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How to Get Cost-Effectiveness Analysis Right? The Case of Vaccine Economics in Latin America

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ABSTRACT

Background: In middle-income countries, vaccines against pneumococcal disease, rotavirus, and human papilloma virus are in general more costly, not necessarily cost saving, and less consistently cost-effective than earlier generation vaccines against measles, diphtheria, tetanus, and pertussis. Budget impact is also substantial; public spending on vaccines in countries adopting new vaccines is, on average, double the amount of countries that have not adopted. Policymakers must weigh the costs and benefits of the adoption decision carefully, given the low coverage of other kinds of cost-effective health and nonhealth interventions in these same settings and relatively flat overall public spending on health as a share of gross domestic product (GDP) over time. **Objective:** This paper considers lessons learned from recent vaccine cost-effectiveness analyses and subsequent adoption decisions in Latin America a, largely under the auspices of the Pro Vac Initiative. **Results:** The paper illustrates how small methodological choices and seemingly minor technical limitations of cost-effectiveness models can have major implications for the studies' conclusions, potentially influencing countries' subsequent vaccine adoption decisions. **Methods:** We evaluate the ProVac models and technical outputs against the standards and framework set out by the International Decision Support Initiative Reference Case for economic evaluation and consider the practical effects of deviations from those standards. **Conclusions:** Lessons learned are discussed, including issues of appropriate comparators, GDP-based thresholds, and use of average versus incremental cost-effectiveness ratios as a convention are assessed. The article ends with recommendations for the future.

Keywords: cost-effectiveness, developing countries, Latin America, vaccination.

Key points

- Cost-effectiveness analyses to inform new vaccine introduction in low- and middle-income countries is increasingly seen as critical to the maximizing the efficiency and impact of vaccination programs.
- This paper considers technical lessons learned from recent vaccine cost-effectiveness analyses and subsequent adoption decisions in Latin America, largely under the auspices of the ProVac initiative. The program has made enormous strides in defining models, sharing expertise with policymakers and promoting use of evidence in vaccine adoption decision using evidence.
- The paper also illustrates how small methodological choices and seemingly minor technical limitations of cost-effectiveness models can have major implications for studies' conclusions, potentially influencing countries' subsequent vaccine adoption decisions.

Introduction

Middle-income countries face special pressures and circumstances when considering adoption of second-wave vaccines, specifically those against rotavirus, human papilloma virus, and the 7, 10, and 13 serotypes of pneumococcal disease (PCV7, PCV10 and PCV 13). These new vaccines are in general more costly, not necessarily cost saving, and less consistently cost-effective in different settings than earlier vaccines against measles, diphtheria, tetanus and pertussis. Budget impact can also be substantial; public spending on vaccines in countries adopting new vaccines is – on average – double the amount of countries that have not adopted. Policymakers must weigh the costs and benefits of the adoption decision carefully, given the low coverage of other kinds of cost-effective health and non-health interventions in these same settings and relatively modest growth in overall public spending on health over time.

This paper considers the technical lessons learned from the past decade of vaccine evaluation and adoption decisions in Latin

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America, primarily conducted with support from the ProVac initiative. ProVac was launched in 2004 as the first large-scale, systematic effort to support governments in conducting their own economic evaluation of vaccines. A decade later, ProVac is the source of the majority of such evaluations in Latin America and the Caribbean, having achieved notable operational and technical successes while applying a novel approach to an issue of tremendous importance. Yet the Latin American experience over the past decade also shows how seemingly small methodological choices can deeply affect the outcome and utility of economic evaluation, leading to risk of sub-optimal resource allocation decisions. These technical lessons have important implications for the future evolution of the field of economic evaluation and other efforts to support development of more evidence-based priority-setting mechanisms in low- and middle-income countries. The experience also illustrates remaining political barriers to evidence-based decision-making, which are further elucidated in a complementary working paper.

This paper considers the technical lessons learned after ten years of ProVac support for vaccine evaluation in Latin America. The remainder proceeds as follows. Section two discusses the special challenge of second-wave vaccine introduction in middle-income countries; section three then describes how the design of the ProVac initiative addresses gaps in country capacity for evidence-based decision-making around vaccine adoption. With reference to the framework and standards established in the Gates Reference Case for Economic Evaluation [1], the paper next considers how ProVac models rate against established technical standards and key technical lessons learned from the Latin American experience (section four). Finally, the paper concludes with a discussion of how the ProVac model relates to the broader ecosystem of priority-setting in low- and middle-income countries (section five).

To Adopt or Not to Adopt? The Special Challenge of Second-Wave Vaccine Introduction in Middle Income Countries

The history of mass vaccination has progressed in two major waves. The first wave, taking place in the 1960s and 70s, saw the introduction of several inoculations against major childhood killers, most notably measles, mumps, and rubella (MMR); oral polio vaccine (OPV); and diphtheria, pertussis, and tetanus (DPT). These vaccines were uniformly low-cost, with a price tag of under $1 per dose everywhere in the world; they were also cost-saving in the very short-term, as averted infections also averted the costs associated with treatment and hospitalization. And of course, the averted disease burden represented a major humanitarian achievement, saving many children from death before their fifth birthdays.

The second wave, covering the period between the 2000 and the present day, has seen the introduction of new vaccines against rotavirus, human papilloma virus, and the 7, 10, and 13 serotypes of pneumococcal disease (PCV7, PCV10 and PCV 13). These vaccines are a major medical breakthrough against major causes of death and morbidity. Yet compared to first-wave vaccines, they are in general more costly, not necessarily cost-saving, and less consistently cost-effective. A fourth vaccine introduced during this period, against Haemophilus influenza type B (HiB), falls into an intermediate zone, found to be cost-saving in some settings but not others.

As first-wave vaccinations saved lives and money almost immediately at a very low cost, public payers were eager to subsidize their introduction so long as they had sufficient budgetary space to do so. With the health and fiscal benefits so obviously exceeding the costs, the vaccine introduction decision was relatively straightforward and uncontroversial.

In contrast, the decision to introduce costlier second-wave vaccines can be more complicated, requiring careful attention to affordability and cost-effectiveness compared to other health priorities that compete for scarce public funds. New vaccines must compete for resources against other interventions to target the same disease, as well as against completely unrelated interventions to address other diseases. For example, the rotavirus vaccine can be compared to other health sector interventions to prevent or control diarrheal diseases such as oral rehydration therapy, hygiene education, and breastfeeding promotion; it can also be compared to health sector interventions to prevent or treat malaria, HIV, and tuberculosis. Cost-effectiveness analysis is needed to weigh the costs and benefits of second-wave vaccine introduction and inform an evidence-based decision on adoption.

The potential budget impact of second-wave vaccines is substantial. As in higher-income countries [2], vaccination budgets are far higher in middle-income countries that have introduced second-wave vaccines when compared to their peers that have not yet done so. Figure 1 compares vaccine expenditure in middle-income countries by introduction status of the pneumococcal and rotavirus vaccines. Public expenditure on vaccines (mean or median) as a share of GDP is more than double (per live birth) when compared to countries that have not introduced the vaccines.

As is self-evident, the price of second-wave vaccines is an important determinant of their overall cost-effectiveness and affordability, making effective price negotiation of paramount importance. Low-income countries (and some transitioning lower-middle income countries) have benefitted from Gavi efforts to pool demand and lead negotiations, enabling lower prices. Most high-income countries, on the other hand, rely on strong domestic institutions and capacity to evaluate the costs and benefits of second-wave vaccines and thereby negotiate moderate prices with industry. Within the current global order, however, many middle-income countries – home to most of the world's poor and ill, and including most countries in Latin America – are stuck on the uncomfortable middle ground, with some ability to pay but with limited technical and institutional capacity to conduct economic evaluation, assess budget impact, and negotiate effectively on price. The presence of the PAHO's Revolving Fund has to some extent centralized the issue of price negotiation in Latin America and the Caribbean away from country governments, but not all countries in the region participate, or participate consistently, in the Fund procurement mechanism. Further, outside the PAHO region in non-Gavi countries, price negotiation remains a major challenge.

The challenge facing middle-income countries is compounded by the structure of the market for second-wave vaccines. Although most new vaccines have remained on-patent during the period of this research, almost all products face competition from a comparator vaccine produced and marketed by a second company. For example, the pneumococcal vaccine has been produced by Pfizer as Prevenar© (7 [now retired from market] and 13 valent) and by GSK as Synflorix©; the rotavirus vaccine is produced as RotaTeq© by MSD Sanofi and as Rotarix© by GSK; and the HPV vaccine is produced as Gardasil© by MSD Sanofi and as Cervarix© by GSK. While each company and product has its own pricing strategy in each country (and for each payer agency), in many cases the products compete head-to-head for public sector market share. This market structure has resulted in highly variable vaccine prices, the result of intense negotiations between public purchasers and industry.

The vaccine market in middle-income countries is a large and important one for both national and international manufacturers. Globally, vaccine sales amount to $24 billion each year for the three companies that concentrate 70% of the market [3].