ABSTRACT. Objective. To analyze the costs and benefits of influenza vaccination of healthy school-aged children.

Design. The analysis was based on data from the literature. Total costs included direct medical costs for vaccination, physician visits, and treatment as well as indirect costs. Indirect costs were in the form of lost productivity when working parents stayed home to care for ill children or to take children to an office for vaccination. The total costs of vaccination strategies were compared with the total cost of not vaccinating. For the base case, the vaccine was assumed to have no effect on rates of otitis media.

Setting. Two hypothetical scenarios were investigated 1) individual-initiated vaccination and 2) vaccination in a group-based setting. The former scenario required the child to be accompanied to a clinic by a parent during usual work hours.

Results. Vaccination resulted in a net savings per child vaccinated of $4 for individual-initiated vaccination and of $35 for group-based vaccination. The savings were caused primarily by averted indirect costs. Moderate increases in the cost of vaccination or reductions in the rate of influenza would eliminate the savings for individual-initiated vaccination but not for group-based vaccination. Alternatively, if influenza vaccination was effective in reducing rates of otitis media, the net savings from vaccination would be substantially higher than the base case.

Conclusion. Vaccination of school-aged children against influenza could have substantial financial benefits to society, especially if performed in a group-based setting. Pediatrics 1999;103(6). URL: http://www.pediatrics.org/cgi/content/full/103/6/673; influenza, cost-effectiveness, vaccination, children, cost.

Influenza causes illness among all age groups with significant morbidity among the elderly and other high-risk groups. A secondary effect of influenza is its ability to disrupt communities by causing school and work-place absenteeism.12 This lost productivity, the indirect costs of influenza, creates a substantial cost to our society.

Numerous studies have suggested that immunization in communities would not only prevent infection but would also reduce the indirect economic costs. For example, recent studies have documented the cost-effectiveness of vaccination of healthy working adults and in the elderly.2,3

Considering the public health and economic problems that are associated with influenza, vaccination of school-aged children may help control the spread of disease and reduce the economic costs. There are several reasons to consider vaccination of children. Although children are at low risk for complications of influenza, the disease causes them discomfort and often requires them to stay home from school.1,4 Time lost from school attributable to illness can result in missed learning opportunities. Infection rates are much higher in children than in adults.5-7 Moreover, children are efficient spreaders of the disease and a major factor in the introduction of influenza into households.8 Finally, working parents may have to stay home to care for a sick child, resulting in lost productivity. Vaccinating healthy workers would not eliminate the lost productivity caused by caring for ill children.

We investigated the cost of vaccinating school children in two hypothetical settings 1) a relatively inefficient system in which individuals schedule appointments for their children at physician offices during the parent or guardian’s normal work hours and 2) a relatively efficient system in which children are vaccinated in a group setting that does not require parents to take time off from work. An example of the latter scenario could be a health fair or school-based vaccination.

METHODS

The population was to be made up of school-aged children in kindergarten through grade 12. The cost of each vaccination strategy was compared with a nonvaccination strategy to obtain the net cost. Results were expressed as the net cost (or net savings) per vaccine recipient. Net cost included direct and indirect costs. Indirect costs included the time lost from work by working parents. Time was lost from work when working parents stayed home with ill children and when the disease was transmitted to a parent from the child. Under the individual-initiated vaccination strategy, time was lost from work when a working parent had to visit a physician’s office or clinic to get the child vaccinated. In the following description, the terms “parent,” “mother,” or “father” refer to a parent, guardian, or other adult who is a primary caretaker of the child.

Direct Cost of Vaccination

The cost of influenza vaccination has been reported to be as low as $4 including the costs of the vaccine, supplies, advertising, mailings, personnel, and administrative costs. This figure was the cost to a staff-model health maintenance organization for influenza vaccination of enrollees attending the doctor’s offices. In another study, these same costs were found to total $10 per recipient when patients were recruited through advertisements to
attend an outpatient clinic. For the purposes of this analysis, the more conservative $10 figure was used to represent the cost of an individual-initiated physician office visit for influenza vaccination. It was assumed that the group-based vaccination strategy would be more efficient and that the direct cost of vaccination would be $4 per dose. Sensitivity analysis was performed to determine the effect of increased vaccine costs on the analysis. It was assumed that unvaccinated children <9 years of age would require an initial vaccination series consisting of 2 doses. In subsequent years, it was assumed that only a single vaccination was required. To be conservative, it was assumed that no child had received previously the primary series. This had the effect of increasing the average cost of the vaccine per child by 1/13. Other costs and probabilities were derived from the literature (Table 1).

Other Direct Costs
Direct costs included the cost of a physician visit for the ill children and for the secondary contacts that sought medical care. According to the National Health Interview Survey, a physician was contacted during 32.5% of influenza illnesses in school-aged children, but only 83.3% of these contacts were face-to-face visits. Thus, it was assumed that a face-to-face physician visit occurred during 27.1% of all influenza cases in school-aged children. The cost for a physician visit was assumed to be $51 based on the cost of an average visit to a pediatrician. The cost for adults to visit a physician was assumed to be $69.51, and 27.1% of ill adults were assumed to visit a physician.

Indirect Costs
Indirect costs included time lost from work that accrued when an employed caretaker had to stay home with an ill child. The National Health Interview study found that there were .793 school days lost per school-aged child annually attributable to influenza. This is nearly identical to the findings of a randomized, placebo-controlled trial that found that unvaccinated children missed .79 days of school per year because of influenza illness. The .793 figure was adopted for this analysis and represented the average burden of illness in the population; children with influenza-associated illness would have more lost school days and uninfected children would not miss school because of influenza.

It was assumed that all infected children required an adult caretaker to stay home with them. Sometimes, the caretaker might not be used in which case no indirect costs were incurred. For the purposes of the analysis, it was assumed that the mother (or another female caretaker) would be the primary caretaker of an ill child. This visit was assumed to be $51 based on the cost of an average visit to a pediatrician. It was assumed that the group-based vaccination strategy would be more efficient and that the direct cost of vaccination would be $4 per dose. Sensitivity analysis was performed to determine the effect of increased vaccine costs on the analysis. It was assumed that unvaccinated children <9 years of age would require an initial vaccination series consisting of 2 doses. In subsequent years, it was assumed that only a single vaccination was required. To be conservative, it was assumed that no child had received previously the primary series. This had the effect of increasing the average cost of the vaccine per child by 1/13. Other costs and probabilities were derived from the literature (Table 1).

Key Assumptions

| Cost of individual-initiated vaccination | $10 | 2 |
| Cost of vaccination in a group setting | $4 | 3 |
| Proportion of children requiring a 2-dose initial series | 1/13 | 9 |
| Efficacy of vaccine | | |
| Base case | 56% | 1 |
| Best case | 75% | 4 |
| Worst case | 43% | 2 |
| Risk of transmission from an infected child to an adult in household | 18% | 23 |
| Proportion of households with 2 parents | 72% | 24 |
| Probability that mother is employed | 76% | 12 |

The individual-initiated vaccination strategy involved vaccination of children in a physician’s office during regular work hours. In families in which the mother worked full-time, it was assumed that 4 hours of wages would be lost if vaccinations were provided in a physician’s office. This provided a conservative estimate of the cost of vaccination. Lower costs would be possible if physicians provided evening hours or if mothers had unpaid caretakers available to accompany their child.

It is certainly possible that an employed male in the household might take off work to be with a sick child rather than a woman. However, we used the salary of working women rather than working men to provide a more conservative estimate of the indirect costs of influenza.

We assumed that if the mother worked, she had no source of free child care in the household and that she would have to take off work to care for a sick school-aged child. This may not be strictly true. In some cases, an unemployed family member or friend might be available to take care of a sick child while the mother continued working. However, national estimates on this possibility were not available. We chose to examine this effect in the sensitivity analysis by varying the proportion of women who would have to take time off from work.

Indirect costs also included the time lost from work attributable to secondary transmission to an employed adult. A sick adult with influenza was assumed to take 1.5 days off work. For the purposes of the baseline analysis, two groups were assumed to be at risk for time lost from work attributable to secondary transmission: 1) working mothers of ill children and 2) working fathers in the 72% of households in which a married couple was present. When fathers were present in the household, it was assumed that 97% would be employed.

Probabilities
In the United States, annual influenza rates range from 10% to 20% of the general population, but the rate is much higher in children. For this analysis, the annual incidence of influenza in children was taken from a prospective study and was 47.7/100 school-aged children <11 years of age, and 40/100 between the ages of 11 and 17 years. These numbers correlate well with results from the National Health Interview Survey of 45 708 US households that found an average rate of 46.3/100 children per year. Other longitudinal studies have found that 40% to 54% of school children acquired the infection. Lower infection rates may be present in some years or in some settings. The effect of lower rates was investigated by sensitivity analysis.

Studies to investigate the efficacy of the vaccine have used various methodologies resulting in a range of values. The ability of the vaccine to prevent infection, influenza-type symptoms, and missed school days has been studied. The inactivated influenza vaccine has been shown to be up to 80% to 90% effective in preventing infection in children. However, not all infections are asymptomatic enough to result in missed school days. Two recent studies found that influenza vaccination reduced missed school days by 56% and 75%. Similarly, the inactivated vaccine was found to be 62% to 73% effective in preventing influenza-type illness in school-aged children. However, Nichol et al. found the vaccine to reduce missed work days by only 43% in adults. For our analysis, the vaccine was assumed to be 56% effective. The effect of varying this number from 43% to 75% was investigated by sensitivity analysis.

The side effects from vaccination of healthy working adults are
minor. We assumed that no costs would be incurred from vaccine side effects. Low-grade fever is the most common reported side effect. Sensitivity analysis was used to investigate the impact on results if all children with low-grade fevers stayed home from school for 1 day. The risk of Guillain Barré in vaccine recipients <45 years of age was found recently to be 0.23. Sensitivity analysis was used to investigate the impact of a rate of Guillain Barré that was similar to the rate in older adults: 1 case per million recipients.

The risk of transmitting influenza from an ill child to an adult contact was assumed to be 18% based on a prospective study by Hayden and colleagues that was confirmed by older studies. This transmission rate seems low because some adults would have already acquired the infection outside the home, and others would be immune or semimmune.

In 1997, married couples made up 72% of all households with families. For these households, it was assumed that 2 adults per household would be at risk to acquire influenza from an infected child. For all other households, only 1 adult was assumed to be at risk.

Influenza vaccination may also prevent otitis media infections. However, there are no prospective studies of the effect of influenza vaccination on the incidence of otitis media in school-aged children. For the purposes of the base case analysis, the vaccine was postulated to have no effect on the incidence of otitis in school-aged children. This assumption was investigated by sensitivity analysis.

RESULTS

Vaccination of school-aged children with the inactivated vaccine resulted in a net cost savings of $3.99 per child under the individual-initiated strategy. Under the group vaccination strategy, influenza vaccination would result in a net cost savings of $34.79 per child vaccinated. The cost savings were primarily attributable to averted indirect costs (Table 2).

Sensitivity Analysis

Our results were based on certain assumptions about the probability of disease and the characteristics of the vaccine. Sensitivity analysis was performed by varying key assumptions to determine the point at which the vaccine no longer resulted in a net cost savings. This showed that vaccination remained cost-effective even with wide variation in the assumptions.

For example, if indirect costs were excluded from the analysis, individual-initiated vaccination would no longer result in a net cost savings, but rather would result in a net cost of $6. In this instance, the cost of time lost from work caused during vaccination and illness was eliminated from the analysis. The net savings for group-initiated vaccination would be retained if only direct costs were considered.

For the original analysis, we assumed an 56% efficacy rate. In the best case scenario, if the efficacy of the influenza vaccine were 75%, the net cost savings attributable to vaccination would increase. For example, individual-initiated vaccination would result in a total $17.25 savings per vaccine recipient. In the worst case, with only a 43% efficacy, the group-based vaccination program would continue to result in a net cost savings, but the individual-initiated vaccination would not (Table 3). The efficacy of the vaccine may be lower in years where the fit with circulating strains is poor. However, the efficacy would have to drop below 10% to negate the cost savings of a group-based vaccination program.

We examined cost-effectiveness over a range of vaccination costs. Under the individual-initiated vaccination strategy, caretakers had to miss work to take children to be vaccinated. The large indirect cost associated with the lost work time was far in excess of the vaccine and administration costs. If the vaccination costs were raised by $4 per recipient, there would no longer be a net cost savings attributable to individual-initiated vaccination. If vaccination cost $20 per child, group-based vaccination would result in a net cost savings of $19 per vaccine recipient. In fact, under the group vaccination strategy, vaccination costs would have to exceed $39 per child to eliminate the net cost savings caused by vaccination.

Several factors might increase the cost of vaccination. Notably, we did not include the costs of serious complications or fatalities caused by vaccination because recent studies have not found evidence of these occurrences. Even if all these children stayed home from school for 1 day, the cost of side effects per vaccine recipient would only be $1.36. From the above sensitivity analysis, it may be seen that the cost of side effects would have to exceed $34 per child to erase the cost savings attributable to group-based vaccination.

The incidence of influenza vaccine-associated Guillain Barré syndrome in subjects <45 years of age was found to be 0 in a recent study. The risk in older adults was ~1 per million doses of the vaccine. If this level of risk occurred in children, a case of Guillain Barré would have to cost >$34 million to negate the cost savings attributable to group-based vaccination.

We assumed that parents needed to take time off from work to get their children vaccinated. If mothers vaccinated >1 child during the half-day, this cost would be lower.

Influenza rates vary from year to year. If rates were 90% of the base rate that we assumed, individual-initiated vaccination would no longer result in a net cost savings. Only if rates were ≤15% of the base

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**TABLE 2. Costs of Influenza and Net Savings Attributable to Vaccination**

<table>
<thead>
<tr>
<th></th>
<th>Direct Costs of Influenza</th>
<th>Indirect Costs of Influenza</th>
<th>Vaccination Costs</th>
<th>Total</th>
<th>Net Cost (Savings)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No vaccination</td>
<td>$8.49</td>
<td>$61.33</td>
<td>$0</td>
<td>$69.82</td>
<td></td>
</tr>
<tr>
<td>Individual-initiated</td>
<td>$3.73</td>
<td>$26.99</td>
<td>$35.11</td>
<td>$65.83</td>
<td>(3.99)</td>
</tr>
<tr>
<td>Group-based vaccination</td>
<td>$3.73</td>
<td>$26.99</td>
<td>$4.31</td>
<td>$35.03</td>
<td>(34.79)</td>
</tr>
</tbody>
</table>

All figures are per school-aged child eligible for vaccination. All numbers are rounded off to the nearest $.01.
rate, would the net savings from group-based vaccination be eliminated.

We assumed that wages were lost for children with working mothers, because the mother would stay home to take care of the ill child. However, some working mothers may have unpaid caretakers available to them such as neighbors or relatives. The unpaid caretakers are at risk to acquire influenza, but do not incur lost wages. Unpaid caretakers would also be available to accompany the child to a doctor’s office to get vaccinated. Sensitivity analysis showed that the presence of unpaid caretakers had little effect on the outcome of the analysis. For example, vaccination under either strategy continued to result in a net cost savings even if 90% of the working mothers had unpaid caretakers.

In some cases, an employed father will choose to stay home with an ill child. Because men’s wages are usually higher than those of women,12 this would enhance the savings attributable to vaccination.

The base case did not include the possibility that vaccination might reduce otitis media. It has been estimated that virtually all children with otitis media visit a physician and that the annual incidence of otitis is 13.6/100 school-aged children.10 Unfortunately, the proportion of otitis attributable to influenza is not known. In two studies of preschool children, 30% of otitis was prevented by both the inactivated vaccine and an investigational live attenuated vaccine.27,28 If this efficacy was true for school-aged children, there would be additional savings from influenza vaccination. To be specific, there would be a total net savings of $20 for individual-initiated vaccination and $50 for group-based vaccination. It was assumed that all children with otitis visited a physician.10

We based family transmission rates on a prospective treatment trial and literature showing that children are the major vectors of disease transmission in families and communities.8 Transmission of the virus to employed adults other than the mother or father would further enhance the attractiveness of vaccination. The latter is likely to occur,8 but is difficult to quantify.

We analyzed the cost of influenza vaccination using a steady-state model. In other words, only 1/13 of children were assumed to receive 2 doses of the vaccine. Although some authors do not advocate a 2-dose initial series, most recommend it for unvaccinated children who are <9 years of age. It is possible that some children will have already received the vaccine before starting school or in other settings. This would decrease the total cost of vaccination of school-aged children. Alternatively, if a mass vaccination program were introduced, it is likely that most children under age 9 would require 2 doses of vaccine in the start-up year. This would increase the start-up costs of a program.

**DISCUSSION**

Influenza vaccination of school children would result in a net cost savings from a societal perspective. A hypothetical low-cost, group-based vaccination program that did not require parents to take time off from work resulted in substantial savings. Such a program would be similar to the work-based vaccination program proposed by Nichol et al2 in their analysis of vaccinating healthy, working adults against influenza.

Our analysis found that the indirect economic effects were central to the benefits of immunization. The importance of the indirect economic effects of influenza vaccination was also demonstrated in a recent study on the effectiveness of influenza vaccination of healthy, working adults.2 Clearly, worker absenteeism attributable to illness in workers or their children is a major consequence of influenza within the community.

Older studies have suggested that mass immunization of school children would be an appropriate strategy for reducing the spread of influenza within communities.29–31 There are several reasons for targeting this group. First, school children are an easy group to reach and offer an excellent opportunity for mass immunization. School-based immunization programs or health fairs would preclude the need for a visit to a physician’s office to receive the vaccine. Furthermore, children and schools are the major pathways that spread influenza to families and neighborhoods.3-7 In an older but important study, Monto et al31 followed the influenza infection rates in the town of Tecumseh, Michigan, in which >85% of the children were vaccinated and the adjacent unvaccinated community of Adrian, Michigan. The mean illness rate in all age groups in Adrian was three times higher than in Tecumseh. In addition, school absenteeism in Tecumseh was reduced markedly.

Additional impetus for vaccinating school-aged children comes from the recent development of a novel, intranasal influenza vaccine. The nasal spray delivery system may provide significant advantages over needle injection, especially in terms of patient/parent acceptance.32 Our analysis shows that the cost of the nasal vaccine will be a critical component in determining its cost-effectiveness.

Side effects of vaccination are shown to be minor in children. However, no vaccine is completely safe or risk-free. Sensitivity analysis showed that the cost savings from vaccination were retained even if all children with minor side effects stayed home from school. Currently, more catastrophic side effects such as Guillain Barré syndrome are believed to be rare.

<table>
<thead>
<tr>
<th>TABLE 3.</th>
<th>Sensitivity Analysis: Efficacy and Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy of Vaccine</td>
<td>Reference</td>
</tr>
<tr>
<td>Best case</td>
<td>75%</td>
</tr>
<tr>
<td>Best case</td>
<td>56%</td>
</tr>
<tr>
<td>Worst case</td>
<td>43%</td>
</tr>
</tbody>
</table>
Indeed, the recent analysis by the Centers for Disease Control and Prevention found no Guillain Barré syndrome associated with the vaccination of children. Possibly, more widespread vaccination would result in detection of cases of this syndrome. Economically, rates similar to those found in older adults would not negate the cost savings from vaccination. Some parents may not be willing to vaccinate children even if the risk of serious complications approaches 0.

On the other hand, we did not consider deaths from influenza, complications of infection, or hospitalizations. These events are rarely associated with influenza in healthy children or healthy adults. However, it seems reasonable to conclude that vaccination would potentially prevent a small number of deaths, complications, and hospitalizations and that total cost savings would be augmented. Potential reductions in cases of otitis media would also contribute to the benefits of vaccination. Finally, we did not include any potential benefits from herd immunity, because it is not clear what proportion of children would have to be vaccinated to induce benefits in unvaccinated persons. If any herd immunity did occur, this would further enhance the benefits of vaccination.

The primary goal of an influenza vaccination program in school-aged children would be to prevent illness in the population and to prevent disruption in the community. In that spirit, we analyzed the magnitude of the number of lost school days and worker absenteeism attributable to influenza and the potential to mitigate these societal losses with available means. The pain and suffering from influenza infection, although not readily quantifiable, would also be reduced significantly by vaccination.

CONCLUSION

In summary, we believe that influenza vaccination of school-aged children could result in a net cost savings from a societal perspective and have health benefits within the community. Policymakers should give serious attention to a vaccination strategy that targets school-aged children and takes advantage of emerging epidemiologic, technological, demographic, and societal factors.

REFERENCES

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