ORIGINAL INVESTIGATION

Benefits of Influenza Vaccination for Low-, Intermediate-, and High-Risk Senior Citizens

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Background: Vaccination rates for healthy senior citizens are lower than those for senior citizens with underlying medical conditions such as chronic heart or lung disease. Uncertainty about the benefits of influenza vaccination for healthy senior citizens may contribute to lower rates of utilization in this group.

Objective: To clarify the benefits of influenza vaccination among low-risk senior citizens while concurrently assessing the benefits for intermediate- and high-risk senior citizens.

Methods: All elderly members of a large health maintenance organization were included in each of 6 consecutive study cohorts. Subjects were grouped according to risk status: high risk (having heart or lung disease), intermediate risk (having diabetes, renal disease, stroke and/or dementia, or rheumatologic disease), and low risk. Outcomes were compared between vaccinated and unvaccinated subjects after controlling for baseline demographic and health characteristics.

Results: There were more than 20 000 subjects in each of the 6 cohorts who provided 147 551 person-periods of observation. The pooled vaccination rate was 60%. There were 101 619 person-periods of observation for low-risk subjects, 15 482 for intermediate-risk, and 30 450 for high-risk subjects. Vaccination over the 6 seasons was associated with an overall reduction of 39% for pneumonia hospitalizations ($P<.001$), a 32% decrease in hospitalizations for all respiratory conditions ($P<.001$), and a 27% decrease in hospitalizations for congestive heart failure ($P<.001$). Immunization was also associated with a 50% reduction in all-cause mortality ($P<.001$). Within the risk subgroups, vaccine effectiveness was 29%, 32%, and 49% for high-, intermediate-, and low-risk senior citizens for reducing hospitalizations for pneumonia and influenza (for high and low risk, $P\leq.002$; for intermediate risk, $P = .11$). Effectiveness was 19%, 39%, and 33% (for each, $P\leq.008$), respectively, for reducing hospitalizations for all respiratory conditions and 49%, 64%, and 55% for reducing deaths from all causes (for each, $P<.001$). Vaccination was also associated with direct medical care cost savings of $73 per individual vaccinated for all subjects combined ($P = .002$). Estimates of cost savings within each risk group suggest that vaccination would be cost saving for each subgroup (range of cost savings of $171 per individual vaccinated for high risk to $7 for low risk), although within the subgroups these findings did not reach statistical significance (for each, $P\geq.05$).

Conclusions: This study confirms that healthy senior citizens as well as senior citizens with underlying medical conditions are at risk for the serious complications of influenza and benefit from vaccination. All individuals 65 years or older should be immunized with this vaccine.

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INFLUENZA IS a major cause of illness, suffering, and death in the United States and worldwide. Each year 10% to 20% of the US population becomes ill.[1] Individuals aged 65 years or older are particularly susceptible to the complications of influenza, experiencing more than 90% of these complications that may include not only pneumonia but also exacerbations of underlying medical conditions such as chronic heart and lung disease[2-4] and even death. In the United States, this burden includes hundreds of thousands of excess hospitalizations,[1,5] tens of thousands of excess deaths,[3,4,6] and billions of dollars in health care costs.[7]

Annual vaccination is recommended as the mainstay of efforts to prevent influenza for the elderly by the Advisory Committee on Immunization Practices of the US Public Health Service,[8] the American College of Physicians,[9] and others. The World Health Or-

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SUBJECTS AND METHODS

GROUP HEALTH SERIAL COHORT STUDIES: SETTING AND SUBJECTS

Group Health Inc is a staff model health maintenance organization with more than 300 000 members in the Minneapolis and St Paul area, Minn. It has 21 clinics and 350 salaried physicians. In 1992 Group Health Inc became affiliated with HealthPartners Inc, a parent company providing integrated health care in coordination with several health care plans and administrative services.

Beginning with the 1989 influenza vaccination season, Group Health Inc piloted a modified version of the Minneapolis Veterans Affairs Medical Center influenza vaccination program,[25] and in 1990 the program was implemented in all the Group Health Inc clinics.[26] This highly successful program has achieved and sustained vaccination rates in excess of 60% for elderly members of the plan. Previously, we reported on the health and economic benefits associated with influenza vaccination of all elderly members of this managed care organization for the years 1990-1991 through 1992-1993.[27] We continued to conduct cohort studies for 3 additional seasons, 1993-1994 through 1995-1996, using methods similar to those in our original study. These new data pooled with the original 3 years of data collection now provide a database with consistent data elements and 147 551 person-periods of observation for the elderly members of this managed care organization. This study represents one of a series of studies assessing the impact of vaccine-preventable diseases and benefits of vaccination among the members of this managed care organization.

All members of the staff model plan were included in the cohort for the respective study season if they were 65 years or older on October 1 for the study year (the beginning of the vaccination season) and if they were enrolled continuously throughout both the vaccination season (October through December) and subsequent influenza season (the outcome period).

INFLUENZA SEASONS (OUTCOME PERIODS)

As with the first 3 years of the project, for the fourth through sixth seasons, the dates of the influenza seasons were selected based on surveillance information obtained from the Minnesota Department of Health.[28-30] This influenza surveillance system includes information from passive reporting of school and nursing home outbreaks as well as laboratory identification of influenza isolates from specimens sent to the Minnesota Department of Health laboratories. The information collected is used to estimate both the level of influenza activity in the state as well as the type of influenza viruses circulating for a given season. The dates of first isolates were similar for these 3 years (November 11, 1993, November 28, 1994, and November 15, 1995), and we selected November 15 as the starting date for each season. For each season, 85% to 100% of all influenza isolates were obtained on or before April 1. To be consistent with our original study, we therefore defined the end of each season as March 31. In all cases, the dates of the influenza seasons included the total period of peak activity for each year.

DATA COLLECTION

All study data were obtained from the linked, administrative databases of Group Health Inc. Baseline information for the study subjects included demographic characteristics as well as information on prior health care utilization and previous outpatient and inpatient diagnoses listed in the databases. The specific diagnoses and their associated codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*)[31] are as

ganization[10] has also suggested that elderly individuals be targeted for immunization. Despite these recommendations, influenza vaccine is underused. In the United States, 40% to 50% or more of targeted individuals fail to receive the vaccine each season.[11,12] Worldwide underuse of influenza vaccine is also observed.[13,14]

Among the elderly, individuals with underlying medical conditions such as cardiopulmonary disease are at especially high risk for the serious complications of influenza.[5,15-17] There is widespread consensus regarding the importance of vaccination for this group.[13] Patients and providers may be less convinced of the benefits of influenza vaccination for low-risk senior citizens. Uncertainty about the risks of influenza and benefits of vaccination for healthy elderly individuals may result in health care providers less frequently recommending vaccination for this group or in patients less frequently accepting the vaccine.[18-20] This may in part explain why in the United States, vaccination rates are lower for elderly individuals without underlying conditions than they are for high-risk elderly individuals.[21] Results from the 1994 National Health Interview Survey, for example, showed that the vaccination rate of elderly individuals with heart disease was 67.5% vs a rate of 51.7% for individuals without heart disease; the vaccination rate for elderly individuals with chronic lung disease was 71.2% vs 56.6% for individuals without lung disease (Centers for Disease Control and Prevention, Atlanta, Ga, unpublished data, December 1997). Uncertainty about the benefits of vaccination may also partially account for the considerable international variation in influenza vaccination recommendations and policies and incomplete agreement regarding the merits of age-based policies that recommend routine immunization for all elderly individuals.[13]

Few studies have assessed the benefits of influenza vaccination among senior citizens while differentiating subjects according to risk category. A placebo-controlled trial in the Netherlands conducted among low-risk senior citizens demonstrated that vaccination was associated with a 58% reduction in clinical and serologic influenza.[22] A serial case-control study conducted over 9 seasons in the 1980s showed that influenza vaccination was associated with significant reductions in hospitalizations for pneumonia and influenza among both high-risk and low-risk senior citizens.[234] However, while vaccination was cost saving among high-risk senior citizens, vaccination did not produce net direct medical care

follows: heart disease (*ICD-9-CM* codes 393-398, 410-414, 425, 428, 429), lung disease (*ICD-9-CM* codes 491-496, 500-518), diabetes mellitus (*ICD-9-CM* code 250), chronic renal disease (*ICD-9-CM* codes 581, 582, 585, plus code 39.95 for dialysis from *Current Procedural Terminology, Fourth Revision* [*CPT4*]),[32] rheumatologic disease (*ICD-9-CM* codes 446, 710, 714), and dementia or stroke (*ICD-9-CM* codes 290-294, 331, 340, 341, 348, 438). These diagnoses were selected because they are associated with a higher risk for developing influenza-associated complications. Information on the receipt of pneumococcal vaccine during the previous 12 months (*CPT4* code 907.32) and influenza vaccination status for the study season (*CPT4* code 907.24) was also collected.

Subjects were also grouped into mutually exclusive categories according to their risk status. High risk was defined as having a baseline diagnosis of heart or lung disease. Intermediate risk was defined as having a baseline diagnosis of diabetes, renal disease, rheumatologic disease, or dementia and/or stroke, but not having underlying heart or lung disease. Low risk was defined as having none of these baseline diagnoses.

The primary outcomes were hospitalizations for pneumonia and influenza (*ICD-9-CM* codes 480-487) and deaths from any cause. Secondary outcomes included hospitalizations for all respiratory conditions (*ICD-9-CM* codes 460,462, 465, 466, 480-487, 500-518), hospitalizations for congestive heart failure (*ICD-9-CM* code 428), and hospitalization costs for all respiratory conditions and congestive heart failure combined. The diagnostic categories for the outcomes were selected to be consistent with previously identified categories of complications of influenza. Hospitalization costs reflected the charges submitted for each hospitalization episode.

STATISTICAL ANALYSIS

Bivariate comparisons for vaccinated and unvaccinated subjects were conducted using Student *t* tests and χ^2 tests for continuous and categorical variables, respectively. For the multivariate analyses, the units of analysis were person-periods of observation. Multivariate analyses comparing outcomes between the 2 groups while controlling for covariates and potential confounders were conducted using general linear (analysis of covariance) and logistic regression analysis models (SPSS for Windows 95, version 7.5, SPSS Inc, Chicago, Ill). Variables included in the models were age; sex; vaccination status; baseline diagnoses of heart disease, lung disease, diabetes, renal disease, rheumatologic disease, or stroke and/or dementia; number of previous hospitalizations and physicians' visits; and history of pneumonia. For those analyses specific to risk categories, the relevant baseline diagnoses were excluded from the models. Vaccine effectiveness was calculated as the percentage reduction in outcomes among vaccinated subjects compared with unvaccinated subjects. Mortality reduction among vaccine recipients was calculated from the results of the logistic regression analysis. Because the outcome events were rare, the adjusted odds ratio was used as an approximation of the relative risk. Thus, mortality reduction was calculated as (1 – odds ratio) × 100%. Cost savings associated with vaccination were calculated from the institution's perspective as direct savings associated with vaccination by comparing hospitalization costs between vaccinated and unvaccinated subjects. After subtracting the costs of the vaccination program (including vaccine, supplies, and administration costs), the difference in mean costs for vaccinated and unvaccinated subjects was then calculated.

Mean Cost Savings =
(Mean Hospitalization Costs for Unvaccinated Subjects)
– (Mean Hospitalization Costs for Vaccinated Subjects)
– (Mean Costs of the Influenza Vaccination Program).

Total Cost Savings =
(Mean Cost Savings) × (No. of People Vaccinated).

cost savings among the low-risk senior citizens. An earlier study[24] in the same health care organization demonstrated significant reductions in hospitalizations for pneumonia during an epidemic season for high-risk senior citizens, but did not show a benefit for senior citizens without underlying cardiopulmonary disease. We conducted this study to further clarify the benefits of influenza vaccination for low-risk senior citizens while concurrently documenting the benefits for intermediate- and high-risk senior citizens from the same population and over the same period.

RESULTS

There were more than 20 000 subjects in each of the 6 cohorts who provided a total of 147 551 person-periods of observation. The overall vaccination rate was 60%. The baseline characteristics of the subjects are shown in **Table 1**. Vaccinated subjects were generally more likely than unvaccinated subjects to be male, to have baseline risk conditions such as underlying heart or lung disease, to have received pneumococcal vaccine in the previous year, and to have higher rates of resource utilization such as physician visits. Unvaccinated subjects, on the other hand, were more likely to have a history of dementia or stroke. There were 101 619 subjects in the low-risk group (68.9%), 15 482 in the intermediate-risk group (10.5%), and 30 450 in the high-risk group (20.6%). The influenza vaccination rates for each group were 56%, 64%, and 69%, respectively.

The characteristics of the 6 influenza seasons and the numbers of outcomes are shown in **Table 2**. Influenza activity exceeded the epidemic threshold for 2 or more consecutive weeks for all the seasons except 1990-1991.[33-37] There was a good to excellent match between vaccine and circulating virus strains each year with the exception of 1992-1993 when the match for the A/H3N2 component was poor (N. Cox, PhD, Centers for Disease Control and Prevention, written communication, February 1997). Over the 6 seasons, there were a total of 1010 hospitalizations for pneumonia and influenza, 4125 hospitalizations for all respiratory conditions, 1615 hospitalizations for congestive heart failure, and 1345 deaths.

The estimates of vaccine effectiveness for hospitalizations and death for all elderly subjects by season are shown in **Figure 1**. Vaccine effectiveness was remark-

ably consistent over the 6 years. On average (**Table 3**), vaccination was associated with a 39% reduction in hospitalizations for pneumonia and influenza ($P<.001$), a 32% decrease in hospitalizations for all respiratory conditions ($P<.001$), and a 27% decrease in hospitalizations for congestive heart failure ($P<.001$). Immunization was also associated with a 50% reduction in deaths from all causes ($P<.001$).

The intermediate- and high-risk categories were associated with increasing rates of the study outcomes when compared with low-risk subjects. Adjusted odds ratios for intermediate- and high-risk subjects, respectively, for the primary study outcomes were 1.56 (95% confidence interval [CI], 1.23-2.02) and 3.26 (95% CI, 2.76-3.86) for any hospitalization for pneumonia and influenza, and 2.67 (95% CI, 2.26-3.16) and 3.33 (95% CI, 2.90-3.82) for all-cause mortality. For the secondary outcomes, the adjusted odds ratios for intermediate- and high-risk subjects were 1.52 (95% CI, 1.31-1.78) and 4.76 (95% CI, 4.30-5.23) for any hospitalization for acute and chronic respiratory disease, and 2.55 (95% CI, 1.98-3.29) and 10.32 (95% CI, 8.70-12.23) for any hospitalization for congestive heart failure. Because of the large numbers of subjects in the low-risk category, however, the numbers of outcomes in this group were substantial: 32% of the hospitalizations for pneumonia and influenza, 30% of the deaths, 26% of hospitalizations for all respiratory conditions, and 16% of hospitalizations for congestive heart failure.

The results of the analyses assessing vaccine effectiveness by risk group are shown in Table 3. High-risk subjects had the highest event rates and largest absolute reductions in events when vaccinated. However, all the groups benefited from vaccination with fewer hospitalizations for pneumonia and influenza and for all respiratory conditions, and with fewer deaths from all causes; estimates of vaccine effectiveness were similar across the groups for these outcomes (**Figure 2**). The benefits of vaccination were less consistent across the risk groups with regard to hospitalizations for congestive heart failure; vaccination was most strongly associated with fewer episodes among the high-risk subjects.

Hospitalization costs for respiratory conditions and congestive heart failure over the 6 seasons were lower among all vaccinated subjects by $78 (95% CI, $27-$128; $P = .002$) (Table 3). After subtracting the costs of the vaccination program, the net savings associated with influenza vaccination were $73 per person vaccinated for all subjects combined. The point estimates for the net savings per person vaccinated by risk category were $166 for high-risk subjects, $117 for intermediate-risk subjects, and $7 for low-risk subjects (for individual risk groups, $P \geq .05$).

Table 1. Baseline Characteristics of Study Subjects

Characteristic	Vaccinated (n = 87 898)	Unvaccinated (n = 59 653)	P
Mean ± SD age, y	72.5 ± 5.7	72.7 ± 6.7	<.001
Male, %	44.7	40.9	<.001
Inpatient diagnoses previous 12 mo, %			
Lung disease	2.6	2.2	<.001
Heart disease	4.8	3.5	<.001
Outpatient diagnoses previous 12 mo, %			
Lung disease	10.1	6.9	<.001
Heart disease	16.5	11.1	<.001
Diabetes mellitus	11.9	7.9	<.001
Chronic renal disease	2.3	1.7	<.001
Dementia or stroke	2.5	4.8	<.001
Rheumatologic disease	2.2	1.5	<.001
Mean ± SD No. of hospitalizations during previous 12 mo	0.23 ± 0.7	0.24 ± 1.0	.01
Pneumonia during previous 12 mo, %	4.2	3.5	<.001
Mean ± SD No. of physician visits during previous 12 mo	13.1 ± 11.8	8.9 ± 12.0	<.001
Pneumococcal vaccination during previous 12 mo, %	11.3	4.5	<.001

COMMENT

Age-based strategies targeting all elderly individuals are more effective than risk disease–based strategies.[38] In this

Table 2. Characteristics of Influenza Seasons and Study Outcomes*

Year	Influenza Seasons	Circulating Virus Strains	No. of Subjects	Mean No. per 1000 Person-Periods			Deaths, No. (%)
				HPI	HACRC	HCHF	
1990-1991	11/1/90-3/31/91	B	25 532	4	20	9	153 (0.6)
1991-1992	11/15/91-3/31/92	A/H3N2	26 369	8	31	5	265 (1.0)
1992-1993	12/15/92-3/31/93	B A/H3N2	26 626	6	29	4	241 (0.9)
1993-1994	11/15/93-3/31/94	A/H3N2	23 567	10	40	19	290 (1.2)
1994-1995	11/15/94-3/31/95	A/H3N2 B	24 765	8	27	17	248 (1.0)
1995-1996	11/15/95-3/31/96	A/H3N2 A/H1N1	20 792	5	20	14	148 (0.7)

*HPI indicates hospitalization for pneumonia and influenza; HACRC, hospitalizations for all acute and chronic respiratory conditions; and HCHF, hospitalizations for congestive heart failure. Data for the first 3 years, 1990-1991 through 1992-1993, have been adapted from earlier work by the authors.[27]

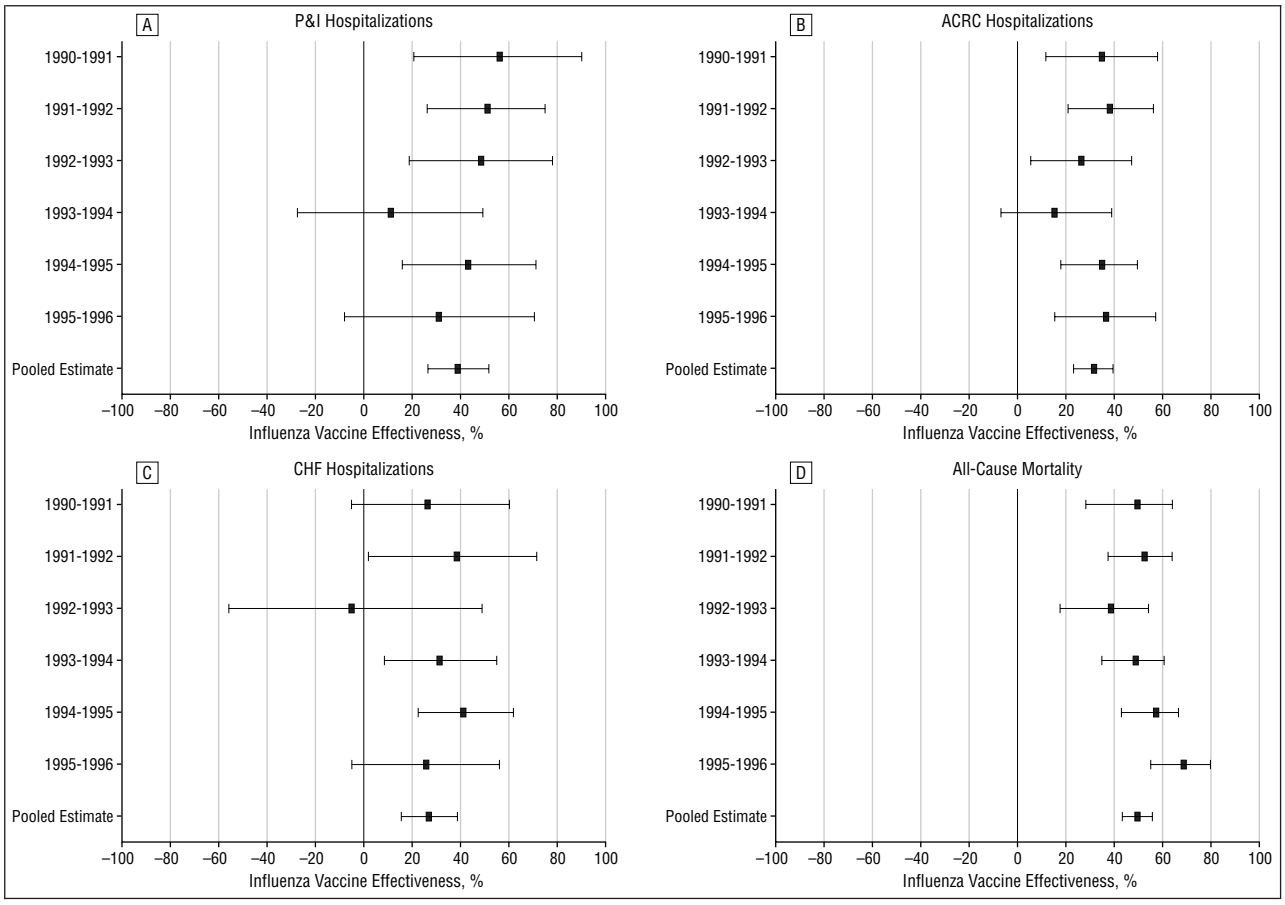

Figure 1. *Influenza vaccine effectiveness over 6 consecutive seasons: reductions in hospitalizations for pneumonia and influenza (P&I) (A), all respiratory conditions (B), and congestive heart failure (CHF) (C), and in reducing deaths from all causes (D). Shown are the point estimates for effectiveness along with the 95% confidence interval. Values to the right of 0 indicate that vaccination reduces outcome event rates; to the left of 0, vaccination increases outcome event rates; and ACRC, all acute and chronic respiratory conditions. Data for 1990-1991 through 1992-1993 have been adapted from Nicholson et al.[13] For the pooled estimates, data for 1990-1991 through 1995-1996 have been combined to provide 147 551 person-periods of observation.*

study, we have provided further evidence supporting such strategies by showing that the benefits of influenza vaccination extended to all elderly subjects regardless of risk category. Over the 6-year period, vaccination of low- as well as intermediate- and high-risk senior citizens was associated with significant reductions in complications of influenza such as hospitalizations for pneumonia and influenza and respiratory conditions and with fewer deaths from all causes.

Consistent with the findings of other investigators, subjects in our study who had a diagnosis of cardiac or pulmonary disease were at substantially increased risk for hospitalization and death when compared with subjects in the low-risk group.[5,15-17] While this high-risk group represented only 20.6% of all subjects in the study, they experienced 56% of the hospitalizations for pneumonia and 53% of the deaths. Nevertheless, intermediate- and low-risk senior citizens also experienced significant numbers of complications of influenza—a finding with significant public health implications. All groups benefited from vaccination.

The benefits of vaccination in our study extended not only to improved health but also to lower direct medical care costs. For all risk groups combined, the net cost savings were $73 per person vaccinated. Vaccination also appeared to be cost saving within each risk group with point estimates of net savings from $166 for high-risk subjects to $7 for low-risk subjects, although these estimates did not reach statistical significance because of the substantial variations within the subgroups. Other investigators have also found that influenza vaccination of the elderly results in direct medical cost savings for the influenza season[23,39-43] and that it is highly cost-effective per year of life saved when compared with other diagnostic or therapeutic interventions.[43-45] In 1 study, however, investigators[23] compared hospitalization costs for pneumonia between high- and low-risk subjects and found that vaccination of high- but not low-risk subjects was associated with direct medical care cost savings. Our findings may differ from that study in part because of the broader range of outcomes included in the cost analysis.

This study provides additional evidence that the impact of influenza and benefits of vaccination for the elderly span a wide range of health outcomes, including hospitalization for pneumonia and influenza, all respiratory conditions, and death.[2-6,46] Vaccination was also associated with fewer hospitalizations for congestive heart failure, although this association was strongest for high-risk subjects, many

Table 3. Effectiveness of Influenza Vaccination in Reducing Primary and Secondary Outcomes Among Higher-Risk and Lower-Risk Subjects*

Outcomes	All Subjects		High Risk		Intermediate Risk		Low Risk	
	Vaccinated (n = 87 898)	Unvaccinated (n = 59 653)	Vaccinated (n = 20 930)	Unvaccinated (n = 9520)	Vaccinated (n = 9910)	Unvaccinated (n = 5572)	Vaccinated (n = 57 058)	Unvaccinated (n = 44 561)
Primary Outcomes								
P & I hospitalizations, mean per 1000	5.3	8.7	16.8	23.5	6.8	9.8	2.2	4.4
Difference	3.4 (2.3 to 4.5)		6.8 (2.5 to 11.0)		3.1 (−0.8 to 7.0)		2.2 (1.3 to 3.0)	
Effectiveness	39% (26% to 52%)		29% (11% to 47%)		32% (−8% to 71%)		49% (29% to 69%)	
P	<.001		.002		.12		<.001	
Death, all causes								
Odds ratio	0.50 (0.44 to 0.56)		0.51 (0.43 to 0.59)		0.36 (0.27 to 0.48)		0.45 (0.37 to 0.55)	
Effectiveness	50% (44% to 56%)		49% (41% to 57%)		64% (52% to 73%)		55% (45% to 63%)	
P	<.001		<.001		<.001		<.001	
Secondary Outcomes								
ACRC hospitalizations, mean per 1000	22.8	33.3	84.4	104.4	17.2	28.0	8.6	12.7
Difference	10.5 (7.6 to 13.3)		20.0 (7.7 to 32.2)		10.8 (2.8 to 18.8)		4.2 (2.3 to 6.0)	
Effectiveness	32% (29% to 40%)		19% (7% to 31%)		39% (10% to 67%)		33% (18% to 47%)	
P	<.001		.001		.008		<.001	
CHF hospitalizations, mean per 1000	9.2	12.7	40.2	46.6	7.6	7.7	2.2	2.8
Difference	3.4 (1.9 to 4.9)		6.4 (−0.4 to 13.2)		0.09 (−3.5 to 3.7)		.6 (−0.3 to 1.4)	
Effectiveness	27% (15% to 39%)		14% (−1% to 28%)		1% (−45% to 48%)		21% (−9.2% to 50%)	
P	<.001		.07		.96		.17	
Costs for ACRC and CHF hospitalizations, mean per person	$355	$433	$1200	$1371	$269	$392	$152	$164
Difference	$78 ($27 to $128)		$171 (−$42 to $384)		$122 (−$1 to $245)		$12 (−$24 to $48)	
Effectiveness	18% (6% to 30%)		12% (−3% to 28%)		31% (0% to 62%)		7% (−15% to 29%)	
P	.002		.11		.05		.52	

*Data have been combined for 1990-1991 through 1995-1996 providing 147 551 person-periods of observation. High risk indicates subjects with a baseline diagnosis of heart or lung disease; intermediate risk, subjects with a baseline diagnosis of diabetes, rheumatologic disease, renal disease, or dementia/stroke; low risk, subjects who had none of the previously listed baseline diagnoses; P & I, pneumonia and influenza; ACRC, all acute and chronic respiratory conditions; and CHF, congestive heart failure. Values with parentheses are 95% confidence interval. Outcomes have been adjusted for the baseline characteristics as noted in the "Methods" section.

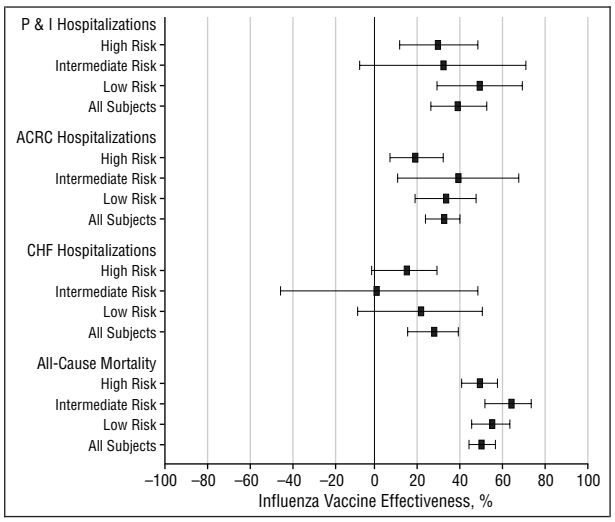

Figure 2. *Influenza vaccine effectiveness among low-, intermediate-, and high-risk subjects. The risk categories are as defined in the "Methods" section. Values to the right of 0 indicate that vaccination reduces outcome event rates; to the left of 0, vaccination increases outcome event rates; P & I, pneumonia and influenza; ACRC, all acute and chronic respiratory conditions; and CHF, congestive heart failure.*

of whom had preexisting cardiac disease. The magnitude of reduction in the outcomes among vaccinated subjects also provides indirect evidence that influenza is directly or indirectly responsible for a large percentage of these events during the influenza season; this held true for low- as well as intermediate- and high-risk subjects. For all senior citizens, the influenza-attributable proportion of these outcomes is undoubtedly substantial but frequently unapparent and unrecognized.

Studies in other populations have highlighted the health benefits associated with influenza vaccination of community-dwelling senior citizens. A placebo-controlled trial[22] from the Netherlands confirmed that vaccination reduced clinical and serologic influenza illness among the elderly by 58%. Observational studies[39-50] from the United States, Canada, and the United Kingdom have demonstrated that vaccination is associated with lower rates of complications of influenza such as hospitalization for pneumonia and influenza and for pneumonia together with other respiratory conditions.[47,50] Several studies have also shown lower death rates from all causes[47,51] or from influenza.[52] A recent meta-analysis has confirmed the benefits of vaccination for elderly residents of long-term care facilities with significant reductions in respiratory illness, hospitalization, and death.[53] Most of these studies evaluated

the benefits of vaccination over 1 or 2 seasons and included fewer outcomes than were evaluated in this study. In our study, we have shown how the benefits of vaccination can also be consistent and substantial over multiple, consecutive seasons.

Strengths of this study include the large study population, inclusion of multiple, consecutive seasons, and the use of the cohort design, the strongest design for observational or noninterventional studies. We also collected information on baseline risk characteristics to adjust for differences in risk factors between vaccinated and unvaccinated subjects and to identify the independent contribution of vaccination to the occurrence of outcome events. Nevertheless, a limitation of all observational studies is the difficulty in performing adequate risk adjustment in the multivariate analyses.[54] In the absence of randomization, it is always possible that there were significant, unmeasured differences between the comparison groups that may have influenced the study findings and conclusions. Misclassification of vaccination status may also have occurred in this study, most likely because of incomplete recording in the administrative databases. However, we have previously shown that the Group Health Inc databases are highly accurate in capturing influenza vaccination status, with 93% agreement between medical records and the computerized databases (K.L.N., unpublished data, September 1995). Furthermore, even if misclassification occurred to any significant extent, this most likely would have biased the study findings to a negative conclusion.

CONCLUSIONS

Millions of elderly individuals fail to receive influenza vaccine each year. Our study confirms that healthy senior citizens as well as senior citizens with underlying medical conditions suffer the serious complications of influenza and that they benefit substantially from vaccination. All individuals aged 65 years or older should be immunized with this vaccine.

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