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A cost-minimisation analysis: comparison of acellular versus whole-cell hexavalent paediatric vaccination strategies in Argentina

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A cost-minimisation analysis: comparison of acellular versus whole-cell hexavalent paediatric vaccination strategies in Argentina

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Abstract

Background: Argentina's National Immunization Program currently administers a pentavalent whole-cell pertussis (wP) vaccine (diphtheria, tetanus, pertussis, hepatitis B, and *Haemophilus influenzae* type b) alongside inactivated poliovirus vaccine (IPV) during infancy. Hexavalent vaccines, with IPV incorporated into the formulation, combining protection against six diseases (diphtheria, tetanus, pertussis, hepatitis B, *Haemophilus influenzae* type b, and poliomyelitis) in a single injection, and are available either wP or acellular pertussis (aP) antigens. By consolidating two injections into one, hexavalent formulations could streamline delivery, reduce the number of injections infants receive, and improve tolerability and compliance. To inform potential schedule modifications, this cost-minimisation analysis compared the societal costs of implementing wP or aP hexavalent vaccination schemes in Argentina.

Methods: This was a cost-minimization analysis conducted from a societal perspective, comparing wP and aP hexavalent vaccination schemes in Argentina. The study population comprised infants born in Argentina between 2021 and 2023, stratified by healthcare market, gestational age, and birth weight. Costs included direct medical costs, parental costs, and the cost of vaccine acquisition and administration. Total vaccine-related costs were disaggregated into vaccine acquisition, programmatic costs, and adverse event (AE) management costs for each scheme. All costs were presented in 2025 US dollars.

Results: Total societal costs were lower for the aP hexavalent scheme ($84.9M) compared with the wP hexavalent scheme ($93.2M), yielding savings of $8.3M (8.9%). Although vaccine acquisition costs were $24.5M higher for the aP scheme, these were offset by a $32.8M (54.6%) reduction in AE management costs. In the public sector, which accounts for 94% of administered

doses, the aP scheme reduced total costs by $9.1M. Premature infants experienced the largest proportional reductions in AE-related costs. Sensitivity analyses confirmed the robustness of findings, with greater savings observed under higher coverage assumptions and when applying higher AE rates.

Conclusion: This analysis demonstrates that the aP hexavalent scheme is associated with lower overall societal costs than the wP hexavalent scheme in Argentina.

Keywords: vaccination, cost-minimisation, paediatric, health outcomes, pertussis

1 Introduction

Immunisation programmes have substantially reduced global morbidity and mortality from vaccine-preventable diseases, contributing to a decline in deaths among children under five from nearly 13 million in 1990 to 5 million in 2020 [1]. Combination vaccines have further improved immunisation coverage by providing protection against multiple diseases in a single visit and simplifying programmatic and logistical demands [2–4].

In Argentina, children routinely receive a pentavalent vaccine containing diphtheria toxoid, tetanus toxoid, whole-cell pertussis (wP), *Haemophilus influenza*e type b (Hib), and hepatitis B (HepB) surface antigens (wP pentavalent vaccine [DTwP-HepB-Hib]) at 2, 4, and 6 months of age, with a first booster at 15–18 months of age [5]. An inactivated polio vaccine (IPV) is administered concomitantly at 2, 4, and 6 months of age, with a booster at 5 years of age. A hexavalent vaccine containing acellular pertussis (aP) antigens, with IPV incorporated into the formulation (aP hexavalent vaccine) [6, 7], is available through private prescription and for high-risk, pre-term infants in the public health program through the Revolving Fund (RF) of the Pan American Health Organization (PAHO).

In a previous cost-minimisation analysis [8], we demonstrated that while replacing the wP pentavalent + IPV schedule with the aP hexavalent schedule was associated with a modest increase in vaccine acquisition costs, it resulted in lower programmatic costs (due to a reduced number of injections) and fewer adverse events and related management costs (attributable to the lower reactogenicity of the aP component relative to that of wP [9, 10]), leading to net cost savings. No studies, however, have evaluated the relative economic impacts of the two hexavalent alternatives in the Argentine setting. Given that both wP and aP hexavalent vaccines

would offer programmatic benefits, a head-to-head economic comparison is needed to inform evidence-based decision-making.

The objective of this study was therefore to conduct a cost-minimisation analysis comparing a hypothetical wP hexavalent (DTwP-HepB-Hib-IPV) scheme against an aP hexavalent (DTaP-IPV-Hib-HepB) vaccination scheme in Argentina from a societal perspective. The analysis incorporated contemporary demographic data, adverse event (AE) rates, healthcare utilisation patterns, and cost inputs to estimate total vaccine-related costs and identify which hexavalent strategy offers the more economically favourable profile.

2 Methods

2.1 Model overview

We performed a cost-minimisation analysis of all infants born in Argentina for vaccination against diphtheria, tetanus, pertussis, Hib, hepatitis B, and polio across public and private health systems. As in our previous analysis, the model used a societal perspective and considered per-dose vaccine coverage rates (AE rates and costs for AE management, vaccine acquisition, logistics, and productivity loss) (Figure 1) [8].

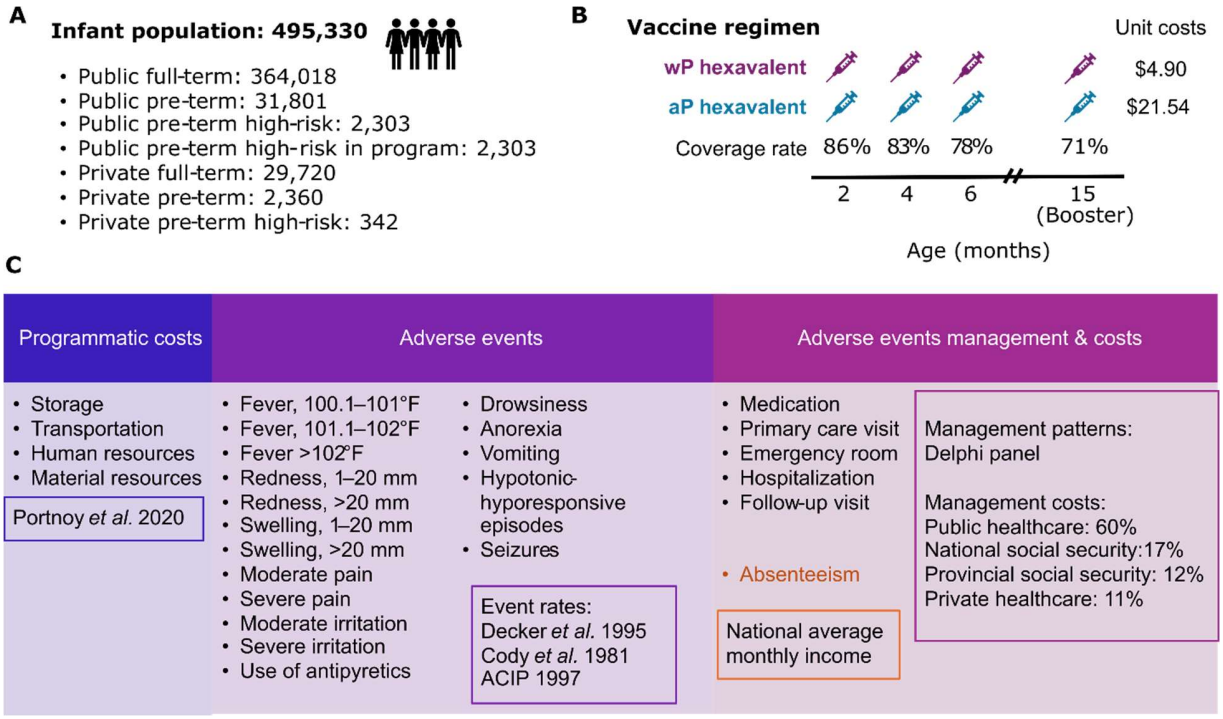


Figure 1. Overview of model schemes and inputs. The total annual infant population was stratified by healthcare market as well as gestational age and birthweight (A). Two vaccination schemes were considered, consisting of four doses and including coverage rates and unit costs (B). Cost inputs included programmatic costs involved in vaccination programs, as well as adverse event management costs and associated parental productivity loss (C). *Cost of a 5-dose bottle of inactivated polio vaccine.

2.2 Population

The study population consisted of infants born in Argentina, using the average annual number of newborns recorded between 2021 and 2023 by the Ministry of Health (Table S1). During this period, an annual average of 46.2 million people and 495,330 live births were registered in Argentina. As previously, infants were categorised into three strata based on gestational age and birth weight: full-term infants were defined as those born at or after 37 weeks' gestation, while pre-term infants were defined as those born before 37 weeks' gestation, and high-risk pre-term infants were defined as those born before 37 weeks' gestation with a birth weight below 1,500 g [8].

2.3 Vaccination schemes

Analyses were conducted under two scenarios, defined by wP hexavalent versus aP hexavalent vaccination schedules (Table 1). Under the wP hexavalent vaccination scheme, all infants being vaccinated in the public sector receive the wP hexavalent vaccine at 2, 4, 6, and 15 months of age, except for half of the high-risk pre-term infants who received the aP hexavalent vaccine as part of the Argentinean public health program for high-risk, pre-term infants (the remaining 50% received the wP hexavalent scheme). In the private insurance sector, all eligible infants received the aP hexavalent vaccine for the primary series (2, 4, and 6 months of age) and 15-month booster regardless of gestational age or birth risk category. Under the aP hexavalent vaccination scheme, all infants receive the aP hexavalent vaccine at 2, 4, 6, and 15 months of age.

Table 1. Vaccine distribution in the model

Sub-population	Public	Private
wP hexavalent vaccination scheme		
≥37 weeks' gestation	wP hexavalent	wP hexavalent
<37 weeks' gestation and ≥1,500 g	wP hexavalent	wP hexavalent
<37 weeks' gestation and <1,500 g	50% wP hexavalent,* 50% aP hexavalent (RF-PAHO)	50% wP hexavalent, 50% aP hexavalent (PAHO)
aP hexavalent vaccination scheme		
≥37 weeks' gestation	aP hexavalent	aP hexavalent
<37 weeks' gestation and ≥1,500 g	aP hexavalent	aP hexavalent
<37 weeks' gestation and <1,500 g	aP hexavalent	aP hexavalent

*Currently, only 50% of high-risk pre-term infants weighing <1500 g at birth have access to the immunisation program using the acellular hexavalent vaccine.
Abbreviations: aP: acellular pertussis; IPV: inactivated polio vaccine; PAHO: Pan American Health Organization; wP: whole-cell pertussis.

Vaccination coverage values were based on the mean rates from 2021 to 2023 (Table S1), indicating 86% received a 1st dose at 2 months of age, 83% a 2nd dose at 4 months of age, 78% a 3rd dose at 6 months of age, and 71% a booster at 15 months of age. The number of doses distributed by the Ministry of Health was assumed to correspond to the entire eligible infant population and was adjusted by the coverage rate, excluding doses administered in the private

insurance sector (Table S2). The effectiveness of the vaccination schemes against the 6 indications was assumed to be equivalent and remain stable with periodic booster doses [11–16].

2.4 Adverse events

As in previous analyses [8, 17], AE rates for wP- and aP-containing vaccines were derived from Decker *et al*. 1995 (Table S3) [10]. These were used because the reported differences between wP- and aP-containing vaccines were smaller than in Zhang *et al*. 2014 [7] and Patterson *et al*. 2018 [9], and thus more conservative. Because Decker *et al*. 1995 did not report AE rates for booster doses [10], the rate following the booster was assumed to be the same as the rate following the third dose of a diphtheria, tetanus, and pertussis vaccine. For serious neurological AEs such as seizures and hypotonic-hyporesponsive episodes, data were obtained from the Advisory Committee on Immunization Practices (ACIP) 1997 and Cody *et al*. 1981 [18, 19], as was done previously [8]. The rate of seizures and hypotonic-hyporesponsive episodes associated with wP-containing vaccines was estimated to be 1 case per 1,750 vaccinated infants (0.57 cases per 1,000 doses), while the rate for aP-containing vaccines was estimated at 0.12 cases per 1,000 doses [18, 19].

2.5 Parameters and associated costs

The parameters and cost components included in this analysis are summarised in Table 2 and Table S8. It was assumed that certain AEs would result in healthcare resource use, including outpatient general practitioner clinic visits, follow-up visits, emergency room visits, and hospitalisations, as well as parental time and travel, with utilisation rates based on expert consensus of paediatricians in Uruguay, selected due to the availability of robust expert consensus data in the absence of locally published Argentine estimates (Table S4–Table S7) [8].

Expert consensus was generated using a Delphi-method survey conducted among 30 expert paediatricians in Uruguay to quantify paediatric attitudes toward AEs following primary vaccination series and booster doses at 2, 4, 6, and 15 months of age [8]. The Delphi methodology, a qualitative information-gathering approach utilising expert consensus, was selected due to the lack of available data for decision-making in this area [20]. Expert selection criteria included academic activity and experience in both public and private healthcare settings, covering ambulatory and hospital environments. The survey comprised 16 semi-structured questions with predetermined and open-ended options for each vaccination dose. Results were expressed as averages with dispersion measures where relevant. This methodology was deemed appropriate for obtaining an approximation of paediatric behaviour regarding vaccine AEs, providing essential data for pharmacoeconomic analysis comparing pentavalent vaccines with wP components versus hexavalent vaccines with aP components. These paediatricians estimated the likelihood of each type of resource use according to the infant's gestational age and the specific vaccine dose. The cost impact of AE management was estimated by combining the proportion of infants experiencing each AE with the management patterns.

Table 2. Parameters and associated unit costs included in the analysis

Variables	US$ per dose or event	Source or assumptions
Direct medical costs (weighted averages)		
Ibuprofen suspension*	3.99	See Table S8
Oral metoclopramide antiemetic drops x 20ml*	5.25	See Table S8
Paediatric outpatient visit†	8.02	See Table S8
Paediatric Emergency Room visit†	13.96	See Table S8
1 day of hospitalisation in the paediatric ward†	90.74	See Table S8
Parental costs		
1 bus trip	0.47	Fare and social fare up to 12 km
1 working day (absenteeism)	15.83	41.5% employment rate
Cost of vaccine acquisition and administration		
wP hexavalent vaccine	4.90	PAHO Revolving Fund 2025 [21]
aP hexavalent vaccine (public health sector)	21.54	PAHO Revolving Fund 2025 [21]
aP hexavalent vaccine (private health sector)*	177.46	See Table S8
Programmatic costs	3.18	Portnoy *et al*. 2020 [22]

*Average

†Weighted average

Note: Prices were converted from Argentine Pesos (Arg$) into US$ using an exchange rate of Arg$1,165=US$1 (May 2, 2025).
Abbreviations: aP: acellular pertussis; IPV: inactivated polio vaccine; NR: not reported; PAHO: Pan American Health Organization; wP: whole-cell pertussis

Healthcare costs were estimated based on a weighted average across public (60%), social security (National: 17%; Provincial: 12%), and private (11%) sectors. For any hospitalisation, a 1-day length of stay was assumed as a conservative estimate. Parental costs included travel expenses to the hospital by bus and productivity losses, which were estimated assuming that one family member lost half a working day when attending an outpatient clinic or emergency room visit and one and a half working days in the case of hospitalisation. These assumptions incorporated a national employment rate of 41.5% and an average monthly income of US$371.93 (Arg$442,596) for 24 working days. Programmatic vaccination costs, including labour, supply chain, service delivery, and capital components, were derived from Portnoy *et al*. 2020 [22]. Vaccine and programmatic costs were sourced in US dollars, while all other costs

were initially collected in Argentine pesos and converted to US dollars using an exchange rate of Arg$1,165 per US$1 based on the Banco Nación rate from May 2, 2025. All costs were expressed in 2025 values.

2.6 Sensitivity analyses

In the first sensitivity analysis, the vaccination coverage for each dose was set to 95% for vaccines administered by the Ministry of Health, and 100% for each dose administered in the private sector. In the second sensitivity analysis, AE rates from Zhang *et al.* 2014 were used (Table S9) [7].

3 Results

3.1 Base case analysis

Total vaccine-related costs, disaggregated into vaccine acquisition, programmatic, and AE management costs, were estimated for each of the vaccination schemes (Figure 2A, Table 3, Table S10, and Table S11). Total costs were for the aP hexavalent scheme were $84.9 million ($182 per child), $8.3 million (8.9%) lower than those of the wP hexavalent scheme, $93.2 million ($200 per child). AE management costs constituted the largest proportion of total costs for the wP hexavalent scheme ($60.0 million; 64%), whereas vaccine acquisition costs constituted the largest proportion of total costs for the aP hexavalent scheme ($53.0 million; 64%). While vaccine acquisition costs were $24.5 million (86.1%) higher for the aP hexavalent vaccination scheme, the AE management costs were $32.8 million lower (-54.6%), resulting in the cost-minimisation of the aP scheme. AE management costs were lower for the aP hexavalent scheme across all cost categories, including medication, inpatient care, primary care visits,

emergency department visits, and follow-up visits (Figure 2B and Table S12). Acquisition of the aP hexavalent vaccine accounted for most of the total vaccine acquisition costs across both schemes (Table S13).

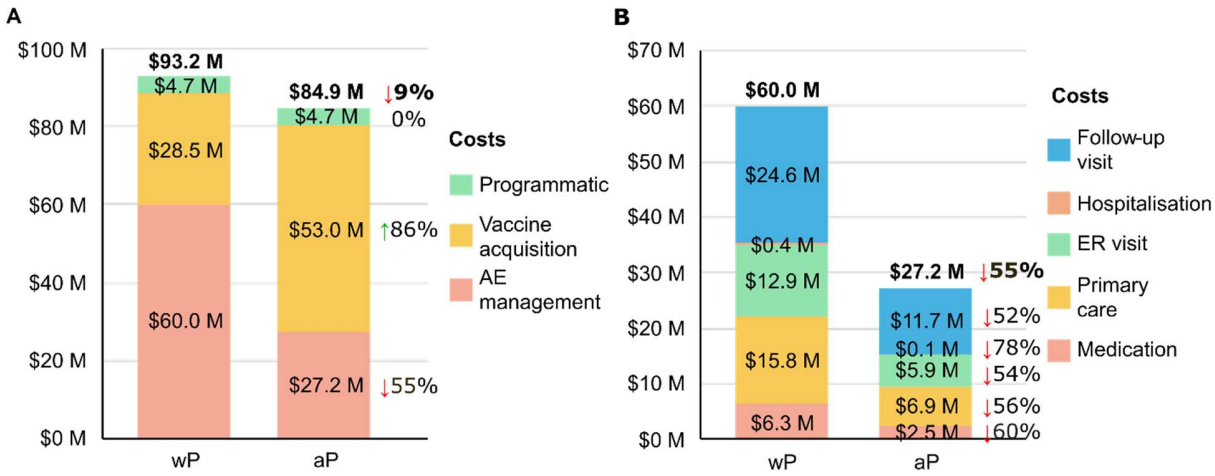


Figure 2. Costs of the current and alternative vaccination schemes across healthcare sectors (A), and a breakdown of the adverse event management costs (B).

Table 3. Summary of costs of the vaccination schemes overall and in the public sector

	All sectors		Public sector	
	wP hexavalent vaccination scheme	aP hexavalent vaccination scheme	wP hexavalent vaccination scheme	aP hexavalent vaccination scheme
Total cost, $ millions	93.16	84.90	70.09	61.00
Incremental total cost, $ millions (%)	Ref	−8.26 (−8.87%)	Ref	−9.10 (−12.98%)
Vaccine acquisition cost, $ millions	28.45	52.96	7.36	31.86
Incremental vaccine acquisition costs, $ millions (%)	Ref	24.51 (86.13%)	Ref	24.50 (333.03%)
AE management cost, $ millions	60.01	27.23	58.03	24.43
Incremental AE management costs, $ millions (%)	Ref	−32.77 (−54.60%)	Ref	−33.60 (−57.90%)
Programmatic cost, $ millions	4.70	4.71	4.70	4.70
Incremental programmatic costs, $ millions (%)	Ref	0.01 (0.10%)	Ref	0.00 (0.00%)

Abbreviations: aP: acellular pertussis; IPV: inactivated polio vaccine; wP: whole-cell pertussis

3.2 Public sector costs

Public sector costs (representing 94% of all vaccine administrations) were estimated by vaccination scheme and cost category. Total public sector costs were $61.0 million for the aP hexavalent scheme ($152 per child) and $70.1 million for the wP hexavalent scheme ($175 per child) (Figure 3A and Table S11). This $9.1 million (13.0%) difference was attributable to lower AE management costs for the aP scheme ($24.4 million versus $58.0 million; $33.6 million [42.1%] difference), which offset the $24.5 million (331.1%) higher vaccine acquisition costs.

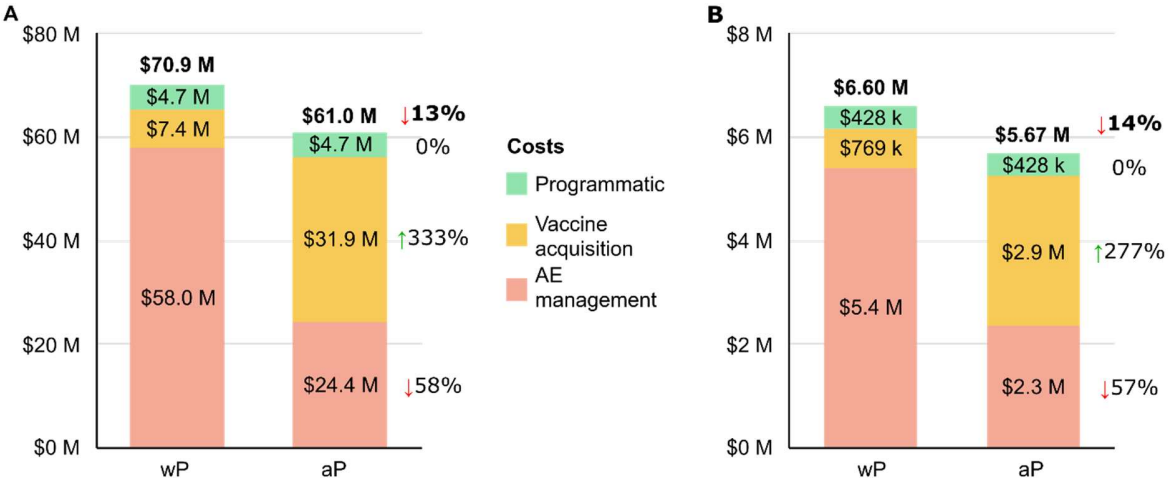


Figure 3. Costs of the current and alternative vaccination schemes to the public sector for all infants (A), and for pre-term infants (B).

The aP hexavalent scheme was associated with fewer AE-related healthcare resource uses and indirect costs than the wP hexavalent scheme, including 946,879 fewer medication administrations, 533,110 fewer primary care visits, 308,687 fewer emergency department visits, and 2,868 fewer hospitalisations (Table S14). In addition, the aP hexavalent scheme was associated with 3,783,405 fewer parental bus journeys and 1,654,129 fewer missed workdays.

3.3 All premature infants in the public sector

Total public sector costs for vaccinating all premature infants were $6.60 million for the wP hexavalent scheme ($181 per child) and $5.67 million for the aP hexavalent scheme ($156 per child) (Figure 3B and Table S11). The aP hexavalent scheme had 376.8% higher vaccine acquisition costs compared with the wP hexavalent scheme ($2.90 million versus $769 thousand) and lower AE management costs ($2.35 million versus $5.40 million; $3.05 million [78.5%] difference).

3.4 Sensitivity analyses

Sensitivity analyses were conducted to assess the robustness of results under alternative assumptions. In the scenario assuming a vaccination rate of 95%, total vaccine-related costs were $106.1 million for the wP hexavalent scheme and $96.9 million for the aP hexavalent scheme, corresponding to a $9.2 million cost difference (8.7%) (Figure 4A). Vaccine acquisition costs were higher for the aP hexavalent scheme ($59.2 million) than the wP hexavalent scheme ($29.9 million), a 65.8% difference. Despite higher acquisition costs, total costs were lower for the aP hexavalent scheme due to a 75% reduction in AE management costs ($32.1 million) compared with the wP hexavalent scheme ($70.6 million).

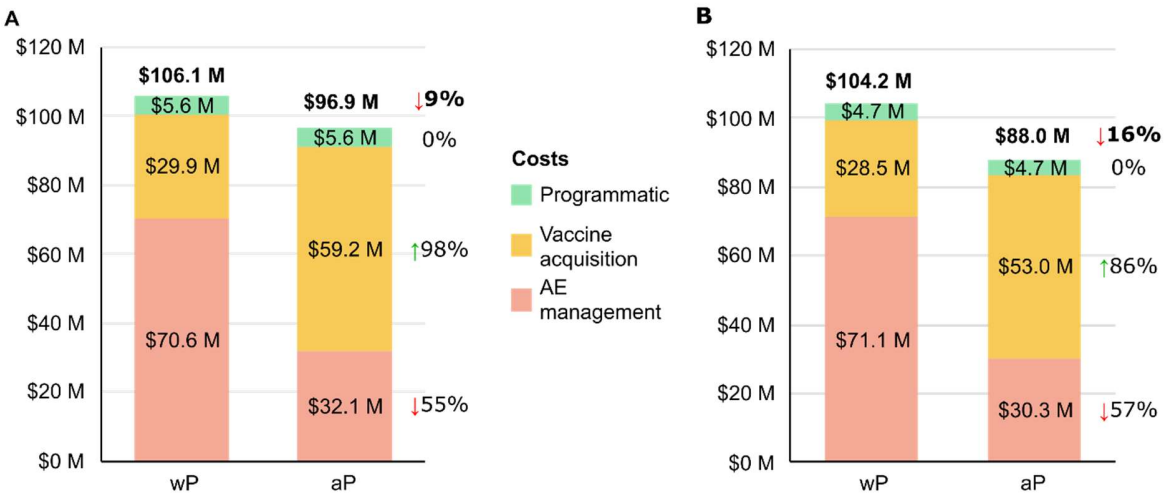


Figure 4. Costs of the current and alternative vaccination schemes in scenarios in which vaccination coverage is 95% overall (A), and in the scenario using vaccine adverse event rates from Zhang *et al.* 2014 [7] (B).

In a second sensitivity analysis using AE rates reported by Zhang *et al*. 2014 [7] rather than the more conservative rates from Decker *et al*. 1995 [10], total vaccine-related costs were $104.2 million for the wP hexavalent scheme and $88.0 million for the aP hexavalent scheme, corresponding to a cost reduction of $16.2 million (15.5%) (Figure 4B). Vaccine acquisition costs remained higher for the aP hexavalent scheme ($53.0 million) compared with the wP hexavalent scheme ($28.5 million), a 60.1% difference. Lower total costs for the aP hexavalent scheme were attributable to 80.5% lower AE management costs, $71.1 million in the wP hexavalent scheme versus $30.3 million in the aP hexavalent scheme.

4 Discussion

We conducted an economic evaluation modelling the costs of wP and aP hexavalent infant vaccination strategies for the primary series and 15-month booster in Argentina, assuming equivalent effectiveness but retaining differences in their safety profiles. Across the overall healthcare system and the public healthcare system specifically, greater vaccine acquisition costs

associated with the aP hexavalent vaccination scheme were more than offset by reductions in AE management costs. While this is the first health-economic comparison of the wP and aP hexavalent vaccine schedules worldwide, previous analyses of switching from a wP pentavalent vaccine + IPV to aP hexavalent vaccine have emphasised the lower costs of AE management with aP hexavalent vaccine schedule, consistent with results reported here [8, 17, 23]. Cost-minimisation with the aP hexavalent scheme was observed across the entire healthcare system, within the public sector alone, and among premature infants in the public sector, with the largest economic impact observed in premature infants due to their higher vulnerability to AEs and greater need for healthcare utilisation. A sensitivity analysis using higher AE rates reported by Zhang *et al.* 2014 resulted in a larger cost difference between schemes, as these higher AE rates per visit substantially increased the costs, primarily because higher reported AE rates per visit substantially increased the costs of the wP hexavalent vaccination scheme [7]. Under these assumptions, the economic benefit of the aP hexavalent vaccination strategy became more pronounced.

Sensitivity analyses explored the impact of increasing vaccination coverage to the national target of 95% at each visit. As expected, total costs increased for both strategies. However, the economic advantage of the aP hexavalent scheme was widened with the increased number of administered doses, driven by the greater increase in AE management costs with the wP hexavalent scheme.

The findings of this analysis have direct relevance for Argentina's national immunisation programme, which currently administers the wP pentavalent vaccine alongside separate IPV doses in the public sector. Transitioning to a universal hexavalent schedule would consolidate two injections into one, reducing the logistical complexity of simultaneous multi-vaccine

administration at each visit and potentially improving parental adherence and coverage rates. From a procurement standpoint, wP and aP hexavalent vaccines are already available through the PAHO Revolving Fund, providing an established regional mechanism for public sector acquisition. While the higher acquisition cost of the aP hexavalent vaccine compared to the wP hexavalent vaccine represents an upfront budgetary consideration, our analysis demonstrates that this is more than offset by reductions in AE management costs. Phased implementation, for example by prioritising high-risk pre-term infants in the public sector, where the economic benefit per child is greatest, could improve access while managing the budgetary transition. Taken together, these findings support the case for a formal policy review of the hexavalent vaccine strategy within Argentina's national immunisation programme.

The economic benefit of the aP hexavalent scheme was most pronounced among premature infants, for whom AE management costs were 78.5% lower than under the wP hexavalent scheme. This finding carries important equity implications. Premature infants are disproportionately represented in lower socioeconomic groups, are more likely to be managed within the public health system and are at greatest clinical risk from vaccine-related AEs, making the case for universal access to aP hexavalent vaccine both economically and ethically important [24, 25]. Achieving universal aP hexavalent coverage to all premature infants in the public sector would reduce AE burden in the most vulnerable population at lower total cost to the health system and should be considered a priority.

While the present analysis provides a conservative estimate of the economic value of the aP hexavalent strategy by assuming equivalent effectiveness, it does not capture the full burden of AEs on affected children and their families. Future work should therefore prioritise a cost-utility analysis incorporating long-term quality of life outcomes, which would provide a more complete

basis for comparing the two hexavalent strategies. The present model is confined to costs and does not capture the lasting burden that serious neurological AEs can place on affected children and their families; accounting for these impacts would be expected to further strengthen the economic case for the aP hexavalent strategy.

4.1 Strengths and limitations

This study has several strengths. It applies the same methodological framework previously used for models in Chile [17] and in Argentina [8], ensuring methodological consistency and comparability across settings and time. Our approach allows vaccine safety to be assessed from an economic perspective, capturing not only direct health effects in children but also healthcare resource use and system-level costs associated with AEs, which differ substantially between wP and aP formulations. Throughout the analysis, conservative assumptions were applied to AE rates to avoid overstating the economic advantage of the aP hexavalent scheme. Base case AE rates were derived from Decker *et al*. 1995 [10], which reported smaller differences between wP- and aP-containing vaccines than Zhang *et al*. 2014 [7] or Patterson *et al*. 2018 [9], and therefore favour the wP hexavalent scheme. Similarly, rates for serious neurological AEs seizures and hypotonic-hyporesponsive episodes were drawn from Cody *et al*. 1981 and ACIP [18, 19], yielding an estimate of 0.57 per 1,000 doses, despite rates as high as 2.91 per 1,000 doses being reported elsewhere [26]. The consistent use of conservative AE inputs means that the base case results represent a lower bound of the true economic advantage of the aP hexavalent strategy.

Several limitations should be noted. First, paediatrician attitudes toward AE management were derived from a 2021 Delphi-based survey conducted in Uruguay. Although major differences are not expected, social norms, clinical practices, and health system organisation may differ in

Argentina, which could influence AE management patterns and associated costs. More broadly, the Delphi methodology represents a qualitative consensus rather than a quantitatively representative assessment, so some variability in real-world practice is likely.

Second, several cost and pricing assumptions should be considered. Drug prices were estimated using a simple unweighted average and do not account for differential utilisation patterns. The cost of the wP hexavalent vaccine was based on the cost of single-dose vials. Although the PAHO Revolving Fund also offers 10-dose vials at a lower nominal per-dose cost, these were not considered for two reasons: to maintain methodological consistency with prior analyses in the region, and because open-vial wastage in routine immunisation settings means the effective per-dose cost may exceed the nominal price and Argentina-specific wastage data were unavailable to model this accurately. Productivity losses related to AEs were estimated assuming only one parent or caregiver was absent, and family travel costs assumed a single caregiver traveling by public bus. Scenarios involving multiple caregivers, alternative transport modes, or private vehicles, which could entail higher costs, were not considered. These limitations suggest that some indirect costs may be underestimated.

Third, certain structural features of the model may not fully reflect real-world programmatic conditions. Firstly, programmatic factors associated with concomitant vaccine administration were not explicitly captured. In Argentina, three vaccines are administered concomitantly at the 2- and 4-month visits (wP pentavalent, IPV, and 13-valent pneumococcal conjugate vaccine), with wP pentavalent and IPV also administered at 6 months of age. Simultaneous administration may lead to missed or delayed doses due to supply constraints, parental reluctance, or child discomfort, which were not captured in the model. Differences in observed coverage rates across vaccines illustrate this limitation. Additionally, since AEs such as pain and fever may occur

concomitantly in the same child, there is a theoretical risk that a single HCRU event could be counted more than once across different AE categories. A thorough review of the relevant literature did not yield data on the number of discrete AE episodes per child, making adjustment for potential co-occurrence unfeasible and a limitation of the analysis. Nevertheless, any potential overestimation of HCRU applies equally to both treatment arms, preserving the comparability of the cost difference between them, and the analysis remains intentionally conservative.

5 Conclusion

Adopting the aP hexavalent vaccination scheme in Argentina is projected to be less costly than adopting a wP hexavalent scheme, including within the public health sector. While absolute cost estimates are influenced by assumptions regarding vaccination coverage and AE rates, scenarios with higher coverage and alternative AE inputs consistently demonstrated greater economic benefits for the aP hexavalent vaccine strategy. These findings are robust across sensitivity analyses and align with the base case comparison of the wP hexavalent schedule and the aP hexavalent schedule, supporting the potential greater value of transitioning to an aP hexavalent rather than a wP hexavalent vaccination program from both health system and societal perspectives.

List of abbreviations

AE: adverse event
aP: acellular Pertussis
ER: emergency room
Hib: *Haemophilus influenza*e type b
IPV: inactivated polio vaccine
NR: not reported
PAHO: Pan American Health Organization
WGA: weeks' gestation age at birth
wP: whole-cell Pertussis

Declarations

Ethics approval

Not applicable

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information file.

Competing interests

The study was funded by Sanofi, but they did not participate in the analysis. The authors have no other conflicts of interest to declare.

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Authors' contributions

All authors participated in the collection of costs (Table 2); all authors contributed to the drafting of the manuscript and its revisions; all authors analysed the results; the CINVE team (IO, CG, LL, HD) defined the materials and methods; CINVE team is responsible of Delphi Model. All authors read and approved the final manuscript.

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