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How cost effective is switching universal vaccination from PCV10 to PCV13? A case study from a developing country

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ABSTRACT

Background: Children immunization with pneumococcal conjugate vaccine (PCV) had profound public health effects across the globe. Colombian adopted PCV10 universal vaccination, but PCV incremental impact need to be revalued. The objective of this analysis was to estimate the cost-effectiveness of switch to PCV13 versus continue PCV10 in Colombian children.

Methods: A complete economic analysis was carried-out assessing potential epidemiological and economic impact of switching from PCV10 to PCV13. Epidemiological information on PCV10 impact was obtained from lab-based epidemiological surveillance on pneumococcal isolates at the Colombian National Institute of Health. Economic inputs were extracted from the literature. Incremental PCV13 effectiveness was based in additional serotypes included. Comparisons among alternatives were evaluated with the Incremental Cost-Effectiveness Ratio (ICER) at a willingness to pay of one GDP per capita (USD$ 6631) per Year of Live Saved (YLS). All costs were reported in 2014USD. Deterministic and probabilistic sensitivity analyses were performed, and 95% confidence interval reported.

Results: After four years using PCV10 for universal vaccination on children the Colombian health surveillance system showed a relative increment on non PCV10 isolates. To change from PCV10 to PCV13 would avoid 587 (CI95% −49–1008) ambulatory Rx community-acquired pneumoniae (CAP), 1622 (CI95% 591–2343) Inpatient RxCAP, 10 (CI 95% 6–11) pneumococcal meningitis, and 79 (CI95% 76–98) deaths. ICER per YLS was USD$ 2319 (CI95% Dominated – USD$ 4225) for Keep-PCV10 and USD$ 1771 (CI95% USD$ 1285–9884) for Switch-to PCV13. In spite of its cost-effectiveness Keep-PCV10 is an extended dominated alternative and Switch-to PCV13 would be preferred. Results are robust to parameters changes in the sensitivity analyses.

Conclusion: A national immunization strategy based in Switch-to PCV13 was found to be good value for money and prevent additional burden of pneumococcal disease saving additional treatment costs, when compared with to Keep-PCV10 in Colombia, however additional criteria to decision making must be taken into account.

1. Introduction

Infections due to *Streptococcus pneumoniae* are major causes of morbidity, hospitalization, and mortality in children and adults. *S. pneumoniae* causes invasive pneumococcal disease (IPD) such as meningitis and bacteremia as well as non-invasive disease, including community-acquired pneumonia (CAP) and acute otitis media (AOM) [1,2]. O'Brien et al estimated in 2000 there were about 14.5 million cases of serious pneumococcal disease around the world with 826 thousand deaths in children less than 5 years old [3]. In Latin America and the Caribbean (LAC), during 2009 were estimated between 12,000 and 28,000 deaths due to pneumococcus, 182 thousand hospitalization and 1.4 million outpatient consults [4,5].

Colombia already evaluated the cost-effectiveness of the Pneumococcal Conjugate Vaccines (PCV) and implemented in 2011 the universal vaccination at free of charge with ten-valent PCV (PCV10) in a 2 + 1 schedule (2, 4 and 12 months) for children less than one year old, through the public health system [6]. The PCV10 implementation, the cost-effective alternative at that moment, produced a switch on the pneumococcal serotypes reported to the SIREVA II initiative after six years [7–9]. Especially a relative increase in 19A serotype had been observed, similarly to other countries those included PCV10 [10]. Compared with the initial Colombian

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cost-effectiveness analysis (CEA), new evidence had emerged about disease occurrence, vaccine effectiveness and costs of pneumococcal disease. For the Colombian Ministry of Health (MoH) is needed to evaluate the up-to-date cost-effectiveness of the available PCVs in the Colombian children population, to reconsider the initial decision about the PCV to be finance through the Expanded Program on Immunization (EPI).

In spite of the initial PCV10 inclusion in the Colombia EPI was informed and discussed with a CEA, the effectiveness of this intervention should be monitored in the population and the inclusion of other alternatives considered for the decision-makers considering the new available evidence, seeking the bigger population welfare. To update the cost-effective profile of available PCVs is useful for EPI's manager to wisely invest the scarce public resources. The objective of this analysis was to estimate the cost-effectiveness to switch the immunization to PCV13 versus to continue PCV10 vaccination in the Colombian children.

2. Methods

2.1. Model and target population

We adapted a previous built simulation model [6] for the present CEA. Due to pneumococcal disease incidence and mortality vary across ages, we implemented an age-dependent Markov model, including a cohort of children younger than one year old (870,130 children according with the *Departamento Nacional de Estadística – DANE*), followed up to the life expectancy (76 years). This population corresponds to the total target vaccination groups for PCV in Colombia in a 2 + 1 doses schedule applied at 2, 4 and 12 months of age. Five states were included: Healthy, AOM, Radiological confirmed CAP, Pneumococcal Meningitis, and death (Fig. 1). The model runs in MS Excel with annual cycles and implemented half cycle corrections. Transitions between states were based in annual probabilities. The occurrence of related pneumococcal disease was considered only during the first five years of life.

2.2. Setting and location

Colombian is a middle-income tropical country located in northwestern South America. The health system is funded entirely by public resources and delivered by both public and private providers. Immunization is delivered in Colombia through this public health system free of any charge for the target population, mainly under one-year children. Vaccines and immunization supplies are bought directly by the MoH and distributed to public and private health facilities, most of them of primary care, that deliver the immunization shots in a continuous way during all the year. The MoH defines the vaccines included in the EPI, through discussion in a National Immunization Technical Advisory Group (NITAG).

2.3. Comparators

In the present CEA three alternatives were evaluated: (1) No vaccination (leave the PCV vaccination), (2) Continue the PCV10 vaccination, and (3) Switch to PCV13 vaccination. To model the current Colombian pneumococcal related burden an additional scenario was simulated (Initial PCV10 vaccination), however it was not included in the comparison to evaluate the cost-effectiveness ratios (Fig. 1). PCV10 covers serotypes 1, 4, 5, 6B,

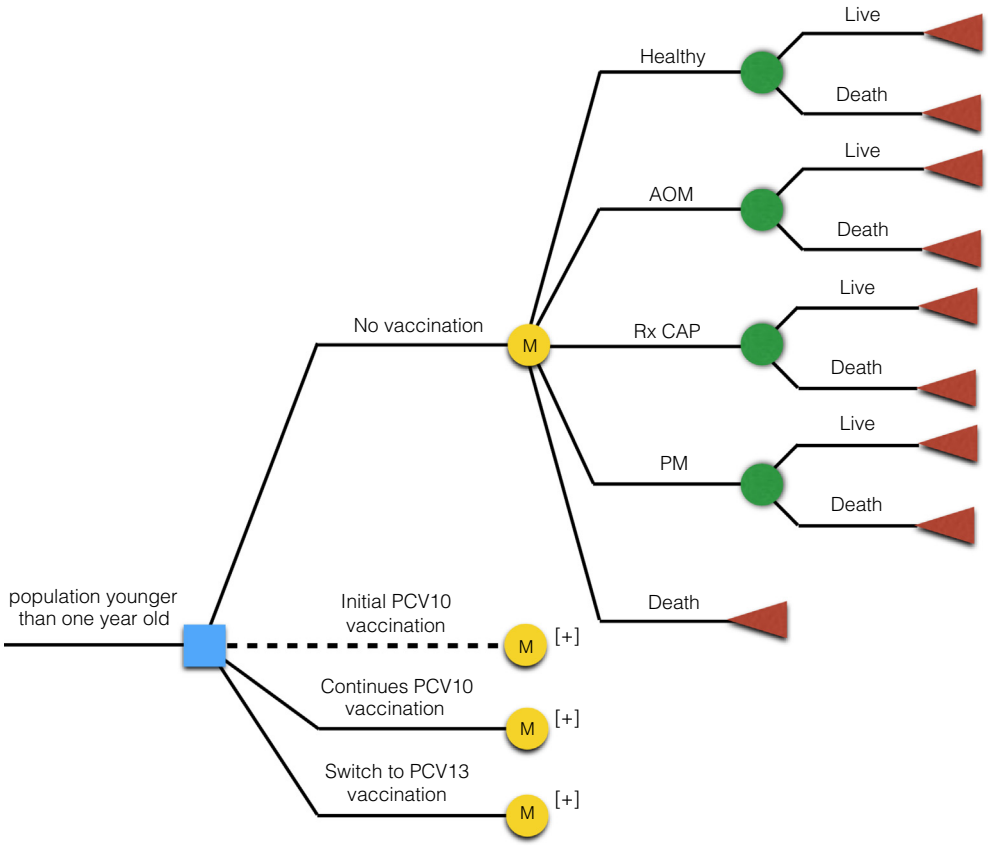


Fig. 1. Decision tree model for the PCVs costs-effectiveness analysis. Colombia, 2014. AOM: Acute Otitis Media; Rx CAP: Radiological confirmed community-acquired pneumonia; PM: Pneumococcal Meningitis. The mark [+] in the 'M' node means inclusion of the showed Markov model. Dashed line represents a base line scenario to model the impact of the considered alternatives.

7F, 9V, 14, 18C, 19F and 23F, conjugated to Non-typeable *Haemophilus influenzae* (NTHi) protein D. PCV13 covers in addition serotypes 3, 6A and 19A, and use as carrier the diphtheria-derived protein CRM(197).

2.4. Demographic and epidemiological parameters

Based on parameters included in previous model [6], a literature review was performed to identify recent publications about the demographic and epidemiological parameters to update the estimation of the pneumococcal related burden of disease in Colombian children (Table 1) [5,11–14]. We included the new serotype distribution (after the PCV10 introduction) reported by SIREVA II for invasive isolates during 2011 to 2014 period, at the Colombian National Health Institute.

Burden of pneumococcal related disease was estimated with the included parameters in each of the model arms that included immunization. The burden of disease in the vaccination arms were estimated based in the serotype coverage vaccine effectiveness. The impact of keeping PCV10 or switching to PCV13, were modeled on the initial estimation for PCV10 vaccination strategy (Table 1).

2.5. Vaccine effectiveness

The vaccine effectiveness against all-cause CAP and pneumococcal meningitis were estimated based in data reported for PCV7 [15,16] adjusted by coverage of pneumococcal serotypes. For all-cause AOM, the PCV10 effectiveness was extracted from the recent COMPAS study [17], while for the PCV13 estimation was based in the PCV7 effectiveness against AOM [16] adjusted by serotypes coverage. Effect against pneumococcal related disease was assumed constant during the first five years of life in vaccinated children. No herd effect was taken into account for any vaccine strategy.

2.6. Costs

Cost of the health states (CAP, AOM, and PM) were obtained from a Latin American's estimation, with measurements for the

Table 1
Parameters and distributions used in the model for the CEA of PCV10 and PCV13 in Colombian Children, 2014.

Parameter	Mean value	Inferior limit	Superior limit	Distribution	Reference
Evaluation year	2014				
Vaccination cohort	870,130			Fixed	*DANE*
Discount rate	3%				
Pneumococcal-related disease occurrence					
Before PCV10 introduction					
Pneumococcal meningitis probability	0.00004	0.00002	0.00006	Beta (3, 3)	[11,12]
Ambulatory all-cause Rx CAP probability	0.0036	0.0033	0.0038	Beta (4, 5, 3)	[11–13]
Inpatient all-cause Rx CAP probability	0.0063	0.0060	0.0068	Beta (2, 3)	[11–13]
All-cause AOM probability	0.3020	0.25	0.35	Beta (3, 25, 3)	[12,14]
Case Fatality ratio pneumococcal meningitis*	37%	33%	54%	Beta (0, 7, 3)	[5,12]
Case Fatality ratio all-cause pneumonia*	3%	2%	6%	Beta (1, 3)	[5,12]
After PCV10 introduction					
Pneumococcal meningitis probability	0.00001	0.00001	0.00002		Adjusted from the model
Ambulatory all-cause Rx CAP probability	0.0028	0.0023	0.0033		
Inpatient all-cause Rx CAP probability	0.0050	0.0042	0.0059		
All-cause AOM probability	0.2054	0.1661	0.2501		
Vaccine effectiveness					
PCV10 before its introduction					
All-cause AOM	16%	−1%	30%	Log-normal	[17]
All-cause Rx CAP	20%	4%	35%		[15] *adjusted by coverage in SIREVA 2007–2008*
Pneumococcal meningitis	71%	48%	82%		[16] *adjusted by coverage in SIREVA 2007–2008*
PCV10 after its introduction					
All-cause AOM	16%	−1%	30%	Log-normal	[17]
All-cause Rx CAP	8%	2%	14%		[15] *adjusted by coverage in SIREVA 2011–2014*
Pneumococcal meningitis	50%	35%	59%		[16] *adjusted by coverage in SIREVA 2011–2014*
PCV13 after PCV10 introduction					
All-cause AOM	13%	9%	19%		[16] *adjusted by coverage in SIREVA 2011–2014*
All-cause Rx CAP	17%	4%	28%		[15] *adjusted by coverage in SIREVA 2011–2014*
Pneumococcal meningitis	69%	48%	79%		[16] *adjusted by coverage in SIREVA 2011–2014*
Costs (USD)					
Care cost per case					
Inpatient CAP	$1163	$930	$1395	Beta (3, 3)	[18] *for low income countries*
Ambulatory CAP	$104	$84	$125	Beta (3, 3)	
Pneumococcal meningitis	$1421	$1137	$1705	Beta (3, 3)	
AOM	$122	$97	$146	Beta (3, 3)	
Immunization costs					
PCV-10 dose	$14.12			Fixed	MoH communication
PCV-13 dose	$15.68			Fixed	
Administration cost per dose	$1	$0.5	$2	Beta (1, 5, 3)	Assumption
Wastage rate	10%	5%	15%	Beta (3, 3)	
Doses per complete schedule	3			Fixed	
Immunization coverage	90%			Fixed	

Rx CAP: Radiological confirmed community acquired pneumonia; AOM: Acute Otitis Media.
* Keep constant after PCV-10 introduction.

Colombian children population [18]. Those costs estimations were obtained from either physicians' interviews and WHO—choosing Interventions that are Cost Effective (WHO-CHOICE) project [19]. Coverage of the vaccination was assumed in 90% for each vaccination alternatives. An administrative cost of USD $ 1 per dose, and a wastage rate of 10% were assumed. Costs per dose of PCV were reported by the Colombian MoH and correspond to prices of the Pan American Health Organization (PAHO) revolving fund. All costs were adjusted to 2014 American dollars (exchange rate of COP$ 2392.46 per USD$ 1)

2.7. Cost-effectiveness analysis

A CEA was made to calculate the Incremental Cost-Effectiveness Ratio (ICER) for each alternative y terms of costs per Year of Life Saved (YLS) including all causes of death during the time horizon of the life expectancy to evaluate the impact of competing causes of death. Pneumococcal disease and its associated costs were only considered during the first five years of life. The ICER calculation was made considering in numerator the net costs of each alternative and in denominator their incremental effectiveness (additional YLS). Costs and results were discounted to the recommended discount rate of 3%. The evaluation was carried out from the third payer perspective (Colombian Health System) and in a competitive scenario, because all the evaluated alternatives are mutually exclusive.

2.8. Sensitivity analyses

Deterministic and probabilistic sensitivity analyses (DSA and PSA) were made for epidemiological parameters, vaccines' effectiveness, and costs included in the model. All parameters were included with their probability distributions to include their uncertainty, according with the uncertainty reported in the original information source. In general, probabilities use Beta, costs use Gamma, and relative risks use log-normal distributions. For the PSA, a Monte Carlo simulation with ten thousand iterations was performed, in order to evaluate each expected value of the ICER in the distribution of costs, diseases likelihood, and effectiveness for each strategy, reporting mean and 95% confidence intervals of the results. An acceptability curve was constructed with the Expected Net Benefits and a willingness to pay (WTP) threshold equal to 1 GDP per capita (USD$ 6631) per YLS. The 95% confidence intervals (CI 95%) are reported for all estimations.

3. Results

Table 2 shows the estimations of burden of pneumococcal-related disease, including cases, deaths, discounted YLS, and net costs for each evaluated alternative in the cohort during first five years of life. Estimations of the avoided cases for each alternative are presented in Table 3. In general, switching to PCV13 would avoid additional cases of pneumococcal-related diseases, except for AOM, where keep PCV10 avoids more cases than PCV13.

Costs of treatment of pneumococcal-related disease in absence of PCV vaccination rise to USD$ 111.8 million (CI95% USD$ 98.3–125.3 million), including all-cause AOM and all-cause Rx CAP. The annual costs of PCV immunization program were estimated in USD$ 38.8 million (CI95% USD$ 37.1–40.8 million) for PCV10 and USD$ 42.9 million (CI95% USD$ 41.0–44.9) for PCV13.

3.1. Cost-effectiveness analysis

Table 4 shows health outcomes, costs, and the ICERs in a competitive setting, excluding initial PCV10 introduction. Fig. 2 shows

Table 2
Burden of pneumococcal-related disease in a Colombian children cohort until 5 years of life by vaccine alternative, 2014.

	AOM	Ambulatory Rx CAP	Inpatient Rx CAP	Pneumococcal meningitis	Deaths due to ambulatory Rx CAP	Deaths due to inpatient Rx CAP	Deaths due to pneumococcal meningitis	Deaths due to TOTAL deaths	Immunization cost	Discounted Lived Years of Life	Discounted net Costs (Immunization + care costs)
No Vaccination	719,246 (679,970–753,117)	15,210 (14,492–15,840)	26,626 (25,573–27,878)	171 (111–232)	455 (308–740)	796 (539–1288)	63 (40–92)	1314 (911–2096)	US$ 0 (US$ 0–0)	22,033,197 (22,032,920–22,033,727)	US$ 111,788,343 (US$ 98,341,713–125,300,458)
PCV10 introduction	665,955 (594,540–732,076)	12,109 (10,246–14,104)	21,781 (18,427–25,430)	61 (35–100)	372 (238–617)	651 (417–1077)	23 (13–38)	1046 (680–1719)	US$ 38,839,273 (US$ 37,113,972–40,778,044)	22,039,502 (22,035,408–22,045,532)	US$ 138,790,310 (US$ 124,194,609–153,882,673)
Keep PCV10	609,660 (492,255–724,000)	11,049 (9065–13,249)	20,441 (16,774–24,593)	45 (26–73)	339 (215–561)	611 (383–1018)	17 (9–28)	967 (617–1595)	US$ 38,839,273 (US$ 37,113,972–40,778,044)	22,041,356 (22,036,464–22,048,668)	US$ 130,708,962 (US$ 113,316,439–149,265,872)
Switch to PCV13	619,187 (549,462–686,831)	10,463 (8057–13,298)	18,820 (14,430–24,002)	35 (20–62)	312 (189–527)	563 (338–957)	13 (7–23)	888 (541–1497)	US$ 42,871,020 (US$ 41,046,954–44,881,760)	22,043,212 (22,037,108–22,052,047)	US$ 133,994,945 (US$ 119,684,712–148,832,830)

Rx CAP: Radiological confirmed community acquired pneumonia; AOM: Acute Otitis Media. Confidence interval 95% in parenthesis.

Table 3
Avoided Burden of pneumococcal-related disease for PCV10 introduction, keep PCV10 and switch to PCV13 strategies in Colombian children (less than 5 years old), 2014.

	OMA	Ambulatory Rx CAP	Inpatient Rx CAP	Pneumococcal meningitis	Deaths due to ambulatory Rx CAP	Deaths due to inpatient Rx CAP	Deaths due to pneumococcal meningitis	TOTAL deaths
PCV10 introduction (actual impact)	53,291 (21,041–85,430)	3101 (1736–4246)	4845 (2447–7146)	111 (76–132)	83 (70–123)	145 (121–212)	41 (27–54)	268 (232–377)
Keep PCV10	56,294 (8076–102,285)	1060 (855–1181)	1339 (837–1653)	16 (9–27)	33 (23–56)	40 (34–58)	6 (4–10)	79 (63–123)
Switch to PCV13*	-9527 (-57207 – 37,169)	587 (-49–1008)	1622 (591–2343)	10 (6–11)	27 (26–34)	48 (46–61)	4 (2–5)	79 (76–98)

Rx CAP: Radiological confirmed community acquired pneumonia; AOM: Acute Otitis. Mean values reported and Confidence interval 95% into parenthesis.
* Avoidable events estimated with respect to Keep PCV10.

Table 4
ICER for the modeled vaccination alternatives in Colombian children (less than 5 years old), 2014.

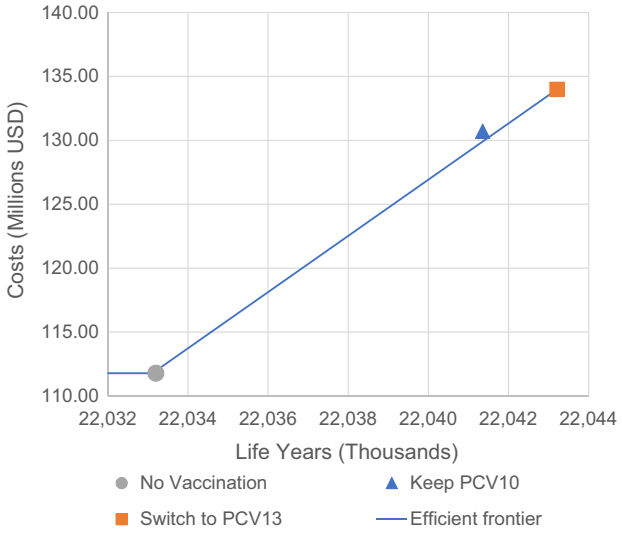
Alternative	Deaths due to pneumococcal related disease	Years of Life Lived	Total costs	Avoided deaths*	Years of Life Saved (YLS)*	Additional costs*	ICER (USD per YLS)
No Vaccination	1314 (911–2096)	22,033,197 (22,032,920–22,033,727)	USD$ 111,788,343 (USD$ 98,341,713–125,300,458)				
Keep PCV10	967 (617–1595)	22,041,356 (22,036,464–22,048,668)	USD$ 130,708,962 (USD$ 113,316,439–149,265,872)	Extended Dominated			
Switch to PCV13	888 (541–1497)	22,043,212 (22,037,108–22,052,047)	USD$ 133,994,945 (USD$ 119,684,712–148,832,830)	426 (370–599)	10,015 (4188–18,320)	USD$ 22,206,602 (USD$ 21,342,999–23,532,372)	USD$ 2217 (USD$1285–5096)

* Estimated compared to relevant alternative. ICER: Incremental cost effectiveness ratio. Confidence interval 95% in parenthesis.

the cost-effectiveness plane of the present comparisons. The more expensive alternative is Switch to PCV13, but it is the more effective alternative with 1856 (CI95% 644–3379) additional YLS with respect to Keep PCV10. It becomes the cost-effective alternative with an ICER of USD$ 2217 (CI95% USD$ 1285–5096) per additional YLS. Keep PCV10 is an extended dominated (ED) alternative. Its ICER compared with No Vaccination would be USD$ 2319 (USD$ 1604–4225) but comparing Switch to PCV13 with Keep PCV10 would estimate an ICER of US$ 1770 (US$ −128–9889). If a decision-maker were willing to pay enough for Keep PCV10 seem worthwhile then they will also be willing to pay the additional costs to move to PCV13 because the ICER is lower [20].

3.2. Sensitivity analyses

Fig. 3 shows the acceptability curve of the CEA based in the Monte Carlo simulations and the probabilistic distribution of all included parameter (according with Table 1). Above a WTP of USD$ 2000 per YLS 'switch to PCV13' alternative begin to be likely the most cost-effective alternative. To WTP values around USD$ 6000 per YLS (near to the Colombian GDP per capita), there is a 90% of likelihood of 'Switch to PCV13' to be the most cost-effective alternative.



Keep PCV10 is an extended dominated (ED) alternative in spite of been cost-effective in the comparison with no vaccination.

Fig. 2. Cost-effectiveness plane and efficient frontier CEA of Keep PCV10 vs PCV13 in Colombian children (less than 5 years old), 2014. Keep PCV10 is an extended dominated (ED) alternative in spite of been cost-effective in the comparison with no vaccination.

4. Discussion

Our results indicate that to continue PCV10 vaccination in Colombian children would had additional health outcomes to good value for money ratio, however, including recent evidence about the effectiveness of available PCVs and new pneumococcal serotypes distribution patterns, switching from PCV10 to PCV13 would be the cost-effective alternative in the Colombian setting as showed in the competitive analysis. The PCV13 inclusion would reduce more cases of Rx CAP, PM, deaths and YLLs than to keep PCV10. However, PCV10 would prevent more AOM cases then PCV13.

Currently there is no published CEA assessing the economic and epidemiological impact of switching from one PCV to another. Many LAC countries have currently introduced PCV10 and some of them have assessed its effectiveness. In most cases it has demonstrated a moderate effectiveness against Rx confirmed CAP and all cause pneumonia [21], but incremental PCV13 benefits are under discussion. The value for money of this change should be evaluate from the decision maker perspective and this research is a contribution in that sense.

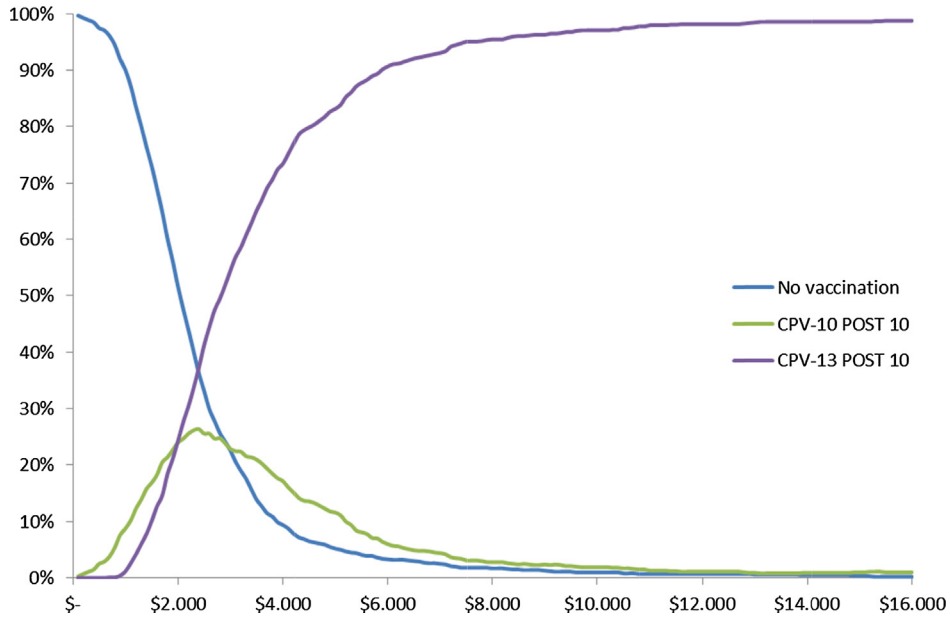


Fig. 3. Acceptability curve of the CEA of Keep PCV10 and PCV13 in Colombian children (less than 5 years old), 2014.

Our main challenge to assess the potential impact of switching between PCV vaccines is the lack of good evidence on the incremental efficacy of PCV13 to prevent invasive and non-invasive pneumococcal disease. There is no experimental field trial comparing efficacy of both vaccines head to head. The best evidence available to date is reports on effectiveness from geographies where different PCV vaccines have been implemented sequentially (PCV7, PCV10 and PCV13) [22]. This precludes us to fully guaranteed that benefits of switching from one to another would produce all the forecasted benefits. However, mechanistic evidence suggests that PCV13 may act effectively against a surge in 19A serotype. England and Wales estimated the vaccine efficacy using the 'indirect cohort' method in which non-vaccine types IPD cases are selected as controls. The PCV13 effectiveness (≥1 dose) against PCV13 serotypes (including 6C) was 69% after switching from PCV7 to PCV13 [23].

Other evidence reports no differences in effectiveness between PCV10 and PCV13 vaccines. Oliveira et al. assessed the evidence on clinical effectiveness of both vaccines in LAC countries using a systematic review [21]. They did not find any study comparing directly both vaccines and they concluded that there was no evidence of any given vaccine being superior to the other one. Furthermore, most studies did not include a control group and a large proportion of them were based on analysis of secondary data from different countries with different surveillance systems which make differences in country results barely comparable. No LAC study evaluates the impact of switching between vaccines [21].

The main reason to obtain a worst cost-effectiveness profile for PCV10 with respect to our previous analysis [6] was that the most recent and high quality available evidence about all cause OMA PCV10 effectiveness [17] is most conservative than the previous reported by Prymula [24], however it still considers effects more than only on pneumococcal included serotypes. With the new effectiveness data, the costs savings of the additional OMA cases avoided related to Non-typeable *Haemophilus influenzae* (NTHi) do not exceed the benefits of the additional pneumococcal serotypes included in PCV13, according with the parameters included in the present model.

Cost-effectiveness results can be change along the time and require continuously evaluation because variation in the model key driver inputs and new available alternatives could adjust the decision. Emergent evidence can change the initial cost-effectiveness estimation, and decision makers could adjust their decisions. Initial impact of the intervention can change the setting where the technology was modelled, as occurred in Colombia with the PCVs. These highlight the importance of use models in the economic evaluation of intervention, especially in absence of complete and perfect information.

Other studies in Colombia have reproduced PCV's CEA in a similar context, but some shortcomings in their designs can be argued. Díaz et al. [25], also showed a better PCV13 cost-effectiveness profile versus PCV10. However, they implemented a deterministic model before the initial PCV10 introduction, with the corresponding serotype distribution and with PCV10's AOM effectiveness only adjusted by pneumococcal serotype distribution and therefore less than PCV13's AOM effectiveness. In addition, that study was funded by the industry. Ordoñez et al. [26] also carried out a CEA of PCV10 versus PCV13 in Colombian children reporting that PCV13 is a cost-saving strategy compared with PCV10. That study also did not consider impact on AOM different to pneumococcal and include average attention costs attention that look pretty inflated. For example, they reported a care cost of US$ 11,595 for meningitis and US$ 1854 for pneumonia while we used more conservative estimates: US$ 1421 for meningitis, US$1163 for inpatient Rx CAP, and US$ 104 for ambulatory Rx CAP. In addition these authors underestimated AOM costs (US$ 40) [26]. All of these adjustments play against the PCV10 cost-effectiveness profile.

A central issue of discussion in the PCVs competitive analysis is the serotype replacement and cross effectiveness, especially if sequential PCV implementation is carried out. We modeled the setting of the initial PCV10 implementation and compared it with the actual serotype distribution. Colombia is one of the LAC countries within the SIREVA initiative which enables us to monitor changes in serotype distribution after vaccine introduction. Raw data comparing 2007–2009 and 2011–2014 period showed that serotypes 19A, 3 and other not PCV included have increased (4% to 13%, 3% to 8% and 12% to 30%, respectively). It was pretty similar with the figure predicted after the initial PCV10 introduction (Supplementary Table 1), except for serotype 6A, which was expected a 17% but now we have 11% and 6% for Pneumonia and meningitis, respectively (Supplementary Table 1). According with these forecasting 19A serotype is no raising more than predicted. It is as an

apparent effect over the proportion of the total serotypes but by the decrease in the other PCV10 included serotypes.

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.vaccine.2018.07.078.

The cost-effectiveness analysis is a piece of evidence to consider the value for money of a health intervention. One important reason to conduct the present analysis was to inform to Colombian national health authorities to make a decision on whether there was added value in shifting from PCV10 to PCV13. National authorities in Colombia have been compelled to analyze that issue since the surveillance system have informed on a remarkable increase on 19A and 3 serotypes after PCV10 introduction [27]. The impact of this analysis in public health in Colombia and other developing countries is to highlight the cost-effectiveness of the PCV13 in a competitive scenario against PCV10 and as long as the additional serotype coverage translate to a higher effectiveness, however programmatic adjustments of the switching should be considered in each particular setting. Other criteria, beside the CEA, should be evaluated for the decision makers to change to PCV13 or introduce it in the EPI. Although the decision making should be evidence informed, and CEA help in it, other legitimate rationalities participate in the process.

This analysis has limitations. First, as we already mentioned, we are assuming an incremental PCV13 effectiveness without head to head clinical or population analysis. In the case of similar effectiveness profile, additional cost of PCV13 with no additional health benefits will make PCV10 the best option. We rely on the usual assumptions implemented in PCVs' CEAs, however additional evidence about the real world PCVs effectiveness is needed. Second, we did not evaluate the burden of pneumococcal disease beyond the premature mortality, however is important to mention that pneumococcal related disease, different to OMA, is still responsible of many infant deaths in developing countries. Include morbidity dimension in the denominator of the ICER as avoided disability, because we consider their care cost only in the numerator, could adjust the cost-effectiveness of the interventions in favor of the one that prevent more non-lethal cases. Third, we did not include herd effect in the analysis. It goes beyond the unvaccinated children and include adult population. In this sense, our results are from a conservative scenario and if we include the herd effect the effectiveness profile will be a little better in a proportional way for all vaccination strategies. In essence, this inclusion will affect the total burden of pneumococcal disease estimate, but not the reported ICER. Fourth, we did not include sequels' attention costs, then the avoided costs due to the occurrence of less cases are underestimated. It is also proportional to each compared alternative and it would not have a significative impact in the estimated ICER between vaccines. Fifth, we did not evaluate the programmatic adjustments needed to do the effective switching to PCV13, for example the adjustment in the schedule of children with one of two doses of PCV10. It should be evaluated for the decision makers and would affect the cost-effectiveness of the program during the transition period. However, here is reported the ICER of the total adjustment of the immunization strategy. The ICER during the transition will be a value between the ICERs reported by us for switch to PCV13 and keep PCV10.

5. Conclusion

In Colombian context after the initial inclusion of PCV10 in children younger than one year of age, switch to PCV13 could show better health outcomes, but PCV10 would have lower immunization costs, and still be a cost-effective alternative compared with no vaccination. From the cost-effectiveness point of view, with these results, to switch to PCV13 would be the preferred policy in the competitive analysis. Colombian MoH must consider the Government priorities when deciding on the best option. This study is an effort to provide the best available evidence to inform a vaccine decision-making in Colombia, with result with potential impact in the health of population, especially the youngest and more vulnerable people with action that are fiscally responsible.

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Conflict of interest statement

The authors declare that they have not conflict of interest.

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