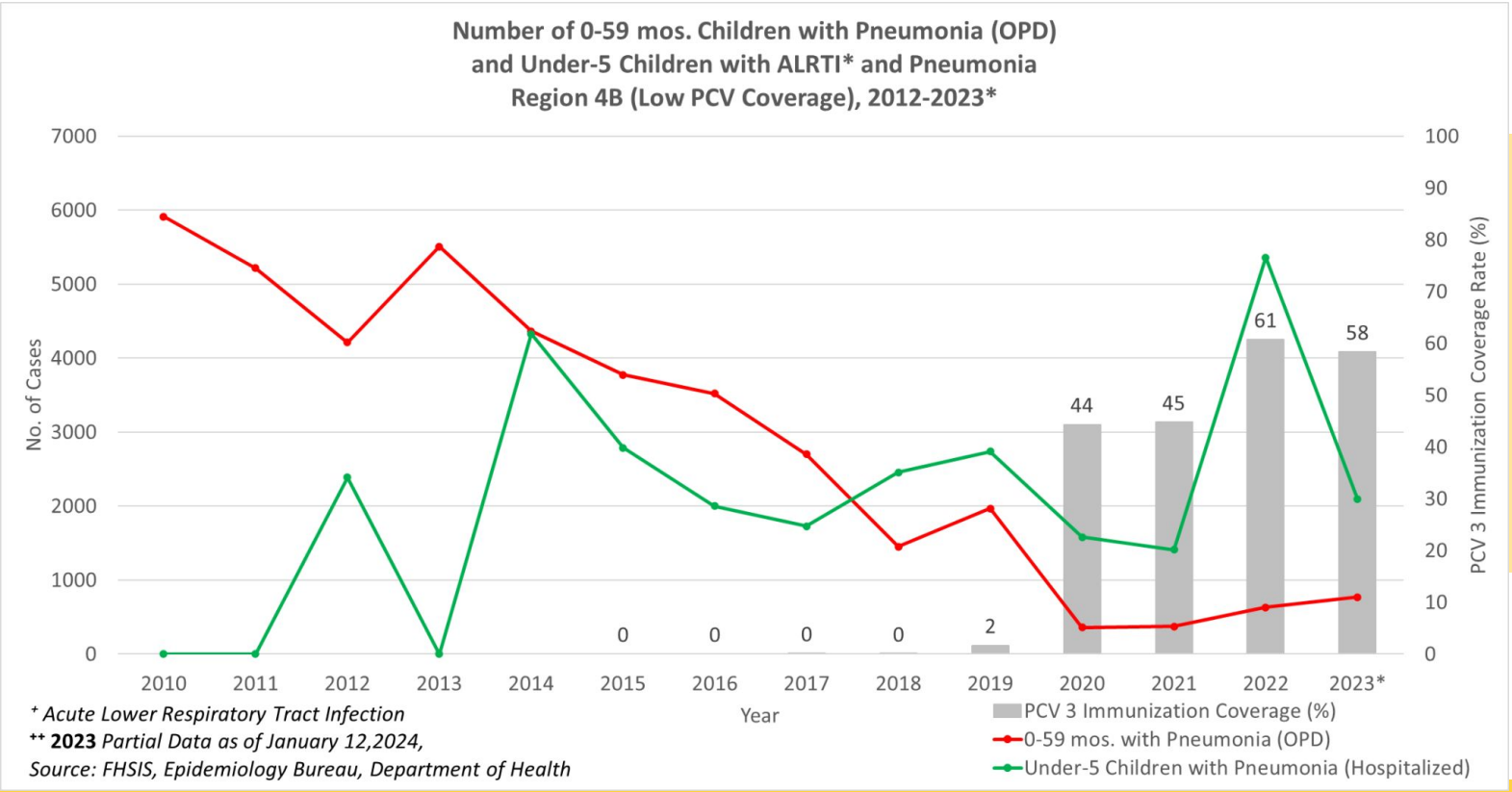


* *Acute Lower Respiratory Tract Infection*
** **2023** *Partial Data as of January 12,2024,*
Source: FHSIS, Epidemiology Bureau, Department of Health

Decreasing trend of outpatient pneumonia cases from 2019-2023.

Hospitalized pneumonia and ALRTI featured exponential increase in 2011 before dropping in 2012, and increasing from 2013 until 2015. From then on, a decreasing trend was seen until 2023.

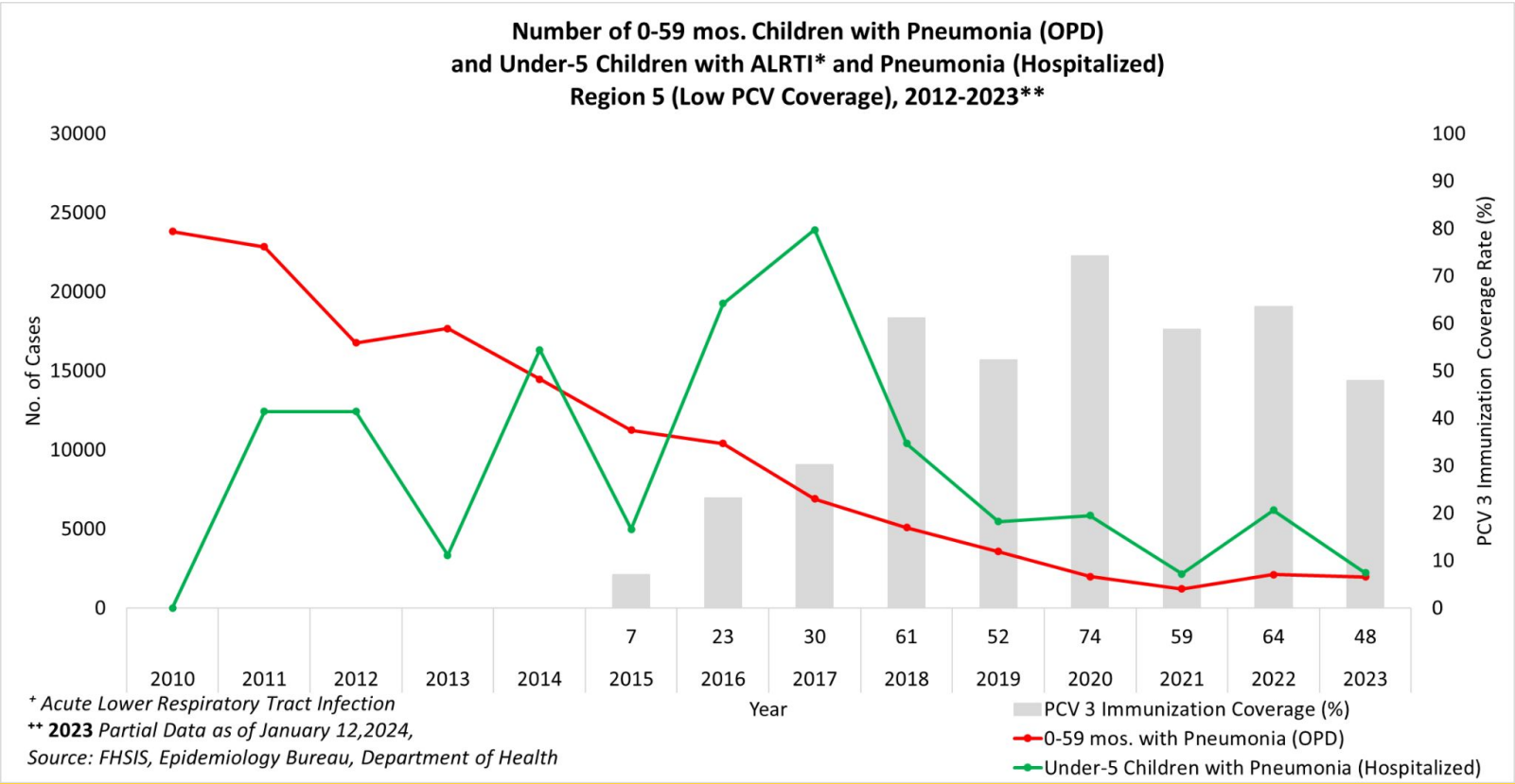
Burden of the Disease: *Region 4B (low PCV coverage area)*



⁺ *Acute Lower Respiratory Tract Infection*
⁺⁺ **2023** *Partial Data as of January 12,2024,*
Source: FHSIS, Epidemiology Bureau, Department of Health

Decreasing trend of outpatient pneumonia cases from 2019 to 2023, and also for hospitalized pneumonia and ALRTI (2019 to 2021) with a sudden spike in 2022 followed by an abrupt decline in 2023.

Burden of the Disease: *Region 5 (low PCV coverage area)*



* *Acute Lower Respiratory Tract Infection*

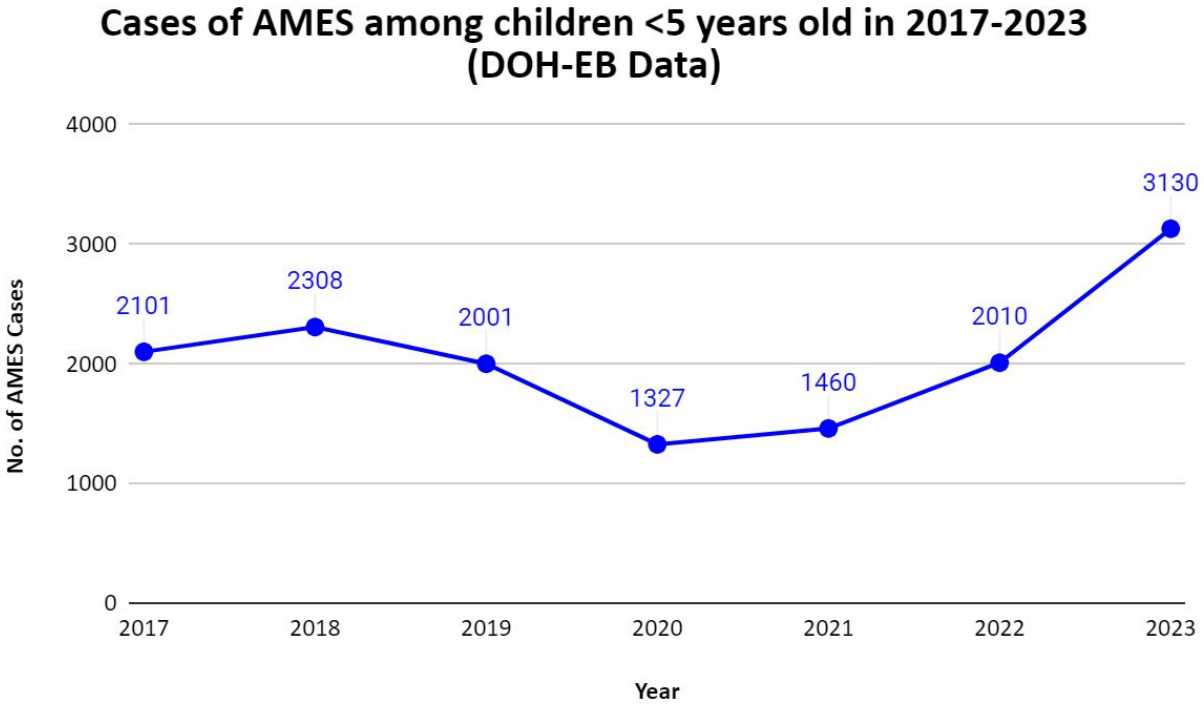
** **2023** *Partial Data as of January 12,2024,*

Source: FHSIS, Epidemiology Bureau, Department of Health

Decreasing trend of outpatient pneumonia cases and hospitalized pneumonia and ALRTI from 2017 to 2023

DOST

Burden of the Disease, *(DOH-EB Data on AMES from **bacterial cause**)*



A decrease in AMES cases from 2018-2020 was seen before gradually increasing from 2020-2023.

Note: No data specific for pneumococcal meningitis

PCV use and pneumococcal serotypes (ST) in the country

Data sources:

***1. Antimicrobial Resistance Surveillance Program (ARSP) of the RITM-DOH**:* Collects routine culture and sensitivity results from 24 sentinel sites

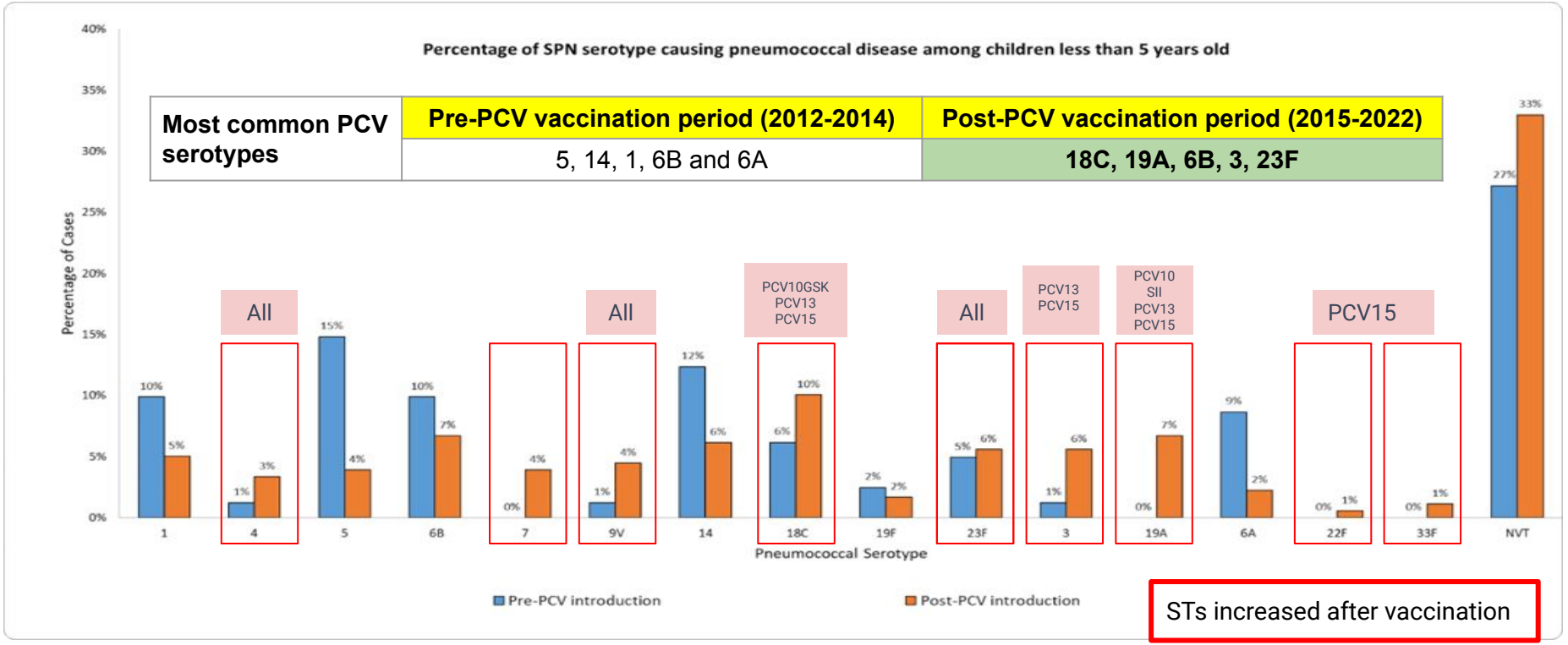
- Isolates from invasive disease specimens (blood and cerebrospinal fluid) as well as noninvasive specimens such as sputum
- Serotyping is done on pneumococcal isolates

***2. Acute Meningitis and Encephalitis Syndrome (AMES) surveillance of the Epidemiology Bureau of the DOH**:* collects data on the etiology of suspected meningitis-encephalitis cases using cerebrospinal fluid specimens.

Figure 1. Regional representation in the ARSP 2022

*From 2021 ARSP Annual Report

PCV use and pneumococcal serotypes (ST) in the country



Percentage of isolates causing vaccine type and non- vaccine type pneumococcal disease in children less than 5 years old, pre and post PCV13 introduction, 2012-2022 (N= 280). *Source: RITM, 2023.*

PCV use and pneumococcal serotypes (ST) in the country

Most common serotypes	**Pre-PCV vaccination period**	**Post-PCV vaccination period**
	5, 14, 1, 6B and 6A	ST18C and 19A
Biggest decrease in prevalence from pre- to post-PCV period	• 5 (78%)→Present in all • 6A (74%)→Present in PCV10SII, 13&15 • 1 and 14 (50%)→Present in all	
Biggest increase in prevalence from pre- to post-PCV period	• 19A (7x)→Present in PCV10SII, 13&15 with cross-reactivity for PCV10GSK • 3 (6x)→Present in PCV13 &15 • 9A (4x)→Non-vaccine ST (not included in Top10 STs)	
Increase in proportion of non-vaccine serotypes (NVT) from pre-PCV to post-PCV periods	• 27% to 37%	
Limitations	• Relatively small number of isolates reported (passive nature of the surveillance) • Lack of a clinical case definition for the surveillance • Variability in specimen collection, storage and reporting *Note: These are the same limitations of the evidence used during the previous assessment*	

Serotypes in PCV products

Vaccine	Serotypes (% prevalence) Top 10 most prevalent														
	18C (10%)	19A (7%)	6B (7%)	3 (6%)	23F (6%)	14 (6%)	1 (5%)	5 (4%)	7F (4%)	9V (4%)	4 (3%)	19F (2%)	6A (2%)	22F (1%)	33F (1%)
PCV7	■		■		■	■				■	■	■			
PCV10GSK	■	■	■		■	■	■	■	■	■	■	■			
PCV10SII		■	■		■	■	■	■	■	■		■	■		
PCV13	■	■	■	■	■	■	■	■	■	■	■	■	■		
PCV15	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■

*Shaded boxes indicate serotypes included in the corresponding PCV product
*cross reactivity

C2: Clinical efficacy, effectiveness and safety

C2.1: Efficacy and effectiveness

Overview of available evidence: Clinical Efficacy and Effectiveness

	PCV10-GSK	PCV13	PCV10-SII	PCV15
Outcome 1: IPD	vs. Hepatitis B vaccine, no vaccination	vs. no vaccination	None	None
	RCT (k=1) • Palmu, 2013 *Observational (k=5)* • Savulescu, 2022 (ST19A) • Domingues, 2014 • Jokinen, 2015 (ST3,ST6A,ST19A) • Rinta-Kokko, 2018 (ST6A,ST19A) • Brandileone, 2018 (ST3,ST6A,ST19A)	*RCT (k=0)* *Observational (k=1)* • Savulescu, 2022 (ST3, ST6A, ST19A) • Varon, 2015 • Moore, 2016		
	vs. PCV7	vs. PCV7		
	RCT (k=0) *Observational (k=1)* • Naucler, 2017 (ST3, ST6A, ST19A)	*SR (k=1)* • Sings, 2018 (ST3) *RCT (k=0)* *Observational (k=6)* • Waight, 2015 • Jayasinghe, 2017 • Naucler, 2017 (ST3, ST6A, ST19A) • Varon, 2015 ((ST3, ST6A, ST19A) • Picazo, 2019 (ST6A,ST19A) • Van der Linden, 2016 (ST6A,ST19A)		

Overview of available evidence: Clinical Efficacy and Effectiveness

Outcome 2: Clinical Pneumonia	**PCV10-GSK**	**PCV13**	**PCV10-SII**	**PCV15**
	vs. Hepatitis B vaccine, no vaccination	vs. no vaccination, PCV7	None	None
	SR (k=1) • Alicino, 2017 RCT (k=1) • Kilpi, 2018 Observational (k=0)	*SR (k=1)* • Alicino, 2017 *Observational (k=1)* • Becker-Dreps, 2014		
Outcome 3: Acute Otitis Media	**PCV10-GSK**	**PCV13**	**PCV10SII**	**PCV15**
	vs. other vaccines	vs. PCV7	None	None
	RCT (k=2) • Vesikari, 2016 • Saez-Llorens, 2017	*Observational (k=1)* • Pichichero, 2018 (ST3,ST6A, ST19A)		
		vs. no vaccine		
		Observational (k=1) • Kawai, 2018		

Overview of available evidence: Clinical Efficacy and Effectiveness

	PCV10-GSK	PCV13	PCV10-SII	PCV15
Outcome 4: Nasopharyngeal Carriage	vs. Other vaccine, no vaccination	vs. no vaccination	None	None
	RCT (k=2) • Temple, 2021 • Saez-Llorens, 2017 (ST6A,ST19A)	*RCT (k=1)* • Temple, 2021 *Observational (k=3)* • Heinsbroek, 2018 • Britton, 2021		
	vs. PCV7	vs. PCV7		
	Observational (k=1) • Bosch, 2015	*RCT(k=1)* • Dagan, 2013 (ST3, ST6A, ST19A) *Observational (k=1)* • Kaur, 2016		

Summary of Evidence for Clinical Efficacy and Effectiveness

Consistently favors vaccine
inconsistent direction
nonsignificant difference
✔ = number of studies
X = no evidence
S=significant; NS=non-significant

- No study comparing any of the vaccines to each other for the ff outcomes: IPD, AOM, Pneumonia
- 1 study comparing PCV10 and PCV13 with each other in terms of nasopharyngeal carriage
- No studies on clinical outcomes for PCV10SII and PCV15

Clinical Outcomes	PCV10-GSK	PCV13	PCV10-SII	PCV15
IPD	✔✔✔✔✔✔✔ *(Case-control=2, Cohort=4, RCT=1)* *VERY LOW to HIGH*	✔✔✔✔✔✔✔ *(Cohort=5, Case-control=2)* *VERY LOW to HIGH*	X	X
IPD due to ST3 *Present in PCV13&PCV15*	✔✔✔ (Cohort=3) *VERY LOW*	✔✔✔✔ *(Case-control=2 S, Cohort=2 NS)* *VERY LOW to LOW*	X	X
IPD due to ST6A *Present in PCV13, PCV10-SII, & PCV15*	✔✔✔✔ (Cohort=4, [2S, 2NS]) *VERY LOW*	✔✔✔✔ *(Case-control=1 S, Cohort=3[2NS, 1S])* *VERY LOW to MODERATE*	X	X
IPD due to ST19A *(Present in PCV13, PCV-10SII, & PCV15, PCV10-GSK with cross-reactivity)*	✔✔✔✔✔ *(Cohort=4 [1 NS, 3S], Case-control=1NS)* *VERY LOW*	✔✔✔ *(Case-control=1S, Cohort=2 [1NS, 1S])* *VERY LOW to LOW*	X	X
Pneumonia	✔ *(RCT=1), MODERATE*	✔ *(Cohort = 1), VERY LOW*	X	X
	✔ *(SR=1) *Intervention: PCV10/PCV13, VERY LOW*			
AOM	✔✔ *(RCT=2), MODERATE*	✔✔ *(Cohort=2[1S, 1NS]), VERY LOW to LOW*	X	X
AOM due to ST3 *Present in PCV13&PCV15*	X	✔ *(Cohort=1), VERY LOW*	X	X
AOM due to ST6A *Present in PCV13, PCV10-SII, & PCV15*	X	✔ *(Cohort=1), VERY LOW*	X	X
AOM due to ST19A *Present in PCV13, PCV10SII, & PCV15, PCV10-GSK with cross-reactivity)*	X	✔ *(Cohort=1), VERY LOW*	X	X

Summary of Evidence for Clinical Efficacy and Effectiveness

Consistently favors vaccine
inconsistent direction
nonsignificant difference
✔ = number of studies
X = no evidence
S=significant; NS=non-significant

- No study comparing any of the vaccines to each other for the ff outcomes: IPD, AOM, Pneumonia
- 1 study comparing PCV10 and PCV13 with each other in terms of nasopharyngeal carriage
- No studies on clinical outcomes for PCV10SII and PCV15

Clinical Outcomes	PCV10-GSK	PCV13	PCV10-SII	PCV15
NP Carriage	✔✔✔ *(RCT= 2[1S, 1NS], Cohort=1NS/S)* *VERY LOW to MODERATE*	✔✔✔✔✔ *(RCT= 2NS, Cohort=3[2S,1NS])* *VERY LOW to HIGH*	X	X
	✔ *(RCT= 1) *Intervention: PCV10 vs PCV13* *LOW*			
NP Carriage *due to ST3* *Present in PCV13& PCV15*	X	✔ *(RCT= 1)* *MODERATE*	X	X
NP Carriage *due to ST6A* *Present in PCV13, PCV10-SII, & PCV15*	✔ *(RCT= 1)* *LOW*	✔ *(RCT= 1)* *HIGH*	X	X
NP Carriage *due to ST19A* *Present in PCV13, PCV10-SII, PCV15, PCV10-GSK with cross-reactivity*	✔ *(RCT= 1)* *LOW*	✔ *(RCT= 1)* *HIGH*	X	X

C2.2: Immunogenicity

Overview of available evidence: Immunogenicity

Outcome	PCV10-GSK	PCV13	PCV10-SII	PCV15
Outcome 1: Against ST3 ***Present in PCV13, PCV15***	VS PCV13 • Pomat, 2019 • Temple, 2019	VS PCV7 • Payton, 2013 • Amdekar, 2013 • Huang, 2012 • Weckx, 2012 • Kieninger, 2010 • Snape, 2010 • Yeh, 2010 • Esposito, 2010 • Bryant, 2010 See studies VS PCV10-GSK See studies VS PCV15		VS PCV13 • Suzuki, 2023 • Martinon-Torres, 2023 • Benfield, 2023 • Lupinacci, 2023
Outcome 2: Against ST6A ***Present in 10-SII, PCV13, PCV15***	VS PCV13 • Pomat, 2019 • Temple, 2019 VS PCV7 • Vesikari, 2009 • Wysocki, 2009 See studies VS PCV10-SII	VS PCV7 • Payton, 2013 • Amdekar, 2013 • Huang, 2012 • Weckx, 2012 • Kieninger, 2010 • Snape, 2010 • Yeh, 2010 • Esposito, 2010 • Bryant, 2010 See studies VS PCV10-GSK See studies VS PCV10-SII See studies VS PCV15	VS PCV10-GSK • Clarke 2021 • Adigweme, 2023 • PH3 India RCT VS PCV13 • Clarke 2020 • Adigweme, 2023 • PH3 India RCT	

Overview of available evidence: Immunogenicity

Outcome	PCV10-GSK	PCV13	PCV10-SII	PCV15
Outcome 3: Against ST19A ***(with cross-reactivity)*** ***Present in 10-SII, PCV13, PCV15***	VS PCV13 • Pomat, 2019 • Temple, 2019 VS PCV7 • Bermal, 2009 (PHL) • Bermal, 2009 (Poland) • Vesikari, 2009 • Wysocki, 2009 See studies VS PCV10-SII	VS PCV7 • Payton, 2013 • Amdekar, 2013 • Huang, 2012 • Weckx, 2012 • Kieninger, 2010 • Snape, 2010 • Yeh, 2010 • Esposito, 2010 • Bryant, 2010 See studies VS PCV10-GSK See studies VS PCV10-SII See studies VS PCV15	VS PCV10-GSK • Clarke 2021 • Adigweme, 2023 • PH3 India RCT VS PCV13 • Clarke 2020 • Adigweme, 2023 • PH3 India RC	VS PCV13 • Suzuki, 2023 • Martinon-Torres, 2023 • Benfield, 2023 • Lupinacci, 2023
Outcome 4: Against ST22F/33F ***Present in PCV15***		See studies vs PCV15		VS PCV13 • Suzuki, 2023 • Martinon-Torres, 2023 • Benfield, 2023 • Lupinacci, 2023

Overview of available evidence: Immunogenicity

Outcome 5: Against PCV shared STs *Present in all*	PCV10-GSK	PCV13	PCV10-SII	PCV15
Against ST18C **Against ST6B** **Against ST23F** **Against ST14** **Against ST1**	VS PCV7 • Bermal, 2009 (PHL) • Bermal, 2009 (Poland) • Vesikari, 2009 • Wysocki, 2009 VS PCV13 • Pomat, 2019 • Temple, 2019	VS PCV7 • Kieninger, 2010 • Bryant, 2010 • Yeh, 2010 • Payton, 2013 • Esposito, 2010 • Weckx, 2012 • Huang, 2012 • Amdekar, 2013 • Snape, 2010 See studies VS PCV10GSK See studies VS PCV10-SII See studies VS PCV15	VS PCV10-GSK • Clarke 2021 • Adigweme, 2023 • PH3 India RCT VS PCV13 • Clarke 2020 • Adigweme, 2023 • PH3 India RCT	VS PCV13 • Suzuki, 2023 • Martinon-Torres, 2023 • Benfield, 2023 • Lupinacci, 2023

Overview of available evidence: **Immunogenicity**

Outcome 5: Against PCV shared STs *Present in all*	PCV10-GSK	PCV13	PCV10-SII	PCV15
Against ST5	VS PCV7 • Vesikari, 2009 • Wysocki, 2009 • VS PCV13 • Pomat, 2019 • Temple, 2019	VS PCV7 • Kieninger, 2010 • Bryant, 2010 • Yeh, 2010 • Payton, 2013 • Esposito, 2010 • Weckx, 2012 • Huang, 2012 • Amdekar, 2013 • Snape, 2010 See studies VS PCV10GSK See studies VS PCV10SII See studies VS PCV15	VS PCV10-GSK • Clarke 2021 • Adigweme, 2023 • PH3 India RCT VS PCV13 • Clarke 2020 • Adigweme, 2023 • PH3 India RCT	VS PCV13 • Suzuki, 2023 • Martinon-Torres, 2023 • Benfield, 2023 • Lupinacci, 2023
Against ST7F				
Against ST9V				
Against ST4		VS PCV7 • Kieninger, 2010 • Bryant, 2010 • Yeh, 2010 • Payton, 2013 • Esposito, 2010 • Weckx, 2012 • Huang, 2012 • Amdekar, 2013 See studies VS PCV10GSK See studies VS PCV15		

DOST

Key Findings on the Immunogenicity of PCV products

All PCV products are equivalent
Some PCV products are equivalent, the rest have no studies
Some PCV products are equivalent, some have lower % responders
With inconclusive findings

Serotype	Prevalence (%)	Present in PCV…	Key findings
18C	10	*PCV10-GSK, PCV13, PCV15, PCV7* *Not in PCV10SII*	***No data for PCV10SII; the rest not different*** • PCV10GSK = PCV7 (k=4) • PCV13 = PCV7 (k=9) • PCV10GSK = PCV13 (k=2) • PCV13 = PCV15 (k=4) • *PCV10SII: No studies vs any PCVs*
19A	7	*PCV13,PCV10-SII, PCV15* *Not in PCV10GSK but with cross-rx*	***All four PCVs are not different*** • PCV7 ≤ PCV10GSK and PCV13 (k=4 for PCV10GSK, k=9 for PCV13) • PCV10GSK = PCV13 (k=2) • PCV10SII = PCV13 (k=3) • PCV10SII ≥ PCV10GSK (k=3) • PCV15 = PCV13 (k=4)
6B	7	All	***PCV10SII at a disadvantage; the rest are generally not different*** • PCV10GSK ≤ PCV7 (k=4) • PCV7 ≥ PCV13 (k=9) • PCV10GSK = PCV13 (k=2) • PCV10SII ≤ PCV13 and PCV10GSK (k=3 for PCV13, k=3 for PCV10GSK) • PCV15 = PCV13 (k=4)
3	6	*PCV13, PCV15*	***PCV13 had greater % responders than PCV10GSK. PCV15 is noninferior to PCV13*** • No studies for PCV10GSK vs PCV7 and PCV13 • PCV7 ≤ PCV13 (k=9) • PCV10GSK < PCV13 (k=2) • PCV10GSK has lower mean titers compared to PCV13 (at 4 months) • PCV15 = PCV13 (k=4)

Key Findings on the Immunogenicity of PCV products

All PCV products are equivalent
Some PCV products are equivalent, the rest have no studies
Some PCV products are equivalent, some have lower % responders
With inconclusive findings

Serotype	Prevalence (%)	Present in PCV…	Key findings
23F	6	All	***All PCVs are generally not different but PCV10SII is inferior to PCV13 in 1 study*** • PCV10GSK = PCV7, PCV13, PCV10SII (k=4 for PCV10GSK, k=3 for PCV10SII, k=2 for PCV10GSK vs PCV13) • PCV10SII ≤ PCV13 (k=3) • PCV13 = PCV7 (k=9) • PCV15 = PCV13 (k=4)
14	6	All	***All four PCVs are not different*** • PCV7 = PCV10GSK = PCV13 = PCV10SII = PCV15 (k=4 for PCV10GSK, k=9 for PCV13, k=3 for PCV10SII, k=4 for PCV15)
1	5	*PCV10GSK, PCV13, PCV10SII, PCV15*	***All four PCVs are not different*** • PCV10GSK and PCV13 ≥ PCV7 • PCV10GSK = PCV10SII = PCV13 • PCV13 = PCV15 ST1 (k=4 for PCV10GSK, k=9 for PCV13, k=3 for PCV10SII, k=4 for PCV15) ST5, 7F (k=2 for PCV10GSK, k=9 for PCV13, k=3 for PCV10SII, k=4 for PCV15)
5	4	*PCV10GSK, PCV13, PCV10SII, PCV15*	
7F	4	*PCV10GSK,PCV13, PCV10SII,PCV15*	
9V	4	All	***All four PCVs are not different*** • PCV7 = PCV10GSK = PCV13 = PCV10SII = PCV15 (k=2 for PCV10GSK, k=9 for PCV13, k=2 for PCV10GSK vs PCV13, k=3 for PCV10SII, k=4 for PCV15)

Key Findings on the Immunogenicity of PCV products

All PCV products are equivalent
Some PCV products are equivalent, the rest have no studies
Some PCV products are equivalent, some have lower % responders
With inconclusive findings

STs not included in the 10 most prevalent STs	Prevalence (%)	Present in PCV…	Key findings
4	3	*PCV10-GSK, PCV13, PCV15, PCV7* *Not in PCV10SII*	***No data for PCV10SII; the rest not different*** • PCV10GSK = PCV7 (k=4) • PCV7 = PCV10GSK = PCV13 = PCV15 • No studies for PCV10SII vs other PCVs (k=2 for PCV10GSK, k=9 for PCV13, k=2 for PCV10GSK vs PCV13, k=4 for PCV15)
6A	2	PCV10 SII, PCV13, PCV15 *Not in PCV10GSK*	***PCV15 and PCV13 are not different, PCV10SII vs PCV13 inconsistent*** • PCV10GSK< PCV7 (k=2) • PCV13 ≥ PCV7 (k=9) • PCV15 = PCV13 (k=4) • PCV10SII ≥ PCV10GSK (k=3) • PCV10SII <, =, or > PCV13 *[inconsistent evidence] (k=3)* • *No studies comparing PCV10SII and PCV15*
22F	1	*PCV15*	**PCV15 is superior to PCV13** PCV15 > PCV13 (k=3)
33F	1	*PCV15*	**PCV15 is superior to PCV13** PCV15 > or non-inferior to PCV13 (k=3)

C2.3: Clinical Safety

Overview of available evidence: **Safety**

Outcome	PCV10-GSK	PCV13	PCV10-SII	PCV15
Outcome 1: Local AEs	VS unspecified comparator • Silfverdal, 2017	VS PCV7 • Thompson, 2013	VS PCV10-GSK • Clarke, 2021 • Adigweme, 2023 VS PCV13 • Clarke, 2020 • Adigweme, 2023	
Outcome 2: Solicited general AEs/systemic AEs	VS unspecified comparator • Silfverdal, 2017	VS PCV7 • Thompson, 2013	VS PCV10-GSK • Clarke, 2021 • Adigweme, 2023 VS PCV13 • Clarke, 2020 • Adigweme, 2023	
Outcome 3: ≥1 AE				VS PCV13 • Suzuki, 2023 • Martinon-Torres, 2023 • Benfield, 2023 • Lupinacci, 2023 • Banniettis, 2022 • Banniettis, 2023

Overview of available evidence: **Safety**

Outcome	PCV10-GSK	PCV13	PCV10-SII	PCV15
Outcome 4: Vaccine related AE/ Treatment-emergent AE				VS PCV13 • Suzuki, 2023 • Martinon-Torres, 2023 • Benfield, 2023 • Lupinacci, 2023 • Banniettis, 2022 • Banniettis, 2023
Outcome 5: Serious AEs	VS unspecified comparator • Silfverdal, 2017	VS PCV7 • Thompson, 2013	VS PCV10-GSK • Clarke, 2021 • Adigweme, 2023 VS PCV13 • Clarke, 2020 • Adigweme, 2023	
Outcome 6: Deaths	VS unspecified comparator • Silfverdal, 2017	VS PCV7 • Thompson, 2013	VS PCV10-GSK • Clarke, 2021 VS PCV13 • Clarke, 2020 • Adigweme, 2023	VS PCV13 • Suzuki, 2023 • Martinon-Torres, 2023 • Benfield, 2023 • Lupinacci, 2023 • Banniettis, 2022 • Banniettis, 2023

Summary of Evidence for Clinical Safety

Safety Outcomes	PCV10-GSK	PCV13	PCV10-SII	PCV15
Solicited Local Adverse Events	✔ (vs unspecified comparator) (1 SR: Non-RCTs, k=21) *Very Low* Incidence of local AES higher after booster than after primary vaccination. Most frequently reported: redness after primary and pain after booster vaccination.	✔ (vs PCV7) (SR: RCTs, k=13) *Moderate* Rates of tenderness, swelling, redness after any dose were similar between PCV13 and PCV7	✔✔ (vs PCV10-GSK) (RCTs=2) RR 0.941 (0.766, 1.156) *Low* ✔✔ (vs PCV13) RR 1.093 (0.783, 1.525) (RCTs=2) *Low*	
Solicited Systemic AEs	✔ (vs unspecified comparator) (1 SR: Non-RCTs, k=21) *Very Low* Most frequently reported solicited general AE: irritability, Grade-3 fever(>40.0°C): 0.1% after primary vaccination. Other grade-3 solicited general AEs were reported after no more than 3.9% of primary doses	✔ (vs PCV7) (SR: RCTs, k=13) *Moderate* Rates of fever (most were mild), decreased appetite, irritability, sleep disturbances were similar between PCV13 and PCV7	✔✔ (vs PCV10-GSK) (RCTs=2) RR 0.969 (0.777, 1.210) *Low* ✔✔ (vs PCV13) (RCTs=2) RR 0.966 (0.685, 1.360) *Low*	
>1 AE				✔✔✔✔✔ (vs PCV13) (RCTs=5) RR 1.00 (0.99, 1.01) *High*

Summary of Evidence for Clinical Safety

Safety Outcomes	PCV10-GSK	PCV13	PCV10-SII	PCV15
Unsolicited AEs	✔ (vs unspecified comparator) (1 SR: Non-RCTs, k=21) *Very Low* Most common: nasopharyngitis	✔ (vs PCV7) (1 SR: RCTs, k=13) *Moderate* 65.6% vs. 64.7%		
Vaccine related AEs	✔ (vs unspecified comparator) (1 SR: Non-RCTs, k=21) *Very Low* Most common: pyrexia	✔ (vs PCV7) (1 SR: RCTs, k=13) *Moderate* 5.2% vs 6.6% Pyrexia and injection site reactions		✔✔✔✔✔ (vs PCV13) (RCTs=5) RR 1.00 (0.99, 1.01) **High**
Serious AEs			✔✔ (vs PCV10-GSK) (RCTs=2) RR 1.031 (0.639, 1.663) *Low* ✔✔ (vs PCV13) (RCTs=2) RR 2.00 (0.885, 4.521 *Low* 2-6% of PCV10SII (most common: bronchiolitis and gastroenteritis), none vaccine related	✔✔✔✔✔ (vs PCV13) (RCTs=5) RR 1.03 (0.88, 1.19) *Moderate* Vaccine-related SAEs: 4 in PCV13 (3 pyrexia, 1 febrile seizure), 5 in PCV15 (4 pyrexia, 1 non-febrile seizure)

Summary of Evidence for Clinical Safety

Safety Outcomes	PCV10-GSK	PCV13	PCV10-SII	PCV15
Serious AEs (including deaths)	✔ (vs unspecified comparator) (1 SR: Non-RCTs, k=21) *Very Low* Nonfatal SAE rate: 11.3%, 0.06 (14% causally related) 21 deaths (0.09%), 1 causally related: sudden death of a 6-week-old HIV-negative child - possible aspiration or smothering	✔ (vs PCV7) (1 SR: RCTs, k=13) *Moderate* **SAEs (vaccine-related):** 0.13% (1 *febrile convulsion and pyrexia, 1 pyrexia, 1 bronchitis, and 1 inconsolable crying, 1 allergy, 1 bronchiolitis)* vs 0.18% (2 *febrile convulsion, 1 infantile spasms, 1 nephroblastoma, and 1 pyrexia)* **Death:** 0.063% vs 0.036% - all SIDS; unrelated to vaccine		
Deaths			✔ (vs PCV10GSK) (RCTs=1) *Low* ✔ (vs PCV113) (RCTs=2) *Low* 2 deaths in the PCV10SII group **were not vaccine-related**	✔✔✔✔✔ (vs PCV13) (RCTs=5) Death RR 0.97 (0.16, 5.81) *Moderate* All 5 deaths in the trial **were not vaccine-related**

C3: Cost Effectiveness

Methodology

Overview:

- Markov model adapted from Kulpeng (2013)using the TreeAge software was used to calculate and compare costs and health outcomes of the following:

(a) $PCV10^{GSK}$ versus ‘no vaccination’

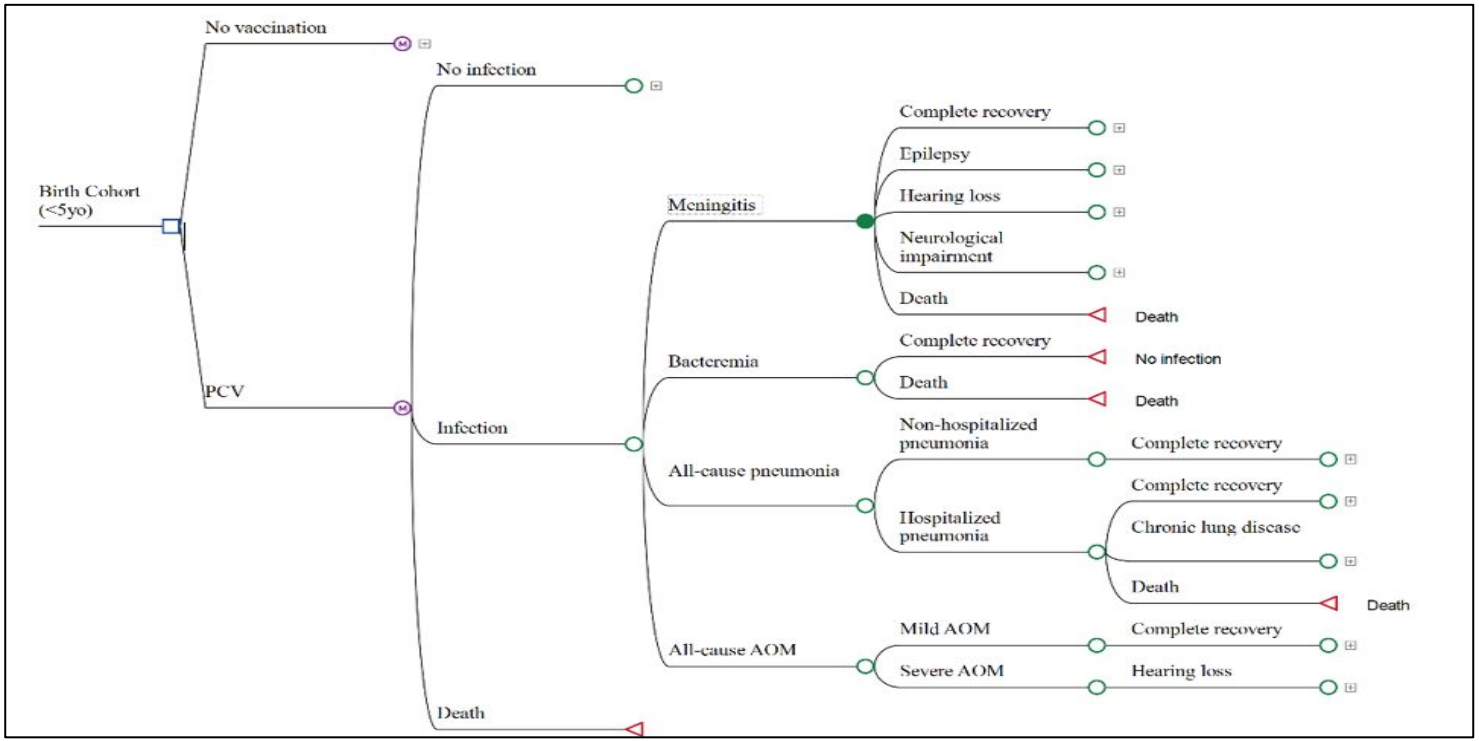
(b) PCV13 versus ‘no vaccination’

(c) $PCV10^{SII}$ versus ‘no vaccination’

(d) PCV15 versus ‘no vaccination’

(e) against each other

Markov model from 2020 PCV reassessment, adapted from Kulpeng et al. 2013:



Model constructed in TreeAge:
https://drive.google.com/file/d/1BKIDPw4IP2wRZoHWqm5VgqxoEtPEiGcC/view?usp=drive_link

- The following assumptions were applied to the model:

1. The infant would receive a complete three-dose schedule to achieve intended effects.

2. For the base-case analysis, evidence from RCTs for efficacy of $PCV10^{GSK}$ against IPD (Palmu, 2013), pneumonia (Kilpi, 2018) and AOM (pooled data from Saez Lorenz 2017 and Vesikari 2017) were used. We assumed the same efficacy with PCV13 which was adjusted based on local serotype coverage.

3. We did not find any published clinical efficacy results for $PCV10^{SII}$ and PCV15 for this review. Hence, for the base-case scenario, we assumed the same efficacy as $PCV10^{GSK}$ and adjusted for serotype coverage of PCV10-SII and PCV15.

- The following assumptions were applied to the model:

4. We also ran an alternative scenario where VE values from observational studies were used. Since there were no clinical effectiveness studies for PCV10-SII and PCV15, we used the VEs from observational studies for PCV10-GSK and PCV13, respectively. For $PCV10^{SII}$, VE was adjusted according to its serotype coverage relative to $PCV10^{GSK}$ while for PCV15, we used VE from PCV13 studies and VE was adjusted to include coverage for ST 3, 6A, 22F and 33F.

5. $PCV10^{GSK}$ is cross-reactive on serotype 19A, hence effective for clinical outcomes evaluated. This will be used for the base-case scenario.

- The following assumptions were applied:

6. PCV10-GSK vaccine effectiveness on AOM against *H. influenzae* was not considered since only one study looked into the effect of PCV10-GSK in reducing AOM caused by *H. influenzae* and the results were not significant.

7. For the base-case analysis, we will use 70% as the assumed PCV coverage.

8. The duration of PCV protection is five years, with or without herd immunity. Herd immunity is gained on the assumption that 80% of the target population is vaccinated.

9. Only one type of infection can occur per year, though more than one infection may occur in the time horizon assessed. Long-term sequelae could only occur once in patients aged <15 years.

- The following assumptions were applied:

10. We only used multidose preparations as this is recommended by HTAC and is the present practice; except for PCV15 which is only available in a single-dose preparation.

11. For sensitivity analysis, we considered no efficacy of PCV10-GSK against ST19A.

12. For sensitivity analysis, we considered no efficacy of PCV13 and PCV15 against ST3.

13. For sensitivity analysis, we considered no efficacy of PCV10-SII against ST23, ST6.

Input parameters for base-case and one-way sensitivity analysis

1. Costs/Prices

	Mean	Low	High	Remarks	Reference
cost_AOM	16,293.98	11,394.77	22,356.05	Range	PhilHealth 2018-2022
cost_AOMmild	230.67	189.01	629.97		PSO-HNS 2016; DPRI Aug. 2023
cost_bacteremia	32,554.41	20,864.07	41,779.06		PhilHealth 2018-2022
cost_chroniclungdisorder	16,609.70	11,536.48	20,826.75		PhilHealth 2018-2022
cost_epilepsy	23,197.02	15,357.08	31,335.51		PhilHealth 2018-2022
cost_hearingloss	47,468.02	42,153.00	52,214.82	+10%	2020 PCV HTA, adjusted for inflation
cost_hospitalizedpneumonia	20,705.39	15,544.76	22,325.66	Range	PhilHealth 2018-2022
cost_meningitis	58,405.60	40,244.02	67,736.07		PhilHealth 2018-2022
cost_neurodevelopmentaldisorder	25,236.29	6,949.27	44,617.00		PhilHealth 2018-2022
cost_nonhospitalizedpneumonia	305.83	275.57	494.14		PIDSP 2021; DPRI Aug. 2023
Price_PCV10GSK	1,180.69	1,062.62	1,298.76	+/-10%	Marketing authorization holder
Price_PCV10SII	991.80	892.62	1,090.98		
Price_PCV13	2,293.55	2,064.20	2,522.91		
Price_PCV15	3,128.16	2,815.34	3,440.97		

Input parameters for base-case and one-way sensitivity analysis

2. Incidence & Utility

Philippine population under 5 y.o.: PSA, 2023

	Mean	Low	High	Remarks	Reference
i_PD	0.4134	0.2807	0.6551	95% CI	Inferred
i_allcausepneumonia	0.6967	0.5984	0.7891		McAllister et al, 2019
i_AOM	0.3029	0.2102	0.4014		Caro et al, 2014
i_bacteremia	0.0002	0.0001	0.0003		Wahl et al, 2018
i_death_othercauses	0.0269	0.0205	0.0357		Sharrow et al, 2022
I_meningitis	0.0002	0.0001	0.0003		Wahl et al, 2018
i_epilepsy	0.0649	0.05841	0.07139	+/-10%	Salonga et al., 2019
i_hearingloss	0.039	0.0351	0.0429		Salonga et al., 2019
i_neurologicalimpairment	0.2922	0.26298	0.32142		Salonga et al., 2019
i_death_meningitis	0.129	0.1161	0.1419		Salonga et al., 2019
i_death_bacteremia	0.3	0.27	0.33		Wahl et al, 2018
i_hospitalizedpneumonia	0.105	0.0945	0.1155		Lupisan et al, 2019
i_chroniclungdisease	0.0894	0.08046	0.09834		Cai et al., 2018
i_death_pneumonia	0.047	0.0423	0.0517		Dembele et al, 2019
i_severeAOM	0.2	0.18	0.22		Anggraeni et al, 2019
u_AOM	0.9984	0.89856	1		
u_Bacteremia	0.9852	0.88668	1		
u_chronic_lungdisorder	0.59	0.531	0.649		
u_Epilepsy	0.64	0.576	0.704		Kulpeng et. al (2013)
u_hearing_loss	0.55	0.495	0.605		
u_Meningitis	0.9638	0.86742	1		
u_neurodevelopment_impairment_MMR	0.69	0.621	0.759		
u_Pneumonia	0.991	0.8919	1		
u_PD	0.921	0.8289	1		Mangen et al. 2015

Input parameters for base-case and one-way sensitivity analysis

3. Vaccine Efficacy, vaccine coverage, and discount rate

	Mean	Low	High	Remarks	Reference
VE_PCV10GSK_AOM	0.1000	0.0200	0.1700	95% CI	Meta-analysis of Vesikari 2016 and Saez Lorenz, 2017; adjusted
VE_PCV10GSK_IPD	0.5294	0.3337	0.5754		Palmu, 2013; adjusted
VE_PCV10GSK_pneumonia	0.2800	0.1300	0.4100		Kilpi, 2018; adjusted
VE_PCV10SII_AOM	0.0806	0.0161	0.1370		Meta-analysis of Vesikari 2016 and Saez Lorenz, 2017; adjusted
VE_PCV10SII_IPD	0.4266	0.2689	0.4637		Palmu, 2013; adjusted
VE_PCV10SII_pneumonia	0.2256	0.1048	0.3304		Kilpi, 2018; adjusted
VE_PCV13_AOM	0.1136	0.0227	0.1931		Meta-analysis of Vesikari 2016 and Saez Lorenz, 2017; adjusted
VE_PCV13_IPD	0.6013	0.3791	0.6536		Palmu, 2013; adjusted
VE_PCV13_pneumonia	0.3181	0.1477	0.4657		Kilpi, 2018; adjusted
VE_PCV15_AOM	0.1165	0.0233	0.1981		Meta-analysis of Vesikari 2016 and Saez Lorenz, 2017; adjusted
VE_PCV15_IPD	0.6168	0.3888	0.6704		Palmu, 2013; adjusted
VE_PCV15_pneumonia	0.3262	0.1515	0.4777		Kilpi, 2018; adjusted
discountrate	0.07	0.03	0.1	N/A	HTA Methods Guide
vaccinecoverage	0.7	0.5	0.9	N/A	Assumption: actual and target coverage

Base Case

(using VE from RCTs; all vaccine-specific serotypes)

Vaccines	Vaccine Efficacy from RCT			Cost Per Person (Php)	Effectiveness (QALY)
	Pneumonia	IPD	AOM		
PCV10-GSK	0.28	0.5294	0.1	11,332.48	9.52
PCV10-SII	0.2256	0.4266	0.0806	12,485.62	9.32
PCV13	0.3181	0.6013	0.1136	10,862.03	9.66
PCV15	0.3262	0.6168	0.1165	10,968.49	9.69

RESULTS

Comparison		Incremental Cost (Php)	Incremental Effectiveness (QALY)	ICER (Php/QALY gained)	Interpretation
PCV10-GSK	vs no vaccination	-5,714.44	0.96	-5,952.54	All PCV vaccines dominate *no vaccination* **Cost-saving**
PCV10-SII		-4,561.30	0.76	-6,001.71	
PCV13		-6,184.89	1.1	-5,622.63	
PCV15		-6,078.43	1.13	-5,379.14	

Scenario A

Assumption: VEs were adapted from observational studies of PCV10-GSK and PCV13, then adjusted for local serotype coverage of the vaccine

Vaccines	Vaccine Efficacy from Obs Studies			Cost Per Person (Php)	Effectiveness (QALY)
	Pneumonia	IPD	AOM		
PCV10-GSK	0.12	0.4879	0.2589	11,125.45	9.38
PCV10-SII	0.0967	0.3932	0.2085	12,265.84	9.21
PCV13	0.26	0.5503	0.2941	10,450.42	9.54
PCV15	0.2667	0.5645	0.3017	10,559.86	9.57

RESULTS

Comparison		Incremental Cost (Php)	Incremental Effectiveness (QALY)	ICER (Php/QALY gained)	Interpretation
PCV10-GSK	vs no vaccination	-5,921.47	0.82	-7,221.30	All PCV vaccines dominate *no vaccination* **Cost-saving**
PCV10-SII		-4,781.08	0.65	-7,355.51	
PCV13		-6,596.50	0.98	-6,731.12	
PCV15		-6,487.06	1.01	-6,422.83	

Scenario B

Assumption: The computation of the input VE does not include contentious serotypes.

Vaccine Brand	ST content	Contentious ST removed from the VE calculation	Remarks (Why ST is contentious?)
PCV10-GSK	18C, 6B, 23F, 14, 1, 5, 7F, 9V, 4, 19F, 19A (cross-reactivity)	19A	**Assumed cross-reactivity of PCV10 against 19A, assumed no effectiveness.** *Same assumption with 2020 reassessment*
PCV10SII	19A, 6B, 23F, 14, 1, 5, 7F, 9V, 6A	23F & 6B	Assumed no effectiveness because of inconsistent immunogenicity findings on **PCV10SII against 23F and 6B** *No assumption in the 2020 reassessment*
PCV13	18C, 19A, 6B, 3, 23F, 14, 1, 5, 7F, 9V, 4, 19F, 6A	3	Assumed no effectiveness because of **inconsistent clinical effect of PCV13 vs ST3** *(Assume for PCV15 as well)* *Same assumption with 2020 reassessment*
PCV 15	18C, 19A, 6B, 3, 23F, 14, 1, 5, 7F, 9V, 4, 19F, 6A, 22F, 23F	3	Assumed no effectiveness because of **inconsistent clinical effect of PCV13 vs ST3** *No assumption in the 2020 reassessment*

Scenario B

Assumption: The computation of the input VE does not include contentious serotypes

Vaccines	Vaccine Efficacy from RCTs			Cost Per Person (Php)	Effectiveness (QALY)
	Pneumonia	IPD	AOM		
PCV10-GSK (w/o ST19A)	0.28	0.4677	0.10	11,922.37	9.41
PCV10-SII (w/o ST23F & 6B)	0.1658	0.3135	0.0592	13,812.30	9.11
PCV13 (w/o ST3)	0.2909	0.55	0.1039	11,476.16	9.56
PCV15 (w/o ST3)	0.2990	0.5654	0.1068	11,584.40	9.59

RESULTS

Comparison		Incremental Cost (Php)	Incremental Effectiveness (QALY)	ICER (Php/QALY gained)	Interpretation
PCV10-GSK	vs no vaccination	-5,124.55	0.85	-6,028.88	All PCV vaccines dominate *no vaccination* **Cost-saving**
PCV10-SII		-3,234.62	0.55	-5,881.13	
PCV13		-5,570.76	1.00	-5,570.76	
PCV15		-5,462.52	1.03	-5,303.42	

Scenario C

Assumption: If 80% of the target population is vaccinated, the rest of the 20% of the population will be protected through herd effects

Vaccines	Vaccine Efficacy from RCTs			Cost Per Person (Php)	Effectiveness (QALY)
	Pneumonia	IPD	AOM		
PCV10-GSK	0.28	0.5294	0.1	10,204.20	9.71
PCV10-SII	0.2256	0.4266	0.0806	11,570.96	9.47
PCV13	0.3181	0.6013	0.1136	9,517.21	9.90
PCV15	0.3262	0.6168	0.1165	9,578.09	9.94

RESULTS

Comparison		Incremental Cost (Php)	Incremental Effectiveness (QALY)	ICER (Php/QALY gained)	Interpretation
PCV10-GSK	vs no vaccination	-6,842.72	1.15	-5,937.52	All PCV vaccines dominate *no vaccination* **Cost-saving**
PCV10-SII		-5,475.96	0.91	-5,986.08	
PCV13		-7,529.71	1.34	-5,635.47	
PCV15		-7,468.83	1.38	-5,427.75	

Current Scenario: Comparing Newer PCVs vs PNF-listed PCVs (PCV13, PCV10-GSK)

Current Scenario (vs PCV13)					
Comparison		**Incremental Cost** (Php)	**Incremental Effectiveness** (QALY)	**ICER** (Php/QALY gained)	**Interpretation**
PCV10-SII	**PCV13**	1,623.59	-0.34	**-4,775.26**	**PCV10SII** is dominated by PCV13
PCV10-GSK		470.45	-0.14	**-3,360.36**	**PCV10-GSK** is dominated by PCV13
PCV15		106.46	0.03	**3,548.67**	**PCV15** has higher costs with marginally higher QALY vs PCV13

Current Scenario (vs PCV10-GSK)					
Comparison		**Incremental Cost** (Php)	**Incremental Effectiveness** (QALY)	**ICER** (Php/QALY gained)	**Interpretation**
PCV10-SII	**PCV10-GSK**	1,153.14	-0.20	**-5,765.70**	**PCV10SII** is dominated by PCV10-GSK
PCV13		-470.45	0.14	**-3,360.36**	**PCV13** dominates PCV10-GSK
PCV15		-363.99	0.17	**-2,141.12**	**PCV15** dominates PCV10-GSK

DOST

Vaccine rollout: 2015-2021→ PCV13; From 2022 onwards→PCV10GSK

ce Considered

PCV versus each other *(1 of 4)*

Similar directions and interpretation for the other three scenario analyses (Scenario A, B, & C)

Base case (using VE from RCTs; all vaccine-specific serotypes)

PCV Comparison		Incremental Cost (Php)	Incremental Effectiveness (QALY)	ICER (Php/QALY gained)	Interpretation
PCV10-GSK	**vs PCV10-SII**	-1,153.14	0.20	**-5,765.70**	**PCV10-GSK** dominates PCV10SII
	vs PCV13	470.44	-0.14	**-3,360.36**	**PCV10-GSK** is dominated by PCV13 and PCV15
	vs PCV15	363.99	-0.17	**-2,141.12**	
PCV10-SII	**vs PCV10-GSK**	1,153.14	-0.20	**-5,765.70**	**PCV10SII** is dominated by PCV10-GSK, PCV13, and PCV15
	vs PCV13	1,623.59	-0.34	**-4,775.26**	
	vs PCV15	1,517.13	-0.37	**-4,100.35**	
PCV13	**vs PCV10-GSK**	-470.44	0.14	**-3,360.36**	**PCV13** dominates PCV10-GSK and PCV10-SII
	vs PCV10-SII	-1,623.59	0.34	**-4,775.26**	
	vs PCV15	-106.46	-0.03	**3,548.67**	**PCV13** has less costs with marginally lower QALY vs PCV15
PCV15	**vs PCV10-GSK**	-363.99	0.17	**-2,141.12**	**PCV15** dominates PCV10-GSK and PCV10-SII
	vs PCV10-SII	-1,517.13	0.37	**-4,100.35**	
	vs PCV13	106.46	0.03	**3,548.67**	**PCV15** has higher costs with marginally higher QALY vs PCV13

DOST

PCV versus each other *(2 of 4)*

Scenario A (using VE from Observational studies, all vaccine-specific serotypes)					
PCV Comparison		**Incremental Cost** (Php)	**Incremental Effectiveness** (QALY)	**ICER** (Php/QALY gained)	**Interpretation**
PCV10-GSK	**vs PCV10-SII**	-1,140.39	0.17	**-6,708.18**	**PCV10-GSK** dominates PCV10SII
	vs PCV13	675.03	-0.16	**-4,218.94**	**PCV10-GSK** is dominated by PCV13 and PCV15
	vs PCV15	565.59	-0.19	**-2,976.79**	
PCV10-SII	**vs PCV10-GSK**	1,140.39	-0.17	**-6,708.18**	**PCV10SII** is dominated by PCV10-GSK, PCV13, and PCV15
	vs PCV13	1,815.42	-0.33	**-5,501.27**	
	vs PCV15	1,705.98	-0.36	**-4,738.83**	
PCV13	**vs PCV10-GSK**	-675.03	0.16	**-4,218.94**	**PCV13** dominates PCV10-GSK and PCV10-SII
	vs PCV10-SII	-1,815.42	0.33	**-5,501.27**	
	vs PCV15	-109.44	-0.03	**3,648.00**	**PCV13** has less costs with marginally lower QALY vs PCV13
PCV15	**vs PCV10-GSK**	-565.59	0.19	**-2,976.79**	**PCV15** dominates PCV10-GSK and PCV10-SII
	vs PCV10-SII	-1,705.98	0.36	**-4,738.83**	
	vs PCV13	109.44	0.03	**3,648.00**	**PCV15** has higher costs with marginally higher QALY vs PCV13

PCV versus each other *(3 of 4)*

Scenario B (using VE from RCTs; removed contentious serotypes)					
PCV Comparison		**Incremental Cost** (Php)	**Incremental Effectiveness** (QALY)	**ICER** (Php/QALY gained)	**Interpretation**
PCV10-GSK	**vs PCV10-SII**	-1,889.93	0.3	**-6,299.77**	**PCV10-GSK** dominates PCV10SII
	vs PCV13	446.21	-0.15	**-2,974.73**	**PCV10-GSK** is dominated by PCV13 and PCV15
	vs PCV15	337.97	-0.18	**-1,877.61**	
PCV10-SII	**vs PCV10-GSK**	1,889.93	-0.3	**-6,299.77**	**PCV10SII** is dominated by PCV10-GSK, PCV13, and PCV15
	vs PCV13	2,336.14	-0.45	**-5,191.42**	
	vs PCV15	2,227.90	-0.48	**-4,641.46**	
PCV13	**vs PCV10-GSK**	-446.21	0.15	**-2,974.73**	**PCV13** dominates PCV10-GSK and PCV10-SII
	vs PCV10-SII	-2,336.14	0.45	**-5,191.42**	
	vs PCV15	-108.24	-0.03	**3,608.00**	**PCV13** has less costs with marginally lower QALY vs PCV15
PCV15	**vs PCV10-GSK**	-337.97	0.18	**-1,877.61**	**PCV15** dominates PCV10-GSK and PCV10-SII
	vs PCV10-SII	-2,227.90	0.48	**-4,641.46**	
	vs PCV13	108.24	0.03	**3,608.00**	**PCV15** has higher costs with marginally higher QALY vs PCV13

DOST

PCV versus each other *(4 of 4)*

Scenario C (with herd immunity)					
PCV Comparison		**Incremental Cost** (Php)	**Incremental Effectiveness** (QALY)	**ICER** (Php/QALY gained)	**Interpretation**
PCV10-GSK	**vs PCV10-SII**	-1,366.76	0.24	-5694.83	**PCV10-GSK** dominates PCV10SII
	vs PCV13	686.99	-0.19	**-3615.74**	**PCV10-GSK** is dominated by PCV13 and PCV15
	vs PCV15	626.11	-0.23	**-2722.22**	
PCV10-SII	**vs PCV10-GSK**	1,366.76	-0.24	**-5694.83**	**PCV10SII** is dominated by PCV10-GSK, PCV13, and PCV15
	vs PCV13	2,053.75	-0.43	**-4776.16**	
	vs PCV15	1,992.87	-0.47	**-4240.15**	
PCV13	**vs PCV10-GSK**	-686.99	0.19	**-3615.74**	**PCV13** dominates PCV10-GSK and PCV10-SII
	vs PCV10-SII	-2,053.75	0.43	**-4776.16**	
	vs PCV15	-60.88	-0.04	**1,522.00**	**PCV13** has less costs with marginally lower QALY vs PCV15
PCV15	**vs PCV10-GSK**	-626.11	0.23	**-2722.22**	**PCV15** dominates PCV10-GSK and PCV10-SII
	vs PCV10-SII	-1,992.87	0.47	**-4240.15**	
	vs PCV13	60.88	0.04	**1,522.00**	**PCV15** has higher costs with marginally higher QALY vs PCV13

Summary Table 2020 ICER values (SDV)

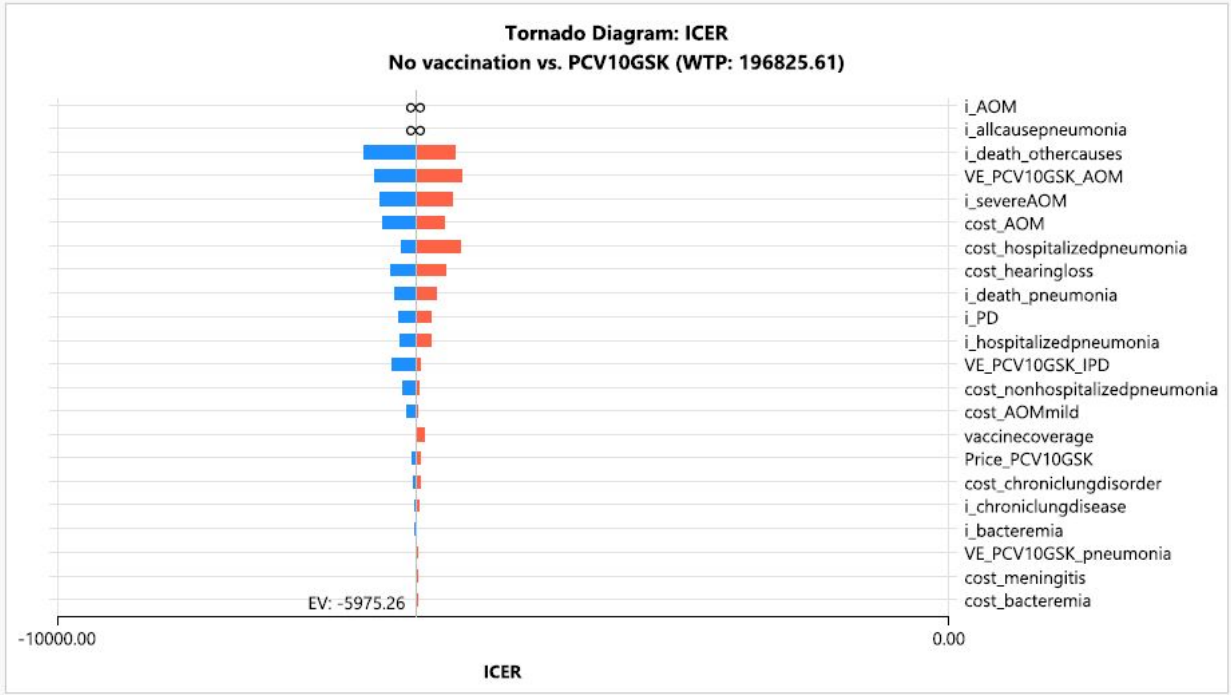
	PCV10 versus 'no vaccination'				PCV13 versus 'no vaccination'				PCV10 versus PCV13			
	Inc. Cost	Inc. LY	Inc. QALYs	ICER/QALY PHP	Inc. Cost	Inc. LY	Inc. QALYs	ICER/QALY PHP	Inc. Cost	Inc. LY	Inc. QALYs	ICER/QALY PHP
Without herd immunity *(50% coverage; Scenario 2)*	996	0.0371	0.0441	22,606	966	0.0435	0.0517	18,667	29.74	0.0065	-0.0077	-3,860
With herd immunity *(90% coverage; Scenario 4)*	-948	0.0690	0.0767	-12,369	-1,418	0.0818	0.0898	-15,794	470	0.0119	-0.0131	-35,797

Summary of 2020 Assessment ICER values (MDV)

	PCV10 versus 'no vaccination'				PCV13 versus 'no vaccination'				PCV10 versus PCV13			
	Inc. Cost	Inc. LY	Inc. QALYs	Cost/QALY PHP	Inc. Cost	Inc. LY	Inc. QALYs	Cost/QALY PHP	Inc. Cost	Inc. LY	Inc. QALYs	Cost/QALY PHP
Without herd immunity *(50% coverage; Scenario 1)*	126	0.0358	0.0429	2,947	350	0.0421	0.0504	6,932	-223	0.0063	-0.0075	29, 605
With herd immunity (90% coverage; Scenario 3)	-1,816	0.0685	0.0754	-24,080	-2,037	0.0804	0.0885	-23,006	221	0.0119	-0.0131	-16,837

dered

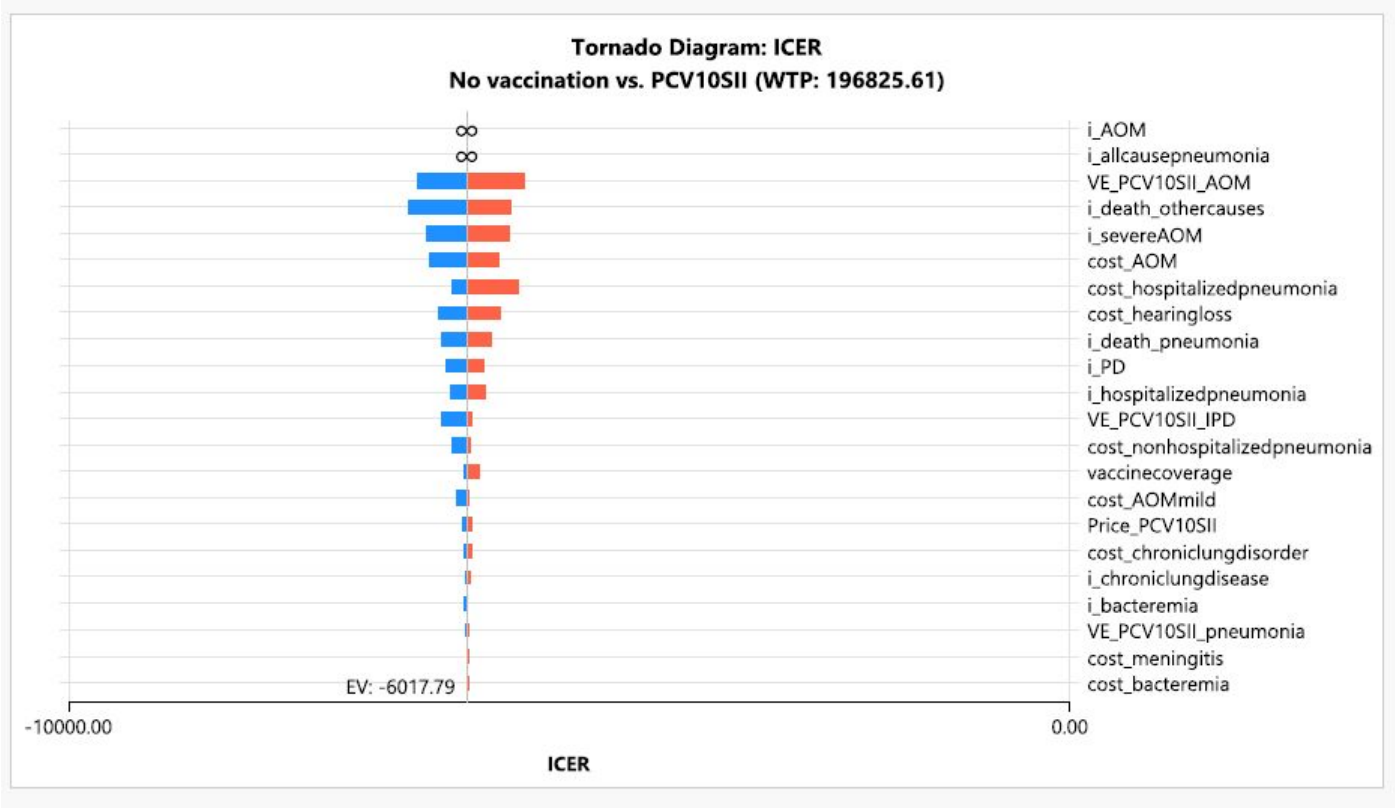
One-way Sensitivity Analysis



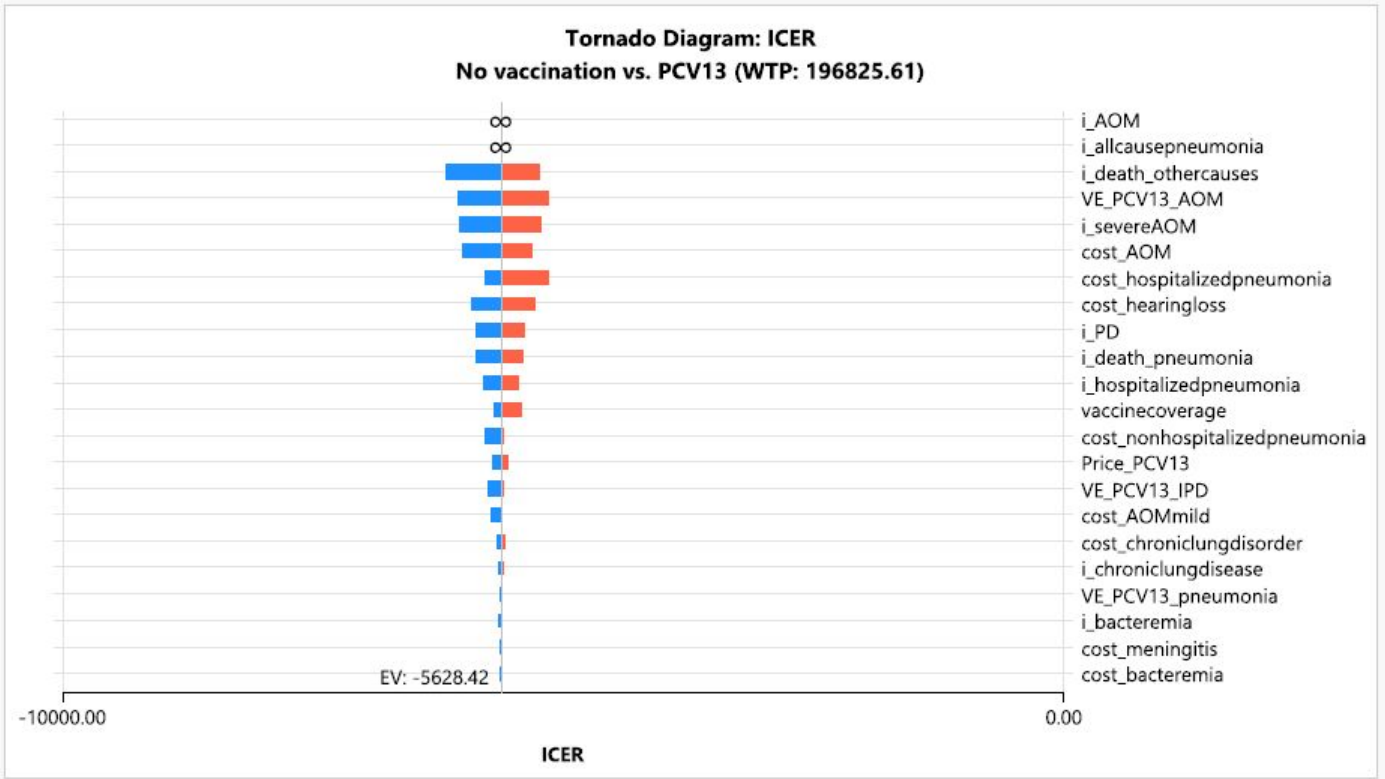
Blue = range of parameters with most favorable outcome
Orange = range of parameters with least favorable outcomes

The longer the bars (blue or orange) , the greater impact on ICER and vice versa

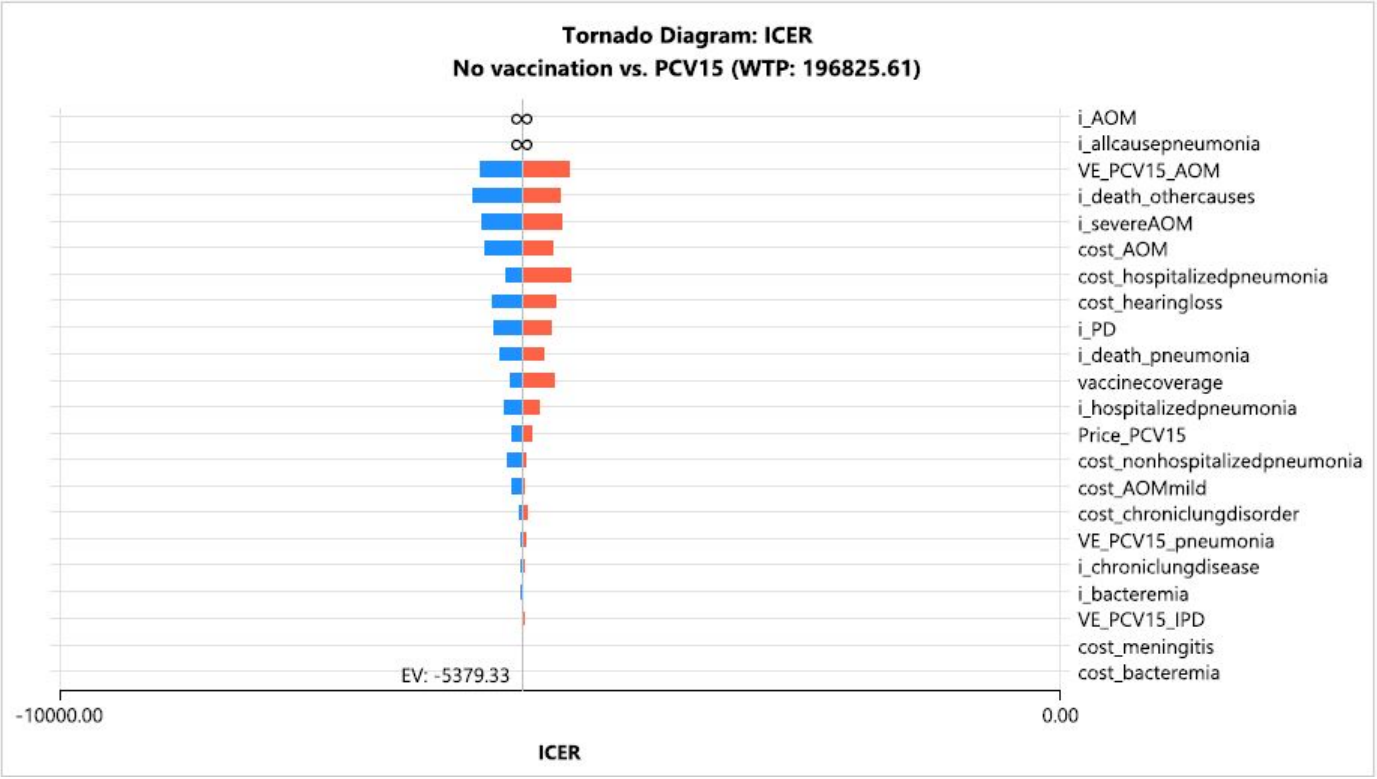
One-way Sensitivity Analysis



One-way Sensitivity Analysis



One-way Sensitivity Analysis



One-way Sensitivity Analysis

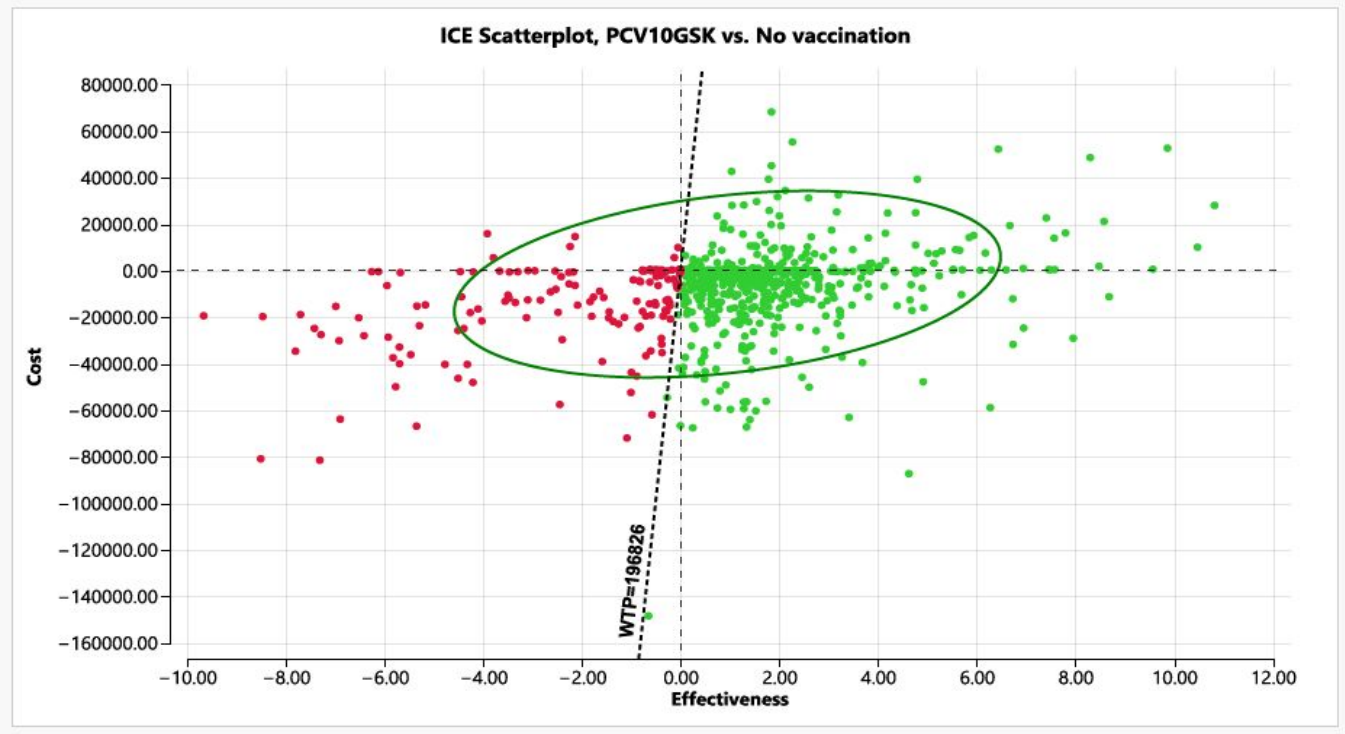
Summary:

- Both PCV10GSK and PCV10SII are most sensitive to the incidence rates of AOM and all-cause pneumonia. Also, VE against AOM and the costs associated with treating AOM and pneumonia are significant factors.

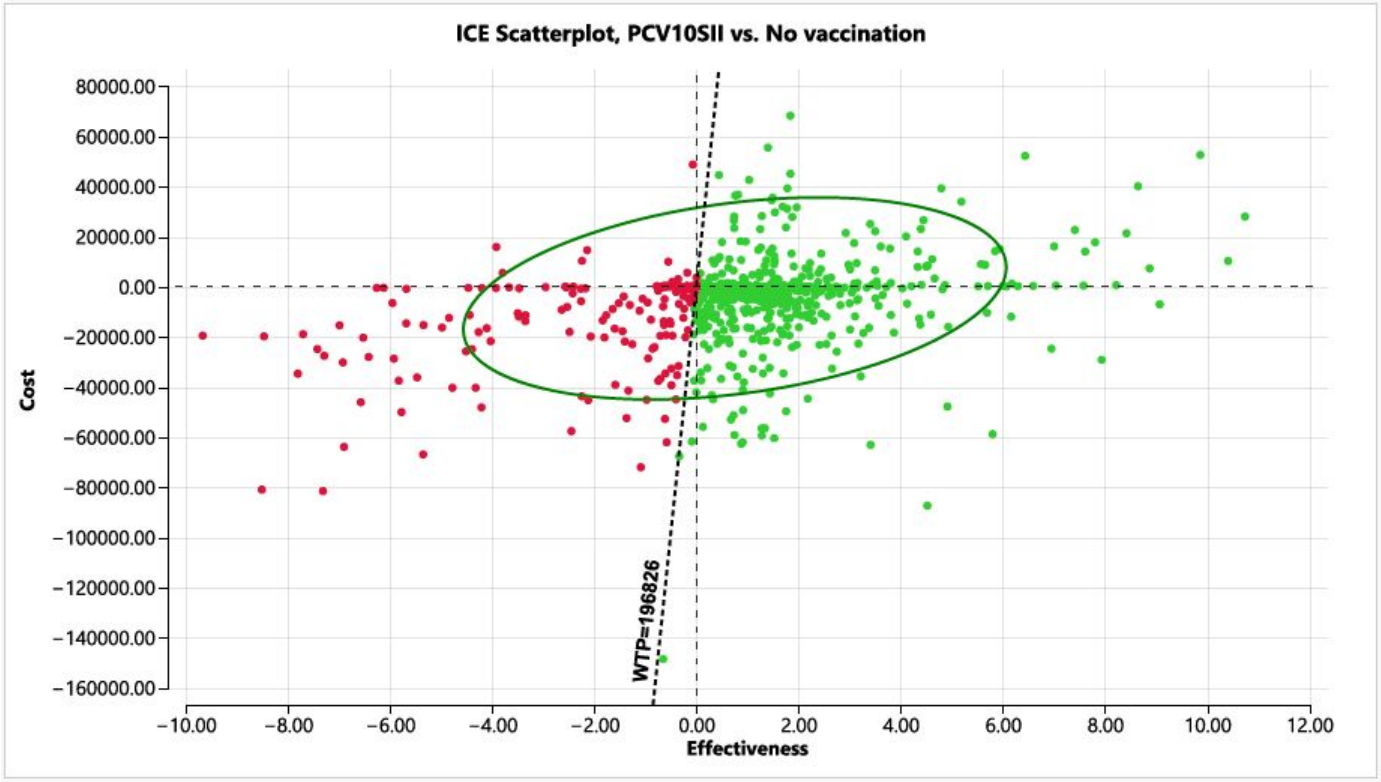
- While PCV13 is also influenced by AOM and pneumonia incidence rates and treatment costs, it shows a broader sensitivity to the incidence of severe pneumococcal diseases and VE against AOM.
  > slightly more resilient, as it considers a wider range of impactful factors

- PCV15 is sensitive to the incidence rates of AOM and pneumonia and the treatment costs. However, it also showed sensitivity to vaccine coverage rates and VE against both AOM and pneumonia.

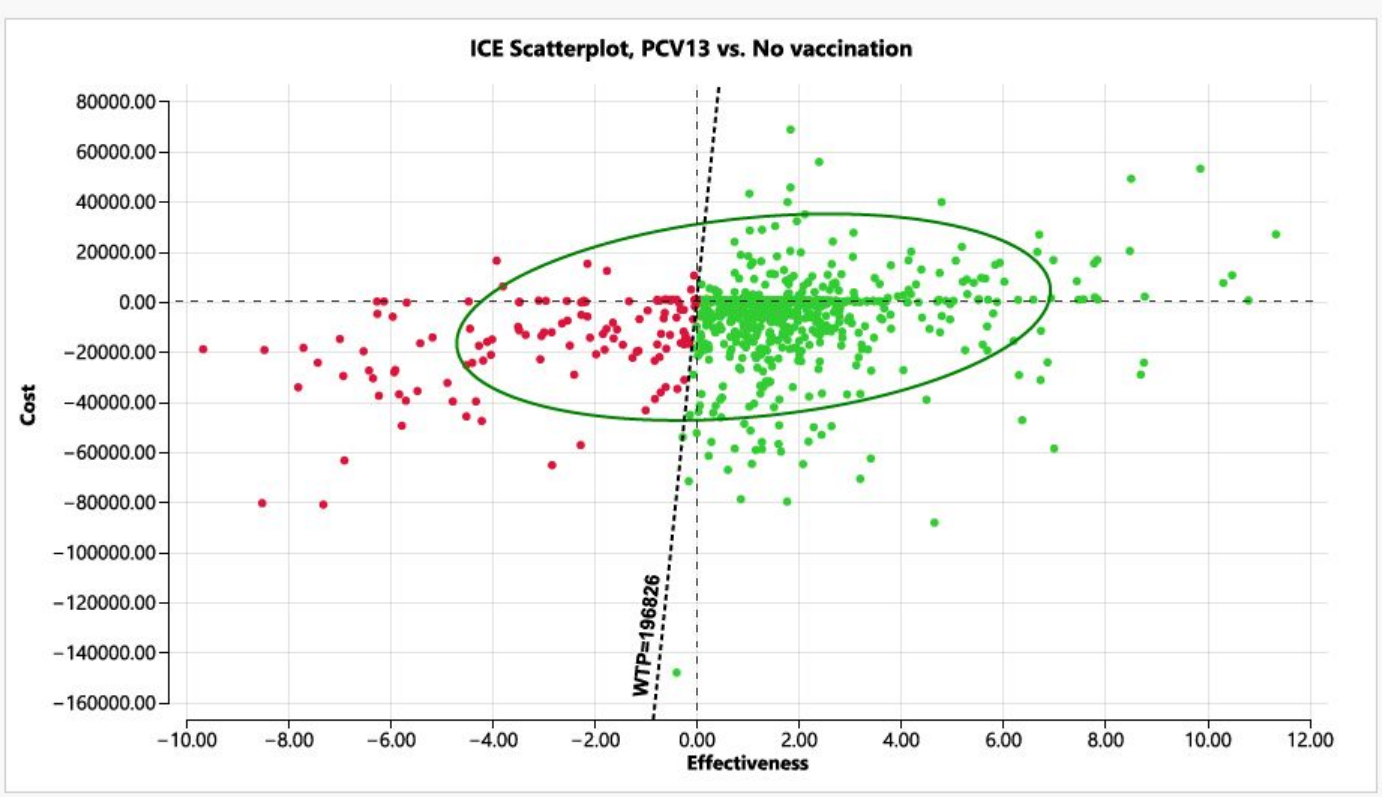
Probabilistic Sensitivity Analysis



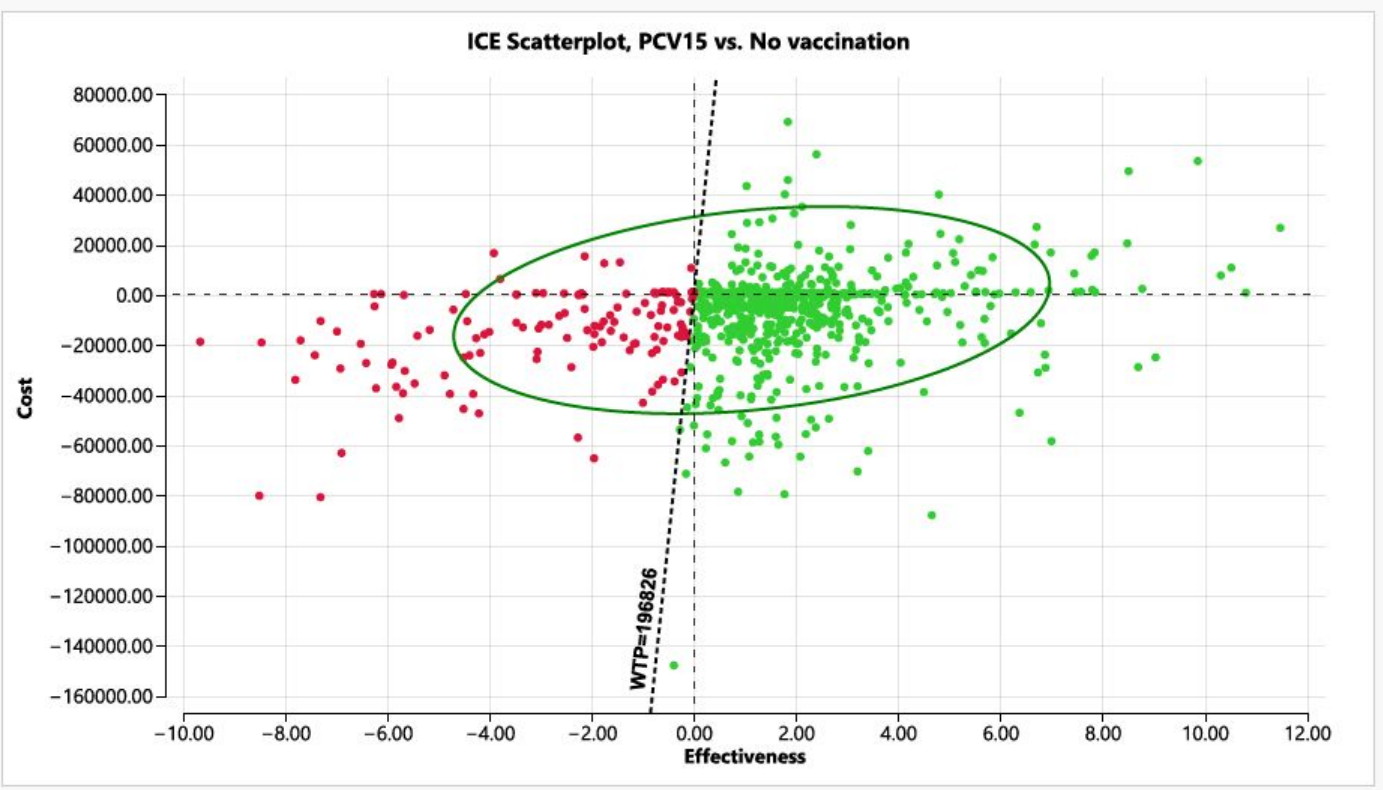
Probabilistic Sensitivity Analysis



Probabilistic Sensitivity Analysis



Probabilistic Sensitivity Analysis

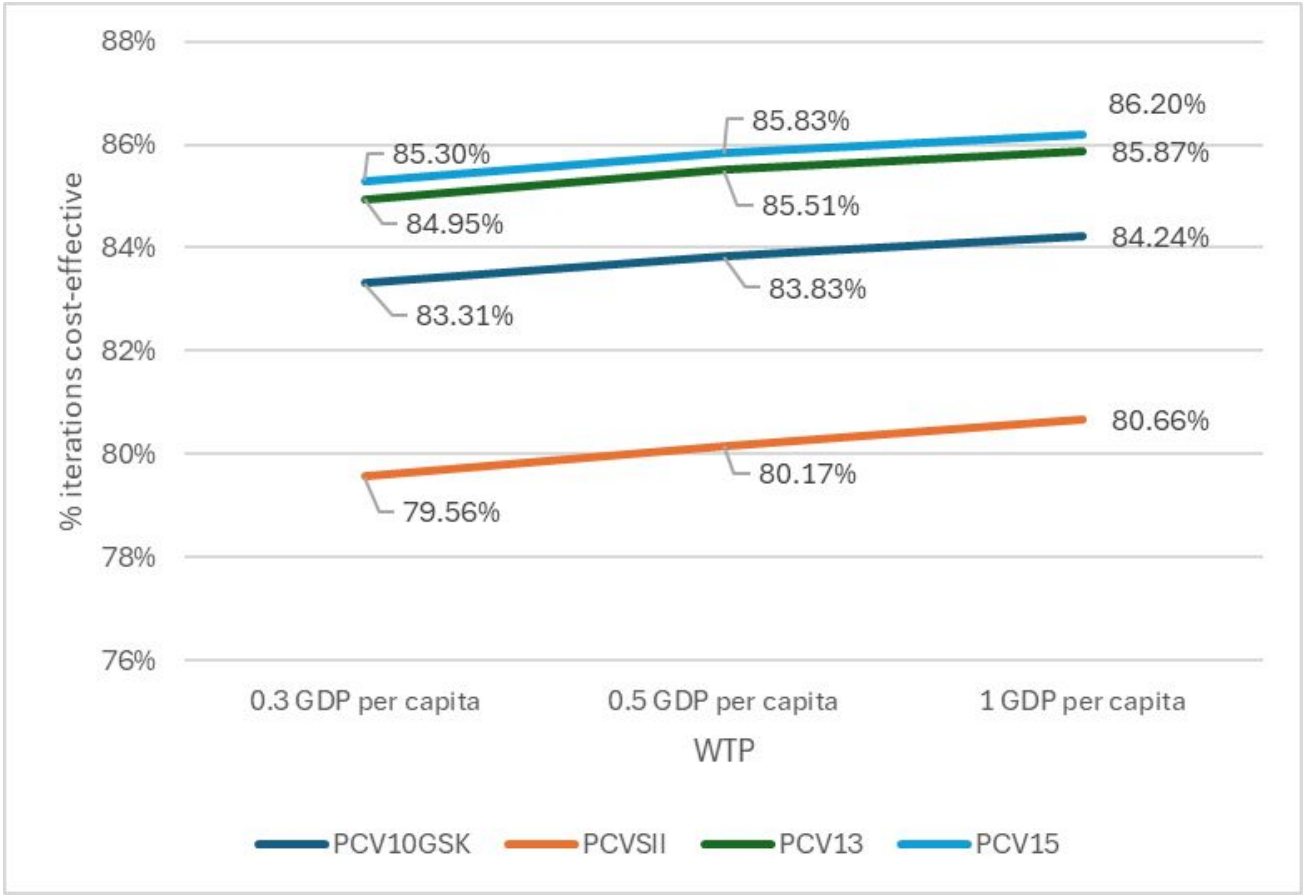


Probabilistic Sensitivity Analysis

Summary:

- PCV10GSK - cost-effective in a majority of scenarios, with over 70% of cases showing that it is either more effective and less costly or more effective and slightly more costly.
- PCV10SII – cost-effective in approximately 66% of scenarios.
- PCV13 - highly cost-effective in over 73% of scenarios, with a strong likelihood of being more effective and either less costly or cost-effective within acceptable limits.
- PCV15 - cost-effective in approximately 73% of scenarios.

CE Acceptability Curve



- The horizontal lines indicate that the probability of each vaccine being cost-effective is constant or has little effect across the WTP range.
- The CEAC considers the entire distribution of possible ICERs generated in the PSA.

C4: Budget Impact Analysis

5-year Budget Impact Analysis

Target vaccine coverage: 90% of projected population

Year	Projected Population (U1yo) (in millions)	PCV10GSK (in Php billions)		PCV10SII (in Php billions)		PCV13 (in Php billions)		PCV15 (in Php billions)		No Vaccination (in Php billions)
		Vaccination Cost	Treatment Cost	Vaccination Cost	Treatment Cost	Vaccination Cost	Treatment Cost	Vaccination Cost	Treatment Cost	Treatment Cost
2024	2.20	2.34 B	24.03 B	1.96 B	26.72 B	4.54 B	22.14 B	6.20 B	21.73 B	37.52 B
2025	2.21	2.35 B	24.18 B	1.98 B	26.88 B	4.57 B	22.27 B	6.23 B	21.86 B	37.75 B
2026	2.23	2.37 B	24.32 B	1.99 B	27.04 B	4.60 B	22.41 B	6.27 B	22.00 B	37.98 B
2027	2.24	2.38 B	24.47 B	2.00 B	27.20 B	4.63 B	22.54 B	6.31 B	22.13 B	38.20 B
2028	2.25	2.40 B	24.61 B	2.01 B	27.36 B	4.65 B	22.68 B	6.35 B	22.26 B	38.43 B
5 year budget impact		**11.84 B**	**121.62 B**	**9.94 B**	**135.20 B**	**22.99 B**	**112.04 B**	**31.36 B**	**109.97 B**	**189.87 B**
Total Budget Impact		**133.45 B**		**145.14 B**		**135.03 B**		**141.33 B**		**189.87 B**

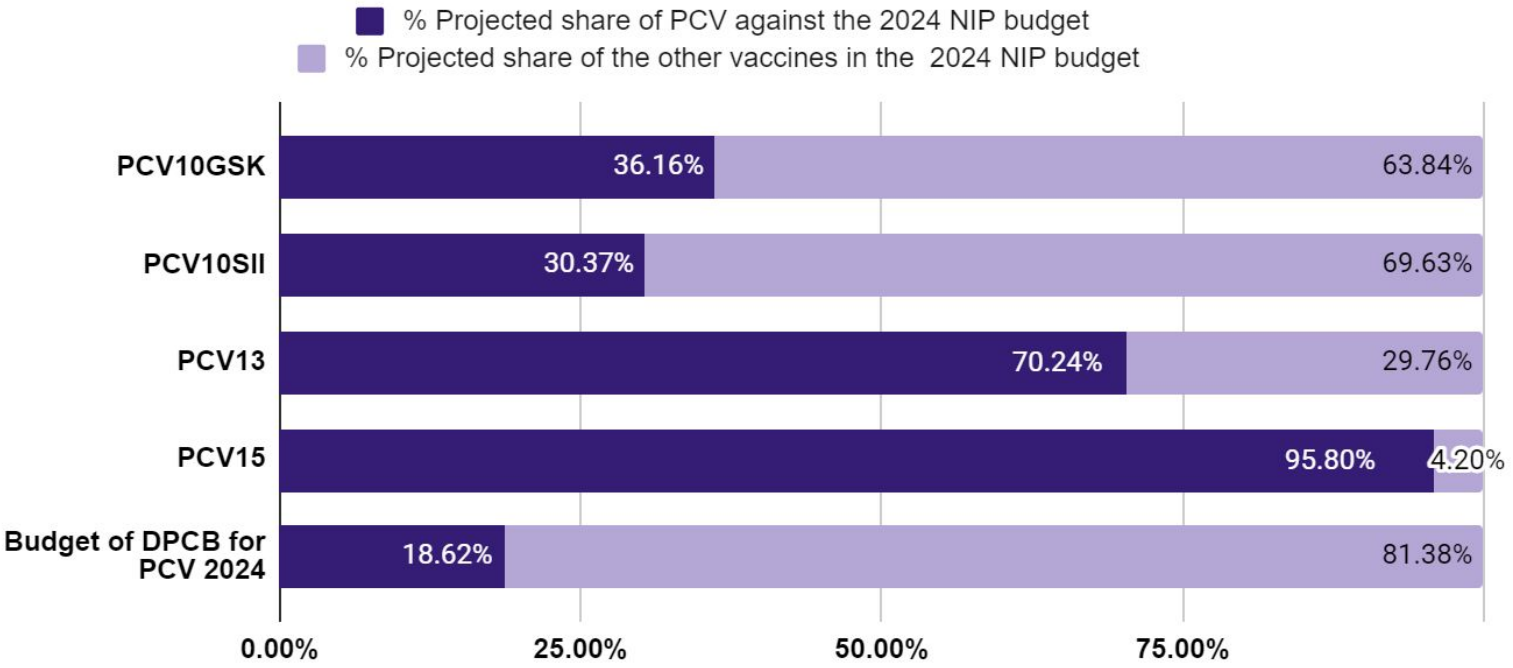
The overall budget impact of vaccination, which takes into account the vaccination and treatment costs, is lower than the budget impact of no vaccination. Focusing on the vaccination cost, the 5-year budget needed for PCV10GSK is Php 1.9B higher than PCV10-SII; the 5-year budget needed for PCV13 is Php 11.2 B higher than PCV10-GSK; while the 5-year budget needed for PCV15 is Php 8.4B higher than PCV13.

5-year Budget Impact Analysis (2020 Assessment)

Table 5.5 *Budgetary impact of PCV10 and PCV13 compared with 'no vaccination' in billions PHP*

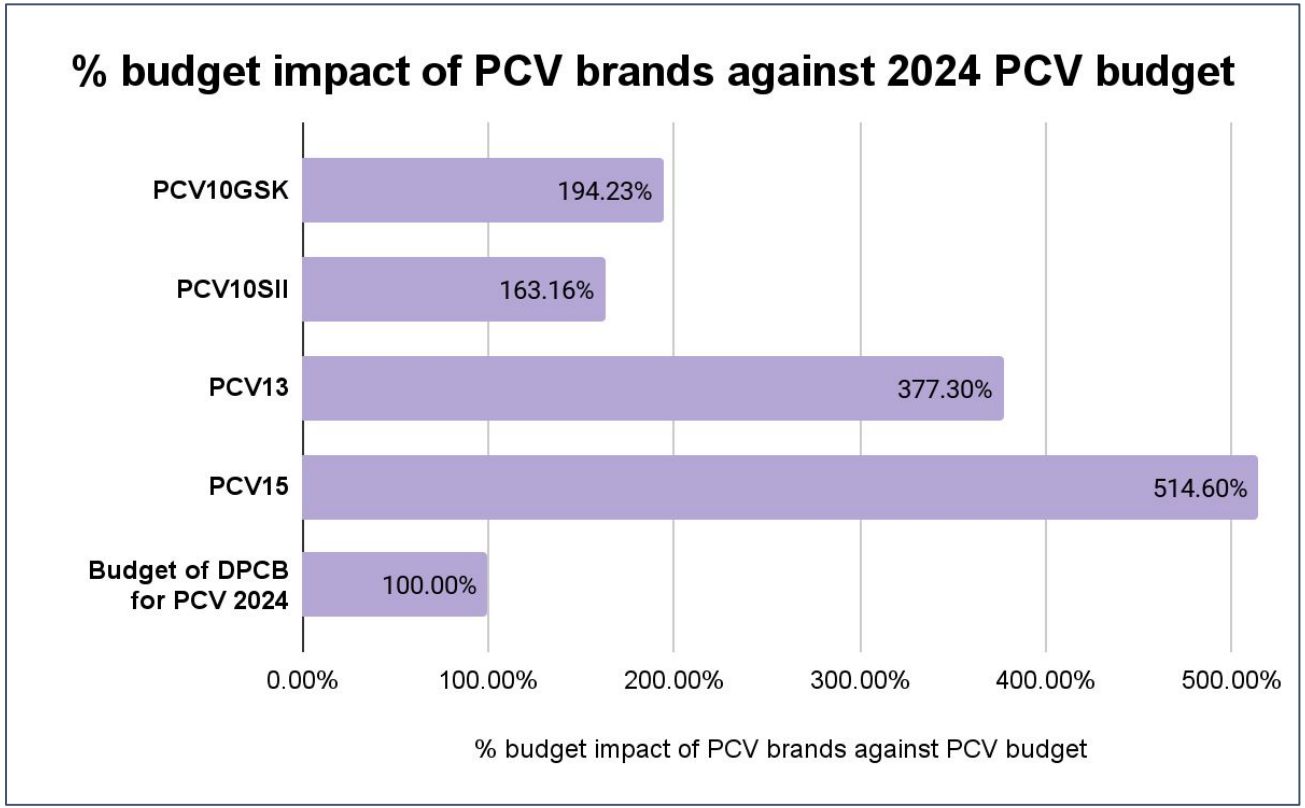
Year	Scenario 1 (MDV, 90% coverage)				Scenario 2 (SDV 90% coverage)				'No vaccination'
	PCV10		PCV13		PCV10		PCV13		
	Vaccination Cost	Treatment Cost	Vaccination Cost	Treatment Cost	Vaccination Cost	Treatment Cost	Vaccination Cost	Treatment Cost	Treatment Cost
2020	3.78	18.85	4.88	18.67	5.87	18.85	6.40	18.67	20.26
2021	3.83	33.02	4.94	32.68	6.00	33.02	6.48	32.68	34.86
2022	3.87	45.42	5.01	44.89	6.02	45.42	6.56	44.89	47.81
2023	3.91	54.82	5.06	54.10	6.09	54.82	6.64	54.10	57.77
2024	3.96	62.53	5.12	61.64	6.16	62.53	6.72	61.64	66.01
5 year Budget Impact	19.99	214.56	25.01	211.99	30.15	214.64	32.80	211.99	226.71
Total Budget Impact	**233.92**		**237.96**		**244.79**		**244.79**		**226.71**

PCV budget impact for the pediatric vaccination against the 2024 NIP budget



NIP Budget for 2024 = Php 6,467,880,022.00
Budget for PCV in 2024 = Php 1,204,070,000.00

Denominator: NIP budget

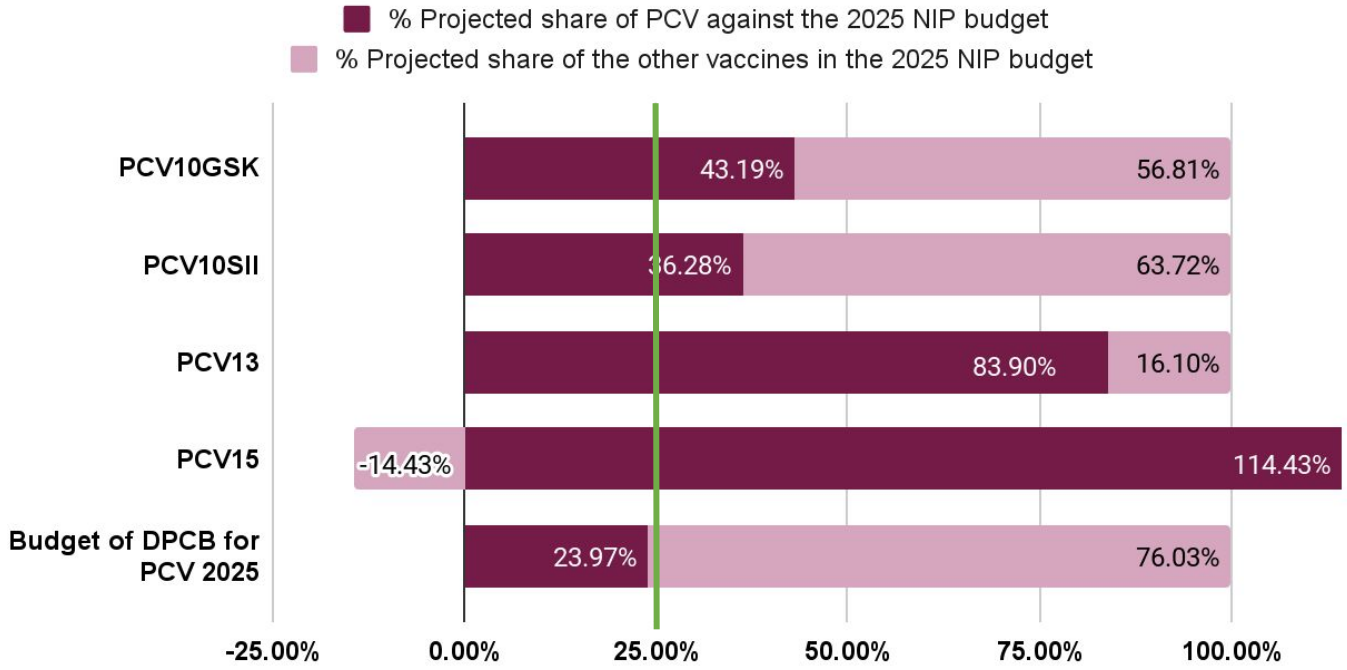


To be able to give 3 doses of PCV to 90% of the target population in 2024, the budget for PCV will need to be increased by the following, respective of each brand:

- PCV10GSK: 94.23% or 1.9x (+Php 1.1B)
- PCV10SII: 63.16% or 1.6x (+Php 760.4 M)
- PCV13: 277.30% or 3.8x (+Php 3.3B)
- PCV15: 414.60% or 5.1x (+Php 5B)

Denominator: PCV budget

PCV budget for the pediatric vaccination against the 2025 NIP budget

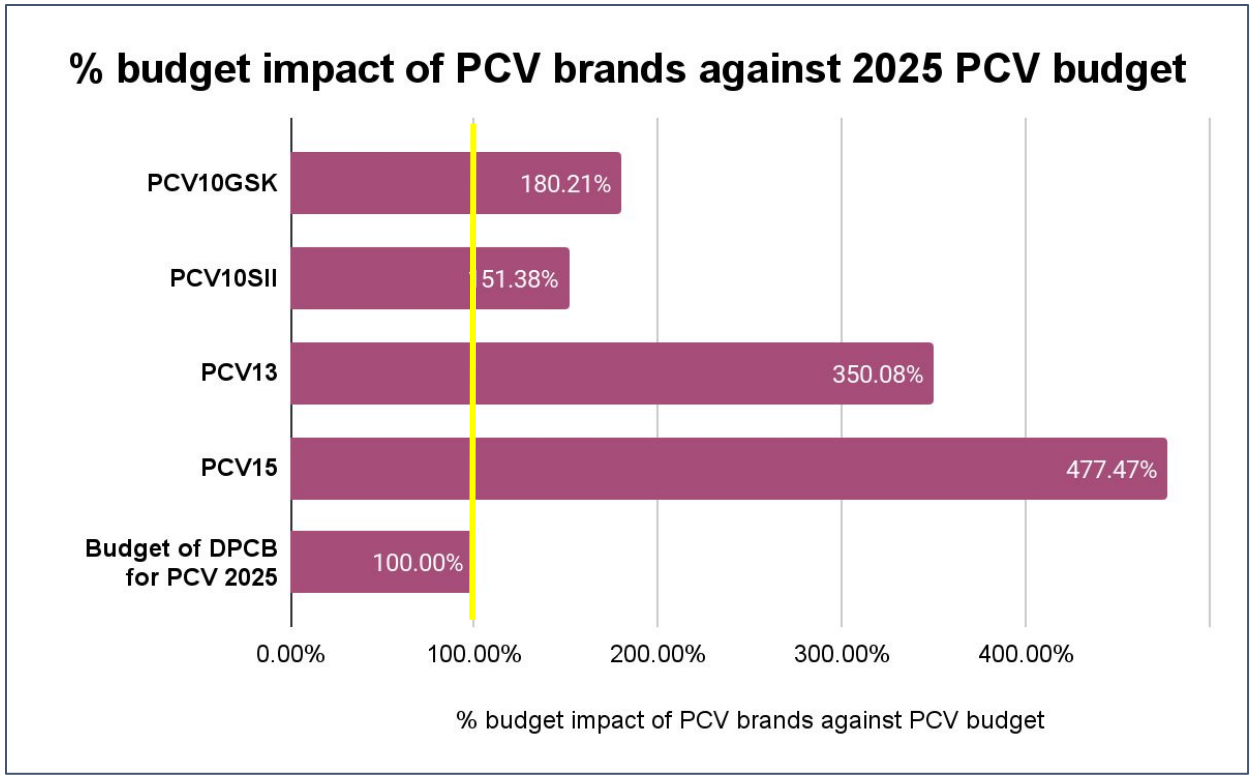


Between 2024 and 2025, the total NIP budget decreased (by 15.8%) but the PCV budget allocation increased (by 8.4%)

If PCV15 will be procured, the total NIP budget will not be enough for PCV alone.

NIP Budget for 2025= Php 5,447,897,413.74
Budget for PCV in 2025 = Php 1,305,653,220.00

Denominator: NIP budget



To be able to give 3 doses of PCV to 90% of the target population in 2025, the budget for PCV would need to be increased by the following, respective of each PCV brand:

- PCV10GSK: 80.21% or 1.8x (+Php 1B)
- PCV10SII: 51.38% or 1.5x (+Php 670.9M)
- PCV13: 250.08% or 3.5x (+Php 3.3B)
- PCV15: 377.47% or 4.8x (+Php 5B)

Denominator: PCV budget

C5: Household Financial Impact

Household Financial Impact of Pneumococcal Disease

Note: Outlier claims (claims <Php 1000) were removed from the dataset	# of paid claims	Hospitalization Cost (Reference excel sheet)		
		Range (Php)	Average (Php)	Median (Php)
Under 5	560,700	1,001.70 to 265,918,968.00	27,315.81	15,700.00
Pneumonia, High Risk *(ICD J13.3; J15.43; J15.93; J18.03;J18.13)*	3,810	2,013.98 to 1,528,102.12	49,275.54	34,593.28
Pneumonia Moderate Risk *(ICD J13.2; J15.42; J15.92; J18.02, J18.12)*	127,700	1,001.70 to 20,524,700.00	18,566.83	15,000.00
Meningitis *(ICD G03.8, G03.9)*	1,552	1,298.00 to 2,955,872.11	65,647.42	41,088.68
Sepsis *(ICD A40.3, A40.8, A40.9, A41.8, A41.9)*	47,668	1,016.00 to 265,918,968.00	65,708.04	33,005.66
Otitis Media *(ICD H65.1,9; H66.1-4,9)*	2,820	1,255.00 to 207,373.95	16,174.62	10,559.50
Newborn Sepsis *(ICD P36.1 P36.8, P36.9)*	377,150	1,002.50 to 154,897,010.00	25,129.47	14,650.00

Source of data: PhilHealth claims from 01 Jan 2017 to 25 March 2023

Recommendation: Evidence Considered

DOST

Household Financial Impact of Pneumococcal Disease

Note: Outlier claims (claims <Php 1000) were removed from the dataset **(Reference excel sheet)**	Median claims cost (Php)	Range of OOP payments (Php)	Median OOP payments (Php)	Ave % Coverage of PhilHealth
Under 5	14,450.00	0 to 265,886,968.00	1,100.00	77.26%
Pneumonia, High Risk	32,000.00	0 to 1,496,102.12	3,000.00	81.18%
Pneumonia Moderate Risk	15,000.00	0 to 20,507,700.00	595.02	81.52%
Meningitis	25,700.00	0 to 2,930,172.11	15,261.58	63.06%
Sepsis	32,000.00	0 to 265,886, 968.00	1,033.22	79.24%
Otitis Media	7,800.00	0 to 199,573.95	3,139.78	66.57%
Newborn Sepsis	13,450.00	0 to 154,882,360.00	1,264.00	75.66%

Source of data: PhilHealth paid claims for pneumococcal disease in children <5 y.o. from 01 Jan 2017 to 25 March 2023

Recommendation: Evidence Considered

DOST

Proportion of pneumonia cases with government funding for treatment

Number of paid claims for high-risk and moderate-risk pneumococcal pneumonia (2017-2023) Ref. PHIC	Number of nonhospitalized all-cause pneumonia (2017-2023) Ref. DOH FHSIS	Number of hospitalized all-cause pneumonia (2017-2023) Ref. DOH FHSIS
131,510	737,457	949,996

$$\frac{\text{Number of paid claims}}{\text{Number of hospitalized + non hospitalized all cause pneumonia cases}} = 7.79\%$$

Household Financial Impact of Nonhospitalized Pneumonia

Treatment regimen	Antibiotic product	Total cost for the treatment regimen per patient Ref: Drug Price Watch	Total cost for the treatment regimen for all patients with nonhospitalized pneumococcal pneumonia (N=51,622)
Amoxicillin trihydrate at 40-50mg/kg/day Q8 for 7 days	Amoxicillin 250mg/5mL suspension 60mL bottle	₱366.94	**₱18,942,176.68**
Amoxicillin trihydrate at 80-90mg/kg/day Q12 for 5 to 7 days	Amoxicillin 250mg/5mL suspension 60mL bottle	₱440.33	**₱22,730,715.26**
Amoxicillin-clavulanate at 80-90mg/kg/day Q12 for 5 to 7 days	Co-Amoxiclav 250mg+62.5/5mL suspension 100mL bottle	₱680.01	**₱35,103,476.22**
Cefuroxime at 20-30mg/kg/day Q12 for 7 days	Cefuroxime 125mg/5mL 70mL bottle	₱1,801.45	**₱92,994,451.90**

Note: Amoxicillin and amoxicillin-clavulanate granules/powder for suspensions are included in the PhilHealth Konsulta Package

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

Ethical and Social Impact

Methodology

- *Data collection strategy:* Semi-structured questionnaires (open-ended)
  - Adapted and revised the 2020 HTA PCV Report questionnaire
- *Participants:* Parents/caregivers of infants for immunization **(N=25)**
- *Sampling:* Convenience sampling - conducted during immunization days
  - 1 tertiary hospital in Manila (n=7)
  - 1 barangay health center in Manila (n=7)
  - 1 rural health unit in Rizal (n=11)

Ethical and Social Impact *(1 of 2)*

	Result	Other comments
Important considerations on the choice of PCV	Effectiveness of the vaccine **n=18/25 (72%)**	
Important characteristics of discussed PCV products	More diseases prevented because the vaccine covers more serotypes **(Mean rank 1.32)**	
Preferred PCV to be included in the immunization program	Vaccine that may have a limited number of serotype coverage (10 serotypes) and may be less expensive so that more children can be given the vaccine **n=17/25 (68%)**	
On whether the brand, country of origin, or the pharmaceutical company is important	Yes **n=14/25 (56%)**	•Vaccines are safer •Have better quality •More effective •They "trust" vaccines coming from known companies

Results

Important characteristics of discussed PCV products	Mean rank
More diseases prevented because the vaccine covers more serotypes	1.32
More children can be vaccinated	1.88
Lower-priced vaccine	2.8

Results

Preferred PCV to be included in the immunization program	N
Vaccine that may have a limited number of serotype coverage (10 serotypes) and may be less expensive so that more children can be given the vaccine	**n=17 (68%)**
Vaccine with the most number of serotype coverage (15) and the most expensive which may limit the number of children who can be vaccinated	n=6 (24%)
Vaccine which covers 13 serotypes but was the second most expensive vaccine	n=2 (8%)

Results

On Branding	No. (N=25)
On whether the brand, country of origin, or the pharmaceutical company is important	**n=14 (56%)**
Not important	n=11 (44%)

- Vaccine are safer
- Have better quality
- More effective
- They “trust” vaccines coming from known companies

- Believe that “generic” medicines including vaccines are as effective as the “branded” ones and they never had any bad experiences using them

Ethical and Social Impact *(2 of 2)*

	Result	Other comments
Perceived issues or challenges parents face when vaccinating their children	Vaccine price **(Mean rank: 2.13)**	
Perceived hindrances to vaccinating children	•Access to government programs **n=16/25 (64%)** •Issues related to the knowledge of parents **n=10/25 (40%)**	•long queues at the health center •vaccine stockouts •limited schedules when vaccines are given •unapproachable health workers

Results

Perceived issues or challenges parents face when vaccinating their children	Mean rank
Vaccine price	2.13
No time to get to the vaccination schedule of the health center	3.30
Lack of information about vaccines	3.43
Lack of government support to facilitate the vaccination of your children	4.13
Distance of the health center is far from their residence	4.48
Family members who are against vaccination	5.39
Religion is against vaccination	6.52
Gender or sex of your child	6.61

Ethical and Social Impact: Summary of findings

- Parents prefer a PCV product that would give the “most” protection to their children, i.e. the product with the most serotypes covered.
- However, given the situation that a less expensive PCV product may mean that more children can be given the vaccine, they would choose this product.
- This survey also showed that challenges and hindrances to immunization of their children include factors that have to do with finances such as vaccine price, factors that affect access of parents to immunization services such as distance from centers and limited vaccination schedules, and lack of information and trust in the health system.

Legal Impact

- DPCB Financial and Supply Chain Monitoring Division (FSCMD) and NIP require the following in a vaccine product for the it to be procured for the program:
    a. **WHO-prequalification**
    b. **Vaccine vial monitors (VVM)**
- Multi-dose vial preparations are not required for the NIP.
- The requirement for the WHO pre-qualification is indicated in AO 2019-0041
- WHO pre-qualification process: VVM is a critical characteristic (WHO 2014).

Recommended STs in 2020	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F

	PCV13 (Prevenar)	PCV10 GSK (Synflorix)	PCV 10 SII (Pneumosil)	PCV15 (Vaxneuvance)
Serotypes included in the Vaccine	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F	1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, 23F	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, and 33F
Vaccine vial monitor	Yes, Type 30	Yes, Type 30	Yes, Type 30	No
WHO prequalification	Yes	Yes	Yes	No

Legal Impact

VI. SPECIFIC GUIDELINES

A. Selection of products

1. The designated DOH clearing houses for drugs and medicines are the following:

    a. For DOH Central Office – Pharmaceutical Division
    b. For Regional Offices – Regional Therapeutics Committee
    c. For Specialty and Retained Hospitals – Therapeutics Committee

2. The CPR must be valid for the entire period of the award. If the CPR is about to expire, the supplier must have submitted a copy of an application of renewal to the FDA at least 3 months before the expiry date (a copy of the expiring CPR which is stamped with an "extension of validity" shall be submitted as proof);

3. If applicable, requirement for WHO Pre-qualification shall be imposed for essential drugs and vaccines procured for special DOH programs such as the EPI, TB, HIV/AIDS program and Rabies program.

Legal Impact

4.3.2 Critical characteristics

Compliance with 'critical' characteristics is also compulsory. However, if upon screening of the PSF the PQ Secretariat identifies a deviation from the characteristic value, then the PQ Secretariat will refer the application to the PSPQ SC and inform the manufacturer of the screening results (see Table 3 below and Figure 2 on page 16). The PSPQ SC can then make a recommendation, consulting with the manufacturer, vaccine procuring agents such as UNICEF SD and additional technical experts when considered necessary, to accept or reject the application and the evaluation of the PSF. Table 3 shows critical characteristics and their values.

Table 3: Critical vaccine characteristics and characteristic values

Characteristic	Applies to ...	Value
Vaccine vial monitor (VVM)	All vaccines	Proof of feasibility and intent to apply a VVM to the proposed vaccine, as defined below. The vaccine presented for prequalification presents data confirming that it has a thermostability profile that will enable it to be matched to a current WHO-approved VVM type (VVM2, VVM7, VVM14 or VVM30) or a future VVM type that may be approved by WHO (WHO/IVB/07.04[9]). Signed declaration, as part of the cover letter submitted along with the file for prequalification confirming that the manufacturer will apply a VVM to the vaccine and has the technical capacity to do so if requested by the purchasing specifications.

DOST

Health Systems Impact

Methodology

a. *Public health sector*
   - *Data collection strategy:* Semi-structured FGD (open-ended)
     - Used some questions from the tool developed by HTAC
     - Facilitated through online and face-to-face meetings
   - *Participants:* NIP Coordinators/Health officers **(N=28)**
   - *Sampling:* Convenience sampling
     - 4 regional offices
     - 2 city health offices
     - 1 rural health unit

a. *Private practitioners*
   - *Data collection strategy:* Survey questionnaire (Google Forms)
     - Adapted and revised 2020 HTA Report survey questionnaire tool
   - *Participants:* private practitioners **(N=14)**
   - *Sampling:* Convenience sampling

Health Systems Impact: Public Sector *(1 of 4)*

Experiences during the switch from PVC13 to PCV10[GSK]		
FGD Topic	**Reactions from health centers staff to the PCV switch**	**Reactions from parents/caregivers of their client**
Acceptability	•Questions the reasons for the shift from a PCV with higher serotype coverage to one with lower serotype coverage •Comments that the decision on the switch may be based more on economic than on clinical grounds. •Comment that they would be watching out for a possible increase in pneumonia cases •Impression that the announcement of the switch was "sudden" so this had a negative connotation with the implementers as they felt they were caught unaware •These were addressed with orientation from the higher levels of the health system on the PCV switch with the evidence used as the basis for the switch.	• No reported refusals from the parents nor any significant change in vaccination rates due to the PCV switch • Focus of communication with parents was PCV being given are anti-pneumonia vaccines that have been approved for use by gov't. • Parents whose infants had received 1 or 2 doses of PCV13 from private MDs and wanted to complete the PCV series with the public health centers. • Concerns raised were from urbanized communities. These concerns were not brought up by the CHDs which covered RHUs or smaller communities. • Refusals from parents were related more to the multiple vaccinations scheduled for 6-week- old infants.

Health Systems Impact: Public Sector *(2 of 4)*

Experiences during the switch from PVC13 to PCV10^{GSK}		
FGD Topic	**Reactions from health centers staff to the PCV switch**	**Reactions from parents/caregivers of their client**
Supply chain management	•There were no reported challenges in this area during the switch from PCV13 to PCV10-GSK.	N/A
Training and handling and preparation	•Implementers had to get used to the multidose PCV10-GSK in terms of administration, storage and handling and in monitoring and reporting •No report of errors in vaccine administration due to this change in preparation •Addressed by giving trainings and orientations	N/A
Adverse event	•No reported adverse events related to PCV during the time of the switch •1 reported adverse event which was investigated and assessed to be not related to the vaccine product	N/A

Health Systems Impact: Public Sector *(3 of 4)*

Perceived advantages and disadvantages of inclusion of either PCV10^{SII} or PCV15		
FGD Topic	**PCV10SII**	**PCV15**
Acceptability	• Any gov't-approved and scientifically-proven effective and safe PCV are acceptable • Parents rely on their trust in government agencies and health workers in their communities	• Preferred if price is not prohibitive (because of the perceived higher possible coverage of streptococcal serotypes) • Single dose preparations are easier to monitor and administer
Supply chain management	• Advantage: Multidose PCV products require less cold chain equipment (CCE) space • VVM is very important in regions and provinces with hard-to-reach communities • Disadvantage: Multidose vials have higher wastage rates and require more effort to monitor	• Advantages: o Most centers preferred a multidose preparation but there were also some which preferred single dose preparations. o Single dose vials are easier to administer and to monitor. o Less wastage • Disadvantages: o Single dose vaccines require more CCE space o No VVMs.

Health Systems Impact: Public Sector *(4 of 4)*

Perceived advantages and disadvantages of inclusion of either PCV10^{SII} or PCV15		
FGD Topic	**PCV10SII**	**PCV15**
Potential for higher immunization coverage rates	• Lower-cost vaccines would ensure sustainability and expansion of the PCV program as well as free up resources for other priority programs	• More expensive PCV may affect sustainability and supply which can subsequently affect potential for higher vaccination coverage rates.
Training and handling	• No foreseen impact related to training or staff skills for multi-dose vaccines	• Single dose preparations in a pre-filled syringes are easier to administer
	• Switch from one brand of PCV to another as this would entail additional training on the new PCV	

Health Systems Impact: Private Practitioners *(1 of 2)*

Perspectives and preferences on PCV products	
Perceived percentage of private practitioners' patient pool who receive immunization from public health centers	• Half of the respondents (n=7) estimate that more than half of their patients also avail of immunizations from public health centers
Perceived reasons why patients avail vaccination from public health centers	• Price: vaccines in health centers are free – 14 out of 14 (100%)
Patients' preference for private clinics over public health centers for immunization services.	• Lack of vaccines in health centers 11 out of 14 (78.6%)

Health Systems Impact: Private Practitioners *(2 of 2)*

Perspectives and preferences on PCV products	
Preferred PCV product among private health practitioners	• Most preferred: PCV13 – Mean rank of 1.57 • Least preferred: PCV10-SII – Mean rank of 3.14
Reasons for most preferred PCV product	• Because of the number of serotypes covered – 11 out of 14 (78.6%) • Related to price which may make this more affordable for my patients – 6 (42.9%)
Reasons why this PCV is the least preferred	• Because of the number of serotypes covered – 8 out of 14 (57.1%) • Related to price – 6 (42.9%)
Acceptability of different PCV products	• 1 being not at all acceptable and 5 being completely acceptable • PCV13 – Mean score of 4.7 • $PCV10^{SII}$ - Mean score of 2.8
Importance of brands, country of origin or manufacturer as factors in choosing PCV products	• Important – 10 out of 14 (71%) • Brand – associated with safety, efficacy, quality and credibility of product

Health Systems Impact: Summary of findings

- The switch from PCV13 to PCV10-GSK did not result in any significant challenges to acceptability from implementors or health clients. Important considerations for a PCV product is its **effectiveness and the number of diseases** it can prevent.
- There were no reported challenges to implementation of a PCV switch. Public health practitioners note the importance of **training and timely coordination** on any change in implementation of the immunization program. There were no hesitation with parents regarding the change in PCV product. The importance of proper communication with parents was emphasized.
- Challenges faced by parents in vaccinating their children have to do more with **vaccine prices and the ease of access** to the programs rather than hesitancy to receive vaccinations.
- Among private practitioners, **PCV13 was the product of choice** primarily because of the **number of serotypes covered and its relative affordability** for their patients.

Thank you!