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Cost-effectiveness analysis of 10- and 13-valent pneumococcal conjugate vaccines in Peru

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ABSTRACT

Objective: To evaluate the cost-effectiveness of introducing the 10-valent pneumococcal conjugate vaccine (PCV10) versus the 13-valent PCV (PCV13) to the National Immunization Schedule in Peru for prevention of pneumococcal disease (PD) in children <5 years of age.
Methods: The integrated TRIVAC vaccine cost-effectiveness model from the Pan American Health Organization's ProVac Initiative (version 2.0) was applied from the perspective of the Government of Peru. Twenty successive cohorts of children from birth to 5 years were evaluated. Clinical outcomes were pneumococcal pneumonia (PP), pneumococcal meningitis (PM), pneumococcal sepsis (PS) and acute otitis media from any causes (AOM). Measures included prevention of cases, neurological sequelae (NS), auditory sequelae (AS), deaths and disability adjusted life years (DALYs). A sensitivity analyses was also performed.
Findings: For the 20 cohorts, net costs with PCV10 and PCV13 were US$ 363.26 million and US$ 408.26 million, respectively. PCV10 prevented 570,273 AOM; 79,937 PP; 2217 PM; 3049 PS; 282 NS; 173 AS; and 7512 deaths. PCV13 prevented 419,815 AOM; 112,331 PN; 3116 PM; 4285 PS; 404 NS; 248 AS; and 10,386 deaths. Avoided DALYs were 226,370 with PCV10 and 313,119 with PCV13. Saved treatment costs were US$ 37.39 million with PCV10 and US$ 47.22 million with PCV13. Costs per DALY averted were US$ 1605 for PCV10, and US$ 1304 for PCV13. Sensitivity analyses showed similar results. PCV13 has an extended dominance over PCV10.
Conclusion: Both pneumococcal vaccines are cost effective in the Peruvian context. Although the net cost of vaccination with PCV10 is lower, PCV13 prevented more deaths, pneumococcal complications and sequelae. Costs per each prevented DALY were lower with PCV13. Thus, PCV13 would be the preferred policy; PCV10 would also be reasonable (and cost-saving relative to the status quo) if for some reason 13-valent were not feasible.

1. Introduction

Streptococcus pneumoniae (SP) is an important cause of pneumonia, meningitis and other invasive pneumococcal diseases (IPD) in children <5 years of age, especially in developing countries [1–3]. Each year, IPD is the cause of over half a million deaths in children <5 years worldwide [4], with more than 10,000 of those deaths in Latin America and the Caribbean (LAC) [5]. It is estimated to be the most common cause of vaccine-preventable deaths in children <5 years in the region of the Americas [5] and IPD treatment is responsible for a significant economic burden [6].

Although there are more than 90 serotypes of SP [7], not all cause disease. The new pneumococcal conjugate vaccines (PCV) protect against the serotypes most commonly associated with invasive disease [4,8]. In Peru, the 7-valent PCV (PCV7) was added to the

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National Immunization Schedule in 2009 by the *National Immunization Program of the Ministry of Health (MINSA)* [9]. PCV7 had been proven effective in preventing IPD [8] and providing modest protection against all-cause acute otitis media (AOM) [10].

In 2011, however, PCV7 was withdrawn from the global market and replaced by higher valence vaccines: the 10-valent (PCV10) (Synflorix®, GlaxoSmithKline) and the 13-valent (PCV13) (Prevenar 13®, Wyeth/Pfizer). PCV10 added three additional serotypes—1, 5 and 7F—plus a Non-Typeable *Haemophilus influenzae* (NTHi) protein carrier that could protect against AOM [11]. PCV13 covers an additional three—3, 6A and 19A (i.e., six more than PCV7) [12]. Evidence shows that their safety and immunogenicity profiles of these higher valences vaccines are similar to that of PCV7 and they do not interference with other vaccines in young children [11,12]. Since these two higher valence vaccines differ in serotypes covered, NTHi protein carrier, and unit price per dose, their impact as a public health intervention could differ. Economic evaluations (EE) should play an important role in decision-making regarding their adoption [13].

In this context, the *National Institute of Health* of Peru (Instituto Nacional de Salud, INS), the MINSA scientific research branch that provides evidence for public health decision-making, with support from the ProVac Initiative of the Pan American Health Organization (Washington, DC, USA; PAHO) [14,15], carried out this EE. The study objective was to evaluate the cost-effectiveness of introducing the PCV10 versus the PCV13 to the National Immunization Schedule for prevention of IPD in children <5 years of age in Peru.

2. Methods

2.1. General modeling approach and comparators

This study employed the TRIVAC cost-effectiveness model, developed by the London School of Hygiene and Tropical Medicine in collaboration with the PAHO ProVac Initiative [14,15]. The pneumococcal component of TRIVAC (version 2.0) [16] was adapted for Peru to conduct the cost-effectiveness analysis (CEA) from the perspective of the Government of Peru, including direct costs borne by its public health system—MINSA and the *EsSalud* Social Security System [17].

Since PCV7 had been withdrawn from the market, PCV10 and PCV13 were compared to having no PCV vaccination program. The incremental cost-effectiveness of the less costly vaccine was compared to that of the more costly to estimate whether the additional benefits would be worth the additional cost.

The TRIVAC model was populated with data on demographics, disease burden, local vaccine serotype distribution, vaccine efficacy, health services utilization, health service costs and vaccination program costs.

It followed 20 stacked cohorts of children from birth to death. IPD cases and deaths were only considered for the first 5 years of life, but permanent meningitis sequelae, life-years gained (LYG) and Disability Adjusted Life-Years (DALY) were calculated over the life-time of each birth cohort. The model estimated the number of cases, deaths and sequelae due to *S. pneumonia*, as well as associated costs in scenarios with and without vaccination. These outputs were then used to calculate health impact (e.g., DALYs averted), economic impact (e.g., net costs, incremental program costs and treatment costs averted), cost-effectiveness (e.g., cost-per-death averted) and cost-utility (e.g., cost-per-DALY averted). The results from each cohort were combined and used to report both the cumulative and annual health benefits and costs associated with each scenario [16].

DALYs were estimated using the disability weights defined for each disease syndrome by the World Health Organization (WHO) [18] and the life-expectancy-at-birth estimated for each cohort by the *National Institute of Statistics and Informatics* of Peru (INEI), using validated international methods [19]. A 3% discount rate for both costs and benefits was used and did not include age weighting (preference for life-years gained during productive years of life) [20,21]. A Gross Domestic Product Per Capita (GDP-PC) for the year 2011 of US$ 6009 (1 US$ = 2.80 PEN [Peruvian Nuevos Soles]) was used as the cost-effectiveness threshold.

The model calculated the number of cases of all-cause AOM, pneumococcal pneumonia, pneumococcal meningitis and pneumococcal sepsis by multiplying the incidence rate by the estimated life-years at risk between birth and 5 years of age. Life-years at risk were calculated for each birth cohort using projections for the number of births and the infant and child mortality rate. Fig. 1 shows the general model structure. In the scenario with vaccination, the total number of averted cases was estimated by multiplying the number of cases in each age group (<3 months, 3–5 months, 6–8 months, 9–11 months, 12–23 months, 24–35 months, 36–47 months, 48–59 months) by the dose- and age-specific program coverage (using DTP1/2/3 timing of vaccination as a proxy), the dose-specific vaccine efficacy and the vaccine-type coverage. Other factors were varied in "what-if" scenario analysis (e.g., waning protection, herd effects <5 years, serotype replacement, low efficacy, low program coverage). Deaths were estimated by applying the reported case-fatality ratio (CFR) to estimates of the number of cases post-vaccination. Pneumococcal meningitis sequelae were obtained by multiplying meningitis survivors (total estimated cases minus deaths) by the estimated proportion of those children that would develop neurological and auditory sequelae [16].

Costs were estimated based on the number of children vaccinated according to vaccine coverage per dose and adjusted for wastage, freight, handling and extra system costs, which included all other incremental costs, in addition to the vaccine and supply procurement. An average number of ambulatory visits and hospitalizations were estimated for disease type and multiplied by the weighted average cost per case. The cost per case was derived from the proportion receiving care by provider type and the associated treatment cost per provider. To estimate the life-time costs associated with meningitis sequelae, an average estimated annual cost until death was assigned [16].

2.2. Demographics

INEI provided data on the number of live births per year, infant mortality rate and life expectancy at birth for each of the 20 cohorts. Mortality rate in children <5 years of age was obtained from United Nations Department of Economic and Social Affairs' Population Division [22]. This demographic information was included for each of the 20 birth cohorts (2012–2031) and four previous cohorts (2008–2011). The latter was needed to calculate more accurate 'annual' events and the cost of the first 5 years of the vaccination program.

2.3. Disease burden

Pneumococcal pneumonia, pneumococcal meningitis, pneumococcal sepsis and all-cause acute otitis media were evaluated. AOM was included due to the etiologic role of NTHi in this disease [23,24]. Disease burden data on pneumococcal syndromes in Peru is sparse, and there are concerns about how representative the available data is and whether the full extent of disease is being detected in laboratories. Consequently, we have included a description of how disease incidence and CFRs were derived for each syndrome studied; Table 1 shows the estimates. Low and high range estimates were defined to explore the "what if" scenario analysis.