

A Narrative Review of Pneumococcal Conjugate Vaccine Choices for Greater Access and Protection against Pneumococcal Diseases in the Philippines

Maria Margarita M. Lota, MD, MHPEd,^{1,2} Ma. Rosario Z. Capeding, MD,²
Fernando B. Garcia, Jr., MPA, PhD,³ John Robert C. Medina, RMT, MD, MHS,⁴
Jeremiah A. Serrano,^{5,6} Carlo R. Lumangaya,⁵ and Vicente Y. Belizario, Jr., MD, MTM&H⁷

¹Department of Medical Microbiology, College of Public Health, University of the Philippines Manila, Manila, Philippines

²Asian Hospital and Medical Center, Muntinlupa, Philippines

³Department of Health Policy and Administration, College of Public Health, University of the Philippines Manila, Manila, Philippines

⁴Institute of Clinical Epidemiology, National Institutes of Health, University of the Philippines Manila, Manila, Philippines

⁵College of Public Health, University of the Philippines Manila, Manila, Philippines

⁶FHI 360, Makati, Philippines

⁷Department of Parasitology, College of Public Health, University of the Philippines

ABSTRACT

Background. Pneumococcal vaccination has been widely used for the prevention of pneumococcal disease, with two types of vaccines available since 2009. With the World Health Organization (WHO) recommendation of incorporating pneumococcal conjugate vaccines (PCVs) in National Immunization Programs (NIPs) worldwide, a ten-valent PCV (PHiD-CV) was initially introduced in the Philippines in 2012. This, however, transitioned to the use of the 13-valent PCV (Pevnar) subsequent to the recommendation of the Formulary Executive Council in 2014.

Objective. This review aimed to present evidence on pneumococcal disease and vaccine inclusion in the Philippine NIP from 2005 - 2021.

Methods. This narrative review compiled articles on *Pneumococcus* from January 2005 to October 2021, sourcing literature from databases such as BIOSIS Preview, CAB Direct, Embase, Google Scholar, and others.

Results. In the Philippines, there was a shift in prevalent serotypes of *Streptococcus pneumoniae* among children under five following the introduction of PCV13 in the National Immunization Program in 2014, with serotype 14 becoming the most common by 2018, and a significant reduction in isolates reported in 2020, where only serotypes 5, 19A, and 23F were identified among invasive strains. The immunogenicity results of a potential vaccine candidate should be factored into the overall evidence when conducting a reassessment of PCV.

Conclusion. As part of the decision making about the inclusion of the PCVs in the NIP of the Philippines, various factors such as local epidemiology, vaccine supply, cost, and programmatic characteristics must be carefully weighed. Enhancing laboratory and surveillance capacity are essential to provide evidence-based decision-making in terms of existing serotype distribution and antimicrobial resistance (AMR) profile in the country. With the introduction of a new affordable formulation of a 10-valent PCV offering a comparable serotype coverage, the reassessment of choice of PCV with the consideration of all three formulations, namely PCV13, PHiD-CV, and SIPL-PCV, may be warranted.

Keywords: 10-valent pneumococcal conjugate vaccine, 13-valent pneumococcal vaccine, pneumococcal vaccines, pneumosil, Philippines



Paper presentation – 53rd APACPH Conference, September 22-23, 2022; Marriott Manila Hotel, Pasay City, Philippines.

eISSN 2094-9278 (Online)

Published: March 31, 2025

<https://doi.org/10.47895/amp.v59i4.10372>

Copyright: The Author(s) 2025

Corresponding author: Maria Margarita M. Lota, MD, MHPEd

Department of Medical Microbiology

College of Public Health

University of the Philippines Manila

625 Pedro Gil St., Ermita, Manila 1000, Philippines

Email: mmlota@up.edu.ph

ORCID: <https://orcid.org/0000-0002-5336-3804>

INTRODUCTION

Pneumococcal disease is caused by the bacterium *Streptococcus pneumoniae* that remains to be a significant public health concern. Pneumococcal vaccination has long been available for the prevention of pneumococcal disease. Since 2009, two pneumococcal vaccines have been in widely used to prevent this infection particularly, in pediatric populations.¹ The 10-valent pneumococcal conjugate vaccine (PCV), also known as PHiD-CV, targets serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, and 23F, while the 13-valent vaccine, also known as PCV13, covers equivalent serotypes with the addition of 3, 6A, and 19A. In 2019, a new formulation of a 10-valent PCV, Pneumosil® Serum Institute of India Pvt Ltd Pneumococcal Conjugate Vaccine (SIPL-PCV), was prequalified by the World Health Organization (WHO).² The serotypes included in SIPL-PCV (1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, 23F) were selected based on cost, coverage, and competitiveness with other PCVs (Table 1).

The WHO recommended the inclusion of PCV in National Immunization Programs (NIPs) worldwide, with a 3-dose schedule either with two primary doses plus one booster dose (2p+1) or three primary doses with no booster.³ This should be complemented by the implementation of other disease prevention and control measures. Considerations for the selection of a PCV for inclusion in the NIP should be based on programmatic characteristics, vaccine supply, vaccine price, regional and local prevalence of vaccine serotypes, and antimicrobial resistance (AMR) patterns.

In the Philippines, the NIP initially included the use of PHiD-CV in 2012 but transitioned to the use of PCV13 subsequent to the recommendation of the Formulary Executive Council in 2014.⁴ In 2020, the Philippine Health Technology Assessment Council (HTAC) conducted a reassessment to review the clinical efficacy and effectiveness as well as the cost-efficiency of both PHiD-CV and PCV13, and recommended the procurement of a vaccine for locally relevant serotypes. While HTAC’s reassessment addressed clinical and cost considerations, this review was initiated in 2021 to explore additional factors that may influence PCV selection. New data may have emerged particularly from the changing serotype distribution in the local and regional context, the development of AMR, and new vaccine options, that maybe incorporated in vaccine assessment for the NIP. Specifically, this narrative review aimed to provide the evidence, between 2005 to 2021, on pneumococcal disease

trends and the inclusion of vaccines in the Philippine NIP. By examining these data, the review sought to present the broader considerations that should be included into vaccine policy decisions, beyond cost-efficiency alone, such as alteration of serotype prevalence, AMR patterns, and programmatic considerations relevant to the Philippine context. This narrative review remains timely and important for ongoing discussions around the inclusion of newer PCV formulations in the NIP.

METHODS

This narrative review was conducted from October 2021 to March 2022 and included articles on Pneumococcus published from January 2005 to October 2021. Published literature were retrieved from the following databases: BIOSIS Preview, CAB Direct, Embase, Google Scholar, PLoS NTD, PubMed, Science Direct, Web of Science, and WHOLIS. Search terms used were “Pneumococci”, “Pneumococcus”, “*S. pneumoniae*”, “*Streptococcus pneumoniae*”, “PCV10”, “PCV13”, “Synflorix”, “Pevnar”, and “Pneumosil”, singly or combined. This provided an extensive yet specific gathering of relevant literature. The articles were assessed for relevance and quality, to provide a comprehensive overview of the evidence within the specified time frame. In addition to the retrieved articles, published reports from the WHO, and other international regulatory agencies, as well as the local Department of Health (DOH), Research Institute of Tropical Medicine (RITM), and the HTAC that were relevant to the review were also included. This thorough compilation of sources guarantees that the narrative review is well-grounded and encompasses a diverse range of evidence to reinforce our conclusions.

Ethical Considerations

The research protocol was screened and exempted from review by the University of the Philippines Manila Research Ethics Board (UPMREB 2021-010-EX).

RESULTS

The results of this narrative review provide insights into the distribution of pneumococcal serotypes across different regions and periods. The following sections detail the most common serotypes found worldwide, with a specific focus on the Asia Pacific region and the Philippines. These findings

Table 1. PCV Types, Brands, and Serotypes Included in their Formulation

Type	Brand	Serotype												
		1	3	4	5	6A	6B	7F	9B	14	18C	19A	19F	23F
PCV10	PHiD-CV													
	SIPL-PCV													
PCV13	Pevnar13													

highlight the variation in serotype prevalence before and after the introduction of pneumococcal vaccines, illustrating the impact of vaccination programs on serotype distribution.

Pneumococcal Serotype Distribution

In more than 90 identified serotypes of *S. pneumoniae*, 6-11 of these serotypes accounted for more than 70% of all invasive pneumococcal disease (IPD) worldwide before the use of pneumococcal vaccines.³ Each of these serotypes differ in terms of capacity to invade the human body, as well as overall virulence and AMR profile.⁵

Prior to the introduction of PHiD-CV and PCV13, the most common serotypes of *S. pneumoniae* worldwide were serotypes 1, 5, 6A, 6B, 14, 19F, and 23F (Table 2), which contributed to more than 50% of all the cases of invasive pneumococcal disease (IPD).

Due to limited samples and incomplete data from Asian countries, country-specific surveillance studies were grouped according to their respective Asia Pacific subregions to determine whether there is a specific serotype pattern within the region (Table 3).⁷ Based on this data, common serotypes varied across Asia Pacific countries. However, looking into some of specific subregions reveal common serogroups. In East and North-East Asia, serogroup 19 (19A and 19F) and serogroup 15 (15A, 15B and 15C) were common in most of its representative countries. In South-East Asia, serogroup 6 (6A and 6B), serogroup 19 (19A and 19F), and serotypes 23F and 14 were present in most isolates. For South and South-West Asia, there was no common distribution, and

for North Central Asia, not enough surveillance data for the other countries in the region were found to have a basis for comparison.

These differences may be attributed to the varying use of vaccines in these countries, particularly the type of PCV which was utilized, the year in which it was included in the NIP, and the period of data collection. As the utilization of these vaccines continues, serotype distribution is expected to change as noted by earlier studies that monitored variations in serotype distribution after the prolonged use of a certain PCV.⁸ This can be observed in the rise of non-vaccine serotypes (NVTs), serotypes not within the formulation of the vaccine in use.

In Southeast Asia, serogroup 6 (6A and 6B), serogroup 19 (19A and 19F), and serotypes 23F and 14 were the most prevalent serotypes based on more recent studies.⁹⁻¹³

In the Philippines, prior to the inclusion of PCV13 in the NIP in 2014, the prevailing serotypes among children less than five years of age were 5, 6A, 14, 1, 18C, and 23F, with serotypes 5 and 6A being most common.⁴ In 2018, a change in the prevailing serotypes and a reduction in the distribution of most PCV13 serotypes were observed. Serotype 14 was the most common, followed by serotypes 18C, 1, and 23F, as well as serotype 19A, which was not seen in previous studies.⁴ In 2020, a total of 210 isolates were reported, which was 63.86% lower than the reported isolates from the previous year. This was also true for the number of invasive *S. pneumoniae* isolates used for serotyping (n=4), wherein only three serotypes were identified, namely, serotypes 5, 19A and 23F.¹⁴

The HTAC recommendation that was adopted by the DOH was the procurement of a multi-dose vial (MDV) preparation of the PCV for the locally relevant serotypes in the country, which include serotypes 1, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F.⁴

Surveillance data on serotype distribution in each country may be limited and should not be the sole consideration in determining vaccine choice. Regional serotype distribution may also be considered as this could be a more reliable indicator as opposed to just local studies with limited sampling that may skew disease distribution in the country.¹⁵ The WHO recommends that countries monitor their epidemiologic profile through high-quality sentinel and population-based surveillance for pneumococcal disease and periodic nasopharyngeal (NP) carriage surveys.³

DISCUSSION

This narrative review highlights several key findings regarding the distribution of pneumococcal serotypes globally, with specific insights into the Asia Pacific region and the Philippines. This section discusses the implications of these findings in relation to vaccine strategies, immunogenicity, antimicrobial resistance (AMR), and the potential coverage of different pneumococcal conjugate vaccines (PCVs).

Table 2. Common Pneumococcal Serotypes per Region, 1980-2007 (Johnson et al., 2010)⁶

Region	Common Serotype	Proportion of IPD (%)
Africa	14	13.0
	1	11.7
	5	10.7
	6A	9.4
Asia	14	11.6
	6B	11.5
	23F	9.7
	1	9.5
Europe	14	23.9
	6B	13.7
	19F	8.2
	23F	7.1
Latin America and the Caribbean	14	26.5
	6B	9.5
	5	8.5
	1	8.4
North America	14	29.2
	6B	13.4
	19F	10.3
	18C	8.0
Oceania	14	23.7
	6B	12.0
	19F	8.9
	18C	5.9

Table 3. *S. pneumoniae* Serotype Surveillance Studies on Children under Five Years of Age in Asian Countries

Region	Country	Period	PCV type (Year of Inclusion in NIP)	Common Serotype	Source
East and North-East Asia (ENEAs): China, Korea, Japan, Hong Kong, Macao, Mongolia	China	2000 - 2016	PCV7 (2003-2013) PCV13 (2016*)	19F (26.4%) 19A (25.8%) 14 (15.1%)	Fu et al., 2019
	Hong Kong	2010 - 2013	PCV7 (2009) PHiD-CV (2010) PCV13 (2011)	19F (17.9%) 15B (10.3%) 15C (9.6%) 6A (7.1%)	Ho et al., 2015
	Japan	2015 - 2017	PCV13 (2013)	24F (24.2%) 12F (14.3%) 15A (14.3%)	Nakano et al., 2019
	Korea	2008 - 2014	PHiD-CV (2009) PCV13 (2010)	19A (37.5%) 11A (12.5%) 23A (12.5%)	Kim et al., 2016
North Central Asia (NCA): Armenia, Azerbaijan, Georgia, Kazakhstan, Russia, Tajikistan, Turkmenistan, Uzbekistan	Russia	2009 - 2013	PCV13 (2014)	19F (21.7%) 6B (12.8%) 23F (10.1%) 14 (9.0%) 6A (8.4%)	Mayanskiy et al., 2014
South-East Asia (SEA): Brunei, Cambodia, Indonesia, Lao, Malaysia, Myanmar, Philippines, Singapore, Thailand, Timor Leste, Vietnam	Cambodia	2012 - 2018	PCV13 (2015)	6B (17.3%) 14 (17.3%) 19A (16.0%) 1 (12.3%)	Turner et al., 2020
	Indonesia	2018 - 2019	PCV13 (2020)	6A/B (28.9%) 23F (16.1%) 19F (9.4%)	Daningrat et al., 2020
	Malaysia	2014 - 2017	PCV13 (2013)	14 (26.9%) 6B (19.6%) 19A (11.8%) 6A (10.6%)	Arushohty et al., 2019
	Thailand	1990 - 2017	PCVs not included in the NIP	6B (20.3%) 23F (16.1%) 14 (14.2%) 19A (8.1%)	Hocknell et al., 2019
	Vietnam	2012 - 2018	PCVs not included in the NIP	19F (32%) 6A (16%) 6B (12%) 23F (12%) 15A (12%)	Vo et al., 2020
South and South-West Asia (SSWA): Afghanistan, Bangladesh, Bhutan, India, Iran, Maldives, Nepal, Pakistan, Sri Lanka, Turkey	Bangladesh	2007 - 2013	PHiD-CV (2015)	2 (16%) 1 (10%) 6B (7%) 14 (7%) 5 (7%)	Saha et al., 2016
	India	2011 - 2015	PCV13 (2017)	14 (14%) 1 (14%) 5 (10%) 19F (9%)	Manoharan et al., 2017
	Iran	2013 - 2016	PCVs not included in the NIP	23F (24.5%) 19F (18.9%) 19A (7.5%) 9V (7.5%)	Houri et al., 2017
	Pakistan	2009 - 2013	PHiD-CV (2012)	18 (18.6%) 14 (11.9%) 12F (10.2%) 23B (10.2%)	Shakoor et al., 2014

*Year made available but not included in NIP

Immunogenicity

Despite the evidence of cross-protection against 6A and 19A, there is limited opsonophagocytic assay (OPA) data on the functional activity of cross-reacting antibodies following PHiD-CV primary or booster vaccination, but in the studies that are published, OPA responses to PHiD-CV are significantly lower than that of PCV13.¹⁵ For both PHiD-CV and PCV13, there was a high immunogenicity for all 10 of their common serotypes. For the additional serotypes in PCV13, namely 3, 6, and 19A, the vaccine produces high levels of functional antibodies.¹⁶ The efficacy of SIIPL-PCV is expected to be equivalent to PCV13 and PHiD-CV as the immunogenicity data has revealed non-inferiority to currently available vaccines.

Invasive Pneumococcal Disease

Following the introduction of PHiD-CV and PCV13, there was a significant reduction of invasive pneumococcal disease (IPD) caused by the vaccine serotypes in both dosing schedules. However, there was little evidence that the two vaccines had a difference in the extent of reduction in vaccine type IPD. In a study, while this reduction in IPD can be observed in serotypes 6A and 19A for PCV13, no reduction in serotype 3 was demonstrated.¹⁶ A study in Turkey revealed that both vaccines had similar impact on meningitis, pneumonia, and bacteremia but PHiD-CV showed greater reductions in AOM-related consultations and hospitalizations.¹⁷ The WHO report further elaborates that evidence for a direct or indirect reduction in serotype 3 IPD following PCV13 was inconclusive, while no impact was observed for PHiD-CV against serotype 3 IPD in either vaccine-eligible or ineligible cohorts. While PHiD-CV appears to be effective in reducing 19A disease, there is very limited data to fully support the impact of PHiD-CV on IPD caused by 3, 6A, and 19A.³

In terms of protection, the direct inclusion of certain serotypes in the vaccine formulation as opposed to relying on cross-protection from other serotypes, may not offer the same level of protection.¹⁸ This is supported by surveillance data from Brazil, Chile, and Colombia that showed an increase in the prevalence of serotype 19A among the children since the introduction of PHiD-CV in their NIP.¹⁹⁻²¹ The more recent evidence suggests a substantial change in the epidemiology of IPD, which provides a basis for a review of vaccine choice with possible consideration of the use of a vaccine that offers direct protection against the prevailing serotypes.¹⁶

PCV13 provides direct protection against additional serotypes 3, 6A and 19A, while PHiD-CV relies on cross-protection from serotypes 6B and 19F for serotypes 6A and 19A, respectively.¹⁵ The WHO has recommended the use of PCV13 in settings where the burden of pneumococcal disease attributed to serotypes 19A and 6A is significant. Immunogenicity data which serves as a serologic correlate of protection and is used as a basis of non-inferiority by the WHO, may provide evidence in conducting a reassessment of PCV.³

Antimicrobial Resistance

AMR is a rapidly growing global concern due to the emergence and spread of pathogens that have developed new resistance mechanisms. While AMR is a naturally occurring phenomenon due to genetic changes, resistance is largely driven by the misuse and overuse of antibiotics and insufficient prevention and control of infectious diseases. According to the WHO, *S. pneumoniae* was listed as one of the eight bacteria of international concern for AMR.²² Of the prevalent pneumococcal serotypes globally, serotypes 19A, 6A, 19F, 14, 6B, 9V, 35B, 23A, and 15A (in descending order) are most commonly associated with AMR.⁵ In all six WHO regions, *S. pneumoniae* has exhibited non-susceptibility to penicillin.²³ Furthermore, a more recent study by Kim and colleagues on the resistance profile of *S. pneumoniae* in Asian countries revealed a marked increase in penicillin resistance from 4.9% in 2008-2009 to 9.0% in 2012-2017, where serotypes 19F (49.4%), 19A (28.6%), and 11A (7.8%) were found to be non-susceptible.²⁴ The Philippines has also seen a recent increase in AMR rates of *S. pneumoniae* based on the Antimicrobial Resistance Surveillance Program (ARSP) (Department of Health - Research Institute for Tropical Medicine, 2021) reports (Table 4).¹⁴ However, data on the AMR among specific serotypes are not available.

Vaccines play an important role in reducing the impact of AMR either through the reduction of the pathogen and/or specific serotypes targeted by the vaccine, or through the prevention of febrile illnesses, preempting the need for antibiotics.^{25,26} Knowing the resistance profile of a particular pathogen will contribute to determining the potential impact that a vaccine can have to counteract AMR. This will also inform vaccine development, targeting priority serotypes which have not been included in currently available vaccines and will provide key information on how vaccine utilization can be maximized to address the current AMR pattern. AMR was not taken into consideration in the recent health technology assessment, which carries patient, healthcare, and economic implications.

Table 4. Resistance Rates for Different Antimicrobials against *S. pneumoniae*, 2019-2020 (ARSP, 2021)¹⁴

Antimicrobial	Resistance Rate (%)	
	2019	2020
Penicillin	13.2	16.5
Co-trimoxazole	13.9	22.2
Erythromycin	9.0	10.4
Ceftriaxone	1.2	4.3
Levofloxacin	1.5	1.3
Clindamycin	6.4	4.6
Linezolid	0.0	1.2
Tetracycline	12.3	16.9
Vancomycin	0.0	0.5
Meropenem	0.0	0.0

Potential Coverage of Different PCVs in the Philippines

Following the introduction of PHiD-CV and PCV13, there was a significant reduction of IPD caused by vaccine serotypes in both dosing schedules (2+1 or 3+0). However, there was no evidence that the two vaccines had a difference in the extent of reduction in vaccine-type IPD. While this reduction in IPD can be observed in serotypes 6A and 19A for PCV13, no reduction in serotype 3 was demonstrated. On the other hand, there is very limited data to fully support the impact of PHiD-CV on IPD caused by serotypes 6A and 19A. As such, the WHO recommends countries having high prevalence of 19A and 6C to use a vaccine containing serotypes 19A and 6A.³

In the Philippine context, a study by Haasis and colleagues calculated the serotype coverage of PHiD-CV and PCV13. Using a Markov model with one year cycle length which includes Philippine data on epidemiological parameter, direct and indirect effects of vaccine efficacy, the estimated lifetime cost and outcomes for PCV10 and PCV 13, as well as the theoretical coverage of SI IPL-PCV were calculated to compare with the currently available vaccines (Table 5).²⁶ While the study by Haasis and colleagues has shown that PCV13 has coverage on serotype 3, recent studies have shown that data on PCV13 impact on serotype 3 were inconclusive, with most studies showing no impact.^{4,5,9,11}

The evidence on serotype distribution on the 2020 HTAC recommendation was based on the RITM surveillance data which found that from 2015 to 2019, the ten common serotypes in both PHiD-CV and PCV13 and serotype 19A accounted for approximately 48% of IPD isolates.²⁸ The additional two serotypes of PCV13, serotypes 3 and 6A comprised 7% of the IPD isolates while NVTs comprised 45% of all serotypes.⁴ However, there is a need to conduct a follow up study using up-to-date surveillance data on serotype coverage.

Prior to the inclusion of PCV13 in the NIP in 2014, serotypes 5 and 6A were most common. A follow up survey in 2018 revealed a reduction in the distribution of most PCV13 serotypes with serotype 14 as most common, followed by serotypes 18C, 1, and 23F as well as serotype 19A which was not seen in previous studies.⁴ In contrast, serogroups 6 and 19 were most prevalent in the SEA region.⁹⁻¹³

Given that 6A was among the most prevalent serotypes prior to the inclusion of PCV13 in the NIP, the utilization of a vaccine not including this serotype could potentially cause a resurgence of cases due to 6A, which can also occur for serotype 19.¹⁹⁻²¹ This could cause serious consequences as serotypes 19A and 6A are the most resistant serotypes globally⁵ and regionally.

In relation to the higher valency vaccines, the 2022 ARSP Annual Report revealed the different *S. pneumoniae* serotypes of positive isolates from children aged five years old and below (Table 6).²⁹ However, only 20 positive isolates were

Table 5. Percent Coverage of Different PCVs in Children under Five Years Old (n=93) in the Philippines. Adopted from Haasis et al. (2015)²⁷

Serotype	PCV10		PCV13 Pneumovax 13
	PHiD-CV (Synflorix)	SI IPL-PCV (Pneumosil)*	
4	4.30	-	4.30
6B	9.68	9.68	9.68
9V	0.00	0.00	0.00
14	11.83	11.83	11.83
18C	1.08	-	1.08
19F	1.08	1.08	1.08
23F	6.45	6.45	6.45
1	6.45	6.45	6.45
5	9.68	9.68	9.68
7F	0.00	0.00	0.00
3	-	-	5.38
6A	-	6.45	6.45
19A	-	7.53	7.53
Total Coverage	50.54	59.15	69.89 64.51**

*hypothetical coverage; **adjusted coverage of PCV13 considering WHO (2021) evidence

Table 6. *S. pneumoniae* Serotypes in Children Aged Five Years Old and below (n=20) in the Philippines (ARSP, 2023)²⁹

Serotype	Number of positive isolates (%)	Serotype coverage				
		PCV 10		PCV13	PCV15	PCV20
		PHiD-CV	SI IPL-PCV	Pneumovax13		
6B	2 (10)					
19A	4 (20)					
10A	2 (10)					
15B	1 (5)					
6C	1 (5)					
10	1 (5)					
15	1 (5)					
23A	1 (5)					
15C	1 (5)					
16F	1 (5)					
35B	1 (5)					
No data	4 (20)					

recorded. Based on this data, the coverage of the different types of PCV were 10%, 30%, and 45% for PHiD-CV, both SIIP-PCV and PCV15, and PCV20, respectively. Of the isolates, 35% were non-PCV serotypes. The data from the 2022 ARSP Annual Report, though limited by the small sample size of only 20 positive isolates, provides insight into the serotype distribution of *S. pneumoniae* among children aged five and below. The varying vaccine coverage suggests that PCV20 offers the broadest protection against pneumococcal disease in this population. However, the presence of 35% non-PCV serotypes highlights a potential gap in current vaccination strategies, as a significant proportion of the pneumococcal serotypes causing infections are not covered by existing vaccines. This finding emphasizes the need for continuous monitoring of serotype prevalence, potential updates to vaccine formulations, and a reassessment of immunization strategies to ensure optimal protection, especially as the pneumococcal landscape evolves. The data underscores the importance of surveillance and suggests that reliance solely on current vaccines may leave some children vulnerable to infections from non-vaccine serotypes.

In the HTAC recommendation, immunogenicity studies were used as a method to evaluate the efficacy and determine the immunological markers as substitute endpoints for clinical protection.⁴ The WHO guidelines include the use of immunogenicity data in order to predict the efficacy of a candidate vaccine.³⁰ Further, these immunogenicity data are also used in non-inferiority trials due to ethical considerations of administering placebo when there is a vaccine of established efficacy. Findings on the immunogenicity of a candidate vaccine may thus be considered in the body of evidence in conducting a reassessment of PCV. In addition, available findings on the real-world data of an approved molecule may also be submitted as evidence for reassessment.

Data on cost-effectiveness analysis and budget impact analysis may be incorporated in a reassessment of evidence as new formulations will incur a different program cost and thus will have a different budgetary impact as compared to that of currently assessed formulations. The coverage of each vaccine may also be recomputed using current surveillance data as the changes in serotype distribution may have significant impact as the most recent study was done in 2015.

CONCLUSION

The review highlights the shifting pneumococcal serotype distribution in the Asia Pacific region, emphasizing the importance of continued surveillance to guide vaccine policies in the Philippines. The inclusion of PCVs in the NIP must be made with careful consideration of various factors contextualized in the Philippine setting. Apart from evaluating programmatic characteristics, vaccine supply, and vaccine price, enhancing laboratory and surveillance capacity will be necessary for evidence-based decision-making with respect to the evolving profile of serotype distribution and

AMR. Furthermore, these factors may be considered by other countries as part of their criteria in the selection of the appropriate type of PCV for inclusion in their respective NIPs. With the availability of a new 10-valent PCV formulation with a lower vaccine price and a comparable coverage for prevailing serotypes, the reassessment of choice of PCV with the consideration of all three formulations, namely PCV13, PHiD-CV, and SIIP-PCV, may be warranted to ensure the better protection against local serotypes and resistant strains. The emergence of evidence from research on newer vaccines and their impact on serotype distribution and AMR will enhance vaccine policies and ensure timely updates to the Philippine NIP for sustained pneumococcal control.

Acknowledgments

The authors would like to express their gratitude to Mr. Romulo Neri for his technical input on the study. The authors would also like to thank Faberco Life Sciences Inc. for providing financial support for this research.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

Funding Source

The study received funding from Faberco Life Sciences Inc.

REFERENCES

1. World Health Organization. Introduction of pneumococcal vaccine PCV10, two dose presentation: a handbook for district and health facility staff [Internet]. 2013 [cited 2021 Oct]. Available from: <https://apps.who.int/iris/bitstream/handle/10665/90378/?sequence=1>
2. Alderson M, Sethna V, Newhouse L, Lamola S, Dhere R. Development strategy and lessons learned for a 10-valent pneumococcal conjugate vaccine (PNEUMOSIL®). Hum Vaccin Immunother. 2021 Aug 3;17(8):2670-7. doi: 10.1080/21645515.2021.1874219. PMID: 33541250. PMCID: PMC8492432.
3. World Health Organization. Pneumococcal conjugate vaccines in infants and children under 5 years of age: WHO position paper—February 2019. Wkly Epidemiol Rec [Internet]. 2019 Feb 22;94(8):85-103 [cited 2021 Nov]. Available from: <https://apps.who.int/iris/handle/10665/310970>.
4. Ceria-Pereña J. Reassessment of 10-versus 13-valent Pneumococcal Conjugate Vaccines in the Philippines: Evidence Summary. Department of Health [Internet]. 2020 HTA Report version 1.0 [cited 2021 Oct]. Available from: <https://hta.dost.gov.ph/wp-content/uploads/2024/02/PCV-Full-HTA-Report-FINAL-.pdf>
5. Hackel M, Lascols C, Bouchillon S, Hilton B, Morgenstern D, Purdy J. Serotype prevalence and antibiotic resistance in Streptococcus pneumoniae clinical isolates among global populations. Vaccine. 2013 Oct 1;31(42):4881-7. doi: 10.1016/j.vaccine.2013.07.054
6. Johnson HL, Deloria-Knoll M, Levine OS, Stoszek SK, Freimanis Hance L, Reithinger R, Muenz LR, O'Brien KL. Systematic evaluation of serotypes causing invasive pneumococcal disease among children under five: the pneumococcal global serotype project. PLoS Med. 2010 Oct 5;7(10):e1000348. doi: 10.1371/journal.pmed.1000348. PMID: 20957191. PMCID: PMC2950125.

7. United Nations. Asia and the Pacific SDG Progress Report 2020 [Internet]. United Nations; 2020 [cited 2021 Oct]. Available from: <https://www.un-ilibrary.org/content/books/9789210049580>.
8. McIntosh E, Reinert R. Global prevailing and emerging pediatric pneumococcal serotypes. *Expert Rev Vaccines*. 2011 Jan 1;10(1):109-29. doi: 10.1586/erv.10.145. PMID: 21162687.
9. Arushothy R, Ahmad N, Amran F, Hashim R, Samsudin N, Azih CR. Pneumococcal serotype distribution and antibiotic susceptibility in Malaysia: a four-year study (2014–2017) on invasive pediatric isolates. *Int J Infect Dis*. 2019 Mar 1;80:129-33. doi: 10.1016/j.ijid.2018.12.009. PMID: 30576811.
10. Hocknell R, Cleary D, Srifeungfung S, Clarke S. Serotype distribution of disease-causing *Streptococcus pneumoniae* in Thailand: a systematic review. *Vaccine*. 2019 May 27;37(24):3159-66. doi: 10.1016/j.vaccine.2019.04.085. PMID: 31030920.
11. Turner P, Leab P, Ly S, Sao S, Miliya T, Heffelfinger JD, et al. Impact of 13-valent pneumococcal conjugate vaccine on colonization and invasive disease in Cambodian children. *Clin Infect Dis*. 2020 Apr 10;70(8):1580-8. doi: 10.1093/cid/ciz481. PMID: 31124635.
12. Daningrat W, Paramaiswari W, Putri HM, Safari D. Antimicrobial resistance profile of *Streptococcus pneumoniae* in children <5 years of age in sea nomads population in Indonesia. *Int J Infect Dis*. 2020 Dec 1;101:13. doi: 10.1016/j.ijid.2020.09.071. PMID: 32971448.
13. Vo T, Phan T, Ngo H, Pham H, Ho T. Antibiotic susceptibility of invasive *Streptococcus pneumoniae* isolates in southern Vietnam. *Int J Infect Dis*. 2020 Dec 1;101:53-4. doi: 10.1016/j.ijid.2020.09.172. PMID: 32980590.
14. Department of Health - Research Institute for Tropical Medicine. Antimicrobial Resistance Surveillance Program: Annual Report Summary 2020 [Internet]. 2021 [cited 2021 Oct]. Available from: <https://arsp.com.ph/publications/>
15. Cohen O, Knoll M, O'Brien K, Ramakrishnan M, Constenla D, Privor-Dumm L, et al. Pneumococcal conjugate vaccine (PCV) product assessment [Internet]. Balt MD Johns Hopkins Bloom Sch Public Heal. 2017 Apr [cited 2021 Oct]. Available from: https://terrance.who.int/mediacentre/data/sage/SAGE_Docs_Ppt_Oct2017/9_session_PCV/Oct2019_session9_PCV_PRIMEsummary.pdf
16. World Health Organization. Considerations for Pneumococcal Conjugate Vaccine (PCV) Product Choice. 2021 [cited 2021 Oct]. Available from: <https://apps.who.int/iris/bitstream/handle/10665/344915/9789240030602-eng.pdf>
17. Mariyam A, Olbrecht J, Ozakay A, Eken V, Meszaros K. Cost-effectiveness comparison of pneumococcal conjugate vaccines in Turkish children. *Value Health Reg Issues*. 2019 Sep 1;19:34-44. doi: 10.1016/j.vhri.2018.11.007. PMID: 30776766.
18. Avila-Aguero ML, Ulloa-Gutierrez R, Falleiros-Arlant LH, Porras O. Pneumococcal conjugate vaccines in Latin America: are PCV10 and PCV13 similar in terms of protection against serotype 19A? *Expert Rev Vaccines*. 2017 Jul 3;16(7):657-60. doi: 10.1080/14760584.2017.1334555. PMID: 28565977.
19. Camacho Moreno G, Imbachi LF, Leal AL, Moreno VM, Patiño JA, Gutiérrez IF, et al. Emergence of *Streptococcus pneumoniae* serotype 19A (Spn19A) in the pediatric population in Bogotá, Colombia as the main cause of invasive pneumococcal disease after the introduction of PCV10. *Hum Vaccin Immunother*. 2020 Sep 1;16(9):2300-6. doi: 10.1080/21645515.2019.1710411. PMID: 31902341. PMID: PMC7660594.
20. Cassiolato AP, Almeida SC, Andrade AL, Minamisava R, Brandileone MC. Expansion of the multidrug-resistant clonal complex 320 among invasive *Streptococcus pneumoniae* serotype 19A after the introduction of a ten-valent pneumococcal conjugate vaccine in Brazil. *PLoS One*. 2018 Nov 29;13(11):e0208211. doi: 10.1371/journal.pone.0208211. PMID: 30496263. PMID: PMC6264776.
21. Potin M, Fica A, Wilhem J, Cerda J, Contreras L, Escobar C, Moreno G, Muñoz A, Véliz L. Opinion of the Immunization Advisory Committee of the Chilean Society of Infectiology: pneumococcal conjugate vaccine in children and the emergence of serotype 19A. *Rev Chilena Infectol*. 2016 Jun;33(3):304-6. doi: 10.4067/S0716-10182016000300009. PMID: 27598249.
22. World Health Organization. Global Antimicrobial Resistance and Use Surveillance System (GLASS) Report 2019 [Internet]. 2020 [cited 2021 Nov]. Available from: <https://iris.who.int/bitstream/handle/10665/332081/9789240005587-eng.pdf?sequence=1>.
23. Shankar PR, Balasubramaniam R. Antimicrobial resistance: global report on surveillance 2014. *Australas Med J* [Internet]. 2014 May 1;7(5):237 [cited 2021 Nov]. Available from: <https://iris.who.int/bitstream/handle/10665/112642/?sequence=1>.
24. Kim S, Chung D, Song J, Baek J, Thamlikitkul V, Wang H, Carlos C, Ahmad N, Arushothy R, Tan S, Lye D. Changes in serotype distribution and antimicrobial resistance of *Streptococcus pneumoniae* isolates from adult patients in Asia: emergence of drug-resistant non-vaccine serotypes. *Vaccine*. 2020 Aug 27;38(38):6065-73. doi: 10.1016/j.vaccine.2019.09.065. PMID: 31563534.
25. World Health Organization. Global antimicrobial resistance surveillance system: manual for early implementation [Internet]. 2015 [cited 2021 Oct]. Available from: <https://apps.who.int/iris/bitstream/handle/10665/188783/9789245549406-chi.pdf>
26. Klugman K, Black S. Impact of existing vaccines in reducing antibiotic resistance: primary and secondary effects. *Proc Natl Acad Sci U S A*. 2018 Dec 18;115(51):12896-901. doi: 10.1073/pnas.1721095115. PMID: 30559199. PMID: PMC6304921.
27. Haasis MA, Ceria JA, Kulpeng W, Teerawattananon Y, Alejandria M. Do pneumococcal conjugate vaccines represent good value for money in a lower-middle-income country? A cost-utility analysis in the Philippines. *PLoS One*. 2015 Jul 1;10(7):e0131156. doi: 10.1371/journal.pone.0131156. PMID: 26131964. PMID: PMC4488293.
28. Department of Health - Research Institute for Tropical Medicine. Antimicrobial Resistance Surveillance Program: Data Summary Report 2019 [Internet]. 2020 [cited 2021 Nov]. Available from: <https://arsp.com.ph/publications/>
29. Department of Health - Research Institute for Tropical Medicine. Antimicrobial Resistance Surveillance Program: Annual Report Summary 2022 [Internet]. 2023 [cited 2023 Apr]. Available from: <https://arsp.com.ph/publications/>
30. Sheets R, Kang HN, Meyer H, Knezevic I. WHO informal consultation on the guidelines for evaluation of the quality, safety, and efficacy of DNA vaccines, Geneva, Switzerland, December 2019. *NPJ Vaccines*. 2020 Jun 18;5(1):52. doi: 10.1038/s41541-020-0197-2. PMID: 32587837. PMID: PMC7304312.