Cost-Utility Analysis of Pneumococcal Vaccines for Older Adults Available in Costa Rica

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INTRODUCTION

- Pneumococcal disease (PD) is a significant cause of morbidity and mortality worldwide in children and older adults [1-2]. *Streptococcus pneumoniae* (SP) is the most common cause of community-acquired pneumonia (CAP), which can develop into invasive pneumococcal disease (IPD), manifesting as meningitis or bloodstream infection (BSI) [2-3]. SP is classified into serotypes according to the polysaccharide capsule antigens; the distribution of serotypes and the incidence of CAP and IPD varies by country and population age group [2].
- Two pneumococcal vaccines are currently available in the National Immunization Program (NIP) for adults in Costa Rica: 13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (PPSV23) [4]. PCV13 is also available in the pediatric NIP [4]. These vaccines differ both in the design and in the number of serotypes contained (13 vs. 23) and in their capacity to generate an effective immune response [5-6]. Protein conjugation as in PCV13 is desirable as it elicits T-cell-dependent immune response, a more robust immunogenicity, and an improved memory for SP polysaccharide antibodies [6].
- Although routine use PCV13 in pediatric NIPs has demonstrated reduced PD in children (including indirect protection in older adults), there is still a substantial vaccine-preventable disease burden among older adults [7-10]. The clinical trial CAPiTA and real-word-evidence studies have demonstrated the impact of PCV13 on PD in older adults [11-12]. While PPSV23 prevents IPD, it has not been shown to reduce CAP incidence or death in adults with or without chronic diseases [13].
- Implementing a mass vaccination program requires an economic evaluation to estimate the clinical and economic benefits of different vaccination strategies in older adults to prevent PD.

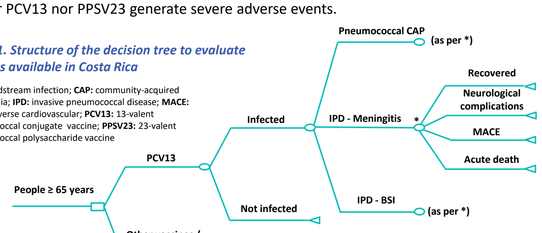
OBJECTIVES

- The aim of the study was to estimate the clinical and economic values of different vaccination strategies with PCV13 and PPSV23 in adults ≥65 years from the public healthcare perspective of Costa Rica.

METHODS

- We conducted a **cost-utility analysis** focused on the population of adults ≥ 65 in Costa Rica, with 500,000 individuals distributed across different age groups based on national population projections [14]. **Time horizon considered:** 5 years.
- **Five vaccination strategies were compared to no vaccination:** *PCV13 alone; PPSV23 with additional PPSV23 at year 5 (PPSV23+PPSV23); PCV13+PPSV23 (same year); and PCV13+PPSV23 with additional PPSV23 at year 5 (PCV13+PPSV23+PPSV23).*
- A **decision tree model** includes branches for each comparator **(Fig. 1)** and assumes neither PCV13 nor PPSV23 generate severe adverse events.

Figure 1. Structure of the decision tree to evaluate vaccines available in Costa Rica



BSI: bloodstream infection; **CAP:** community-acquired pneumonia; **IPD:** invasive pneumococcal disease; **MACE:** major adverse cardiovascular; **PCV13:** 13-valent pneumococcal conjugate vaccine; **PPSV23:** 23-valent pneumococcal polysaccharide vaccine

- **Health outcomes considered:** pneumococcal CAP and IPD and their sequelae (neurological deficit, hearing loss, epilepsy caused by meningitis, and major adverse cardiovascular events [(MACE]) related to SP infections). We assumed no waning for PCV13 over 5 years per the CAPiTA results [11]; PPSV23 was also assumed not to wane to simplify the model.
- Due to unavailability of data, we assumed that the distribution of pneumococcal serotypes in Costa Rica was comparable to that in Colombia, a country sharing similar geographic and social circumstances [15].

METHODS (continued)

- **Costs:** Vaccine costs are from PAHO tariffs; vaccine administration costs were assumed to be $1 per vaccine; healthcare costs were estimated using a bottom-up technique from a consultancy with experts. All costs are in USD2022. Costs and outcomes were discounted 3.5% annually.
- **Heterogeneity** was characterized through subgroup analysis in a range of age groups: 65-74 years, 75-84 years, and ≥85 years [16]. **Probabilistic sensitivity analysis (PSA)** was conducted using Monte Carlo simulations (n=1000) and its results are presented in **cost-effectiveness acceptability curves.**
- The analysis was performed from the perspective of the third-party payer responsible for mass vaccination programs in the country.

RESULTS

Study Parameters

- **Table 1** provides data on the assumptions made for incidence rates of pneumococcal infections in Costa Rica, with the proportion caused by SP in adults for each infection.

Table 1. The age group in Costa Rica adjusted the annual incidence rate of CAP, meningitis, and bloodstream infection.

	65-74 years	75-84 years	≥85 years	Source
Hospital-treated CAP	0.74 %	1.31 %	2.08 %	[16]
Outpatient CAP	0.26 %	0.38 %	0.86 %	[16]
All CAP	1.00 %	1.69 %	2.94 %	
Meningitis	0.02 %	0.03 %	0.06 %	[16,17]
Bloodstream infection	0.37 %	0.62 %	1.08 %	[16,18]
Total	1.39 %	2.34 %	4.08 %	

CAP: community-acquired pneumonia

Table 2. Efficacy of PCV13 and PPSV23 to prevent pneumococcal infections in older adults, adjusted by the type of infection

Vaccines efficacy by type of infection	Mean	Min	Max	Sources
PCV13 CAP	45.6 %	21.8 %	62.5 %	[11]
PCV13 IPD	75.0 %	41.4 %	90.8 %	[11]
PPSV23 CAP	0.0 %	0.0 %	0.0 %	[13]
PPSV23 IPD	67.1 %	9.5 %	88.0 %	[13]
PCV13 + PPSV23 CAP*	45.6%	21.8%	62.5%	[11,13]
PCV13 + PPSV23 IPD	75.0%	41.4 %	90.8 %	[11,13]

CAP: community-acquired pneumonia; **IPD:** invasive pneumococcal disease; **PCV13:** 13-valent pneumococcal conjugate vaccine; **PPSV23:** 23-valent pneumococcal polysaccharide vaccine. *The model is only applying vaccine efficacy to CAP due to serotypes covered in PCV13.

- **Table 2** shows the efficacy of PCV13 and PPSV23 in preventing pneumococcal infections in older adults adjusted by the type of infection; the efficacy of these vaccines must be adjusted by serotype distribution in each vaccine (i.e., no cross-immunity with serotypes not included in the vaccines).
- Annual incidence rates of pneumococcal infections were further adjusted by age group and vaccine efficacy while considering serotype distribution according to the type of vaccine.

Table 3. Health care costs of the different manifestations of pneumococcal disease and its complications, Costa Rica, 2022.

Clinical manifestation	Healthcare costs
Hospital-treated community-acquired pneumonia (general ward)	$ 3,134
Outpatient community-acquired pneumonia	$ 282
All CAP (weighted average)*	$ 2,486
Meningitis	$ 6,408
Bloodstream infection	$ 6,408
Hearing loss	$ 550
Neurological deficit (annual cost)	$ 5,500
Epilepsy (annual cost)**	$ 1,155
General cardiac complications	$ 698
Heart failure	$ 416
Acute coronary syndrome	$ 821
Cardiac arrhythmia	$ 1,000

CAP: community-acquired pneumonia. *The weighted average assumes that 75 % of older adults with pneumonia require hospital treatment (73% in the general ward and 2 % in ICU) and 25 % receive outpatient treatment. The cost of ICU in CAP is the same for IPD ** Annual epilepsy costs were obtained from literature [19], and adjusted to local drug prices.

- The healthcare costs of different pneumococcal diseases were estimated by experts as depicted in **Table 3.**
- The study evaluated the basal quality-adjusted life years (QALYs) of the population of interest at the beginning of the observation period, as well as the QALYs from patients with PD and epilepsy. Disutilities for neurological deficits or hearing loss were also included in the model.

Cost-Utility Analysis

Table 4. Total healthcare costs, QALYs, and Incremental Cost-Effectiveness Ratio (ICER) adjusted by age group of the different pneumococcal vaccination strategies available in Costa Rica.

	No Vaccine	PCV13	PPSV23 + PPSV23	PCV13 + PPSV23 + PPSV23	PPSV23	PCV13 + PPSV23
Total costs	$59,168,473	$52, 954,330	$65,973,890	$62,275,366	$60,916,952	$57,665,307
Total QALYs	1,810,387	1,820,643	1,811,537	1,821,007	1,811,478	1,820,810
Δ Costs		-$6,214,144	$6,805,417	$3,106,893	$1,748,478	- $1,503,166
Δ QALYs		10,256	1,150	10,620	1,091	10,423
ICER ≥ 65 years		**-$606**	**$5,920**	**$293**	**$1,603**	**-$144**
ICER 65-74 years		-$305	$9,553	$977	$3,518	$352
ICER 75-84 years		-$736	$4,357	-$3	$779	-$359
ICER ≥ 85 years		-$1,002	$1,129	-$608	-$922	-$798

WTP threshold was assumed to be 1 GDP per capita in Costa Rica (USD 12,509). **QALY:** quality-adjusted life years; **ICER:** Incremental Cost-Effectiveness Ratio; **WTP:** Willigness to Pay; **GDP:** Gross Domestic Product

- **Table 4** presents the main CUA results for people ≥ 65 years as well as ICERs adjusted by age group. All vaccination strategies were estimated to prevent more disease and yielded more QALYs than no vaccination.
- PCV13 alone and PCV13 + PPSV23 were cost-saving compared to no vaccination in people ≥ 65 years, however, only PCV13 alone saved costs in all age groups, and the other strategies were cost-effective.
- The study found a relevant difference in QALYs obtained with all strategies that include PCV13 compared to those without it.
- **PSA** with 1 GDP/QALY as the WTP threshold showed 84.3% probability of PCV13 being the favored strategy in people 65-74 years; 66.3% in people 75-84 years, while PCV13+PPSV23+PPSV23 has a 51.3% chance to be most favored in people ≥ 85 years (Figures 2-4). Not vaccinating against pneumococcus in older adults was unlikely to be a good option.

Sensitivity Analysis

Figure 2. WTP curves for pneumococcal vaccination strategies available in Costa Rica in people between 65-74 years.

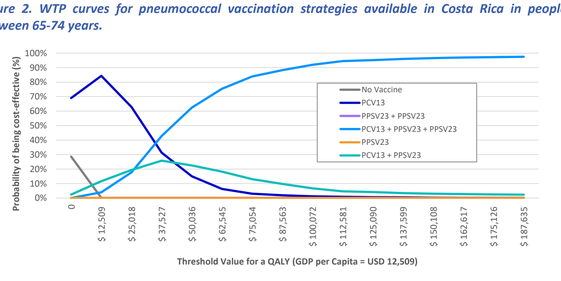


Figure 3. WTP curves for pneumococcal vaccination strategies available in Costa Rica in people between 75-84 years.

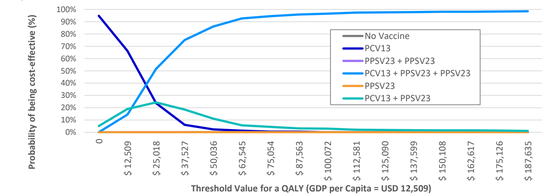
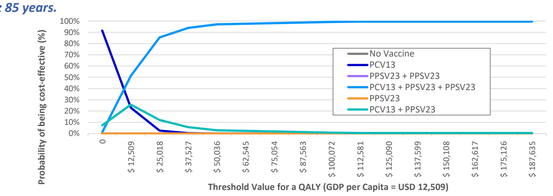


Figure 4. WTP curves for pneumococcal vaccination strategies available in Costa Rica in people ≥ 85 years.



DISCUSSION

- The CUA of different vaccination strategies in adults over 65 indicates that vaccination with PCV13 alone and PCV13+PPSV23 compared to no vaccination could save Costa Rica''s healthcare system $ 6.2 million and $ 1.5 million, respectively. All other vaccination schedules are cost-effective, but only PCV13 and PCV13+PPSV23 save costs in people ≥ 65 years.
- PSA also showed that the strategies that include PCV13 in combination with PPSV23 (sequential schedule) had greater efficiency and lower costs than those that do not. Other studies done worldwide show consistent results that strategies including PCV13 + PPSV23 are either cost-saving or cost-effective [20-22].
- Our results suggest that PCV13 alone or combined with PPSV23 are the best options in most age groups considered in the study in Costa Rica. PCV13 alone was the most cost-saving strategy for preventing CAP and IPD in all older adults.
- One of the strengths of this economic model was evidencing the clinical and economic impact that preventing PD has on MACE related with pneumococcal infections. Recent observational studies have found significant risk of cardiovascular complications in patients with pneumococcal CAP or IPD [23,24].
- In conclusion, vaccinating older adults with PCV13 with or without PPSV23 is likely to improve health and provide a net savings for the Costa Rican healthcare system.

DISCLOSURES

Pfizer sponsored this study.

For questions, please contact **jaime.ordonez@trueconsulting.co**

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