CHAPTER 8

Influence of high risk medical conditions on the effectiveness of influenza vaccination among elderly members of three large managed care organizations

Hak E[1,2], Nordin J[2], Wei F[2], Mullooly J[3],
Poblete S[4], Strikas R[5], Nichol KL[6]

Author affiliations:
[1] Julius Center for General Practice and Patient Oriented Research, University Medical Center Utrecht
[2] HealthPartners Research Foundation, Bloomington, MN, USA
[3] Kaiser Permanente Northwest, Portland, OR, USA
[4] Oxford Health Plans, New York, NY, USA
[5] Centers for Disease Control and Prevention, Atlanta, GA, USA
[6] VA Medical Center and University of Minnesota, Minneapolis, MN, USA

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Background Little is known about the influence of specific high risk medical conditions on the risk for the serious complications of influenza or the effectiveness of influenza vaccination among the elderly. We therefore conducted this serial cohort study to assess the risk for hospitalization or death and the effectiveness of influenza vaccination among subgroups of elderly members of three geographically disparate US managed care organizations including persons with cardiopulmonary disease, diabetes, immune-suppression, other high-risk conditions and healthy elderly.

Methods For the 1996-97 and 1997-98 influenza seasons, the following data were obtained on elderly members of each plan using administrative and clinical computer databases: demographic information, baseline health care use, co-morbid conditions, influenza vaccination status, and outcomes during the influenza seasons (hospitalization for pneumonia and influenza (P&I) and all-cause death). Outcomes in vaccinated and unvaccinated elderly members according to risk and disease specific subgroups were compared after controlling for age, gender, other co-morbidities and prior health care use.

Findings 122,974 and 158,454 elderly persons were included in the two study cohorts. The vaccination rates were 57.7% the first year and 58.1% the second year. Among unvaccinated persons, hospitalizations for pneumonia and influenza or death occurred in 8.2/1,000 healthy persons and 38.4/1,000 high-risk persons in year 1 and 8.2/1000 and 29.3/1000 in year 2. After adjustments, vaccination was associated with a 48% reduction in the combined outcome of hospitalization or death (95% confidence interval (CI) 42% to 52%) in year 1 and 31% (95% CI 26% to 37%) in year 2. Effectiveness estimates were statistically significant and generally consistent across the healthy and high-risk subgroups in both years. The absolute risk reduction, however, was higher among high-risk persons than among healthy elderly persons in each year (18.0 events prevented with vaccination per 1000 high risk persons vs 3.8 events per 1000 healthy persons in year 1 and 8.5 events prevented with vaccination per 1000 high risk persons vs 3.5 events per 1000 healthy persons in year 2). For years 1 and 2, 55 and 118 high risk persons needed to be vaccinated to prevent one hospitalization or death. Among healthy persons, 264 and 290 needed to be vaccinated in order to prevent one outcome.

Interpretation Influenza causes significant morbidity and mortality in all subgroups of elderly persons and individuals in both high risk and healthy subgroups may substantially benefit from vaccination. However, the impact of influenza is highest in those with high-risk medical conditions.

Key words: Influenza, immunization, elderly, administrative database, epidemiology

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Annual influenza epidemics continue to impose an enormous health and economic burden on society, especially among the elderly.[1,2] Immunization against influenza has been demonstrated to be effective in reducing associated morbidity and mortality[3-6] and cost-saving among seniors.[7] Despite evidence for its cost-effectiveness, however, current immunization rates remain unsatisfactory. In the United States, for example, more than 30% of the elderly fail to receive the vaccine each season.[8] Similarly low vaccine uptake rates have been reported in other countries.[9] Apart from differences in health care, studies have shown that among the main reasons for compliance with vaccination recommendations are the recommendations of health care providers and belief in the impact of influenza and the safety and effectiveness of the vaccine.[10-12]

Underlying conditions, such as cardio-pulmonary disease, are well known risk factors for serious influenza-associated complications.[3-6,13,14] However, the clinical effectiveness of influenza vaccination among persons with specific chronic, high risk medical conditions has not been well described, and this may lead to uncertainties regarding the benefits of vaccination in these groups. On the other hand, information on the rates of serious complications of influenza in healthy elderly are limited and suggest a lower impact than among elderly with high-risk disease.[15,16] Two previous cohort studies were inconclusive with regard to benefits in low risk seniors.[17,18] These findings may help to explain suboptimal vaccination rates in seniors and likely have contributed to widespread international variation in immunization recommendations.[19]

Age-based immunization policies are attractive both from an organizational and health- economical point of view. However, additional information clarifying issues of individual risk for the serious complications of influenza and the benefits of vaccination may help policy makers and program planners design more effective vaccination programs or to prioritize vaccine delivery when vaccine supplies are inadequate.[20,21] In a prospective cohort study using administrative and clinical databases of three health plans in the US, we therefore determined the occurrence of influenza and pneumonia hospitalizations and death from all causes during the 1996-97 and 1997-98 influenza epidemics, and the effectiveness of influenza vaccination in preventing these outcomes in specific high-risk subgroups of elderly plan members. These subgroups included persons with cardiopulmonary disease, diabetes, immune-suppression, other high risk diseases and healthy elderly.

Methods

Setting

This study is part of an ongoing collaborative effort between three large managed care organizations from geographically disparate locations across the US to pool data derived from their linked administrative and clinical databases in order to provide timely assessments of influenza vaccination effectiveness. HealthPartners (HP) is a nonprofit health maintenance organization with about 890,000 members in Minnesota and Wisconsin. It offers coverage for 280,000 members through a staff model health maintenance organization, while the other members are covered through a network health maintenance organization model. Kaiser Permanente Northwest Division (KPNW) provides health care services to nearly 420,000 persons in Portland, Oregon-Vancouver, Washington. Oxford Health Plans (Oxford) provide health benefit plans to 1.8 million members in New York, New Jersey, Pennsylvania and Connecticut. In all, over 3 million members receive medical care from these health plans. For study purposes, the same definitions for diagnoses and outcomes were used.

Study subjects

Eligibility criteria to be included in the two study cohorts were: member of one of the three health plans aged 65 years or older as of October 1, 1996 in the first year and October 1, 1997 for the second year and continuous enrollment for the one-year period prior to October 1 for each study year through the outcome period. The continuous enrollment period was required to ensure complete capture of outcome data as well as enough prognostic information to allow for adjustment of potential incomparability between comparison groups.[22] The health plans cover institutionalized persons as well community dwelling persons. Because capture of vaccination status was thought to be incomplete for institutionalized people, they were excluded from the study. For the 1996/97 and 1997/98 study years, there were 122,974 and 158,454 eligible plan members among the three health plans, combined.

At baseline, eligible subjects were classified into seven non-mutually exclusive groups according to entries of relevant codes in the *International Classification of Diseases, Ninth revision, Clinical Modification* (ICD-9-CM) in outpatient clinic or hospital databases 12 months prior to September 30, 1996 in year 1 and September 30, 1997 in year 2: (1) combination of pulmonary (ICD-9-CM codes 011, 460, 462, 465-66, 480-511, 512.8, 513-17, 518.3, 518.8, 519.9, 714.81) and cardiac disease (ICD-9-CM codes 093, 112.81, 130.3, 391, 393-98, 402, 404, 410-29, 745-6, 747.1-747.49, 759.82, 785.2, 785.3), (2) pulmonary disease, (3) cardiac disease, (4) diabetes and other endocrine disorders (ICD-9-

CM codes 250-1), (5) immune suppression [renal disease (ICD-9-CM codes 274.1, 403, 580-91, 593.71-593.73, 593.9), immune-deficiency or organ transplants (ICD-9-CM codes 042, 079, 279, V08, V42), hematological cancer (ICD-9-CM codes 200-208) or non-hematological cancer (ICD-9-CM codes 140-198, 199.1)], (6) other comorbid conditions [dementia or stroke (ICD-9-CM codes 290-4, 331, 340-1, 348, 438), vasculitis or rheumatologic diseases (ICD-9-CM codes 446, 710, 714 - 714.4, 714.8, 714.89, 714.9), and (7) healthy elderly (having none of the previously listed diagnostic codes in their records). Other baseline data that were obtained included age and gender, number of any hospitalizations or outpatient visits, and whether a person had a hospitalization for influenza or pneumonia in the previous year.

Influenza vaccination and seasons

The health plans offered their members vaccination with the trivalent inactivated influenza virus vaccine current for each season. During the 1996-97 epidemic influenza activity was widespread in most US states, exceeding baseline levels for more than 5 consecutive weeks. Circulating influenza strains predominated by the H_3N_2 A-type matched well with the components of the vaccine of that year.[23] In 1997-98, the level of influenza activity was similar, but another influenza A virus, the A/H_3N_2/Sydney-like virus, became the predominant strain in most areas in the US.[24] That year's vaccine containing A/H_3N_2/Wuhan-like virus was poorly matched to the predominant circulating virus. Influenza seasons were defined as follows on the basis of influenza surveillance data from the Centers for Disease Control: Year 1: HealthPartners: November 22, 1996 through May 24, 1997; Oxford: October 5, 1996 through May 3; Kaiser: November 22, 1996 through March 22. Year 2: HealthPartners: December 7, 1997 through March 28, 1998; Oxford: November 23, 1997 through April 4, 1998; Kaiser: December 21, 1997 through March 7, 1998. Influenza vaccination status was ascertained from the computerized data bases of each plan.

Primary outcome measure

Excess hospitalizations and deaths during influenza seasons are strongly and linearly correlated.[25] As others have done,[26] we used as our primary study outcome the combined outcome of a hospitalization for pneumonia or influenza (P & I, ICD9-CM codes 480 - 487) or death. We used this combined outcome to enhance the power of our study and to provide more precise estimates of vaccine effectiveness within the disease-based high-risk subgroups.

Data analysis
Each participating health plan center extracted data of eligible subjects from their linked databases and forwarded these data to the coordinating data management center at HealthPartners. With EPI-Info, version 6, (CDC, Atlanta, Georgia, USA) we estimated that a minimal cohort size of 27,000 would give us an 85% chance of detecting a reduction of at least 20 percent in outcome events among recipients of the influenza vaccine. For this calculation we assumed an immunization rate of 55%, an event rate of 3% and a two-sided alpha level of 0.05. Bivariate analysis using SPSS for Windows, version 9.0, (SPSS Inc., Chicago, Illinois, USA) included Student T-tests for continuous and chi-square tests for categorical variables to test for differences between comparison groups. Multivariable logistic regression was used to assess the association of vaccination status with the study outcome measures while controlling for age, gender, co-morbid medical conditions, prior health care use (hospitalizations and outpatient visits) and whether the person had previously been hospitalized for pneumonia and influenza. In addition, site was also included in the models. For analyses according to specific subgroups, the relevant underlying medical conditions were excluded from the model. Adjusted odds ratio's (OR) and their 95% confidence intervals (95% CI) as approximations of relative risks were calculated. Vaccine effectiveness (VE) was determined as 1- OR times 100 percent. Absolute risk reductions per 1,000 vaccinees (ARR) were calculated as the vaccine effectiveness (VE) times the outcome rate in unvaccinated persons. The number needed to treat (i.e. vaccinate) to save 1 outcome (NNT) was calculated as (1/ARR)*1000.[27]

Results

Data on 122,974 and 158,454 seniors were captured for the 1996-97 and 1997-98 study years, respectively. The vaccination rates for all three sites combined were 57.7% in year 1 and 58.1% in year 2. For both years, vaccinated subjects were somewhat older and generally more likely to have high risk medical conditions than were unvaccinated subjects. (table 1) Vaccinated persons also had higher numbers of outpatient visits during the baseline period. Both groups had similar rates of hospitalization during the baseline period.

There were 1961 outcome events (hospitalizations for pneumonia or influenza or deaths) in year 1 and 2555 outcome events in year 2 (table 2). Unvaccinated persons had higher event rates than vaccinated persons in each subgroup and for both years. Vaccination was associated with a reduction in

Table 1. Baseline characteristics of study subjects by year*

	1996-97 (N = 122,974)			1997-98 (N = 158,454)		
	Vaccinated n = 71,005	**Unvaccinated n = 51,969**	**P Value**	**Vaccinated n = 92,001**	**Unvaccinated n = 66,453**	**P Value**
Mean age (SD)	74.2 (6.3)	74.0 (6.9)	<0.001	74.3 (6.4)	73.9 (6.8)	<0.001
Female sex	56.0%	58.9%	<0.001	56.0%	59.7%	<0.001
High risk	46.9%	40.7%	<0.001	62.9%	51.1%	<0.001
Heart & lung disease	7.2%	6.1%	<0.001	12.7%	10.5%	<0.001
Lung disease	16.0%	13.0%	<0.001	28.0%	22.3%	<0.001
Heart disease	27.7%	24.2%	<0.001	33.8%	27.6%	<0.001
Diabetes	13.2%	10.6%	<0.001	15.2%	12.1%	<0.001
Immune suppresssion	6.0%	5.5%	<0.001	18.5%	14.0%	<0.001
Other comorbid conditions	5.0%	6.3%	<0.001	5.7%	5.8%	0.23
Number of hospitalizations during 12 month baseline period (SD)	0.21 (0.60)	0.12 (0.65)	0.91	0.22 (0.62)	0.22 (0.68)	0.44
Number of outpatient visits during 12 month baseline period (SD)	10.02 (12.13)	9.23 (14.93)	<0.001	13.49 (14.77)	10.87 (17.02)	<0.001
Having had a hospitalization for pneumonia or influenza during 12 month baseline period	1.0%	1.1%	0.07	0.8%	0.8%	0.94

* Shown are data pooled for the three sites. High risk denotes having at least one of the following comorbid conditions listed as an outpatient or inpatient diagnosis during the 12 month baseline period: heart disease, lung disease, diabetes, immune suppression (having renal disease, hematologic or non-hematologic cancer or solid organ transplant) or other comorbid conditions (dementia/stroke, vasculitis or rheumatologic disease). SD denotes standard deviation.

Table 2. Numbers of outcome events among vaccinated and unvaccinated study subjects*

Risk Group	Season 1996-97 Number of Outcomes	Risk Group	Season 1997-98 Number of Outcomes
All		All	
vaccinated (n = 71,005)	896 (1.3%)	vaccinated (n = 92,001)	1293 (1.4%)
unvaccinated (n = 51,969)	1065 (2.0%)	unvaccinated (n = 66,453)	1262 (1.9%)
Healthy		Healthy	
vaccinated (n = 37,693)	201 (0.5%)	vaccinated (n = 34,155)	164 (0.5%)
unvaccinated (n = 30,843)	254 (0.8%)	unvaccinated (n = 32,489)	267 (0.8%)
High risk		High risk	
vaccinated (n = 33,312)	695 (2.1%)	vaccinated (n = 57,846)	1129 (2.0%)
unvaccinated (n = 21,126)	811 (3.8%)	unvaccinated (n = 33,964)	995 (2.6%)
Having heart & lung disease		Having heart & lung disease	
vaccinated (n = 5112)	229 (4.5%)	vaccinated (n = 11,728)	423 (3.6%)
unvaccinated (n = 3173)	262 (8.3%)	unvaccinated (n = 6,984)	394 (5.6%)
Lung disease		Lung disease	
vaccinated (n = 11,377)	344 (3.0%)	vaccinated (n = 25,727)	645 (2.5%)
unvaccinated (n = 6737)	388 (5.8%)	unvaccinated (n = 14,842)	555 (3.7%)
Heart disease		Heart disease	
vaccinated (n = 19,639)	471 (2.4%)	vaccinated (n = 31,094)	743 (2.4%)
unvaccinated (n = 12,596)	548 (4.4%)	unvaccinated (n = 18,350)	661 (3.6%)
Diabetes		Diabetes	
vaccinated (n = 9390)	185 (2.0%)	vaccinated (n = 13,966)	323 (2.3%)
unvaccinated (n = 5525)	197 (3.6%)	unvaccinated (n = 8,025)	255 (3.2%)
Immune suppression		Immune suppression	
vaccinated (n = 4281)	214 (5.0%)	vaccinated (n = 17,055)	484 (2.8%)
unvaccinated (n = 2882)	247 (8.6%)	unvaccinated (n = 9,287)	477 (3.2%)
Having other comorbid conditions		Having other comorbid conditions	
vaccinated (n = 3531)	107 (3.0%)	vaccinated (n = 5,230)	119 (2.3%)
unvaccinated (n = 3278)	228 (7.0%)	unvaccinated (n = 3,872)	174 (4.5%)

*High risk denotes having at least one of the following comorbid conditions listed as an outpatient or inpatient diagnosis during the 12 month baseline period: heart disease, lung disease, diabetes, immune suppression (having renal disease, hematologic or non-hematologic cancer or solid organ transplant) or other comorbid contitions (dementia/stroke, vasculitis or rheumatologic disease).

Table 3. Effectiveness of influenza vaccination in reducing the risk of hospitalization for pneumonia and influenza or death from all causes*

Risk Group	1996-97 Vaccine Effectiveness (95% CI)	1996-97 P Value	1997-98 Vaccine Effectiveness (95% CI)	1997-98 P Value
All	48% (42% to 52%)	<0.001	31% (26% to 37%)	<0.001
Healthy	46% (34% to 56%)	<0.001	42% (28% to 52%)	<0.001
High risk	47% (40% to 53%)	<0.001	29% (22% to 35%)	<0.001
Having heart & lung disease	47% (35% to 57%)	<0.001	28% (17% to 38%)	<0.001
Lung disease	48% (38% to 56%)	<0.001	27% (18% to 36%)	<0.001
Heart disease	49% (42% to 56%)	<0.001	30% (21% to 37%)	<0.001
Diabetes	50% (37% to 60%)	<0.001	21% (6% to 34%)	0.009
Immune suppression	43% (30% to 53%)	<0.001	39% (30% to 47%)	<0.001
Other comorbid conditions	56% (44% to 66%)	<0.001	39% (24% to 51%)	<0.001

*High risk denotes having at least one of the following comorbid conditions listed as an outpatient or inpatient diagnosis during the 12 month baseline period: heart disease, lung disease, diabetes, immune suppression (having renal disease, hematologic or non-hematologic cancer or solid organ transplant) or other comorbid contitions (dementia/stroke, vasculitis or rheumatologic disease). CI denotes confidence interval.

Table 4. Absolute risk reductions associated with vaccination and corresponding numbers of persons needed to vaccinate to prevent one outcome*

Risk Group	1996-97 Event rate per 1000 unvaccinated persons	Absolute risk reduction per 1000 persons vaccinated	Numbers needed to vaccinate to prevent one outcome	1997-98 Event rate among unvaccinated persons	Absolute reduction with vaccination	Numbers needed to vaccinate to prevent one outcome
All	20.5	9.8	102	19.0	5.9	170
Healthy	8.2	3.8	264	8.2	3.5	290
High Risk	38.4	18.0	55	29.3	8.5	118
Having heart & lung disease	82.6	38.8	26	56.4	15.8	63
Lung disease	57.6	27.6	35	37.4	10.1	99
Heart disease	43.5	21.3	47	36.0	10.8	93
Diabetes	35.7	17.8	56	31.8	6.7	150
Immune suppression	85.7	36.9	27	51.4	20.0	50
Having other comorbid conditions	69.6	39.0	26	44.9	17.5	57

* The absolute risk reduction per 1000 persons vaccinated = (event rate in unvaccinated persons) * (vaccine effectiveness [table 3]). The numbers need to vaccinate to prevent one outcome = (1/absolute risk reduction)*1000. High risk denotes having at least one of the following comorbid conditions listed as an outpatient or inpatient diagnosis during the 12 month baseline period: heart disease, lung disease, diabetes, immune suppression (having renal disease, hematologic or non-hematologic cancer or solid organ transplant) or other comorbid contitions (dementia/stroke, vasculitis or rheumatologic disease).

Figure 1a. **Influenza Vaccine Effectiveness 1996-97**

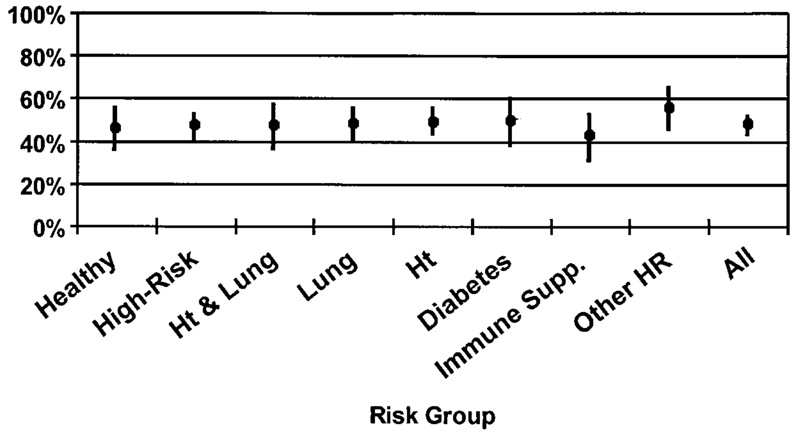
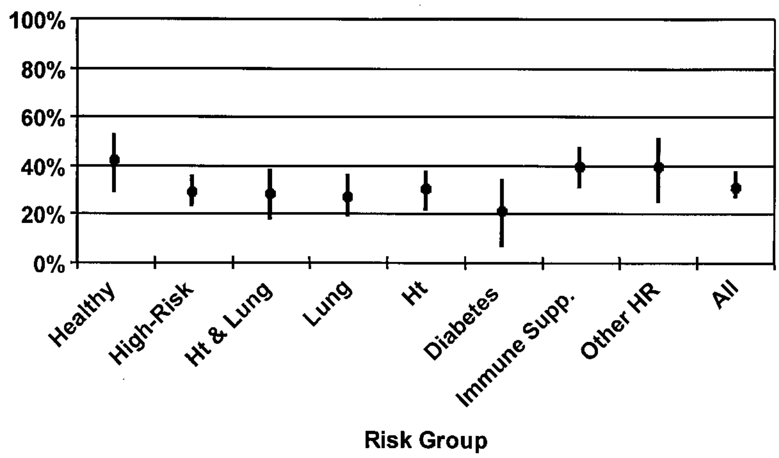


Figure 1b. **Influenza Vaccine Effectiveness 1997-98**



the combined outcome of a P & I hospitalization or death from any cause of 48% (95% CI 42% -52%) in year 1 and 31% (95% CI 26% to 37%) in year 2 (table 3). When analyzed according to subgroup, influenza vaccination was consistently effective across each of the disease-specific categories in both years as well as among the healthy subgroup (table 3, figure 1a & 1b).

As expected, the absolute benefits of vaccination varied by subgroup (table 4). Among healthy persons, 3.8/1,000 healthy persons were saved from hospitalization for pneumonia and influenza or death with vaccination whereas vaccination prevented 18.0/1,000 elderly with high risk medical conditions from experiencing one of these complications during year 1. Findings in year 2 were similar with an absolute risk reduction of 3.5 per 1,000 healthy elderly persons and 8.5 per 1,000 high risk elderly persons. The numbers needed to treat to prevent one outcome also reflect the higher level of absolute benefits experienced by the high-risk subgroups. In year 1, 26 to 56 persons in the various high-risk subgroups would have to be vaccinated in order to prevent one outcome while 264 healthy persons would have to be vaccinated in order to prevent one outcome (table 4). In year 2, the NNT's were 50 to 150 among persons in the high-risk subgroups and 290 for healthy persons (table 4).

Discussion

This study is unique in that the size of the cohorts allowed us to obtain precise estimates of clinical influenza vaccine effectiveness across different high-risk subgroups of seniors and to demonstrate the consistency of vaccine effectiveness across the specific risk groups. Our results also demonstrate that rates of hospitalization for pneumonia and influenza or death were highest among unvaccinated persons with high risk conditions including heart and lung disease and those with immune suppression and lowest in seniors without high-risk medical conditions which is in accordance with other studies.[3-7, 16] Thus, the absolute benefits from vaccination were highest among the high risk seniors. Nevertheless, vaccination provided benefits in all of the subgroups including the healthy elderly with reductions in risk for hospitalization or death of 9.8 events per 1,000 vaccinated persons in year 1 and 5.9 events per 1,000 vaccinated persons in year 2.

Previous studies of the benefits of influenza vaccination among elderly persons with chronic lung disease have also shown significant benefits with vaccination. Hak et al.[28] found that influenza vaccination was associated with a 50% reduction in influenza associated complications including pneumonia, cardiac disease or death among such patients. Vaccine effectivenss was even higher at 80% among persons who also had pre-exsisting cardiovascular disease. Nichol et al.[29] found that influenza vaccination of elderly persons with chronic lung disease was also highly beneficial. Vaccination in that study was associated with a 52% reducation in hospitalizations for pneumonia and influenza and a 70%

reduction in deaths. Since a recent randomized controlled trial showed that the risk of pulmonary complications resulting from vaccination is, althoug present, relatively small among adult asthmatics,[30] these results clearly support a vaccination policy for these patients.

Persons in our study with immune suppression who were vaccinated experienced substantially fewer influenza-associated complications than did their non-immunized counterparts. This is in agreement with results of a recent sero-conversion study among patients with lung cancer[31] and a randomized controlled trial of influenza vaccine effectiveness among HIV-infected persons.[32] In the latter study, vaccine recipients had no influenza infection whereas 25% of the saline placebo recipients attracted influenza: a protective efficacy of 100% (95% CI 73-100%).

Diabetics are also at higher risk for serious complications from influenza and benefitted from vaccination. Colquhoun and colleagues performed a case-control study among diabetics and estimated that influenza vaccination reduced hospital admissions for influenza, pneumonia or diabetic events by 79%.[33] US data from the Behavioral Risk Factor Surveillance System showed that most states would not reach the objective for 2000 to increase immunization rates >60% in these patients.[34] Our finding support additional immunization efforts for these groups.

Govaert et al. randomly allocated 1,838 healthy elderly persons to influenza vaccine or placebo.[15] The incidence of clinical influenza infection was 20 and 30 per 1,000 in vaccinees and non-vaccinees, respectively and the vaccine effectiveness was 47%. The absolute reduction in risk was 10 influenza cases per 1,000 vaccinated persons, a finding of unclear clinical meaning because the outcome included both mild and severe influenza illnesses but did not include influenza-associated complications. However, we have shown that an absolute reduction in serious outcomes of 3.5 to 3.8 per 1,000 healthy elderly persons can be attained which highlights the importance and potential benefits of immunization even for low risk seniors.

Even during the second year of the study when there was a poor match between the predominant circulating virus (A/Sydney/H3N2) and the corresponding vaccine strain,[24] we demonstrated a significant level of vaccine effectiveness in all of the subgroups we studied, although the level observed was somewhat lower than seen in the first year of the study. This finding suggests that there was some degree of cross protection afforded by the vaccine. Varying levels of cross protection have been observed in other studies conducted during years when there is a poor vaccine - circulating virus strain match.[35]

Several limitations of this study deserve comment. The use of a non-experimental study design may result in the potential incomparability of prognosis among vaccinees and non-vaccinees.[22] Confounding may have led to unequal balance of average risk of outcomes between the comparison groups. We were able to capture data on co-morbidity, age, gender and baseline health care use, and adjusted for their presence in the analyses. Nevertheless, our results should be interpreted with some caution.

Misclassification of vaccination status may have occurred in this study, most likely due to failure to capture vaccination status. If such misclassification were substantial, this likely would have biased the study findings to lower vaccine effectiveness rates. However, data were available from two health plans which suggest that misclassification of vaccination status was probably minimal. Data from a member survey conducted in 1995 for HealthPartners show that more than 95% of the plan seniors who were vaccinated reported receiving their influenza vaccinations at a health plan site[36] and that agreement between medical records and the computerized data bases is in excess of 90% for vaccination status.[16] Likewise, the results from annual membership surveys conducted from 1990 through 1995 at Kaiser-Permanente indicate that over 90% of elderly plan members who were immunized received their vaccine at a health plan site. Furthermore, chart audits from the plan indicate that over 98% of influenza vaccinations are recorded in their computerized database. (J Mullooly, PhD, personal communication, 1/2001).

We did not include other outcomes associated with influenza infections such as acute respiratory or cardiac disease or diabetes events leading to clinic visits or hospitalizations.[2,4,7,16] We limited our analysis to the serious influenza associated outcomes of P & I hospitalization and all-cause death because the attributable fraction due to influenza infections is relatively high during influenza seasons.[1] However, the overall absolute health benefits of vaccination might have been underestimated.[4,7,16]

We lacked information on pneumococcal vaccination status. In a recent cohort study among elderly persons with chronic pulmonary disease, two-thirds of patients had received this vaccine.[37] Results showed that reductions associated with pneumococcal vaccination were additive to those of influenza vaccination. However, it is unclear how this might have affected the estimates for effectiveness in other subgroups.[38]

It often takes an enormous effort to increase influenza vaccination coverage in a large-scale prevention program despite the fact that the vaccine is inexpensive, well-tolerated and effective. Health policy makers, physicians and patients need valid and precise information to justify ongoing support of such strategies. This type of evidence is also helpful in identifying highest priority groups for vaccination when there is a delay or shortage of vaccine supplies as is the case in the US for the 2000-2001 season.[20,21] In case of an influenza pandemic a substantial shortfall of vaccine will likely occur as well and such information will undoubtedly be of use in that event.

Our data support current age-based recommendations for the immunization of all persons aged 65 years and older.[39] Both healthy and high-risk seniors enjoy substantial benefits from vaccination, and age-based strategies have been more effective than risk condition-based vaccination strategies in achieving high vaccination rates.[40] However, our findings also highlight the fact that elderly with underlying medical conditions do have significantly higher rates of hospitalization and death, and therefore the absolute reduction in outcomes per 1,000 vaccinated persons is higher in these groups. Thus, while all persons 65 years or older benefit from vaccination and should be targeted for annual immunization, efforts should be renewed especially to ensure vaccination among those with cardiopulmonary disease, diabetes, cancer, transplants or immune-deficiency, and other high-risk conditions.

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