Influenza Vaccination

Health Impact and Cost Effectiveness Among Adults Aged 50 to 64 and 65 and Older

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Background: Influenza causes approximately 36,000 deaths per year in the United States despite the presence of an effective vaccine. This assessment of the value of influenza vaccination to the U.S. population is part of an update to the 2001 ranking of clinical preventive services recommended by the U.S. Preventive Services Task Force. The forthcoming ranking will include the new recommendation of the Advisory Committee on Immunization Practices to extend influenza vaccination to adults aged 50 to 64 years.

Methods: This service is evaluated on the two most important dimensions: burden of disease prevented and cost effectiveness. Study methods, described in a companion article, are designed to ensure consistency across many services.

Results: Over the lifetime of a birth cohort of 4 million, it is estimated that about 275,000 quality-adjusted life years (QALYs) would be saved if influenza vaccination were offered annually to all people after age 50. Eighty percent of the QALYs saved (220,000) would be achieved by offering the vaccine only to persons aged 65 and older. In year 2000 dollars, the cost effectiveness of influenza vaccination is $980 per QALY saved in persons aged 65 and older, and $28,000 per QALY saved in persons aged 50 to 64. When the costs of patient time and travel are excluded, the cost effectiveness ratio of vaccinating 50- to 64-year-olds decreases to $7200 per QALY saved, and vaccinating those aged 65 and older saves $17 per person vaccinated.

Conclusions: Influenza vaccination is a high-impact, cost-effective service for persons aged 65 and older. Vaccinations are also cost effective for persons aged 50 to 64.
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Introduction

Influenza epidemics cause, on average, 36,000 deaths per year in the United States. As part of the adult immunization schedule, the Advisory Committee on Immunization Practices (ACIP) recommends annual influenza vaccinations for both persons aged 65 and older (due to increased risk for complications) and for persons aged 50 to 64 years, due to a higher prevalence of certain chronic medical conditions among this group.[1,2]

Influenza vaccination coverage increased throughout the 1990s, but significant gaps remain between current vaccination levels and *Healthy People 2010* goals. Between January and March 2004, 70.3% of adults aged 65 years and older and 40.6% of those aged 50 to 64 years reported an influenza shot in the last 12 months. Hispanic and non-Hispanic black adults aged 65 and older reported much lower vaccination coverage: 54.3% and 50%, respectively.[3] Only one third of high-risk groups aged less than 65 were vaccinated (those with cardiovascular disease or respiratory diseases, among others).[4]

This assessment of the health impact and cost effectiveness of influenza immunization for the population aged 50 and older and the accompanying articles[5–8] in this issue of the *American Journal of Preventive Medicine* are part of the update to Partnership for Prevention's 2001 ranking of 30 clinical preventive services.[9,10] The National Commission on Prevention Priorities (NCPP) guided development of the updated ranking. The NCPP chose to evaluate services based on the same criteria used previously: (1) clinically preventable burden (CPB) as a measure of health impact, and (2) cost effectiveness.[9,10] This article describes the updated estimates of CPB and cost effectiveness for influenza vaccination, reflecting new evidence, more thorough review and analyses, and the revised recommendation of the ACIP to extend vaccinations to persons aged 50

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to 64 years. The marginal value of adding the 50- to 64-year-old age group was of particular interest.

Methods

A detailed description of the study methods can be found in the companion article[8] and in a technical report available online.[11] The methods were designed primarily to ensure consistency in estimating a service's CPB and cost effectiveness across many services that differ substantially from one another, while managing an enormous volume of evidence. Key aspects of the methods used to evaluate all services and applications of those methods that are specific to the evaluation of influenza vaccination are summarized here. The main objective was to estimate the CPB and cost effectiveness of offering influenza vaccine to individuals aged ≥50 years; however, separate estimates by age groups (50 to 64 and ≥65) were also produced.

Evidence Gathering

Two sets of standardized search strategies were developed for the overall prioritization study (one for effectiveness and cost-effectiveness data and a second for burden of disease and cost data). Each strategy included four levels, where Level 1 included the most current literature and data sources, and each subsequent level extended to less current sources and sources less likely to yield useful data. The Level-1 search used PubMed for English-language articles dating from 1992 and was limited to MeSH major terms, title word terms, and phrases. The Cochrane Collaboration reviews were also searched from 1992.[8]

For influenza vaccination, a Level-1 search[8,11] was performed for data on the burden of disease, quality of life, effectiveness, delivery rates, patient adherence to vaccination offers, and cost effectiveness. The search was extended to Levels 2 and 3[8,11] to identify additional literature on the effectiveness of influenza vaccinations in preventing mortality, vaccination rates, the antigenic match of each year's vaccine, and patient adherence to offers for influenza vaccination.

The searches identified 27 articles on the effectiveness of influenza vaccinations in preventing influenza-like illness or influenza-associated mortality.[12–38] Two studies were subsequently identified[39,40] in a recent systematic review.[41] Eleven studies were excluded for reasons that included small sample sizes, potential error in case identification or vaccination status, no or uncertain accounting for potentially important selection effects, populations that could not be generalized to the target population for this service, and beginning vaccinations after the start of an outbreak.[14,17,20,23–25,27,29,30,37,38] More detail on reasons for excluding studies may be found in the technical report for influenza vaccination available online (prevent.org/ncpp.htm).

The Level-1 search for cost-effectiveness studies identified 14 articles.[16,28,30,42–52] Three articles[28,30,52] were abstracted that either expressed results in terms of dollars per life year saved (or quality-adjusted life years saved) or net savings and also met each of the following criteria: provided a clear base-case estimate of cost effectiveness, was published since 1990, expressed results in U.S. dollars, and included the majority of the ≥50 age group.

Estimating Clinically Preventable Burden

Clinically preventable burden was defined as the proportion of disease, injury, and death prevented by the service in a typical practice if the service were offered to 100% of the target population at regular intervals as recommended. This model for estimating CPB was analogous to a simplified cost-effectiveness model. Results of algebraic calculations performed at the base-case estimate of each variable are reported. The details of the algebraic models used to derive CPB are available in each service's technical report. Conceptually, CPB was simply the product of burden of disease and effectiveness. CPB was measured as quality-adjusted life years (QALYs) saved to capture the impact of disease, injury, and premature death.

Clinically preventable burden was based on the delivery of the service to a 1-year U.S. birth cohort (the size of which is defined consistently in this study as 4 million) over the age range that the service was recommended by the U.S. Preventive Services Task Force (USPSTF) or the ACIP. Because all CPB estimates were based on effectiveness in a typical practice, patient adherence to offers to accept the service and to follow up on treatment or changes in behavior was considered for every service. The primary distinction between efficacy and effectiveness was adherence,[8,11] so that:

$$\%\ \text{effectiveness} = \%\ \text{adherence} \times \%\ \text{efficacy}.$$

Clinically preventable burden was estimated independent of current delivery rates to indicate each service's total value, rather than the value of improving delivery rates over current levels for the U.S. population in order to fairly compare services with widely varying current delivery levels.

The values used to estimate CPB for influenza vaccination are shown in Table 1. The "base case" column shows the best available estimate for each variable, and the "range" column shows the range over which the point estimates were varied in the sensitivity analysis. Because the severity of influenza and degree of antigenic match of influenza vaccine vary from year to year, estimates that reflect average influenza seasons over time were created to aid long-term decision making about the priority of influenza vaccinations.

Burden of disease. Estimates of the deaths attributable to influenza were uncertain due to inherent difficulties in measuring influenza's role as a contributing factor in deaths with other conditions such as respiratory diseases and cardiovascular disease.[32,53–55] The current estimate was based on the influenza-associated mortality for all underlying causes of death reported by Thompson et al.[53] for persons aged ≥50 years. Influenza-related mortality with all underlying causes was most consistent with the available estimates of the effectiveness of the vaccine in preventing mortality.

Based on these published data, there would be 84,447 influenza-related deaths among persons aged ≥50 in a U.S. birth cohort of 4 million with current immunization rates, given current influenza mortality rates[53] and number of years at risk among persons aged ≥50.[56] In sensitivity analyses, the lower bound was the incidence rate of influenza-associated illness with underlying causes of death from respiratory and circulatory deaths, and the higher bound was the incidence rate for all underlying causes, which includes deaths associated with both influenza and respiratory syncytial virus.[53]

Table 1. Data used in estimating CPB and CE of influenza vaccine when offered to birth cohort of 4 million starting at age 50

	Base case estimate	Source	Range for sensitivity analysis
Number of person-years between ages 50 and 64	53,357,760	Thompson (2003)[53]	
Number of person-years ≥65	58,699,920	Thompson (2003)[53]	
Annual influenza-related mortality rate per 100,000, ages 50 to 64	12.5	Riddiough (1983)[50]	± 25%
Annual influenza-related mortality rate per 100,000 ages ≥65	132.5	Riddiough (1983)[50]	± 25%
Vaccination rate in 50- to 64-group in 1990s	34.2%	CDC[3], Heilman (1990)[54]	± 25%
Vaccination rate in ≥65 group in 1990s	57.4%	CDC[3], Heilman (1990),[54] Cox (1998)[55]	± 25%
Annual incidence rate of influenza-like illness in unvaccinated individuals	0.1511	Ahmed (1997),[13] Barker (1980),[15] Fedson (1993),[19] Jullooly (1994),[28] Arias (2002),[56] Singleton (2000)[57]	0.09 to 0.25
Annual hospitalization rate for pneumonia or influenza in unvaccinated individuals aged 50 to 64	0.0010	Ahmed (1997)[13]	0.000 to 0.0020
Annual hospitalization rate for pneumonia or influenza in unvaccinated individuals aged ≥65	0.00900	Nichol (1996),[29] Nichol (1994),[30] Nichol (1999)[31]	0.0085 to 0.0111
Adherence with vaccine	85.0%	CDC[58]	75% to 95%
Efficacy of influenza vaccine in preventing influenza-related mortality	42.9%	Coffield (2001),[9] Bridges (2000),[16] Howells (1975),[25] Nichol (1994),[30] Nichol (2003)[32]	
Efficacy of vaccine in preventing influenza-like illness	18.9%	Ahmed (1997),[13] Barker (1980),[15] Fedson (1993),[19] Jullooly (1994),[28] Nichol (1998),[33] Taylor (1992),[36] Treanor (1992)[37]	10% to 30%
Efficacy of influenza vaccine in preventing hospitalizations for influenza and pneumonia	36.6%	Maciosek (2001),[10] Ahmed (1995),[12] Bridges (2000),[16] Edwards (1994),[18] Howells (1975),[25] Nichol (1996),[29] Nichol (1994),[30] Nichol (1999),[31] Nichol (2003)[32]	25% to 50%
Duration of illness in years for influenza-like illness (=1 week)	0.0192	Jullooly (1994)[28]	0.5 to 2 weeks
Duration of illness in years for influenza hospitalizations (=2 weeks)	0.0385	See text	1 to 3 weeks
Quality-of-life reduction per year (QALY weight)	0.30	See text	0.20 to 0.40
Cost per hospitalized case, ages 50 to 64	$7,276	Frank (1985)[43]	± 25%
Cost per hospitalized case, ages ≥65	$8,278	Frank (1985)[43]	± 25%
Percent of non-hospitalized cases receiving care	47%	Frank (1985)[43]	35% to 60%
Cost per outpatient treated case, all ages	$198	Frank (1985)[43]	± 25%
Per vaccination healthcare costs	12.59	Ahmed (1997),[13] Howells (1975),[25] Meiklejohn (1989),[27] Frank (1985)[43]	$6 to $18
Per vaccination patient time and travel costs	21.16	van Essen (1997)[64]	$10.58 to $35.27
Discount rate	3%	See text	

CE, cost effectiveness; CPB, clinically preventable burden; QALY, quality-adjusted life year.

To adjust this estimate of mortality to reflect mortality in the absence of the vaccine, estimates of current delivery rates and efficacy of the vaccine were needed.[8,11] During the 1990s, the average annual vaccination rate reported in the National Health Interview Survey was 34.2% for ages 50 to 64 and 57.4% for ages ≥65.[3,57,58] The delivery rate for each age group was used to adjust the age group–specific mortality rates.

To quantify the incidence of influenza-like illness in the absence of vaccines, observed incidence rates among individuals who have not been vaccinated were used. Sixteen estimates of the incidence of influenza-like illness in unvaccinated adults aged <70 were recorded from four studies that were abstracted for vaccine effectiveness data[16,18,31,59] and from one additional study of zanamivir.[60] Most study populations were dominated by working-age adults; some included a small portion of children. Only one study provided estimates of influenza-like illness among unvaccinated, community-living older adults.[22]

The included studies provided too few estimates to determine reliably separate incidence rates for younger and older adults. Therefore, the estimates of the six included studies were combined.[16,18,22,31,59,60] The included studies used different measures of influenza illness including influenza-like illness, febrile illness, upper respiratory tract illness, and febrile upper respiratory tract illness. The included studies covered influenza seasons of 1983–1984 through 1989–1990, 1992–1993, 1997–1998, and 1998–1999. To estimate the incidence in an average-risk year, an estimate for each year was calculated, and then the mean incidence and median incidence across years were estimated. Estimates for each year reflected the average estimate for all studies that include that particular year. If a study reported estimates for multiple definitions of influenza-like illness, the estimates were averaged to create a single estimate for the study for each included year. Calculated in this way, the mean annual incidence rate over these six influenza seasons was 15.1% among unvaccinated individuals.

Three studies provided hospitalization rates for influenza or pneumonia for individuals aged ≥65 years who had not received the influenza vaccine.[32–34] These studies reported on the populations served by three managed care plans in the Midwest, Northeast, and Northwest over ten influenza seasons: 1990–1991 through 1999–2000. Among the included estimates, the mean annual incidence rate per person of hospitalizations across the included influenza seasons was 0.9%. We were unable to identify appropriate estimates of influenza and pneumonia hospitalization rates for unvaccinated adults aged 50 to 64 years. Therefore, we used an estimate of one hospitalization per 1000 among unvaccinated individuals aged 50 to 64 years.[16]

Patient adherence. Estimates were scarce of adherence with clinician recommendations to be vaccinated. The best estimate was from an Ohio study of three interventions aimed at increasing provider adherence to immunization guidelines,[61] which reported the portion of patients aged ≥65 years who were offered and accepted influenza vaccinations. Averaged across the three study arms, 85.6% of patients who were offered the vaccination were vaccinated. This estimate was similar to the vaccination rates achieved by reminder letters and postcards sent to older adults in three European studies identified during the Level-1 search.[62–64] In sensitivity analysis, the current vaccination rate in the ≥50 age group (55%) was used as the lower bound.[57]

Vaccine efficacy. The studies on which the estimates of efficacy were based include five randomized controlled trials,[16,18,22,31,39] seven observational studies,[13,32–36,40] and five case–control studies.[12,13,19,21,28] Five studies[12,19,28,33,35] provided estimates of the efficacy of vaccinations in preventing mortality among adults. These studies were from three different countries (United Kingdom,[12] Canada,[19] and the United States[28,33,35]), and among them covered all influenza seasons between 1980–1981 and 1995–1996. An average estimate was created for each included influenza season and the average across seasons was used in the calculations (42.9%).

Seven studies[16,18,22,31,36,39,40] provided estimates of the efficacy of influenza vaccinations in reducing the incidence of influenza-like illness. The mean efficacy across the included influenza seasons (calculated as described above) was 18.9%.

Nine studies[13,15,19,21,28,32–35] contributed estimates of the efficacy of influenza vaccinations in reducing hospitalizations for pneumonia or influenza, using various diagnoses codes and including a wide range of influenza seasons during the 1980s and 1990s. The vast majority of the study populations were aged ≥65 years. The mean efficacy of the vaccine in reducing hospitalizations for influenza and pneumonia was 36.6%.

Years and quality of life lost. There was a significant risk of overstating life years lost due to influenza. The estimate of prevented mortality reflected deaths from all causes that happen to be concurrent with an influenza infection. Many of these deaths were among individuals with other chronic conditions. The observation period for all effectiveness studies was limited to the influenza season, making it impossible to determine when deaths would have occurred without vaccinations. Therefore, the average life expectancy at death was first calculated using the weighted average of life expectancy in 5-year age groups from life tables,[56] and the age at death for mortality with the International Classification of Diseases (ICD)-9 codes[65] used by Thompson et al.[53] for "underlying respiratory and circulatory deaths." Then, to create a more conservative estimate of CPB, 75% of this estimate was used as the base-case estimate for life expectancy at death, and 50% and 100% of this estimate were used as the lower and upper bounds in sensitivity analysis.

Calculations of QALYs lost attributable to nonfatal cases required estimates of the duration of illness and the reduction in quality of life for each case. The average quality-of-life reduction from nonhospitalized cases was approximated using the standard quality-of-life reduction of 0.30 for acute conditions.[8,11] It was assumed that this reduction occurred for an average of 1 week per episode.[31] An average duration of 2 weeks was used for hospitalized cases.

Estimating Cost Effectiveness

Cost effectiveness was measured as the net cost of the preventive service divided by the number of QALYs saved. The standards recommended for the "reference case" of the Panel on Cost Effectiveness in Health and Medicine (PCEHM)[66] were followed to produce comparable estimates of cost effectiveness across preventive services in the accompanying ranking. Using a societal perspective, net costs were defined as the value of resources used in providing the preventive service and any follow-up services minus the resource savings from averted disease or injury. The PCEHM recommendation on including the value of patient time losses resulting from illness, injury, and treatment in the societal perspective varies with the source of the quality-of-life data. In most cases, these disease costs should be excluded; they were excluded from all cost-effectiveness estimates in the ranking to provide consistency. QALYs saved in the cost-effectiveness measure were consistent with QALYs saved in the CPB measure; however, costs and benefits were discounted at a 3% annual rate in the cost-effectiveness measure.

For each service, the cost effectiveness of providing the service as recommended was estimated relative to no provision of the service. Cost-effectiveness estimates from the literature were used when available. Adjustments were made to ensure consistency across services. When existing studies were not adequate, even with substantial adjustment, or did not exist, new cost-effectiveness estimates were developed based on the CPB estimates.

Three[28,30,52] of 14 cost-effectiveness studies that were abstracted met the criteria stated above. However, each had

Table 2. CPB and CE by age group for birth cohort of 4 million

	Age ≥50	Age 50–64	Age ≥65
Cases of influenza-like illness prevented[a]	2,638,621 (23.5)	1,296,889 (24.3)	1,341,732 (22.9)
Hospitalizations prevented[a]	180,810 (1.6)	16,583 (0.3)	164,227 (2.8)
Deaths prevented[a]	40,477 (0.4)	2,851 (0.05)	37,626 (0.04)
CPB (QALYs saved)	274,881	54,415	220,466
Direct cost of immunizations	$1,199,653,037	$571,230,806	$628,422,231
Value of patient time and travel	$2,015,469,432	$959,692,671	$1,055,776,761
Direct cost savings	$1,821,591,392	$286,979,679	$1,534,611,713
CE ($/QALY saved)	5,858	28,044	980
Net cost per person vaccinated	$15.64	$28.44	$4.00
CE with medical costs only	n.d.	7,182	n.d.
Net cost per person vaccinated with medical costs only	$(5.52)	$7.28	$(17.16)

[a]Per 1,000 person-years in parentheses.
CE, cost effectiveness; CPB, clinically preventable burden; n.d., not defined; QALY, quality-adjusted life year.

several significant limitations for the purposes, including the exclusion of individuals aged 50 to 64 years, lack of an estimate of life years saved or quality-adjusted life years saved (in two studies that found cost savings), and only marginally recent cost data, among others. Therefore, a new cost-effectiveness estimate was produced based on the CPB estimate to provide an update that included individuals aged 50 to 64 years, was methodologically comparable to the cost-effectiveness estimates of other services that were evaluated, and yielded a complete sensitivity analysis.

A cost-effectiveness study by Meltzer et al.[46] provided detailed reporting of model design and results, including online appendixes. For the cost-effectiveness estimate, Meltzer's study was used as the source for most variables not included in the CPB estimate, including age group–specific influenza costs (inflation adjusted to year 2000 dollars). Estimates of cost per case for adults aged 20 to 64 years were applied to the narrower age group of 50 to 64.

The per-case cost estimates for treating influenza from Meltzer et al.[46] are shown in Table 1 after inflation adjustment. Cases treated in the hospital (inclusive of the individual's outpatient costs) are shown separately from cases treated only in the outpatient setting. Because the difference among outpatient costs by age group from Meltzer et al.[46] was negligible, a simple average of their age group–specific outpatient costs was used. These estimates were applied to the annualized incidence and hospitalization rates from the CPB calculations. The Meltzer et al.[46] estimate that 47% of all nonhospitalized cases receive outpatient care was used.

The cost of the vaccine, vaccine administration, and vaccine wastage were the average of four estimates of private-sector costs adjusted to year 2000 dollars,[16,28,30,46] including the midpoint of the range used by Meltzer et al.[46] It was assumed that 2 hours are required to receive the vaccination, but only half this time is attributable to the vaccination itself because some patients receive one or more other services at the same time. Average hourly earnings plus benefits in 2000[67] were used to estimate the value of patient time. The resulting estimate of the value of patient time was $21.16 in year 2000 dollars per person vaccinated. This estimate is close to that used by Bridges et al.[16] ($14.70 in 1999 dollars) and within the range used by Meltzer et al.[46] ($8 to $39 in 1995 dollars). For sensitivity analysis, the value of time was changed by 25% in both directions, and the portion of the 2 hours attributable to influenza vaccination varied from 33% to 67%.

Results

The main results are shown in the first numeric column of Table 2. Offering influenza vaccination to all people in a birth cohort of 4 million starting at age 50 would prevent approximately 2.64 million cases of influenza-like illness, 180,000 hospitalizations, and 40,500 deaths over the lifetime of a birth cohort. Preventing these events yielded a total of 275,000 QALYs saved.

The average annual net cost of this vaccination is $1.5 billion in year 2000 dollars. Using the quality-of-life estimates, duration of illness, and vaccine efficacy used for CPB, cost effectiveness is $4600 per QALY saved.

Of the 275,000 QALYs saved (without discounting), 220,000 are achieved by vaccinating adults aged ≥65, and 54,000 more are added by extending the recommendation to adults aged 50 to 64. Using the base-case estimates, the marginal cost effectiveness of immunizing the group aged 50 to 64 is $28,000 per QALY saved, and is $7200 per QALY saved if the costs necessary for patient time and travel are excluded. Finally, to facilitate comparisons to prior studies, the cost effectiveness of vaccination in the ≥65 age group alone was estimated and found to be $980 per QALY saved including patient time costs for travel and visit, and a savings of $17 per person vaccinated without these costs.

Sensitivity Analysis

In single-variable sensitivity analysis, CPB was most sensitive to the variables related to mortality rates, vaccine efficacy in preventing mortality, adherence, and average life expectancy gained per death prevented. Decreasing influenza mortality rates, vaccine efficacy in preventing mortality and adherence produced a lower multivariate sensitivity analysis[11] estimate of 90,800 QALYs saved. Increasing mortality rates, vaccine efficacy in preventing mortality, and life expectancy produced an upper multivariate sensitivity analysis estimate of 639,000 QALYs saved.

In the estimate of cost effectiveness, the most important variables were the cost of the vaccine, the value of patient time to receive the vaccine, and the efficacy of the vaccine in preventing hospitalizations. The estimates of mortality incidence, efficacy of the vaccine in preventing mortality, years of life gained per death prevented, incidence of hospitalization, and costs of hospitalizations were also influential variables. Simultaneously decreasing the costs of the vaccine and the cost of patient time to receive the vaccine, while increasing the efficacy of the vaccine in reducing hospitalizations, produced the lower multivariate sensitivity analysis estimate of $7.25 saved per person vaccinated. Simultaneously increasing the cost of patient time to receive the vaccine while decreasing mortality incidence and the years of life gained per death prevented produced a positive cost-effectiveness ratio of $22,000 per QALY saved.

Discussion

These simplified models, which were designed to promote consistency in the evaluation of many services, provided transparent estimates of the benefits and cost effectiveness of offering influenza vaccine to a birth cohort of 4 million individuals starting at age 50. Like all models, the accuracy of the estimate is limited by the accuracy of the most influential data points. Some of the most uncertain data points were found to be the most influential, including patient time costs to receive the vaccine, the efficacy of the vaccine in preventing mortality and hospitalizations, mortality incidence, and years of life gained per death prevented. These data points were either not directly observed or were observed in populations that may not be generalizable to the U.S. population.

The incidence rates for nonfatal cases were observed in unvaccinated populations. These populations may have received partial protection from living in the community with vaccinated populations. Therefore, the use of these data may have caused us to understate incidence in the absence of the vaccine. Likewise, efficacy estimates based on comparisons between those who received the vaccine and those who did not receive the vaccine but were living in the community with individuals who did receive the vaccine may be biased.

The estimates of effectiveness against hospitalizations and deaths are based entirely on observational studies. If more-frail individuals fail to receive the vaccine, then comparisons of those who did and did not receive the vaccine may cause the estimates of effectiveness against hospitalizations and death to be overstated.[41,68] The potential impact of this bias was reduced by limiting hospitalizations to those for influenza and pneumonia, and limiting deaths to influenza-associated deaths. However, this does not eliminate the potential for the estimated health impact and cost savings to be overstated by this bias.

Broader definitions of influenza-related hospitalizations were considered. However, suitable estimates were not found. The available incidence data of hospitalizations for respiratory illness and cardiovascular disease[19,29,30,33] were based on any diagnostic code in the medical claims form rather than just the primary diagnosis. Therefore, they may have included a substantial number of the influenza and pneumonia hospitalizations that were already included in the estimate of the incidence of hospitalizations.

This estimate of $28,000 per QALY saved among persons aged 50 to 64 indicates that adding all 50- to 64-year-olds to the recommended delivery group falls within reasonable cost-effectiveness intervals. However, the model does not include enough detail to evaluate the cost effectiveness of vaccinating all persons aged 50 to 64 versus vaccinating only those in this age group who are at higher risk for complications from influenza. Although the marginal cost effectiveness of vaccinating 50- to 64-year-olds who are not at increased risk may be poor relative to some alternative uses of resources, the simplified message resulting from an age-based recommendation may extend the reach into the high-risk group further than a complicated risk-based recommendation.[1]

The PCEHM recommendations were followed to exclude savings from productivity gains in order not to double-count the value of time in terms of dollars in the numerator of the cost-effectiveness ratio and in QALYs in the denominator. These potential savings may be an important additional factor for employers to consider in identifying priorities for their populations aged 50 and older.

Three cost-effectiveness studies were abstracted on the influenza vaccine for adults aged ≥65 years that reported results in terms of U.S. dollars and either QALYs or years of life. One estimated that increasing immunization rates in Medicare recipients by providing coverage for the vaccine would cost Medicare $145 per life year saved (LYS) in the early 1990s ($232/LYS in year 2000 dollars).[52] Mullooly et al.[28] estimated that $1.10 was saved per person vaccinated in a Portland OR health maintenance organization (HMO) in the 1980s ($2.53 saved in year 2000 dollars).[28] Finally, Nichol et al.[30] found an average savings of $123 per person vaccinated over 3 years in a Minneapolis HMO in the early 1990s (approximately $182 saved in year 2000 dollars). In comparison, it was estimated that the cost effectiveness for persons aged 65 and older is $550 per QALY saved when the costs of time to receive vaccination are included, and that vaccinations save $18 per person when time costs are excluded.

Jefferson et al.[41] recently completed a systematic review of the effectiveness of influenza vaccinations in individuals aged 65 and older. Although analyzed somewhat differently and over a broader selection of the literature, their estimates of the efficacy of the influenza vaccine in preventing hospitalizations (26% to 45%) and mortality (42% to 60%) are comparable to those in the current analysis (37% and 43%, respectively). However, Jefferson et al.[41] did not find influenza vaccination to be effective in reducing influenza-like illness or confirmed influenza cases in community-living older adults. They calculated a non–statistically significant relative risk of 1.05 based on three observational studies in adults aged over 65, while the 19% effect size calculated for these CPB and cost-effectiveness estimates were based on two randomized controlled trials and one observational study among individuals aged 65 and older, and three randomized controlled trials and one observational study in younger adults. The estimates among younger adults were slightly lower than those among older adults, and therefore are not the reason for finding a positive effect.

Conclusions

These estimates indicate that influenza vaccinations for adults should remain a high-priority service. Neither new evidence nor the change in the recommended age group to include individuals aged 50 to 64 alter substantially the health impact or the cost effectiveness of adult influenza vaccinations.

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