Economic Evaluation of the 7-Vaccine Routine Childhood Immunization Schedule in the United States, 2001

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Objective: To evaluate the economic impact of the routine US childhood immunization schedule: diphtheria and tetanus toxoids and acellular pertussis; tetanus and diphtheria toxoids; *Haemophilus influenzae* type b conjugate; inactivated poliovirus; measles, mumps, and rubella; hepatitis B; and varicella vaccines.

Design: Decision tree–based analysis was conducted using population-based vaccination coverage, published vaccine efficacies, historical data on disease incidence before vaccination, and disease incidence reported for 1995-2001. Costs were estimated using the direct cost and societal (direct and indirect costs) perspectives. Program costs included vaccine, administration, vaccine-associated adverse events, and parent travel and time lost. All costs were inflated to 2001 US dollars, and all costs and benefits in the future were discounted at a 3% annual rate.

Participants: A hypothetical 2001 US birth cohort of 3 803 295 infants was followed up from birth through death.

Main Outcome Measures: Net present value (net savings) and benefit-cost ratios of routine immunization.

Results: Routine childhood immunization with the 7 vaccines was cost saving from the direct cost and societal perspectives, with net savings of $9.9 billion and $43.3 billion, respectively. Without routine vaccination, direct and societal costs of diphtheria, tetanus, pertussis, *H influenzae* type b, poliomyelitis, measles, mumps, rubella, congenital rubella syndrome, hepatitis B, and varicella would be $12.3 billion and $46.6 billion, respectively. Direct and societal costs for the vaccination program were an estimated $2.3 billion and $2.8 billion, respectively. Direct and societal benefit-cost ratios for routine childhood vaccination were 5.3 and 16.5, respectively.

Conclusion: Regardless of the perspective, the current routine childhood immunization schedule results in substantial cost savings.

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N UMEROUS STUDIES[1-33] HAVE demonstrated the cost savings of childhood vaccination in the United States. However, in most cases, studies focused on single vaccines, and widely different methods and assumptions were used, which prevents adequate comparisons. To date, we know of no study that has examined the benefits and costs of the routine childhood immunization schedule using consistent methods and assumptions.

Vaccines are one of the greatest achievements of biomedical science and public health and represent one of the most effective tools for the prevention of diseases.[34] The introduction and widespread use of vaccines have resulted in dramatic declines in the United States in the morbidity, disability, and mortality caused by a variety of infectious diseases, including diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b (Hib), poliomyelitis, measles, mumps, rubella, hepatitis B virus (HBV), and varicella.[35-37] The current routine immunization schedule represents nearly 8 decades of vaccine development.[38-45]

Some of the economic studies still being cited as evidence that older vaccines result in net savings are now more than 20 years old. The prices of these vaccines, their formulations and uses, and the cost of medical care for the diseases they prevent have changed across the years; for example, 2 doses of measles, mumps, and rubella (MMR) vaccine are now recommended; inactivated poliovirus (IPV) vaccine has replaced oral poliovirus vaccine; and acellular pertussis vaccine has replaced whole-cell pertussis vaccine. Given that immunization is a cornerstone of preventive health care for children and that US vaccine financing mechanisms are still less than perfect, an updated and comprehensive eco-

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nomic evaluation is important and useful for making future policy decisions regarding childhood vaccination.

We applied a decision analysis model using population-based surveillance of diseases, published vaccine efficacies, historical data on disease incidence before vaccination, and disease incidence reported around 1995-2001, along with the available estimates of current costs of treating diseases and complications and administering vaccines. The objective of this study was to provide a comprehensive economic evaluation of routine childhood immunization with diphtheria and tetanus toxoids and acellular pertussis (DTaP); tetanus and diphtheria toxoids (Td); Hib conjugate; IPV; MMR; hepatitis B (HB); and varicella vaccines in the United States, addressing current costs and benefits. Although recommended for routine immunization, pneumococcal conjugate and influenza vaccines are not included in this study because they are not yet fully implemented (ie, they are relatively newly recommended by the Advisory Committee on Immunization Practices).

METHODS

DECISION ANALYSIS MODEL

We developed a decision tree as the basis for our model (**Figure 1**) and then evaluated the effect of routine childhood vaccination with DTaP, Td, Hib, IPV, MMR, HB, and varicella vaccines on a hypothetical US birth cohort of 3 803 295 children (the estimated number of births in 2001 [http://www.census.gov/population/projections/nation/detail/p2001_10.a]) from birth through death. The Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices routinely recommends 5 doses of DTaP,[46] 3 or 4 doses of Hib,[47] 4 doses of IPV,[40] 2 doses of MMR,[48] 3 doses of HB,[49] and 1 dose of varicella vaccine.[44] Additional booster doses of Td are required every 10 years, and the first booster dose may be given at 11 to 12 years of age.[39] Our analysis is based on coverage attained in the United States as estimated by the 2000 National Immunization Survey, the 1999 National Health Interview Survey, and the 2000-2001 School and Childcare Vaccination Surveys.

We calculated net present values (NPVs) and benefit-cost ratios (BCRs) for all 7 vaccines together. The analyses were performed from 2 perspectives: direct cost (direct medical and nonmedical costs) and societal (direct and indirect costs). All costs were inflated to 2001 dollars, and all costs and benefits in the future were discounted at a 3% annual rate for the base case analysis.

The data used in this analysis were compiled from a variety of sources: the published literature, including surveillance data, study data, and expert consensus; several large, computerized data sets; and CDC unpublished data. When it was necessary to make estimates about the incidence of disease and complications from multiple publications, results from existing meta-analyses were used as the estimates if possible. Otherwise, conservative assumptions were made, thereby intentionally underestimating the benefits of vaccination.

ESTIMATING THE BURDEN OF DISEASES WITHOUT VACCINATION

The age-specific annual incidence rates of diphtheria, tetanus, pertussis, Hib, poliomyelitis, measles, mumps, rubella, and varicella diseases in the United States in the prevaccine era were
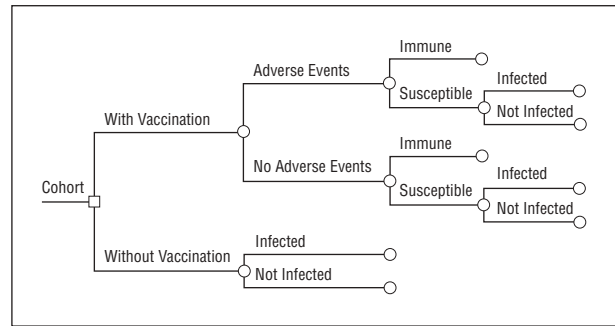

Figure 1. Simplified decision tree.

Table 1. Diphtheria, Tetanus, Pertussis, Hib, Poliomyelitis, Measles, Mumps, Rubella, and Varicella Annual Incidence Rates Without and With Vaccination*

	Without Vaccination (ie, Prevaccine Era)	With Vaccination (ie, Data by 2000)
Diphtheria†	600	0.001
Tetanus†	0.3	0.015
Pertussis†	4720	33
Hib meningitis‡	104	0.1
Hib epiglottitis‡	9.4	0.004
Hib septicemia‡	12	0.05
Hib pneumonia‡	13.4	0.05
Hib cellulitis‡	14.7	0.009
Hib arthritis‡	2.7	0.004
Hib, other invasive disease‡	1.3	0.05
Poliomyelitis, paralytic†	31	0
Measles§	10 641	1
Mumps†	6205	7
Rubella†	3300	0.2
Varicella‖	9839	1091

Abbreviation: Hib, *Haemophilus influenzae* type b.
*Data are given per 100 000 population. The incidence estimates used in the analysis varied by age.
†Estimates are for children 5 to 9 years old.
‡Estimates are for children 1 year old.
§Estimates are for children 2 to 4 years old.
‖Estimates are for children 1 to 4 years old.

estimated or obtained from the National Health Interview Survey and the literature (**Table 1**).[5,6,10,22,39,50-59] **Table 2** lists the health care utilizations for each of these diseases as appropriate. For diphtheria and tetanus, all cases were assumed to be hospitalized, with case-fatality ratios of 10%[5,39,57] and 15%,[5,39,56] respectively. Age-specific probabilities of pertussis hospitalizations and case-fatality ratios were used in the analysis.[5,60,61] In the base case analysis, the case-fatality ratio for Hib was estimated to be 3.78%.[6,10,53] For poliomyelitis, we assumed that 40% of the cases were paralytic and that 60% were nonparalytic.[59,62] We also assumed that all the paralytic cases needed acute care; that 22.4% had minor residual deficit, 41.4% had moderate residual deficit, and 24.3% had severe residual deficit without severe respiratory problems; and that 2% had severe respiratory problems.[14,63,64] This analysis also included postpoliomyelitis syndrome as part of the long-term course of poliomyelitis.[65-67] The case-fatality ratio for paralytic cases was assumed to be 3%.[68]

In the base case analysis, the estimated case-fatality ratios were 0.08% for measles infection,[69] 5% for measles encephalitis,[22] and 0.46% for thrombocytopenia after measles infection.[70] We assumed that the subacute sclerosing panencepha-

Table 2. Probabilities and Costs of Hospitalizations and Outpatient Visits for Selected Vaccine-Preventable Diseases*

	Probability of Hospitalization, %	Hospitalization Days, No.	Cost of Hospitalization, $	Cost per Outpatient Visit, $
Diphtheria	100	6.1	10 897	64.06
Tetanus	100	16.7	65 826	64.06
Pertussis	0.65-30	5.5-15.0	6908-14 380	64.06-111.19
Hib				
Acute cases	50-100	2.00-7.29	2638-24 557	63.81-226.53
Sequelae in meningitis	5-30	2.84-26.75	11 676-31 594	199.18-366.20
Poliomyelitis	5-100	4.0-17.0	4993-32 439	64.06
Measles	11-100	1.3-10.9	2587-29 556	56.83-337.95
Mumps	1-100	2.8-8.7	7184-29 556	70.63-356.85
Rubella	0.1-100	2.6-8.7	3135-29 556	57.05-417.85
Congenital rubella syndrome				
Hospitalization for investigation	100	13.6	39 934	70.78
Heart surgery	100	8.9	23 795	NA
Cataract surgery	100	2.2	5638	NA
HB	0.001-100	3.9-11.0	10 050-17 358	137-384
Varicella	0.1-2.1	3.1-9.3	2654-14 189	53-163

Abbreviations: HB, hepatitis B; Hib, *Haemophilus influenzae* type b; NA, not applicable.

*All costs are given in 2001 US dollars. Some estimates used in the analysis varied by age, outcome of diseases, and with vs without vaccination program.

litis rate was 10 per million measles cases.[20,71,72] The incidence of congenital rubella syndrome, its complications, and its associated costs were estimated from the literature.[22,73,74] For varicella, age-specific probabilities of hospitalizations and case-fatality ratios were used.[75,76]

In the United States, the prevalence of HB surface antigen positivity among women of childbearing age was assumed to be 0.57%, with 15% of these women being HB e antigen positive.[26,77] The prevalence of anti–HB core antibody at age 5 years is 0.56%, and the lifetime risk of HBV infection is 6.1%.[78] We assumed that 90% of infants born to HB surface antigen–positive/HB e antigen–positive women and 10% of infants born to HB surface antigen–positive/HB e antigen–negative women become perinatally infected. We assumed that acute HB occurs in 1% of perinatal infections, 6% of early childhood infections (after birth through 5 years old), and 30% of late infections (>5 years old through adulthood).[26] We assumed that 0.1% of infants and 0.6% of young children, adolescents, and adults who develop acute HB will develop fulminant hepatitis, and the mortality of fulminant HB is assumed to be 70%.[23,24,26,79,80] We assumed that 90% of infants, 30% of young children, and 6% of adolescents and adults who become infected will develop chronic HB infection.[26] Long-term sequelae develop in 25% of chronic infections from perinatal or early childhood infection and in 15% of chronic infections from late infection; sequelae include chronic persistent hepatitis, chronic active hepatitis, cirrhosis, and primary hepatocellular carcinoma.[26,79-83]

ESTIMATING THE BURDEN OF DISEASES WITH VACCINATION

For all diseases except varicella and HB, we used surveillance data from the National Notifiable Diseases Surveillance System to estimate the burden of diseases with vaccination in 2001. Incidence data were averaged for the 6 years from 1995 through 2000. For varicella, because it is not a nationally notifiable disease, we used the average incidence for the 2 sites (Antelope Valley, Calif, and West Philadelphia, Pa) in the Varicella Active Surveillance Project[36] during 2000 to estimate the total number of varicella cases in the United States. We assumed that 20.9% of these cases involved persons who had previously received varicella vaccine and that these were thus much milder than

cases among unvaccinated persons. For HB, because acute cases were underreported and chronic cases were not reported to the National Notifiable Diseases Surveillance System, we decided to use an established decision tree model[26] and the efficacy of the vaccine[84] to estimate the likelihood of HB infection and sequelae in vaccinated and unvaccinated children in the cohort.

COSTS ASSOCIATED WITH DISEASE

Direct Costs

Direct health care costs include those associated with the treatment, complications, and sequelae of diseases. Outpatient and inpatient costs were included in the analysis. The cost of outpatient visits, the average duration of hospitalization, and hospitalization costs for each condition related to these diseases or congenital rubella syndrome were obtained from HCUPnet,[85] the Marketscan database,[86] and published and unpublished studies (Table 2).*

We assumed that the annual cost of epilepsy and hemiplegia during a 50-year life span was $1693[88]; the annual special education cost for severely disabled children until age 18 years was $16 750[89]; the average annual long-term care cost for patients with poliomyelitis and severe respiratory problems during a 30-year life span was $137 220[90-93]; the annual cost for the long-term care of individuals with moderate and severe mental retardation during a 50-year life span was $31 059 and $78 448, respectively[10]; and the cost for periodic hearing aid evaluation is $243 per year and for hearing aids (binaural) is $1141 per year.[94]

Indirect Costs

Our model estimated the productivity losses due to premature mortality and the indirect costs from permanent disability as well as opportunity costs associated with caregivers who missed work to care for their sick children or patients themselves for missed work. To estimate the productivity losses from premature mortality, we used the human capital approach.[95] Costs for work loss were determined by the number of days of missed work (for the illness, for a resulting disability, or for the provision of care to sick children) multiplied by the daily wage rate

*References 5, 6, 10, 13, 14, 20, 22, 26, 87.

Table 3. Probabilities and Costs of Adverse Reactions*

	Rate (per 100 000 Doses)	Probability of Hospitalization, %	Hospitalization Days, No.	Cost of Hospitalization, $	Cost per Outpatient Visit, $
DTaP vaccine					
Hypotonic hyporesponsive episodes	8	12.50	7.1	8460	64.06
Uncomplicated seizures	10	12.50	5.2	8481	64.06
Protracted crying/screaming	63	0.50	2	3157	64.06
Anaphylaxis	2	100	1.9	5268	64.06
Hib vaccine					
Fever	2000	0	NA	NA	NA
MMR vaccine					
Additional outpatients visits for minor reactions	50	0	NA	NA	64.51
Parotitis	1600	1	3	8898	124.31
Arthralgia/arthritis	1000	1	2	9405	140.07
Febrile seizures	33	10	2	5446	419.86
Thrombocytopenic purpura	3	40	4.8	22 776	417.85
Anaphylaxis	0.1	100	2.89	16 092	153.25
Aseptic meningitis	0.1	25	3	18 983	143.68
Encephalitis	0.1	100	8.7	29 556	337.95
Varicella vaccine					
Rash	2000	0	NA	NA	NA
Additional outpatient visits	1000	0	NA	NA	64.06
Pneumonia	0.2	58	5.5	13 864	111.19
Herpes zoster	1.4	5	2	4944	92.76

Abbreviations: DTaP, diphtheria and tetanus toxoids and acellular pertussis; Hib, *Haemophilus influenzae* type b; MMR, measles, mumps, and rubella; NA, not applicable.

*All costs are given in 2001 US dollars. We assumed that there were no adverse reactions for tetanus and diphtheria toxoids, inactivated poliovirus, and hepatitis B virus vaccines and that other adverse events not mentioned herein were rare for other vaccines.

associated with the value of lost wage-earning work and the imputed value of housekeeping and home care activities. Appropriate values, taken from published studies,[95] the Bureau of Labor Statistics, and the Bureau of the Census, were applied for the general working population and for parents who missed work to care for their sick children. We assumed that the days of morbidity were distributed randomly throughout the week.

COSTS AND ADVERSE EVENTS ASSOCIATED WITH VACCINATION

Routine childhood vaccines are purchased with public and private funds. The distribution of publicly purchased vs privately purchased vaccines was derived from the CDC Vaccine Management database and from voluntary manufacturer reports to the CDC. Overall, approximately 55% of all US childhood vaccines were publicly purchased in 2001. The public and private prices for all vaccines were obtained from the CDC Vaccine Price List in 2001. We assumed that the average total cost to distribute (transport from the manufacturer to the site where administered) a dose of public vaccine was $0.68 and that the overall rate of vaccine wastage (public and private sectors) was 12%.[10,22] The federal excise tax that supports the National Vaccine Injury Compensation Program (http://www.hrsa.gov/osp/vicp) was included in all vaccine prices.

Most vaccines for children are administered by private sector providers. National Immunization Survey data indicate that approximately 76% of children obtained their vaccines from private providers, and 24% from public providers. The cost for administering a vaccine during a visit to a public clinic was estimated to be $5.23. In the private sector, we used an administration cost of $18.65.[10,22]

We used the same assumptions as previous economic studies,[10,22] and we assumed that the cost of caregiver travel to the clinic was $3.50 and that 2 hours away from work was needed to take the child for vaccination. We assumed that the average cost for these caregivers was $8.50 per hour. We calculated the indirect caregiver costs using the estimate of the average number of vaccination visits for each child derived from National Immunization Survey, National Health Interview Survey, and School and Childcare Vaccination Surveys data. We assumed that there were a mean of 7.8 vaccination visits for each child by age 12 years.

Vaccination coverage rates by age and number of doses administered were estimated for children in the cohort aged 1 to 3 years using 2000 National Immunization Survey data and aged 4 to 6 years using 1999 National Health Interview Survey and 2000-2001 School and Childcare Vaccination Surveys data. By 19 to 35 months of age, 94.1% of the children had received 3 or more doses of DTaP vaccine, 93.4% had received 3 or more doses of Hib vaccine, 89.5% had received 3 or more doses of poliomyelitis vaccine, 90.5% had received 1 or more doses of MMR vaccine, 90.3% had received 3 or more doses of HB vaccine, and 67.8% had received 1 or more doses of varicella vaccine.[96] By 6 years of age, 95% of the children had received 3 or more doses of DTaP vaccine, 94% had received 3 or more doses of Hib vaccine, 94% had received 3 or more doses of poliomyelitis vaccine, 95% had received 1 or more doses of MMR vaccine, and 93% had received 3 or more doses of HB vaccine. For varicella, we assumed that in a fully implemented program, 93% of the children would receive 1 or more doses of varicella vaccine.

The frequency and cost of care for adverse events associated with each of the vaccines is summarized in **Table 3**.

NPV AND BCRs

The benefits of routine childhood immunization consist of the savings from reduced morbidity and mortality resulting from vaccine use, including direct medical and nonmedical and indirect costs. The costs associated with the vaccination program include the vaccines, their administration, parent travel and time lost, and adverse events associated with these vaccines. The NPV is the most widely used summary measure in economic analysis to determine the return on any investment

Table 4. Health and Economic Outcomes for Selected Vaccine-Preventable Diseases With and Without a Vaccination Program*

	Without Vaccination Program				Prevented or Saved by Vaccination Program			
	Cases, No.	Deaths, No.	Direct Costs (Million), $	Total Costs (Million), $	Cases, No.	Deaths, No.	Direct Costs (Million), $	Total Costs (Million), $
Diphtheria	247 214	24 721	2358	24 930	247 212	24 721	2358	24 930
Tetanus	153	23	8	29	146	22	8	28
Pertussis	2 662 307	1049	2265	3668	2 614 874	1008	2193	3545
Hib	17 530	663	1434	2696	17 469	661	1430	2689
Poliomyelitis	60 974	723	2084	4890	60 974	723	2084	4890
Measles	3 433 722	2795	2646	5875	3 433 036	2794	2645	5874
Mumps	2 100 718	11	936	1459	2 095 917	11	934	1456
Rubella	1 786 334	14	88	381	1 784 030	14	88	380
Congenital rubella syndrome	616	68	115	173	602	66	112	169
HB	232 001	3427	168	1272	207 353	3024	149	1121
Varicella	3 788 807	70	205	1184	3 160 391	57	173	993
Total	**14 330 376**	**33 564**	**12 307**	**46 557**	**13 622 004**	**33 101**	**12 174**	**46 075**

Abbreviations: HB, hepatitis B; Hib, *Haemophilus influenzae* type b.
*Costs are rounded and given in US dollars.

Table 5. Summary of Costs and Benefit-Cost Ratios*

	Direct Costs (Million), $	Societal Costs (Direct + Indirect) (Million), $
Disease costs without immunization program	12 307	46 557
Disease costs with immunization program	133	482
Costs averted	12 175	46 075
Immunization program costs†	2293	2789
Net present value (net savings)	9881	43 286
Benefit-cost ratio	5.3:1	16.5:1

*All costs are given in US dollars.
†Direct program costs included vaccine, administration, parent travel, and direct costs for treatment of adverse events. Societal costs included direct program costs and parent time lost for vaccination and treatment of adverse events.

and in this case is the sum of the discounted benefits from the routine childhood vaccination program minus the sum of the discounted costs. The NPV can be written as follows:

$$NPV = \sum_{t=0}^{T} \frac{B_t}{(1+r)^t} - \sum_{t=0}^{T} \frac{C_t}{(1+r)^t},$$

where B_t and C_t are the benefits and costs, respectively, in year t; T is the life expectancy; and r is the annual discount rate.

The BCRs also provide a summary measure to determine the return on any investment. In this analysis, the BCR is equal to the discounted costs averted by the vaccination program divided by the discounted vaccination program costs. The BCR can be calculated as follows:

$$BCR = \sum_{t=0}^{T} \frac{B_t}{(1+r)^t} \Big/ \sum_{t=0}^{T} \frac{C_t}{(1+r)^t}.$$

SENSITIVITY ANALYSES

Sensitivity analyses were used to assess the robustness of the economic estimates and to estimate the impact of potential changes to the vaccination program. Univariate sensitivity analy-

ses were performed to assess the effect of varying (1) the rates of adverse events; (2) the postvaccination disease incidence rates; (3) the total direct and indirect costs without vaccination; (4) the proportion of vaccines purchased in the public vs private sector; (5) the vaccine administration costs; (6) the vaccine wastage rate; (7) the inclusion of federal, state, and local vaccination program management expenditures; (8) the costs associated with parent travel and time lost; and (9) the discount rate. Each new variable was introduced by itself in the sensitivity analyses. We also performed the worst-case scenario analysis: the combination of the worst case of items 1 to 7.

RESULTS

BASE CASE ANALYSIS

Table 4 summarizes the expected diphtheria, tetanus, pertussis, Hib, poliomyelitis, measles, mumps, rubella, congenital rubella syndrome, HBV, and varicella cases and deaths, as well as the associated economic burden with and without a vaccination program. Without a routine childhood vaccination program, the model estimated that in a cohort of 3 803 295 children, approximately 14.3 million cases of these diseases would occur, resulting in 33 564 deaths. These cases would result in direct costs of $12.3 billion and societal costs of $46.6 billion. Disease-associated costs with vaccination were $0.1 billion and $0.5 billion, respectively. The direct and societal costs of the routine childhood vaccination program with DTaP, Td, Hib, IPV, MMR, HB, and varicella vaccines were estimated to be $2.3 billion and $2.8 billion, respectively (**Table 5**). The calculated NPVs (net savings) of the routine childhood vaccination program from the direct cost and societal perspectives were $9.9 billion and $43.3 billion, respectively. The direct and societal BCRs for the routine vaccination program were 5.3 and 16.5, respectively.

SENSITIVITY ANALYSES

Table 6 gives the direct and societal BCRs after sensitivity analysis, and **Figure 2** shows the related tornado graph for the societal BCRs. When we doubled

the adverse events rate used in the base case analysis, the direct and societal BCRs became 5.2 and 16.3, respectively. To evaluate the extent to which underestimation of disease incidence in the postvaccination era may have affected our analysis, we ran the model using postvaccination diphtheria, tetanus, pertussis, measles, mumps, and rubella rates that were 1000% of the rates in the base case analysis. The direct and societal BCRs did not change substantially. The incidences, costs, and patterns of treatment of some diseases likely have changed across time even without vaccination. For the worse-case scenario, if the total direct and indirect costs without vaccination were reduced by 20%, the related direct and societal BCRs became 4.2 and 13.2, respectively. If 100% of these 7 vaccines were purchased at private sector prices and administered by the private sector, the total direct and societal vaccination program costs increased to $2.8 billion and $3.3 billion, and the related direct and societal BCRs became 4.3 and 13.8, respectively. If the administration costs in the public and private sectors were doubled, the related direct and societal BCRs became 3.7 and 12.3, respectively. With a lower or higher wastage rate, the BCRs changed only slightly. When federal, state, and local vaccination program management expenditures (approximately $700 million based on estimated costs for 2001 and including section 317 of the Public Health Services Act, Vaccines for Children program, state and local funds, and part of the National Vaccine Injury Compensation Fund, which covered the vaccines administered before October 1, 1988) were included, the direct and societal BCRs were 4.1 and 13.2, respectively. In the worst case, which included all the worse-case scenarios mentioned previously herein, the related direct and societal BCRs were 1.8 and 6.5, respectively.

If we assumed no costs associated with parent travel and time lost (because most routine vaccination occurs during well-child care visits at which other services are delivered), the related direct and societal BCRs were 5.5 and 20.8, respectively. Finally, with higher discount rates (ie, 8%), the direct BCR decreased slightly and the societal BCR (6.1 for 8%) decreased by two thirds from the base case.

COMMENT

The results of this study show that for the 2001 US birth cohort alone, routine childhood immunization with DTaP, Td, Hib, IPV, MMR, HB, and varicella resulted in substantial cost savings (~$10 billion and >$43 billion from the direct cost and societal perspectives, respectively) and has high BCRs: for every dollar spent, the vaccination program saves more than $5 in direct costs and approximately $11 in additional costs to society.

The sensitivity analysis found the results to be most sensitive to discount rate, yet even with the worst-case scenario, the BCRs were still greater than 1. Our results remained stable across a wide range of vaccine wastage rate estimates. In recent years, approximately half of the childhood vaccines have been purchased at public sector prices through programs such as the Vaccines for Chil-

Table 6. Benefit-Cost Ratios: Univariate Sensitivity Analysis

	Benefit-Cost Ratio	
	Direct Cost Perspective	Societal Perspective
Base case*	5.3	16.5
200% Base case adverse events rate (1)	5.2	16.3
1000% of base case incidence rate after vaccination (2)	5.0	16.1
20% Reduction of total direct and indirect costs (3)	4.2	13.2
100% of Vaccine purchased by private providers (4)	4.3	13.8
200% of Base case administration cost (5)	3.7	12.3
Wastage rate = 0%	5.6	17.3
Wastage rate = 25% (6)	5.0	15.8
Federal, state, and local vaccination program management expenditures were added (7)	4.1	13.2
Worst-case scenario (combination of 1-7 above)	1.8	6.5
0% Indirect caregiver cost and travel cost for vaccination	5.5	20.8
Discount rate = 0%	8.4	46.9
Discount rate = 5%	4.4	10.0
Discount rate = 8%	3.7	6.1

*Base case: wastage rate = 12% and discount rate = 3%.

dren Program and the State Child Health Insurance Program.[97,98] In our sensitivity analysis, increasing the proportion of vaccines purchased by private providers did not substantially change BCRs. This finding is important because costs are higher for privately purchased and administered vaccines compared with publicly purchased and administered vaccines. The role of the private sector in administering vaccines is expected to continue to increase with insurance reform to improve vaccination coverage rates in children (ie, first dollar laws) and the increasing delivery of vaccines by managed care organizations.[99] The BCRs remained high when all vaccines were purchased in the private sector, so one might conclude that there is no need for public purchase. However, this 1-way sensitivity analysis did not account for changes in immunization rates that might result from higher vaccine prices. Neither does it address equity issues associated with public purchase, such as vaccine access for the underserved and the public good of preventing infectious disease with vaccines.

This study has some limitations. Some of the cost data used in the analysis may not be representative because we derived some of the cost estimates from commercial databases. Also, by not including items such as pain and suffering to the family and friends of the ill patients, our model underestimated the benefit of the immunization program. In addition, by increasing the number of physician con-
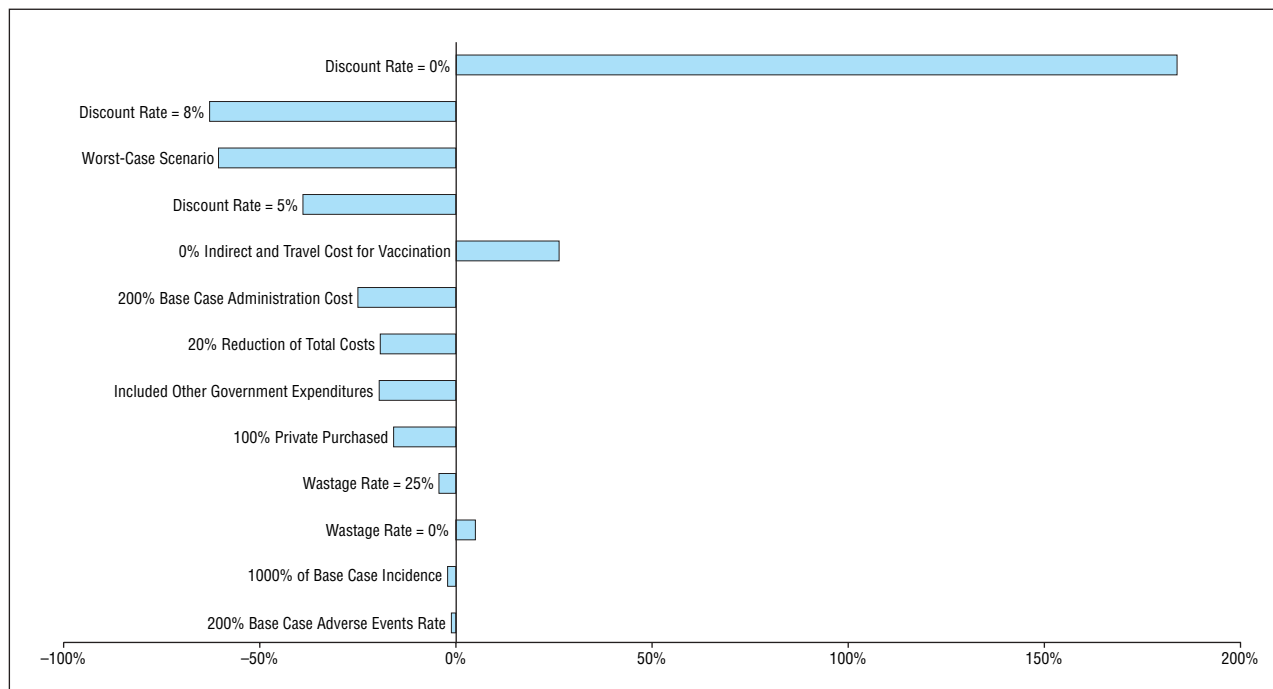
Figure 2. Sensitivity analysis: societal benefit-cost ratios (baseline=16.5).

tacts, vaccination programs introduce indirect benefits by adding new opportunities for the provision of other preventive counseling and services. Regarding varicella, the vaccination program was not mature in 2001, and 6 years after vaccine licensure, full reduction of varicella cases had not yet occurred, so our model underestimated the benefits of the fully implemented varicella program. Furthermore, regarding varicella vaccination, we made the conservative assumption that all the children received vaccine regardless of a history of chickenpox. We also did not analyze for undefined impacts of varicella vaccination on risk of herpes zoster in either vaccinees or persons with a history of chickenpox.

Data on the probability distributions of variables are unavailable, which prevents us from conducting a Monte Carlo simulation for a multivariate probabilistic sensitivity analysis and estimating confidence intervals. Also, this analysis does not include hospital infection control costs and costs to the public sector, such as surveillance officers and outbreak response, and neither does it include the indirect costs of diagnostic and confirmatory laboratory testing for persons with compatible illnesses. Whereas some diagnostic testing has long been conducted for treatment purposes, the establishment of vaccination and disease control programs generally leads to substantial increases in testing, particularly for viral illnesses, such as measles or rubella.

Finally, as in most economic analyses, caution should be exercised in interpreting and generalizing these results. For example, we did not include pneumococcal conjugate and influenza vaccines, and so this analysis should not be viewed as an analysis of the whole immunization program in the United States. In addition, we did not consider the future cost of disease if we stop vaccination now, and neither did we estimate the marginal cost of increasing vaccination coverage from current levels. Neither did

we address the vaccine supply and demand issues and the benefits for vaccine producers.

This analysis will be helpful in understanding the economic effects of the immunization program under current circumstances. Administrators and policy makers may use the results to obtain sustained support for programs, make needed modifications, and guide future programs. Overall, as the burden of disease decreases owing to the use of vaccines, this type of analysis will help ensure that society remains aware of the tremendous return on the investment in vaccines, measured not only in dollars but in health. Conversely, if the current high vaccination coverage levels are not maintained, vaccine-preventable diseases will recur along with the health burden, deaths, and costs to the medical system and society.

Despite the substantial success in achieving high immunization coverage and in reducing vaccine-preventable diseases in children, challenges remain. Efforts must continue to reach 2010 goals of 90% coverage for selected vaccines and to reduce remaining socioeconomic and racial/ethnic disparities in coverage and to improve adult and adolescent immunization rates. Concerns related to the safety of vaccines can lead to declining coverage if not appropriately addressed.[100] As newer and better vaccines (some of which are much more expensive) and combination vaccines become available, they will need to be incorporated into the already complex, increasingly expensive immunization system. Pertussis is the only disease for which children are routinely vaccinated that is not at historically low levels in the United States. Because the coverage among vaccine-eligible age groups remains high and the effectiveness of acellular pertussis vaccine has been demonstrated to be high in postlicensure evaluations, new strategies are needed to further reduce the incidence of pertussis.

The current immunization program with these 7 vaccines is cost saving, although newer vaccines (eg, varicella and pneumococcal conjugate) have proved to be more expensive than older ones. However, future recommendations should not be limited to vaccines that demonstrate cost savings. To do so would place them at a comparative disadvantage that few other prevention interventions could meet and would likely lead to missed opportunities to provide good value to society by prevention of diseases.

Because of the success of the current routine childhood vaccination program, diphtheria, tetanus, pertussis, Hib, poliomyelitis, measles, mumps, and rubella are no longer major health threats in the United States, and the threat of HB and varicella is substantially decreased. Although not reflected in this analysis and difficult to quantify, a dramatic decrease in the loss and suffering of patients, family, and friends is also a direct result of this achievement. Routine childhood vaccination against diphtheria, tetanus, pertussis, Hib, poliomyelitis, measles, mumps, rubella, HB, and varicella in the United States is a remarkable medical accomplishment that achieves significant public health benefit at a substantial cost savings.

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