

Cost-utility analysis on the inclusion of pneumococcal vaccines in the national immunization program for older adults in the Philippines – Evidence from a middle-income country in Asia

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Title

Cost-utility analysis on the inclusion of pneumococcal vaccines in the national immunization program for older adults in the Philippines – Evidence from a middle-income country in Asia

Short title

Pneumococcal vaccines for older adults in Philippines

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Declarations

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Author contributions

HV, JA, PFR study conceptualization. RAHC, JCC, MMD, NB, DS, XT data collection. HV performed the data analysis. HV, JA, PFR wrote the first draft. RAHC, JCC, MMD, NB, DS, XT provided critical inputs and reviewed the manuscript. JA, PFR supervision of the project. All authors approved the contents of the manuscript.

Ethics Statement and Consent to Participate

The study was done according to the Declaration of Helsinki and relevant national regulations. The study was reviewed by University of the Philippines Manila Review Ethics Board (UPMREB 2024-0207-EX, 4 March 2024) and exempted from full review because it used publicly available data. Informed consent was not required because no human participants were involved.

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Conflicts of Interest

None

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Data availability

All data used in the analysis are publicly available. The datasets supporting the conclusions of this article are included within the article and its additional file.

Abbreviations

CEAC, cost-effectiveness acceptability curve

GDP, gross domestic product

HTA, health technology assessment

HTAC, Health Technology Assessment Council of the Philippines Council for Health

Research and Development

ICD-10, International Statistical Classification of Diseases and Related Health Problems 10th

Revision

ICER, incremental cost-effectiveness ratio

IPD, invasive pneumococcal disease

NBPP, non-bacteremic pneumococcal pneumonia

NMB, net monetary benefit

PCV, pneumococcal conjugate vaccine

PCV13, 13 valent pneumococcal conjugate vaccine (Pevnar 13 ®)

PCV15, 15-valent pneumococcal conjugate vaccine (Vaxneuvance ®)

PhilHealth, Philippine Health Insurance Corporation

PHP, Philippine peso

PPV23, 23-valent pneumococcal polysaccharide vaccine (Pneumovax 23®)

QALY, quality-adjusted life years

VE, vaccine effectiveness

WHO, World Health Organization

WTP, willingness-to-pay

Abstract

Background: Pneumococcal disease remains a substantial cause of morbidity and mortality among older adults. This study evaluated the cost-effectiveness and budget impact of four pneumococcal vaccination strategies among adults aged 60 years and older in the Philippines.

Methods: A Markov model with seven health states (healthy, meningitis, bacteremia with pneumonia, bacteremia without pneumonia, non-bacteremic pneumococcal pneumonia [NBPP], disability/sequelae, death) was used to simulate a 15-year time horizon under annual cycles. Four strategies were compared: no vaccination, PPV23 alone, sequential PCV13 followed by PPV23, and sequential PCV15 followed by PPV23. The analysis used a healthcare system perspective, with costs and outcomes discounted at 7% annually. The willingness-to-pay (WTP) threshold was set at PHP 173,742.26 per quality-adjusted life year (QALY), equivalent to 75% of the 2024 GDP per capita. Epidemiologic parameters, vaccine effectiveness, waning rates, utility values, and cost inputs were derived from local and international sources. One-way and probabilistic sensitivity analyses (PSA) were performed, and cost-effectiveness acceptability curves (CEACs) were generated. A budget impact analysis (BIA) estimated financial implications over a five-year period (2025–2029) at 95% vaccination coverage.

Results: Compared with no vaccination, PPV23 alone had the lowest incremental cost-effectiveness ratio (ICER: PHP 3,705.50 per QALY) and the highest net monetary benefit (NMB: approximately PHP 1.31 million). PCV13 followed by PPV23 and PCV15 followed by PPV23 had ICERs of PHP 19,289.21 and PHP 23,453.88 per QALY, respectively. Vaccine coverage against IPD was the most influential parameter in sensitivity analyses. PSA indicated PPV23 was cost-effective in nearly all simulations at the specified WTP threshold,

with a CEAC-derived probability exceeding 90%. In the BIA, only PPV23 was associated with net cost savings relative to no vaccination after accounting for vaccine procurement, wastage and storage. PCV13 plus PPV23 was projected to cost PHP 16.69 billion more than PPV23 alone, and PCV15 plus PPV23 was projected to cost PHP 20.9 billion more than PPV23 alone and PHP 4.21 billion more than PCV13 plus PPV23.

Conclusion: Among the four strategies evaluated, PPV23 alone was associated with the lowest ICER and lowest impact on budget. Sequential PCV13/PPV23 and PCV15/PPV23 strategies were associated with additional health gains but at a higher cost.

Keywords: cost-effectiveness, economic evaluation, pneumococcal vaccines, adults, invasive pneumococcal disease, Philippines

Introduction

Pneumococcal disease remains an important cause of morbidity and mortality among older adults, particularly because the risk of severe disease increases with age and underlying chronic conditions. In the Philippines, pneumonia is consistently among the top 10 causes of morbidity, and pneumococcal disease contributes substantially to severe respiratory and invasive infections. In a prospective study of 535 patients aged ≥ 14 years hospitalized with community-acquired pneumonia in a rural Philippine setting, *Streptococcus pneumoniae* (pneumococcus) accounted for 10.5% of cases and was the most frequently isolated organism from positive blood cultures (15 of 24 bacterial isolates).¹ Nationally, however, pneumococcal disease surveillance remains limited, and published epidemiologic data on invasive pneumococcal disease (IPD) in Philippine adults are lacking. Available evidence from Asia demonstrates a substantial age gradient in IPD incidence, ranging from 26 per 100,000 among adults aged ≥ 65 years in rural Thailand to 1,147 per 100,000 in Taiwan, with reported adult case-fatality rates of 18–40%.² These data underscore the need for locally relevant evidence to inform vaccination policy.

Pneumococcal vaccination is an established strategy for preventing pneumococcal disease in older adults. Two vaccine types are currently available in the Philippines: the 23-valent pneumococcal polysaccharide vaccine (PPV23) and pneumococcal conjugate vaccines (PCVs), including PCV13 and PCV15.^{3–5} Unlike PPV23, PCVs induce mucosal immunity and reduce carriage of vaccine-type pneumococci, providing a biological rationale for their use in sequential vaccination schedules.⁶ Philippine policy currently provides PPV23 to indigent adults aged ≥ 60 years through the national pneumococcal immunization program.⁷ Although national coverage increased from $<1\%$ in 2019 to approximately 7% in 2023, uptake remains limited.⁸ International recommendations increasingly incorporate PCV-based

schedules, including PCV15 followed by PPV23, reflecting evolving evidence and vaccine availability.⁹

The choice of pneumococcal vaccine strategy therefore has implications for both population health and healthcare resource allocation. The World Health Organization recommends that decisions regarding adult pneumococcal vaccination consider local disease burden, cost-effectiveness, and operational feasibility.¹⁰ This is particularly relevant in the Philippines, where epidemiologic evidence is incomplete, vaccine coverage is low, and public resources for adult immunization are constrained. Although PPV23 is currently used within the national program for older adults,¹¹ the economic consequences of replacing or complementing it with PCV13 or PCV15 followed by PPV23 have not been established in the Philippine context.

We therefore conducted a cost-utility analysis of pneumococcal vaccination strategies for adults aged ≥ 60 years in the Philippines. We compared PPV23 alone with PCV13 followed by PPV23 and PCV15 followed by PPV23, using no vaccination as the reference strategy, and assessed incremental costs, quality-adjusted life-years (QALYs), and cost-effectiveness under alternative assumptions of vaccine effectiveness and parameter uncertainty. By quantifying the costs and health outcomes associated with each strategy over a 15-year time horizon, the analysis addresses a key evidence gap for national decisions on adult pneumococcal vaccination and resource allocation.

Methods

We developed a Markov model to simulate the health and economic outcomes associated with pneumococcal vaccination strategies among Filipino adults aged ≥ 60 years over a 15-year time horizon. The model was adapted from previous study which evaluated pneumococcal vaccination among adults aged ≥ 65 years in Thailand.¹² The model compared four strategies: (a) no vaccination, (b) PPV23 alone, (c) PCV13 followed by PPV23, and (d) PCV15 followed by PPV23. Pairwise comparisons between vaccination strategies were also performed. The evaluated strategies corresponded to vaccination schedules under consideration by the Philippine Department of Health.

Model structure

The model comprised seven health states: healthy, meningitis, bacteremia with pneumonia, bacteremia without pneumonia, non-bacteremic pneumococcal pneumonia (NBPP), disability or sequelae, and death (Figure 1). At model entry, all individuals were assumed to be in a healthy state. During each model cycle, individuals could remain healthy or develop invasive pneumococcal disease (IPD, which comprises meningitis, bacteremia with pneumonia, and bacteremia without pneumonia) or non-bacteremic pneumococcal pneumonia (NBPP). Following infection, individuals could recover, develop long-term sequelae, or die. Recovered individuals were subsequently considered to be in a healthy state. All individuals were also exposed to age-specific all-cause mortality throughout the model.

The model was implemented in TreeAge Pro (TreeAge Software, LLC, United States) and used to simulate disease progression, costs, and health outcomes over the specified time horizon. Transition probabilities, costs, and utility values were assigned to the relevant health states and applied at each model cycle.

Model Assumptions

Adults receiving sequential vaccination were assumed to receive both vaccines in the specified sequence. Base-case vaccine coverage was assumed to be 95%. Individuals could experience a maximum of one pneumococcal infection per year but could experience infections in multiple years over a 15-year time horizon. We used this time horizon based on the assumption that vaccine effectiveness wanes to zero 15 years after vaccination. Long-term sequelae could occur only once. Multidose preparations were used for PCV13, whereas single-dose preparations were used for PCV15 and PPV23.

Vaccine protection was assumed to wane over time for all vaccine products. For PCV13 and PCV15, protection was assumed to persist for 15 years, with no decline during the first 5 years followed by a linear decline to zero over the subsequent 10 years. For PPV23, protection was assumed to decline linearly from the first year after vaccination and reach zero by year 15.

Model input parameters

Epidemiologic and demographic parameters were obtained from national demographic data, published literature, and international databases (Appendix Table S1, Table S2, Table S3).

Population estimates for adults aged ≥ 60 years were obtained from the Philippine Statistics Authority 2026 population projections.¹³ Disease incidence and prevalence estimates were primarily obtained from the Global Burden of Disease 2021^{14,15} database and supplemented with local and international surveillance and cohort studies.^{1,16–24} Parameters included the incidence of pneumococcal meningitis, bacteremia with and without pneumonia, and NBPP.

Model incidence estimates were derived by combining reported incidence rates, case-fatality ratios, and the proportion of disease attributable to *Streptococcus pneumoniae*. Incidence rates were applied to the target population and adjusted according to pneumococcal attribution and disease setting, including hospitalized, outpatient, invasive, and non-invasive cases. Parameter uncertainty was represented using reported confidence intervals where available; otherwise, uncertainty bounds of $\pm 20\%$ of the point estimate were applied.

Disease-specific mortality was estimated by applying case fatality ratios from systematic reviews and country-specific studies to the estimated number of cases. Age-specific case-fatality ratios were used where available. Mortality from causes other than pneumococcal disease was based on Philippine Statistics Authority mortality estimates for 2023. The proportion of pneumococcal cases resulting in long-term disability or sequelae was obtained from published literature.

Vaccine efficacy and effectiveness

Vaccine effectiveness (VE) against IPD and NBPP was obtained from randomized controlled trials and observational studies and adjusted for the serotype coverage of each vaccine formulation (Appendix Table S4). For the base-case analysis, PPV23 effectiveness estimates were primarily derived from Tsai et al. (2015) for IPD and Maruyama et al. (2010) for NBPP.^{25,26} Effectiveness estimates for PCV13+PPV23 and PCV15+PPV23 were informed by observational studies, including Hasegawa et al. (2024) and Heo et al. (2021).^{27,28} Where direct evidence for PCV15 was unavailable, its effectiveness was based on PCV13 sequential vaccination estimates and adjusted according to PCV15 serotype coverage. Confidence intervals from source studies were used to define uncertainty ranges where available.

An alternate-effectiveness scenario incorporated pooled and randomized trial evidence from Ortqvist et al. (1998), Bonten et al. (2015), and pooled analyses of Ortqvist et al. (1998) and Maruyama et al. (2010).^{26,29,30} This scenario incorporated wider VE ranges, including negative lower bounds, to represent uncertainty in vaccine effectiveness. VE was decomposed according to PCV and PPV23 contributions, with adjustment for overlapping and non-overlapping serotypes.

For the base-case analysis, VE waning estimates for IPD and NBPP were based on the waning assumptions reported by Ngamprasertchai et al. (2023) (Appendix Table S5).¹² PPV23 effectiveness against IPD and NBPP was modeled to decline annually from 68.7% and 56.05%, respectively, to zero by year 15. For sequential PCV13+PPV23 and PCV15+PPV23 strategies, initial effectiveness was set at 42.36% for IPD and 33.61% for NBPP, with no decline in effectiveness decline during the first 5 years and subsequent linear waning to zero by year 15.

Utilities

Health-state utility weights were used to estimate quality-adjusted life-years (QALYs) and were derived from published literature (Appendix Table S6).^{12,24} Base-case utility weights were 0.4 for meningitis, 0.5 for bacteremia and pneumonia, and 0.3 for long-term neurological sequelae, including epilepsy, hearing loss, neurocognitive impairment, and behavioral problems. Uncertainty ranges were generally defined as $\pm 20\%$ of the base-case estimates based on the available evidence.

Cost

The analysis was conducted from the healthcare system perspective and included direct medical costs associated with pneumococcal disease, sequelae, outpatient treatment, and vaccination. Disease-related costs were primarily based on 2025 PhilHealth (national health insurance) case rates, guided by ICD-10 codes and published literature for sequelae (Appendix Table S7).^{22,31} Mean direct medical costs were PHP 50,115 for meningitis, PHP 62,400 for bacteremia without pneumonia and with pneumonia, and PHP 29,250 for hospitalized NBPP. Uncertainty bounds of $\pm 20\%$ were applied to these estimates.

Costs assigned to sequelae were PHP 15,210 for seizure/epilepsy, PHP 45,435 for hearing loss, PHP 18,525 for neurocognitive impairment, and PHP 15,210 for behavioral problems. Outpatient treatment costs for non-hospitalized NBPP were estimated using the Drug Price Reference Index and Philippine Society for Microbiology and Infectious Diseases guidelines, resulting in an estimated cost of PHP 179.51.^{32,33} Cost inputs were obtained from different reference years according to data availability, and no inflation adjustment was applied.

Vaccine procurement prices were obtained from manufacturers and redacted (Table S6). Vaccine costs were adjusted for wastage and storage costs based on calculations used and provided by the Department of Health. For single-dose preparations, 5% of the unit cost was added for wastage and 8% for storage. For multidose preparations, 10% was added for wastage and 4% for storage. These vaccine cost inputs were redacted.

Cost inputs were obtained from different reference years according to data availability, and no inflation adjustment was applied.

Discounting and economic outcomes

Costs and health outcomes were discounted at 7% annually over a 15-year time horizon. The primary outcome was the incremental cost-effectiveness ratio (ICER), expressed as cost per QALY gained. Incremental costs and QALYs were calculated for each vaccination strategy relative to the comparator. Strategies that were more costly and less effective than an alternative were classified as dominated. Net monetary benefit (NMB) was also calculated.

The base-case willingness-to-pay (WTP) threshold was PHP 173,742.26 per QALY gained, corresponding to 75% of the 2024 Philippine GDP per capita. Cost-effectiveness was assessed by comparing the ICER with the specified WTP threshold.

Sensitivity analyses

One-way and probabilistic sensitivity analyses were conducted to characterize parameter uncertainty. One-way sensitivity analyses varied individual parameters across their prespecified uncertainty ranges and assessed their effects on the ICER. Probabilistic sensitivity analysis simultaneously varied model parameters according to their assigned probability distributions. Results were presented using cost-effectiveness planes and cost-effectiveness acceptability curves (CEACs), which estimated the probability that each strategy was cost-effective across different WTP thresholds.

Expert consultation and validation

The model structure, key input parameters, and preliminary results were reviewed through consultation with experts in Markov modeling, epidemiology, and pneumococcal disease. The model structure, key input parameters and preliminary results were reviewed through consultations with experts from the Subcommittee on Vaccines and subsequently by the Health Technology Assessment Council (HTAC) of the Philippine Department of Science and

235 Technology. The model structure, key input parameters and preliminary results were
236 reviewed through consultations with experts from the Health Technology Assessment
237 subcommittee on vaccines and subsequently by the Health Technology Assessment Council
238 (HTAC) of the Philippine Department of Science and Technology.³⁴

239

240 *Ethics review and consent to participate*

241 The study was done according to the Declaration of Helsinki and relevant national
242 regulations. The study was reviewed by University of the Philippines Manila Review Ethics
243 Board (UPMREB 2024-0207-EX, 4 March 2024) and exempted from full review because it
244 used publicly available data. Informed consent was not required because no human
245 participants were involved.

Results

1. Base-case cost utility analysis

The no-vaccination strategy had the lowest cost at PHP 300.45 per person and generated 7.40 QALYs (Table 1). PPV23 increased costs to PHP 794.43 per person and generated 7.48 QALYs, corresponding to an incremental gain of 0.09 QALYs compared with no vaccination. PCV13+PPV23 and PCV15+PPV23 had higher costs of PHP 1,588.97 and PHP 1,867.17 per person, respectively, and each generated 7.46 QALYs.

Compared with no vaccination, PPV23 had an ICER of PHP 5,710.75 per QALY gained. The ICERs for PCV13+PPV23 and PCV15+PPV23 were PHP 19,289.21 and PHP 23,453.88 per QALY gained, respectively (Table 1). PPV23 had the highest NMB at PHP 1,299,492.65. NMB was PHP 1,295,275.39 for PCV13+PPV23 and PHP 1,294,997.19 for PCV15+PPV23 (Table 1).

In pairwise comparisons, PPV23 was less costly and more effective than both sequential strategies (Table 2). Compared with PPV23, PCV13+PPV23 cost PHP 794.54 more per person and generated 0.02 less QALYs. Compared with PPV23, PCV15+PPV23 cost PHP 1,072.74 more per person and generated 0.02 less QALYs. Thus, both sequential strategies were dominated by PPV23.

PCV13+PPV23 and PCV15+PPV23 generated the same number of QALYs. PCV13+PPV23 cost PHP 278.20 less per person than PCV15+PPV23. The sequential strategies were therefore subject to extended comparison with PPV23, given their higher costs and lower effectiveness.

2. Sensitivity analyses

To test the robustness of the base-case findings, both one-way sensitivity analysis and probabilistic sensitivity analysis were conducted. These analyses were performed to determine whether the conclusions of the model remained consistent under different assumptions and to provide greater confidence in the reliability of the results.

2.1. One-way sensitivity analysis

One-way sensitivity analyses examined the effects of variation in vaccine effectiveness, vaccine coverage, costs, utility values, disease incidence, case-fatality rates, and discount rates on the ICERs (Figure 2a–c).

For PPV23 versus no vaccination (Figure 2a), vaccine coverage produced the largest variation in the ICER. Other influential parameters were vaccine efficacy against invasive pneumococcal disease (IPD), incidence of pneumococcal infection, discount rate and PPV23 price. Across the tested parameter ranges, the ICER remained below the WTP threshold of PHP 173,742.26 per QALY gained.

For PCV13+PPV23 versus no vaccination (Figure 2b), vaccine coverage was the largest driver of ICER variation. The incidence of pneumococcal infection, discount rate and combined vaccine price also produced changes in the ICER. The ICER remained below the WTP threshold across the tested parameter ranges except when there is a substantial low vaccine coverage rate (19.2%).

For PCV15+PPV23 versus no vaccination (Figure 2c), vaccine coverage efficacy was also the largest driver of ICER variation, followed by incidence of pneumococcal infection,

discount rate and combined vaccine price. The ICER remained below the WTP threshold across the tested parameter ranges except when there is a substantial low vaccine coverage rate (22.1%).

2.2. Probabilistic sensitivity analysis

Probabilistic sensitivity analysis simultaneously varied all model parameters according to their specified probability distributions to characterize joint parameter uncertainty (Figure 3a–c). Additional pairwise probabilistic sensitivity analyses are presented in the Appendix (Appendix Figure S1a–S1f).

For PPV23 versus no vaccination (Figure 3a), 99.90% of simulations were cost-effective at a WTP threshold of PHP 173,742.28 per QALY gained. Mean ICER for the simulations was PHP 8,942.32 which was substantially below the WTP threshold. Most simulations were located in the northeast quadrant of the cost-effectiveness plane, indicating positive incremental costs and positive incremental QALYs. No simulations showed no vaccination to be dominant over PPV23.

For PCV13+PPV23 versus no vaccination (Figure 3b), most simulations showed positive incremental costs and positive incremental QALYs. Mean ICER for the simulations was PHP 56,696.17 which was below the WTP threshold. At the WTP threshold of PHP 173,742.28 per QALY gained, 98.8% of simulations were cost-effective. The remaining simulations were distributed around the origin and above the cost-effectiveness threshold.

For PCV15+PPV23 versus no vaccination (Figure 3c), most simulations showed positive incremental costs and positive incremental QALYs. Mean ICER of the simulations was PHP

67,505.74 which was below the WTP threshold. At the WTP threshold of PHP 173,742.28 per QALY gained, 98.4% of simulations were cost-effective. The distribution of simulations indicated greater incremental costs relative to the incremental QALY gain than for PPV23 alone.

2.3. Cost-effectiveness Acceptability Curve

The cost-effectiveness acceptability curve showed the probability of each strategy being cost-effective across increasing WTP thresholds (Figure 4). At low WTP thresholds, no vaccination had the highest probability of cost-effectiveness. As the WTP threshold increased, the probability for no vaccination decreased, while that for PPV23 increased toward 100%.

At WTP thresholds of PHP 115,828.17, PHP 173,742.26, and PHP 231,656.35, corresponding to 0.5, 0.75, and 1.0 times GDP per capita, respectively, PPV23 had the highest probability of being cost-effective. The probabilities for PCV13+PPV23 and PCV15+PPV23 remained low across the evaluated WTP range.

2.4. Cost utility analysis using alternative scenarios (vaccination strategies)

Results of the alternative cost-utility scenarios are presented in Appendix Table S8. Under the alternate assumptions, PCV13+PPV23 and PCV15+PPV23 generated higher QALYs and lower ICERs than in the base-case analysis. PPV23 continued to have a low ICER and the highest or near-highest NMB across the evaluated scenarios.

3. Budget impact analysis

The budget impact analysis estimated the 5-year financial consequences of four vaccination strategies for adults aged ≥ 60 years in the Philippines: no vaccination, PPV23 alone, PCV13 followed by PPV23, and PCV15 followed by PPV23. Disease-related costs for IPD and non-bacteremic pneumococcal pneumonia were based on PhilHealth case rates and median hospitalization costs. Alternate scenarios using a lower target population coverage of 40% which represented the elderly indigent population. Vaccine waning assumptions were consistent with those used in the cost-utility analysis.

Vaccination coverage was assumed to reach 95% of the target population in 2026, with the remaining 5% vaccinated in the subsequent year. This pattern was applied annually, resulting in 5% of each annual cohort remaining unvaccinated by 2030. Annual and cumulative program costs included vaccine, wastage and storage costs, and disease-management costs. Incremental budget impact was calculated relative to no vaccination. No inflation adjustment was applied to cost inputs from different reference years. Model assumptions and input parameters are provided in Appendix Table S9.

Over the 5-year horizon, all vaccination strategies reduced treatment costs relative to no vaccination. When vaccination costs were included, PPV23 alone had a lower total cost than no vaccination under all scenarios using both the base-case (PhilHealth case rates) and alternate cost scenarios (median hospitalization cost) and both 95% vaccination coverage and 40% vaccination coverage.

PCV13+PPV23 had lower total costs than PCV15+PPV23 but higher total costs than PPV23 alone and no vaccination across the evaluated scenarios except in the scenario with a 40% vaccination coverage using median hospitalization costs (Appendix Table S10).

370 PCV15+PPV23 had the highest total costs in all scenarios except in the scenario with the
371 40% vaccination coverage using median hospitalization costs where no vaccination had a
372 total higher cost than all three vaccination regimens.
373
374 Considering vaccination costs alone, under all scenarios, PPV23 had the lowest total cost.
375 Under base-case scenario of 95% vaccination coverage using PhilHealth case rates and base-
376 case vaccine effectiveness, PCV13+PPV23 cost PHP 16.69 billion more than PPV23 alone,
377 whereas PCV15+PPV23 cost PHP 20.9 billion more than PPV23 alone and PHP 4.21 billion
378 more than PCV13+PPV23.
379

Discussion

Our cost-utility analysis found that PPV23 alone had the lowest ICER (incremental cost-effectiveness ratio) and highest NMB (net monetary benefit) compared with no vaccination, while sequential PCV13+PPV23 and PCV15+PPV23 strategies incurred substantially higher costs with smaller QALY gains. These findings were consistent across one-way and probabilistic sensitivity analyses, with PPV23 remaining cost-effective in 99.9% of probabilistic simulations at a WTP (willingness-to-pay) threshold of PHP 173,742.26 per QALY gained.

The main goal of our study was to determine whether the current adult vaccination strategy in the Philippines, consisting of PPV23 alone, should be supplemented with conjugate vaccine-based, given international recommendations favoring pneumococcal conjugate vaccines³⁵ and evidence suggesting improved immunogenicity with sequential vaccination.^{30,36} We hypothesized that the addition of PCV13 or PCV15 would provide greater health gains among older adults and high-risk populations that would justify their higher acquisition costs. However, this was not observed in our study.

The primary reason PPV23 emerged as the most cost-effective strategy was that the incremental clinical benefits associated with adding a conjugate vaccine were relatively small compared with the substantial increase in program costs. Although immunogenicity studies consistently demonstrated enhanced immune responses with sequential PCV13+PPV23 and PCV15+PPV23 regimens,³⁷⁻⁴⁰ clinical effectiveness data supporting superior protection against invasive pneumococcal disease (IPD) and non-bacteremic pneumococcal pneumonia (NBPP) were limited for the PCV13 regimen and absent for the PCV15 regimen,⁴¹⁻⁴³ and most available evidence was derived from observational studies.^{27,28,44,45} In contrast, PPV23

has a substantially larger body of effectiveness evidence, including population-based studies showing significant protection against IPD in older adults.^{25,26,29,46–49} These effectiveness estimates formed the basis of the economic model and favored PPV23 because observed differences in clinical outcomes between strategies were modest relative to differences in vaccine costs.

Also, it should be noted that most published effectiveness studies assessing conjugate vaccines in adults were conducted in high-income countries with mature pediatric PCV programs,^{41–43} where substantial herd protection had already altered circulating serotypes and disease epidemiology.⁵⁰ Comparable population-based effectiveness studies evaluating sequential PCV and PPV23 strategies in low-and- middle-income settings such as the Philippines are lacking. Consequently, the available evidence may not fully capture the potential benefits of conjugate vaccine strategies in the local context. Until stronger local effectiveness and surveillance data became available, the combination of broader serotype coverage, demonstrated effectiveness against IPD, lower acquisition costs, and favorable budget impact explains why PPV23 alone remained the dominant and most cost-effective strategy in this assessment.

Unlike the recent adult PCV13 model by Santiaguel et al. (2025), which compared PCV13 with a two-dose PPV23 schedule using vaccine effectiveness estimates derived from international sources,⁵¹ the present HTA incorporates effectiveness estimates from a comprehensive synthesis of clinical studies in adults and evaluates all vaccination strategies under consideration by the national immunization program (PCV13+PPV23, PCV15+PPV23, or PPV23 alone). In addition, we included PCV15, which was recently approved for adult use in the Philippines.³ While the previous study favored PCV-based approach, the current

evaluation found PPV23 alone to provide the most favorable balance of health gains, cost-effectiveness, and budget impact in the Philippine context. The preference for a single-dose strategy also reflects its lower acquisition and delivery costs compared with a sequential PCV–PPV23 schedule requiring two vaccine doses. However, the selection of PPV23 alone was based not solely on its lower cost, but on the overall balance of clinical benefits, economic value, and budgetary implications in the Philippine setting, consistent with the vaccination strategy under consideration by the national immunization program.

Strengths and limitations

Our study input parameters were reviewed by various stakeholders, which included clinical experts, health economists, representatives from patient organizations, and the industry. This was also moderated by the Health Technology Assessment Council which has the government mandate to conduct these assessments in the country. Unlike previous Philippine economic evaluations that relied heavily on assumptions from international data, the present study incorporated a comprehensive systematic review and meta-analysis of adult pneumococcal vaccine effectiveness and calibrated effectiveness estimates using local serotype surveillance data. This approach increases the relevance of the findings to the Philippine setting.

Nevertheless, this study has several limitations. First, the model used was a static model. Static models assume that the risk of infection remains constant over time and do not fully account for changes in population immunity, herd protection, serotype replacement, or shifts in serotype prevalence resulting from vaccine introduction, which are known to be seen in countries which introduced the vaccines.⁵² As a result, the model may underestimate the broader population-level benefits of vaccination, particularly for conjugate vaccines that may reduce nasopharyngeal carriage and transmission.^{53,54} We tried to mitigate this by doing

several scenarios and sensitivity analysis. We also used vaccine serotype VEs from literature and adjusted the VEs used using local serotype surveillance data.

Second, there is lack of local epidemiologic, vaccine effectiveness and utility data for input into the model. Although local sources such as the Antimicrobial Resistance Surveillance Program (ARSP),⁵⁵ Acute Meningitis and Encephalitis Syndrome (AMES) surveillance data (personal communication), PhilHealth databases, and demographic data from the Philippine Statistical Authority^{13,23} were used whenever available, many key parameters had to be derived from international studies. This limitation was particularly important for sequential vaccination strategies involving PCV13+PPV23 and PCV15+PPV23, for which very few effectiveness studies were available and no direct effectiveness studies were identified for PCV15+PPV23. Consequently, several model assumptions were required regarding vaccine effectiveness, waning, and disease outcomes. To minimize bias, preference was given to studies conducted in populations with healthcare systems, disease epidemiology, and socioeconomic characteristics similar to those of the Philippines.^{25–29} Furthermore, vaccine-effectiveness inputs were inferred using local serotype prevalence and coverage data to improve external validity. Nevertheless, uncertainty remains regarding the true effectiveness of sequential vaccination strategies in the Philippine population.

Third, the costing component was limited by the availability of local cost data. In the base-case analysis, direct medical costs were derived primarily from PhilHealth case rates, reflecting the healthcare payer perspective adopted in this study. However, PhilHealth reimbursement rates may not fully reflect the actual costs incurred by healthcare facilities or the total expenditures borne by the healthcare system.^{56,57} They may underestimate resource utilization, particularly among patients with prolonged hospital stays, intensive care

requirements, complications, or catastrophic illness.^{56,57} To partially address this limitation, we conducted alternative analyses using median actual hospitalization costs in addition to PhilHealth case rates, thereby testing the robustness of the results under different costing assumptions. Importantly, the overall conclusions regarding the relative cost-effectiveness of the assessed vaccination strategies remained largely unchanged across these alternative costing scenarios.

Fourth, local disease surveillance for pneumococcal disease remains limited. The Philippines currently lacks a comprehensive national surveillance system specifically designed to measure the burden of invasive pneumococcal disease and pneumococcal pneumonia. Existing sources are based on passive or sentinel surveillance systems with relatively small numbers of serotyped isolates.^{55,58} As acknowledged in this study, this data may not accurately represent the true distribution of circulating serotypes nationally. Consequently, estimates of vaccine-type disease burden and vaccine coverage against circulating serotypes should be interpreted with caution. Nevertheless, these represent the best available local data and are likely more appropriate for decision making than relying solely on international serotype distributions.

Finally, the model did not explicitly incorporate broader societal benefits of adult vaccination, including reductions in caregiver burden, productivity losses among working-age adults, long-term disability-related costs, and potential indirect protection conferred to unvaccinated populations. Therefore, the economic value of vaccination may be underestimated, particularly for strategies that reduce disease transmission or prevent long-term sequelae. Future studies incorporating dynamic transmission modeling, more comprehensive local costing data, and strengthened national pneumococcal surveillance would further reduce

uncertainty and improve future assessments of adult pneumococcal vaccination strategies in the Philippines.

Implications

From 2019 to 2023, the childhood pneumococcal vaccination coverage remained below 80%, which is below its target of 95%.^{59,60} Thus, we re-iterate the recommendation of WHO recommendations to improve childhood vaccination coverage which has a proven protective benefit on the disease transmission at a population level. At the same time, strengthening pneumococcal surveillance, including serotype monitoring and carriage studies, is essential to better understand local epidemiology and inform future vaccine policy.^{52,61} Given the ongoing development of higher-valency pneumococcal vaccines,^{10,62} periodic reassessment of vaccine effectiveness, serotype distribution, and cost-effectiveness will be necessary to ensure that vaccination strategies remain aligned with local disease patterns and provide optimal value for the healthcare system.^{10,63}

Conclusion

The current vaccination strategy (PPV23 alone) was the least costly vaccination strategy and had the lowest ICER and highest NMB compared with no vaccination. PCV13 followed by PPV23 and PCV15 followed by PPV23 incurred higher costs and generated fewer QALYs than PPV23 alone. Although these findings support the current vaccination strategy of older adults in the Philippines, improvement of childhood immunization and improvement of pneumococcal surveillance are needed to help the country make a more informed decision.

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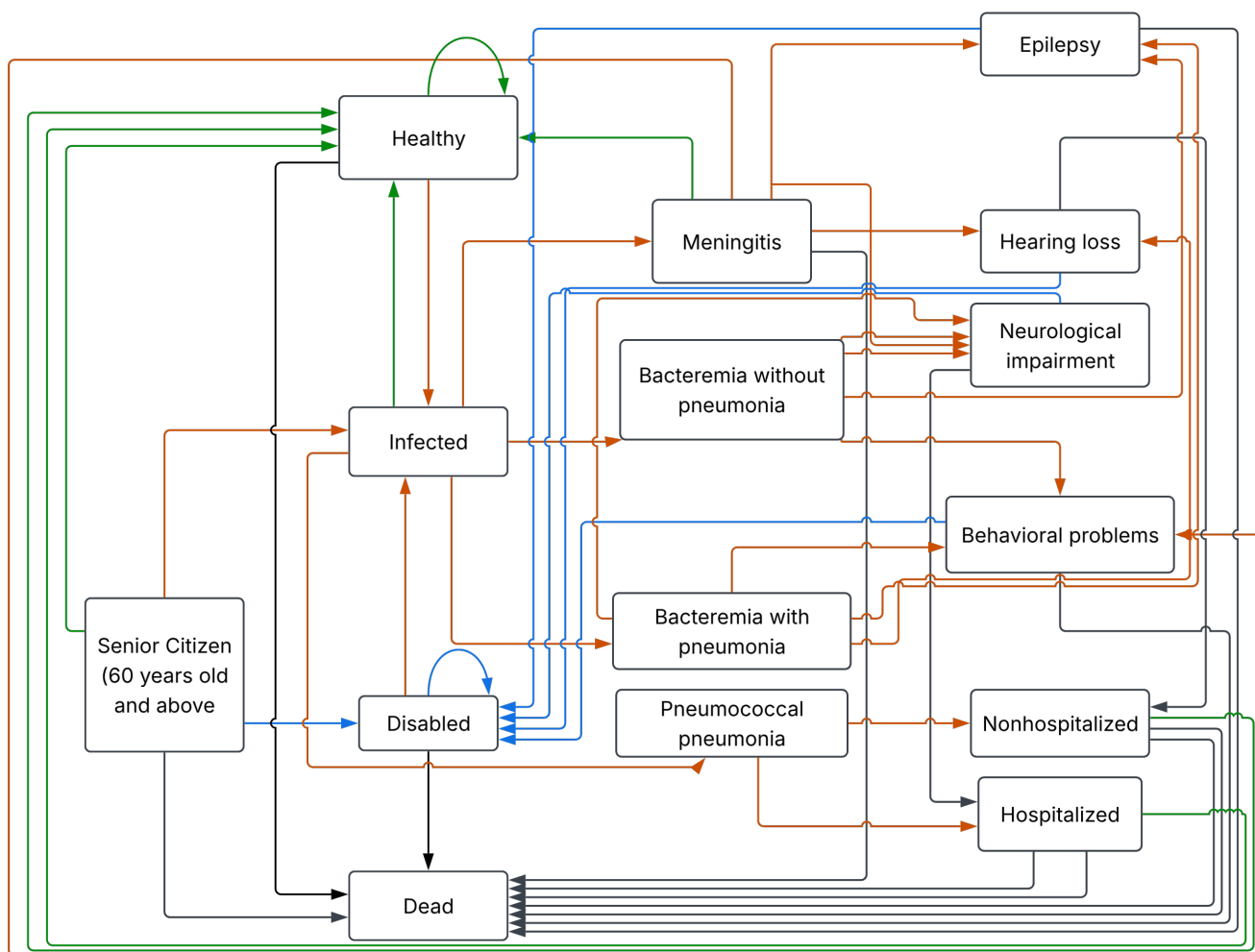
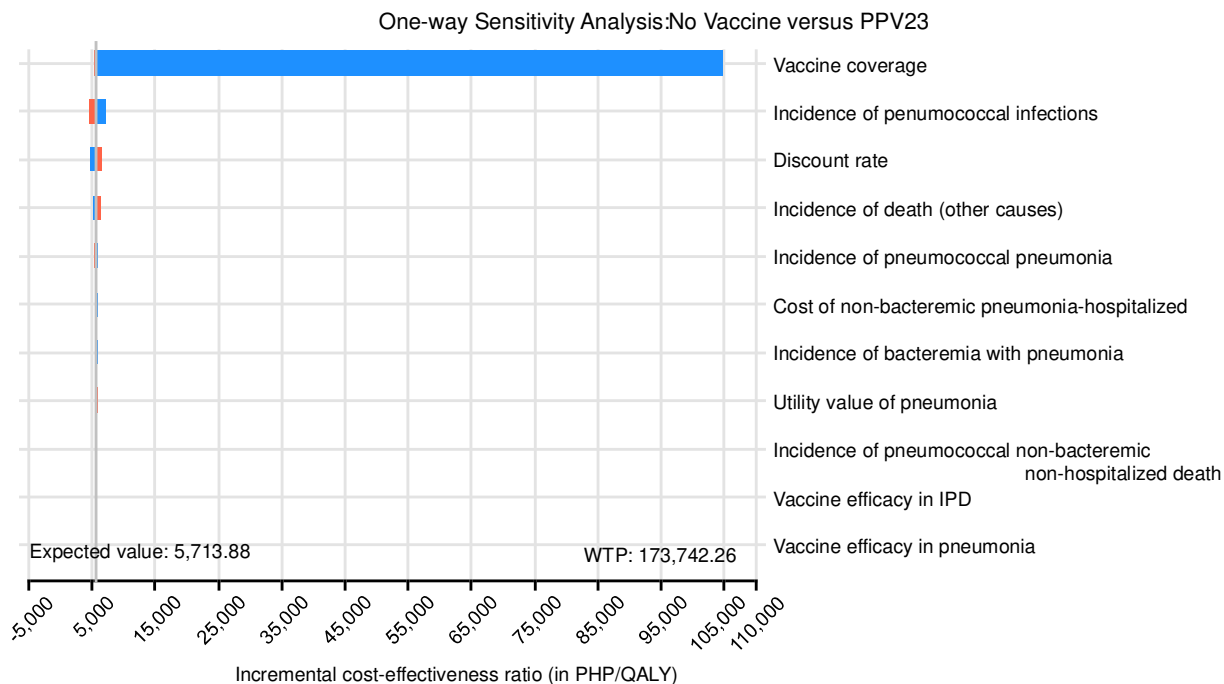
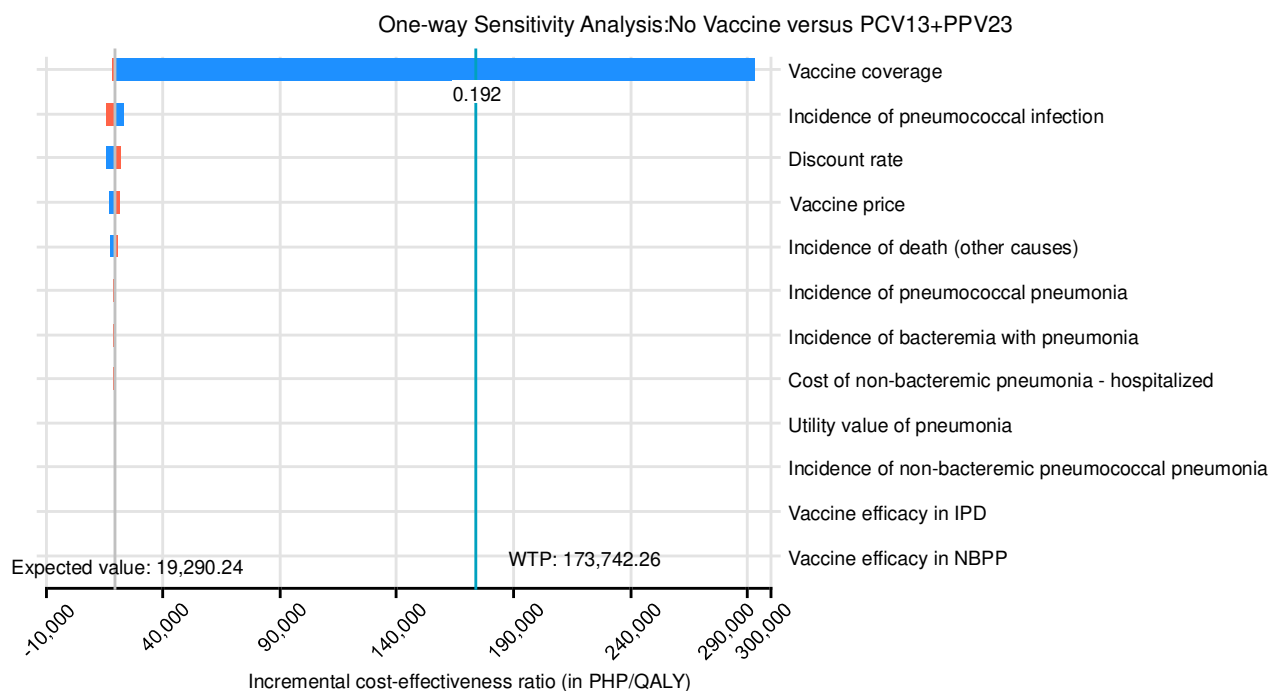


Figure 1. Schematic depiction of Markov model used

a) No vaccination versus PPV23



b) No vaccination versus PCV13 and PPV23



c) No vaccination versus PCV15 and PPV23

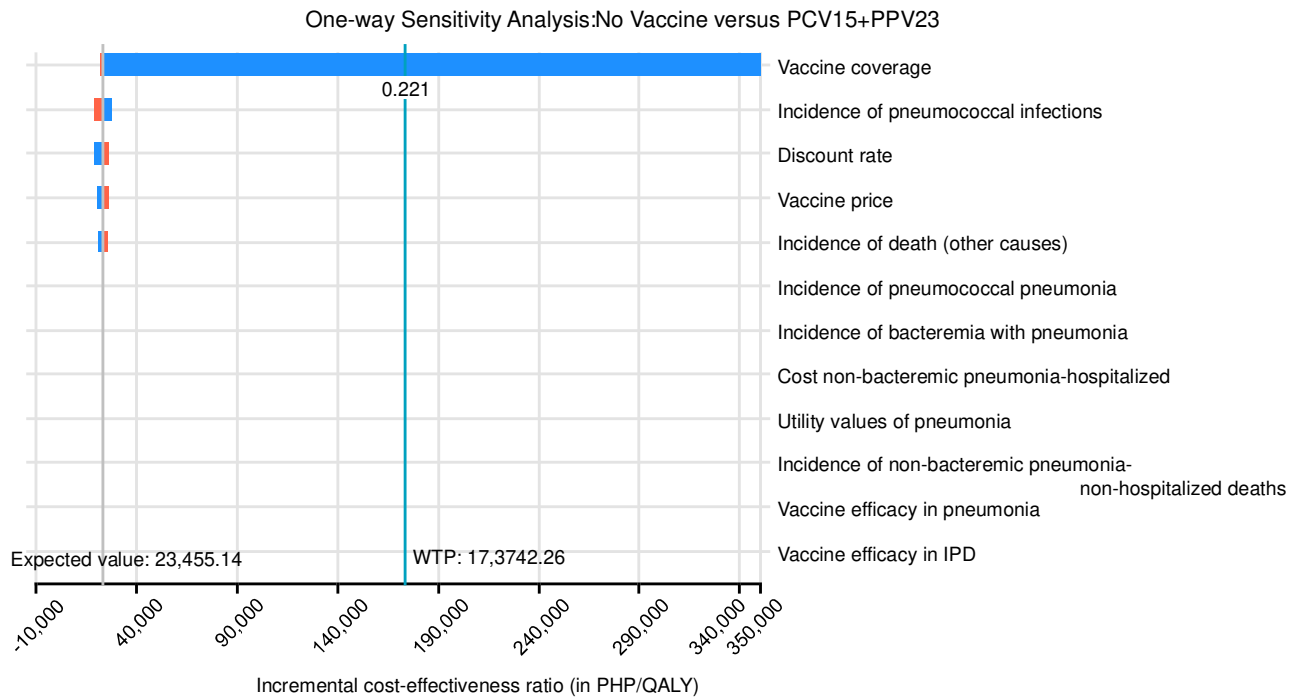
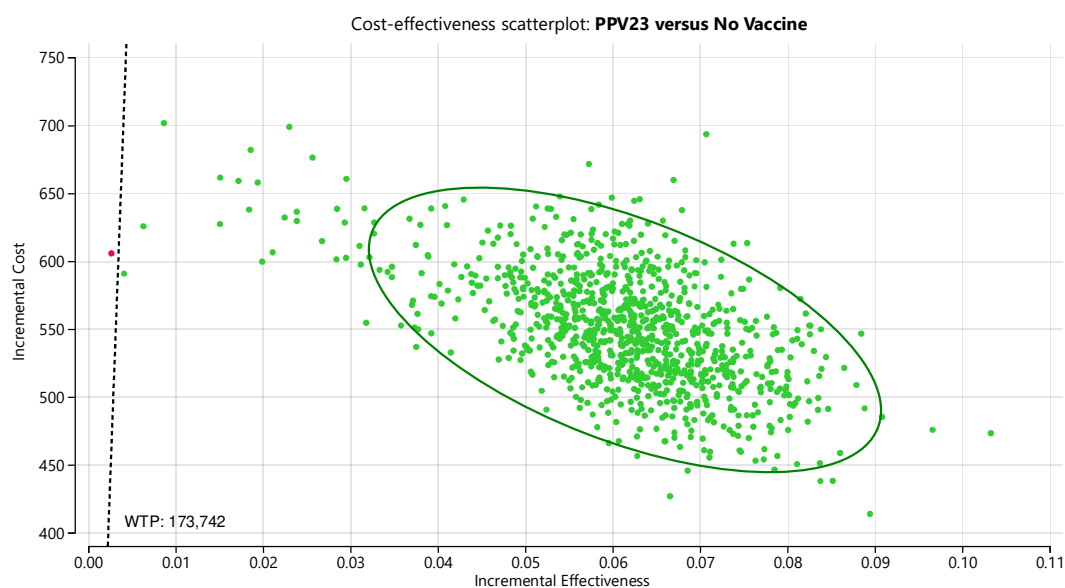


Figure 2. One- way sensitivity analysis using tornado diagram (bars show the outcome swing for each variable varied from low to high while holding others constant. Inputs are ranked vertically by largest impact to smallest on incremental cost-effectiveness ratio, ICER). We included a) PPV23 vs No vaccination, b) PCV13 and PPV23 versus No vaccination, and c) PCV15 and PPV23 versus No vaccination as scenarios for possible implementation

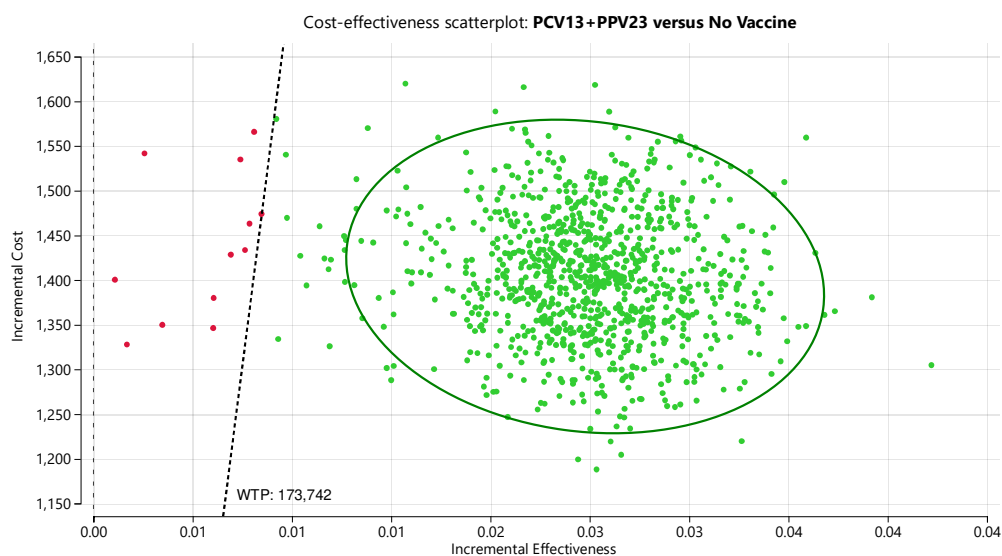
a) PPV23 versus No vaccination



Incremental Cost	Incremental Effectiveness	ICER	No. of Iteration	Proportion	Interpretation
IC<0	IE>0	Superior	0	0	-
IC>0	IE>0	ICER<173,742.26	999	0.999	PPV23 is 99.9% cost-effective
IC<0	IE<0	ICER>173,742.26	0	0	-
IC>0	IE>0	ICER>173,742.26	1	0.001	PPV23 is 0.1% beyond WTP
IC<0	IE<0	ICER<173,742.26	0	0	-
IC>0	IE<0	Inferior	0	0	-
IC=0	IE=0	0/0	0	0	-

**Mean ICER PHP8,942.32/QALY*

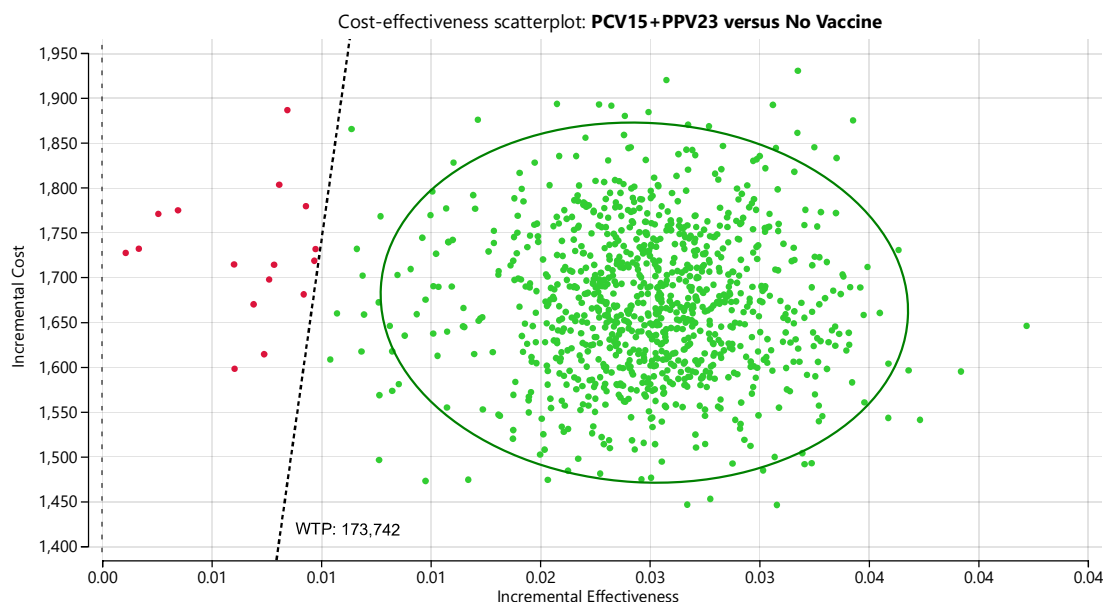
b) PCV13 and PPV23 versus No vaccination



Incremental Cost	Incremental Effectiveness	ICER	No. of Iteration	Proportion	Interpretation
IC<0	IE>0	Superior	0	0	-
IC>0	IE>0	ICER<173742.26	988	0.988	PCV13&PPV23 is 98.8% cost-effective
IC<0	IE<0	ICER>173742.26	0	0	-
IC>0	IE>0	ICER>173742.26	12	0.012	In 1.2% iterations, ICER of PCV13&PPV23 is greater than WTP
IC<0	IE<0	ICER<173742.26	0	0	-
IC>0	IE<0	Inferior	0	0	-
IC=0	IE=0	0/0	0	0	-

* Mean ICER PHP56,696.17/QALY

c) PCV15 and PPV23 versus No vaccination



Incremental Cost	Incremental Effectiveness	ICER	No. of Iteration	Proportion	Interpretation
IC<0	IE>0	Superior	0	0	-
IC>0	IE>0	ICER<173742.26	984	0.984	PCV15&PPV23 is 98.4% cost-effective
IC<0	IE<0	ICER>173742.26	0	0	-
IC>0	IE>0	ICER>173742.26	16	0.016	In 1.6% iterations, ICER is greater than WTP
IC<0	IE<0	ICER<173742.26	0	0	-
IC>0	IE<0	Inferior	0	0	-
IC=0	IE=0	0/0	0	0	-

*Mean ICER PHP67,505.74/QALY

Figure 3. Probabilistic sensitivity analysis using scatter plot (Each point represents one simulation iteration mapping the incremental cost against incremental QALYs. The diagonal dotted line marks the willingness-to-pay threshold; points below the

line indicate cost-effective outcomes. The ellipse represents the 95% confidence interval, enclosing the majority of simulated iterations to show the joint uncertainty about costs and QALYs. Red dots indicate simulations that crossed the willingness to pay threshold). We included a) PPV23 vs No vaccination, b) PCV13 and PPV23 versus No vaccination, and c) PCV15 and PPV23 versus No vaccination as scenarios for possible implementation

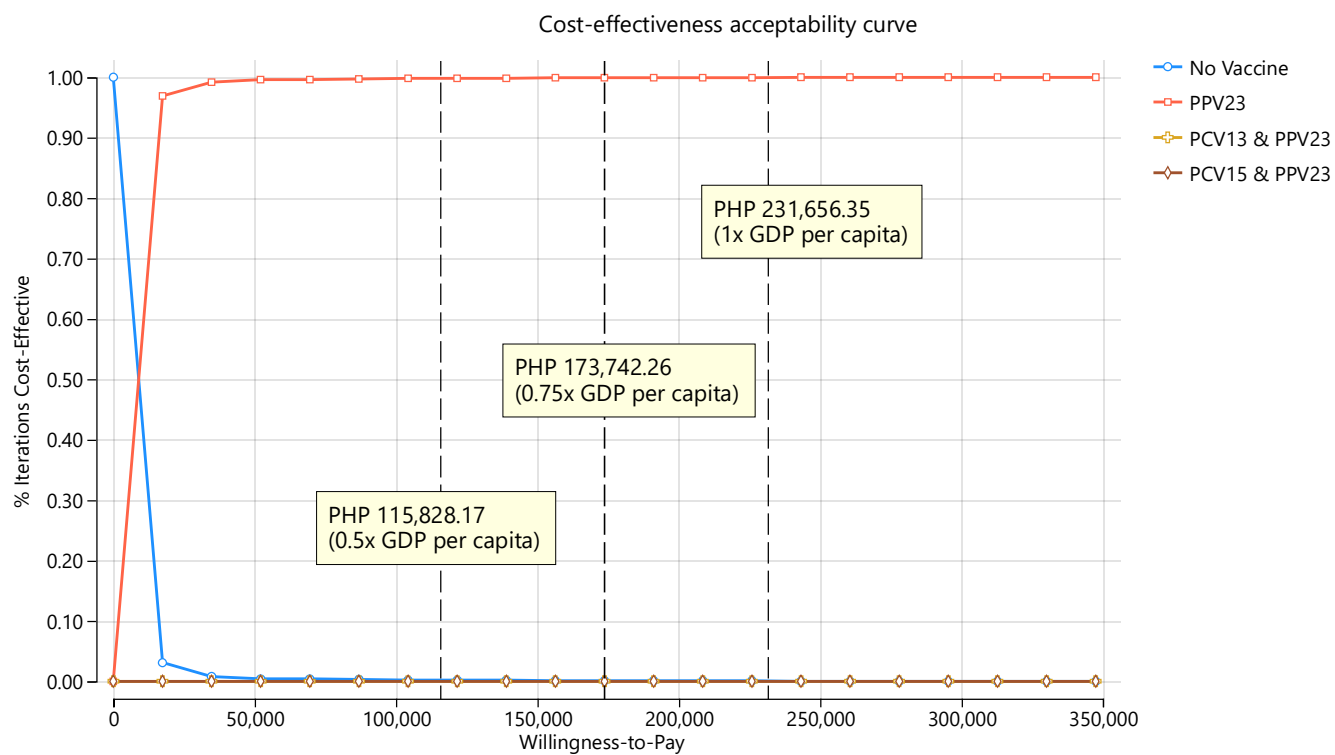


Figure 4. Cost-effectiveness acceptability curve

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [TablesOct42026.docx](#)
- [AppendixSep272026.docx](#)
- [CHEERSChecklistOct42026.docx](#)