Interdisciplinary Epidemiologic and Economic Research Needed to Support a Universal Childhood Influenza Vaccination Policy

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Recent research indicates that influenza vaccination of children may decrease the influenza disease burden in adults to a greater extent than targeting vaccination to populations at high risk of serious disease. Possible new policies reflecting these results would add groups most likely to transmit disease to existing vaccination recommendations. Interdisciplinary research combining epidemiology with economics is needed to answer critical questions about the desirability and feasibility of potential new policies, such as what additional resources medical providers might need to expand vaccination to larger groups or what opportunity costs parents might incur in vaccinating their children annually. In this paper, the authors provide background for some of the changes in influenza vaccination rates and disease and discuss existing information gaps and research methods capable of closing these gaps. They provide several examples of interdisciplinary studies that have incorporated both economics and epidemiology or health policy issues. These studies are representative of a variety of stakeholder perspectives needed to determine whether community-based, universal childhood vaccination policies would be more efficacious and cost-effective than strategies targeted toward persons at high risk of disease complications.

INTRODUCTION

Between 1980 and 2001, the influenza vaccination rate for people over age 64 years increased from approximately 20 percent to 65 percent (1). However, instead of falling, numbers of influenza-associated deaths increased during the same time frame, with 90 percent of those deaths occurring among the elderly (2–4). Reasons for this conundrum include the aging of the population, which increases the baseline risk of mortality; an increase during the late 1990s in A/H3N2 influenza seasons, which are usually associated with higher mortality than seasons with other influenza strains; and increases in the population of patients with underlying conditions that increase the risk of complications from influenza. Failure to see marked reductions in mortality may also be related to lower effectiveness of influenza vaccines in the elderly as compared with younger populations (5). The frail elderly have the lowest rates of vaccine-induced protection against influenza (30–40 percent) in comparison with healthy younger adults (70–90 percent) (6–8). While influenza vaccination of the elderly still results in reductions in mortality and other complications, there is a substantial burden of illness that is not being prevented through a strategy focused specifically on vaccinating the elderly.

Recently, scientists have begun to investigate whether universal childhood vaccination, in addition to vaccination of the elderly, would prevent a greater proportion of influenza morbidity and mortality in the entire community. While the burden of influenza is greatest in the elderly, the attack rate is greater in children, making them very efficient disease vectors. There is a growing body of evidence supporting the hypothesis that vaccinating children directly protects them and indirectly protects adults more effectively than does vaccinating just the elderly, by reducing transmission of disease in the community (9).
Support for a potential policy of universal childhood vaccination comes from a retrospective study of Japan’s policies—first mandatory, then voluntary—of vaccinating all school-aged children against influenza annually between 1962 and 1994 (10). Calculated numbers of pneumonia and influenza deaths attributed to influenza in the elderly were substantially reduced during the years that the policy was in effect. After Japan stopped vaccinating schoolchildren, there was a marked increase in influenza-related morbidity and mortality among the elderly (10). This pattern suggests that decreasing disease transmission from children to the community led to less exposure to influenza viruses among the elderly. However, these results are not directly comparable to the US population, for two reasons. Throughout the study period, a much lower proportion of high-risk and elderly adults were vaccinated in Japan than in the United States. Furthermore, a much greater proportion of Japanese schoolchildren live in the same households as their grandparents, making child-to-adult disease transmission more likely (10).

There is some US research supporting a policy of universal childhood vaccination against influenza because of the overall societal benefits that might accrue from such a policy. A simulation model constructed by Halloran and Longini (11) indicated that vaccinating 20 percent of schoolchildren would reduce influenza-related mortality in the elderly more than would vaccinating 90 percent of persons over age 64 years. A study in Texas compared the incidence of medically attended acute respiratory illness among adults in communities where 20–25 percent of children aged 1.5–18 years had been vaccinated over a 3-year period with the incidence in communities where children had not been vaccinated. Among adults aged 35 years or older who were living in child-vaccinated communities, medically attended acute respiratory illness was reduced 8–18 percent compared with communities where children had not been vaccinated. Among adults aged 35 years or older who were living in child-vaccinated communities, medically attended acute respiratory illness was reduced 8–18 percent compared with communities where children had not been vaccinated (12). During the 1968–1969 influenza season, approximately 85 percent of schoolchildren in Tecumseh, Michigan, were vaccinated. Adult disease rates in Tecumseh were three times lower than those in a nearby town in which the population was largely unvaccinated (13).

This epidemiologic research supports a potential major change in policy—a move toward universal childhood vaccination in addition to the current approach targeting persons at high risk of influenza complications, particularly the elderly. To address the concerns of stakeholders regarding the potential difficulties of implementing universal vaccination of children, interdisciplinary research in economics and epidemiology has recently appeared incorporating some measures (e.g., elasticity) and models (e.g., simulation) from mainstream economics that are not usually found in traditional economic evaluations (e.g., cost-effectiveness, cost-benefit, and cost-utility analyses). Some of this research produces results from the perspective of individual stakeholders (e.g., parents, medical providers) rather than the traditional societal perspective. This interdisciplinary economic and epidemiologic research is very useful in answering the questions of various stakeholders whose compliance would be critical in implementing universal childhood influenza vaccination.

There would be challenges involved in implementing universal vaccination of children aged 5–18 years. This new policy would mean vaccinating an estimated additional 56 million people during a short time frame each fall (14). Aside from the need for more epidemiologic research, there needs to be research examining the additional economic costs of implementing such a policy and the resources that would be saved as a result of implementing such a policy. A few of the many potential questions that might be addressed are:

1. If vaccination of schoolchildren decreases disease transmission to adults, it should also decrease the costs of treating influenza-related illness, decrease numbers of hospitalizations, and keep children in school for more days each year. How much money will Medicare and other insurance carriers save in disease-treatment costs as compared with increased vaccination costs?
2. How safe is influenza vaccine in the school-aged population? Will safety assurances encourage/discourage parents, who will potentially incur lost wages to vaccinate their children each year or, alternatively, save on lost wages both by not caring for sick children and by not getting sick themselves? What value would parents place on helping their children avoid illness?
3. Do medical practitioners have the capacity to vaccinate large numbers of children in a short time frame? Would they be sufficiently reimbursed for vaccination to want to incur the additional costs necessary to vaccinate their patients? What losses would medical practitioners incur if vaccinating children stopped them from administering other medical care that might be reimbursed at a higher rate?

MATERIALS AND METHODS

There is a small but growing number of health-economics researchers adding to the essential findings of traditional economic evaluations by using other types of modeling, looking at questions from perspectives other than those of society, and incorporating epidemiologic findings into their models. For this paper, we searched the ECONLIT and MEDLINE databases using combinations of the terms “influenza,” “vaccination,” “adults,” “child,” and “universal” to find interdisciplinary literature published during 2004 and 2005 that represented economic-epidemiologic research not limited to economic evaluation. Articles with outcomes expressed in dollar terms that delayed the results of time, motion, or time-motion studies were not used. We found seven articles that fell into this category. We discuss all seven, explaining how each publication can help inform policy-makers about influenza vaccine policy and implementation of that policy.

RESULTS

The US health-care market is a public-private partnership with many stakeholders (public and private insurers, public health advocates, physicians, consumers, etc.). In the face of rising health-care costs, public health researchers are
turning more frequently to economic experts for evaluation of public health protocols, including vaccination. Experts in all economic specialties, including health economics, investigate ways to allocate limited resources between competing needs. Traditionally, health economists have used economic evaluation to answer single-issue questions (e.g., those that compare a new vaccine with an existing vaccine or no vaccine).

However useful and well-done they may be, economic evaluations of influenza vaccination and disease often do not address the broader policy issues raised by elected officials, who are charged with funding programs that have competing demands. The traditional standard in health economics has been to examine issues from a societal perspective. Although a societal perspective is often necessary, it does not address the specific interests of stakeholders who are facing the increasing costs associated with compliance with public health recommendations or who might not understand the benefit they would receive by decreasing illness costs.

As a result of these issues, some researchers in public health, including health economists, are beginning to use methods other than economic evaluation to address more complex questions from the perspective of specific stakeholders. For example, in a recent article, Szuks stated, “Government agencies need to understand the consequences of influenza, including the economic sequelae, in order to make informed choices in the context of health care policy” (15, p. 26). This type of research would help stakeholders understand why participating in implementation of vaccination policy is in their best interest. The studies discussed below examined questions from a variety of perspectives and employed methods that are not frequently used in economic evaluations.

Consumer choice

Even though influenza vaccination for the elderly has been proven effective at reducing expensive influenza-associated sequelae (7, 8) and there are no out-of-pocket Medicare-patient costs for vaccination, many elderly persons still do not get an annual influenza vaccination. In their study, Parente et al. (16) relied on a fundamental principle of microeconomics: that consumers need information on different options in order to make rational choices about how to best spend their limited resources. In this tradition, Parente et al. developed a model theorizing that consumers who were unaware of Medicare benefits, including coverage of influenza vaccination or mammography, would use these preventive health measures less often than consumers who were educated about their benefit coverage. Uneducated consumers would incorrectly believe that they had to pay for preventive services if they did not know that these services were covered by Medicare.

To test their theory, Parente et al. (16) linked data from supplemental questions in the Medicare Current Beneficiary Survey to rates of vaccination and mammography use by Medicare patients and measured benefit use in an applied model. During the influenza season following administration of the Medicare Current Beneficiary Survey questionnaire, 85 percent of consumers over age 64 years who were both aware of Medicare policies and had previously been vaccinated and 63 percent of consumers who were aware of the policies but had never before been vaccinated put in an administrative claim for influenza vaccine. Only 39 percent of respondents who were uninformed about their Medicare benefits received vaccinations during the same season. The authors concluded that “strategies to educate the insured Medicare population about coverage of preventive services may have substantial social value” (16, p. 25).

Work in this genre has several policy uses, one of which would be the potential to address insurance carriers’ concerns about the perceived costs of vaccinating many more children each year. Insurance carriers would worry about losing vaccinated clients, for whom they would have lower associated illness costs, and acquiring unvaccinated clients, for whom they would have higher associated illness costs. However, with a fully implemented universal influenza vaccination policy, insurance companies would probably both lose and acquire vaccinated clients. There are studies showing that children and adolescents of parents with health insurance covering vaccination are more likely to receive all vaccinations in a timely manner (17, 18). There is no reason to assume that the results from these studies would not apply to influenza vaccination for children and adolescents. In turn, vaccinated children and adolescents are probably less likely to become ill or pass along illness to their parents, saving insurance carriers the costs of physician visits and use of medications by sick parents and their children.

Household illness expenses

Most economic evaluations do not incorporate factors that are difficult to quantify (e.g., household labor or time lost from work for care of an ill child), so household expenses incurred in providing patient care are rarely taken into account. This makes it difficult to provide persuasive arguments regarding individual interests in favor of vaccination. During the Australian winter months of July through December 2001, Lambert et al. conducted a prospective cohort study in 118 Melbourne children between 12 and 71 months of age” (19, p. 509). The children did not have previous high-risk conditions. The parents completed a symptom diary card for each day that the child was in the study, as well as records of direct and indirect expenses for the care of sick children. There were subsequently 202 incidents of influenza-like illness, 89 physician visits, and 42 prescriptions for antibiotics. The average cost of each episode, without hospitalization, was $241 (Australian). The main “drivers” of illness-associated costs were parental time taken to care for the ill child and use of nonprescription medicines. Furthermore, families were responsible for 87 percent of the costs of illness in a child, and families with the lowest incomes and most substantial resource constraints had the highest average costs.

To our knowledge, there have been no US studies of the opportunity costs and/or indirect costs incurred by parents in caring for sick children with influenza or influenza-like
illnesses. The Lambert et al. study (19) is a good example of the type of research that is critical in evaluating the opportunity costs faced by families, defined as the difficult choice parents must make between work responsibilities and caring for sick children. The caretakers in the lowest-paid jobs, which are the jobs least likely to allow flexible leave time with pay, are the ones that incur the highest indirect costs. An argument for universal childhood vaccination might be made on the basis that averting childhood illness would minimize both opportunity costs and indirect costs and constraints faced by overburdened parents.

**Elasticity**

One fundamental economic tool not often used by health economists or epidemiologists is measurement of elasticity. In simple terms, elasticity measures how much a dependent variable changes in response to changes in an independent variable. Elasticity is a neutral value that can move in either a positive direction or a negative direction. Ohkusa (20) conducted a cost-benefit analysis by researching the elasticity between recipient copays (independent variable) and the probability that the elderly would be vaccinated (dependent variable) in 12 large Japanese cities. He obtained vital statistics data on influenza- and pneumonia-related mortality from the Japanese government. The study showed that a reduction in the vaccination copay by approximately ¥1,000 (~$8 US) increased vaccination rates enough to prevent approximately 400 deaths per year in the average large city. Ohkusa concluded that subsidization of influenza vaccination for the elderly would be cost-beneficial to the government of Japan (20).

Elasticity measures are a useful way to convey the economic benefits of the effectiveness of vaccination to policy-makers. Unlike sensitivity analyses, which are often one-way measures, elasticity measures allow for two-way variations in both dependent variables and independent variables. A US study carried out along similar lines that examined the tradeoff between increased expenses for influenza vaccination and decreased expenses related to decreased illness would be useful to insurance decision-makers, who would have to decide whether or not to cover the vaccination of increased numbers of people.

**Simulation modeling**

Several recent economic studies have relied on simulation modeling for their results. Simulation modeling enables researchers to create theoretical populations on the basis of a few data points. It is a useful tool when 1) real-world data are lacking or 2) observing the effects of a public health intervention on a live population is either difficult or unethical.

Coleman et al. (21) used simulation and other modeling techniques to determine the costs incurred by different-sized medical practices when vaccinating adults against influenza during either scheduled office visits or unscheduled vaccination clinics. In most cases, providing vaccine to adults at the national average reimbursement rate was an economic loss for medical practices. Following the release of the results of the study, Medicare increased reimbursement to physicians for the administrative costs associated with vaccinating adults. More studies of this type are needed in pediatric and family practices to identify the resources required to vaccinate large numbers of children each year and to inform policy-makers deciding how best to provide the resources necessary for vaccination services.

Meltzer et al. (22) used a Monte Carlo simulation to calculate net economic returns from vaccinating children against influenza each year. As do many epidemiologic investigators, these authors used the Medicaid database to obtain original data with which to set parameters, including definitions of children at high risk of influenza, for three age-specific cohorts (6–23 months, 6–59 months, and 5–14 years). Each cohort comprised 1,000 children and different proportions of high-risk children (0 percent, 10 percent, and 100 percent). The authors varied the costs of vaccination from $30 per dose to $60 per dose. The results of the model varied depending on the influenza attack rate, the percentage of high-risk children, age group, and cost. Vaccinating 100 percent of high-risk children resulted in a median net savings to society. Vaccinating cohorts of children with no high risk did not result in cost savings, but vaccinating cohorts of children with some high risk resulted in different break-even points for each cohort.

This study makes a valuable beginning contribution to our understanding of the direct costs and savings associated with universal childhood influenza vaccination. In particular, models like this account for the nonrandom distribution of high-risk children in the population and are particularly useful in analyzing whether or not campaigns targeting unvaccinated populations are a better use of public monies than generalized vaccination campaigns. Meltzer et al. (22) acknowledged in their Discussion section that serious gaps in observed data did not allow them to account for the indirect costs of influenza in children, such as parental time lost from work, or the effects of influenza on children in different circumstances. Furthermore, their model did not include any factors examining potential decreases in disease transmission from children to adults. Reproduction of this study to include potential cost savings from herd immunity and consideration of indirect costs (such as those associated with caring for ill children) would be very valuable.

Weycker et al. (23) used a stochastic simulation model to track influenza transmission in a community. This permitted virtual examination of disease transmission from children to adults according to different levels of childhood vaccination. Disease burden declined in adults in inverse relation to the vaccination levels of children. Influenza vaccination of 20 percent of children aged 6 months–18 years resulted in a 46 percent reduction in the total number of influenza cases, while 80 percent coverage reduced disease by 91 percent. Direct medical costs and work loss due to influenza morbidity and care of sick children all decreased with the decrease of illness burden in the simulated community. At 80 percent coverage, the cost savings per vaccinated child were $35 in direct medical costs and $139 in indirect costs, such as reduction in parental lost-work time.

Clinical trials can be constructed to answer multiple questions simultaneously and provide highly credible...
DISCUSSION

Influenza infection continues to produce high rates of morbidity and mortality, especially among the elderly; therefore, an enhanced strategy is needed to reduce the influenza disease burden. One option would be to recommend vaccinating all children to decrease disease transmission in the community and protect other population groups indirectly by decreasing their exposure to the virus. Research combining epidemiology with economics would produce valuable results to help policy-makers evaluate whether or not a new, community-based policy should be adopted and to help stakeholders understand why complying with this type of policy might be in their best interests.

Economic researchers can use tools other than economic evaluation to determine the resources needed to implement policies from the viewpoints and needs of different stakeholders. One example would be modeling the trade-off decision insurance carriers make between paying more for illness and paying less for prevention. Influenza vaccination is effective, but new policies might result in more optimal prevention of the burden of influenza in the community. Epidemiology is essential in determining the best ways to reduce this burden, but when paired with economic modeling methods and theories, interdisciplinary research produces more useful results for policy-makers than either discipline does on its own. Such research provides all stakeholders with the foundation they need to make informed decisions regarding vaccine policies. Ultimately, this type of research will help ensure successful implementation of any new influenza vaccination policies.

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