Economic and health burden of rotavirus gastroenteritis for the 2003 birth cohort in eight Latin American and Caribbean countries

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Suggested citation Rheingans RD, Constenla D, Antil L, Innis BL, Breuer T. Economic and health burden of rotavirus gastroenteritis for the 2003 birth cohort in eight Latin American and Caribbean countries. Rev Panam Salud Publica. 2007;21(4):192–204.

ABSTRACT

Objective. *To estimate the health and economic burden of rotavirus gastroenteritis in hospital and outpatient settings in eight Latin American and Caribbean countries (Argentina, Brazil, Chile, Dominican Republic, Honduras, Mexico, Panama, and Venezuela).*

Methods. *An economic model was constructed using epidemiological data from published articles, national health administration studies, and country-specific cost estimates. For each of the eight countries, the model estimated the rotavirus outcomes for the 2003 birth cohort during the first five years of life. The main outcome measures included health care costs, transportation costs, lost wages, and disease burden expressed in disability-adjusted life years. Estimates were expressed in 2003 US dollars. All future costs and disability-adjusted life year estimates were discounted at a rate of 3%. Sensitivity analyses evaluated the impact of specific variables on the medical cost of treating rotavirus.*

Results. *For every 1 000 children born during 2003 in the eight Latin American and Caribbean countries studied here, we estimated that rotavirus gastroenteritis would result in an average of 246 outpatient visits, 24 hospitalizations, 0.6 deaths, and US$ 7 971 in direct medical costs during their first five years of life. The incidence of rotavirus-associated outpatient visits and the cost of outpatient visits were predicted to have the largest impact on the total medical cost per child.*

Conclusions. *Rotavirus gastroenteritis is likely to result in substantial disease and economic burden to health systems in Latin American and Caribbean countries, and the foreseeable burden should be an important consideration in evaluating the cost-effectiveness of vaccination.*

Key words Rotavirus; gastroenteritis; costs and cost analysis; cost of illness; models, economic; Latin America; Caribbean Region.

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Rotavirus is the most important viral cause of acute gastroenteritis in children under 5 years of age, causing severe dehydrating diarrhea and vomiting in infants and young children worldwide. In Latin America, it is estimated that rotavirus gastroenteritis is associated with more than 15 000 deaths in under children under 5 years of age (1). In addition, several studies have documented that rotavirus gastroenteritis is a common cause of hospitalization in children of this age group (1–7). A recent review of 28 studies of children hospitalized with severe diarrhea in Latin America

found that 31% to 38% of those hospitalizations were attributed to rotavirus gastroenteritis (8).

Although the main impact of rotavirus gastroenteritis is the morbidity and mortality it causes in children, information on the economic burden of disease can aid decisionmakers in choosing interventions to improve health. With the development of rotavirus vaccines, information on the economic burden of rotavirus and the potential costs averted by vaccination can provide decisionmakers with an estimate of the net impact of vaccination on financial resources, either in the health sector or for society as a whole.

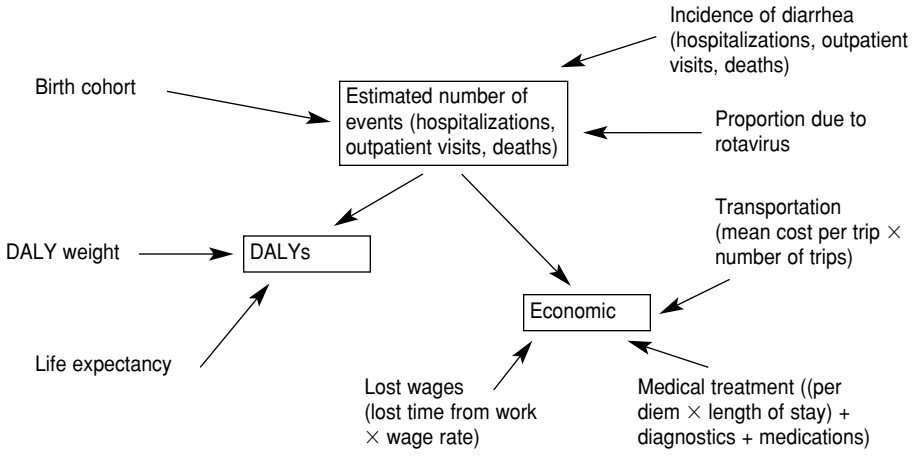
Few studies have evaluated the economic burden imposed by rotavirus gastroenteritis in Latin America. Among publications retrieved by a MEDLINE search of health economic studies of rotavirus or gastroenteritis from 1995 to 2005, only one study was undertaken in Latin America (6). According to this study, the Peruvian Ministry of Health was estimated to spend over US$ 2.6 million annually to treat young children with rotavirus gastroenteritis (6).

The purpose of this study was to estimate the impact of rotavirus gastroenteritis in children on the cost of direct medical treatment to the health care system in eight Latin American and Caribbean countries: Argentina, Brazil, Chile, the Dominican Republic, Honduras, Mexico, Panama, and Venezuela. In addition to health care costs, nonmedical direct (e.g., transportation) and indirect costs (e.g., productivity losses) were also considered. The results should provide insight into the reductions that could be achieved in the disease and economic burden by preventing rotavirus infection.

METHODS

The estimates provided in this analysis of the cost of rotavirus gastroenteritis to the health care system and society were obtained with a generalized model populated with epidemiological and cost data for the eight Latin American and Caribbean countries. The model estimated the expected rotavirus gastroenteritis-associated health outcomes and costs during the first five years of life for the 2003 annual birth cohort in each country (Figure 1). Country estimates were based on a combination of country-specific data and extrapolation from other countries for which data were lacking. Simulation techniques were used to calculate ranges for these estimates.

FIGURE 1. Framework for estimating the health and economic burden of rotavirus gastroenteritis in terms of disability-adjusted life years (DALYs)



The eight countries were selected to provide estimates for different representative settings within Latin America and the Caribbean, so geographic range and income diversity were considered in choosing the countries. Income levels ranged from a per capita gross domestic product (GDP) of 2003 US$ 1 001 in Honduras, a lower-middle-income country, to a per capita GDP of 2003 US$ 6 121 in Mexico, an upper-middle-income country (9). Larger countries were selected to cover a significant portion of the Latin American and Caribbean population. The availability of epidemiological data for a specific country was considered, although it was not a necessary condition for inclusion.

The primary perspective for this analysis was that of society as a whole, including the direct medical costs, direct nonmedical costs, and indirect costs associated with medical treatment in formal inpatient and outpatient settings. Direct medical costs included the costs of tests, medication, supplies, facilities, and personnel needed for treatment. Nonmedical direct costs included the cost of transportation to and from the medical facility. Indirect costs were based on caregiver productivity losses that occur as a result of the child being sick. The main outcome measures were: (1) the health care costs of rotavirus gastroenteritis during the first five years of life for an annual birth cohort, (2) the nonmedical direct and the indirect costs for each cohort, and (3) the disease burden expressed in disability-adjusted life years (DALYs). All estimates were based on the expected events and costs for an annual birth cohort until 5 years of age, after which rotavirus infection rarely causes severe morbidity or mortality. Estimates were expressed in 2003 US$. All future costs and DALYs estimates were discounted at a rate of 3%.

Estimating disease burden of rotavirus gastroenteritis

For each country, the epidemiological burden of rotavirus gastroenteritis was estimated for the 2003 birth cohort until the age of 5 years. A quantitative model was used to predict the expected events during the first five years of life. Predicted estimates were

modeled over time rather than by directly following the cohort prospectively in an epidemiological study for the five-year period. The key outcomes included hospitalizations, outpatient visits, and deaths. The risks of hospitalization, outpatient visit, and death were based on the cumulative risk of each event due to acute gastroenteritis, and the proportion of those events associated with rotavirus. Estimates of the number of events were calculated based on the 2003 birth cohort size and the estimated age distribution of each event.

Hospitalization. The 5-year cumulative risk of hospitalization for rotavirus gastroenteritis was estimated for each country based on epidemiological data from published articles and national health administration studies. Published estimates of hospitalization for diarrheal disease and rotavirus gastroenteritis were available for children under 3 years of age in Chile (4, 10), and for children under 5 years of age in Venezuela (4, 10). Because the Chilean study reported the rotavirus hospitalization rate for children under the age of 3 years, the incidence rate was converted to the under-five rate on the basis of published estimates (3, 7, 11–13). The 5-year cumulative risk of hospitalization for rotavirus in Venezuela was adjusted since only one-third of the "hospitalized cases" reported in the study were actual admissions for overnight care or longer.[4]

The 5-year cumulative incidence of hospitalization for diarrhea in Argentina, Brazil, Honduras, and Mexico was based on national administrative data (14–18). Because national administrative data do not include hospitalizations that occur in the private health care sector, the rates were adjusted to include this sector (5, 18–20). Data for the incidence of hospitalization for diarrhea in the Dominican Republic and Panama were unavailable; therefore, cumulative incidence estimates for the two countries were based on the mean rate for Argentina, Brazil, Chile, Honduras, Mexico, and Venezuela (4, 10, 14–18).

The total number of hospitalizations of children under 5 years of age for diarrhea recorded by the various sources was divided by the birth cohort (21) to obtain the five-year cumulative incidence of hospitalization for diarrhea in each of the eight countries. The proportion of hospitalizations for rotavirus infection was based on published estimates for Argentina (5), Brazil (22–28), Chile (4), Mexico (29), and Venezuela (10). Because published estimates were not available for the Dominican Republic, Honduras, and Panama, the proportion of hospitalizations for diarrhea attributed to rotavirus for these countries was estimated based on other countries in Latin America and the Caribbean (4–6, 11, 29). The cumulative risk of hospitalization for rotavirus gastroenteritis was then calculated by multiplying the cumulative risk of hospitalization for diarrhea by the proportion attributed to rotavirus gastroenteritis.

Outpatient visits. The five-year cumulative incidence of outpatient visits for rotavirus gastroenteritis was estimated from published and administrative data. Published estimates of outpatient visits for rotavirus gastroenteritis were available in Chile for children under 3 years of age (4) and in Venezuela for children under 5 years of age (10). The Chilean data were adjusted to a five-year risk on the basis of published estimates (30, 31), and were adjusted to include data regarding nonemergency visits (32). The incidence of outpatient visits for rotavirus in Venezuela was adjusted to include outpatient visits in nonhospital settings, with data that were based on interviews with eight Venezuelan physicians.

The five-year cumulative incidence of outpatient visits for diarrhea in Argentina, Honduras, Mexico, and Panama was calculated from national administrative data (16–18, 33, 34), and adjusted for inclusion of the private sector (5, 18, 20, 35). Because data were unavailable for Brazil and the Dominican Republic, the cumulative risk of an outpatient visit due to diarrhea in these two countries was based on the mean risk calculated for Argentina, Chile, Honduras, Mexico, Panama, and Venezuela.

For Brazil, Chile, and Venezuela the proportion of outpatient visits for diarrheal disease attributed to rotavirus was based on published data (4, 10, 36–39). The proportion of outpatient visits attributed to rotavirus diarrhea for the Dominican Republic, Honduras, Mexico, and Panama was based on extrapolation from other countries in Latin America and the Caribbean (4–6, 10, 40). For Argentina, the rotavirus proportion was based on a published study (5) and a personal communication.[5] The cumulative risk of an outpatient visit for rotavirus gastroenteritis was calculated by multiplying the cumulative risk of an outpatient visit for diarrhea by the proportion attributed to rotavirus gastroenteritis.

Mortality. The five-year cumulative incidence of diarrheal mortality was based on country-specific estimates, using ICD-10 categories A00–A09 (41). National administrative data on deaths from diarrhea were available for Argentina, Brazil, Mexico, Panama, and Venezuela (21, 42–45). Estimates of the risk of death due to diarrheal disease in Chile and the Dominican Republic were based on the WHO Mortality Database (46). For Honduras, estimates were based on the Pan American Health Organization estimate of mortality in children under 5 years of age (21), and on a national survey estimate of the proportion attributable to diarrhea (47). The five-year cumulative risk of death due to diarrheal disease was then calculated by dividing the estimated number of deaths due to diarrheal disease in under-five children by the birth cohort of each country (21). The cumulative risk of death due to rotavirus gastroenteritis was calculated by multiplying the risk of death due to

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diarrheal disease by the proportion of deaths from diarrhea attributed to rotavirus. Because no studies estimated the proportion of deaths from diarrhea attributed to rotavirus, the proportion was assumed to be the same as that for hospitalized cases.

Disability-adjusted life years. In addition to estimating the number of events, the disease burden was also expressed in terms of DALYs, an index that makes comparisons with other diseases possible. The DALYs estimate includes two components: years of life lost (YLLs) due to premature mortality, and years lived with disability (YLDs). The former was calculated based on the average country-specific life expectancy at birth and 1 year of age (48). To calculate YLDs, only morbidity from a disease severe enough to require medical care was considered. This component was calculated from default disability weights from the Global Burden of Disease Study (49) and the World Health Organization's guidelines for cost-effectiveness studies (50), assuming an average duration of illness of six days (51). Because of the short duration of illness from gastroenteritis, YLDs contributed very little to the DALYs estimate, so the estimate was based primarily on the YLLs. To ensure comparability, a discount rate of 3% and age weighting were included (49).

Table 1 summarizes the values used to calculate the disease burden for rotavirus gastroenteritis.

Estimating medical costs associated with rotavirus gastroenteritis

The economic burden of rotavirus gastroenteritis to the health care system in the eight countries was estimated by combining the number of each type of event with information on the costs associated with the event. This information was combined in a spreadsheet-based decision-analytic model. For hospital and outpatient events, these were partitioned into the cost of the visit (including facilities and personnel) and the cost of the resources used for treatment (diagnostic tests and medication). For each country, baseline estimates were based on resource use information from a prospective rotavirus surveillance study and facility-specific cost data. To compare costs among countries, two alternative sources of cost estimates were used: (1) the WHO-CHOICE (Choosing Interventions that are Cost Effective) project (52) and (2) estimates obtained from physician interviews.

Prospective rotavirus surveillance study. Economic cost data were collected as part of an ongoing rotavirus gastroenteritis surveillance study done prior to a randomized vaccine trial (53). The prospective study was conducted in one or more sites in each of the eight countries. Participating sites generally consisted of secondary- or tertiary-level facilities that provided inpatient and outpatient care to children. Eligible cases were children less than 24 months of age who came to the center with severe gastroenteritis, defined as an episode of diarrhea (the passage of three or more loose or watery stools within a 24-hour period), with or without vomiting, that required overnight hospitalization or rehydration therapy equivalent to World Health Organization (WHO) plan B (oral rehydration therapy) or plan C (intravenous rehydration therapy), in a medical facility such as a hospital, clinic, or supervised rural health care center. At each site, economic data were collected for a sample of approximately 60 inpatients and 60 outpatients. Sample size was determined based on the recommendation of the WHO guide to costing diarrheal disease (54) in order to ensure an estimated mean direct medical cost within 15% of the actual mean. Stool samples were tested for rotavirus with an enzyme-linked immunoassay.

Health economic data were collected during 2003. The surveillance study contained an economic component to calculate the direct medical costs, direct nonmedical costs, and indirect costs associated with rotavirus gastroenteritis. A cost questionnaire was administered to the caregivers of patients with gastroenteritis. Questions asked about nonmedical direct costs (cost of transporting the child to the hospital and visiting the child in the hospital) and indirect costs (time lost from paid work to care for the child). Investigators also reported patient data regarding the length of stay and the utilization of diagnostics and medication to treat gastroenteritis.

Survey data were analyzed using SAS statistical software (SAS Institute Inc., Cary, North Carolina, United States of America). Separate estimates were generated for inpatients and outpatients. Inpatients were those who were classified as inpatients and spent a minimum of one day in the hospital, and outpatients were those who were not classified as inpatients and spent a maximum of one day at the hospital or clinic. For countries in which outpatients can stay at the hospital "under observation" but are not admitted, the outpatient definition was adapted to include patients who stayed for more than one day at the center's rehydration facility.

Health care costs were calculated as the sum of the visit cost at the hospital or outpatient setting, the cost of diagnostics, and the cost of medication. Estimates of the hospital per diem costs were based on information from hospital finance departments of public health care facilities, with the exception of Chile since per diem data were available from private facilities as well. The cost per stay as an inpatient was calculated by multiplying the per diem rate (which includes the cost of accommodation, administration, food, and personnel) by the duration of stay (between three and four days).

The cost per outpatient visit was calculated as the weighted mean of the cost of visiting a pediatrician, general practitioner, emergency room, or rehydration facility based on the proportion of patients seen in each of these four outpatient settings. This information was obtained from physician interviews done in 2003. Health care utilization patterns varied by country; however, the proportion seen by a pediatrician or in an emergency department was generally greater than the

TABLE 1. Input variables and ranges used for estimating the economic burden of rotavirus gastroenteritis for the 2003 birth cohort in eight Latin American and Caribbean countries

Variable (source)	Argentina	Brazil	Chile	Dominican Republic	Honduras	Mexico	Panama	Venezuela
Birth cohort, 2003 (21)	726 000	3 471 000	286 000	203 000	206 000	2 285 000	70 000	582 000
5-year risk of hospitalization for for gastroenteritis (4, 10, 14–18)[a]	0.093	0.112	0.060	0.065	0.038	0.018	0.065	0.070
Upper and lower bounds[b]	0.08, 0.11	0.10, 0.13	0.05, 0.07	0.05, 0.08	0.03, 0.04	0.01, 0.02	0.05, 0.08	0.06, 0.08
Proportion of gastroenteritis hospitalizations due to rotavirus[a] (4–6, 10, 22–29, 40)	0.34	0.31	0.47	0.37	0.37	0.40	0.37	0.33
Upper and lower bounds	0.29, 0.39	0.26, 0.36	0.40, 0.54	0.30, 0.44	0.30, 0.44	0.34, 0.46	0.30, 0.44	0.28, 0.38
5-year risk of an outpatient visit for gastroenteritis (4, 10, 16–18, 33, 34)[a]	1.38	1.08	0.69	1.08	1.07	1.06	1.13	1.15
Upper and lower bounds[b]	1.17, 1.59	0.81, 1.35	0.59, 0.79	0.81, 1.35	0.91, 1.23	0.90, 1.22	0.96, 1.30	0.98, 1.32
Proportion of gastroenteritis outpatient visits due to rotavirus (4–6, 10, 36–40)[a]	0.26	0.19	0.34	0.25	0.25	0.25	0.25	0.23
Upper and lower bounds[b]	0.22, 0.30	0.16, 0.22	0.29, 0.39	0.20, 0.30	0.20, 0.30	0.20, 0.30	0.20, 0.30	0.20, 0.27
5-year risk of death for gastroenteritis (per 1 000 births) (21, 41–45)[a]	0.40	2.30	0.10	5.90	8.70	1.01	1.44	2.00
Upper and lower bounds[b]	0.34, 0.46	1.96, 2.65	0.09, 0.12	5.02, 6.79	7.40, 10.01	0.86, 1.16	1.22, 1.66	1.70, 2.30
Proportion of gastroenteritis deaths due to rotavirus[c]	0.34	0.31	0.47	0.37	0.37	0.40	0.37	0.33
Upper and lower bounds[b]	0.27, 0.41	0.25, 0.37	0.38, 0.56	0.30, 0.44	0.30, 0.44	0.32, 0.48	0.30, 0.44	0.26, 0.40
Proportion seen in private sector (4, 5, 18–20, 35)	0.46	0.25	0.27	Data unavailable	0.12	0.15	0.07	Data unavailable
Gross domestic product per capita (2003 US$) (9)	3 381	2 788	4 591	1 821	1 001	6 121	4 328	3 319
Average life expectancy (years) (47)	74.2	68.9	75.8	69.6	69.1	74.0	74.1	73.8
Mean female hourly wage (US$) (59–62)	0.87	1.58	2.11	0.71	0.53	1.86	2.10	1.05

[a] The shape of the distribution was defined as triangular distribution since the true population value was more likely to be closer to the chosen value for the analysis than the minimum or maximum values defined by the range.
[b] The upper and lower bounds of the distributions were the ones used in the sensitivity and uncertainty analyses.
[c] The proportion of gastroenteritis mortality attributable to rotavirus was based on the proportion of hospitalizations attributable to this diagnosis. The shape of the distribution was defined as uniform since the true population value was equally likely to be any value within the specified range.

proportion seen by a general practitioner or in a rehydration facility. Costs for these types of outpatient visits were based on the average costs for public facilities.

Mean total diagnostic and medication costs for treating gastroenteritis were calculated for both inpatients and outpatients for each country. The unit cost for each diagnostic test was based on estimates provided by the finance departments of public hospitals, and costs associated with medications were based on the listing of medications and national formularies (55, 56).

Alternative health care cost estimates. To compare the findings across countries, we also estimated inpatient and outpatient visit costs with a standardized approach developed by WHO for its WHO-CHOICE project (52) and data from cost studies of diarrhea (57). The WHO-CHOICE project provided estimates of the per-diem and per-visit cost of public health care facilities for 14 epidemiological categories based on geographical region and mortality stratum. The per-diem and per-visit cost estimates included the cost of the facility, personnel, equipment, and food, and excluded the cost of medications and diagnostic tests (52). Based on information from cost studies of diarrheal disease conducted in Mexico and the Philippines, we estimated that these costs would add 33% to the cost of hospitalization, and 65% to the cost of outpatient visits (57).

Because the WHO-CHOICE model was developed using year-2000 international dollars, all costs were converted to 2003 US$ using the consumer price index, purchasing power parity conversion factors, and official exchange rates (9, 58). "International dollars" are used to express the value of a quantity in a local currency based on its purchasing power compared to a US$ rather than the actual exchange rate. A hospital per-diem rate was estimated for each country as a weighted average of estimates for public primary-, secondary-, and tertiary-level facili-

ties, using the proportions of each from the multicountry study (59). The cost of hospitalization was calculated as the product of the per-diem cost and a duration of 3.5 days (6, 60, 61). Country-specific outpatient visit costs were calculated by adjusting the WHO-CHOICE regional estimate proportionally to the country-specific hospital per-diem cost.

The second alternative approach used physician interviews to estimate resource utilization for the treatment of rotavirus gastroenteritis, along with facility- and country-specific unit cost estimates. Interviews of four to eight physicians in each country, mostly from public health settings, were conducted in 2003 to characterize the typical management of rotavirus gastroenteritis. Interviews included questions regarding care for patients with moderate rotavirus gastroenteritis, and for patients with severe rotavirus gastroenteritis.

Estimating societal costs of rotavirus gastroenteritis

In addition to health care costs, nonmedical direct (e.g., transportation costs) and indirect costs (e.g., productivity losses) were also calculated based on the prospective rotavirus surveillance study. Caregivers of inpatients and outpatients were asked how much money they spent to transport their child or themselves to the health facility. Caregivers were also asked to quantify time lost from paid work due to their child's illness. The average indirect cost was estimated by multiplying the mean hours lost by the mean female hourly wage for each of the countries (62–65).

Uncertainty and sensitivity analyses

Although country-specific data on the epidemiology of the disease and the associated health care costs were available for most countries, the quality and relevance of the data were limited for others, a limitation that created uncertainties regarding the final economic burden estimates. Two approaches were used to address this uncertainty: sensitivity and uncertainty analyses. A one-way sensitivity analysis was conducted by varying individual input parameters by ± 20% to assess their impact on the economic burden in each country. An uncertainty analysis was conducted to evaluate the overall impact of uncertainty on the estimates, to develop upper and lower bounds for the estimates, and to assess the contribution of individual parameters to overall uncertainty.

For each country, burden estimates were calculated in a spreadsheet-based decision-analytic model that estimated the frequency of different events and the costs associated with each. A Monte Carlo model was developed based on this model. In Monte Carlo analysis, individual point estimates of parameters are replaced with distributions of potential values (66). In a series of iterations, individual values are randomly selected from each of the distributions, and results are calculated and stored. The process is repeated for a large number of iterations (10 000 in this case). The final product is a distribution of potential outcomes that describe the likely range of actual expected results.

For national disease burden variables, distributions were used to characterize the cumulative incidence of illness outcomes (hospitalization, outpatient visits, and death) in each country, and the proportion due to rotavirus. The distributions specified a range around the value chosen for analysis, and described the likelihood that the true population value would be the value chosen. Wider distributions were used for countries for which the estimates were extrapolated from other countries. For the cost variables, input distributions were based on the mean costs and standard errors from the baseline analysis described above. Table 1 shows the best estimates and distributions used in the analysis.

Upper- and lower-bound uncertainty limits (5% and 95%) were estimated for the key output parameters: direct medical costs and total societal costs for each country. In addition, a contribution-to-variance analysis was done to determine the contribution of the individual input parameters to the overall uncertainty regarding total societal costs.

RESULTS

Disease burden

In the eight countries together, which represent 68% of the total annual births in Latin America, rotavirus gastroenteritis was predicted to be responsible for approximately 2 000 000 outpatient visits, 190 000 hospitalizations, and 5 000 deaths for the annual birth cohort. In each of the countries, per 1 000 children, rotavirus gastroenteritis was predicted to result in 205 to 359 outpatient visits, 7 to 35 hospitalizations, and 0.05 to 3.2 deaths (Table 2). The DALYs resulting from these events ranged from 2 to 107 per 1 000 children, with lower rates observed in higher-income countries due to lower mortality.

Economic burden

The mean predicted costs (direct medical, direct nonmedical, and indirect) for hospital and outpatient events associated with gastroenteritis are shown in Table 3. In each of the countries, direct medical costs were estimated to account for the majority of the total costs of hospitalizations and outpatient visits. The cost of medications and diagnostics was expected to account for 5% to 25% of the medical costs of hospitalization, and 30% to 75% of the costs of outpatient visits. The total estimated medical costs per hospitalization ranged from US$ 72.49 in the Dominican Republic to US$ 190.12 in Panama, and the total estimated medical costs per outpatient visit ranged from US$ 6.54 in the Dominican Republic to US$ 33.99 in Chile. The calculated treatment costs for hospital and outpatient events were consistent with estimates provided by the two alternative methods (WHO-CHOICE and physician interviews).

TABLE 2. The burden of rotavirus gastroenteritis in eight Latin American and Caribbean countries, estimated as the expected number of events for the 2003 birth cohort during the first five years of life

	Argentina	Brazil	Chile	Dominican Republic	Honduras	Mexico	Panama	Venezuela	Total
Birth cohort	726 000	3 471 000	286 000	203 000	206 000	2 285 000	70 000	582 000	7 829 000
Events									
Hospitalizations	22 956	120 513	8 008	4 882	2 896	16 086	1 684	13 502	190 528
Outpatient visits	260 489	712 249	66 924	54 810	55 105	605 525	19 775	153 648	1 928 525
Deaths	99	2 475	13	443	663	923	37	384	5 038
DALYs[a]	3 549	83 365	543	14 823	22 120	31 768	1 277	13 098	170 542
Events per 1 000 births									
Hospitalizations	32	35	28	24	14	7	24	23	24
Outpatient visits	359	205	234	270	268	265	283	264	246
Deaths	0.1	0.7	0.05	2.2	3.2	0.4	0.5	0.7	0.6
DALYs	5	24	2	73	107	14	18	23	22

[a] DALYs = disability-adjusted life years.

TABLE 3. Estimated costs in 2003 US dollars of treating rotavirus gastroenteritis in the 2003 birth cohort during the first five years of life in eight Latin American and Caribbean countries, using prospectively collected cost data and two alternative methods for estimating health care costs

	Argentina	Brazil	Chile	Dominican Republic	Honduras	Mexico	Panama	Venezuela
Hospitalization	No. = 60	No. = 43	No. = 41	No. = 29	No. = 32	No. = 49	No. = 196	No. = 55
Per diem cost	39.67	35.07	41.70	16.64	24.36	50.98	53.00	19.91
Total accommodation cost[a]	142.81	129.76	125.10	66.56	95.00	173.33	153.70	81.63
Diagnostics and medication	20.39	21.21	40.27	5.93	24.75	14.11	36.42	43.31
Total direct medical costs	163.20	150.97	165.37	72.49	119.75	187.44	190.12	124.94
Alternative estimates of direct medical costs								
Alternative 1[b]	133.56	123.13	189.74	80.87	57.50	263.53	201.43	164.00
Alternative 2[c]	194.10	179.16	178.59	78.35	124.07	227.92	163.70	81.70
Transportation	7.12	1.49	12.72	1.99	2.83	7.36	8.99	4.91
Indirect cost	11.57	18.58	18.27	5.43	2.60	21.08	15.81	8.85
Outpatient visit	No. = 50	No. = 52	No. = 53	No. = 224	No. = 38	No. = 66	No. = 91	No. = 21
Per visit cost	5.62	5.39	14.01	4.49	5.81	13.30	15.88	5.48
Diagnostics/medication	7.65	5.42	19.98	2.05	15.96	10.86	12.54	17.79
Total direct medical costs	13.27	10.81	33.99	6.54	21.77	24.16	28.42	23.27
Alternative estimates of direct medical costs								
Alternative 1[b]	12.06	11.12	17.13	7.31	5.20	23.79	18.18	14.80
Alternative 2[c]	8.41	12.64	20.13	5.84	12.93	18.51	17.48	9.87
Transportation	0.49	0.04	0.66	2.05	1.95	1.58	3.46	1.55
Indirect cost	2.09	8.35	7.64	4.47	2.26	13.54	9.44	4.10

[a] Total accommodation cost = per diem cost × average length of stay. For the eight countries, the average length of stay of in days was: Argentina, 3.6; Brazil, 3.7; Chile, 3.0; Dominican Republic, 4.0 (based on physician interviews); Honduras, 3.9; Mexico, 3.4 (based on the hospital-based surveillance study and physician interviews); Panama, 2.9; and Venezuela, 4.1.
[b] Alternative 1, WHO-CHOICE and data from diarrheal cost studies (51).
[c] Alternative 2, physician interview data obtained in 2003.

Table 4 shows the estimated health care system and societal costs of these rotavirus-associated events for the 2003 birth cohort in each country, and upper and lower uncertainty limits for these estimates. From the health care system perspective, the average estimated direct medical costs ranged from US$ 3 400 to over US$ 16 000 per 1 000 births, with higher costs tending to occur in the higher-income countries. In all countries except Argentina and Brazil, where rotavirus hospitalization rates are higher, the majority of the total costs were predicted to result from outpatient visits. From the societal perspective, total estimated costs (including nonmedical and indirect costs) of rotavirus gastroenteritis ranged from US$ 5 000 to almost US$ 19 000 per 1 000 births. Overall, direct

TABLE 4. The estimated economic burden, in 2003 US$, of rotavirus gastroenteritis in the 2003 birth cohort during the first five years of life in eight Latin American and Caribbean countries

	Argentina	Brazil	Chile	Dominican Republic	Honduras	Mexico	Panama	Venezuela
Direct medical costs								
Hospitalization	3 685 584	17 813 038	2 233 323	346 417	339 574	2 952 068	313 370	1 662 273
Outpatient visit	3 375 524	7 519 460	2 407 961	350 184	1 172 105	14 290 600	549 018	3 491 822
Total	7 061 108	25 332 499	4 641 283	696 601	1 511 679	17 242 669	862 387	5 154 096
Uncertainty range	6 067 380 to 8 126 045	21 765 457 to 29 111 179	3 885 593 to 5 469 498	559 376 to 844 638	1 253 134 to 1 791 978	14 595 840 to 19 788 196	732 265 to 1 003 551	4 423 414 to 5 955 345
Nonmedical direct costs								
Hospitalization	160 027	175 807	99 730	9 512	8 025	143 323	14 818	64 910
Outpatient visit	124 677	27 829	43 145	109 752	104 960	2 141 118	66 833	232 626
Total	284 704	203 636	142 875	119 264	112 986	2 284 441	81 651	297 536
Indirect costs								
Hospitalization	260 045	2 192 280	137 756	21 175	7 373	332 006	26 059	116 996
Outpatient visit	531 784	5 809 228	480 473	195 413	121 646	8 008 492	182 343	615 334
Total	791 829	8 001 508	618 230	216 588	129 019	8 340 498	208 402	732 330
Total costs								
Hospitalization	4 105 656	20 181 125	2 470 809	377 105	354 972	3 427 397	354 247	1 844 179
Outpatient visit	4 031 985	13 356 517	2 931 579	655 349	1 398 712	24 440 211	798 194	4 339 782
Total	8 137 641	33 537 642	5 402 388	1 032 454	1 753 684	27 867 608	1 152 441	6 183 961
Uncertainty range	7 026 852 to 9 315 473	28 714 867 to 38 649 243	4 575 937 to 6 313 709	844 021 to 1 235 194	1 457 934 to 2 069 514	23 244 283 to 32 609 187	981 935 to 1 337 970	5 260 654 to 7 184 664
Cost per 1 000 births								
Direct medical costs	9 726	7 298	16 228	3 432	7 338	7 546	12 320	8 856
Nonmedical direct costs	392	59	500	588	548	1 000	1 166	511
Indirect costs	1 091	2 305	2 162	1 067	626	3 650	2 977	1 258
Total	11 209	9 662	18 889	5 086	8 513	12 196	16 463	10 625

medical costs accounted for 73% of the total estimated cost in the eight countries. Hospitalization events accounted for 17% to 70% of direct estimated medial costs, and 12% to 60% of total estimated costs in each country.

Sensitivity and uncertainty

The results of the one-way sensitivity analysis are shown in Table 5. The table reports the estimated cost per 1 000 children in 2003 US$ for each country, using three scenarios: baseline, a 20% increase in the selected value, and a 20% decrease. Compared to the baseline figures, a 20% increase or a 20% decrease in rotavirus hospitalization or outpatient visit incidence resulted in a 2% to 12% and an 8% to 18% change in total costs, respectively. Similarly, a 20% increase or decrease in average direct medical costs for hospitalization or outpatient visits resulted in a 2% to 11% and a 4% to 13% change in total costs, respectively.

The results of the uncertainty analyses are shown in Table 4 and Table 6. Upper and lower uncertainty bounds are provided in Table 4 for the estimates of direct medical and societal costs of rotavirus gastroenteritis. The uncertainty limits were smallest when country-specific data were available for estimating key epidemiological parameters (Argentina, Chile, and Venezuela).

The contribution-to-variance analysis summarized in Table 6 examined the effect of selected input parameters on the total estimated cost of rotavirus gastroenteritis in each country. Uncertainty in the incidence of outpatient visits for diarrhea and the proportion of these visits ascribed to rotavirus diarrhea contributed at least 7% to the overall uncertainty in the economic burden for each country, although the contribution was much higher in some countries such as the Dominican Republic, Honduras, Mexico, and Panama. The incidence of hospitalization for diarrhea and the proportion of hospitalizations ascribed to rotavirus diarrhea were highest in Brazil, where these factors accounted for 16% to 17% of the overall uncertainty. Direct medical costs were a relatively larger source of variability in countries for which there was more certainty regarding country-specific epidemiological inputs (e.g., hospitalizations in Argentina or Chile, and outpatient visits in Honduras). Indirect costs for hospitalizations contributed a small fraction to the overall uncertainty; however, indirect costs for outpatient visits made larger contributions to overall uncertainty, especially in Brazil, Mexico, Panama, and Venezuela.

TABLE 5. Sensitivity analysis based on the effect of changes in rotavirus incidence and cost estimates on the total estimated economic burden for the 2003 birth cohort in eight Latin American and Caribbean countries, expressed in 2003 US$ per 1 000 children for the first five years of life

Variable	Argentina	Brazil	Chile	Dominican Republic	Honduras	Mexico	Panama	Venezuela
Rotavirus hospitalization incidence[a]								
–20%	10 078	8 499	17 162	4 714	8 168	11 896	15 451	9 992
Base case	11 209	9 662	18 889	5 086	8 513	12 196	16 463	10 625
+20%	12 340	10 825	20 617	5 458	8 858	12 496	17 476	11 259
Rotavirus outpatient incidence								
–20%	10 098	8 893	16 839	4 440	7 155	10 057	14 183	9 134
Base case	11 209	9 662	18 889	5 086	8 513	12 196	16 463	10 625
+20%	12 320	10 432	20 940	5 732	9 871	14 335	18 744	12 117
Direct medical cost from hospitalizations								
–20%	10 194	8 636	17 328	4 745	8 183	11 938	15 568	10 054
Base case	11 209	9 662	18 889	5 086	8 513	12 196	16 463	10 625
+20%	12 224	10 689	20 451	5 427	8 843	12 454	17 359	11 197
Direct medical cost from outpatient visits								
–20%	10 279	9 229	17 206	4 741	7 375	10 945	14 895	9 425
Base case	11 209	9 662	18 889	5 086	8 513	12 196	16 463	10 625
+20%	12 139	10 096	20 573	5 431	9 651	13 447	18 032	11 825

[a] For each variable, the table shows the effect of a 20% increase or of a 20% decrease on the total economic burden of rotavirus gastroenteritis, compared to the baseline value.

TABLE 6. Cost and uncertainty range for the total estimated cost of rotavirus gastroenteritis in each country, in 2003 US$, along with contribution (percentage) of selected input variables to the variance in cost estimates for the 2003 birth cohort during the first five years of life in eight Latin American and Caribbean countries

	Argentina	Brazil	Chile	Dominican Republic	Honduras	Mexico	Panama	Venezuela
Total cost (2003 US$)	8 137 641	33 537 642	5 402 388	1 032 454	1 753 684	27 750 765	1 152 441	6 183 961
Uncertainty range (2003 US$)	7 026 852 to 9 315 473	28 714 867 to 38 649 243	4 575 937 to 6 313 709	844 021 to 1 235 194	1 457 934 to 2 069 514	23 244 283 to 32 609 187	981 935 to 1 337 970	5 260 654 to 7 184 664
Variables								
Incidence of hospitalization for diarrhea	14%	17%	8%	10%	1%	< 1%	< 1%	4%
Incidence of hospitalization for rotavirus	13%	16%	8%	6%	2%	< 1%	7%	4%
Incidence of outpatient visits for diarrhea	12%	20%	10%	33%	22%	28%	18%	22%
Incidence of outpatient visits for rotavirus	13%	7%	13%	21%	38%	51%	37%	22%
Direct medical costs from hospitalization	28%	15%	46%	23%	6%	< 1%	3%	15%
Direct medical costs from outpatient visits	15%	4%	8%	< 1%	25%	2%	12%	12%
Indirect costs from hospitalization	< 1%	2%	< 1%	< 1%	< 1%	< 1%	< 1%	< 1%
Indirect costs from outpatient visits	4%	18%	7%	5%	4%	17%	10%	19%

DISCUSSION

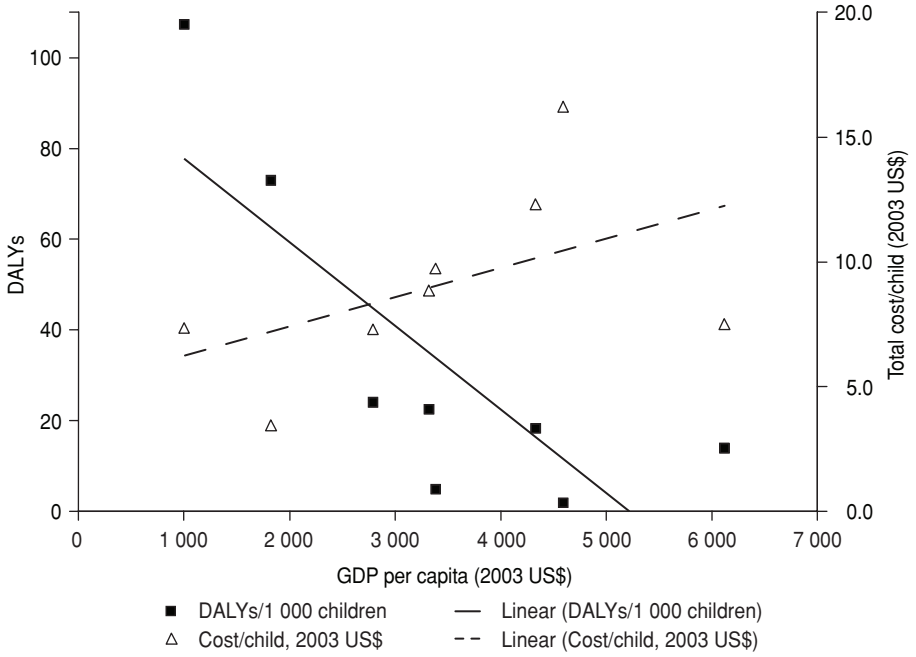
The study demonstrates that rotavirus gastroenteritis can be expected to result in a large health and economic burden in the eight Latin American and Caribbean countries studied. For every 1 000 children born, rotavirus gastroenteritis was estimated to result in an average of 246 outpatient visits, 24 hospitalizations, 0.6 deaths, and 2003 US$ 7 971 in direct medical costs

during their first five years of life. These rates translated into estimates of approximately 2 000 000 outpatient visits, 190 000 hospitalizations, 5 000 deaths, and US$ 62.4 million in direct medical costs for the 2003 annual birth cohort by the age of 5 years. Direct medical expenses from hospitalizations and outpatient visits were predicted to account for costs of up to US$ 16 per child (US$ 3.4 to US$ 16.2, depending on the country). When productivity losses for caregivers and additional out-of-pocket expenses were also considered, the estimated societal cost rose to almost US$ 19 per child (US$ 5.1 to US$ 18.9, depending on the country). For the eight countries together, rotavirus gastroenteritis was estimated to lead to costs of US$ 85 million (including societal costs) for the 2003 birth cohort. This estimate did not include additional costs associated with cases that are treated at home or by traditional healers and pharmacists.

The estimated number of deaths due to rotavirus in the current study is lower than the estimates by Parashar and colleagues, which were based on regression analysis rather than country-specific data (1). The observed differences were greatest for Chile, Argentina, and Mexico, all of which are upper-middle-income countries. Because most of the studies used in Parashar's regression model were from low-income and lower-middle-income countries (1), their model may not perform as accurately for higher-income countries.

In terms of public health, deaths and hospitalizations for severe cases of gastroenteritis are of greatest concern. However, from an economic perspective, outpatient visits are also of concern since they can generate a large portion of the costs of rotavirus gastroenteritis. Outpatient visits accounted for an estimated 30% to 83% of the direct medical costs in each country, and accounted for an even greater fraction of the total estimated societal costs (40% to 88%). The proportion of total costs associated with outpatient visits was higher in countries with lower rates of rotavirus hospitalizations, such as Mexico and Honduras.

FIGURE 2. Estimated economic and health burden of rotavirus diarrhea for the 2003 birth cohort in eight selected Latin American and Caribbean countries, by per capita gross domestic product (GDP), as measured in disability-adjusted life years (DALYs)/1 000 children and cost per child (2003 US$)



Rotavirus gastroenteritis was predicted to result in substantial disease and economic burdens in each of the eight countries studied; however, the pattern differed slightly among countries. As expected, the greatest disease burden (in terms of DALYs) was predicted for lower-middle-income countries, especially the Dominican Republic and Honduras. In contrast, the greatest economic burden was foreseen in upper-middle-income countries due to their higher treatment costs per child and higher productivity losses. Variability in health care costs may be due to differences in treatment patterns (medications, diagnostics, and relative importance of inpatient and outpatient treatment) and input costs (primarily labor).

Figure 2 shows the predicted health and economic burdens of rotavirus (DALYs per 1 000 births and total cost per child) by per-capita income in each of the countries. Although higher-income countries tended to have higher economic burdens, and lower-income countries tended to have higher health burdens, many middle-income countries had large health and economic burdens associated with rotavirus gastroenteritis. This may reflect real differences between countries. For children who have access to timely medical attention, rotavirus gastroenteritis is likely to generate economic costs. For children with little access to medical care, gastroenteritis may be more likely to result in mortality (an increase in DALYs).

The sensitivity and uncertainty analyses provide an important tool for assessing the validity of the burden estimates presented here. Although there is uncertainty about the country-specific epidemiological and economic inputs used in the model, the overall uncertainty bounds presented in Table 4 suggest that the economic burden estimates are quite robust. In countries where uncertainty bounds are wider, estimates could be improved with additional data for input variables that contribute the most to overall uncertainty. This is particularly true for countries where epidemiological estimates were extrapolated from other countries.

The primary limitations of this study relate to the availability of country-specific incidence data for severe rotavirus gastroenteritis events. The potential impact of these data limitations was systematically assessed in the sensitivity and uncertainty analyses to determine their importance. Another limitation is that the study did not include the costs borne by families for treatment of rotavirus gastroenteritis in less formal settings, including treatment at home or by traditional healers. As a result, the estimates presented here are likely to underestimate the total economic burden of rotavirus gastroenteritis.

The evidence presented in this study lends support to the conclusion that rotavirus gastroenteritis can be expected to produce substantial morbidity, mortality, and health care system costs in Latin America and the Caribbean. For every 1 000 children born in 2003, we estimate that rotavirus will result in 246 outpatient visits, 24 hospitalizations, 0.6 deaths, and US$ 7 971 in direct medical costs during their first five years of life. The eight countries studied here may spend an estimated total US$ 62.4 million annually in direct medical costs arising from the treatment of rotavirus gastroenteritis. When the costs of transportation and time lost from work are included, the total estimated societal burden of rotavirus gastroenteritis is approximately US$ 86 million for the eight countries. This estimate does not include the additional non-medical costs borne by families, or the costs of treatment in less formal settings, which may comprise an important proportion of the total economic burden imposed by rotavirus. Although rotavirus is often described as a democratic virus because it infects almost all children by the age of 5 years, the nature of the resulting burden can differ greatly. In higher-income countries the economic burden is likely to be greater, whereas in lower-income countries it is the health burden that can be expected to be greater.

As vaccines become available to control rotavirus gastroenteritis, information on the economic and health burden of disease in Latin America and the Caribbean, as well as in other regions, becomes more important. Health care resources used to treat rotavirus gastroenteritis could be used to address other health challenges or to offset the costs of vaccination. These economic burden estimates provide the foundation for further evaluations of the cost-effectiveness of rotavirus vaccination.

Acknowledgments. Financial support for this project was provided by GlaxoSmithKline Biologicals. The authors would like to acknowledge the help of GSK Medical Advisors (salaried employees) for their valuable input in generating epidemiological data. The GSK Medical Advisors were: Yolanda Cervantes, GSK-Mexico; Marisol Navarrete, GSK-Chile; Eduardo Ortega, GSK-Caribbean and Central American Region; Pilar Rubio, GSK-Brazil; Ricardo Ruttiman, GSK-Argentina; José Tavares, GSK-Brazil; and Juan Pablo Yarzabal, GSK-Venezuela. We are indebted to Miguel O'Ryan, Maribel Rivera, Jorge Gómez, Irene Pérez-Schael, and Alexandre Linhares for their assistance with identifying epidemiological data and for their general support of the study. We also thank Ralf Clemens for reviewing the manuscript.

Note on conflict of interest. The Pan American Health Organization (PAHO) has purchased vaccines from GlaxoSmithKline, and PAHO has also received contributions from GlaxoSmithKline. While the *Revista Panamericana de Salud Pública/Pan American Journal of Public Health* is affiliated with PAHO, the *Revista/Journal* is an independent scientific publication whose articles do not necessarily reflect the opinions or official positions of PAHO on specific issues. The mention of particular companies or of certain manufacturers' products in the *Revista/Journal* does not imply that they are endorsed or recommended by PAHO in preference to other ones of a similar nature. As with all other research articles published in the *Revista/Journal*, this article went through the regular process of peer review by outside experts.

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Manuscript received 18 July 2005. Revised version accepted for publication on 16 October 2006.

Carga económica y de morbilidad de la gastroenteritis por rotavirus en la cohorte de nacidos en 2003 en ocho países de América Latina y el Caribe

RESUMEN

Objetivo. Estimar la carga económica y de morbilidad de la gastroenteritis por rotavirus en hospitales y servicios ambulatorios de ocho países de América Latina y el Caribe (Argentina, Brasil, Chile, Honduras, México, Panamá, República Dominicana y Venezuela).

Métodos. Se elaboró un modelo económico a partir de datos epidemiológicos de artículos publicados, estudios de autoridades sanitarias nacionales y los estimados de costos específicos de cada país. El modelo calculó las consecuencias de la infección por rotavirus en los primeros cinco años de vida de la cohorte de nacidos en 2003 en cada uno de los ocho países estudiados. Las principales medidas de valoración fueron los costos de la atención sanitaria, los costos de transportación, los salarios perdidos y la carga de morbilidad expresada en años de vida ajustados por discapacidad. Los estimados se expresaron en dólares estadounidenses del año 2003. Se empleó una tasa de descuento de 3% para los cálculos de costos y años de vida ajustados por discapacidad de los años siguientes. El impacto de las variables específicas sobre los costos clínicos del tratamiento de la infección por rotavirus se realizó mediante análisis de sensibilidad.

Resultados. Se estimó que durante los primeros cinco años de vida, la gastroenteritis por rotavirus provoca en promedio 246 consultas externas, 24 hospitalizaciones, 0,6 muertes y gastos médicos directos por US$ 7 971,00 por cada 1 000 niños nacidos en 2003 en los ocho países estudiados de América Latina y el Caribe. Se prevé que la frecuencia de visitas médicas asociadas con la infección por rotavirus y los costos por consultas externas tengan el mayor impacto en los costos clínicos totales por niño.

Conclusiones. La gastroenteritis por rotavirus puede representar una considerable carga económica y de morbilidad para los sistemas sanitarios de los países de América Latina y el Caribe. Se debe prestar una especial atención a la carga previsible al evaluar la efectividad en función del costo de la vacunación contra rotavirus.

Palabras clave Infecciones por rotavirus, gastroenteritis, costos y análisis de costo, costo de enfermedad, modelos económicos, América Latina, Región del Caribe.