

Economic Evaluation of Use of Diphtheria, Tetanus, and Acellular Pertussis Vaccine or Diphtheria, Tetanus, and Whole-Cell Pertussis Vaccine in the United States, 1997

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Objective: To compare the economic costs and benefits associated with using either diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP) or diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTwP) in the United States in 1997.

Design: Standard cost-benefit analysis, from both the societal and health care system perspectives, was performed for each combination vaccine as well as for the pertussis components singly.

Setting: A simulated cohort of 4.1 million children from birth to age 15 years.

Main outcome measures: Net costs (savings) and benefit-cost ratios (BCRs)

Results: Without a vaccination program, diphtheria, tetanus, and pertussis disease caused more than 3 million cases and more than 28 000 deaths, at a cost of \$23.6 bil-

lion. From the societal perspective, net savings because of the use of DTaP and DTwP were \$22.510 million and \$22.623 million, respectively. The net savings from the acellular pertussis component and the whole-cell pertussis component only were \$4.362 million and \$4.474 million, respectively. Benefit-cost ratios for DTaP from a societal and health care system perspective were 27:1 and 9:1, respectively. Sensitivity analyses of key variables did not result in appreciable changes in results.

Conclusions: Compared with no program, vaccination with DTaP or DTwP resulted in substantial savings, regardless of the perspective taken and for all sensitivity analyses conducted. Compared with DTwP, use of DTaP generated a small cost increase that might be offset by the value of other factors, such as increased confidence in pertussis vaccination resulting from reduced adverse events.

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THE INTRODUCTION and widespread use of a combined diphtheria and tetanus toxoids and whole-cell pertussis vaccines (DTwP) in the late 1940s in the United States led to a reduction of more than 95% in morbidity and mortality from each of these diseases.¹ Although the use of diphtheria and tetanus toxoids has been strongly supported, use of whole-cell pertussis vaccine has been controversial because of the frequency of local and systemic adverse events and an alleged association with permanent brain damage. Although this latter association has not been proven, it led to reduced acceptance of DTwP in the United Kingdom, Sweden, Japan, and Germany in the 1980s.² Acellular pertussis vaccines, made from purified components of *Bordetella pertussis*, were developed to reduce vaccine-related adverse events.^{3,4}

Recent studies have found combined diphtheria and tetanus toxoids and

acellular pertussis vaccines (DTaP) to be safe and to have an efficacy against pertussis disease similar to that previously published for DTwP.⁵⁻⁸ In 1997, DTaP was recommended for routine use among infants and young children in the United States.^{9,10} Although DTaP vaccines are associated with significantly fewer adverse events,^{11,12} they are more expensive than DTwP. Few investigators in the United States have conducted an economic analysis of the benefits and costs of using either DTaP or DTwP.^{13,14} An analysis by Battelle using 1994 cost estimates found a benefit-cost ratio (BCR) for DTwP of 30:1 from the societal perspective and 6:1 from the health sector perspective.¹⁴ This analysis did not consider use of DTaP for the full vaccination series.

To quantify possible economic differences between DTaP and DTwP vaccines, we analyzed 2 scenarios: exclusive use of each vaccine according to the recommended schedule for childhood im-

MATERIALS AND METHODS

We adapted the standard cost-benefit model used by Batelle Inc, Arlington, Va, to evaluate the benefits and costs of a US vaccination program to prevent diphtheria, tetanus, and pertussis in which either DTaP or DTwP was used compared with no vaccination program.^{14,15} We examined the impact of vaccination on a hypothetical US birth cohort of 4.1 million children, evaluated from birth through age 15 years.¹⁶ The 1997 childhood immunization schedule, which recommends 5 doses of vaccine (1 dose at age 2 months, 4 months, 6 months, 15 to 18 months, and 4-6 years), was assumed. We conducted the analyses from 2 perspectives (societal and health care system).

The equations for the standard cost-benefit model used in this study are presented below:

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

where the net present value (NPV) (or net benefit of vaccination with DTaP or DTwP) is the sum of the discounted benefits from vaccination program minus the sum of the discounted costs; j , vaccine candidate ($j=1$, diphtheria, $j=2$, tetanus, and $j=3$, pertussis); B_t , benefits from the vaccination program in year t ; C_t , costs of the vaccination program in year t ; T , the planning horizon (15 years); and r , discount rate.

The equation used for calculating the benefits of a vaccination program is B_t =total disease burden without vaccination program–total disease burden with vaccination program. In this formula, disease burden is defined as the costs of all hospitalized cases plus costs of nonhospitalized cases. The equation used for calculating the costs of a vaccination program is C_t =total costs of vaccination + total costs of vaccine-associated adverse events.

These 3 equations were used to estimate the BCR of vaccination with either DTaP or DTwP, compared with no vaccination. This is expressed as follows:

$$BCR_t = \sum_{t=0}^T B_t / \sum_{t=0}^T C_t.$$

Benefit-cost ratios for the acellular pertussis and whole-cell pertussis components were calculated using vaccine price plus the cost of treating vaccine-related adverse events as the program costs. Costs associated with vaccine administration, transportation of parent and child, and lost parental productivity were assumed to be borne by the diphtheria and tetanus component.

ESTIMATING DISEASE BURDEN WITHOUT VACCINATION

When no published data were available, the conclusions of an expert panel conducted by Batelle Inc on February 22, 1993, were used (**Table 1**).¹⁴ The panel members were Kathryn Edwards, MD, Scott Halperin, MD, Erik Hewlett, MD, and Edward A. Mortimer, Jr, MD. Based on review of diphtheria incidence rates in the prevaccine era¹⁷ and after the introduction of diphtheria toxoid, the expert panel estimated that in the absence of vaccination, the age-specific incidence of diphtheria would be similar to that observed during the prevaccine period. The expected number of tetanus cases in the absence of vaccination was estimated from the rate of tetanus observed among unvaccinated children in the US during 1981-1991.¹⁴ The age-specific risk of contracting pertussis was calculated based on incidence data from Sweden during the early 1980s¹⁸ and US data from the 1920s,¹⁹ both of which suggested a cumulative pertussis incidence of 70% by age 15 years. The age-specific likelihood of hospitalization was based on a study of bacteriologically confirmed case patients hospitalized in Sweden.²⁰

ESTIMATING DISEASE BURDEN WITH VACCINATION

To determine the number of cases of diphtheria, tetanus, and pertussis occurring in the presence of a vaccination program, we used the average of the annual number of reported cases for each disease between 1986 and 1996 in the United States stratified by age (<1 year, 1-4 years, 5-9 years, and 10-14 years).²¹⁻³¹ Based on studies showing comparable efficacy of DTaP and DTwP, the same reduction in disease burden was used for DTaP and DTwP in the base case. Rates for each disease were adjusted for underreporting and applied to the birth cohort of 4.1 million. We assumed that 50% of diphtheria (Centers for Disease Control and Prevention, unpublished data) and 80% of tetanus cases³² were unreported. For pertussis, the age-specific disease burden was estimated from national surveillance data on hospitalized cases³³ (adjusted for 70% underreporting³⁴), and divided by the probability of hospitalization.³⁵⁻³⁷

VACCINE-ASSOCIATED ADVERSE EVENTS

Minor vaccine-associated adverse events were defined as local reactions at the injection site (eg, pain, redness,

munization in the United States compared with no vaccination program.

RESULTS

BASE CASE

Without a vaccination program, for a cohort of 4.1 million children, the model estimated that 2.87 million pertussis cases would occur, resulting in 1131 deaths; 276 750 diphtheria cases, resulting in 27 675 deaths; and 165 tetanus cases, resulting in 25 deaths. From the societal perspective, these cases would cost \$23 536.5 million with approximately \$18 772.4 million (80%) for diphtheria and \$4770.1 million (20%) for pertussis (**Table 2**).

In the presence of either a DTaP or DTwP vaccination program, the number of diphtheria, tetanus, and pertussis cases would be reduced by more than 99%, 93%, and 96%, respectively (Table 2). The societal cost of vaccinating with DTaP was estimated at \$866.5 million, which is \$113 million greater than the \$753.7 million that would be spent on a DTwP vaccination program (Table 2). From a societal perspective, the BCR for the DTaP vaccination program was 27:1, and the BCR for the DTwP vaccination program was 31:1 (Table 2). The BCR for DTaP, from the health care system perspective, was estimated to be 9:1.

The incremental costs of vaccinating with acellular pertussis vs whole-cell pertussis was \$113 million (\$148.7 million in additional vaccine costs minus \$35.8 million

swelling) or mild systemic reactions, such as low-grade fever, vomiting, and anorexia. The frequency of minor adverse events associated with both DTaP and DTwP was estimated by averaging the results of clinical trials for vaccines licensed for use in the United States in 1997 (Table 1).^{5,6,12}

Major reactions to DTaP or DTwP were those identified in the 1991 and 1994 Institute of Medicine reports as having scientific evidence of a causal relationship with DTwP.^{38,39} These reactions were hypotonic hyporesponsive episodes, uncomplicated seizures, protracted crying or screaming, anaphylaxis, and acute encephalopathy with no permanent sequelae. Probabilities for these conditions were based on published estimates^{11-13,38,39} and clinical trials (Table 1).^{5,6,9,10} The base-case analysis for DTwP included the possibility of vaccine-associated encephalopathy occurring at a frequency of 0.57 cases per 100,000 doses. In the base-case analysis, it was assumed that DTaP was not associated with acute encephalopathy.

COSTS ASSOCIATED WITH DISEASE

Data on costs of disease and adverse events were obtained from a variety of published studies,^{13,40} the 1987 National Medical Expenditures Survey,⁴¹ and from the Codman Research Group's 1990 hospital discharge database.⁴² All diphtheria and tetanus cases were assumed to be hospitalized and disease burden costs were calculated from the average length of hospital stay and average costs per case.¹⁴ Information on the probabilities of pertussis-related complications and their associated costs was used to calculate pertussis disease burden costs. Physician costs for inpatients were based on average hospital stay, assuming 1 physician visit per day of hospitalization.^{43,44} All costs were standardized to 1997 dollars, using the medical care component of the consumer price index.⁴⁵ All costs and benefits that were assumed to occur in the future were discounted at a 3% annual rate.

COSTS ASSOCIATED WITH VACCINATION

The direct cost of vaccination was the sum of vaccine price per dose, vaccine administration costs, and costs associated with vaccine adverse events. It was assumed that 50% of vaccinations are given in the public sector and 50% in the private sector. For DTaP, a weighted average vaccine price of \$13.87 (Table 1) was used based on the 1997 private

sector and federal contract vaccine prices for licensed DTaP vaccines (Centers for Disease Control and Prevention, unpublished data). For DTwP, a weighted average vaccine price of \$5.71 was used based on the 1996 private sector and federal contract vaccine prices (Centers for Disease Control and Prevention, unpublished data). Prices included \$2.25 per dose tax that supports the National Vaccine Injury Compensation Program.⁴⁶

Direct nonmedical costs included travel to the clinic or physician's office at \$3 for a round trip drive of 10 miles or \$1.50 each way for public transportation. The weighted average cost of administering either DTaP or DTwP was estimated to be \$12.65 per dose. To calculate indirect costs, we assumed that a caretaker's time off from work to take his or her child for vaccination was an average of 2 hours of lost productivity at a cost of \$17.50.⁴⁷

Vaccination coverage rates by age and number of doses administered were obtained for children aged 0 to 6 years (Centers for Disease Control and Prevention, unpublished data). The data reflect recent gains in vaccination coverage rates, with 93% of 19- to 35-month-old children having received 3 or more doses of DTP/diphtheria and tetanus vaccinations.⁴⁸ We estimated that by age 6 years, 98% of children have received 4 or more doses of DTwP/DTaP. To calculate the maximum number of doses of vaccine required for the program, we assumed 21.5% vaccine wastage.⁴⁹

SENSITIVITY ANALYSES

Univariate sensitivity analyses were performed to test the effect of the following key parameters on the cost-benefit of DTaP: (1) a lower (80%) and upper bound (98.5%) for acellular pertussis vaccine effectiveness; (2) higher program costs of \$12.2 million (Table 1); (3) a discount rate of 5%; and (4) variation of the probabilities of some major vaccine-related adverse events (hypotonic hyporesponsive episodes, uncomplicated seizures, and protracted crying) (Table 1).

Threshold values for the price of DTaP and the effectiveness of the acellular pertussis vaccine were calculated. The threshold value for DTaP price was the price at which the net present value (NPV) of the DTaP vaccination program equaled the NPV of the DTwP program. The threshold value for the effectiveness of acellular pertussis vaccine was the vaccine effectiveness at which the NPV of an acellular pertussis vaccine program equaled the NPV of the whole-cell pertussis program.

for reduced costs of vaccine adverse events) (Table 2). Cost savings for vaccination with acellular pertussis were \$4360.8 million and for vaccinating with whole-cell pertussis were \$4473.7 million (Table 2). From the societal perspective, BCRs were estimated to be 20:1 for acellular pertussis and 41:1 for whole-cell pertussis.

SENSITIVITY ANALYSES

The BCRs for DTaP when acellular pertussis effectiveness was set at 80% and 98.5% were 26:1 and 27:1, respectively (**Table 3**). With higher program costs, the BCR decreased from 27:1 to 25:1 at the 3% discount rate. Using higher program costs, a discount rate of 5%, and lower and higher estimates of vaccine adverse events only

slightly reduced the BCRs of DTaP vaccination (Table 3). The threshold price for a dose of DTaP ranged from \$13.87 at 98.5% vaccine effectiveness to \$7.65 at 96% vaccine effectiveness (**Figure 1**). At current vaccination costs, the NPV of acellular pertussis equaled that of whole-cell pertussis if vaccine effectiveness was 98.5% (**Figure 2**).

COMMENT

Diphtheria, tetanus, and pertussis are major public health concerns in the United States because of their potential to cause a substantial health and economic burden. Our study shows that a vaccination program that achieves high coverage levels with either DTaP or DTwP is highly cost beneficial and results in substantial cost savings. Regard-

Table 1. Input Variables and References*

Input Variables	Vaccines, Base-Case		References
	DTaP	DTwP	
Disease and Complication Rates (per 100 000)			
Diphtheria			
Without vaccination†	6750	6750	Estimated
With vaccination‡			
Hospitalized	0.05	0.05	Estimated
Death	0.005	0.005	Estimated
Tetanus			
Without vaccination†	4.02	4.02	Estimated
With vaccination‡			
Hospitalized	0.28	0.28	Estimated
Death	0.042	0.042	Estimated
Pertussis			
Without vaccination†			
Not hospitalized	66 686	66 686	Estimated
Hospitalized	3314	3314	Estimated
Death	27.59	27.59	Estimated
Seizures	117.00	117.00	Estimated
Pneumonia	823.81	823.81	Estimated
Encephalopathy	10.75	10.75	Estimated
No complications	2360.40	2360.40	Estimated
With vaccination‡			
Not hospitalized	2708	2708	33, 34
Hospitalized	126.43	126.43	33, 34
Death	1.01	1.01	33, 34
Seizures	3.42	3.42	34
Pneumonia	26.12	26.12	34
Encephalopathy	0.32	0.32	34
Complications	96.60	96.60	Estimated
Major Adverse Events			
HHE	8 (4-14)§	57§	13
Physician visit, %	50	50	13
Hospitalized, %	12.5	12.5	13
Anaphylaxis	2§	2§	38
Physician visit, %	100	100	14
Hospitalized, %	100	100	14
Uncomplicated seizures	10 (4-26)§	57§	11
Physician visit, %	100	100	14
Hospitalized, %	12.5	12.5	13
Protracted crying/screaming	63 (12-127)§	31§	40
Physician visit, %	10	10	14
Hospitalized, %	0.5	0.5	14
Acute encephalopathy		0.57§	38
Physician visit, %		100	13
Hospitalized, %		100	13
Minor adverse events, %	37	61	37
Other Variables, %			
Vaccination coverage	93	93	48
Vaccine effectiveness	96 (80-98.5)	96	
Annual discount rate	3 (5)	3	

less of the vaccine used or the perspective taken, the BCR (which measures the return for every dollar invested) of the vaccination program was always more than 1.0. These findings provide a compelling case for public and private sectors in the United States to maintain the high vaccination coverage levels achieved among infants and young children.

Sensitivity analyses of the effect of higher program costs, lower pertussis vaccine effectiveness, a discount rate of 5%, or a higher frequency of major adverse events

Table 1. Input Variables and References* (cont)

Input Variables	Vaccines, Base-Case		References
	DTaP	DTwP	
Cost of Disease and Adverse Events Associated With Vaccination, \$ (1997 Dollars)			
Physician visit	55	55	43, 44
Telephone consultation	15	15	17
Diphtheria			
Hospital	9043	9043	42
Tetanus			
Hospital	55 736	55 736	42
Pertussis			
Ambulatory visit	157	157	17
Hospital	9154	9154	42
HHE	6890	6890	42
Uncomplicated seizures	7013	7013	42
Protracted crying/screaming	2607	2607	42
Acute encephalopathy	14 641	14 641	42
Anaphylaxis	4429	4429	42
Vaccine-associated costs, \$			
Average vaccine price and excise tax			
DTwP#	5.71		CDC unpublished data
DTaP#	13.87		CDC unpublished data
Whole-cell pertussis**	3.62		CDC unpublished data
Acellular pertussis**	11.78		CDC unpublished data
Administration cost††	12.65		Estimated
Transportation cost	3.00		Estimated
Higher program administration	12 223 221		Estimated
Unaccounted vaccine (wastage)	51 675 824		Estimated
Parental time (lost productivity/h)‡‡	8.75		47

*DTaP indicates diphtheria, tetanus, and acellular pertussis vaccine; DTwP, diphtheria, tetanus, and whole-cell pertussis vaccine; HHE, hypotonic hyposensitive episodes; and CDC, Centers for Disease Control and Prevention.

†Rates per 100 000 children. Estimated disease burden without vaccination is based on the average number of cases reported during the prevaccine era divided by the cohort of 4.1 million children and multiplied by 100 000.

‡Rates per 100 000 children. Estimated based on the average number of cases reported in the annual summaries of notifiable diseases, United States, 1986 to 1996,²¹⁻³¹ divided by the cohort of 4.1 million children and multiplied by 100 000.

§The range noted was used in a 1-way sensitivity analysis. Rate per 100 000 doses of vaccine administered.

||Estimate calculated by using the estimated length of stay and average cost per hospital day (mean cost per day/length of stay).

¶Estimates obtained from the World Health Organization. International Classification of Diseases, Ninth Revision (ICD-9). Geneva, Switzerland: World Health Organization; 1977:code 323.5 (encephalopathy).

#Based on CDC estimates, it was assumed that 50% of vaccinations are given in the public sector and 50% in the private sector; a weighted average vaccine price was calculated using these percentages.

**Acellular pertussis and whole-cell pertussis vaccine costs were calculated by subtracting the price of diphtheria and tetanus vaccine from the price of either DTaP or DTwP.

††The weighted mean vaccine administration cost between public and private sectors was calculated by assuming that 50% of vaccinations were given in each sector.

‡‡The annual median hourly earnings for men and women participating in the labor market in a full- or part-time job.⁴⁷

Table 2. Results of the Base-Case Analyses of Health and Economic Outcomes and Benefit-Cost Ratios of DTaP/DTwP and Acellular/Whole-Cell Pertussis Vaccination Program*†

Parameters	Vaccine Type			
	DTaP	DTwP	Acellular Pertussis Only	Whole-Cell Pertussis Only
Health Outcomes				
Cases and deaths without vaccination				
Diphtheria cases	276 750	276 750		
Deaths	27 675	27 675		
Tetanus cases	165	165		
Deaths	25	25		
Pertussis cases	2 870 001	2 870 001	2 870 001	2 870 001
Deaths	1131	1131	1131	1131
Cases and deaths with vaccination‡				
Diphtheria cases	2	2		
Deaths	0.2	0.2		
Tetanus cases	12	12		
Deaths	2	2		
Pertussis cases	116 224	116 224	116 224	116 224
Deaths	41	41	41	41
Economic Outcomes (Disease Costs), \$\$				
Without vaccination (in millions)				
Diphtheria	18 772.4	18 772.4		
Tetanus	21.0	21.0		
Pertussis	4770.1	4770.1		
Total Cost	23 563.5	23 563.5	4770.1	4770.1
Total Cost HCS 	4755.0	4755.0	2546.3	2546.3
With vaccination (in millions)				
Diphtheria	0.1	0.1		
Tetanus	1.5	1.5		
Pertussis	184.9	184.9		
Subtotal	186.5	186.5	184.9	184.9
Subtotal HCS 	99.7	99.7	99.7	99.7
Vaccine program costs (in millions)				
Vaccine¶	252.7	104.1	214.7	66.0
Administration#	230.5	230.5	0.0	0.0
Transportation	54.7	54.7	0.0	0.0
Parental productivity	318.9	318.9	0.0	0.0
Adverse events	9.7	45.5	9.7	45.5
Subtotal	866.5	753.7	224.4	111.5
Subtotal HCS 	547.6	434.8	224.3	111.2
Total Program Costs	1053.0	940.2	409.3	296.4
Total Program Costs HCS 	647.3	534.2	324.0	210.9
Net cost (savings in millions)	22 510.5	22 623.3	4360.8	4473.7
Net cost HCS (savings in millions)	4107.7	4220.8	2222.3	2335.4
Benefit-cost ratios	27:1	31:1	20:1	41:1
Benefit-cost ratios HCS	9:1	11:1	11:1	22:1

*DTaP indicates diphtheria, tetanus, and acellular pertussis vaccine; DTwP, diphtheria, tetanus, and whole-cell pertussis vaccine; and HCS, health care system perspective.

†Value of health and economic outcomes are estimated based on model parameters. Costs and benefits are discounted at 3% and expressed in 1997 dollars. Numbers in the table are rounded.

‡Data used are based on the mean disease incidence (Centers for Disease Control and Prevention, unpublished data, 1986-1996) applied to a birth cohort of 4.1 million over a 15-year period (birth to age 15 years).

§Disease costs are calculated as the sum of the direct and indirect costs.

||The details of the calculated numbers for this perspective were not shown but are available on request from the authors.

¶Vaccine cost includes excise tax of \$2.25.

#A mean vaccine administration cost of \$12.65 was used (assuming a 50/50 private/public vaccination level).

associated with DTaP did not greatly alter the positive BCR. Benefit-cost ratios remained more than 25:1 from the societal perspective and more than 7:1 from the health care system perspective for each of these analyses, indicating the robustness of the base-case estimates.

Using DTaP instead of DTwP led to a net increase in vaccination program costs; however, DTaP was still shown to be highly cost beneficial. For the net savings

of the DTaP vaccination program to equal those of the DTwP program, the average price for a dose of DTaP would need to decrease from \$13.87 per dose to \$7.65 per dose. A decrease in vaccine price might occur in the future with increased competition and higher volumes of vaccine purchased.

Adding either acellular or whole-cell pertussis to an existing 5-dose schedule of diphtheria and tetanus

Table 3. Univariate Sensitivity Analysis of the Impact of Altering Health and Economic Outcomes for Vaccination With DTaP or Acellular Pertussis Alone*†

Parameters	DTaP	Acellular Pertussis
80% Vaccine Effectiveness for Acellular Pertussis		
Cases of pertussis	574 000	574 000
Deaths	226	226
NPV (in millions), \$	21 741.8	3592.3
BCR	26:1	17:1
98.5% Vaccine Effectiveness for Acellular Pertussis		
Cases of pertussis	43 055	43 055
Deaths	17	17
NPV (in millions), \$‡	22 623.8	4474.2
BCR	27:1	21:1
BCR		
Higher program costs	25:1	5:1
5% Discount rate	25:1	5:1
Lower vaccine adverse event rates§	27:1	5:1
Higher vaccine adverse event rates§	27:1	5:1

*DTaP indicates diphtheria, tetanus, and acellular pertussis vaccine; NPV, net present value; and BCR, benefit-cost ratio.

†The results shown are for the societal perspective. Values in the table are rounded.

‡Measures the magnitude of the discounted economic benefit received in the DTaP or acellular pertussis vaccination program.

§Values from Table 1.

toxoids resulted in prevention of an estimated 2.75 million pertussis cases and 1090 pertussis deaths. These disease burden costs outweighed the costs of either vaccine and any associated adverse events. Regardless of the perspective taken or the vaccine used, net cost savings of vaccination against pertussis were positive. This finding is similar to that in an earlier study by Koplan et al,⁴⁰ which found a savings of \$1.1 billion in direct medical costs from a health sector perspective and a BCR of 3:1. In 1984, Hinman and Koplan¹³ updated the earlier estimates using more current disease incidence data and rates of adverse events and still found net cost savings and a BCR of 11:1.

It is possible that our model over estimates some of the economic benefits obtained when vaccinating against diphtheria, tetanus, and pertussis. When calculating benefits, we used the consensus from an expert panel that the disease burden without vaccination would be equal to that of the prevaccination era before the introduction of mass immunizations. In developed countries, however, the incidence of many infectious diseases, including diphtheria, tetanus, and pertussis, were declining before the introduction of universal immunization.^{50,51}

In 1997, after licensure of DTaP vaccines in the United States, the Advisory Committee on Immunization Practices, American Academy of Pediatrics, and American Academy of Family Physicians recommended routine use of acellular pertussis vaccines among infants and young children in the United States.^{9,10} Although policymakers were mindful of the slight economic advantage of DTwP over DTaP as shown in this study, the following factors played a role in the decision

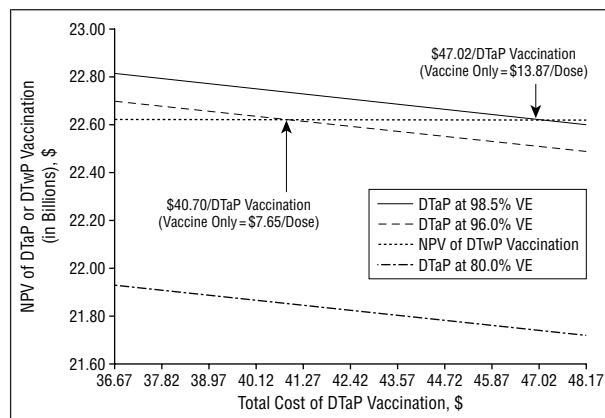


Figure 1. Sensitivity analysis of the impact of varying the cost of vaccination and vaccine effectiveness (VE) on the net present value (NPV) of combined diphtheria, tetanus, and acellular pertussis (DTaP) vaccination compared with the NPV of combined diphtheria, tetanus, and whole-cell pertussis (DTwP) vaccination. Total costs indicate both direct and indirect costs.

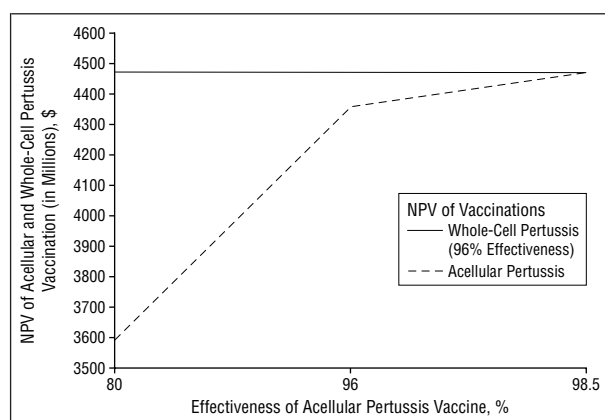


Figure 2. Sensitivity analysis of the changes in the net present value (NPV) of acellular pertussis vaccine with changes in vaccine effectiveness compared with the NPV of whole-cell pertussis vaccine.

to use acellular pertussis vaccines: (1) parents and providers would have increased confidence in vaccination from the use of a vaccine associated with fewer adverse events; (2) the production of acellular pertussis vaccines could be better standardized with more rigorous quality control than could production of whole-cell pertussis vaccines; and (3) acellular pertussis vaccines may be used as a booster dose in adolescents and adults with potential further decrease in pertussis disease. These considerations, and the fact that the use of DTaP generates net savings, support the decision to switch from using DTwP to DTaP.

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