Project Cost-effectiveness of New Vaccines for Adolescents in the United States

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ABSTRACT

BACKGROUND. Economic assessments that guide policy making on immunizations are becoming increasingly important in light of new and anticipated vaccines for adolescents. However, important considerations that limit the utility of these assessments, such as the diversity of approaches used, are often overlooked and should be better understood.

OBJECTIVE. Our goal was to examine economic studies of adolescent vaccines and compare cost-effectiveness outcomes among studies on a particular vaccine, across adolescent vaccines, and between new adolescent vaccines versus vaccines that are recommended for young children.

METHODS. A systematic review of economic studies on immunizations for adolescents was conducted. Studies were identified by searching the Medline, Embase, and EconLit databases. Each study was reviewed for appropriateness of model design, baseline setup, sensitivity analyses, and input variables (ie, epidemiologic, clinical, cost, and quality-of-life impact). For comparison, the cost-effectiveness outcomes reported in key studies on vaccines for younger children were selected.

RESULTS. Vaccines for healthy adolescents were consistently found to be more costly than the health care or societal cost savings they produced and, in general, were less cost-effective than vaccines for younger children. Among the new vaccines, pertussis and human papillomavirus vaccines were more cost-effective than meningococcal vaccines. Including herd-immunity benefits in studies significantly improved the cost-effectiveness estimates for new vaccines. Differences in measurements or assumptions limited further comparisons.

CONCLUSION. Although using the new adolescent vaccines is unlikely to be cost-saving, vaccination programs will result in sizable health benefits.

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Key Words: cost-effectiveness, adolescents, vaccines

Abbreviations: HPV—human papillomavirus
LYS—life-years saved
QALY—quality-adjusted life-year
MPV4—meningococcal polysaccharide vaccine
MCV4—meningococcal conjugate vaccine
Tdap—tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis

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Assessing the economic considerations of health care interventions is becoming increasingly important for policy making. When these assessments identify the greatest population health gains for a given expenditure of resources, they can help decision-makers apportion limited health care dollars: potential cost savings may be used to justify program expenditures, or costs that exceed potential savings may be assessed fairly against competing health priorities.

Early vaccination programs have been shown to be highly effective and cost-saving in children. However, the relatively higher price of recently introduced vaccines for adolescents (and, for that matter, of all new vaccines), combined with the financial and programmatic constraints faced by immunization programs, underscores the need...
for economic analyses to guide new recommendations. In this context, thorough assessments of immunizations for adolescents are needed to estimate the relative costs of achieving health benefits.

COMPLEXITY OF VACCINE ECONOMICS

Partly because methods and assumptions vary, assessing economic considerations of immunizations is complex, and assessments of adolescent immunizations are no exception. Among the most critical elements to look for in economic analyses of immunizations are whether the studies encompass the full range of potential costs and benefits and whether they follow recommended standards for reporting outcomes.3 For example, are all cost and health outcomes fairly and appropriately estimated? Is the potential benefit of herd immunity included? Are uncertainties, risks, and robustness of the results properly assessed? If important uncertainties are not addressed in an analysis, are they identified as limitations? Furthermore, the adolescent population adds more challenges for thorough economic evaluations of new vaccines. Adolescents are among the least frequent consumers of preventive health services, particularly in the late teenage years; thus, new and potentially costly interventions may be needed to reach them and ought to be addressed.

The main objective of this article was to review studies on the cost-effectiveness of 2 groups of vaccines for adolescents: those in use for several years, including vaccines to prevent hepatitis B, hepatitis A, and influenza, and those that have been recently approved and recommended, including the human papillomavirus (HPV), meningococcal conjugate, and pertussis vaccines. To place the new adolescent vaccines in context, cost-effectiveness comparisons were undertaken among studies on a particular vaccine, across adolescent vaccines, and between new adolescent vaccines versus vaccines that are recommended for young children. Finally, a number of unanswered questions and cautions, were examined, and presented in the form of limitations, for those who are in a position to try to compare current economic studies for policy decision-making. Our overall aim was to showcase the challenges in relying on a single cost-effectiveness estimate from a single study without fully understanding what underpinned each estimate.

METHODS

Literature Reviewed on Adolescent Vaccines

We searched the Embase, Medline, and EconLit databases by using the search terms “adolescents” (or age group 10–19 years) and “cost” or “cost-effectiveness” or “cost-benefit or economic” along with the specific disease term (ie, “hepatitis,” “human papillomavirus,” “influenza,” “meningococcal,” “pertussis”). We included studies published through 2005 but used no lower bound on the publication date. Excluded were non-US studies (with the exception of 1 study on pertussis from Canada), studies that did not include the target ages or consider routine vaccination, and studies with designs that did not provide results on the value of vaccination (eg, cost-of-illness studies were excluded). We also included relevant unpublished manuscripts on recently recommended vaccines (in press or submitted) that met these criteria.

Review Process

Studies were grouped according to disease. Team members independently conducted reviews and prepared preliminary summaries. Uncertainties about the data and methods used in these analyses were identified. The characteristics of each study were grouped into the categories depicted in Table 1. The table depicts the full range of inputs and outputs that may comprise an economic analysis of a vaccine. In our assessment, we highlighted similarities and differences, with a focus on those studies that adhered most closely to recommended standards for conducting economic analyses (see Tables 1 and 2).5,9 In an attempt to make the studies (performed over the course of several years) as comparable as possible, cost values published before December 2003 were adjusted to 2004 US dollars by using the Gross Domestic Product deflator. This strategy helped to smooth out differences such as lower vaccine cost estimates from studies performed years ago.

Comparison Approach

Typically, for any set of economic studies, inputs and assumptions vary. Thus, for each set of studies on a particular adolescent vaccine we examined key inputs (eg, vaccine doses and costs, assumed vaccine coverage, and if herd immunity was included) and commented on their comparability. We took the same approach when looking across vaccines.

For the basic comparison, in addition to discussing the salient inputs and assumptions, we examined outcome measures of vaccination-program effectiveness and cost-effectiveness from both the direct health care payer and societal perspectives. Following recommendations in health economics,5–9 outcomes mainly considered for our comparisons were life-years saved (LYS), quality-adjusted life-years (QALY) saved, cost-effectiveness (expressed as cost per LYS and QALY saved), and cost/benefit (expressed as cost/benefit ratio) (see Table 2 for definitions). In Table 3 we have summarized those studies on adolescent vaccination with comparable vaccine costs and for which at least 1 of the cost-effectiveness measures mentioned above was reported. More detailed information appears in the appendices, including summaries of studies that reported different measures or relied, for vaccines in use for several years, on substantially higher vaccine costs than those currently observed.10

Finally, for comparing economic studies for adolescent vaccines with those for vaccines recommended for young children, we selected a few recent and comprehensive studies that evaluated vaccination programs for children.
ANALYSES OF STUDIES

Cost-effectiveness of Current and Recently Recommended Vaccines

Hepatitis Vaccines
Two economic studies on hepatitis A vaccination were reviewed, and both reported cost-effectiveness estimates (Table 3, Appendix 1). The first study considered a monovalent adolescent hepatitis A immunization program.11 The second estimated the incremental health and cost effects of hepatitis A protection for college students by comparing a program with a combined hepatitis A and B vaccine with a program that used only the monovalent vaccine for hepatitis B.12 Assumptions about the likelihood of infection over a lifetime differed by a magnitude (1.67% to 33.3%, respectively), and costs for vaccines were dramatically different ($15.7 to $25.2 per dose, respectively). Vaccine-efficacy estimates and baseline vaccination coverage were similar. In the first study, the cost to the health care system per LYS reached $54 000 ($61 000 in 2004 US dollars) for the general US population, and the cost to society reached $36 000 ($40 000 in 2004 US dollars). A direct comparison to the other study was not possible, because results were presented as QALYs: $12 000 per QALY saved for the health system and cost-saving for society.

Six economic studies12–17 assessed hepatitis B immunization of schoolchildren (including those aged <10 years), adolescents, or young adults (including those aged 19 years). Two studies focused on interventions for specific ethnic groups16,17 (Appendix 2). Four studies reported cost-effectiveness estimates for routine vaccination (Table 3 and Appendix 2). In these 4 studies, differences in vaccine and vaccination costs were sub-
TABLE 2 Definitions of Outcome Measures

Cost-effectiveness analysis: assesses the cost of averting a disease outcome and is typically measured by a ratio of intervention costs versus outcomes averted. The numerator states the monetary value of all resources consumed by the intervention program minus all prevented disease costs (eg, costs of prevented hospitalizations, doctor visits, and prevention of productivity losses resulting from work loss, permanent disability, or premature death). The denominator is a measure of effectiveness in natural units such as cases prevented, lives saved, or, most commonly, LYS. Cost-effectiveness analysis is used to choose between alternative interventions that are aimed at achieving similar outcomes.6,7

Life-years saved (LYS): an effectiveness measure defined as the number of additional years of life expected should disease-specific events leading to premature death not occur.6 Because life expectancy is age specific, LYS are often taken to be the difference between the age-specific life expectancy and the age at which, without intervention, premature death from the disease-specific event could happen.

Cost-utility analysis extends cost-effectiveness analysis by including different outcome measures weighted by a common unit. For health-related analyses, costs and common effectiveness units are derived by using methods recommended by the Panel on Cost-effectiveness in Health and Medicine.8 Outcomes in cost-utility analysis are expressed as cost per change in health status or quality of life.9,10

Quality-adjusted life-year (QALY): a type of quality-of-life measure that is based on individual preferences for states of health. For QALY, a year of perfect health is assigned a value of 1, and death is valued at 0, with most other states of health usually valued between 0 and 1.11 As such, QALYs measure not only years of life saved but also years of function and health preserved. QALYs are highly relevant when disease-specific outcomes lead to both mortality (ie, premature death) and significant morbidity (ie, temporary or permanent disability).

Cost/benefit analysis: places dollar values on all significant health and nonhealth outcomes including death, pain and suffering, and property loss so that benefits are directly compared with costs in monetary terms.12,13 Reporting costs and outcomes in a monetary metric facilitates comparison among diverse programs and allows the benefits to be clearly distinguished from the costs. In a cost/benefit analysis, a ratio of the benefits versus costs may be presented. Results may also be presented by subtracting the cost of intervention from the benefits of the intervention (ie, net benefits or savings). In allocating resources, analysts often trade-off the most efficient investments, those with the highest cost/benefit ratios or net benefits, against investments with a broader reach that can produce a larger total benefit with higher cost.14

Cost-saving versus cost-effective: an intervention is said to be cost-saving when the numerator in the cost-effectiveness analysis or cost-utility analysis ratios is negative (ie, when prevented costs are larger than the intervention costs, which makes “doing nothing” more costly). Likewise, in a benefit-to-cost ratio in cost/benefit analysis, values higher than 1 are read as “cost-beneficial,” which means that the benefits of interventions are higher than its costs. An intervention is said to be cost-effective when the intervention has lower costs per outcome avoided compared with some alternative or to some threshold. An intervention that is cost-saving will also be cost-effective, but a cost-effective intervention will not always be cost-saving.

Costs were also reported at $28 000 ($31 000 in 2004 US dollars) per LYS14 or $7600 ($9000 in 2004 US dollars) per QALY gained (the later result was from a study on hepatitis A and B15).

Two additional elements are worthy of mention: (1) despite the growing evidence of the herd-immunity benefits16–20 of vaccinating children and adolescents with hepatitis vaccines, the available literature did not consider the economic benefits of indirect protection, although a few pointed to achieving high coverage rates as a main condition; and (2) vaccinating young children is reported as a more effective and cost-effective strategy than vaccinating adolescents or college students.

Influenza Vaccine

Four studies used various methods to evaluate vaccination programs against influenza for adolescents. One of these studies reported cost-effectiveness estimates21 (Table 3 and Appendix 3), 2 studies reported only cost/benefit ratios,22,23 and 1 study reported a different outcome (cost per healthy LYS) that was not used for comparisons.24 (Appendix 3).

Because underlying comorbidities or other medical conditions increase the likelihood of complications among those who are infected with influenza, studies consistently showed greater economic benefits for vaccinating adolescents at high risk of complications as compared with adolescents who were not at high risk. Using QALYs, Prosser et al21 projected that a mean investment of $10 000 per QALY gained for 12- to 17-year-olds at high risk and $119 000 per QALY gained for 12- to 17-year-olds who were not at high risk would be required (Table 3). In 2 studies, Meltzer et al22,23 found median net savings for influenza vaccination in 5- to 14-year-olds at high risk and 0- to 19-year-olds who were at high risk. One of these 2 studies was conducted under the assumptions of a moderately severe influenza pandemic. In general, the studies suggested that vaccinating adolescents who were not at high risk was not cost-saving in nonpandemic years and that significant investment would be required for vaccinating adolescents who were not at high risk against influenza.21–23

Although vaccinating adolescents at high risk of complications has been consistently found to be more cost-effective (or cost-beneficial) than vaccinating those not at high risk, several unknowns could change the overall picture. For example, it is not known if a recommendation for routine vaccination for all adolescents might improve coverage rates for adolescents at high risk. It also is not known if indirect effects in other populations would improve the cost-effectiveness of vaccinating adolescents who are not at high risk or if annual influenza vaccination would be programmatically and financially feasible. Only Meltzer et al22 considered the question of how increased coverage of individuals at high risk might affect the economic returns from a strategy of universal vaccination in a particular age group. However, the other unknowns were not considered in the studies that we reviewed.
Human Papillomavirus Vaccine

Two vaccines have been effective against HPV in clinical trials when administered before exposure to HPV, and 1 has been licensed and recommended for use. Six published studies have evaluated the effectiveness and cost-effectiveness of HPV vaccination programs (Table 3). Table 3 provides a summary of 4 studies in peer-reviewed journals on prophylactic HPV vaccines that reported cost-effectiveness estimates (Appendix 4). Among the excluded studies was 1 that reported only effectiveness measures without costs and 1 that focused on prioritization of research and development for new vaccines. The cost-effectiveness studies used Markov models of the natural history of HPV and cervical cancer or a disease-transmission model. Base-case estimates of the cost per QALY gained by vaccinations ranged from $15,000 to $24,000. The cost-effectiveness estimate based on the transmission model seemed more favorable to vaccination than the estimates that were based on the Markov models, partly be-

### Table 3: Cost Per LYS and Cost Per QALY Gained of Current and New Vaccines for Adolescents in the United States

<table>
<thead>
<tr>
<th>Vaccine and Target Group</th>
<th>No. of Doses</th>
<th>Cost per Vaccine Recipient, $</th>
<th>Base Case Vaccine Coverage, %</th>
<th>Herd Immunity*</th>
<th>Cost per** Life-Year, Payer, $</th>
<th>Cost per** Life-Year, Societal, $</th>
<th>Cost per** QALY, Societal, $</th>
<th>Ref No.</th>
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</thead>
<tbody>
<tr>
<td><strong>Selected current vaccines</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>Hepatitis A vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>College freshman</td>
<td>3 + Hepatitis B</td>
<td>47</td>
<td>68</td>
<td>No</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>12</td>
</tr>
<tr>
<td>All 15-y-olds or those at high risk in 10 high-incidence states</td>
<td>2</td>
<td>50</td>
<td>70</td>
<td>No</td>
<td>16 000</td>
<td>Savings</td>
<td>—</td>
<td>11</td>
</tr>
<tr>
<td>All 15-y-olds</td>
<td>2</td>
<td>50</td>
<td>70</td>
<td>No</td>
<td>61 000</td>
<td>40 000</td>
<td>—</td>
<td>11</td>
</tr>
<tr>
<td>Hepatitis B vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>College freshman (unvaccinated or at high risk)</td>
<td>3</td>
<td>125</td>
<td>68</td>
<td>No</td>
<td>9000</td>
<td>—</td>
<td>Savings</td>
<td>12</td>
</tr>
<tr>
<td>All unvaccinated</td>
<td>3</td>
<td>85</td>
<td>—</td>
<td>No</td>
<td>31 000</td>
<td>—</td>
<td>—</td>
<td>14</td>
</tr>
<tr>
<td>All unvaccinated</td>
<td>3</td>
<td>85</td>
<td>—</td>
<td>No</td>
<td>36 000</td>
<td>Savings</td>
<td>—</td>
<td>15</td>
</tr>
<tr>
<td><strong>Influenza vaccine</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>12- to 17-y-olds at increased risk of complications</td>
<td>1 yearly</td>
<td>48</td>
<td>—</td>
<td>No</td>
<td>—</td>
<td>750 000</td>
<td>10 000</td>
<td>21</td>
</tr>
<tr>
<td>12- to 17-y-olds healthy or not at high risk</td>
<td>1 yearly</td>
<td>48</td>
<td>—</td>
<td>No</td>
<td>—</td>
<td>8 500 000</td>
<td>119 000</td>
<td>21</td>
</tr>
<tr>
<td><strong>Recently recommended vaccines</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>HPV vaccines (types 16 and 18)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All female 12-y-olds + screening vs screening only</td>
<td>3 + 1 booster</td>
<td>400</td>
<td>70</td>
<td>Yes</td>
<td>—</td>
<td>17 802</td>
<td>15 000</td>
<td>32</td>
</tr>
<tr>
<td>All female 12-y-olds + screening vs screening only</td>
<td>3</td>
<td>377</td>
<td>100</td>
<td>No</td>
<td>—</td>
<td>—</td>
<td>24 000</td>
<td>35</td>
</tr>
<tr>
<td>All female 12-y-olds school based + screening vs screening only</td>
<td>3 + 1 booster</td>
<td>300</td>
<td>70</td>
<td>No</td>
<td>—</td>
<td>32 000</td>
<td>23 000</td>
<td>33</td>
</tr>
<tr>
<td>All female 12-y-olds + first screening at 25 vs 18 y</td>
<td>3</td>
<td>200</td>
<td>100</td>
<td>No</td>
<td>—</td>
<td>45 000</td>
<td>—</td>
<td>31</td>
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<tr>
<td>Meningococcal vaccines</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>MCV4</td>
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</tr>
<tr>
<td>Highly endemic areas only, with catch up</td>
<td>1</td>
<td>83</td>
<td>70</td>
<td>Yes</td>
<td>—</td>
<td>58 000</td>
<td>38 000</td>
<td>33 000</td>
</tr>
<tr>
<td>All 11-y-olds; routine assuming 20 y of protection</td>
<td>1</td>
<td>83</td>
<td>70</td>
<td>No</td>
<td>—</td>
<td>121 000</td>
<td>118 000</td>
<td>30</td>
</tr>
<tr>
<td>All 11- to 17-y-olds; catch-up and routine</td>
<td>1</td>
<td>83</td>
<td>70</td>
<td>Yes</td>
<td>—</td>
<td>147 000</td>
<td>127 000</td>
<td>88 000</td>
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<tr>
<td>All 11-y-olds; routine assuming 10 y of protection</td>
<td>1</td>
<td>83</td>
<td>70</td>
<td>No</td>
<td>—</td>
<td>219 000</td>
<td>205 000</td>
<td>179 000</td>
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<td>MPV4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>First-year college students in dormitories</td>
<td>1</td>
<td>70</td>
<td>80</td>
<td>No</td>
<td>—</td>
<td>306 000</td>
<td>—</td>
<td>40</td>
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<tr>
<td>Pertussis-containing vaccines</td>
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<td></td>
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<tr>
<td>Tetanus, diphtheria, and acellular pertussis vaccine</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>All 12-y-olds</td>
<td>1</td>
<td>10</td>
<td>95</td>
<td>Yes</td>
<td>—</td>
<td>—</td>
<td>Savings</td>
<td>46</td>
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<tr>
<td>All 10- to 19-y-olds</td>
<td>1</td>
<td>37</td>
<td>40</td>
<td>No</td>
<td>—</td>
<td>—</td>
<td>Savings</td>
<td>47</td>
</tr>
<tr>
<td>All 11- to 18-y-olds</td>
<td>1</td>
<td>16</td>
<td>80</td>
<td>Yes</td>
<td>—</td>
<td>22 000</td>
<td>6300</td>
<td>—</td>
</tr>
<tr>
<td>All 11-y-olds</td>
<td>1</td>
<td>15</td>
<td>76</td>
<td>No</td>
<td>—</td>
<td>—</td>
<td>20 000</td>
<td>48</td>
</tr>
</tbody>
</table>

Interventions are grouped according to current vaccines and recently recommended vaccines, and then alphabetically. — indicates that data were not available.

*Herd immunity is included as reductions in either attack rates or secondary attack rates of the unvaccinated.

**Cost per LYS and per QALY gained from publications before 2003 were converted to 2004 US dollars by using the Gross Domestic Product deflator. Reported studies shown here used 3% to annually discount future costs, benefits, and health outcomes. Figures in the columns were rounded to the nearest thousand.

* Depending on the particular study payer’s perspective, figures include either direct medical and direct not-medical costs or only direct medical costs.
cause the transmission models included the potential impact of herd immunity. Two studies evaluated the impact of vaccinating men and women, and found that the inclusion of men in the vaccination programs had only a modest impact on cervical cancer incidence. Benefits of vaccinating men increased, however, as coverage rates among women decreased.

The cost-effectiveness of HPV vaccination also depended on potential savings accrued from less frequent cervical cancer screening. Much of the potential economic benefit of an HPV vaccine would be realized only if the initiation of screening for cervical cancer were delayed until an older age, the interval between screenings were increased, or both. With such changes, HPV vaccination might be cost-effective compared with current HPV screening. Likewise, economic assessments of HPV vaccine have not focused on potential reduction of the incidence of anal, penile, and vulvar carcinoma, for which specific screening is not currently recommended.

A number of factors that might affect the economic analysis and outcome of an HPV vaccination program were also identified in the studies. First, would a vaccination program effectively reach those who were least likely to be protected from cervical cancer by conventional screening programs? Conversely, might vaccination programs favor those who would be protected already through the use of screening? Second, we do not know the effect of high levels of vaccine-induced type-specific immunity on the epidemiology of HPV infection. Is it possible that other potentially oncogenic virus types could become more prevalent and replace those being prevented by the vaccines? Third, little is known about the probability of HPV transmission, which is obviously a key factor in transmission models of the impact of HPV vaccines. Would changes in sexual mixing patterns across risk and age groups significantly affect indirect protection benefits derived from vaccination?

**Meningococcal Conjugate Vaccine**

Vaccines against meningococcal disease based on the polysaccharide capsule have been in use in the United States since the 1970s. Both the older meningococcal polysaccharide vaccine (MPV4) and new meningococcal conjugate vaccine (MCV4) formulations cover serogroups A, C, Y, and W-135, which have caused approximately two thirds of the US cases of meningococcal disease in recent years. Although both vaccines are safe and effective, the newly recommended MCV4 is believed to confer longer protection.

Three studies have assessed the cost-effectiveness of vaccines against meningococcal disease. In the first study, of the newer conjugate formulation at $83 per vaccinated adolescent, assuming the benefits of vaccination would last 22 years and adopting a societal perspective, it was estimated that the median societal cost per LYS would be $121,000 (Table 3).

The second study considered the vaccination using MPV4 for college freshmen who lived in dormitories. This population has a moderately elevated risk of meningococcal disease relative to the general population. Results showed substantial social costs for an MPV4 vaccination program relative to estimated benefits. Compared with an MCV4 vaccination program, the cost per LYS would be much higher for MPV4, in part because of the long duration of immunity conferred by the MCV4 vaccine and the possibility of generating significant indirect protection of unvaccinated persons (Table 3).

It is believed that because adolescents have the highest rates of asymptomatic carriage of *Neisseria meningitidis* as well as behavioral risk factors that facilitate infection, simultaneously vaccinating multiple adolescent cohorts would provide significant and immediate protection to the unvaccinated. In the third study, Ortega-Sanchez et al estimated that a combined catch-up vaccination of healthy adolescents plus an added routine program would prevent 48% of cases caused by vaccine serogroups, with the majority of these benefits (up to 73% of averted cases) being a result of reduced attack rates among unvaccinated groups. The authors assumed that herd-immunity effects were equivalent to recent experiences in the United Kingdom, in which meningococcal serogroup C vaccine conferred sizable indirect protection (Appendix 5). When considering the economic impact, at the same cost of $83 per vaccine used in the first study assessed, a catch-up vaccination program followed by a routine program was estimated to cost society an average of $127,000 per LYS and $88,000 per QALY saved. Compared with routine vaccination of each 11-year-old cohort, catch-up vaccination could cost up to one-fifth less per LYS (Table 3).

Because some counties in the United States often experience higher meningococcal incidence than the general population, the same study found that targeting vaccination campaigns to these counties could decrease the cost per LYS by two thirds of that reported for the general population. Various concerns about the feasibility of this targeted strategy were outlined by the authors.

**Pertussis-Containing Vaccine**

Two adolescent/adult pertussis booster vaccines formulated with tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine adsorbed (Tdap) were recently approved and recommended for use in persons aged 10 to 18 years and the other for those aged 11 to 64 years.

Four economic analyses of adolescent pertussis vaccination suggest that it is likely to be cost-effective or even cost-saving (Table 3 and Appendix 6). The investigators assumed similar vaccine efficacy (85%–88%). However, assumptions about incidence of pertussis and duration of immunity varied substantially (Appendix 6). The studies consistently showed greater economic benefits when higher incidence in adolescents was assumed. None of the studies examined the impact of duration of vaccine-mediated immunity.

Using cost/benefit analysis, Purdy et al calculated a break-even vaccine cost of $37 from the societal perspective. The next 4 studies all included some measure of herd immunity (ie, reduction in disease transmission) and assumed a cost of $10 to $15 of the pertussis component in the Tdap vaccine price (Appendix 6). Prevent-
ing infant deaths from pertussis is a potentially important rationale for vaccinating adolescents and adults. Assuming 12% herd immunity, Iskedjian et al found that adolescent vaccination ranged from cost-saving to a cost to society of $410 per case prevented. Assuming 20% of cases were prevented by herd immunity (the highest value used in any study), Caro et al found that adolescent vaccination would cost $6300 per LYS. In this study, outcomes critically depended on the risk of infection and herd-immunity estimates, with results ranging from cost-saving to $187 000 per LYS. Assuming that herd immunity resulted in a 17% reduction in disease transmission, Lee et al reported a cost of $19 000 per QALY saved and found adolescent vaccination to be cost-effective from both the societal and health care payer perspectives. Differences in outcomes reported, cost per case, LYS and QALYs saved, limited further comparisons.

The 4 economic analyses that considered the impact of herd immunity revealed that the assumptions used regarding reduction in disease transmission were also critical to estimating the cost-effectiveness of interventions. However, these studies also highlighted the uncertainty of estimates regarding how frequently Bordetella pertussis is transmitted from 1 age group to another and how effective adolescent or adult vaccination would be in interrupting transmission to infants.

Cost-effectiveness Comparisons Among Vaccines for Adolescents and With Those Recommended for Young Children

With the exception of pneumococcal conjugate vaccination, childhood immunizations have been shown to be cost-saving, even when considering only direct costs of disease and in every case when indirect costs were included. Disease reduction of 94% to 98% in most childhood vaccines has offset vaccination costs. However, the increasing price of vaccines and greater efforts needed to achieve or sustain programmatic goals (overall coverage of ~90% in preschool-aged children) might increase costs and reduce the net social benefits of childhood vaccination programs.

Among new vaccines, adolescent pertussis vaccination is likely to be as cost-effective as childhood vaccines. In addition to the fact that it is less expensive than other new vaccines, it is believed that pertussis cost-effectiveness will increase, in part, because of the benefits of preventing transmission.

In contrast, studies on adolescent MCV4 and HPV vaccines projected lower cost-effectiveness than that for childhood vaccines (Table 3). Although substantial reductions in meningococcal disease and costs were estimated for MCV4, the reductions were smaller than for childhood vaccination (only 48% reduction for vaccine serogroups in a 10-year period). The 2 studies on MCV4 have also demonstrated that despite the high costs associated with treating a case or, conversely, the large savings in preventing a case, vaccination benefits are offset by the relatively low number of cases and the high vaccine costs. Therefore, publicly funded programs against meningococcal disease would result in net financial loss to payers and society and would be more costly per health outcome than other vaccine recommendations, even with best-case scenario input values.

Given the projected high vaccine effectiveness and the disease burden prevented, reductions of HPV infection and sequelae are expected to partially overcome high vaccination costs. As shown in Table 3, economic studies on routine HPV vaccination in adolescents reported societal costs per LYS between $17 000 and $45 000 and per QALY saved between $15 000 and $24 000. Although less than that for MCV4, these projected estimates show that vaccination programs with HPV might not be as cost-effective as childhood immunizations.

Using a Common Rule of Thumb

To assess their own social cost-effectiveness value, some studies on adolescent vaccines avoided comparing their outcomes with interventions beyond the specific vaccine or when interventions with the same vaccine were for different age groups. Instead, a few studies resorted to a common and controversial rule of thumb. The rule has been that interventions that cost less than $50 000 per QALY saved are defined as societally cost-effective and that interventions between $50 000 and $100 000 should only be adopted if there are additional unpriced benefits such as relieving fear in the community. This rule and its cost thresholds are highly contested as baseless of any economic theory or expert support. Indeed, recent extensive and theoretical studies may suggest threshold values that are much higher and/or context specific. Thus, assessments of cost-effectiveness of any vaccine and, for that matter, of any health intervention that uses this rule of thumb should be avoided.

A more reliable alternative is to perform cost-effectiveness comparisons with other vaccines, as attempted here (see Fig 1), or with other health services. Although more research is needed to standardize economic assessments of diverse health interventions, evaluations of clinical services for adolescents that address, for example, preventing obesity, substance use/abuse, and injuries could serve better to further contextualize the health and economic benefits of adolescent vaccines.

DISCUSSION

Despite the fact that our review reveals a group of economic analyses with widely varying methods, it demonstrates that vaccines for adolescents were consistently not cost-saving for either the health care system or society. Among recently recommended immunizations, meningococcal vaccines are seen as the least cost-effective and pertussis followed by HPV vaccines as relatively the most cost-effective (Fig 1). However, these 3 new vaccines for adolescents are expected to be less cost-effective than most vaccination programs that are recommended for young children. In general, interventions with new vaccines were more cost-effective when herd-immunity benefits were included (Table 3).
Unanswered Questions

Experience from immunization programs suggests that a number of factors could be correlated with capturing promised health and economic benefits for adolescents. The first factor is related to the optimal timing of adolescent vaccination. Studies on routine vaccination of adolescents with new vaccines assumed vaccination would occur at age 11 to 12 years. Delivering vaccines in early adolescence may be most feasible, because 11- to 12-year-olds may be subject to middle school mandates and may be more likely to use medical services than older adolescents. However, most disease burden caused by pertussis or meningococcal infection occurs in the late teen years. Similarly, the likelihood of sexual activity and HPV infection is higher for older teens. Therefore, delaying vaccination to midadolescence just before the peak of disease might provide better direct and herd-immunity benefits, particularly if waning immunity after vaccination is of concern. This trade-off between feasibility and disease burden is answered partially by studies that have proposed the simultaneous vaccination of various cohorts of adolescents or by introducing booster doses in early adulthood.32,33,41

Second, unlike the childhood immunization program, which has achieved high coverage among cohort after cohort with ≥24 immunizations, high coverage has not been attained for the few vaccines that adolescents needed before the recent introduction of 3 new vaccines,4,54 and efforts to strengthen the system and reach most adolescents have been renewed. Achieving high coverage would be highly relevant for the cost-effectiveness of HPV and influenza vaccines for adolescents, because in contrast to the MCV4 and TdaP vaccines, which require only 1 dose, the suggested 3-dose series to fully immunize girls with the HPV vaccine and a yearly dose of influenza vaccine for all adolescents would represent a difficult barrier to achieving high coverage benefits.

Third, interventions with new vaccines were reported to be between 17% and 51% more cost-effective compared with interventions without herd immunity (see Table 3). Two important requirements of achieving herd-immunity benefits are high vaccination coverage and high and long-lasting vaccine effectiveness. Studies on new vaccines assumed persistent coverage across various cohorts and relied on projections of vaccine effectiveness and duration by using data from clinical trials. Although most studies also included some form of sensitivity analysis to test the significance of these variables, in practice, achieving high coverage has proved to be difficult and post-implementation vaccine effectiveness and duration are usually unknown or lower than those reported in clinical trials. These factors may dramatically change their cost-effectiveness values.

Fourth, most studies were based on the assumption of vaccinating in a clinical setting. Other options to improve coverage, and possibly reduce administrative costs
(like school-based immunization), have been considered. However, in addition to concerns that this path could result in missed opportunities for physicians to interact with adolescents about other preventive issues, little is known about costs associated with vaccinating adolescents in alternative settings.

Fifth, newer vaccines for adolescents are expected in the coming years and would add new challenges to adolescent vaccination programs. According to the Institute of Medicine, at least 4 other vaccines (against Chlamydia trachomatis, cytomegalovirus, group B streptococcus, and herpes simplex virus type 2) are under development and could be available in 7 to 10 years for adolescents.36

Sixth, the new adolescent vaccines are viewed to strengthen the so-called “adolescent vaccine platform,” which means that the routinely recommended vaccines for adolescents may provide a prime opportunity to increase the delivery of other needed clinical preventive services or, in fact, may compete with them for time and other resources.61 Certainly, there is also the possibility that adolescents will obtain vaccines in venues that cannot offer comprehensive services, but the aim for adolescents, as for children, is to maintain a medical home.62

Factors That Limit Comparisons
This review identified key limitations for comparing reviewed studies. Among others, a substantially limiting element was the source of specific health-related quality-of-life scores or utilities used in the studies. Most used measures for complications or morbidity conditions came from previous studies or resorted to generic measures that closely resembled those under analysis. Two exceptions were the studies by Lee et al,63 who elicited patients’ preferences for pertussis-related health states, and Prosser et al,21 who elicited community preferences for influenza-related health states. Consistent with Griebisch et al,64 who concluded that QALY scores used in assessing the cost-effectiveness of health interventions for children and adolescents should not yet be regarded as standardized, the observed variations in the source and calculation methods of QALYs across the reviewed studies should also caution the comparisons on cost per QALY gained.

Because the Panel on Cost-effectiveness in Health and Medicine65 strongly recommended the use of QALYs, specifically in an attempt to allow such comparisons, the simultaneous use of cost per LYS when available for comparison might cross-validate the comparisons on cost per QALY gained.

Independent of the measure used, the public health audience could also be a factor of additional controversy. For example, when considering prevention of pertussis versus prevention of cervical cancer, the comparison of the LYS or, for that matter, QALYs gained is not necessarily obvious; that is, does the public really consider a LYS or a QALY gained from preventing a case of pertussis the same as a LYS or QALY gained from preventing a case of cervical cancer? Available evidence demonstrates that societies may be reluctant to allocate health care resources mainly, or even solely, on the basis of cost per QALY gained. In Oregon, the attempt to use QALYs to allocate Medicaid funds was short lived.66 Denmark also has a history of rejecting the use of QALYs as the main tool for allocating health care.67

Two additional limitations were observed. First, differences in safety and efficacy add considerable complexities to the cost-effectiveness comparisons among adolescent vaccines, with some that may be reluctant to allocate health care resources mainly, or even solely, on the basis of cost per QALY gained. In Oregon, the attempt to use QALYs to allocate Medicaid funds was short lived.66 Denmark also has a history of rejecting the use of QALYs as the main tool for allocating health care.67

Beyond comparison restrictions, we should also realize that, for a variety of reasons, we are most likely to be well past the era of routine vaccination efforts that result in cost savings. We also have to acknowledge that as a society we may have, at least initially, limited funds available to begin new vaccination programs for all adolescents. Overall, we are near the point at which future recommendations that lead to increased vaccination not only among adolescents but across all ages will need to systematically compare their health and economic gains when vying for a given amount of social resources. In this context, economic analyses, when properly performed and with solid information, can certainly be illuminating.

ACKNOWLEDGMENTS
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REFERENCES
## APPENDIX 1  Economic Assessments of Hepatitis A Vaccination of US Adolescents

<table>
<thead>
<tr>
<th>Jacobs et al(^{11})</th>
<th>Jacobs et al(^{12})</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population considered</strong></td>
<td>Adolescents (aged 15 y) in 10 states with highest hepatitis A incidence rates</td>
</tr>
<tr>
<td><strong>Base year of analysis</strong></td>
<td>1997</td>
</tr>
<tr>
<td><strong>Perspective taken</strong></td>
<td>Health system and societal</td>
</tr>
<tr>
<td><strong>Risk of infection absent vaccination, % lifetime risk of overt hepatitis A</strong></td>
<td>3.33</td>
</tr>
<tr>
<td><strong>Initial vaccine efficacy, %</strong></td>
<td></td>
</tr>
<tr>
<td>Full series</td>
<td>—</td>
</tr>
<tr>
<td>2 doses</td>
<td>94</td>
</tr>
<tr>
<td>1 dose</td>
<td>85</td>
</tr>
<tr>
<td><strong>Duration of vaccine protection</strong></td>
<td>0.3%–0.6% lose protection annually after full series; 1.6%–2.7% lose protection annually after single dose</td>
</tr>
<tr>
<td><strong>Vaccination costs</strong></td>
<td>$25.15 per dose, including vaccine administration</td>
</tr>
<tr>
<td><strong>Discount rate, % (costs and benefits)</strong></td>
<td>3</td>
</tr>
<tr>
<td><strong>Main cost/benefit measure, result</strong></td>
<td>1.23/1.00</td>
</tr>
<tr>
<td>(medical and work-loss cost reduction/vaccination costs), $</td>
<td></td>
</tr>
<tr>
<td><strong>Main cost-effectiveness measure, result, $</strong></td>
<td></td>
</tr>
<tr>
<td>Per LYS (health system)</td>
<td>13,722</td>
</tr>
<tr>
<td>Per LYS (societal)</td>
<td>&lt;50</td>
</tr>
<tr>
<td>Per QALY saved (health system)</td>
<td>—</td>
</tr>
<tr>
<td>Per QALY saved (societal)</td>
<td>—</td>
</tr>
</tbody>
</table>

— indicates not applicable.
### APPENDIX 2  Economic Assessments of Hepatitis B Vaccination of US Adolescents

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Perspective taken</td>
<td>Health system</td>
<td>Health system and societal</td>
<td>Health system and societal</td>
<td>Societal</td>
<td>Health system and societal</td>
<td>Societal</td>
</tr>
<tr>
<td>Risk of infection absent vaccination, %</td>
<td>2.5 (during 10-y period)</td>
<td>30.0 (lifetime risk)</td>
<td>3.8 (lifetime risk)</td>
<td>4.8 (lifetime risk)</td>
<td>4.16 (lifetime risk)</td>
<td>As high as 80</td>
</tr>
<tr>
<td>Initial vaccine efficacy, %</td>
<td>Full series</td>
<td>90</td>
<td>95</td>
<td>95</td>
<td>99</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td>2 doses</td>
<td>60</td>
<td>85</td>
<td>61</td>
<td>Unclear</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>1 dose</td>
<td>60</td>
<td>35</td>
<td>18</td>
<td>Unclear</td>
<td>35</td>
</tr>
<tr>
<td>Duration of vaccine protection</td>
<td>10 y</td>
<td>Unclear</td>
<td>1% lose protection annually after full series; higher rates for partial series</td>
<td>Unclear</td>
<td>4.5% lose protection annually after vaccination</td>
<td>Unclear</td>
</tr>
<tr>
<td>Vaccination costs, $</td>
<td>225.00 (3-dose series, including administration fees)</td>
<td>341.00 (3-dose series, including all program costs)</td>
<td>90.89 (3-dose series, plus 33.39 for administration fees)</td>
<td>85.00 (3-dose series, including administration fees)</td>
<td>40.02 (3-dose series, plus 45.00 for administration fees)</td>
<td>9.00–22.00 (per dose, plus 5.00–15.00 administration fees)</td>
</tr>
<tr>
<td>Discount rate, % (costs and benefits)</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Main cost/benefit measure, result, $</td>
<td>NR</td>
<td>4.44/1.00 (medical and work-loss cost: vaccination costs)</td>
<td>1.14/1.00 (medical and work-loss cost: vaccination costs)</td>
<td>NR</td>
<td>1.08/1.00 (medical and work-loss cost: vaccination costs)</td>
<td>5.26/1.00 to 4.47/1.00</td>
</tr>
<tr>
<td>Main cost-effectiveness measure, result, $</td>
<td>97,256 per LYS (health system)</td>
<td>11,525 per LYS (health system)</td>
<td>7,600 per QALY saved (health system)</td>
<td>26,000 per LYS (health system)</td>
<td>27,919 per LYS (health system)</td>
<td>9,954 to 11,759 per LYS (societal)</td>
</tr>
</tbody>
</table>

NR indicates not reported.
### Economic Assessments of Influenza Vaccination for US Adolescents

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Population considered, age, y</td>
<td>5–14</td>
<td>0–19</td>
<td>12–17</td>
<td>3–14</td>
</tr>
<tr>
<td>HR</td>
<td>5–14</td>
<td>0–19</td>
<td>12–17</td>
<td>15–24</td>
</tr>
<tr>
<td>NHR</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>15–24</td>
</tr>
<tr>
<td>All</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Perspective taken</td>
<td>Societal</td>
<td>Societal</td>
<td>Societal</td>
<td>Societal</td>
</tr>
<tr>
<td>Risk of infection absent vaccination, %</td>
<td>20–30, 30–40</td>
<td>40 (pandemic year)</td>
<td>6</td>
<td>NR</td>
</tr>
<tr>
<td>Initial vaccine efficacy for 1 dose, %</td>
<td>69 (mean), 77 (median)*</td>
<td>40, 55, 70</td>
<td>69</td>
<td>60</td>
</tr>
<tr>
<td>Duration of vaccine protection, No. of seasons</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Vaccination costs, $ per vaccine recipient</td>
<td>30–60</td>
<td>21–62</td>
<td>48</td>
<td>11</td>
</tr>
<tr>
<td>Discount rate, % (costs and benefits)</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Main cost/benefit measure, result</td>
<td>1</td>
<td>Net savings</td>
<td>Net savings</td>
<td>NR</td>
</tr>
<tr>
<td>2</td>
<td>Net costs</td>
<td>Net savings</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Main cost-effectiveness measure, result, $</td>
<td>1</td>
<td>NR</td>
<td>NR</td>
<td>10 000/QALY saved</td>
</tr>
<tr>
<td>2</td>
<td>NR</td>
<td>NR</td>
<td>119 000/QALY saved</td>
<td>44/HLY gained</td>
</tr>
<tr>
<td>3</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>181/HLY gained</td>
</tr>
</tbody>
</table>

HR indicates at high risk for complications of influenza; NHR, not at high risk; —, not applicable; HLY, healthy life-year; NR, not reported.

*Reports cost per healthy life-year gained.

*Vaccine efficacy was defined by an assumed probability distribution (see Figure 2 in ref 22 for additional details).

*Reference also contains results, in an online appendix, in which effectiveness in 0- to 19-year-olds was assumed at 1 dose: 40% for non-medically attended illness and outpatient visits, 55% for hospitalization, and 40% for death.
## APPENDIX 4  Economic Assessments of HPV Vaccination of US Adolescents

<table>
<thead>
<tr>
<th>Assumptions</th>
<th>Goldie et al(^{35})</th>
<th>Kulasingam and Myers(^{31})</th>
<th>Sanders and Taira(^{33})</th>
<th>Taira et al(^{32})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine efficacy, %</td>
<td>90 Vaccine at age 12 y; current Papanicolaou screening(^a)</td>
<td>90 Vaccine at age 12 y; current Papanicolaou screening(^a)</td>
<td>75 Vaccine at age 12 y and booster at age 22 y; 71% of women have biennial Papanicolaou screening starting at age 24 y</td>
<td>90 Vaccine at age 12 y and booster at age 22 y; 71% of women have biennial Papanicolaou screening starting at age 16 y</td>
</tr>
<tr>
<td>Vaccine strategy combined with cervical cancer screening strategy</td>
<td>100 Vaccine at age 12 y; current Papanicolaou screening(^a)</td>
<td>100 Vaccine at age 12 y; current Papanicolaou screening(^a)</td>
<td>After 10 y 200 Vaccine at age 12 y and booster at age 22 y; 71% of women have biennial Papanicolaou screening starting at age 24 y</td>
<td>After 10 y 200 Vaccine at age 12 y and booster at age 22 y; 71% of women have biennial Papanicolaou screening starting at age 24 y</td>
</tr>
<tr>
<td>Vaccine coverage, %</td>
<td>37.7</td>
<td>100 Vaccine at age 12 y; current Papanicolaou screening(^a)</td>
<td>70 Vaccine at age 12 y and booster at age 22 y; 71% of women have biennial Papanicolaou screening starting at age 16 y</td>
<td>70 Vaccine at age 12 y and booster at age 22 y; 71% of women have biennial Papanicolaou screening starting at age 16 y</td>
</tr>
<tr>
<td>Waning immunity</td>
<td>No waning immunity</td>
<td>After 10 y</td>
<td>After 10 y 300 (100 for booster)</td>
<td>After 10 y 300 (100 for booster)</td>
</tr>
<tr>
<td>Cost of vaccine, $</td>
<td>377</td>
<td>200</td>
<td>300 (100 for booster)</td>
<td>300 (100 for booster)</td>
</tr>
<tr>
<td>Reference comparison strategy</td>
<td>Current Papanicolaou screening(^a)</td>
<td>100% of women have biennial Papanicolaou screening starting at age 18</td>
<td>71% of women have biennial Papanicolaou screening starting at age 16</td>
<td>71% of women have biennial Papanicolaou screening starting at age 16</td>
</tr>
<tr>
<td>Includes herd immunity</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reduction in cervical cancer cases with vaccination/screening strategy compared to reference strategy, %</td>
<td>58.1</td>
<td>36.0</td>
<td>19.9</td>
<td>61.8</td>
</tr>
<tr>
<td>Incremental life expectancy</td>
<td>0.0119 QALY gained</td>
<td>0.0045 y</td>
<td>0.011 QALY gained</td>
<td>0.0168 QALY gained</td>
</tr>
<tr>
<td>Incremental lifetime cost, $</td>
<td>249</td>
<td>246</td>
<td>227.55 per QALY gained</td>
<td>14,583 per QALY gained</td>
</tr>
<tr>
<td>Cost-effectiveness, $</td>
<td>244</td>
<td>246</td>
<td>227.55 per QALY gained</td>
<td>14,583 per QALY gained</td>
</tr>
</tbody>
</table>

\(^a\)Goldie et al [32] estimated current Pap screening as follows: 70.5% of women have Papanicolaou screening in past year, 12.6%, 4.3%, 30% screening in past 2, 3 and 5 years, respectively, and 9.1% are screened in intervals >5 year.

## APPENDIX 5  Economic Assessments of the Meningococcal Vaccination of US Adolescents

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine type</td>
<td>Tetravalent conjugate (MCV4)</td>
<td>Tetravalent conjugate (MCV4)</td>
<td>Tetravalent polysaccharides (MPV4)</td>
</tr>
<tr>
<td>Vaccine efficacy for A/C/Y/W135, %</td>
<td>93 (78–98)</td>
<td>93 (78–98)</td>
<td>85 (80–90)</td>
</tr>
<tr>
<td>Vaccine strategy</td>
<td>Vaccine at age 11 y with routine vaccine all 11- to 17-y-olds with catch-up</td>
<td>Adolescents vaccinated at age 11 y</td>
<td>Cohort of freshmen college living in dormitories</td>
</tr>
<tr>
<td>Vaccine coverage, %</td>
<td>70 (66–95)</td>
<td>70 (16–95)</td>
<td>80 (60–100)</td>
</tr>
<tr>
<td>Waning immunity</td>
<td>No waning immunity during 10 y</td>
<td>After 10y drops 25% and remains there till 22nd year</td>
<td>Efficacy is constant for 4 y and then wanes</td>
</tr>
<tr>
<td>Cost of vaccine, $</td>
<td>83 per dose per vaccine</td>
<td>83 per administered dose (infants require 3 doses, $249 per vaccine recipient)</td>
<td>70 per vaccine</td>
</tr>
<tr>
<td>Reference comparison strategy</td>
<td>No vaccination</td>
<td>No vaccination</td>
<td>No vaccination</td>
</tr>
<tr>
<td>Type of model</td>
<td>Population analysis with a Monte Carlo model; Markov for disease transmission</td>
<td>Cohort analysis with a Monte Carlo model</td>
<td>Cohort analysis with a Monte Carlo model</td>
</tr>
<tr>
<td>Includes herd immunity</td>
<td>Age-specific 57%–66% reduction in unvaccinated attack rate</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Outcomes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent reduction in incidence of disease compared to reference strategy</td>
<td>Annual incidence in population: 13% without heard immunity, 48% with herd immunity</td>
<td>45% (adolescent cohort)</td>
<td></td>
</tr>
<tr>
<td>Life-years prevented (undiscounted)</td>
<td>3683 LYS annually</td>
<td>1798 (adolescent)</td>
<td>177 life-years in 4 y of a cohort of freshmen initially living in dormitories</td>
</tr>
<tr>
<td>Cost per LYS, $</td>
<td>38 000 highly endemic areas, 127 000 general population with herd immunity</td>
<td>121 000 (adolescent)</td>
<td>297 000 (in 2003 dollars)</td>
</tr>
<tr>
<td>Cost per QALY saved, $</td>
<td>33 000 highly endemic areas, 88 000 general population</td>
<td>118 000 (adolescent)</td>
<td>No</td>
</tr>
</tbody>
</table>
### APPENDIX 6  Economic Assessments of the Pertussis Vaccination of US Adolescents and Adults

<table>
<thead>
<tr>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Population considered, age, y</td>
<td>11–18 (in US)</td>
<td>12 (in Ontario, Canada)</td>
<td>14 (in Quebec, Canada)</td>
</tr>
<tr>
<td>Base year of analysis</td>
<td>2002</td>
<td>2003</td>
<td>2004</td>
</tr>
<tr>
<td>Time horizon, y</td>
<td>Lifetime</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Perspective taken</td>
<td>Societal and health care payer</td>
<td>Societal and Ministry of Health</td>
<td>Societal and Ministry of Health</td>
</tr>
<tr>
<td>Risk of infection absent vaccination, incidence per 100,000 person-years</td>
<td>2 to 43 (infants, children, adolescents, and adults)</td>
<td>511 (adolescents only)</td>
<td>511 (adolescents only)</td>
</tr>
<tr>
<td>Initial vaccine efficacy, %</td>
<td>85</td>
<td>85</td>
<td>85</td>
</tr>
<tr>
<td>Duration of vaccine protection</td>
<td>Efficacy of 0% at 10 y</td>
<td>Efficacy of 85% at 10 y</td>
<td>Efficacy of 85% at 10 y</td>
</tr>
<tr>
<td>Herd immunity, %</td>
<td>(1) 20</td>
<td>(1) 12</td>
<td>(1) None</td>
</tr>
<tr>
<td></td>
<td>(2) 5</td>
<td></td>
<td>(2) 17</td>
</tr>
<tr>
<td></td>
<td>(3) 35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccination costs, $</td>
<td>15.74 (US dollars)</td>
<td>15.72 (Canadian dollars)</td>
<td>15.72 (Canadian dollars)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discount rate, %</td>
<td>3 (costs and benefits)</td>
<td>3% (costs), 0–3 (benefits)</td>
<td>3% (costs), 0–3 (benefits)</td>
</tr>
<tr>
<td>Main cost/benefit measure, result (societal perspective)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main cost-effectiveness measure, result (societal perspective), $</td>
<td>(1) 6300 per LYS</td>
<td>Cost-saving</td>
<td>410 per case prevented</td>
</tr>
<tr>
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</tbody>
</table>

NR indicates not reported.
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