Original Article

Cost-effectiveness analysis of pneumococcal conjugate vaccines in preventing pneumonia in Peruvian children

Edward Mezones-Holguín*[1,2], Rafael Bolaños-Díaz*[1,3], Víctor Fiestas[1], César Sanabria[3], Alfonso Gutiérrez-Aguado[4,5], Fabián Fiestas[1], Víctor J Suárez[1,5], Alfonso J Rodríguez-Morales[6], Adrián V Hernández[1,2]

[1] *Unidad de Análisis y Generación de Evidencias en Salud Pública (UNAGESP), Centro Nacional de Salud Pública, Instituto Nacional de Salud, Lima, Peru*
[2] *School of Medicine, Universidad Peruana de Ciencias Aplicadas, Lima, Peru*
[3] *Faculty of Economics, Universidad Nacional Mayor de San Marcos, Lima, Peru*
[4] *Ministry of Economy and Finance, Government of Peru, Lima, Peru*
[5] *Postgraduate School, Universidad Cesar Vallejo. Lima, Peru*
[6] *Public Health and Infection Research Group, Faculty of Health Sciences, Universidad Tecnológica de Pereira, Pereira, Risaralda, Colombia*

* Authors contributed equally to this work.

Abstract

Introduction: Pneumococcal pneumonia (PP) has a high burden of morbimortality in children. Use of pneumococcal conjugate vaccines (PCVs) is an effective preventive measure. After PCV 7-valent (PCV7) withdrawal, PCV 10-valent (PCV10) and PCV 13-valent (PCV13) are the alternatives in Peru. This study aimed to evaluate cost effectiveness of these vaccines in preventing PP in Peruvian children <5 years-old.

Methodology: A cost-effectiveness analysis was developed in three phases: a systematic evidence search for calculating effectiveness; a cost analysis for vaccine strategies and outcome management; and an economic model based on decision tree analysis, including deterministic and probabilistic sensitivity analysis using acceptability curves, tornado diagram, and Monte Carlo simulation. A hypothetic 100 vaccinated children/vaccine cohort was built. An incremental cost-effectiveness ratio (ICER) was calculated.

Results: The isolation probability for all serotypes in each vaccine was estimated: 38% for PCV7, 41% PCV10, and 17% PCV13. Avoided hospitalization was found to be the best effectiveness model measure. Estimated costs for PCV7, PCV10, and PCV13 cohorts were USD13,761, 11,895, and 12,499, respectively. Costs per avoided hospitalization were USD718 for PCV7, USD333 for PCV10, andUSD 162 for PCV13. At ICER, PCV7 was dominated by the other PCVs. Eliminating PCV7, PCV13 was more cost effective than PCV10 (confirmed in sensitivity analysis).

Conclusions: PCV10 and PCV13 are more cost effective than PCV7 in prevention of pneumonia in children <5 years-old in Peru. PCV13 prevents more hospitalizations and is more cost-effective than PCV10. These results should be considered when making decisions about the Peruvian National Inmunizations Schedule.

Key words: pneumonia; pneumococcal; pneumococcal vaccines; cost-effectiveness; immunization programs; Peru.

J Infect Dev Ctries 2014; 8(12):1552-1562. doi:10.3855/jidc.5855

(Received 04 September 2014 – Accepted 28 October 2014)

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Introduction

Background

Infections due to *Streptococcus pneumoniae* are major causes of morbidity, hospitalization, and mortality in children. *S. pneumoniae* causes invasive pneumococcal diseases (IPDs) (*e.g.*, meningitis and bacteremia) and non-invasive pneumococcal diseases (*e.g.*, community-acquired pneumonia [CAP] and acute otitis media [AOM]) [1-4]. Prevention is complex because there are 94 serotypes. However, approximately 80% of all IPDs are caused by 20 serotypes [1,5].

Introduction of pneumococcal conjugate vaccines (PCVs) occurred in the United States in 2000, and later in Europe in 2001, when the Food and Drug Administration (FDA) and the European Medicines Agency (EMA), respectively, authorized the 7-valent vaccine (PCV7). This vaccine included serotypes 4,

6B, 9V, 14, 18C, 19F, and 23F [6,7]. In other regions of the world, such as Southeast Asia and Latin America, and the Caribbean, PCVs have been approved for use since 2005 and 2007, respectively [8,9]. Peru included PCVs in 2009 [10]. PCV7 has been demonstrated to be effective in preventing CAP and IPDs in children [11-14]. However, years after its introduction, there has been a change in *S. pneumoniae* serotype distribution [9,14-16].

In 2009 in Europe and in 2010 in the United States, the 10-valent (PCV10) vaccine, which added serotypes 1, 5 and 7F to PCV7 serotypes, and the 13-valent (PCV13) vaccine, which further added serotypes 3, 6A and 19A to PCV10 serotypes, were introduced to cover a broader range of serotypes [17-21]. In order to support the adoption of PCVs for vaccination schedules of immunization programs, cost-effectiveness studies have been performed in various countries [22-29]. However, in Latin America, few previous studies have evaluated the pharmacoeconomic and economic impact of PCV10 and PCV13 [26,30-35]; none of these studies were conducted in Peru by a non-pharmaceutically funded institution.

In 2011, the manufacturer of PCV7 stopped its worldwide distribution. Therefore, PCV7 had to be replaced by PCV10 or PCV13. In this context, economic evaluations (EEs) are necessary tools for choosing to include either PCV10 or PCV13 in the Peruvian National Immunizations Schedule (PNIS). EEs are instruments that measure costs and health effects and describe the comparative efficiency of services and health interventions (*e.g.*, drugs, technologies, procedures, public health interventions). Among them, the cost-effectiveness analysis (CEA) is the most important [36,37-67].

Objective

We estimated the cost-effectiveness of PCV10 and PCV13 in the prevention of pneumococcal pneumonia (PP) in children under five years of age in Peru, considering current vaccination with PCV7 as the baseline strategy.

Methodology

Target population, setting, location, and study perspective

A cost-effectiveness analysis from the perspective of the government was conducted. The population included a hypothetical cohort of children under five years of age in Peru, and the cost estimation was based on 2011 information from the Peruvian Ministry of Health (MINSA). The international recommendations for performing health economic evaluations were used [38]. Peru ranked 82 in the Human Development Index (0.737) in 2013 (reported in 2014); it is a high human development country with a life expectancy of 74.8 years and a gross national income (GNI) per capita of USD 11,280 [68].

This study included three phases. The first phase involved a systematic search of literature for estimating PCV effectiveness. The second phase included the development of a costing frame related to the intervention and treatment. Finally, the third phase was the development of a pharmacoeconomic model comparing PCV7, PCV10, and PCV13 alternatives. The time span for all interventions was three years, and an annual discount rate of 3% was used [36].

The PNIS for 2011 included three doses (2+1) of PCV, two doses in the first year and a third dose at 12 months or more in the second year [39]. Although other PCV studies used three doses plus a booster (3+1) in children between two months and two years of age, the Pan American Health Organization (PAHO) and the World Health Organization (WHO) expert panels recommend three doses for any PCV as the minimum number to be considered in a vaccination schedule [40]. For this study, three doses (2+1) were considered to be the complete schedule of vaccination against *S. pneumoniae*.

Health outcomes and measurement of effectiveness

Vaccine effectiveness for all alternatives was defined as that which prevented or avoided hospitalizations due to PP. The main goal of the Peruvian government is the reduction of child mortality and malnutrition; PP is strongly associated with these conditions. Hence, the MINSA's request was focused on PP as the main outcome.

Systematic search of literature

First, an investigation was undertaken to determine whether PCV7, PCV10, and PCV13 intervention among children under five years of age reduces the incidence of pneumonia, meningitis, or acute otitis media. Studies were selected from a search of papers in the following databases: Cochrane Library, PubMed/MEDLINE, EMBASE, Latin American Literature on Health Sciences (LILACS), and Scientific Electronic Library Online (SciELO). Studies from January 2005 to December 2010 were selected. References identified were limited to randomized controlled trials (RCTs), observational studies, and systematic reviews with or without meta-analysis

(MA), conducted in children under five years of age. Review papers, editorials, and conference abstracts were excluded.

Three searches were used.

Search 1 included ("7-valent pneumococcal* vaccine") AND ("pneumonia" OR "meningitis" OR "acute otitis media");

Search 2 included ("10-valent pneumococcal* vaccine") AND ("pneumonia" OR "meningitis" OR "acute otitis media"); and

Search 3 included ("13-valent pneumococcal* vaccine") AND ("pneumonia" OR "meningitis" OR "acute otitis media").

Second, an exhaustive review of references in the primary identified sources was done to complement the systematic search. National and international experts were asked to provide additional bibliographical searches and knowledge about additional available studies not identified by investigators. Given that no studies were found for meningitis and acute otitis media, the CEA was done for pneumonia only, specifically for PP, as this allowed the evaluation of pneumococcal serotype distribution in the country.

Estimation of resources and costs

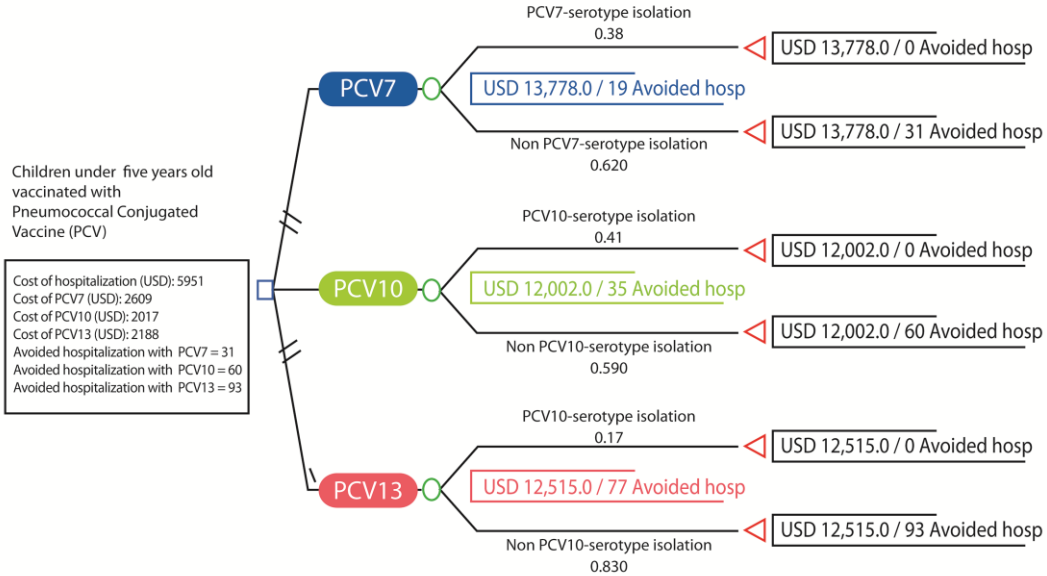
Costs were calculated based on real costs from the perspective of the MINSA according to the PNIS. Direct medical costs for inpatient care, including average diagnosis and treatment costs of hospitalized patients with pneumococcal pneumonia, were obtained from three major general hospitals in Lima: Hospital Nacional Arzobispo Loayza, Hospital San Juan de Lurigancho, and Instituto Nacional de Salud del Niño. For cost estimations of PCV10 and PCV13, manufacturers of PCVs were contacted. Also, approximately 15% of the direct costs were estimated to be indirect costs, according to Ministry of Health calculations. All currency values were expressed in USD for 2011, which was the year the model was developed (1 USD = 2.8 Peruvian nuevos soles).

Pharmacoeconomic model

A decision tree analysis-based model was used. This represented the probable clinical evolution in a temporal horizon of three years, applying three alternative preventing interventions with PCV7, PCV10, and PCV13. Each branch of the model decision tree represented one of these preventing options, and the final results of each of the branches combine the serotype isolation in the corresponding vaccine with associated cost and final clinical effectiveness (avoided hospitalizations) (Figure 1).

For outcome assessment, the relation of cost-effectiveness for each option was calculated, with the most efficient option being the one with the lowest value. Also, the incremental cost-effectiveness ratio (ICER) of all the alternatives was estimated; this evaluated the necessary cost to avoid an extra hospitalization due to PP.

Figure 1. Decision tree analysis of three PCV varieties



The decision tree model is represented based on the CEA. Branches of the tree show the possible evolution of the interventions, assuming that all can possibly reduce the incidence of pneumonia. At branches, the probabilities of serotype isolation (included in the corresponding vaccine) are represented according the observational available information based on epidemiological data of hospitalized children (Figure 1).

Probabilistic sensitivity analyses were performed to assess the effect of uncertainty around the model results. First, cost-effectiveness acceptability curves were created. Second, considering the best fitted distribution explaining the performance of each variable –normal distribution in the most variables (for building the range of incidence rate for serotypes include in each vaccine, we using in that way, the worse a best scenario) and log-normal distribution in the case of costs– a Monte Carlo simulation was conducted (1,000 simulations were run, each selecting an input within the distribution). This process allowed for the estimation of a range of possible model outcomes. Finally, tornado analysis was done to evaluate the variables with major influence in final cost-effectiveness results [36,41,42].

The software used for the analysis was TreeAge Pro Healthcare.

Results

Study parameters and findings of the systematic search

No systematic reviews, MAs, or RCTs comparing clinical efficacy and effectiveness of PCV10 and PCV13 were found. Two observational studies by Hortal *et al.* [43] and Cedrés *et al.* [44], considered to be relevant sources for the analysis, were selected. These studies were based on epidemiological surveillance information from Uruguay, a middle-income Latin American country with a population of approximately three million. These studies assessed the pneumococcal serotype incidence in a pediatric population of children under five years of age in PCV7 pre-vaccination and post-vaccination periods. This information was used because the baseline serotype distribution (pre-vaccination period) was similar to that of the Peruvian population [45]. Effectiveness data for PCV10 and PCV13 were extrapolated from available data, based on previously used methodologies [24,46-48].

Outcomes

According to Hortal *et al.*, 314 cases of pneumonia were recorded in a population of children under five years of age during the PCV7 pre-vaccination period (2000–2004). Serotype distribution was 52% for PCV7 vaccine-included serotypes (4, 6B, 9V, 14, 18C, 19F, 23F), 34% for additional serotypes included in the PCV10 (1, 5, 7F), 12% for additional serotypes included in the PCV13 (3, 6A, 19A); and 2% for other serotypes not included in these PCVs in Uruguay [43].

Cedrés *et al.* [44], after the introduction of PCV7 in Uruguay, reported 61 cases of PP in a population of children under five years of age vaccinated with PCV7 in the post-vaccination period (2008–2009). Serotype distribution was 38% for PCV7 vaccine-included serotypes; 39% for PCV10 vaccine-included additional serotypes; 15% for PCV13 vaccine-included additional serotypes; and 8% for other serotypes not included in these PCVs [44].

The relative risk (RR) of PCV7-serotypes pneumonia between post- and pre-vaccination periods was 0.73; based on these point estimates, a RR reduction of 27% was achieved with PCV7. This has been defined as a direct effect (DE) of PCV7 vaccine in this cohort.

Considering the lack of prospective studies assessing the clinical efficacy of PCV10 and PCV13 until 2009, the pneumonia risk reduction of these vaccines was estimated based on the assumption that both would have the same DE as PCV7. Of note, PCV10 and PCV13 included the same serotypes available in PCV7 plus an additional DE that would correspond to a factor defined in previous studies [24,46-48]. For PCV10, this factor would be estimated as (pre-vaccination PCV10 serotypes incidence [not included in PCV7])/(pre-vaccination PCV7 serotypes incidence). Similarly, the additional DE for PCV13 would be estimated as (pre-vaccination PCV13 serotypes incidence [not included in PCV10])/(pre-vaccination PCV7 serotypes incidence). The total DE of PCV10 would be DE(PCV10) = DE(PCV7) x (pre-vaccination PCV10 serotypes incidence/pre-vaccination PCV7 serotypes incidence), and the total DE for PCV13 would be DE(PCV13) = DE(PCV7) x (pre-vaccination PCV13 serotypes incidence/pre-vaccination PCV7 serotypes incidence).

According to this, given the epidemiological surveillance in Uruguay, the DE for PCV10 would be 0.73 x (0.34/0.52), and for PCV13 would be 0.73 × (0.12/0.52). The final DE would be 0.48 and 0.17 for PCV10 and PCV13, respectively. These values

correspond to a relative risk reduction of 52% and 83%, respectively.

According to the general direction of epidemiology of MINSA [49], the annual incidence of pneumonia is around 130 cases/100,000 children under five years of age. Of these cases, 40% are due to *S. pneumoniae*, which represents approximately 52 cases of PP per 100,000 children under five years of age per year [49]. Based on the reports of the Peruvian National Institute of Health until year 2009 (pre-vaccination introduction year), 62%, 71%, and 82% of isolates would correspond to serotypes included in the PCV7, PCV10, and PCV13 vaccines [45], respectively. Thus, incidence rates would be 32 cases/100,000 for PCV7 serotypes, 37 cases/100,000 for PCV10 serotypes, 43 cases/100,000 for PCV13 serotypes; 9 cases/100,000 would approximately correspond to serotypes not included in current PCVs.

In terms of CEA, the post-vaccination incidence could be estimated to be 38%, 41%, and 17% for the development of pneumonia with serotypes included in PCV7, PCV10, and PCV13, respectively. Considering the DE of these three vaccines and a coverage of 100%, the annual incidence of PP due to serotypes of PCV7 in children under five years of age would decrease from 32 (pre-vaccination period) to 12 cases/100,000 (post-vaccination period; *i.e.*, 52 × 0.62 × 0.38). Thus, overall pneumonia cases would be reduced from 52/100,000 to 32/100,000 per year. Similarly, the annual incidence of PP due to serotypes of PCV10 would be reduced from 37 to 15/100,000 (52 × 0.71 × 0.41); *i.e.*, overall pneumonia cases would be reduced from 52/100,000 to 30/100,000 per year. Finally, pneumonia associated with PCV13 serotypes would decrease from 43 to 7/100,000 (52 × 0.82 × 0.17); *i.e.*, overall pneumonia cases reduced from 52/100,000 to 16/100,000 per year. Although these are only point estimates, a similar distribution of serotypes among hospitalized and non-hospitalized patients is assumed.

According to the decision tree, the probability of serotype isolation would be 38%, 41%, and 17% for PCV7, PCV10, and PCV13, respectively.

Costs

In Table 1, the total cost for a hypothetical cohort of 100 vaccinated children with each PCV in evaluation is shown. PCV7 has the highest cost, and the PCV13 cost is higher than that of PCV10. Those estimations include fixed and variable costs (direct

Table 1. Direct and indirect costs of vaccination with PCV7, PCV10, PCV13

	Costs in USD		
	PCV7	**PCV10**	**PCV13**
Fixed costs	1.17	1.17	1.17
Human resources	0.88	0.88	0.88
Depreciation	0.29	0.29	0.29
Variable costs	21.52	16.37	17.86
Materials and devices	0.72	0.72	0.72
Vaccines	20.00	14.85	16.34
Services	0.80	0.80	0.80
Direct costs (fixed + variable costs)	22.69	17.54	19.03
Indirect costs	3.40	2.63	2.85
Total costs x 1 dose	26.09	20.17	21.88
N° of doses	3	3	3
Total costs x 3 doses	78.28	60.51	65.65
Total costs x 100 vaccinated children	**7,828**	**6,051**	**6,565**

Table 2. Average costs of hospitalization due to pneumonia in children in Lima, Peru

Parameter description	**Quantity**	**Unit price (USD)**	**Total costs (USD)**
Consultation at emergency department (/child)			3.23
X-rays			4.41
Complete blood counts (CBC)			2.33
Hemoculture (1 sample/bottle)			5.03
1 day of hospitalization in a general ward (/child)	7	6.11	42.76
Vial of ceftriaxone	14	0.61	8.50
Syringe d/c of 1 cc c/a of 25' 5/8"	14	0.06	0.90
Costs of hospitalization			59.51

costs) plus indirect costs. Table 2 summarizes the estimated costs of treatment for each hospitalization case at the MINSA institutions. In Table 3, the potential cost for a hypothetical cohort of 100 children vaccinated with PCV7 and hospitalized due to pneumonia is estimated to be USD 13,761. Similarly, for a cohort of 100 PCV10-vaccinated children hospitalized due to pneumonia, a potential cost of USD 11,985 was estimated. Finally, a similar cohort of 100 PCV13-vaccinated hospitalized children with pneumonia would have an estimated potential cost of USD 12,499.

Cost-effectiveness ratio (CE ratio) and incremental cost-effectiveness ratio

An estimation of CE ratios is presented in Table 3. This corresponds to USD 718 for PCV7, USD 333 for PCV10, and USD 162 for PCV13 per avoided hospitalization. These results indicate that interventions with PCV10 and PCV13 are more cost effective than those with PCV7; however, intervention with PCV10 would be less cost effective than with PCV13 when baseline strategy PCV7 is eliminated. Figure 2 shows the point estimates of CE ratio for the three alternatives, considering at the *y*-axis the costs per 100 vaccinated children and at the *x*-axis avoided hospitalizations. For example, the use of PVC7 in 100 children would cost USD 13,800 to avoid 19 hospitalizations. The summary for the analysis of ICER is shown in Table 3. Cost per avoided hospitalization would be lowest with PCV13 (USD 162) than PCV10 (USD 333) and PCV7 (USD 718). PCV7 is less cost effective than PCV10 and PCV13. However, PCV13 would be more cost effective than PCV10 when PCV7 is eliminated, with an estimated ICER of 13.

Sensitivity analysis

In the worst-case scenario for PCV7, no pneumonia cases would be avoided, and in the best-case scenario, 48 cases would be avoided. The worst-case scenario for PCV10 and PCV13 would correspond to the worst-case scenario for PCV7 (0 avoided pneumonia cases), and the DE would be 33 avoided pneumonia cases for PCV10 and 76 for PCV13. The best-case scenario for PCV10 and PCV13 would begin with the best-case scenario for PCV7 (48 avoided cases), plus the DE (66 avoided cases for PCV10, and 88 for PCV13). For cases in which other serotypes were isolated (not included in any of the assessed vaccines), it is assumed that no cases would be avoided (0 avoided pneumonia cases). Acceptability curves for the interventions are shown in Figure 3. The probability of cost effectiveness for PCV13 is around 40% when willingness to pay is USD 0; beginning with a willingness to pay USD 30, PCV13 has a higher probability of cost effectiveness than does PCV10 (> 50%). However, PCV10 and PVC7 were never more cost effective than PCV13 for any level or amount of willingness to pay.

The Monte Carlo probabilistic simulation is presented in Figure 4, showing the scatter plot of PCV13 located at the right-hand side of PCV7 and PCV10, with practically no overlap between PCV13 and PCV10 and little overlap between PCV7 and PCV10. Differences between them are clear, showing that PCV13 and PCV10 are more cost effective than PCV7. Additionally, PCV13 is more cost effective than PCV10, although this intervention has a slightly higher cost. The tornado diagram in Figure 5 shows the most influential variable on the final results of the model.

Table 3. Incremental cost-effectiveness ratio (ICER) analysis for three different pneumococcal conjugates vaccines

	Effectiveness (avoided hospitalizations)	Cost (USD)	Cost effectiveness (USD per avoided hospitalization)	ICER	
PCV7	19.16	13,761	718	Dominated	
PCV10	36.00	11,985	333	-105	PCV10 vs PCV7
PCV13	76.94	12,499	162	13	PCV13 vs PCV10

Table 4. Value parameters of the economic model

Variable	Mean Value (range)	Distribution
Hospitalization cost (USD)	5,951 (5,000 – 7,000)	LogNormal
PCV10 cost (USD)	2,017 (1,800 – 2,500)	LogNormal
PCV13 cost (USD)	2,188 (1,800 – 2,500)	LogNormal
PCV7 cost (USD)	2,609 (2,000 – 3,000)	LogNormal
Avoided hospitalizations with PCV10	60 (40 – 90)	Normal
Avoided hospitalizations with PCV13	93 (40 – 100)	Normal
Avoided hospitalizations with PCV7	31 (20 – 40)	Normal

Figure 2. CE relation between the three vaccine varieties (per 100 children < 5 years of age vaccinated) (AH = avoided hospitalizations)

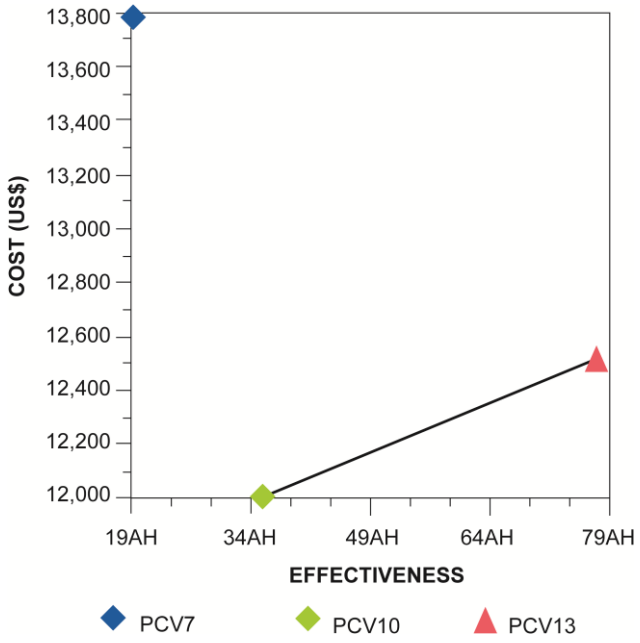


Figure 3. Acceptability curve for three vaccine varieties

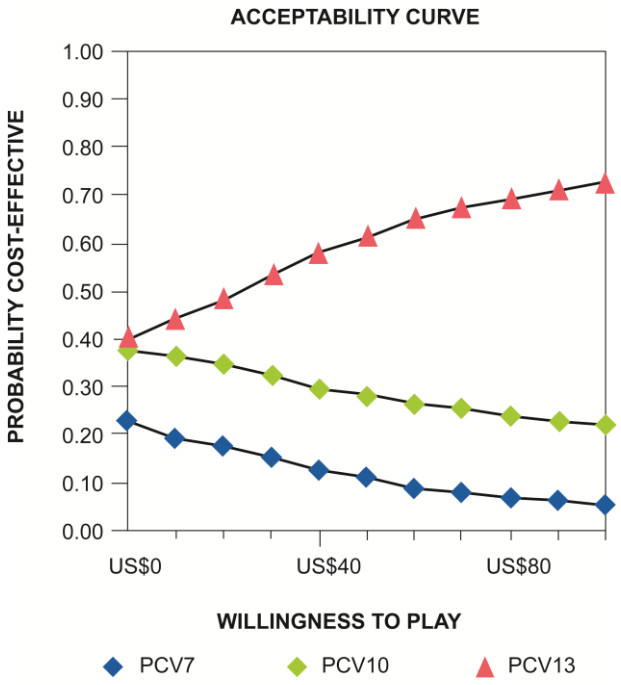


Figure 4. Probabilistic sensitivity test for the three vaccine varieties using the Monte Carlo simulation method

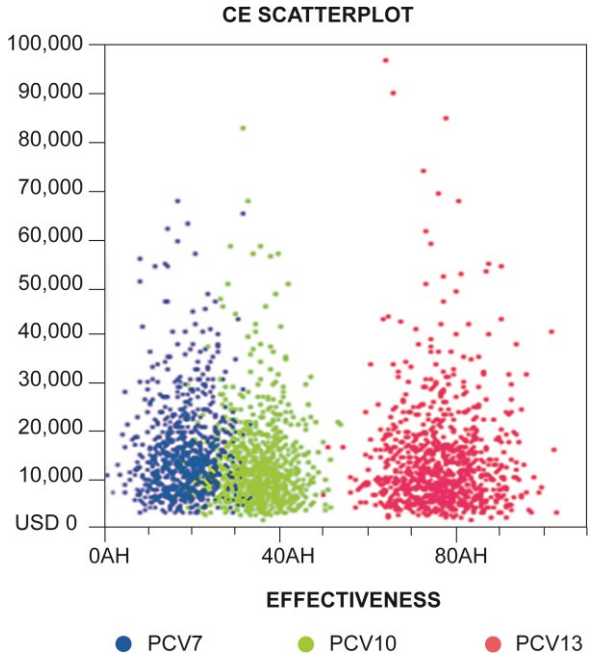
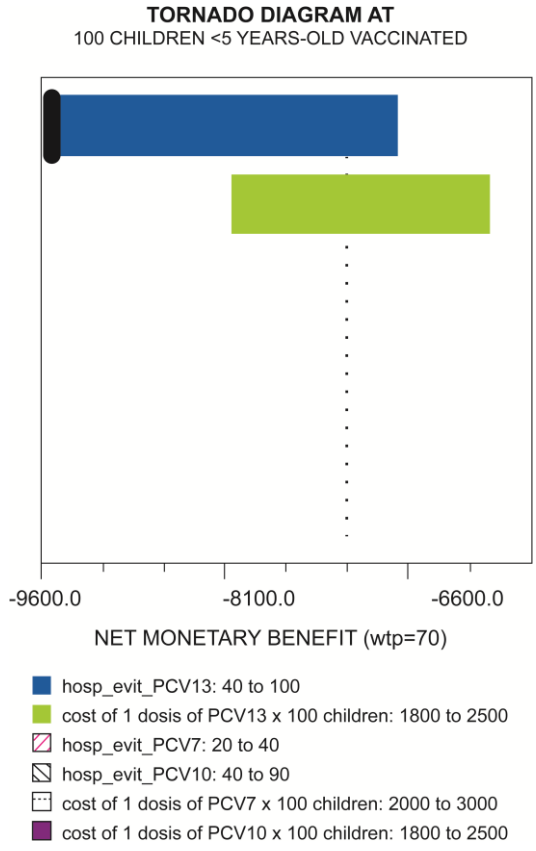


Figure 5. Tornado diagram



According to this, effectiveness variation for pneumonia in PCV13-vaccinated children and cost per dose of PCV13 would be the variables that have a greater impact on the net monetary benefit.

Finally, the values, ranges, and probability distributions for all parameters used to represent uncertainty are shown in Table 4.

Discussion

Our findings show that PCV13 would be more cost effective than PCV10 in the prevention of PP in children under five years of age when PCV7 is eliminated. Moreover, if PCV7 were maintained in the analysis, PCV7 would be less effective than PVC10 and PCV13. These results are due to PVC13's higher effectiveness in preventing more hospitalizations due to pneumococcal pneumonia than PCV10 despite the lower cost of PCV10.

Beneficial effects of PCVs on at-risk populations have been described. The efficacy of PCV7 was demonstrated in clinical trials prior to commercialization [12,50], and it was subsequently introduced into immunization schedules in several countries, including Peru [51]. Moreover, prospective results of efficiency of PCV10 and PC13 are still necessary, particularly for regions such as Latin America and especially Peru. This country has a comprehensive immunization program, in which MINSA provides vaccines to the whole population through the social security system and, in some cases, within the private sector [39,51]. There have been studies assessing cost effectiveness of PCV7 [23,27,28,52], but few studies assessing PCV10 and PCV13 [29,32,35] have been conducted in this part of the world.

This study is a first approach at measuring the efficiency –since EE involves cost and effectiveness related whichever intervention in health [36,37,53]– of available vaccination alternatives to support decision making in Peru. This study is of utmost importance, especially to countries such as Peru with estimated IPD rates in children under 24 months of age in Lima of 18.4 cases/100,000 [4] and where pneumonia is the major problem related to child mortality [54]. Also, EEs are an important tool for making decisions in public health interventions because of their budgetary impact; furthermore, because vaccination programs are provided by the public sector, vaccination programs are among the most frequently studied public health interventions [29,55,56]. This mainly occurs in countries where the financial support for those programs is funded by the government, especially because economic evaluations results are context dependent [37,57]. Given the Peruvian MINSA provides vaccines for all infants and toddlers through the PNIS [39], deciding on an alternative with the highest cost effectiveness and largest reductions in children mortality is mandatory. Thus, in the Peruvian context, the PCV13 vaccine is the best alternative. However, it is important to take into account other conditions or perspectives that could guide the complexity of decision making [37,58].

Our study has some limitations. First, the pharmacoeconomic analysis was not based on direct data of the epidemiological surveillance of Peru because there are no local observational reports for a PCV7 post-vaccination period or any systematic review or RCT which compares directly the efficacy of both vaccines (PV10 and PCV13) to estimate efficacy. We used information from the epidemiological surveillance in Uruguay, a country that had a similar pneumococcal serotypes distribution to Peru in the PCV7 pre-vaccination period [43,44]; thus, we extrapolated the direct effect by standardized international methods [24,46-48]. However, observational designs are of high relevance and utmost importance in CEA [59,60]. The second limitation was our use of only pneumonia as the outcome, to the exclusion of pneumococcal meningitis, sepsis, and otitis media; this was because available evidence is still limited and the record systems for these diseases in Peru are scarce. Third, because we did not categorize the clinical form of pneumonia (empyema, with or without bacteremia), the estimations are limited to uncomplicated PP; we assumed a similar distribution of the complications and development of diseases for all types of serotypes, thus it does not produce any variation in the model. Finally, indirect effect by herd immunity of PCVs was not measured. The estimation of this effect can have a significant clinical impact on a non-vaccinated pediatric population, may decrease the severity given the reduction of invasive serotypes circulation, and eventually also may prevent disease in a non-vaccinated population [61-64]. However, including this estimation could increase the uncertainty of the model, especially when we do not have exact estimations. Also, our model is static, so it may not reflect the real world by including the dynamic transmission of pneumococcal pneumonia in the community, where the indirect effect has important implications [65].

An inherent feature of pharmacoeconomic designs is the fact they are regularly assessed by different

sensitivity tests, which examine the robustness of results against uncertainty of each variable [66]. Thus, the robustness of our results was supported with probabilistic sensitivity tests, in which it was observed that PCV13 is better than the other two alternatives in terms of cost effectiveness in the Peruvian context; this is one of strengths of our study.

According to our results, interventions with PCV10 and PCV13 are more cost effective in the reduction of hospitalizations due to pneumonia than interventions with PCV7, although PCV7 is less cost effective the other two interventions. PCV13 is more cost effective than PCV10. It is necessary to assess the impact of PCVs after their introduction because they are an important investment for the government and because assessment allows for a better use of resources and enhances public health policies [67].

Acknowledgements

This study was funded by Instituto Nacional de Salud, Lima, Peru.

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Corresponding authors

Edward Mezones-Holguín
Unidad de Análisis y Generación de Evidencias en Salud Pública (UNAGESP)
Centro Nacional de Salud Pública, Instituto Nacional de Salud
Av. Tizón y Bueno 276, Lima 11, Peru
Phone: +51-980-652960
Email: emezones@gmail.com

Alfonso J. Rodriguez-Morales
Faculty of Health Sciences, Universidad Tecnológica de Pereira, La Julita,
Pereira 660003, Colombia.
Phone: +57-300-8847448
Email: arodriguezm@utp.edu.co

Conflict of interests: No conflict of interests is declared.