Economic Evaluation of the Routine Childhood Immunization Program in the United States, 2009

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KEY WORDS

diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP), tetanus and diphtheria toxoids vaccine (Td), Haemophilus influenzae type b conjugate vaccine (Hib), inactivated poliovirus vaccine (IPV), measles/mumps/rubella vaccine (MMR), hepatitis B vaccine (HepB), varicella vaccine (VAR), 7-valent pneumococcal conjugate vaccine (PCV7), hepatitis A vaccine (HepA), rotavirus vaccine (Rota), net savings, benefit-cost analysis

ABBREVIATIONS

ABCs—Active Bacterial Core Surveillance
BCR—benefit-cost ratio
DTaP—diphtheria and tetanus toxoids and acellular pertussis vaccine
HepA—hepatitis A vaccine
HepB—hepatitis B vaccine
Hib—Haemophilus influenzae type b conjugate vaccine
IPD—invasive pneumococcal diseases
IPV—inactivated poliovirus vaccine
MMR—measles/mumps/rubella vaccine
NIS—National Immunization Survey
NPV—net present values
PCV7—7-valent pneumococcal conjugate vaccine
Rota—rotavirus vaccine
Td—tetanus and diphtheria toxoids vaccine
VAR—varicella vaccine

Dr Zhou conceptualized the study, carried out the analyses, and drafted the initial manuscript; Dr Shefer conceptualized the study and drafted the initial manuscript; Dr Wenger conceptualized the study and drafted the initial manuscript; Dr Messonnier conceptualized the study and reviewed the manuscript; Ms Wang reviewed the analyses and manuscript; Ms Lopez provided inputs of the analyses and reviewed the manuscript; Dr Moore provided inputs of the analyses and reviewed the manuscript; Dr Cortese provided inputs of the analyses and reviewed the manuscript; Dr Rodewald conceptualized the study and reviewed the manuscript; and all authors approved the final manuscript as submitted.

(Continued on last page)

WHAT'S KNOWN ON THIS SUBJECT: The first evaluation of the economic impact of all vaccines in the routine US childhood immunization schedule assessed the 2001 schedule (excluding pneumococcal conjugate and influenza vaccines) and documented substantial cost savings over the lifetimes of the cohort of children born in 2001.

WHAT THIS STUDY ADDS: This report updates our previous evaluation, and estimates the costs and benefits of vaccinating the cohort of children born in 2009. We include vaccines routinely recommended for children in 2009.

abstract

OBJECTIVES: To evaluate the economic impact of the 2009 routine US childhood immunization schedule, including diphtheria and tetanus toxoids and acellular pertussis, Haemophilus influenzae type b conjugate, inactivated poliovirus, measles/mumps/rubella, hepatitis B, varicella, 7-valent pneumococcal conjugate, hepatitis A, and rotavirus vaccines; influenza vaccine was not included.

METHODS: Decision analysis was conducted using population-based vaccination coverage, published vaccine efficacies, historical data on disease incidence before vaccination, and disease incidence reported during 2005 to 2009. 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 work time lost. All costs were inflated to 2009 dollars, and all costs and benefits in the future were discounted at a 3% annual rate. A hypothetical 2009 US birth cohort of 4 261 494 infants over their lifetime was followed up from birth through death. Net present value (net savings) and benefit-cost ratios of routine childhood immunization were calculated.

RESULTS: Analyses showed that routine childhood immunization among members of the 2009 US birth cohort will prevent ∼42 000 early deaths and 20 million cases of disease, with net savings of $13.5 billion in direct costs and $68.8 billion in total societal costs, respectively. The direct and societal benefit-cost ratios for routine childhood vaccination with these 9 vaccines were 3.0 and 10.1.

CONCLUSIONS: From both direct cost and societal perspectives, vaccinating children as recommended with these vaccines results in substantial cost savings. Pediatrics 2014;133:577–585
In the United States the widespread use of vaccines, frequently cited as among the most effective preventive health care measures, has resulted in dramatic decreases in the incidence of vaccine-preventable diseases and corresponding declines in morbidity and mortality. Remarkable success has been observed not only for vaccines in use for decades, but also for more recently introduced vaccines, including pneumococcal conjugate and rotavirus vaccines.\(^1\)\(^-\)\(^4\) In addition to the health benefits that have accrued from the US immunization program, cost savings have accrued as well. The first evaluation of the economic impact of all vaccines in the routine US childhood immunization schedule assessed the 2001 schedule (excluding the newly added pneumococcal conjugate and influenza vaccines); this evaluation documented substantial cost savings over the lifetimes of the cohort of children born in 2001.\(^7\) The study used consistent methods and assumptions for each vaccine assessed and thus provided comprehensive economic information of uniform consistency for making US vaccine policy and immunization program decisions.

Since the analysis of routinely used vaccines in the 2001 schedule, pneumococcal conjugate vaccine has become widely used, and hepatitis A and rotavirus vaccines were added to the schedule, along with a second dose of varicella vaccine.\(^8\) In addition, costs for vaccination have risen, in part because more vaccines are recommended and because in general newer vaccines are more expensive than older ones. Of note, costs for treatment of vaccine-preventable diseases that do occur have also risen.

This report updates our previous evaluation, using the same methods to estimate the costs and benefits of vaccinating the cohort of children born in 2009, following members from birth to death. We include vaccines routinely recommended for children in 2009: diphtheria and tetanus toxoids and acellular pertussis (DTaP), \textit{Haemophilus influenzae} type b conjugate (Hib), inactivated poliovirus (IPV), measles/mumps/rubella (MMR), hepatitis B (HepB), varicella (VAR), 7-valent pneumococcal conjugate (PCV7), hepatitis A (HepA), and rotavirus (Rota) vaccines. Although recommended for routine immunization, influenza vaccine is not included in this analysis because it is administered annually and methods for assessing costs and impact differ substantially than those for other vaccines.

**METHODS**

**Decision Analysis Model**

We developed 1 decision tree for each vaccine as the basis for our model (see for example, Fig 1) and then evaluated the effect of routine childhood vaccination with DTaP, Hib, IPV, MMR, HepB, VAR, PCV7, HepA, and Rota vaccines on a hypothetical US birth cohort of 4,261,494 children (the estimated number of births in 2009 [http://www.census.gov/popest/states/asrh/les/SC-EST2009-AGESEX-RES.csv]) from birth through death. In the 2009 schedule, the Centers for Disease Control and Prevention (CDC)’s Advisory Committee on Immunization Practices recommended routine administration of 5 doses of DTaP, 3 or 4 doses of Hib (depending on product used), 4 doses of IPV, 2 doses of MMR, 3 doses of HepB, 2 doses of VAR, 4 doses of PCV7, 2 doses of HepA, and 2 or 3 doses of Rota (depending on product used) by age 6 years.\(^9\) Our analysis is based on coverage attained for each of these vaccines in the United States as estimated by the 2009 National Immunization Survey (NIS),\(^10\) Immunization Information Systems\(^11\) available in some areas, and 2009–2010 School and Childcare Vaccination Surveys.\(^12\)

The analyses were performed from 2 perspectives: direct cost (direct medical and nonmedical costs) and societal (direct and indirect costs). Direct medical costs include those associated with treating an initial infection as well as costs associated with complications and sequelae of diseases. Direct nonmedical costs include travel costs, costs for special education of children disabled by diseases, and costs for other supplies for special needs. Indirect costs include the productivity losses owing to premature mortality and permanent disability among cohort members, as well as opportunity costs associated with parents who miss work to care for their sick children or cohort members themselves who miss work owing to vaccine-preventable illness. Benefits of routine childhood immunization are quantified as the savings in direct and indirect costs that accrue from averting morbidity and mortality by vaccination. The costs associated with the immunization program include the vaccines, their administration, parent travel, and work time lost and adverse events associated with these vaccines. All costs were adjusted to 2009 dollars by using general and

![FIGURE 1: Simplified decision tree.](image-url)
medical Consumer Price Indices, and all costs and benefits in the future were discounted at a 3% annual rate. We calculated net present values (NPV) and benefit-cost ratios (BCRs) for all vaccines together. NPV is the sum of the discounted benefits from the routine childhood immunization program minus the sum of the discounted costs, and BCR is equal to the discounted benefits divided by the discounted immunization program costs. The incremental benefit-cost ratios for PCV7, HepA, and Rota vaccines were also calculated.

The data for burden of diseases, costs of diseases, costs for outbreak control, and costs of vaccination and adverse events used in our 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.

### 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, and the prevalence, complications, and perinatal transmission of hepatitis B in the United States in the pre-vaccine era were obtained from the previous analysis (Table 1).7,15–27

For pneumococcal-related diseases, the age-specific estimated incidence rates in the United States in the pre-vaccine era were obtained from the CDC’s Active Bacterial Core Surveillance (ABCs) program (for invasive pneumococcal diseases, or IPD) and the literature (for pneumonia and acute otitis media).28–31 Age-specific pre-vaccine IPD rates and case-fatality rates for IPD were based on data from the ABCs program for 1998 and 1999. All-cause pneumonia incidence and acute otitis media rates were obtained from the literature.28–31

For hepatitis A virus infection, pre-vaccine age- and region-specific incidence estimates were based on the average incidence during 1990 to 1995. For each reported case of hepatitis A we assumed there were 3.28 unreported cases.32 All reported cases were assumed to be icteric (symptomatic with jaundice). The number of additional anicteric cases was estimated by applying age-specific ratios.32 We assumed a 1.40% per year ongoing decline for the logarithm of hepatitis A virus infection rates during the period covered by our analysis.32

For rotavirus disease, we assumed that the cumulative incidence of rotavirus gastroenteritis is 75% in the first 5 years of life.35–38 The cumulative incidence of hospitalization visits attributable to rotavirus gastroenteritis in the first 5 years is 1.70%, the cumulative incidence of outpatient visits is 11.14%, the cumulative incidence of emergency department visits is 5.36%, and the cumulative incidence of deaths is 0.00078%.36

### Estimating the Burden of Diseases With Vaccination

For all diseases except varicella, hepatitis B, pneumococcal diseases, hepatitis A, and rotavirus, we used surveillance data for 2005 to 2009 from the National Notifiable Diseases Surveillance System to estimate the burden of diseases with vaccination in 2009. For varicella, we used the average incidence in 2009 from 4 states (Colorado, Connecticut, Michigan, and Texas) to estimate the total varicella cases in the United States. Based on data from the Varicella Active Surveillance Project, we assumed that 59.5% of reported cases involved persons who had previously received VAR and that these were thus much milder than cases among unvaccinated persons.37 For hepatitis B, because chronic cases were not reported to the National Notifiable Diseases Surveillance System, we used an established hepatitis B decision analysis model38 and the vaccine efficacy estimates39 to estimate the likelihood of hepatitis B infection and sequelae among vaccinated and unvaccinated children in the cohort. For pneumococcal disease, vaccination-era IPD rates and case-fatality rates for IPD were based on data for 2008 to 2009.

### Table 1

#### Annual Incidence Rates of Diphtheria, Tetanus, Pertussis, Hib, Polio, Measles, Mumps, Rubella, HepB, Varicella, IPD, HepA, and Rota (per 100 000)7,15–36

<table>
<thead>
<tr>
<th>Disease</th>
<th>Without Vaccination (ie, Pre-Vaccine Era)</th>
<th>With Vaccination (ie, data by 2009)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria&lt;sup&gt;a&lt;/sup&gt;</td>
<td>600</td>
<td>0</td>
</tr>
<tr>
<td>Tetanus&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.3</td>
<td>0.003</td>
</tr>
<tr>
<td>Pertussis&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4720</td>
<td>12</td>
</tr>
<tr>
<td>Hib&lt;sup&gt;c&lt;/sup&gt;</td>
<td>158</td>
<td>0.1</td>
</tr>
<tr>
<td>Polio, paralytic&lt;sup&gt;d&lt;/sup&gt;</td>
<td>31</td>
<td>0</td>
</tr>
<tr>
<td>Measles&lt;sup&gt;e&lt;/sup&gt;</td>
<td>10 641</td>
<td>0.2</td>
</tr>
<tr>
<td>Mumps&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6205</td>
<td>11.3</td>
</tr>
<tr>
<td>Rubella&lt;sup&gt;b&lt;/sup&gt;</td>
<td>3300</td>
<td>0.01</td>
</tr>
<tr>
<td>HepB&lt;sup&gt;c&lt;/sup&gt;</td>
<td>72.4</td>
<td>5.5</td>
</tr>
<tr>
<td>Varicella&lt;sup&gt;c&lt;/sup&gt;</td>
<td>9859</td>
<td>394</td>
</tr>
<tr>
<td>IPD&lt;sup&gt;b&lt;/sup&gt;</td>
<td>213.6</td>
<td>31.8</td>
</tr>
<tr>
<td>HepA&lt;sup&gt;d&lt;/sup&gt;</td>
<td>14.3</td>
<td>2.5</td>
</tr>
<tr>
<td>Rota&lt;sup&gt;d&lt;/sup&gt;</td>
<td>12 750</td>
<td>6209.1</td>
</tr>
</tbody>
</table>

<sup>a</sup>Incidence estimates used in the analysis varied by age.
<sup>b</sup>Estimates shown are for children age 5 to 9 years.
<sup>c</sup>Estimates shown are for children age 1 year.
<sup>d</sup>Estimates shown are for children age 2 to 4 years.
<sup>e</sup>Estimates shown are for children age 1 to 4 years.
<sup>f</sup>Estimates shown are for children age 2 years in 1 region.
<sup>g</sup>Estimates shown are for children age 2 years.

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PEDIATRICS Volume 133, Number 4, April 2014

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from the ABCs program. All-cause pneumonia incidence and acute otitis media rates were obtained from the literature. For both hepatitis A and rotavirus diseases, we developed hepatitis A and rotavirus decision analysis models, using the efficacies of the vaccines to estimate the likelihood of hepatitis A and rotavirus infections and their sequelae among vaccinated children in the cohort.

**COSTS ASSOCIATED WITH DISEASE**

**Direct Costs**

Direct costs for outpatient and inpatient visits and outbreak control, which was not included in the previous analysis, were covered in the analysis. The cost of outpatient visits, average duration of hospital stay, hospitalization costs, and costs for outbreak control for each condition related to these diseases, including congenital rubella syndrome (Table 2) were obtained from HCUPnet, the Marketscan database, and published and unpublished studies.

**Indirect Costs**

To estimate the productivity losses from premature mortality, we used the human capital approach. Costs for work loss were determined by the number of days of missed work (for provision of care for sick children, for illness among cohort members, or for resulting disability) multiplied by the daily wage rate associated with the value of lost wage-earning work and the imputed value of housekeeping and home-care activities. We assumed the days of morbidity were distributed randomly throughout the week.

**Vaccination Coverage, Costs, and Adverse Events Associated With Vaccination**

Vaccination coverage was based on 2009 NIS data. Overall, ~53% of US childhood vaccines were publicly purchased in 2009 (CDC, unpublished data, 2009). The public and private prices for all vaccines were obtained from the CDC Vaccine Price List in 2009. We assumed that the overall rate of vaccine wastage (public and private sectors) was 5%. The federal excise tax that supports the National Vaccine Injury Compensation Program was not included in all vaccine prices.

NIS data indicate that >80% of children obtained their vaccines from private providers. The cost for administering a vaccine dose during a visit to a private clinic was estimated at $25.68. For the public clinic, we used an administration cost of $7.20. We assumed that caregivers take 2 hours’ time off from work to take the child for vaccination (as per previous economic studies). We assumed that the average cost for these caregivers was $16.75 per hour; and cost for caregiver’s travel to the clinic was $21.60. We assumed that there were no serious side effects for IPV. For HepB, we assumed that 1.1 per 1 000 000 vaccinated children will have anaphylaxis. For PCV7, we assumed that 5 per 1 000 000 vaccinated children will have severe seizure. For HepA, we assumed that 0.17 per 1 000 000 vaccinated children will have severe adverse reactions. For Rota, we assumed that 2250 per 1 000 000 vaccinated infants will have intussusceptions caused by the first dose (based on data from international setting and no documented risk in the United States), and that the case-fatality rate for intussusception is 0.4%.

**Sensitivity Analyses**

Sensitivity analyses were used to assess the robustness of our economic estimates and to estimate the impact of potential changes to the immunization program. Univariate sensitivity analyses were performed to assess the effect of varying: (1) pre-vaccine-era disease incidence rates; (2) vaccine-era disease

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**TABLE 2 Probabilities and Costs of Hospitalizations and Outpatient Visits for Selected Vaccine-Preventable Diseases (All Costs Are in 2009 USD)**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Probability of Hospitalization, %</th>
<th>No. of Hospitalization Days</th>
<th>Cost per Hospitalization, $</th>
<th>Cost per Outpatient Visit, $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>100</td>
<td>6.1</td>
<td>15 004</td>
<td>88</td>
</tr>
<tr>
<td>Tetanus</td>
<td>100</td>
<td>16.7</td>
<td>90 635</td>
<td>88</td>
</tr>
<tr>
<td>Pertussis</td>
<td>0.65–30</td>
<td>5.5–15</td>
<td>9511–19 800</td>
<td>88–153</td>
</tr>
<tr>
<td>Hib</td>
<td>Acute cases</td>
<td>50–100</td>
<td>2–7.29</td>
<td>3632–33 812</td>
</tr>
<tr>
<td></td>
<td>Sequelae among meningitis cases</td>
<td>5–30</td>
<td>2.84–26.75</td>
<td>16 076–43 501</td>
</tr>
<tr>
<td>Poliomyelitis</td>
<td>5–100</td>
<td>4–17</td>
<td>6875–44 665</td>
<td>88</td>
</tr>
<tr>
<td>Measles</td>
<td>11–100</td>
<td>1.3–10.9</td>
<td>3562–40 695</td>
<td>78–465</td>
</tr>
<tr>
<td>Mumps</td>
<td>1–100</td>
<td>2.8–8.7</td>
<td>8982–40 695</td>
<td>97–491</td>
</tr>
<tr>
<td>Rubella</td>
<td>0.1–100</td>
<td>2.6–8.7</td>
<td>4317–49 695</td>
<td>79–575</td>
</tr>
<tr>
<td>Congenital rubella syndrome</td>
<td>Hospitalization for investigation</td>
<td>100</td>
<td>13.8</td>
<td>54 984</td>
</tr>
<tr>
<td>Heart surgery</td>
<td>100</td>
<td>8.9</td>
<td>32 763</td>
<td>32763</td>
</tr>
<tr>
<td>Cataract surgery</td>
<td>100</td>
<td>2.2</td>
<td>7763</td>
<td>7763</td>
</tr>
<tr>
<td>HepB</td>
<td>0.001–100</td>
<td>3.9–11</td>
<td>15 836–23 900</td>
<td>189–529</td>
</tr>
<tr>
<td>Varicella</td>
<td>0.1–2.1</td>
<td>3.1–8.3</td>
<td>3654–19 537</td>
<td>75–224</td>
</tr>
<tr>
<td>Pneumococcal</td>
<td>0–100</td>
<td>6.4–16.8</td>
<td>3356–22 837</td>
<td>76–240</td>
</tr>
<tr>
<td>diseases</td>
<td>HepA</td>
<td>0–100</td>
<td>2–11</td>
<td>11 070–35 064</td>
</tr>
<tr>
<td>Rota</td>
<td>0.5–3.8</td>
<td>2–3.4</td>
<td>2823–4235</td>
<td>119–402</td>
</tr>
</tbody>
</table>

*Some estimates used in the analysis varied by age, outcome of diseases, and with or without vaccination program.*
incidence rates; (3) rates of vaccine adverse events; (4) direct costs; (5) the proportion of vaccines purchased in the public versus private sector; (6) vaccine administration cost; (7) the vaccine wastage rate; (8) vaccination coverage; (9) the inclusion of federal, state, and local immunization program management expenditures and excise tax; and (10) costs associated with parent time lost from work and travel. Each parameter was assessed individually into the sensitivity analyses. We also performed the worst-case scenario analysis: the combination of the worst case of items 1 to 9.

**RESULTS**

**Base Case**

Table 3 summarizes disease cases and early deaths prevented, as well as the direct and societal costs saved by routine childhood immunization. Analyses showed that routine childhood immunization with DTaP, Hib, IPV, MMR, HepB, VAR, PCV7, HepA, and Rota among the cohort of 4,261,494 will prevent ~42,000 early deaths and 20 million cases of disease. The direct and societal costs averted by immunization program were $20.3 billion and $76.4 billion, respectively. The direct and societal costs of the routine childhood immunization program were estimated at $6.7 billion and $7.5 billion, respectively. The NVPs (net savings) of the routine childhood immunization program from the payers’ and societal perspectives were $13.5 billion and $68.8 billion, respectively. The direct and societal costs of the routine childhood immunization program were estimated at $6.7 billion and $7.5 billion, respectively. The NVPs (net savings) of the routine childhood immunization program from the payers’ and societal perspectives were $13.5 billion and $68.8 billion, respectively. The direct and societal costs of the routine childhood immunization program were estimated at $6.7 billion and $7.5 billion, respectively.

**Sensitivity Analyses**

Table 4 shows both the direct and societal BCRs from sensitivity analyses when the value of each parameter was varied in a plausible range. The incidences of some diseases likely have decreased over time even without vaccination. In a conservative scenario, reducing pre-vaccine incidence rates by 10%, the resulting direct and societal BCRs were 2.6 and 9.0, respectively. Disease incidence in the vaccination era may have been underestimated. To test the effect, we modeled vaccination era 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. When we doubled the vaccine adverse event rates used in the base case analysis, the direct and societal BCRs did not change substantially. With a lower or higher wastage rate, the BCRs changed only slightly. When

### Table 3

**Estimated Cases and Deaths Prevented and Costs Saved for Selected Vaccine-Preventable Diseases With a Vaccination Program for 1 Cohort**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cases Prevented</th>
<th>Deaths Prevented</th>
<th>Direct Costs Saved, Million $</th>
<th>Societal Costs Saved (Direct + Indirect), Million $</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diphtheria</td>
<td>275,028</td>
<td>27,503</td>
<td>3654</td>
<td>59,296</td>
</tr>
<tr>
<td>Tetanus</td>
<td>169</td>
<td>25</td>
<td>12</td>
<td>45</td>
</tr>
<tr>
<td>Pertussis</td>
<td>2,950,836</td>
<td>1062</td>
<td>4443</td>
<td>7017</td>
</tr>
<tr>
<td>Hib</td>
<td>18,606</td>
<td>741</td>
<td>1810</td>
<td>3756</td>
</tr>
<tr>
<td>Polio</td>
<td>67,463</td>
<td>800</td>
<td>2898</td>
<td>7259</td>
</tr>
<tr>
<td>Measles</td>
<td>3,835,825</td>
<td>3106</td>
<td>3762</td>
<td>8862</td>
</tr>
<tr>
<td>Mumps</td>
<td>2,312,275</td>
<td>12</td>
<td>1411</td>
<td>2374</td>
</tr>
<tr>
<td>Rubella</td>
<td>1,981,066</td>
<td>15</td>
<td>187</td>
<td>721</td>
</tr>
<tr>
<td>Congenital rubella syndrome</td>
<td>632</td>
<td>70</td>
<td>133</td>
<td>257</td>
</tr>
<tr>
<td>HepB</td>
<td>239,993</td>
<td>3514</td>
<td>240</td>
<td>1770</td>
</tr>
<tr>
<td>Varicella</td>
<td>3,942,646</td>
<td>73</td>
<td>373</td>
<td>1598</td>
</tr>
<tr>
<td>HepA</td>
<td>153,164</td>
<td>36</td>
<td>52</td>
<td>114</td>
</tr>
<tr>
<td>Pneumococcus-related diseases</td>
<td>2,323,952</td>
<td>5056</td>
<td>965</td>
<td>2696</td>
</tr>
<tr>
<td>Rota</td>
<td>1,582,940</td>
<td>19</td>
<td>327</td>
<td>595</td>
</tr>
<tr>
<td>Total</td>
<td>19,685,495</td>
<td>42,032</td>
<td>20,267</td>
<td>76,360</td>
</tr>
</tbody>
</table>

* Costs are rounded and presented in US dollars.
* Included IPD, acute otitis media, and pneumonia.

### Table 4

**BCRs: Univariate Sensitivity Analysis**

<table>
<thead>
<tr>
<th>BCRs From Direct Cost Perspective</th>
<th>BCRs From Societal Perspective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base casea</td>
<td>3.0</td>
</tr>
<tr>
<td>90% of base case pre-vaccine incidence (1)</td>
<td>2.6</td>
</tr>
<tr>
<td>1000% of base case incidence rate after vaccination (2)</td>
<td>2.9</td>
</tr>
<tr>
<td>200% base case adverse events rate (3)</td>
<td>3.0</td>
</tr>
<tr>
<td>20% increase of direct costs (4)</td>
<td>3.6</td>
</tr>
<tr>
<td>20% reduction of direct costs (4)</td>
<td>2.4</td>
</tr>
<tr>
<td>100% of vaccine purchased by private providers (5)</td>
<td>2.6</td>
</tr>
<tr>
<td>200% of base case administration cost (6)</td>
<td>2.2</td>
</tr>
<tr>
<td>Wastage rate = 0% (7)</td>
<td>3.1</td>
</tr>
<tr>
<td>Wastage rate = 10% (7)</td>
<td>2.9</td>
</tr>
<tr>
<td>100% coverage rate (8)</td>
<td>2.6</td>
</tr>
<tr>
<td>Federal, state, and local vaccination program management expenditures were added (9)</td>
<td>2.8</td>
</tr>
<tr>
<td>Worst-case scenario (combination of 1–8 above)</td>
<td>1.2</td>
</tr>
<tr>
<td>0% indirect caregiver cost and travel cost for vaccination</td>
<td>3.2</td>
</tr>
</tbody>
</table>

* Base case: wastage rate = 5%.
federal, state, and local immunization program management expenditures and excise tax (~$560 million based on estimated costs for 2009 and included Section 317 and Vaccine for Children program operations funding) (CDC, unpublished data, 2009) were included, the direct and societal BCRs were 2.8 and 9.4, respectively. In the worst case, which included all the worst-case scenario mentioned previously herein, the related direct and societal BCRs were 1.2 and 5.1, respectively.

**DISCUSSION**

The routine childhood immunization program remains 1 of the most cost-effective prevention programs in public health. Our analysis demonstrates that because of vaccination, US children born in 2009 will suffer 20 000 000 fewer cases of vaccine-preventable diseases and 42 000 fewer early deaths related to those diseases during their lifetimes. From a societal perspective, at a program cost of $7.5 billion, the routine immunization schedule will save a total of $76 billion in direct and indirect costs, resulting in a net savings of $69 billion and a BCR of 10.1. In other words, from a societal perspective, every dollar spent ultimately saves at least 10 dollars.

Our previous analysis of the routine US childhood immunization program, based on the 2001 birth cohort and the recommended vaccines for them that were in common use, estimated a program cost of ~$3 billion, and ~$47 billion in costs averted, a BCR of 16.5:1. Key contributors to the increased costs of the program for the 2009 cohort compared with the 2001 cohort include a 14% increase in the size of the birth cohort itself (from an estimated 3.8 million children in 2001 to 4.3 million in 2009), that 2 of the 3 new vaccines (PCV7 and Rota) are relatively expensive, a second dose of VAR, the increased prices of older vaccines, the increased use of more expensive combination vaccines containing multiple antigens, and increasing administration and travel costs. We used higher administration costs for combination vaccines than single ones to capture some of the additional physician work of vaccine risk and benefit counseling. Unlike the previous analysis, the 11- to 12-year-old tetanus and diphtheria toxoids vaccine (Td) booster was not included in this analysis. In 2005, a recommendation for tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap) replaced the recommendation for Td, and we plan to conduct an analysis of this and other new adolescent vaccines.

Although increased cost of vaccines combined with increased administration and travel costs led to an increase in program costs of ~$4.7 billion in 2009 (from 2.8 billion in 2001 to 7.5 billion in 2009), this program achieved additional savings of nearly $30 billion compared with costs averted in 2001. Despite the additional savings resulting from the program in 2009, the BCR of 10.1 is substantially lower than the 16.5 noted in 2001. This is primarily owing to the attributes of the 3 most recently introduced vaccines (PCV7, HepA, and Rota vaccines) and the diseases they prevent. The diseases prevented by 2 of the new vaccines, rotavirus and hepatitis A vaccines, are less likely to result in lengthy hospitalization or death. For this reason, the BCR of the newer vaccines is reduced. Even with HepA and Rota vaccination levels not yet having achieved maximal coverage, these 3 vaccines will prevent nearly 4 000 000 cases of vaccine-preventable diseases and 5000 deaths in the 2009 birth cohort, with direct and indirect cost savings of ~$3 billion. The incremental societal BCRs for HepA and Rota vaccines were <1, and these 2 vaccines were not cost-saving, but they are still cost-effective from the societal perspective.

The sensitivity analyses highlight several key aspects of the current routine immunization program. First, the early childhood vaccines are very effective and have reduced levels of vaccine-preventable disease to remarkably low levels. Current levels of most vaccine-preventable diseases are so low that modeling a 10-fold increase in reported incidence rates does not alter the BCR substantially. Similarly, these vaccines are safe, and even when modeling adverse events rates far higher than those currently reported, the BCR of the program remains positive. As shown in Table 4, the current model was most sensitive to increases in administration costs. 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. Even with the worst-case scenario, the BCRs were still >1.

Routine childhood immunization coverage in the United States has improved in recent years. Although overall coverage is currently high, several factors could potentially affect this success, including vaccine hesitancy concern by private physicians over insufficient reimbursement for routine childhood immunizations, failure of some insurance plans to cover all recommended vaccines, and the possibility that underinsured children are less likely to be fully immunized than fully privately insured children. Some of these factors highlight economic challenges for ensuring that all US children are protected from vaccine-preventable diseases. Recent health care reform legislation addresses most, but not all, of the challenges to achieving and maintaining optimal vaccination rates among US children.
and may present some opportunities to assess the impact of improved financing support. For example, private insurers will be required to cover the cost of vaccination recommended by the Advisory Committee on Immunization Practices without cost-sharing. Monitoring the impact of these changes on coverage rates will provide useful information for future vaccine financing policy decisions. Data on benefits and costs of the current program will be increasingly important as decisions on immunization program financing are made.

Our evaluation has a number of limitations. We might have underestimated the full impact of the newest vaccines to be introduced (HePA and Rota coverage has not yet reached that of other vaccines). We also underestimated the full impact of PCV7 on pneumococcal disease from herd immunity, which has resulted in significantly reduced disease among children and adults not directly vaccinated with PCV7; this would result in underestimation of the NPV and the BCRs. New 13-valent pneumococcal conjugate vaccine, which replaced PCV7 vaccine, has been licensed and recommended for children in the United States since February 2010. Thirteen-valent pneumococcal conjugate vaccine is more expensive than PCV7. However, it adds 6 additional serotypes, thereby providing more protection against the most common strains of pneumococcal bacteria responsible for severe pneumococcal infections among children.

We also did not include the costs associated with pain and suffering from diseases or the value of potential benefits of the immunization program to children other than immunization itself that accrue from visiting a health care provider to obtain vaccines. Vaccines are developed and used to prevent disease and its attendant consequences, including pain, suffering, long-term disabilities, and death. The increased number of vaccines incorporated into the early childhood schedule has raised questions about the value of the vaccination series. Our analysis demonstrates the substantial health benefits associated with vaccinating young children, as well as an impressive return on the investment of vaccines and immunization services. In this context, our data confirm that the vaccines currently recommended for young children represent not only a major public health victory in terms of disease prevention, but also an excellent public health “buy” in terms of dollars and cents.

ACKNOWLEDGMENTS
We thank Elizabeth Briere, MD, MPH, Bo-Hyun Cho, PhD, Amanda Faulkner, MPH, Kathleen Gallagher, DSc, MPH, Lisa Galloway, MS, Lee Hampton, MD, Qian Li, Jennifer Liang, DVM, Ruth Link-Gelles, MPH, Mona Marin, MD, Jennifer Murphy, MPH, Laura Pabst, MPH, Umesh Parashar, MD, Sarah Schillie, MD, Jane Seward, MBBS, James Singleton, MS, Jacqueline Tate, PhD, Gary Urquhart, MPH, Warren Williams, MPH, Pascale Wortley, MD, and Fan Zhang, PhD for their critical assistance and thoughtful review of this manuscript, and Mary McCauley, MTSc, for her kindly assistance in manuscript preparation.

REFERENCES


48. MarketScan Database. Ann Arbor, MI: The MEDSTAT Group, Inc. 2000


(Continued from first page)
Economic Evaluation of the Routine Childhood Immunization Program in the United States, 2009
Fangjun Zhou, Abigail Shefer, Jay Wenger, Mark Messonnier, Li Yan Wang, Adriana Lopez, Matthew Moore, Trudy V. Murphy, Margaret Cortese and Lance Rodewald
Pediatrics 2014;133;577
DOI: 10.1542/peds.2013-0698 originally published online March 3, 2014;

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