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Evaluating the Cost-Effectiveness and Budget Impact of the 20-Valent Pneumococcal Conjugate Vaccine Among Adults in Taiwan

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Abstract

Background/Objectives. The 13-valent pneumococcal conjugate vaccine (PCV13), followed by the 23-valent pneumococcal polysaccharide vaccine (PPV23; PCV13→PPV23), was recommended for adults with high-risk conditions and all adults aged ≥65 years. With the availability of the 20-valent PCV (PCV20), which provides broader protection against pneumococcal disease, Taiwan CDC recently recommended to replace PCV13→PPV23 with PCV20. However, there is no economic evidence to support the recommendation. Therefore, the objective of the study is to assess the short- and long-term clinical and economic value of PCV20 to support the recommendation. **Methods.** A lifetime cost-effectiveness analysis (CEA) based on a single cohort and five-year budget impact analysis (BIA) based on rolling cohorts were conducted from a healthcare system perspective to evaluate replacing PCV13→PPV23 with PCV20 among high-risk adults aged 18–64 years and all adults aged 65–99 years. **Results.** In CEA, PCV20 was estimated to reduce pneumococcal disease cases by 4,684 and deaths by 160 among the model population (N = 5.5M) over a lifetime horizon. Total costs decreased by NT$2.3 billion while quality-adjusted life-years (QALYs) increased by 944, making PCV20 the dominant strategy versus PCV13→PPV23. BIA showed budget savings of NT $5.4 billion over five years including NT$2.4 billion in the first year. **Conclusions.** Switching to PCV20 for adults with high-risk conditions and all adults aged ≥ 65 years would substantially reduce the burden of pneumococcal disease and related deaths, leading to cost and budget savings for Taiwan's healthcare system.

Keywords: pneumococcal conjugate vaccines; cost-effectiveness analysis; adult vaccination; Taiwan

1. Introduction

Streptococcus pneumoniae, also known as *S. pneumoniae* or *pneumococcus*, is a major cause of mortality and morbidity globally [1]. It is the leading causative pathogen of community acquired pneumonia (CAP) which presents as invasive pneumococcal disease (IPD), including bacteremia and meningitis, and non-invasive disease such as non-bacteremic pneumonia (NBP) [2, 3]. In 2013, Said et al. reported that an estimated 27.3% of CAP was attributable to pneumococcus worldwide [4]. More recently, a systematic review by Lansbury et al. (2022) reported this proportion to be lower (18%) due to the introduction of childhood vaccinations [5]. An older study conducted in Taiwan among adults hospitalized due to CAP found *pneumococcus* to be the most common etiologic agent (40 of 168 patients [23.8%]) in adults with CAP, aligning with global findings [6].

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To reduce the burden of pneumococcal disease, the Taiwanese national pneumococcal immunization program (NIP) has consistently recommended vaccination for both children and adults [7, 8]. The recommendations for adult pneumococcal immunization were recently revised introducing the novel 20-valent pneumococcal conjugate vaccine (PCV20) to replace the sequential regimen of 13-valent PCV13 followed by 23-valent pneumococcal polysaccharide vaccine (PPV23; PCV13→PPV23) [9, 10]. PPV23 protects against 23 IPD-causing serotypes (1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19A, 19F, 20, 22F, 23F, and 33F), 11 of which are unique to PPV23 [11-13]. PCV13 covers 13 serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F) and protects against both IPD and NBP due to pneumococcus, unlike PPV23. Given the combined benefits of PCV13 and PPV23, until recently the sequential regimen of PCV13→PPV23 was recommended for high-risk adults and all adults aged ≥65 years in Taiwan. A 15-valent pneumococcal conjugate vaccine (PCV15), which protects against PCV13 serotypes as well as 22F and 33F, is also available in Taiwan, but not included in the NIP [7, 8].

PCV20 was licensed in Taiwan in December 2024 based on findings from clinical trials [14-17]. PCV20 covers five additional serotypes (i.e., 8, 10A, 11A, 12F, 15B) not included in PCV15 and shares 19 of the 23 serotypes covered by PPV23 [18-21]. Unlike PPV23, PCV20 has a T cell-dependent response mechanism which results in more durable protection than PPV23 [22, 23]. Because of the serotype overlap and vaccine characteristics, most countries where PCV20 is included in the adult vaccination program recommend its use alone (i.e., as opposed to in sequence with PPV23), resulting in more straightforward recommendations. Following the common practice observed in other countries, in January 2026, the simplified single-dose regimen of PCV20 was included in the adult pneumococcal NIP in Taiwan [9, 10]. Therefore, the objective of this cost-effectiveness analysis (CEA) and budget impact analysis (BIA) is to provide timely evidence to support the recommendation and to estimate both the short- and long-term clinical and economic benefits of PCV20 in light of this new recommendation.

2. Materials and Methods

2.1. Model Description

A cost-effectiveness model (CEM) and a budget impact model (BIM), both utilizing a deterministic Markov-type process, were used to project the clinical outcomes and economic costs of IPD and all-cause NBP among adults from a healthcare system perspective in a hypothetical population of adults in Taiwan (Figure 1). Clinical and economic outcomes were projected in the CEM to track a single cohort from model entry until death or the end of the time horizon to estimate lifetime costs and quality-adjusted life-years (QALYs). The BIM used multiple rolling adult cohorts, adding new eligible individuals each year, to estimate the financial impact on the healthcare budget over five years. The model population was characterized based on age (in one-year increments) and risk profile (i.e., low [immunocompetent without underlying medical conditions], moderate [immunocompetent with ≥1 underlying medical condition], or high [immunocompromised]). During the modeling horizon, persons were allowed to transition to a higher risk group (e.g., low → moderate), but not to a lower risk group.

Persons in the CEA and BIA model populations may have received PCV20 alone or PCV13→PPV23 at model entry; those who received PCV13 at model entry were assumed to have received PPV23 in model year 2 (if alive). PCV15 was excluded from the analyses because it is not included in the national pneumococcal immunization program in Taiwan [7, 8], and because Taiwanese surveillance data used in this study suggested that there were no cases of pneumococcal disease attributed to PCV15 non-PCV13 serotypes (see Model Estimation) [5, 24].

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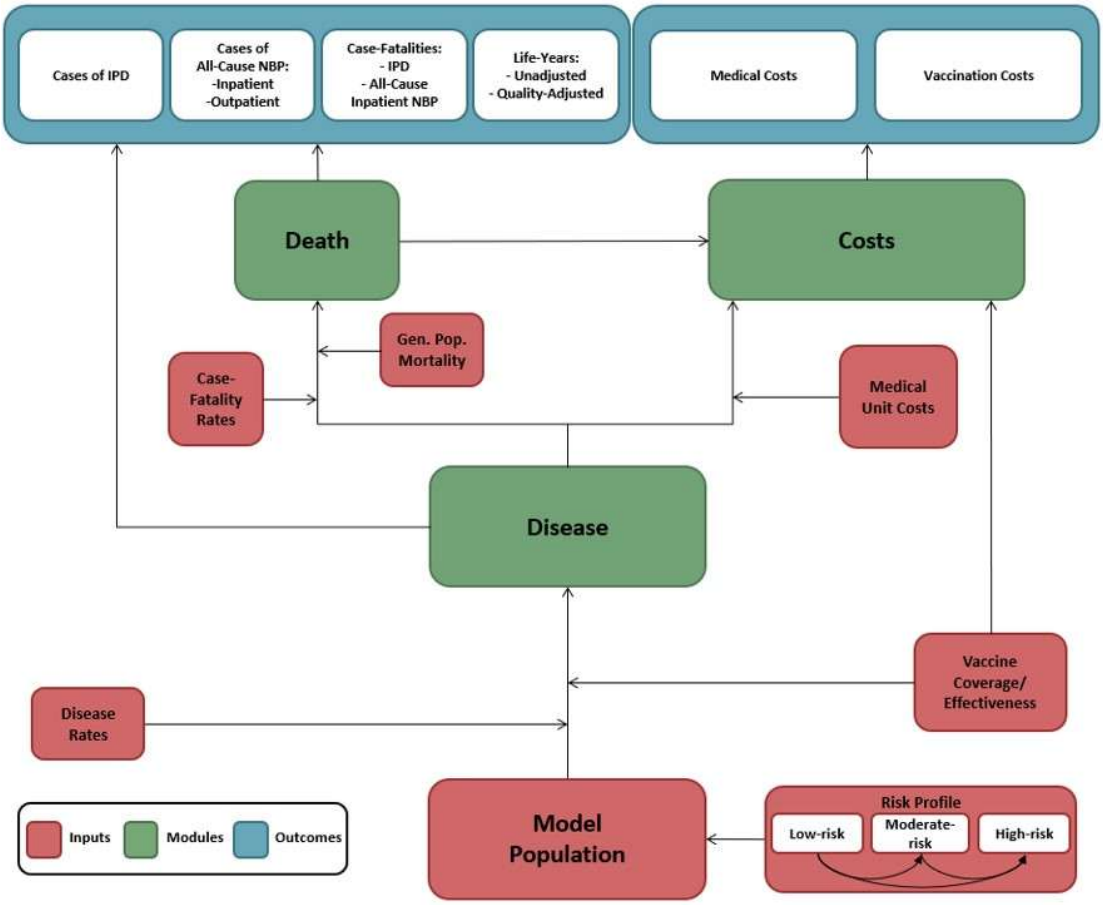

Figure 1. Modeling framework.

Clinical outcomes and economic costs were projected annually for the model populations based on age, risk profile, disease/fatality rates, vaccination status, vaccine type, time since vaccination, and unit costs of vaccination and medical treatment. All IPD cases were considered requiring hospitalization, whereas all-cause NBP was stratified by care setting (inpatient vs. outpatient). Persons vaccinated at model entry may have been at lower risk of future IPD and NBP; the magnitude of the reduction in probability of contracting pneumococcal disease varied based on vaccine(s) received, clinical presentation (i.e., IPD or NBP), proportion of disease that is vaccine-preventable (i.e., vaccine-type), and vaccine effectiveness against vaccine-type disease (which is dependent on age and time since receipt). The models also considered age- and risk-dependent probability of death from IPD, NBP requiring inpatient care, and other causes (i.e., other than IPD and NBP). Expected costs of medical treatment for IPD and NBP were generated using event rates and unit costs specific to the care setting. Costs of vaccination were tallied in the year(s) in which the vaccination occurred (i.e., year 1 for PCV20, years 1 and 2 for the sequential strategies).

2.2. Inputs Estimation

Model inputs were primarily based on published sources and were estimated by age (18-49, 50-64, 65-74, 75-84, and 85-99 years) and risk. In cases where published sources were not stratified by age and risk, techniques of linear interpolation and extrapolation were employed to derive age- and risk-specific values required by the model. All costs are expressed in 2024 New Taiwan dollar (NT$). Methods used in estimation of key model parameters are summarized below; base case model inputs for the population size, disease incidence rates, annual mortality rates, case fatality rates, medical care costs, and utilities are included in Table 1 and for the vaccine effectiveness rates and vaccine uptake in Supplemental Table S1. The estimation of key model parameters is presented below, with

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additional details on inputs provided in the Supplements. Unless otherwise specified, the descriptions apply to both the CEA and BIA.

Population. The Taiwan adult population (N=20,091,471) by single year of age was derived from the overall 2025 Taiwan resident population projected by the Taiwan National Statistics [25] and population pyramid for Taiwan [26]. To estimate the proportion of the population who is at risk of pneumococcal disease, we utilized a previously published study which reports the prevalence of various comorbidities in the general population in Taiwan [27]. Based on the distribution of persons with relevant comorbidities reported in that study, at-risk individuals were stratified into high-risk (defined as persons with cancer, liver disease, or renal disease) and moderate-risk (defined as persons with diabetes, congestive heart failure, coronary syndrome, cerebrovascular disease or chronic pulmonary disease) (Supplemental Table S2) [27]; persons not identified as at-risk were considered low-risk.

Rates of Disease. Age-specific IPD incidence rates were from the 2019 Taiwan CDC surveillance report [24] and were allocated across risk groups using the relative risk of IPD as observed in the United States (US) from 2017/2018 (Pfizer, unpublished observations) and the underlying Taiwan population risk distribution [27]. Age-specific all-cause NBP incidence rates were based on Huang et al. (2022) [28] and were apportioned by care setting based on the proportion of pneumonia treated in the inpatient and outpatient settings from Lu et al. (2020) [29]. Age-specific inpatient rates were allocated across risk groups using the relative risk of hospitalized all-cause NBP from a US study spanning 2013-2015 [30] and the underlying Taiwan population risk distribution [27]. Age-specific outpatient rates were allocated across risk groups based on relative risks of all-cause NBP from Weycker et al. (2016) [31] and the underlying Taiwan population risk distribution [27].

Case-Fatality and Mortality Rates. Age-specific case-fatality rates (CFRs) for IPD were from the 2019 Taiwan CDC surveillance report [24] and apportioned across risk groups using relative risks from the US CDC (Pfizer, unpublished observations) and the risk distribution of persons with IPD in Taiwan [27]. For CFR due to inpatient all-cause NBP, age-specific rates were obtained from Lu et al. (2020) [29] and allocated across risk groups based on relative risks from Averin et al. (2021) [32] and the risk distribution of persons with inpatient all-cause NBP in Taiwan [29, 30]. Outpatient all-cause NBP was assumed not to cause disease-related mortality.

General population mortality rates were based on 2023 life tables from the Taiwan Ministry of the Interior [33] and were allocated across risk groups based on assumed relative risk of mortality and population weights. Mortality rates were downwardly adjusted to account for death due to IPD and all-cause inpatient NBP.

Vaccine Effectiveness. Vaccine effectiveness (VE) against vaccine-type (VT) IPD and NBP for PCV13 and PPSV23 were based on published literature [34-37] and have been used in previously published studies [38-43]. VE-PCV20 against VT disease was assumed to be equivalent to that of PCV13, based on published data evaluating the safety, tolerability, and immunogenicity of PCV20 [44]. VE-PPV23 against VT-NBP was assumed to be zero, based on multiple published sources and in line with base case assumptions used in several economic studies [45-60]. Detailed description of estimation of initial VE and waning assumptions are included in the Supplemental Text file.

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Table 1. Base case model input values for the number of persons, disease incidence rates, annual mortality rates, case fatality rates, medical care costs, and utilities for high-risk patients aged 18-64 years and all patients aged 65-99 years in Taiwan.

	Age/Risk Profile										
	18-49 years	50-64 years	65-74 years			75-84 years			≥85 years		
	High	High	Low	Moderate	High	Low	Moderate	High	Low	Moderate	High
No. of adults	361,455	452,216	1,373,521	1,200,807	381,838	479,038	562,725	212,962	169,480	211,068	88,419
Annual disease incidence (per 100,000)											
IPD	4.6	6.2	1.9	6.0	8.1	2.9	6.9	7.6	4.6	8.2	6.5
Inpatient NBP	271.9	859.3	212.5	1,041.3	2,358.9	683.0	1,980.8	2,868.8	1,056.1	3,062.6	4,435.4
Outpatient NBP	888.6	2,260.3	1,028.2	3,106.4	4,166.4	1,422.1	4,296.5	5,762.6	1,853.4	5,599.9	7,510.7
Annual mortality/case-fatality (per 100)											
General population	0.2	1.0	1.2	1.8	2.2	2.7	4.0	5.2	5.1	7.4	9.7
IPD	8.6	9.8	6.8	12.9	12.0	13.2	17.0	13.2	17.4	21.3	17.9
Inpatient NBP	10.5	11.4	4.5	6.7	10.0	8.6	10.7	11.4	11.6	11.7	15.6
Outpatient NBP	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Medical care costs (per case, NTD)											
IPD	119,179	119,179	119,179	119,179	119,179	119,179	119,179	119,179	119,179	119,179	119,179
Inpatient NBP	48,195	48,195	48,195	48,195	48,195	48,195	48,195	48,195	48,195	48,195	48,195
Outpatient NBP	785	785	785	785	785	785	785	785	785	785	785
CEA Utilities											
General population health-state utilities	0.7190	0.6632	0.8872	0.6984	0.6768	0.8805	0.6711	0.6521	0.8733	0.6438	0.6017
IPD	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300
Inpatient NBP	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300	0.1300
Outpatient NBP	0.0040	0.0040	0.0040	0.0040	0.0040	0.0040	0.0040	0.0040	0.0040	0.0040	0.0040

Abbreviations: CEA, cost-effectiveness analysis; IPD, invasive pneumococcal disease; NBP, non-bacteremic pneumonia; NTD, New Taiwan Dollar.

Serotype Coverage. The percentage of IPD due to vaccine serotypes in year 1 of the modeling horizon was estimated by age using data from the 2019 Taiwan CDC surveillance report [24] (Supplemental Table S3). Although more recent surveillance data (2020, 2021 and 2022) are available, the 2019 surveillance report was employed because, probably as a consequence of the Covid-19 pandemic, substantially reduced numbers of IPD cases were observed in more recent reports. Percentage of all-cause NBP due to vaccine serotypes was estimated by multiplying IPD serotype coverage by the proportion of NBP due to pneumococcus (18%) from Lansbury et al. (2022) [5] (Supplemental Table S4). PCV15 serotype coverage was found to be the same as PCV13 serotype coverage because there was no disease attributable to serotypes 22F and 33F. While PCV13 serotype coverage in 2019 was lower relative to 2015, surveillance data for the years between 2015 and 2019 showed that coverage varied from year to year; hence, no consistent pattern of reduction was observed [12, 24, 61-63]. Therefore, in the CEA base case and the BIA, herd effects from pediatric vaccination were not considered and serotype coverage was constant throughout the duration of the

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modeling horizon. The impact of herd effects from future pediatric PCV20 use was, however, examined in a scenario analysis within the CEA.

Vaccine Coverage. In the CEA, vaccine coverage for PCV13 and PCV20 at model entry was based on assumed uptake: aged 18-49 (7.2%), 50-64 (20%), 65-74 (50%), and 75-99 years (35%) (Pfizer, unpublished observations). For the BIA, we assumed the same vaccine coverage in Year 1; from year 2 to year 5, an annual relative increase in coverage was assumed as follows: 20% for high-risk adults aged 18-64 years, 15% for adults aged 65-74 years, and 10% for adults aged ≥75 years. In both models, all persons who received PCV13 in model year 1 were assumed to receive PPV23 in model year 2, if alive.

Costs. Cost of medical care for IPD, inpatient all-cause NBP, and outpatient all-cause NBP were based on Lu et al. (2022) [64] and were adjusted to 2024 NT$ using the Taiwan consumer price index (CPI) [65]. Costs were assumed to be invariant by age and risk. All vaccine prices employed are confidential. The PCV20 price was assumed to be 10% higher than the PCV13 price (Pfizer, unpublished observations), and PPV23 price was 40% of PCV13 price. Vaccine administration cost was not considered in the model.

Utility and Disutilities. In the CEA, age-specific general population health state utilities were based on Wong et al. (2019) [66]. Because utilities from Wong et al. (2019) are relatively high, they were assumed to reflect baseline utilities for low-risk persons, thus utilities for moderate- and high-risk persons were derived by multiplying utilities from Wong et al. by relative utility values for moderate- and high-risk (vs. low-risk) persons derived from Mendes et al. (2022) [42].

Disease-related disutilities in the CEA were based on published literature. Disutility due to IPD and inpatient NBP was assumed to be 0.13 in the year of occurrence based on Mangen et al. (2017) [67]. For NBP requiring outpatient care only, disutility was assumed to be 0.004 based on Melegaro et al. (2004) [68]. Disutility was assumed to be invariant by age and risk.

2.3. Cost-Effectiveness Analyses

Base Case. Clinical outcomes and economic costs over a lifetime time horizon were evaluated for PCV20 versus PCV13→PPV23 in high-risk adults aged 18-64 years and all adults aged 65-99 years. Analyses were also conducted for subgroups defined on age (i.e., 18-64 and 65-99 years, respectively).

Analyses were conducted from the Taiwan healthcare system perspective; future costs, life-years (LYs), and quality-adjusted LYs (QALYs) were discounted at 3% annually. Incremental cost-effectiveness ratios (ICERs) were calculated based on differences in costs and QALYs for each comparison.

Scenario Analyses. Herd effects from future pediatric PCV20 NIP were incorporated in Scenario Analysis #1. Herd effects were based on the observed serotype coverage patterns in PCV13 serotypes reported in the Taiwan CDC surveillance reports from 2015-2019 [12, 24, 61-63] following the implementation of a pediatric national immunization program with PCV13 in 2015. Relative changes in PCV13 serotypes were applied to PCV20 non-PCV13 serotypes starting in model year 4. Serotype coverage for IPD and NBP with herd effects are presented in Supplemental Tables S5 and S6. In Scenario Analysis #2, only 50% of persons who received PCV13 in model year 1 were assumed to receive PPV23 in model year 2.

Probabilistic Sensitivity Analyses. Probabilistic sensitivity analyses (PSAs) were conducted (1,000 replications) to account for uncertainty surrounding key model parameters. For each input parameter, the appropriate distribution was determined based on information available in the source material (Supplemental Table S7). Cost-effectiveness of PSA results was evaluated relative to a willingness-to-pay (WTP) threshold of 3x gross domestic product (GDP) per capita, a metric commonly employed in countries to assess cost-effectiveness where the local health technology assessment authority does not have a pre-specified threshold.

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2.4. Budget Impact Analyses

Base case analysis evaluated the clinical outcomes and economic costs over a five-year horizon for PCV20 versus PCV13→PPV23 in high-risk adults aged 18-64 years and all adults aged 65-99 years. Analyses were conducted from the Taiwan healthcare system perspective over a five-year horizon; future costs were not discounted in the model. Total cumulative costs, annual costs, and net budget impact were calculated.

3. Results

3.1. Cost-Effectiveness Analysis

Base Case Analyses. With use of PCV13→PPV23 among the high-risk population aged 18-64 years and all adults aged 65-99 years (N = 5,508,375), the model estimated 5,511 cases of IPD, 1,934,376 cases of all-cause inpatient NBP, 3,716,882 cases of all-cause outpatient NBP, and 236,583 disease-related deaths over the lifetime modeling horizon (Table 2). These outcomes corresponded to a total direct cost of NT$75.2 billion—including NT$63.7 billion for medical care and NT$11.5 billion for vaccination. Compared to PCV13→PPV23, use of PCV20 at model entry reduced expected lifetime cases of IPD by 29, all-cause inpatient NBP by 1,483, all-cause outpatient NBP by 3,171, and total disease-related deaths by 160. Given the reduction in cases, expected lifetime total medical care costs were reduced by NT$64.4 million. Furthermore, replacing a two-dose strategy with a single dose of PCV20 decreased total vaccination costs by NT$2.3 billion. With total costs lower by NT$2.3 billion, and discounted life years higher by 1,178 (unadjusted) and 944 (quality-adjusted), PCV20 was estimated to be the dominant strategy (i.e., cost-saving) versus PCV13→PPV23 from the healthcare system perspective. PCV20 was also dominant among subgroups defined on age with estimated cost savings (medical care and vaccination costs) of NT$132.4 million among adults aged 18-64 years and NT$2.2 billion among adults aged 65-99 years (Supplemental Table S8).

Table 2. Cost-effectiveness of PCV20 vs. PCV13→PPV23 in high-risk patients aged 18-64 years and all patients aged 65-99 years in Taiwan (N = 5,508,375) - Base-case.

	PCV13→PPV23	PCV20	Difference
Clinical Outcomes			
No. of Cases			
IPD	5,511	5,482	-29
All-Cause NBP			
Inpatient	1,934,376	1,932,893	-1,483
Requiring Outpatient Care Only	3,716,882	3,713,710	-3,171
No. of Deaths	236,583	236,423	-160
Life-Years (discounted)*	69,827,105	69,828,283	1,178
Quality-Adjusted Life-Years (discounted)*	50,672,027	50,672,971	944
Economic Outcomes			
Total Costs (millions)			
Medical Care	NTD 63,671.5	NTD 63,607.1	-NTD 64.4
Vaccination	NTD 11,482.8	NTD 9,199.2	-NTD 2,283.6
Medical + Vaccination	NTD 75,154.3	NTD 72,806.3	-NTD 2,348.0
Cost-Effectiveness			
Cost per LY	---	---	Dominant
Cost per QALY	---	---	Dominant

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Abbreviations: IPD, invasive pneumococcal disease; LY, life-year; NBP, non-bacteremic pneumonia; NTD, New Taiwan Dollar; PCV, pneumococcal conjugate vaccine; PPV, pneumococcal polysaccharide vaccine; QALY, quality-adjusted life-year. *Life-years, QALYs, and costs have been discounted at a 3% annual rate.

Scenario Analyses. In the scenario assuming herd effects from pediatric use of PCV20 (Scenario Analysis #1), the ICER for PCV20 use remained dominant compared to the sequential strategy among high-risk adults aged 18-64 years and all adults aged 65-99 years (Δ costs: -NT$2.3B; Δ QALYs: 815; Table 3), and in subgroup analyses for both age groups (Supplemental Table S9). In the scenario assuming reduced uptake of PPV23 (50%) in the sequential strategy (Scenario Analysis #2), the ICER for PCV20 use remained dominant compared to the sequential strategy among high-risk adults aged 18-64 years and all adults aged 65-99 years (Δ costs: -NT$789.1M; Δ QALYs: 953; Table 4), and in subgroup analyses for both age groups (Supplemental Table S10).

Probabilistic Sensitivity Analyses. In probabilistic sensitivity analyses of the full model population, 100% of 1,000 of simulations generated ICERs located in the southeast quadrant of the scatterplot and thus projected lower costs and higher QALYs with use of PCV20 versus PCV13→PPV23 (Figure 2). All (100%) of the 1,000 simulations were therefore under the 3x GDP per capita threshold (NT$3.4M) [69].

Table 3. Cost-effectiveness of PCV20 vs. PCV13→PPV23 in high-risk patients aged 18-64 years and all patients aged 65-99 years in Taiwan (N = 5,508,375) - Scenario analysis #1.

	PCV13→PPV23	PCV20	Difference
Clinical Outcomes			
No. of Cases			
IPD	5,453	5,429	-23
All-Cause NBP			
Inpatient	1,930,861	1,929,593	-1,268
Requiring Outpatient Care Only	3,710,239	3,707,514	-2,725
No. of Deaths	236,140	236,004	-135
Life-Years (discounted)*	69,829,068	69,830,085	1,017
Quality-Adjusted Life-Years (discounted)*	50,673,581	50,674,395	815
Economic Outcomes			
Total Costs (millions)			
Medical Care	NTD 63,557.1	NTD 63,501.7	-NTD 55.3
Vaccination	NTD 11,482.8	NTD 9,199.2	-NTD 2,283.6
Medical + Vaccination	NTD 75,039.8	NTD 72,700.9	-NTD 2,338.9
Cost-Effectiveness			
Cost per LY	---	---	Dominant
Cost per QALY	---	---	Dominant

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Abbreviations: IPD, invasive pneumococcal disease; LY, life-year; NBP, non-bacteremic pneumonia; NTD, New Taiwan Dollar; PCV, pneumococcal conjugate vaccine; PPV, pneumococcal polysaccharide vaccine; QALY, quality-adjusted life-year. *Life-years, QALYs, and costs have been discounted at a 3% annual rate.

Table 4. Cost-effectiveness of PCV20 vs. PCV13→PPV23 in high-risk patients aged 18-64 years and all patients aged 65-99 years in Taiwan (N = 5,508,375) - Scenario analysis #2.

	PCV13→PPV23	PCV20	Difference
Clinical Outcomes			
No. of Cases			
IPD	5,521	5,482	-39
All-Cause NBP			
Inpatient	1,934,376	1,932,893	-1,483
Requiring Outpatient Care Only	3,716,881	3,713,710	-3,171
No. of Deaths	236,584	236,423	-161
Life-Years (discounted)*	69,827,093	69,828,283	1,190
Quality-Adjusted Life-Years (discounted)*	50,672,018	50,672,971	953
Economic Outcomes			
Total Costs (millions)			
Medical Care	NTD 63,672.5	NTD 63,607.1	-NTD 65.5
Vaccination	NTD 9,922.8	NTD 9,199.2	-NTD 723.6
Medical + Vaccination	NTD 73,595.4	NTD 72,806.3	-NTD 789.1
Cost-Effectiveness			
Cost per LY	---	---	Dominant
Cost per QALY	---	---	Dominant

Abbreviations: IPD, invasive pneumococcal disease; LY, life-year; NBP, non-bacteremic pneumonia; NTD, New Taiwan Dollar; PCV, pneumococcal conjugate vaccine; PPV, pneumococcal polysaccharide vaccine; QALY, quality-adjusted life-year. *Life-years, QALYs, and costs have been discounted at a 3% annual rate.

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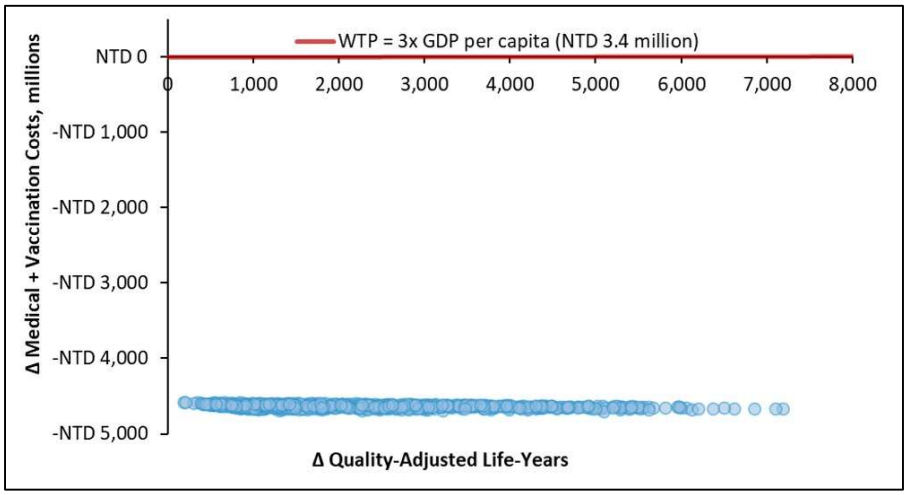

Figure 2. Scatterplot of results of CEA probabilistic sensitivity analyses for PCV20 vs. PCV13→PPV23 in high-risk patients aged 18-64 years and all patients aged 65-99 years in Taiwan (N = 5,508,375). Abbreviations: GDP, gross domestic product; NTD, New Taiwan Dollar; WTP, willingness-to-pay.

3.2. Budget Impact Analysis

Among high-risk adults aged 18-64 years and all adults aged 65-99 years (N = 5,301,030), replacing PCV13→PPV23 with PCV20 would prevent an additional 20 cases of IPD, 1,080 cases of all-cause inpatient NBP, 2,357 cases of all-cause outpatient NBP, and 113 deaths over five years (Table 5, Supplemental Table S11). The reduction in cases would lower medical care costs by NT$56.3 million and vaccination costs by NT$5.4 billion, resulting in total budget savings of NT$5.4 billion from the healthcare system perspective.

In the model population, the vaccine uptake increased cumulatively from 40% in Year 1 to 65% in Year 2, 80% in Year 3, 88% in Year 4, and reaching 93% in Year 5. The reduction in costs was estimated at NTD$2.4 billion in the first year, decreasing over time as the eligible vaccination population gradually declines in subsequent years.

Table 5. Net budget impact of PCV20 vs. PCV13→PPV23 among high-risk adults aged 18-64 years and all adults aged ≥65 years in Taiwan (N=5,301,030).

	PCV20 vs. PCV13-> PPV23					
	Year 1	Year 2	Year 3	Year 4	Year 5	Total
Cumulative vaccine uptake	40%	65%	80%	88%	93%	---
Clinical Outcomes						
No. of Cases						
IPD	-2	-3	-4	-5	-6	-20
All-Cause NBP						
Inpatient	-111	-188	-236	-265	-281	-1,080
Requiring Outpatient Care Only	-253	-420	-518	-571	-596	-2,357
No. of Deaths	-11	-19	-25	-28	-30	-113
Economic Outcomes						
Total Costs (millions)						
Medical Care	-NTD 5.8	-NTD 9.8	-NTD 12.3	-NTD 13.8	-NTD 14.7	-NTD 56.3
Vaccination	-NTD 2,361.7	-NTD 1,453.8	-NTD 833.1	-NTD 457.0	-NTD 251.3	-NTD 5,356.8
Medical + Vaccination	-NTD 2,367.5	-NTD 1,463.5	-NTD 845.4	-NTD 470.8	-NTD 265.9	-NTD 5,413.1

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Abbreviations: IPD, invasive pneumococcal disease; NBP, non-bacteremic pneumonia; NTD, New Taiwan Dollar.

4. Discussion

In this study, we evaluated the public health and economic impact of replacing the current pneumococcal vaccination strategy for adults at high risk of disease and people aged 65 and older in Taiwan with PCV20 considering both long-term and short-term perspectives. Results from the CEA, suggest that use of PCV20 in lieu of PCV13→PPSV23 among high-risk adults aged 18-64 years and all adults aged 65-99 years would be cost-saving (total net costs = -NT$2.3B) over a lifetime horizon from the healthcare system perspective. Use of a single dose of PCV20 remained cost-saving compared to current recommendations in subgroup analysis defined on age, and in scenarios considering potential herd effects from future pediatric use of PCV20 and reduced uptake of PPV23 in the sequential strategy. Results from probabilistic sensitivity analyses in the CEA were consistent with base case results. The BIA conducted over a five-year time horizon found that PCV20 would reduce the clinical burden and result in total budget savings of NT$5.4 billion with annual savings peaking at NT$2.4 billion in the first year. Administering a single dose of PCV20 to adults therefore represents an efficient allocation of healthcare resources and is expected to lead to substantial cost and budget savings for the Taiwanese healthcare system.

To the best of our knowledge, this study is the first economic analysis to assess the clinical and economic value of PCV20 from both long-term and short-term perspectives, providing health economic evidence to support the recent decision to implement PCV20 into the national adult vaccination program. The findings from the cost effectiveness assessment are largely consistent with those from evaluations of a single dose of PCV20 versus a sequential strategy of PCV13 followed by PPV23 among adults in Germany, Argentina, Singapore and the US; we note that current pneumococcal vaccine recommendations in those countries include PCV20 for older adults as well as adults with certain risk conditions [43, 70-72]. Additionally, lower total vaccination costs and the additional protection offered by PCV20 against NBP led to PCV20 being cost-effective or dominant versus PPV23 alone in studies published in Japan, the UK, Denmark, and Norway [42, 73-75]. In comparison, few studies have evaluated the budget impact of PCV20. A study in Dubai concluded that replacing PCV13→PPV23 with PCV20 among non-Emirati at-risk/high-risk adults aged 19-49 and all adults aged ≥50 would, similar to our study, be budget saving [76]. However, a study based in England found that using PCV20 in lieu of PPV23 among at-risk adults aged 18-64 and all adults aged ≥65 resulted in a moderate increase in costs over a five-year period [77]. While both the present study and the cited research[76, 77] suggest a substantial reduction in the burden of pneumococcal disease, differences in budget impact may be explained by variations in country-specific healthcare systems, vaccine pricing, population risk profiles, and implementation strategies.

Limitations due to parameter uncertainty should be noted. First, vaccine effectiveness of PCV20 against VT-IPD and VT-NBP was based principally on PCV13 data; however, actual effectiveness of PCV20 may vary somewhat from PCV13 [34, 35, 78]. Furthermore, recent evidence suggests that PPV23 may provide some, albeit limited, protection against VT-NBP, which was not modeled in the present study [79, 80]. Second, we assumed that 18% of all-cause NBP was due to pneumococcus, based on Lansbury et al. (2022) [5]. However, estimates reported elsewhere suggest that this proportion may be higher [4], which would yield additional cost savings and greater public health benefit; notably, a study conducted in Taiwan suggests that pneumococcus accounts for 23.8% of hospitalizations due to CAP among adults [6]. Third, PCV15 was excluded from the analysis because it is not included in Taiwan's national pneumococcal vaccination program, and both the 2019 Taiwanese surveillance data (employed in analyses) and the most recent Taiwanese surveillance data (2022) showed no cases of pneumococcal disease attributed to PCV15 non-PCV13 serotypes (i.e., serotypes 22F and 33F).

There are also limitations regarding the modeling frameworks. Although some serotype replacement may occur in the real world, this possibility was not considered in the CEA scenario

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assuming pediatric herd effects. The CEA and BIA also excluded other potential downstream adverse outcomes and costs associated with pneumonia, which may conservatively bias against use of PCV20. Furthermore, the analyses did not consider the cost of vaccine administration; however, since PCV20 requires only one administration, unlike the sequential strategy, PCV20 would yield greater cost savings if the cost of vaccine administration had been considered. Finally, BIA is valuable for estimating the short-term costs of implementing new interventions, but restricting outcomes to a five-year timeframe can obscure the full benefits and value for money of a future PCV20 program for adults. This short-term focus also excludes long-term consequences of pneumococcal disease, such as worsening comorbidities, which may result in significant additional costs.

5. Conclusions

With PCV20 now recommended and prioritized over the sequential regimen, its implementation for high-risk adults aged 18–64 years and all adults aged ≥65 years in Taiwan is expected to substantially reduce lifetime cases and deaths from pneumococcal disease. Vaccinating adults with a single dose of PCV20 is an efficient use of healthcare resources and will result in both cost and budget savings for the Taiwanese healthcare system.

Supplementary Materials: The following supporting information can be downloaded at the website of this paper posted on Preprints.org, Table S1: Model input values for vaccine effectiveness and vaccine coverage in high-risk patients aged 18-64 years and all patients aged 65-99 years in Taiwan - CEA base case and BIA. Table S2: Underlying risk distribution in the Taiwan general population, by age - CEA and BIA. Table S3: Percentage of IPD due to vaccine serotypes in model years 1-10, by age - CEA base-case and BIA. Table S4: Percentage of NBP due to vaccine serotypes in model years 1-10, by age - CEA base-case and BIM. Table S5: Percentage of IPD due to vaccine serotypes, by age and year of modeling horizon - CEA scenario analysis #1. Table S6: Percentage of NBP due to vaccine serotypes, by age and year of modeling horizon - CEA scenario analysis #1. Table S7: Probabilistic sensitivity analysis variables sampled and distributional information – CEA. Table S8: Cost-effectiveness of PCV20 versus PCV13→PPV23 in (A) high-risk adults aged 18-64 years in Taiwan (N = 828,517) and (B) all adults aged 65-99 years in Taiwan (N = 4,679,858) - CEA base-case. Table S9: Cost-effectiveness of PCV20 versus PCV13→PPV23 in (A) high-risk adults aged 18-64 years in Taiwan (N = 828,517) and (B) all adults aged 65-99 years in Taiwan (N = 4,679,858) - CEA scenario analysis #1. Table S10: Cost-effectiveness of PCV20 versus PCV13→PPV23 in (A) high-risk adults aged 18-64 years in Taiwan (N = 828,517) and (B) all adults aged 65-99 years in Taiwan (N = 4,679,858) - CEA scenario analysis #2. Table S11: Budget impact of PCV20 vs. PCV13→PPV23 among high-risk adults aged 18-64 years and all adults aged ≥65 years in Taiwan (N=5,301,030)

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Abbreviations

The following abbreviations are used in this manuscript:

BIA	Budget impact analysis
BIM	Budget impact model
CAP	Community-acquired pneumonia
CAPiTA	Community-Acquired Pneumonia Immunization Trial in Adults
CDC	Centers for Disease Control
CEA	Cost-effectiveness analysis
CEM	Cost-effectiveness model
CFR	Case fatality rate
GDP	Gross domestic product
ICER	Incremental cost-effectiveness ratio
IPD	Invasive pneumococcal disease
LY	Life year
NBP	Non-bacteremic pneumonia
NT$/NTD	New Taiwan dollar
PCV13	13-valent pneumococcal conjugate vaccine
PCV15	15-valent pneumococcal conjugate vaccine
PCV20	20-valent pneumococcal conjugate vaccine
PPV23	23-valent pneumococcal polysaccharide vaccine
PSA	Probabilistic sensitivity analysis
QALY	Quality-adjusted life year
RR	Relative rate
VE	Vaccine effectiveness
VT	Vaccine-type
WTP	Willingness-to-pay

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