Original Article

National legislation and spending on vaccines in Latin America and the Caribbean

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Abstract This study examined the dynamics of vaccine spending and vaccine legislation in the Americas Region over the period 1980–2013. Annual vaccine expenditures from thirty-one countries were extracted from the Pan American Health Organization Revolving Fund database. Information on vaccine laws and regulations was provided by the PAHO Family, Gender, and Life Course Unit. Both time series and event history models were estimated. The results show that passing an immunization law led a representative country to increase its vaccine spending, controlling for income, infant mortality, population size, and DPT3 vaccine coverage. Countries with higher vaccine coverage were also more likely to have passed laws. Conversely, higher income countries were less likely to have vaccine laws. Vaccine legislation will likely play a similarly important role in other regions as more countries move towards immunization program ownership.

Keywords: health financing; immunizations, vaccines; Latin America; PAHO

Background and Problem Statement

We address the role vaccine laws have played in the investments Latin American governments have historically made, and continue to make in their national immunization programs. Throughout the twentieth century, public health programs drove mortality decline in Latin America.1 Governments organized and financed them, but they were sustained by popular demand. Institutionalizing water and sanitation
systems, food safety, vector control, immunization, and other key programs required notable increases in public health investments that, over time, were widely seen by the public as valuable public goods. Legal frameworks protected these programs as advocated by various constituencies.

Ongoing demographic changes also favored the passage of vaccine-related legislation in Latin America. Infant and child mortality continued to fall, and life expectancy increased from 52 years in the 1950s to 73 years in 2005–2010. This trend began early in the twentieth century. Economic growth, education levels, and rising labor productivity continued to improve living conditions. Populations increasingly used government health services. Key among these were immunization programs.

The years 1985–1991 were particularly important as countries worked together to eradicate poliomyelitis. Eradicating polio required each country to optimize its immunization program. Countries had to meet the same set of technical benchmarks. Polio vaccine coverage, for example, had to exceed 80 per cent in at least 80 per cent of municipalities or districts. Each person suspected of having polio had to be clinically examined within 48 h, and laboratories had to report on every case within 100 days. If any one country failed, all would be at risk. The Pan American Health Organization (PAHO) provided coordination, technical, and financial support for the Regional polio eradication effort. The Region’s last indigenous polio case occurred in 1991.

Most of the early financing for the polio effort came from external partners, among them USAID, UNICEF, and the Rotary Foundation. Over time, governments also increased their investments, more than quadrupling their expenditures on vaccine and accounting for 95 per cent of immunization expenditures by 1991. By 1995, all but a few national immunization programs were entirely self-financed. These programs continued to perform well through the 1990s and to this day.

Program performance and public spending went hand in hand. Each in its own way, Latin American countries achieved ownership of their immunization programs. By this, we mean that there was sustainable government financing of routine immunization services and maintenance of consistently high technical performance. Countries built the needed technical expertise and garnered political support sufficient to keep the programs financed. For most countries, the evidence suggests this meant passing and enacting new vaccine laws. In 1980, just two

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Latin American countries had vaccine laws. By 2003, nineteen countries had laws with provisions for vaccine financing. These provisions establish line items in the health budget to buy vaccines and syringes — one of the criteria for participation in the PAHO Revolving Fund. By 2011, the number of countries with some type of legal framework had increased to twenty-seven, covering 92 per cent of the Region’s population.

Not all Latin American countries have immunization laws. In a 2009 survey, respondents in nine countries expressed their concern that in the absence of such laws, their national immunization program financing was not assured. In their review article, Trumbo et al examined Latin American vaccine laws, noting that Regional vaccine expenditures rose as the number of countries passing such laws increased.

What caused what? Did immunization spending increase as a result of legislation, or did increased spending cause the governments to pass the laws? We address this question using a two-step longitudinal modeling approach. In the first step, a time series regression model is used to test whether countries with laws were more likely to increase vaccine spending compared to countries without such laws. A two-state hazard model is then fitted to identify factors influencing passage of the laws.

Methods

Many factors in addition to those mentioned earlier affected the probability that a country increased vaccine spending or passed a vaccine law:

- progress against polio and other vaccine-preventable diseases,
- introduction of new technologies and practices,
- widespread public involvement in immunization campaigns, and
- other unmeasured effects.

In addition, countries likely affected each others’ investment and legislative decisions through their use of the Revolving Fund and their participation in the Directing Council and other PAHO structures. In other words, independence cannot be assumed. Both modeling approaches allow for these unobserved and time-varying effects.
Data and variables

We obtained data on vaccine expenditures by country for the years 2000–2013 from the PAHO Revolving Fund.\(^1\) Thirty-one countries and territories purchased vaccines through the Fund at least once over the period. Countries purchased many vaccines recommended by the World Health Organization, including BCG, oral polio, DPT (diphtheria–pertussis–tetanus), measles-containing, and pentavalent vaccines. Vaccine prices did not vary across the countries, but did vary by year, by vaccine, and by presentation (the number of doses per vial). These variations were taken into account in our calculations. Annual vaccine expenditures were computed for each country by multiplying the numbers of doses purchased by the unit price negotiated that year by the Revolving Fund. Expenditures were summed and converted to constant 2013 US dollars using the US Consumer Price Index. Values were logged to approximate normality.

Additional factors affect vaccine expenditures: population size, income, vaccine coverage, infant mortality rate, and the prevalence of vaccine-preventable diseases. The models control for these effects. We extracted annual numbers of births plus infant mortality rates for each country from the United Nations Population Division website.\(^2\) Gross national incomes per capita, measured in constant (2014) dollars, were extracted from the World Development Indicators database.\(^3\) We obtained annual numbers of measles cases and mean coverage levels of third dose of DPT vaccine in each country from the PAHO Immunization Unit. PAHO also provided information on whether and when pneumococcal, rotavirus, and human papillomavirus vaccines were introduced in each country. Using this information, we created dummy variables to indicate the year of each introduction. Quantities purchased, however, were not available to us. Thus, these newer vaccines do not contribute to the summed vaccine expenditures.

An indicator variable was created and coded 1 to denote existence of a vaccine law in a given year, 0 otherwise. We found details of the laws in a database maintained by the PAHO Immunization Unit. A second indicator variable was coded 1 if the law contained an explicit public financing provision, 0 otherwise. Types and total numbers of provisions in each law were measured with polytomous indicators. Continuous variables were lagged and logged to meet model specifications. Variables are described in Table 1.

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Regression model

All models were estimated in Stata 12.0. A time series dataset was prepared covering the period 1980–2013. The following specification was used for the expenditure model:

\[
I_{\text{Exp}}_{it} = \alpha + \beta_1 \text{Law}_{ki(t)} + \beta_2 X_{ki(t)} + u_i + \epsilon_{it},
\]

(1)

where \( I_{\text{Exp}}_{it} \) is the log of the vaccine expenditures observed by Country \( i \) in Year \( t \), \( \alpha \) is the intercept, \( \text{Law}_{it} \) is an indicator for presence of a vaccine law in Country \( i \) at Year \( t \), \( X_{ik(t)} \) is a vector of covariates \( k \) in Country \( i \) in Year \( t \), \( \beta_1 \) and \( \beta_2 \) are parameter vectors, \( u \) is a country-specific random effect, and \( \epsilon \) is an error term assumed to be normally distributed.

Models were fitted using generalized least squares. We adjusted variance estimators using Stata’s robust command. Durbin Watson and Wooldridge tests revealed no autocorrelation in the data. A Hausmann test did not reach significance (\( \chi^2(5) = 2.77, p = 0.10 \)), so the random effects specification was used. Four covariates from Table 1 combined to form the best-fitting model. Substituting lagged DTP3 coverage for contemporaneous coverage improved model fit. A post-estimation Breusch–Pagan Lagrange multiplier test verified that the random effects specification is preferred to a simpler OLS model (\( \chi^2 = 457.7, p < 0.001 \)). Following estimation, we computed elasticities and marginal effects with all other independent variables set to their means.

Table 1: Descriptive statistics of PAHO vaccine law and vaccine expenditures dataset in Latin America and Caribbean countries, 1980–2013

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Mean</th>
<th>SD</th>
<th>Maximum</th>
<th>Minimum</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gross national income p.c</td>
<td>5165</td>
<td>9199</td>
<td>120 490</td>
<td>220</td>
<td>1114</td>
</tr>
<tr>
<td>DPT3 coverage</td>
<td>79.77</td>
<td>20.46</td>
<td>99</td>
<td>3</td>
<td>1089</td>
</tr>
<tr>
<td>Infant mortality rate</td>
<td>30</td>
<td>20</td>
<td>129</td>
<td>5</td>
<td>1105</td>
</tr>
<tr>
<td>No. live births</td>
<td>488 675</td>
<td>953 610</td>
<td>4 312 853</td>
<td>1933</td>
<td>1105</td>
</tr>
<tr>
<td>Measles cases</td>
<td>2089</td>
<td>8541</td>
<td>129 126</td>
<td>0</td>
<td>1115</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dependent variables</th>
<th>Mean</th>
<th>SD</th>
<th>Maximum</th>
<th>Minimum</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine expenditures</td>
<td>4 043 682</td>
<td>7 071 697</td>
<td>45 728 864</td>
<td>0</td>
<td>274</td>
</tr>
<tr>
<td>Vaccine law</td>
<td>0.36</td>
<td>0.48</td>
<td>1.00</td>
<td>0.00</td>
<td>1530</td>
</tr>
</tbody>
</table>

Event history model

In the event history model, countries enter the risk set in 1980 — the first year for which legislative data were obtained. The passage of a vaccine law is the event of interest (failure event). Those not passing a law by 2013 are censored cases. Two countries, Grenada and Honduras, already had vaccine laws prior to 1980; thus, these two cases are left-censored and do not contribute information. To model predictors of the existence of a vaccine law, we used a semi-parametric Cox Proportional Hazards model. The model follows the form

$$\lambda_i(t) = \lambda_0(t) e^{\beta Z_i(t)},$$  \hspace{1cm} (2)

where $\lambda_i(t)$ is the probability (hazard) Country $i$ passed a vaccine law prior to year $t$ conditional on no law being passed in prior years and on a vector of $k$ covariates $Z$, possibly time-varying. Continuous variables $z_k$ are standardized to aid interpretation. $\lambda_0(.)$ is an unspecified baseline hazard function, and $\beta$ is a vector of coefficients to be estimated. Huber–White standard errors are reported using Stata’s robust option.

Exploratory log-rank tests (results not shown) revealed that the hazard of passing a law was significantly higher in countries with the following:

- below median incomes ($\chi^2(1) = 5.64, p = 0.02$),
- above median infant mortality rates ($\chi^2(1) = 2.79, p = 0.10$),
- below median dtp3 coverage levels ($\chi^2(1) = 3.77, p = 0.05$), or
- any reported measles cases ($\chi^2(1) = 3.58, p = 0.06$).

The indicators for new vaccine introductions did not affect survival times. There was insufficient statistical support to perform a log-rank test for vaccine expenditures. We performed post-estimation tests to determine the robustness of the proportionality assumption and of the model in general. Log–log plots showed that neither the covariates nor the residuals were correlated with failure times. Cox–Snell residual plots were linear.

Results

Among the 31 study countries, Table I shows the annual vaccine expenditures averaged $4\,043\,682$ over the period 2000–2013, or
about $8 per infant. Coverage with third dose of DPT vaccine averaged 80 per cent, and the number of measles cases per year per country averaged 2089. Vaccine laws were in place over 36 per cent of the country-years studied. The number of countries with explicit public financing provisions for vaccines in their laws rose from none in 1995 to twenty in 2005 to twenty-nine in 2013.

**Time series regression model**

Regression model results are presented in Table 2. Controlling for the other variable effects, countries with laws spent 98 percent more on vaccines over the period compared to countries without vaccine laws. The marginal effect of having a law was considerable. With other variables set to their means, the predicted vaccine expenditure in countries without laws was $505,792 compared to $1,351,560 for those with laws (results not shown). Infant mortality had a comparable but opposite effect on vaccine spending. Vaccine expenditures were 49 per cent lower among countries in the lower half of the infant mortality

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine law</td>
<td>0.983</td>
</tr>
<tr>
<td>Low infant mortality</td>
<td>-0.492</td>
</tr>
<tr>
<td>Lagged log DTP3 coverage</td>
<td>2.467</td>
</tr>
<tr>
<td>Log GNI per capita</td>
<td>-0.234</td>
</tr>
<tr>
<td>Constant</td>
<td>4.858</td>
</tr>
<tr>
<td>$^g$</td>
<td>0.863</td>
</tr>
<tr>
<td>$^{R^2}$</td>
<td>0.074</td>
</tr>
<tr>
<td>Within</td>
<td>0.194</td>
</tr>
<tr>
<td>Between</td>
<td>0.206</td>
</tr>
<tr>
<td>Overall</td>
<td>23.0^*</td>
</tr>
</tbody>
</table>

| $^a$Dependent variable: Logged government vaccine expenditures, in constant 2013 dollars. |
| $^b$Coded 1 if vaccine law existed, 0 otherwise. |
| $^c$Coded 1 if imr below sample mean, 0 otherwise. |
| $^d$Logged DPT3 vaccine coverage rate, lagged 1 year. |
| $^e$Logged GNI, in 2013 constant dollars. |
| $^f$Significant by Breusch-Pagan test. |
| $^g$Hausmann Test: $\chi^2 = 1.89, p = 0.76$. |
distribution. With other variables at their means, the predicted amount spent on vaccines in the lower mortality countries was $770,581 compared to $1,265,781 in high-mortality countries (results not shown). Income was also negatively associated with vaccine spending, although the relationship is only marginally significant. For every $14 increase in gross national income per capita, vaccine expenditures fell by $100 (elasticity \(-0.143\), standard error \(0.086\), \(z = -1.66\), \(p = 0.096\), 95 per cent confidence interval \(-0.311, 0.026\)). Vaccine spending and immunization program performance, measured by DPT\(_3\) coverage the previous year, were strongly positively associated. An 80 per cent increase in coverage was associated with a $100 increase in spending (elasticity 0.800, standard error 0.280, \(z = 2.86\), \(p = 0.004\), 95 per cent C.I. = \(0.252, 1.348\)). Numbers of measles cases, legal provisions, and the new vaccine introduction indicators were all insignificant and were excluded from the model. As mentioned, many other country-level factors likely affected the amounts governments spent on vaccines. These unobserved effects account for most of the variance measured and are captured in the random effect (\(\rho = 0.86\)).

The key finding in the panel data regression is that vaccine spending was higher if the country had a vaccine law in place, controlling for income and program performance. The next section explores how those laws came to exist.

**Event history analysis**

By 2013, the data show that 26 countries (58 per cent) had some kind of vaccine laws, leaving 16 countries right-censored. The smoothed hazard function for the Latin American countries is shown in Fig. 1. The probability of a country passing a vaccine law was highest around 1985. It fell to near zero in 1990, after which it again rose.

The best-fitting hazard model is shown in Table 3. Income and birth cohort data were missing for the smallest 15 countries, reducing the number of subject countries to 29. Of these, 23 countries passed laws during the period 1980–2013. The probability of passing a law was lower among higher-income countries. Expressed as a hazard ratio, that probability fell by 0.2 per cent for every standard deviation increase in GNI. The hazard rose more markedly with the size of the annual birth cohort, increasing by 29 per cent for every standard deviation increase in the number of births. The probability of passing a
The law was also influenced by immunization program performance (DTP3 coverage). Among countries below the median DTP3 coverage, the probability was just 49 per cent that of countries above the median.

**Discussion**

We examined the dynamics of vaccine spending and vaccine legislation in Latin America over the period 1980–2013. We estimated both panel
data and event history models. Association and temporal order were demonstrated using both approaches. The results suggest a causal link that passing an immunization law led a country to increase its vaccine spending. There were no vaccine expenditure data available prior to 2000, which precluded testing the reverse causal hypothesis. Nor does the study show a causal mechanism.

The covariates reveal clues about the underlying processes affecting both outcomes. Countries with higher incomes were significantly less likely to have passed vaccine laws. One interpretation is that fiscal space in these countries was large enough and sufficiently stable over time for them to internalize the costs without special legislation to earmark or otherwise protect vaccine financing. A second possibility is that citizens in wealthier countries were less exposed to the risk of mortality due to vaccine-preventable diseases and were therefore less vocal about the need for a vaccine law.

Infant mortality levels also affected countries’ vaccine spending decisions. Countries with high infant mortality tended to spend more on vaccines. In high-mortality countries, one might argue that immunization programs are less efficient and less effective; therefore, proportionately more doses of vaccines are needed to protect a given population.

A third factor, affecting both outcomes, was DTP3 coverage, which had independent, additive effects over and above income or mortality. A country with comparatively higher DTP3 coverage spent more, and was more likely to have passed a law, compared to other countries with similar incomes and mortality regimes but lower vaccine coverage levels. Vaccine coverage is a direct measure of vaccine use and therefore of vaccine costs to the governments. High coverage also indicates a successful and high-performing program, making it an even more valuable public good.

In any society, laws are reflections of current social conditions. This truism is illustrated by the development of vaccine-related legislation in Latin America. Legislative action steadily increased among Latin American countries as their immunization programs expanded. Following a prolonged, region-wide debt crisis during the 1980s, most countries experienced sustained economic growth, enabling greater vaccine spending. In the political sphere, there was a secular trend toward democratization in the Region. Politicians found they could win elections by demonstrating support for immunization and other
effective social programs.\textsuperscript{17} Taken together, the results reported here are consistent with this sociological perspective. The rapid declines in child mortality and in fertility, increasing health services utilization, and rising expectations for what government can do are three dimensions of Latin America’s health transition — a complex of epidemiological, demographic, and social shifts plus the adaptation of health services to those shifts.\textsuperscript{18,19}

Our study faced several limitations. The models are necessarily parsimonious, as they examine country-level processes in just one region. More elaborate models might have been fitted were data available from other regions and countries. More qualitative data could shed more light on the underlying mechanisms through which countries actually pass vaccine laws. Our analyses were further limited in that vaccine expenditures prior to 2000 could not be retrieved. As most of the vaccine laws had been passed in the preceding two decades, this meant there was insufficient statistical support to include expenditures as a predictor in the event history model.

Global vaccine coverage levels have been stagnant in recent years. To remedy this, the global immunization community came together in 2010–2011 to create a Decade of Vaccines Global Vaccine Action Plan.\textsuperscript{20} The plan outlines six strategic objectives and includes both public spending and the existence of vaccine legislation as indicators of country commitment. A growing number of African and Asian countries are indeed spending more on immunization and enacting vaccine laws, increasing the likelihood they will achieve the 2020 Global Vaccine Action Plan objectives.\textsuperscript{21} The findings we report here augur well for the prospects of sustainable financing for immunization programs in those regions.

Conclusion

Among a sample of Latin American countries studied, those with vaccine laws spent more on vaccines than countries without them. Less was revealed about the forces leading countries to pass such laws. Additional research is needed to validate and to build on these findings elsewhere, particularly in Eurasian, Asian, and African countries, which are currently engaged in the global polio eradication effort and whose own health transitions continue apace.
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