Cost-effectiveness Analysis of a Rotavirus Immunization Program for the United States

Andrew W. Tucker; Anne C. Haddix, PhD; Joseph S. Bresee, MD; Robert C. Holman, MS; Umesh D. Parashar, MBBS, MPH; Roger I. Glass, MD, PhD

Context.—Rotavirus is the most common cause of severe diarrhea in children, and a live, oral vaccine may soon be licensed for prevention.

Objective.—To estimate the economic impact of a national rotavirus immunization program in the United States.

Design.—Cost-effectiveness was analyzed from the perspectives of the health care system and society. A decision tree used estimates of disease burden, costs, vaccine coverage, efficacy, and price obtained from published and unpublished sources.

Intervention.—The proposed vaccine would be administered to infants at ages 2, 4, and 6 months as part of the routine schedule of childhood immunizations.

Main Outcome Measures.—Total costs, outcomes prevented, and incremental cost-effectiveness.

Results.—A routine, universal rotavirus immunization program would prevent 1.08 million cases of diarrhea, avoiding 34 000 hospitalizations, 95 000 emergency department visits, and 227 000 physician visits in the first 5 years of life. At $20 per dose, the program would cost $289 million and realize a net loss of $107 million to the health care system—$103 per case prevented. The program would provide a net savings of $296 million to society. Threshold analysis identified a break-even price per dose of $9 for the health care system and $51 for the societal perspective. Greater disease burden and greater vaccine efficacy and lower vaccine price increased cost-effectiveness.

Conclusions.—A US rotavirus immunization program would be cost-effective from the perspectives of society and the health care system, although the cost of the immunization program would not be fully offset by the reduction in health care cost of rotavirus diarrhea unless the price fell to $9 per dose.

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ROTAVIRUS is the most common cause of severe diarrhea among young children in the United States.[1,2] In the first 5 years of life, approximately 70% of children will become ill from rotavirus diarrhea,[3,4] 1 in 8 will seek care from a physician,[1] and about 1 in 78 will be hospitalized for severe disease.[1,5] Although rotavirus causes few deaths in the United States,[6] it has recently been estimated to cause 49 000 to 55 000 hospitalizations[5,7] and $564 million in direct medical costs annually among children younger than 5 years.[8] Live, oral vaccines against rotavirus have been developed that are safe and, when administered in 3 doses, prevent 50% to 60% of rotavirus diarrhea and 70% to 100% of severe, dehydrating illness.[9-14] The first live, orally administered, tetravalent, human-rhesus reassortant vaccine (RRV-TV) is currently being reviewed by the Food and Drug Administration for licensure.

In the United States, the decision to implement a national rotavirus vaccine program will be based largely on the expected reduction in severe and costly disease outcomes, particularly hospitalizations, as well as the predicted cost-effectiveness of the program. A previous, preliminary study[8] found that a national rotavirus vaccine program would yield a net savings of $79 million in health care costs and a much larger savings, $466 million, from a societal perspective, given a vaccine price of $20 per dose. However, in the 2 years since this study was published, many of the estimates used in that analysis, including those for disease burden, vaccine efficacy, and costs of care, have changed, potentially affecting the projected cost-effectiveness. Since this analysis may be critical for policymaking, we have revisited the cost-effectiveness study of a national rotavirus vaccine program and developed new estimates, incorporating data specific to the first vaccine expected to be licensed.

METHODS

Study Design

We examined the impact of a rotavirus immunization program in which rotavirus vaccine, RRV-TV, would be administered orally in 3 doses in the first 6 months of life as part of a child's routine immunizations. The impact was measured as the decrease in the disease burden and associated costs during the child's first 5 years of life, when most rotavirus diarrhea occurs.[2,5,15,16] This analysis was applied to the hypothetical 1997 US birth cohort of 3.9 million children.[17]

A decision model was used to calculate total costs, defined as the cost of a national rotavirus immunization program minus the present value of costs attributable to rotavirus diarrhea that would be prevented by such a program. We also estimated the number of adverse outcomes (rotavirus diarrhea, physician and emergency department visits, hospitalizations, and deaths) prevented by such a program. Finally, we calculated cost-

From the Viral Gastroenteritis Section, Respiratory and Enteric Viruses Branch (Mr Tucker and Drs Bresee and Glass); the Prevention Effectiveness Branch, Division of Prevention Research and Analytic Methods, Epidemiology Program Office (Dr Haddix); Epidemic Intelligence Service, Epidemiology Program Office, Centers for Disease Control and Prevention (Dr Parashar); and Office of the Director, Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases (Mr Holman), Atlanta, Ga.

This article was completed by Mr Tucker in partial fulfillment of his thesis for a Master of Public Health degree at the Rollins School of Public Health, Emory University, Atlanta.

Reprints: Roger I. Glass, MD, PhD, Viral Gastroenteritis Section, Centers for Disease Control and Prevention, US Department of Health and Human Services, 1600 Clifton Rd NE, Mailstop G04, Atlanta, GA 30333.

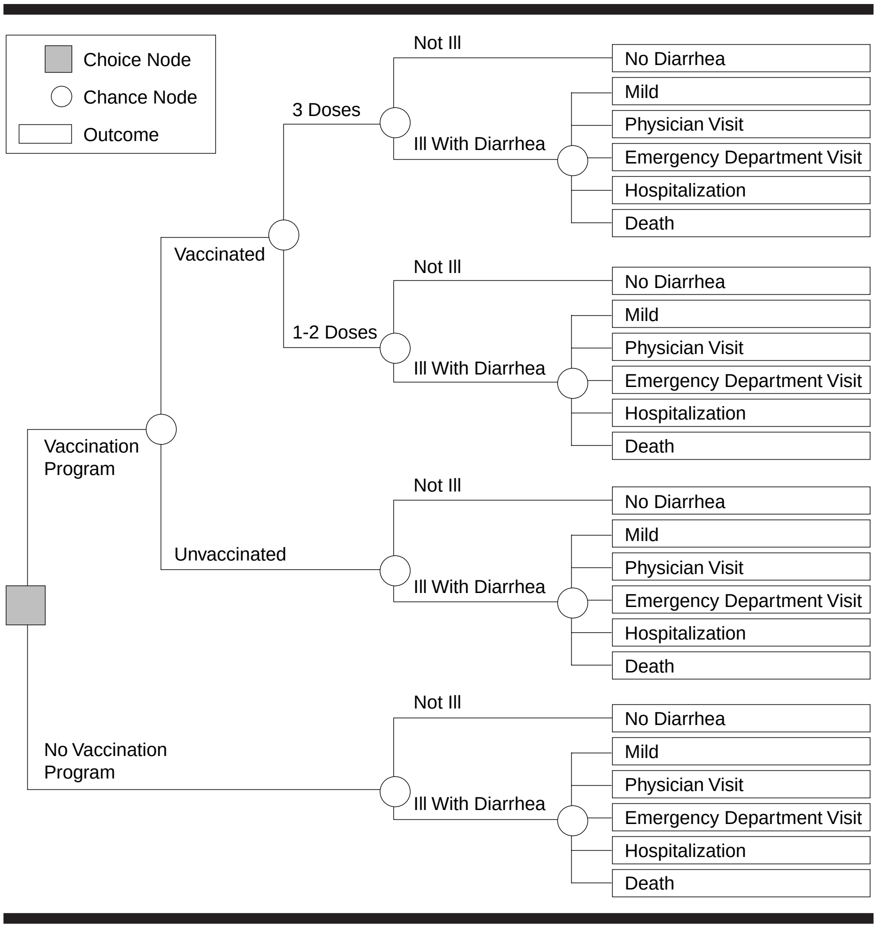

Figure 1.—Decision tree for rotavirus immunization program in the United States. The current practice with no vaccination is compared with a vaccination program in which rotavirus vaccine is included in a national childhood immunization program.

effectiveness, ie, the ratio of the costs divided by the number of cases of rotavirus diarrhea prevented by an immunization program. Cost-effectiveness was analyzed from 2 perspectives: (1) that of the health care system, which includes medical costs associated with rotavirus diarrhea and cost of the immunization program, and (2) that of society, which also includes nonmedical costs, including lost caregiver workdays and the lost lifetime productivity of a child dying.

All costs are in 1996 dollars. Costs and wages published before 1996 were updated using the consumer price index and nonfarm sector payroll index, respectively (indices from the US Department of Commerce, Bureau of Labor Statistics). Disease costs and rotavirus cases that would occur in the future (in cost-effectiveness ratios) have been discounted at an annual rate of 3%. Medical costs of rotavirus cases occur over a 5-year period according to the age-specific incidence estimates for each outcome. Productivity costs associated with rotavirus mortality are estimated for the average life expectancy of a child younger than 5 years.

Decision Analysis Model

We compared rotavirus disease outcomes with and without an immunization program by using a decision-tree model with the SMLTREE decision analysis software, version 2.99 (Roslyn, NY: Jim Hollenberg; 1993) (Figure 1). We analyzed the decision tree to determine the costs of the 2 options: vaccination at current levels of coverage for diphtheria and tetanus toxoids and pertussis (DTP) and the current situation of no immunization program. The vaccine price, coverage, efficacy, disease burden, medical costs, and discount rate used in the decision tree were varied in sensitivity analyses (Tables 1, 2, and 3).

Rotavirus Infection, Morbidity, and Mortality Estimates

Single-year disease totals for children younger than 5 years were summed to provide 5-year cumulative totals for our cohort followed up from birth to age 5 years after adjusting for differences in size of birth cohorts. We chose a base-case estimate of 70% for the cumulative incidence of rotavirus diarrhea in the first 5 years of life, using results of 2 prospective longitudinal studies, and a range from 55% to 85% for sensitivity analysis.[3,4] These incidence rates are consistent with those reported in the placebo groups of 2 of the 3 efficacy trials conducted in the United States,[10,13] but the trials have not included children younger than 6 months and older than 2 years, groups constituting 40% of the severe cases.[5] The longitudinal data also avoid the biases inherent in estimating the incidence from the placebo arm of a vaccine trial.[18-20]

The numbers of physician and emergency department visits and hospitalizations for rotavirus diarrhea were estimated as the percentage of visits or hospitalizations for diarrhea that could be attributed to rotavirus (Table 2). In an analysis of hospital discharge data from 1979 through 1992, Jin and colleagues[7] estimated that 55 000 children aged 0 to 59 months were hospitalized each year for rotavirus diarrhea and that these accounted for 30% of all hospitalizations for diarrhea in this age group. A more recent analysis of National Hospital Discharge Survey data from 1993 through 1995 shows a slight decline in estimated rotavirus hospitalizations.[5] We chose 50 000 hospitalizations per year as our base-case estimate, for a cumulative risk per child by age 5 years of 1.28% (ie, 1 in 78 children is hospitalized for rotavirus diarrhea by age 5 years), with a range of estimates from 30 000 hospitalizations per year (1 in 130 children) to 70 000 (1 in 56 children). No reliable data exist on the national incidence of outpatient visits due to rotavirus diarrhea. Since a smaller fraction of mild vs severe episodes is due to rotavirus,[16,21] we estimated that 20% of all physician visits for diarrhea were due to rotavirus[21,22] and used the method of Jin and colleagues[7] to determine diarrhea cases. Therefore, 372 000 of the 1.86 million physician office visits[23] and 38 000 of the 190 000 hospital outpatient clinic visits[24] for diarrhea were attributed to rotavirus. The cumulative incidence of outpatient physician visits for rotavirus diarrhea would be 10.5% (1 in 9.5 children) during the first 5 years of life. Similarly, we estimated that 20% of emergency department visits for diarrhea were due to rotavirus, providing a national estimate of 160 000 visits for rotavirus[24] or a cumulative incidence by age 5 years of 4.1% (1 in 24 children). For physician visits and emergency department visits, we used a range of 10% to 25% and 10% to 30% of all diarrhea cases, respectively, in sensitivity analysis. Finally, about 20 deaths occur each year due to rotavirus diarrhea among children younger than 5 years,[1,6] for a cumulative incidence by age 5 years of 0.000005 (1 in 195 000 children).

Incidence studies were reviewed to determine the age distribution of disease during the first 5 years of life.[3-6,25] In a recent national study of hospitalizations coded as rotavirus diarrhea, 36% of patients were younger than 1 year, 37% were between ages 1 and 2 years, and 27% were between ages of 2 and 4 years.[5] We applied this distribution to hospitalizations. We estimated that 78% of deaths occurred in the first year on the basis of published data.[6] For less severe outcomes (mild diarrhea, physician visits, and emergency department visits), we used published studies of rotavirus gastroenteritis to estimate that 25%, 36%, and 39% of the cases occur among children younger than 1 year, between 1 and 2 years, and 2 to 4 years, respectively.[3,4,25]

Vaccine Coverage and Efficacy Estimates

Rotavirus vaccine coverage was anticipated to equal rates for DTP coverage since the rotavirus vaccine will likely be recommended to be administered concurrently with DTP at 2, 4, and 6 months.[26] In 1996, 61% of children in the United States received 3 doses, 28% received only 2 doses, 8% received only 1 dose, and 3% received no doses of DTP in their first 6 months of life (Centers for Disease Control and Prevention [CDC], unpublished National Immunization Survey data, 1996). By age 1 year, these percentages become 88%, 7%, 3%, and 2%, respectively. We assumed that rotavirus vaccination would be administered only in the first 6 months of life, and therefore, we used the 6-month data for our base-case estimates. The upper limit of the range of vaccine coverage rates used in the sensitivity analysis (90%, 5%, and 2% of children receiving 3, 2, and 1 dose by age 6 months, respectively) reflects the national goal of the National Immunization Program to achieve higher coverage.[27] The lower limit of the range (30%, 14%, and 4% receiving 3, 2, and 1 dose by age 6 months, respectively), which is half that of current rates, reflects our assumption that rotavirus vaccine uptake may be gradual.

Vaccine efficacy was reviewed for 3 trials of RRV-TV conducted in industrialized countries with the current formulation (4×10^5 plaque-forming units) of vaccine and a US multicenter trial conducted using a lower dose (4×10^4 plaque-forming units) that had similar results[9-11,13] (Table 1). These data provided base-case figures for vaccine efficacy of 50% against rotavirus diarrhea, 70% against physician visits, 75% against emergency department visits, and 85% against hospitalizations and deaths. Ranges of vaccine efficacy were selected to reflect the results of vaccine trials and are consistent with the findings that vaccines are always more effective against severe than mild disease. Since no data were available on the efficacy of partial immunization (1-2 doses), children receiving 1 or 2 doses were assigned an efficacy equivalent to half that of the 3-dose regimen for each outcome.

Table 1.—Efficacy of Rotavirus Vaccine in Developed Countries*

Diarrhea Outcome	Study Group by Author: Bernstein et al, 1995[9]	Rennels et al, 1996[10]	Santosham et al, 1997[13]	Joensuu et al, 1997[11]	Base Case Efficacy† (Range)
Any	57	49	48	68	0.50 (0.40-0.70)
Severe	82	80	88	91	. . .
Hospitalization‡	. . .	100‡	. . .	100‡	0.85 (0.70-0.95)
Emergency department visit	. . .	. . .	. . .	. . .	0.75 (0.50-0.90)
Physician visit	78	73	. . .	. . .	0.70 (0.50-0.90)
Death	. . .	. . .	. . .	. . .	0.85 (0.70-0.95)

*Estimates used for cost-effectiveness analysis of a rotavirus vaccination program in the United States in 1997. Ellipses indicate data not available.
†Estimates are for full vaccination (3 doses). Partial vaccination (1-2 doses) is presumed to give intermediate (50%) protection.
‡The number of hospitalizations prevented was 2 in Rennels et al[10] and 22 in Joensuu et al.[11]

Table 2.—National Disease Burden of Rotavirus Diarrhea Among Children Younger Than 5 Years*

Type of Cases	No. of Cases	Sensitivity Analysis Range	Base Case Cumulative Incidence by Age 5 y, %†
Diarrhea without a rotavirus vaccination program[3,4]	2 730 000	2 145 000-3 315 000	70
No. requiring no medical care	2 109 980	. . .‡	54
No. of physician visits[21-23]	410 000	205 000-492 000	11
No. of emergency department visits[24]	160 000	80 000-240 000	4
No. of hospitalizations[7]	50 000	30 000-70 000	1
No. resulting in death[1,6]	20	. . .‡	.0005

*Estimates used for cost-effectiveness analysis of a rotavirus vaccination program in the United States in 1997.
†Based on birth cohort of 3.9 million in 1997.
‡Ellipses indicate data not available.

Table 3.—Rotavirus Diarrhea Cost Estimates Used in Analysis

Variable	Costs (1996 Dollars): Base-Case Estimates	Range for Sensitivity Analysis
Direct medical costs		
Outpatient visit (physician, laboratory, medication, oral rehydration solution)[29,31]	132	106-158
Emergency department visit*	243	194-292
Hospitalization (room, physician, medications, intravenous fluids, laboratory tests, postdischarge outpatient visit)		
Vaccinated child (2.5 d)[8]	2672	2138-3206
Unvaccinated child (3.4 d)[5,8,28]	3622	2898-4346
Emergency department visit for a dying child[8]	756	605-907
Oral rotavirus vaccine, 1 dose	20	10-30
Vaccine administration, 1 dose[32,33]	10	8-12
Nonmedical costs		
Other direct costs of rotavirus diarrhea (per episode)[29]		
Transportation	16	8-24
Extra diapers	7	. . .†
Forgone earnings of parent/caregiver of child with rotavirus diarrhea (per day)[34]	77	. . .†
Lifetime productivity loss of child to death[34]		
<1 y	984 000	184 000-3 603 000
1-4 y	1 034 000	215 000-3 515 000

*A.C.H., unpublished data, 1997.
†Ellipses indicate that no range of values was used.

Cost Estimates

Medical costs include costs of inpatient, outpatient, and emergency department care, as well as the costs associated with vaccination (Table 3). The cost of hospi-

Table 4.—Rotavirus Health Outcomes and Costs With and Without a Rotavirus Immunization Program*

Variable	No Vaccine Program	With Vaccine Program	Prevented by Vaccine Program	Reduction, %
Events, No.				
Total rotavirus diarrhea	2 730 000	1 652 000	1 078 000	39
Physician visits	410 000	183 000	227 000	55
Emergency department visits	160 000	65 000	95 000	59
Hospitalizations	50 000	16 400	33 600	67
Deaths	20	7	13	65
Costs, $ (thousands)				
Medical costs				
Office visits	51 777	23 144	28 633	55
Emergency department visits	37 264	15 185	22 079	59
Hospital	175 434	43 894	131 540	75
Death (emergency department visits)	15	5	10	67
Vaccine administration	0	96 330	−96 330	. . .†
Cost of vaccine, $20 per dose	0	192 660	−192 660	. . .†
Total Medical Costs	**264 490**	**371 218**	**−106 728**	−40
Nonmedical costs				
Loss of earnings by caregiver	687 779	311 390	376 389	55
Other direct nonmedical	28 577	15 654	12 923	45
Lifetime productivity loss of child to death	19 912	6541	13 371	67
Total Nonmedical Costs	**736 268**	**333 585**	**402 683**	55
Total Cost	**1 000 758**	**704 803**	**295 955**	30

*Data are 5-year estimates for a birth cohort of 3.9 million.
†Ellipses indicate cost incurred.

talization includes the daily room charge, inpatient physician visits, medications, intravenous fluids, laboratory tests, and 1 postdischarge outpatient visit, and is derived from Blue Cross/Blue Shield estimates of the cost of inpatient services.[8] Data from a 1993-1995 national survey[5] and a study in Connecticut[28] indicate that the average hospital stay for a child with rotavirus diarrhea was about 3.4 days; we used this figure for an unvaccinated child. The cost of an outpatient visit, which includes laboratory tests and medications, was derived from a study on the costs of ambulatory care for children with diarrhea[29] and was consistent with current published costs.[30,31] The cost of a regular emergency department visit comes from data obtained during a large diarrhea outbreak in a major US city (A.C.H., unpublished data, July 1997). The cost of treatment for a dying child, including ambulance transportation and 30 minutes of critical care in an emergency department, was derived from Blue Cross/Blue Shield estimates.[8] Our estimated cost to administer the vaccine of $10 per dose (excluding the price of the vaccine) is based on experience with other childhood vaccines[32,33] and does not include an additional physician visit. Finally, we used a base-case figure of $20 per dose as our working estimate of the wholesale cost of the vaccine since the company has provided no range of cost for the vaccine. Medical cost estimates, apart from vaccine price, were increased and decreased by 20% for the upper and lower limits, respectively, in the sensitivity analysis.

The nonmedical costs of an episode of rotavirus diarrhea include travel to seek health care, extra diapers, loss of work time of the caregiver, and lifetime productivity loss of a dying child.[29] The forgone earnings of a parent or guardian[34] include 4 days of wages or salary for a dying child and 3.4 days (unvaccinated) and 2.5 days (vaccinated) for hospitalizations.[5,8] We used the same estimates for less severe rotavirus-related outcomes as they were consistent with duration of illness (diarrhea) data from vaccine trials (Ed Zito, PhD, Wyeth-Ayerst Research, unpublished data, 1995). The discount rate was varied from 0% to 8% in sensitivity analysis. Savings in travel costs when a sick child was not in day care were not included.

Sensitivity Analysis

Starting from the base-case scenario, we performed a univariate sensitivity analysis to examine the range of values for all variables to reflect uncertainties in our estimates (Tables 1, 2, and 3). Best- and worst-case scenarios were also calculated by biasing the model in favor of and against an immunization program, respectively, without varying the vaccine price. Finally, threshold analyses provided the break-even price of a vaccine for different scenarios.

RESULTS

Base-Case Estimate

A rotavirus immunization program in which a US birth cohort of 3.9 million participates is projected to prevent 1.08 million (39%) cases of rotavirus diarrhea during the first 5 years of life, including 227 000 (55%) physician visits, 95 000 (59%) emergency department visits, 34 000 (67%) hospitalizations, and 13 (65%) deaths (Table 4). The annual cost of rotavirus diarrhea is estimated to be $264 million to the health system, 66% of which is because of hospitalizations, and $1.001 billion to society. At a vaccine price of $20 per dose, a rotavirus immunization program would cost $289 million and would save $182 million in direct medical costs and an additional $403 million in indirect costs. Thus, the vaccination program would result in a net loss to the health care system of $107 million, but a net savings to society of $296 million. The incremental cost-effectiveness of immunization (ie, the cost per case prevented) for the base-case ($20) is $103 from the perspective of the health care system. The break-even price of the vaccine is $9 for medical costs and $51 in terms of societal costs at which the cost-effectiveness ratio is $0.

Sensitivity Analysis

Since caregiver loss of earnings accounts for 93% of the nonmedical costs, we lowered the number of workdays lost from 3.4 to 2.4 for unvaccinated children and from 2.5 to 1.5 for vaccinated children. This lowered the net savings to society from $296 million to $218 million. However, univariate analysis indicated that an immunization program would provide a net savings to society under any scenario, and the worst-case scenario provided a $32 million savings. From the health care perspective, the most important determinants of cost-effectiveness were hospitalizations, vaccine price, and vaccine efficacy. The low estimate of 30 000 hospitalizations yielded a ratio of $154 per case prevented ($3 break-even vaccine price), whereas a high estimate of 70 000 hospitalizations provided a ratio of $53 per case prevented ($14 break-even vaccine price) (Figure 2, top). Vaccine prices of $10 and $30 resulted in cost-effectiveness ratios of $10 and $197, respectively. Finally, higher efficacy resulted in improved cost-effectiveness, with the high estimate giving a ratio of $58 ($11 break-even price) compared with the low-efficacy estimate of $166 ($6 break-even price) (Figure 2, bottom). Other variables had much smaller impacts.

The cost-effectiveness ratio changed minimally with vaccine coverage; doubling coverage would double both the cost savings and the cost of the vaccine (represented in the numerator) as well as the cases prevented (represented in the denominator), leaving the ratio unchanged. However, higher coverage would result in lower overall morbidity. For example, the low coverage estimate would prevent only 0.53 million cases, whereas the high estimate would prevent 1.28 million cases. The magnitude of net costs would depend on the vaccine price: higher coverage saves more at a vaccine price below the break-even point, and lower coverage loses less at a vaccine price above the break-even point.

From the health care perspective, the best-case scenario provided a savings of $49 million, while the worst-case scenario resulted in a cost-effectiveness ratio of $239.

COMMENT

This analysis of the cost-effectiveness of a national rotavirus immunization program is based on the latest estimates of the disease burden in the United States and the most recent efficacy trials with the RRV-TV vaccine. We estimate the full cost of rotavirus disease in the United States to be $1 billion, of which $264 million is attributable to medical costs. Introduction of a national rotavirus immunization program would produce a net savings from the societal perspective and cost $103 per case of rotavirus diarrhea prevented from the health care system perspective. Consequently, a rotavirus immunization program would be cost-effective from both perspectives. When examining only the impact on the health care system, the break-even price per dose at which the vaccine would be cost saving would be $9.

This analysis suggests a number of important features in considering the introduction of a rotavirus vaccine. Hospitalization costs, vaccine efficacy, and vaccine price are the main determinants of the cost-effectiveness equation, ie, as vaccine efficacy and the number and cost of hospitalizations increase and the vaccine price decreases, the immunization program realizes greater cost reduction and cost-effectiveness. With the gradual decline of hospitalization rates associated with rotavirus diarrhea in the United States,[5] the value of a rotavirus vaccine has decreased as well. Furthermore, within the changing health care system, some groups, such as health maintenance organizations, may experience even lower rates of hospitalization as the care of patients with diarrheal diseases is shifted from an inpatient to an outpatient setting. Consequently, the value of the vaccine may be less for health maintenance organizations than for settings with higher hospitalization rates. At the same time, companies contracting health services for their employees may perceive that societal costs (ie, lost wages of caregivers) are particularly important since they reflect lost worker productivity and they may opt to pay for the vaccine themselves to ensure continuity in their workforce.

Three previous cost-effectiveness studies of a US immunization program for rotavirus have been performed with different methods and results.[8,35,36] An early study using CDC data[35] in a period before vaccine trial data were available estimated that a rotavirus immunization program would cost the medical system $255 million in 1985 dollars and concluded that a such a program would be extremely cost-effective given a vaccine costing less than $20. Griffiths and colleagues[36] examined the economic impact of a vaccine program based on the results of a placebo group of a vaccine trial in which only 2 children were hospitalized and most care was provided on an outpatient basis. The break-even value of a vaccine was only $4 per dose from a societal perspective, a low estimate perhaps due either to earlier and effective care given by study nurses during continuous follow-up or to the decision to analyze median rather than mean cost per infant, thereby underreporting the major contribution of hospital costs.

The current study updates the analysis of Smith and colleagues,[8] who concluded that a rotavirus immunization program in which a vaccine cost of $20 per dose would yield savings to the health care system of $79 million and to society of $466 million (in 1993 dollars). The favorable results of Smith and colleagues[8] were largely because of a higher estimate of hospitalizations (104 000 per year), a figure obtained by extrapolating the rate of hospitalizations for rotavirus diarrhea in 1980 estimated by Ho and colleagues[37] (68 000 per year) to the birth cohort of children, which had increased 53% from 2.7 million in 1980 to 4.1 million by 1991. The actual number of hospitalizations in 1991, subsequently estimated by Jin and colleagues[7] from the hospital discharge survey, was 55 000 per year. The most recent (1993-1995) estimates indicate that the number of hospitalizations for rotavirus diarrhea in the United States is more likely around 50 000,[5] and rotavirus-associated deaths, estimated at 75 to 125 in 1980,[37] have nearly disappeared since 1985 (20 per year).[6] Since hospitalizations are the major factor accounting for medical costs (ie, 66% of medical costs), this decrease in rotavirus hospitalizations has led to a decline in medical costs, while nonmedical costs have remained the same after adjusting for inflation. In addition, recent vaccine studies provide higher estimates of efficacy against hospitalizations and other outcomes.[9-13]

The current study has a number of limitations in the estimates used in the analysis as well as considerations of herd immunity, increased treatment with oral rehydration therapy, and the unassessed cost of adverse events. The

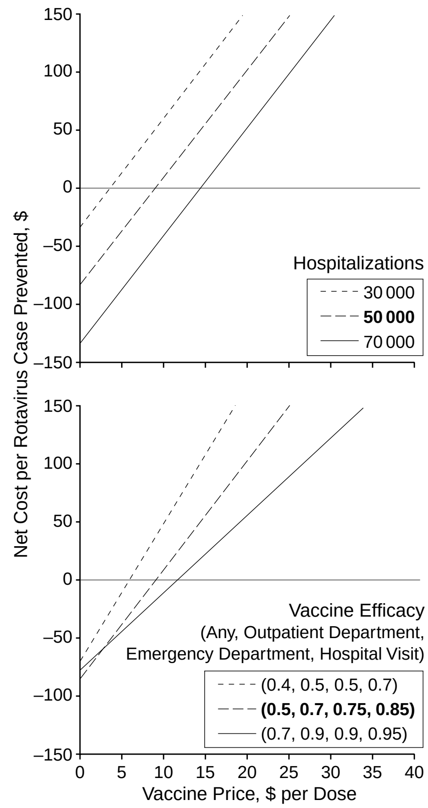

Figure 2.—Cost-effectiveness of a rotavirus immunization program for a range of vaccine prices. The net cost per rotavirus case prevented is examined in a sensitivity analysis over a range of estimates of hospitalizations (top) and vaccine efficacy (bottom). Base-case estimates are in boldface type.

burden of rotavirus disease was extrapolated from all diarrheal events estimated from a diversity of studies. Hospitalizations are the major contributor to medical costs, while salary loss of the caregiver because of mild disease is the main contributor to societal costs. These data on mild disease are least reliable but even the worst-case estimates yield a positive cost-effectiveness ratio. Outpatient and emergency department visits remain difficult to ascertain, especially since rotavirus diarrhea is not coded in these settings,[23,24] and these figures may be of increased importance over time as practice shifts the treatment of diarrhea from the inpatient to the outpatient setting. The use of efficacy estimates from phase 3 trials may either overstate or understate the actual effectiveness of a vaccine when used in routine public health practice. Effectiveness could be less than efficacy if children require all 3 doses for protection, or if protection wanes after 1 or 2 seasons since 14% of cases occur by age 6 months and 28% of cases occur after age 2 years.[5] Effectiveness could be greater than efficacy since children continue to receive missed doses after age 6 months (CDC, National Immunization Survey, unpublished data, 1996) and the potential of herd immunity has not yet been assessed. A new program of oral rehydration therapy might decrease the number of hospitalizations for rotavirus diarrhea but would incur additional costs. Finally, the vaccine incurs some mild side effects (eg, fever after the first dose) and other, less common, but more costly, adverse reactions (eg, hospitalizations) that can only be assessed through postlicensure surveillance.

To date, no price has been assigned to the rotavirus vaccine, and this value will be critical to the ultimate cost-effectiveness equation and determination of the use of the vaccine. Assignment of a price per dose near the break-even point for medical expenses ($9) would make a vaccine program cost-saving under any circumstances. Economic studies of other vaccines have identified cost-effectiveness results comparable to ours,[32,33] and new vaccines, such as varicella-zoster immune globulin, have been introduced at a price intermediate between the break-even point for medical and societal costs. Our cost-effectiveness analysis will need to be reassessed when a vaccine price or range of prices for the private and public sector has been assigned. Similarly, the administrative cost (ie, $10 per dose) may be too large given the oral route of administration and should be reassessed when the product enters use. The decline in disease burden since our last review has led to a shift in the equation on the cost-effectiveness of this vaccine for national use, and its acceptance will likely be because of assessment of societal costs rather than medical costs alone.

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