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Post-introduction economic evaluation of pneumococcal conjugate vaccination in Ecuador, Honduras, and Paraguay

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ABSTRACT

Objective. *A decision-analytic model was constructed to evaluate the economic impact of post-introduction pneumococcal conjugate vaccine (PCV) programs in Ecuador, Honduras, and Paraguay from the societal perspective.*

Methods. *Hypothetical birth cohorts were followed for a 20-year period in each country. Estimates of disease burden, vaccine effectiveness, and health care costs were derived from primary and secondary data sources. Costs were expressed in 2014 US$. Sensitivity analyses were performed to assess the impact of model input uncertainties.*

Results. *Over the 20 years of vaccine program implementation, the health care costs per case ranged from US$ 764 854 to more than US$ 1 million. Vaccination prevented more than 50% of pneumococcal cases and deaths per country. At a cost of US$ 16 per dose, the cost per disability-adjusted life year (DALY) averted for the 10-valent PCV (PCV10) and the 13-valet PCV (PCV13) ranged from US$ 796 (Honduras) to US$ 1 340 (Ecuador) and from US$ 691 (Honduras) to US$ 1 166 (Ecuador) respectively. At a reduced price (US$ 7 per dose), the cost per DALY averted ranged from US$ 327 (Honduras) to US$ 528 (Ecuador) and from US$ 281 (Honduras) to US$ 456 (Ecuador) for PCV10 and PCV13 respectively. Several model parameters influenced the results of the analysis, including vaccine price, vaccine efficacy, disease incidence, and costs.*

Conclusions. *The economic impact of post-introduction PCV needs to be assessed in a context of uncertainty regarding changing antibiotic resistance, herd and serotype replacement effects, differential vaccine prices, and government budget constraints.*

Key words *Streptococcus pneumoniae;* cost-effectiveness evaluation; disability-adjusted life years; pneumococcal vaccines, economics; Ecuador; Honduras; Paraguay.

Pneumococcus is a leading cause of death among children, accounting for 9% of deaths among children 1–59 months old in the year 2008 (1). The burden of pneumococcal disease is especially high in the Latin America and Caribbean (LAC) region, with 1 in 4 children suffering an episode of pneumonia every year (2), a significant proportion of which are caused by *Streptococcus pneumoniae*. Treatment of pneumococcal disease is challenging due to increasing antibiotic resistance (3) and a changing serotype replacement and herd immunity environment, making the use of the pneumococcal conjugate vaccine (PCV) in early childhood an important public health priority.

Three vaccines against pneumococcal disease are currently available. These include the 7-valent PCV (PCV7) Prevnar® (or "Prevenar" in some countries) (Wyeth Pharmaceuticals Inc., a subsidiary of Pfizer Inc., Pearl River, New York,

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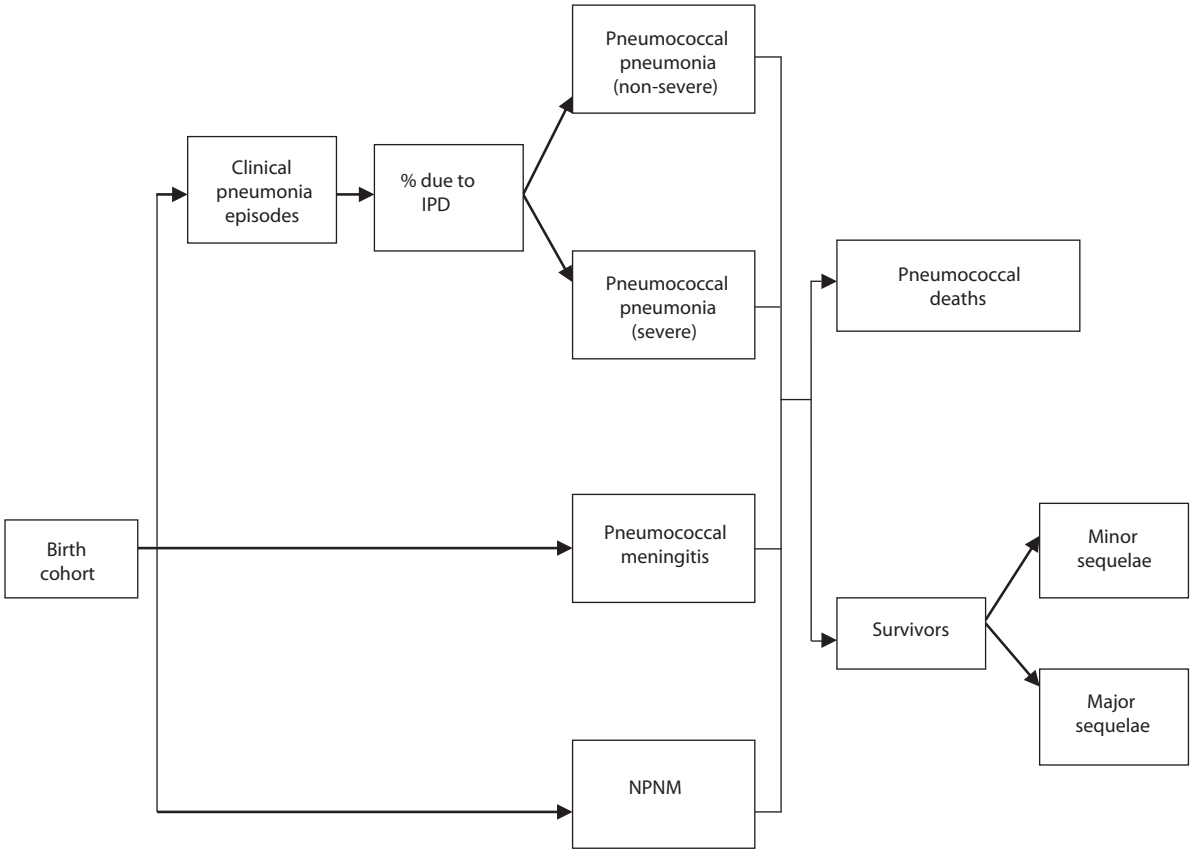
United States) introduced in the United States in 2000, with capsular polysaccharide antigens of seven serotypes. The widespread use of PCV7 caused a reduction of invasive pneumococcal disease (IPD) in vaccinated and unvaccinated groups through herd effects, but also caused an increase in IPD due to non-vaccine serotypes, resulting in serotype replacement, observed among both the vaccinated and unvaccinated (3). Since 2010, two improved pneumococcal conjugate vaccines, the 10-valent PCV (PCV10) Synflorix™ (GlaxoSmithKline Biologicals, Rixensart, Belgium) and the 13-valent PCV (PCV13) Prevnar 13® (Wyeth Pharmaceuticals Inc., a subsidiary of Pfizer Inc.) were made available globally. These vaccines vary by their serotype coverage. PCV10 contains serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F; includes three additional serotypes (1, 5, and 7F), compared to PCV7; and uses protein D from non-typeable *Haemophilus influenzae* (NTHi) as a carrier protein, which may offer additional protection against NTHi (4). PCV13 includes six additional capsular *S. pneumoniae* polysaccharide serotypes (1, 3, 5, 6A, 7F, and 19A) compared to PCV7; the six serotypes are individually conjugated to nontoxic diphtheria as a carrier protein (5). The clinical advantage of these vaccines is difficult to establish. PCV10 may provide higher protection against NTHi (4), whereas PCV13 offers a wider coverage of serotypes causing IPD (5).

This study developed a decision-analytic model to evaluate the economic impact of post-introduction pneumococcal conjugate vaccination programs (PCV10 and PCV13) in Ecuador, Honduras, and Paraguay from the societal perspective.

MATERIALS AND METHODS

A decision-analytic model (Figure 1) was constructed to assess the economic impact of two available pneumococcal conjugate vaccination programs (PCV10 and PCV13). The model integrates health burden estimates with economic burden estimates to develop country-level estimates of the incremental cost-effectiveness ratios (ICERs) of the two vaccines for Ecuador, Honduras, and Paraguay. The ICERs were estimated by calculating the net costs between two possible interventions divided by the net benefits of the interventions. The three countries were selected because of their established surveillance system of bacterial pneumonia and bacterial meningitis and their widespread PCV10 and PCV13 introduction (Paraguay introduced PCV10 in March 2012, and Ecuador and

FIGURE 1. Schematic diagram of economic model used to evaluate cost-effectiveness of the pneumococcal conjugate vaccine (PCV), post-vaccination scenario, Ecuador, Honduras, and Paraguay, 2013–2034[a–c]



[a] Compiled by the author based on the model developed for the current analysis.
[b] IPD: invasive pneumococcal disease.
[c] NPNM: non-pneumonia/non-meningitis.

Honduras introduced PCV13 in August 2010 and April 2011 respectively). In addition, these three countries comprise a significant amount of the burden of pneumococcal diseases in LAC, and have significant financial constraints. Health care authorities in each of these countries have expressed interest in reassessing the economic impact of the PCV post-introduction.

For all children born in a given birth cohort (births between January and December), the model projected the number of person-years lived between 1 and 59 months of age. Person-years were calculated based on estimates of the number of births and the rates of neonatal (< 1 m), infant (< 12 m), and under-5 mortality. Person-years were then multiplied by the incidence of disease per 100 000 per year (in children aged 1–59 months) to estimate the total number of cases expected to occur before all children in the cohort reached 5 years of age. Case fatality ratios (CFRs) were applied to the total number of cases to estimate under-5 deaths due to the disease. A proportion of the survivors were assumed to develop lifelong disability or sequelae.

A comprehensive literature review of epidemiological studies on pneumococcal disease and related syndromes (pneumonia, meningitis, bacteremia, and acute otitis media) occurring after introduction of the vaccine was conducted. Epidemiological data were summarized using medians, interquartile range, and minimum and maximum values to indicate the range of data. Different age categories was developed and serotype coverage for the various pneumococcal conjugate vaccines were calculated. Model inputs are described in detail in Annex 1.

There were no published randomized controlled trial data on vaccine efficacy for PCV10 and PCV13 at the time the analysis was conducted. The efficacy estimates for PCV10 and PCV13 were therefore based on PCV7 efficacy studies (6, 7), using a linear adjustment for serotype coverage in Honduras, Ecuador, and Paraguay.

The model assumed that coverage rates for one, two, and three doses of PCV10 and PCV13 were the same as for one, two, and three doses of diphtheria-tetanus-pertussis vaccine (DTP). As the model included 20 birth cohorts, coverage estimations were needed for the entire 20-year period of model projections.

For all three countries studied, Demographic and Health Surveys (DHS) data (8) were used to estimate the number of outpatient visits and inpatient admissions and the distribution of visits and inpatient admissions by type of provider. The DHS data are from nationally representative household surveys that determine the percentage of cases presenting at health care providers due to various illnesses, including acute respiratory infections (ARIs). All counts for the various providers are then summed and aggregated by eight standard health settings: 1) private: non medical; 2) private: drugstore; 3) private: clinic; 4) private: hospital; 5) government: clinic; 6) government: primary hospital; 7) government: secondary hospital; and 8) government: tertiary hospital. Based on consensus among local health providers, it was assumed that 5% of hospital counts and 5% of counts for provincial/tertiary hospitals were in tertiary-level hospitals. To augment information on treatment in the existing literature, several local health providers were contacted and asked to respond to various surveys. The surveys contained specific questions about the diagnosis and treatment of pneumococcal pneumonia, pneumococcal meningitis, and non-pneumonia/non-meningitis (NPNM). Local health care providers interviewed were pediatricians, infectologists, intensivists, and primary care physicians working in the public sector. Physicians working in the private and social security sectors were also interviewed. A total of 18 physicians in Quito and Guayaquil (Ecuador) responded to the surveys, 21 in Tegucigalpa and Comayagüela (Honduras), and 12 in Asunción (Paraguay).

As costs generally increase with increasing levels of care, the per diem cost of a hospital bed-day and outpatient visit were divided into three levels of care (primary, secondary, and tertiary). The per diem and per visit costs for Ecuador, Honduras, and Paraguay were estimated based on data from the World Health Organization (WHO) CHOICE (CHOosing Interventions that are Cost-Effective) project (9). Total cost per hospitalization was calculated by multiplying the per diem cost by the estimated length of stay reported in the physician interviews. The WHO-CHOICE model was developed using "international dollars"[2] for the year 2000, so the local cost estimates from the three countries were inflated to international dollars for the year 2014 using the consumer price index (CPI) (10).

The base-case analysis was performed from a societal perspective in which all costs borne by health care providers (e.g., hospitalization, ambulatory visits, medications, laboratory tests, surgical interventions, and other procedures) and households (e.g., family out-of-pocket costs and family productivity losses) are included. No economic costs for cases resulting in death, those not seeking formal medical attention, or those requiring extended lengths of stay due to complications or sequelae were included because they were not available. Costs of adverse events associated with vaccination were also excluded because vaccine trial data suggest the safety of the vaccine is equivalent to that of a placebo.

The main outcome measures included the health care costs of pneumococcal disease for 20 birth cohorts, the disease burden and health care system costs averted by vaccination, and the ICER (the cost of the PCV in US$ divided by disability-adjusted life years (DALYs) averted and US$ per life saved or death averted). A DALY is a common measure of illness that captures years of life lost due to premature mortality (YLL) and years lived with disability (YLD). It is also used as a measure of effectiveness in cost-effectiveness analyses. All future costs and DALY estimates were discounted at a rate of 3%, as recommended by WHO (11) and the Global Burden of Disease (GBD) study (12).

Sensitivity analyses were performed by calculating key outcomes (economic burden and cost-effectiveness) for different scenarios likely to influence the cost-effectiveness of vaccination. These scenarios included high- and low-end estimates of the following parameters: vaccine efficacy, disease incidence, CFRs, discount rates, and vaccine price. The discount rates and vaccine prices were also varied (ranging between 0% and 10%).

RESULTS

Based on the model assumptions, before introduction, there would be an

[2] An international dollar has the same purchasing power as one US dollar in the United States.

estimated 863 177 pneumococcal cases, 22 064 associated deaths, and more than 771 000 DALYs for 20 years of birth cohorts (2013–2034), and an estimated 49 929 pneumococcal disease cases and 1 405 deaths during a typical year (Table 1). The majority of pneumococcal cases (93%) are due to severe pneumococcal pneumonia. Across all three countries, more deaths would be related to pneumococcal meningitis than to pneumococcal pneumonia. The latter finding supports the findings of previous studies that show pneumococcal meningitis as the leading cause of pneumococcal deaths (13). In terms of DALYs, lower rates were observed in Paraguay than in Honduras or Ecuador due to Paraguay's lower mortality rate. In addition, YLD contributed very little to the DALY estimate. The DALY estimate was primarily based on YLL as the majority of cases were due to premature mortality.

TABLE 1. Estimated health burden of pneumococcal disease with and without vaccination, Ecuador, Honduras, and Paraguay, 2013–2034[a]

Estimated health burden	Total for the study period (20 birth cohorts)			During a typical year		
	Ecuador	Honduras	Paraguay	Ecuador	Honduras	Paraguay
Without vaccination (current practice)						
Cases	373 108	286 516	203 553	21 606	16 598	11 725
Deaths	7 895	10 130	4 039	513	641	251
DALYs[b] (in 000s)	279	351	141	–[c]	–	–
With vaccination						
Cases	163 632	122 587	100 591	9 529	7 124	5 896
Deaths	3 468	4 337	2 003	226	275	126
DALYs[b] (in 000s)	123	150	70	–	–	–
Benefits of vaccination (averted events)[d]						
Cases	209 477	163 929	102 961	12 077	9 474	5 830
Deaths	4 426	5 793	2 037	287	366	125
DALYs[b] (in 000s)	156	201	71	–	–	–

[a] Compiled by the author based on the study results.
[b] Disability-adjusted life years (undiscounted).
[c] Not applicable.
[d] Based on assumptions about vaccine effectiveness (efficacy and coverage).

TABLE 2. Estimated health service cost of pneumococcal disease for 1) a 20-year period (20 birth cohorts) and 2) a typical year (per 100 000), Ecuador, Honduras, and Paraguay, 2013–2034[a]

Estimated health service cost (borne by health services)	Ecuador	Honduras	Paraguay
		(in 2014 US$)	
Per vaccine for the total study period (20 birth cohorts)	13.21	14.95	18.19
Per vaccine during a typical year (per 100 000)	0.76	0.87	1.05

[a] Compiled by the author based on the study results.

TABLE 3. Estimated incremental cost-effectiveness ratio (ICER) for two types of pneumococcal conjugate vaccines (PCV10 and PCV13) from the societal perspective, by cost per dose, Ecuador, Honduras, and Paraguay, 2013–2034[a]

Type of PCV	ICER (in 2014 US$ per DALY[b] averted, discounted)		
	Ecuador	Honduras	Paraguay
PCV10[c]			
At $32 per dose	2 716	1 588	2 416
At $16 per dose	1 340	796	1 226
At $7 per dose	528	327	446
PCV13[d]			
At $32 per dose	4 289	3 067	3 525
At $16 per dose	1 166	691	1 026
At $7 per dose	456	281	343

[a] Compiled by the author based on the study results.
[b] Disability-adjusted life year.
[c] 10-valent.
[d] 13-valent.

Table 2 shows the estimated health service cost of pneumococcal disease for a 20-year period and a typical year in Ecuador, Honduras, and Paraguay. The health service costs of pneumococcal disease during a typical year ranged from US$ 764 854 (US$ 0.76 per 100 000) to US$ 1 047 628 (US$ 1.05 per 100 000), with higher costs in Paraguay. Over the 20 years of vaccine program implementation, the health care costs of pneumococcal disease borne by society ranged from US$ 13 208 283 (US$ 13.21 per 100 000) to US$ 18 187 067 (US$ 18.19 per 100 000). In all countries, most of the cost resulted from hospitalization. The costs of medications and diagnostics for pneumococcal meningitis were generally higher than those for pneumococcal pneumonia.

Under the base-case scenario, over the 20 birth cohorts, vaccination reduced pneumococcal cases and associated deaths by 56% in Ecuador, 57% in Honduras, and 50% in Paraguay (Table 1). These benefits were greatest in Ecuador because of the higher disease burden in this country. In addition, over the 20 birth cohorts, vaccination prevented 70 927 DALYs in Paraguay, 156 385 in Ecuador, and 200 829 in Honduras (all undiscounted). More DALYs were averted in Honduras than in Ecuador or Paraguay due to Honduras' higher mortality. Over the 20 years of vaccine program implementation, PCV resulted in treatment cost savings of US$ 8.6 million, US$ 7.4 million, and US$ 9.2 million in Honduras, Ecuador, and Paraguay respectively (not shown).

Table 3 shows the results of the cost-effectiveness analyses from the societal perspective. For PCV10, at the higher cost of US$ 32 per dose, the ICER (discounted) ranged from US$ 1 588 per DALY in Honduras to US$ 2 716 per DALY in Ecuador. At a reduced cost of US$ 16 per dose, the ICER (discounted) ranged from US$ 796 per DALY in Honduras to US$ 1 340 per DALY in Ecuador. The PCV10 produced a cost-effectiveness (discounted) ranging from US$ 327 per DALY in Honduras to US$ 528 per DALY in Ecuador when the price of the vaccine was reduced to US$ 7 per dose.

For PCV13, at a cost of US$ 32 per dose, the cost per DALY averted compared to no vaccine ranged from US$ 3 067 (Honduras) to US$ 4 289 (Ecuador). At a reduced cost of US$ 16 per dose and

US$ 7 per dose, the cost per DALY was reduced even further, from US$ 691 (Honduras) to US$ 1 166 (Ecuador) and from US$ 281 (Honduras) to US$ 456 (Ecuador) respectively.

For all three countries, the uncertain parameters that were most likely to influence the ICER of the PCV were the incidence of pneumococcal disease, CFRs, vaccine efficacy rates, discount rates, and price of the vaccine. In countries with higher levels of mortality, the CFRs and vaccine effectiveness against mortality contributed more to overall uncertainty.

DISCUSSION

Findings of the evaluation indicated that pneumococcal disease is an important cause of pneumonia, meningitis, and NPNM in Ecuador, Honduras, and Paraguay. The pattern of disease burden differed by country. As expected, the greatest disease burden (in terms of DALY loss) was in Honduras. In contrast, the greatest economic burden was in Paraguay, due to higher health service costs. Variability in health service costs was due to differences in treatment patterns (medications, diagnostics, and relative importance of hospital and ambulatory treatment) and unit costs. Across countries, more deaths were related to pneumococcal meningitis than to pneumococcal pneumonia.

Findings from this study demonstrate that years after PCV was introduced in Ecuador, Honduras, and Paraguay, routine infant immunization with PCV10 and PCV13 still makes sense in lower-middle-income countries like Ecuador, Honduras, and Paraguay, where the population-wide incidence of pneumococcal disease is high. Childhood PCV met acceptable standards of economic efficiency in all three countries. It is unclear from the findings of the analysis which of the two PCVs to choose, as no direct comparison of all potential PCV candidates was made. While the rate of health care utilization was assumed to be the same in all three countries, the health service costs were higher in Paraguay. Similarly, the incidence rate of pneumococcal disease was high enough in Honduras to maintain a more acceptable ICER than in Paraguay.

From the societal perspective, universal vaccination with PCV has the potential to confer benefits at a cost across all three countries. Health interventions that result in negative net costs are stronger investments because they result in improved health and cost-savings. In practice, few interventions (not even highly effective interventions, such as WHO's Expanded Programme on Immunization (EPI)) meet this standard of cost-savings (11). Based on the results presented here, vaccination for pneumococcal disease is cost-effective, depending on the price of the vaccine.

The interpretation of whether an intervention is cost-effective depends on the standard to which it is compared, or the "cutoff" figure for the value of a DALY or a life year. The standard should reflect how much a decision-maker is willing to invest to gain one DALY (or prevent one death). If the cost per DALY or life year is greater than this, one can say that it is too high, and that PCV is not "worth the cost." If it is less, one might conclude that PCV is a relatively efficient way to produce extra DALYs or life years.

The WHO World Health Report for 2002 suggests that "very cost-effective interventions" are those that "avert each additional DALY at a cost less than the gross national income (GNI) per capita" (13). In addition, interventions with an ICER (US$ per DALY) between one and three times per capita GDP can be considered "cost-effective" (13). With a per capita GNI of US$ 2 840, US$ 1 200, and US$ 1 400, at a vaccine price of US$ 26.35 per dose, universal PCV would be considered very cost-effective in Ecuador and Honduras, and cost-effective in Paraguay, at a cost of US$ 2 640, US$ 1 560, and US$ 2 370 per DALY averted respectively. At a reduced price of US$ 7 and US$ 13 per dose, vaccination would have an even more favorable cost-effectiveness ratio for the three countries analyzed. These findings are consistent with earlier studies that support the use of PCV10 and PCV13 versus PCV7.

Caution should be used when comparing these findings to earlier ones, as vaccination should be compared to country-specific evaluations of the cost-effectiveness of alternative health investments being considered in that country, and within the context of uncertainties regarding vaccine effectiveness, disease burden variations, and price differences. In addition, earlier evaluations did not consider the impact of the vaccine post-introduction.

Study limitations

This post-introduction evaluation faced various challenges, including the lack of pre-vaccine baseline data in all three countries studied. In addition, there were other (non-vaccine) factors affecting disease burden, making it more difficult to evaluate post–vaccine introduction benefits. Conducting these types of studies can also be very resource-intensive and/or technically challenging to implement.

In the current model, the author conservatively assumed that incidence remains constant over time with each successive birth cohort. This is in line with the conclusions of the GBD 2010 study of the Institute for Health Metrics and Evaluation (IHME) and other academic partners (14), which suggest that data on indirect protection are too geographically limited to fully estimate these effects. There is also evidence from at least one published study of settings of indigenous communities with high background rates of pneumonia that the circulating serotypes prevented by the vaccine may be replaced over time by other serotypes, causing IPD and thus negating some of the benefits of the vaccine. The likely extent of this problem in countries with new vaccine introduction is difficult to predict, and there is a general lack of data to parameterize such effects.

The evaluation presented here is conservative in a number of areas. First, the model makes relatively simple assumptions about the projected impact of the vaccine. This is likely to be an over-simplistic method for two reasons. There is evidence that the vaccine reduces the carriage of the organism in the nose and throat of vaccinated children. This reduces the probability that unvaccinated children will come into contact with the organism during their daily contacts. As more children are vaccinated, the incidence of carriage, and therefore pneumococcal disease, is expected to decline with each successive birth cohort. Second, the focus of the evaluation is on three syndromes for which the efficacy of a PCV has been established (pneumococcal meningitis, pneumococcal pneumonia, and NPNM). It is likely that the vaccine would also have an impact on other pneumococcal diseases, such as otitis media, but due to a lack of reliable data, the potential benefits for reducing the incidence of those diseases were not considered in this evaluation. Third, pneumococcal disease in high-risk children (immunocompromised or asplenic) was not considered in the evaluation despite

the higher costs that this subgroup may incur to the health care systems of these countries. This is mainly due to lack of reliable data on the efficacy against pneumococcal disease in high-risk groups for the population studied. Fourth, loss in quality of life resulting from disease morbidity was ignored because of the many conceptual and methodological problems with the use of child utilities.[3] By omitting this measure of effectiveness, the disease burden and the potential benefits of vaccination may have been underestimated. Fifth, the analysis considered the direct effects of vaccination without considering the indirect protective effect on persons never vaccinated. By analogy to other vaccine-preventable infectious diseases, the herd immunity effect could be large and could offset inefficiencies in delivery of full course, on-time vaccination to all children. Using "pre-vaccination" as the comparator in the analysis was a study limitation. However, the differences in the cost-effectiveness ratios were influenced mostly by the health service costs and disease incidence.

Study strengths

Despite the various limitations of this study, a few study strengths should be acknowledged. The current study makes use of country-specific costs of treating pneumococcal disease, making the results of the study more representative of each of the studied countries. Few studies have explored the economic impact of post–PCV introduction and, to the best of the author's knowledge, there have been no previous economic evaluations done post-introduction in countries in the LAC region. The evaluation reported here improves the understanding of the economic impact of PCV, post-introduction, in this setting. It also provides valuable insight to vaccine policy advisory bodies and country-level policymakers in Ecuador, Honduras, and Paraguay by giving them relevant data on vaccine performance. In this way, it not only promotes sustained use of PCV10 and PCV13 but also promotes optimal use of the vaccine in these settings. For countries that have introduced the vaccine, a post-introduction evaluation like this helps to promote sustained use of PCV by providing funding partners with relevant data on vaccine performance.

While simplistic, the model provides a middle ground between two conflicting and uncertain forces (the positive indirect influence of herd immunity, and the negative indirect influence of serotype replacement). Future models should include the option to explore these effects in a more sophisticated way, but until more is known about both effects, the model will continue to use relatively simple, transparent, and conservative assumptions about the possible vaccine impact. Finally, a more thorough investigation of uncertainty should be made in future analyses of the effects of herd immunity and serotype replacement, as there is a lack of understanding about how to model these indirect effects and predict the population impact of PCVs in a reliable way.

Conclusions

This report provides evidence of the benefits of the PCV10 and PCV13 in the form of cost-effectiveness, with additional clinical benefits being produced at additional cost to the health service. The most common benefit of vaccination shown here is that it prevents disease, and in this way preserves good health. Findings underscore the importance of vaccination as a cost-effective intervention for preventing pneumococcal disease. PCV introduction decisions should be reassessed, given the evolving antibiotic resistance environment, herd and serotype replacement effects, differential vaccine prices, and government budget constraints.

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Conflicts of interest. None.

Disclaimer. The sponsors had no role in data collection, analysis, or interpretation of the data, and any views and opinions are solely those of the author. The author holds sole responsibility for the views expressed in the manuscript, which may not necessarily reflect the opinion or policy of the RPSP/PAJPH or the Pan American Health Organization.

[3] Numeric values representing the strength of individual preference for a health-related outcome.

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ANNEX 1. Overview of epidemiological inputs for economic model used to estimate the cost-effectiveness of pneumococcal conjugate vaccines (PCV10 and PCV13), Ecuador, Honduras, and Paraguay, 2013–2034

Study population

For each country, the model evaluates multiple future cohorts (20 in total from 2013–2034), and the number of live births per year expands from 1 993 to 2 048 to represent events in the future years associated with each birth cohort. The author assumed the following age distribution for all invasive pneumococcal syndromes: 2% for children < 3 months, 7% for children 3–5 months, 11% for children 6–8 months, 13% for children 9–11 months, 22% for children 12–23 months, 22% for children 24–35 months, 11% for children 36–47 months, and 11% for children 48–59 months.

Live births per year

Estimates of yearly numbers of births are required five years prior to the year of introduction, and up until 20 years after the year of vaccine introduction. Information is required on children born five years prior to the year of vaccine introduction because annual cases and deaths will include children aged 1–4 years in the first year of introduction. The model uses this trend to generate annual estimates.

Proportion of births in urban areas

The percentage of population living in urban areas per year is calculated by converting five-year trends (2000–2050) into yearly estimates using a linear trend between the midpoints of each five-year period. Because these rates are based on all ages, an adjustment for age is made to better reflect the percentage of births born to women living in urban areas (A1).

Infant mortality per 1 000 live births

The infant mortality rate is the proportion of live births during a specific year that die before the age of 12 months, calculated by converting five-year trends (2000–2050) into yearly estimates using a linear trend between the midpoint of each five-year period. This is used to estimate the number of person-years at risk of infection between 1 and 59 months of age.

Under-five mortality per 1 000 live births

The under-5 mortality rate (U5MR) is the proportion of live births during a specific year that die before the age of 5 years, calculated by converting five-year trends (2000–2050) into yearly estimates using a linear trend between the midpoint of each five-year period. This is used to estimate person-years at risk of infection between 1 and 5 years of age.

Life expectancy at birth

Life expectancy in years at birth is calculated by converting five-year trends (2000–2050) into yearly estimates using a linear trend between the midpoints of each five-year period. These estimates are used to calculate the number of healthy life years gained by vaccination, and are included in calculations of disability-adjusted life years (DALYs).

Burden of pneumococcal disease

Estimates of disease burden are from the Global Burden of Disease (GBD) study (A2). For pneumonia, the pneumococcal disease burden was estimated as an etiologic fraction of the all-cause pneumonia burden. For meningitis or serious invasive pneumococcal disease (IPD), incidence rates and case-fatality ratios (CFRs) were estimated directly. The estimates of cases and deaths represented in this study are assumed to be an underestimate of the true burden of pneumococcal disease in

the countries studied. Uncertainty ranges were provided to account for the paucity of data on high-quality meningitis, non-pneumonia/non-meningitis (NPNM), and pneumonia. No adjustment was made to include cases that occur in the private sector.

Because the data from the Global Burden of Disease (GBD) study (A2) are estimated for the year 2000, the default data were adjusted to better reflect the burden of disease in the years 2010, 2011, and 2012. The author assumed the same incidence rate of disease for years 2010, 2011, and 2012, but CFRs were adjusted to the year 2012 using the United Nations Population Division U5MR estimates (A1), and assuming the percentage of U5MR due to IPD remains the same over time (i.e., the CFRs remain the same over time). In the current model, the author conservatively assumed incidence remains constant over time with each successive birth cohort. This is in line with the conclusions of the GBD study that suggest that data on indirect protection are too geographically limited to fully estimate these effects.

DALYs. The disease burden is also estimated in terms of DALYs (A1). Total DALYs are constructed as the sum of years of life lived with disability (YLD) and years of life lost due to premature mortality (YLL) (age at death subtracted from average life expectancy). This makes the DALY a more comparable measure because it takes account of morbidity and mortality. The DALY loss from mortality (YLL) was calculated based on the average country-specific life expectancy at birth (A1). For the calculation of YLD, only morbidity from disease severe enough to require medical care was considered. YLD was calculated using default disability weights from the GBD study (A2) and WHO's guidelines for cost-effectiveness studies (A3).

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Evaluación económica tras la introducción de la vacunación antineumocócica conjugada en Ecuador, Honduras y Paraguay

RESUMEN

Objetivo. Se construyó un modelo analítico de decisiones para evaluar la repercusión económica posterior a la introducción de los programas de vacunación antineumocócica conjugada (VNC) en Ecuador, Honduras y Paraguay desde la perspectiva de la sociedad.

Métodos. Se hizo un seguimiento de cohortes de nacimiento hipotéticas durante un período de 20 años en cada país. A partir de fuentes de datos primarias y secundarias, se derivaron los cálculos de la carga de morbilidad, la eficacia de la vacuna y los costos sanitarios. Los costos se expresaron en US$ de 2014. Se realizaron análisis de sensibilidad para evaluar la repercusión de las incertidumbres de insumo del modelo.

Resultados. Durante los 20 años de puesta en práctica de los programas de vacunación, los costos sanitarios por caso variaron desde US$ 764 854 a más de US$ 1 millón. La vacunación previno más de 50% de los casos y muertes por neumococo en cada país. A un costo de US$ 16 por dosis, el costo por año de vida ajustado en función de la discapacidad (AVAD) evitado por la VNC 10-valente (VNC10) y la VNC 13-valente (VNC13) varió desde US$ 796 (Honduras) a US$ 1 340 (Ecuador) y de US$ 691 (Honduras) a US$ 1 166 (Ecuador), respectivamente. A un precio reducido (US$ 7 por dosis), el costo por AVAD evitado varió desde US$ 327 (Honduras) a US$ 528 (Ecuador) y deUS$ 281 (Honduras) a US$ 456 (Ecuador), para la VNC10 y la VNC13 respectivamente. Diversos parámetros del modelo influyeron en los resultados del análisis, incluidos el precio de la vacuna, la eficacia de la vacuna, la incidencia de la enfermedad y los costos.

Conclusiones. Las repercusiones económicas tras la introducción de la VNC deben evaluarse en un contexto de incertidumbre con respecto a los cambios en cuanto a la resistencia a los antibióticos, los efectos de la inmunidad de grupo y la sustitución de serotipos, los diferentes precios de las vacunas, y las limitaciones presupuestarias de los gobiernos.

Palabras clave *Streptococcus pneumoniae;* evaluación de costo-efectividad; años de vida perdidos por incapacidad; vacunas pneumocócicas, economía; Ecuador; Honduras; Paraguay.