I
fluenza is a highly contagious viral disease, with widespread outbreaks and epidemics typically occurring in the United States during the winter months. Influenza was responsible for an average of 36,000 deaths per year in the United States from 1990-1999.1 Although rates of infection are highest among children, serious illness and death are most common in individuals over the age of 65 years and those with medical conditions that place them at higher risk for complications,2-5 with people over the age of 65 years accounting for 63% of all influenza-related hospitalizations.6,7 Influenza vaccination has been found to be associated with reductions in hospitalizations for heart disease, cerebrovascular disease, pneumonia, and influenza, while the risk of death from all causes during the influenza season is reduced.6

Even though vaccination rates increased during the 1990s, the Advisory Committee of Immunization Practices from the Centers for Disease Control and Prevention (CDC) recommends using strategies to increase vaccination levels, including reminder systems and standard orders programs.9-12 Economic studies of influenza vaccinations for people over the age of 65 years have shown overall cost savings and reductions in hospitalization and death.13 Similarly, studies of adults under the age of 65 years also show that influenza vaccinations can reduce direct medical costs as well as indirect costs from worker absenteeism.14-22 The Task Force on Community Preventive Services has shown cost-effectiveness studies to range between $3 and $46 per additional vaccine administered,23 whereas client recall and reminder systems have been found to be effective in increasing community demand for vaccines.24-26

This study tested an intervention designed to support the Advisory Committee of Immunization Practices recommendation to increase vaccination level. We estimated the benefits of influenza vaccines for the elderly27-29 and also studied the effect of a nurse advice service, with the goal of reducing inpatient bed days and emergency department (ED) visits for members over the age of 65 years in a preferred provider organization health plan (the Blue Cross and Blue Shield Government-wide Service Benefit Plan).
METHODS

Subjects
All subscribers (households) and their dependents over the age of 65 years enrolled in the Blue Cross and Blue Shield Government-wide Service Benefit Plan in the states of Oklahoma, Rhode Island, Kentucky, California, Arizona, Utah, and Colorado in October 2002 were eligible for the study. Subscribers were either current federal employees or retired federal employees with the Blue Cross and Blue Shield Government-wide Service Benefit Plan as their primary insurance payer.

Study Design
A randomized controlled trial was used to assign members to 1 of 3 groups. The first 2 groups were intervention groups; the third served as a control group. Households in all states had an equal probability of assignment into the intervention group. Once in a group, that subscriber and his or her associated dependents over the age of 65 years remained in that group for the duration of the study. If a member died or changed health plan coverage, the person was still included in the study for the duration of his or her health plan eligibility. The simple randomization code was developed by using a computer random number generator between the values of 0 and 1 so that the control group was 3 times as large as each intervention group.

The 5-month study period was October 15, 2002 through March 15, 2003, when influenza was most likely to occur, although the influenza season can vary from year to year.

Intervention
Because there were 2 mailed interventions, there were 2 separate intervention groups. The objective of 1 of the mailings was to promote receiving influenza vaccination (influenza mailing group). The purpose of the other mailing was to promote the use of a telephonic nurse advice service (nurse advice service mailing group). The goal of each intervention was to reduce influenza-related inpatient bed days and ED visits.

The nurse advice service was sponsored by the Blue Cross and Blue Shield Government-wide Service Benefit Plan and provided through a contract with a third-party vendor. The nurse advice service employed approximately 400 registered nurses through a distributed call center model. A standardized triage system using proprietary symptom-based algorithms and caller education content was used. Members of all 3 groups (control, influenza vaccination mailer, and nurse advice service mailer) had unlimited access to the nurse advice service.

The mailings for the first arm of the intervention (influenza mailing group) were sent at the beginning of the study period (October 1, 2002, and November 1, 2002) to increase the likelihood that a person would read at least 1 of the 2 identical mailings and subsequently receive an influenza vaccination.

The influenza mailer was based on CDC influenza and influenza vaccination clinical content, and was reviewed and approved by physicians board certified in internal medicine and emergency medicine. The mailer included descriptions of high-risk populations and of the beneficial effects of vaccination, the recommended timing for receiving the vaccine, and a recommendation for frequent hand washing.

The mailings for the second arm of the intervention (nurse advice service mailing group) were sent at the beginning and middle of the study period (October 1, 2002, and January 1, 2003, respectively) to increase the likelihood that a person would read at least 1 of the 2 identical mailings and subsequently call the nurse advice service if symptoms developed.

The nurse advice service mailer included a description of influenza symptoms (fever, chills, rhinorrhea, myalgias, and headache) and a brief description of high-risk populations. It also included an invitation to call the nurse advice service at the earliest sign of symptoms and stated that nurse advice service would provide 24/7 telephonic access to a registered nurse who would help persons understand what they could do to start feeling better, when they should see a doctor, and what new or worsening symptoms should prompt a call back to the service or their physician.

The control group was not sent either mailing.

Hypotheses
We tested the hypotheses that encouraging members to receive an influenza vaccine or encouraging members to call a telephonic nurse advice service with mailed prompts would result in fewer condition-related inpatient bed days and ED visits. Physician evaluation and management visits and other outpatient visits also were measured with no hypotheses about their expected change. Recent research suggests that mailed prompts can improve screening rates for osteoporosis in women over the age of 65 years, and it was expected that this intervention with mailed prompts would also influence health behavior.50

Disease and Outcome Definitions
The outcome measures included influenza, pneumonia, heart failure, and other respiratory inpatient bed days, ED visits, physician evaluation and management visits, and other outpatient visits. The diagnosis codes for the outcomes were defined following those used by Nichol et al14 and Davis et al.16 Utilization for pneumonia and influenza was determined by...
International Classification of Diseases, Ninth Revision, Clinical Modification\textsuperscript{11} (ICD-9-CM) codes 480-487. Utilization for congestive heart failure was determined by ICD-9-CM code 428. Utilization for all respiratory conditions was determined by ICD-9-CM codes 460-462, 465, 466, 480-487, and 500-518. Because no diagnosis-related group information was available, the reason for each admission or visit was determined by the most frequent first-listed diagnosis for each admission or visit. Physician evaluation and management visits were determined by looking at all outpatient claims that did not occur on the same day as an inpatient admission or ED visit using Clinical Procedural Terminology codes 99201-99215 or 99241-99245. Other outpatient visits represented the remaining outpatient visits that did not occur on the same day as an inpatient admission or ED visit.

**Statistical Analysis**

To check the randomization, demographic and baseline variables were compared to ensure that there were no significant differences among the 3 groups, as was indicated by the fact that all measured variables were within 1 standard deviation of one another.

The rates of condition-related inpatient bed days, ED visits, physician evaluation and management visits, and other outpatient visits were compared between the intervention and the control groups in the intervention time period. Because randomization was based on clusters (subscribers were randomized rather than individuals), \( P \) values were calculated with a \( \chi^2 \) statistic by using the SAS software (version 9; SAS Institute Inc, Cary, NC) clustering option. Statistical significance of differences of utilization and vaccinations between each group was calculated by using the \( \chi^2 \) statistic generated by “proc genmod” using the “repeated” option in SAS to account for the clustering effect on the variance.\textsuperscript{11}

**Savings Calculation**

Financial savings were calculated by 2 different methods. The first method, the unit cost method, determined savings by multiplying utilization rate differences by the number of people in the intervention group and then by the average unit cost of condition-related visits. The second method, the per member per month (PMPM) method, determined savings by multiplying PMPM differences by the number of member months for the intervention group. This method used actual condition-related visit costs for each person and applied a trimming algorithm that applied a stop-loss to any visit’s costs above the 99th percentile. This stop-loss was applied to limit the impact of outlier visit costs.

The perspective of the savings calculation is that of the health plan. Claims costs represent payments made by the health plan, with no member out-of-pocket costs or health plan costs for already provided benefits.

**RESULTS**

Because the mailings were sent out in bulk, no information was available on undeliverable pieces. Subscribers (households), not individual members, were randomized and sent the 2 mailings to reduce cross-contamination between household members, avoiding the possibility of a husband and wife pair being randomized into different groups.

The total sample size was 134,791 individuals, of whom 26,474 in the intervention group were sent the influenza mailing, and 26,864 in the intervention group were sent the nurse advice mailing; 81,453 were in the control group. The unbalanced study design was influenced by a fixed budget for mailings for the intervention group. Characteristics of intervention and control individuals are shown in Table 1. The randomization appeared to be appropriate for the available demographic variables. Differences between the intervention groups and control group all were less than 1 standard deviation.

Table 2 and Table 3 show the utilization rates per 10,000 people for each intervention group compared with the control group over the 5-month study period of October 15, 2002, through March 15, 2003. Compared with the control group, the influenza mailing intervention group experienced 2.87% (\( P = .033 \)) fewer condition-related inpatient bed days and 7.25% (\( P = .101 \)) fewer condition-related ED visits compared with the control group. No significant differences between groups for physician evaluation and management visits, other outpatient visits, or influenza vaccinations were observed. Influenza vaccinations often are given in settings that do not generate claims, thus limiting the reliability of evidence of influenza vaccinations as seen via administrative claims.

Compared with the control group as shown in Table 3, the nurse advice service mailing intervention group experienced 7.65% (\( P < .001 \)) fewer condition-related inpatient bed days, 6.75% (\( P = .125 \)) fewer condition-related ED visits, 16.13% (\( P = .049 \)) more nurse advice service general health information calls, and 18.43% (\( P < .001 \)) more nurse advice service symptomatic calls, of which there was an increase of 54.14% (\( P = .002 \)) for influenza and upper respiratory illness compared with the control group. No significant differences between groups for physician evaluation and management visits were observed, although there was a lower rate for the intervention group for other outpatient visits: 4.63% (\( P = .001 \)). No significant differences between groups for influenza vaccinations were observed. Influenza
Cost and Utilization Avoidance

**Table 1. Characteristics of the Intervention and Control Groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Influenza Intervention</th>
<th>Nurse Advice Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of households randomized</td>
<td>26,474</td>
<td>26,864</td>
<td>81,453</td>
</tr>
<tr>
<td>Average household size, n</td>
<td>1.3 (0.4)</td>
<td>1.3 (0.4)</td>
<td>1.3 (0.5)</td>
</tr>
<tr>
<td>Average age, y</td>
<td>77.8 (7.5)</td>
<td>77.8 (7.5)</td>
<td>77.7 (7.5)</td>
</tr>
<tr>
<td>Male, %</td>
<td>40.4 (0.5)</td>
<td>40.0 (0.5)</td>
<td>40.4 (0.5)</td>
</tr>
<tr>
<td>Member months, n (5-mo study period)</td>
<td>4.9 (0.7)</td>
<td>4.9 (0.7)</td>
<td>4.9 (0.7)</td>
</tr>
<tr>
<td>Dual Medicare coverage, %</td>
<td>73.6 (0.4)</td>
<td>73.3 (0.4)</td>
<td>73.8 (0.4)</td>
</tr>
<tr>
<td>CHF, %</td>
<td>6.0 (0.2)</td>
<td>6.2 (0.2)</td>
<td>6.1 (0.2)</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>12.1 (0.3)</td>
<td>12.2 (0.3)</td>
<td>12.5 (0.3)</td>
</tr>
<tr>
<td>CAD, %</td>
<td>17.1 (0.4)</td>
<td>16.0 (0.4)</td>
<td>16.5 (0.4)</td>
</tr>
<tr>
<td>COPD, %</td>
<td>6.4 (0.2)</td>
<td>6.5 (0.2)</td>
<td>6.6 (0.2)</td>
</tr>
<tr>
<td>Asthma, %</td>
<td>2.2 (0.1)</td>
<td>2.1 (0.1)</td>
<td>2.2 (0.1)</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>26.5 (0.4)</td>
<td>26.5 (0.4)</td>
<td>26.4 (0.4)</td>
</tr>
<tr>
<td>Arthritis, %</td>
<td>8.1 (0.3)</td>
<td>8.4 (0.3)</td>
<td>8.2 (0.3)</td>
</tr>
<tr>
<td>Depression, %</td>
<td>1.5 (0.1)</td>
<td>1.6 (0.1)</td>
<td>1.6 (0.1)</td>
</tr>
</tbody>
</table>

CAD indicates coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease.

* Differences between the intervention groups and control group were all less than 1 standard deviation.

**Table 2. Utilization Rates for Influenza Mailing Intervention Group and Control Group**

<table>
<thead>
<tr>
<th>Utilization Type</th>
<th>Influenza Intervention Group</th>
<th>Control Group</th>
<th>P</th>
<th>Percent Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient bed days (condition related)</td>
<td>2636.55</td>
<td>2714.45</td>
<td>.033</td>
<td>−2.87</td>
</tr>
<tr>
<td>Emergency department visits (condition related)</td>
<td>225.13</td>
<td>242.72</td>
<td>.101</td>
<td>−7.25</td>
</tr>
<tr>
<td>Physician evaluation and management visits (condition related)</td>
<td>55,504.65</td>
<td>55,580.76</td>
<td>.148</td>
<td>−1.36</td>
</tr>
<tr>
<td>Other outpatient visits (condition related)</td>
<td>2597.64</td>
<td>2617.83</td>
<td>.576</td>
<td>−0.77</td>
</tr>
<tr>
<td>Influenza vaccination rate</td>
<td>2074.11</td>
<td>2076.29</td>
<td>.946</td>
<td>−0.10</td>
</tr>
<tr>
<td>Inpatient bed days (total)</td>
<td>8735.74</td>
<td>8646.34</td>
<td>.176</td>
<td>1.03</td>
</tr>
<tr>
<td>Emergency department visits (total)</td>
<td>1775.70</td>
<td>1748.25</td>
<td>.356</td>
<td>1.57</td>
</tr>
<tr>
<td>Physician evaluation and management visits (total)</td>
<td>29,954.29</td>
<td>30,009.45</td>
<td>.652</td>
<td>−0.18</td>
</tr>
<tr>
<td>Other outpatient visits (total)</td>
<td>27938.73</td>
<td>28,510.55</td>
<td>.00</td>
<td>−2.01</td>
</tr>
</tbody>
</table>

*Utilization rates are calculated by the number of events × sample size × 10,000.

Vaccines were not encouraged in the nurse advice service mailing intervention group.

For nurse advice symptomatic calls, the distributions of nurse recommendations for the nurse advice mailing intervention group and the control group were not statistically different from each other and were as follows: (1) access urgent care was 16.0% for the intervention group and 18.2% for the control group, (2) speak to their provider was 32.1% for the intervention group and 32.2% for the control group, (3) make an appointment with their provider was 14.7% for the intervention group and 14.9% for the control group, and (4) access self-care instructions with monitoring.
was 37.2% for the intervention group and 34.7% for the control group.

Regression analysis was performed on inpatient bed days, which included age and sex as covariates, as part of a sensitivity analysis even though a regression framework was not needed as an analytic tool given the randomized design. The results of the regression analysis showed that the estimated impact of the bed-day rate differed by less than 1% for both intervention groups, thus lending support to an appropriate randomization process.

Table 4 shows the overall financial results. For the influenza mailing intervention group, incremental savings totaled $122,656 for the unit cost method and $63,096 for the PMPM method. For the nurse advice mailing intervention group, incremental savings totaled $309,824 for the unit cost method and $387,783 for the PMPM method. The total cost of the intervention (cost of the mailings) was $32,000, which was allocated evenly for each arm for purposes of calculating a return on investment (ROI) for each arm of the intervention. The ROI was for the mailing that encouraged use of the nurse advice service, not for implementing a nurse advice service for a membership with no already-existing nurse advice service. For the influenza mailing intervention group, the entire cost of influenza vaccines for the influenza mailing group was added to the cost of the intervention.

DISCUSSION

This study provides convincing evidence that a relatively simple mail-delivered prompt to encourage flu vaccination or the use a nurse advice line can have effects on health services utilization rates and generate cost savings.

Influenza vaccination has been shown to decrease influenza morbidity and mortality,\textsuperscript{8,13-22} and nurse advice services have been shown to have the same outcomes as telephonic advice from on-call physicians.\textsuperscript{32} This study was designed to evaluate the efficacy of targeted communications as a tool to reduce condition-related inpatient bed days and ED visits for members over the age of 65 years enrolled in a large commercial health plan. The hypotheses were that these communications would lead to either an increase in vaccination rates or greater use of nurse advice service use, with a corresponding decrease in condition-related ED visits and inpatient bed days. The results indicate that these hypotheses appear to be correct.

To calculate the benefits of the intervention, direct medical cost savings were calculated using condition-related inpatient bed days, ED visits, physician evaluation and management visits, and other outpatient visits. Direct costs for
other utilization types (eg, pharmacy, condition-unrelated visits such as trauma ED visits) were not included. The inclusion of more utilization categories or condition-unrelated visits beyond the targeted intervention would decrease the specificity of the outcomes and would likely increase the variance of estimated impacts of the intervention.

A potential weakness of the study is the use of administrative claims data for analysis. Other literature suggests that the percentage of people over the age of 65 years who report having an influenza vaccine varies between 34.9% and 80.3% and that mailed reminders in a randomized control trial for people over the age of 65 years increased influenza vaccination rates to a level of 35.1% compared with a control group rate of 9.8%. The rate of influenza vaccination as seen through administrative claims in this study was between 20% and 21% and seemed to be in the range of expectations based on previous literature. Influenza vaccinations often are given in settings that do not generate claims, thus limiting the reliability of the evidence of influenza vaccinations in administrative claims. However, it is believed that this would most likely lead to an underestimation of the benefit of the intervention, as members urged to receive influenza vaccination would be more likely (or at least not less likely) to get it, whatever the setting. Other literature suggests that influenza vaccination can reduce hospitalizations for people over the age of 65 years by between 19% and 32%. Inpatient bed days were reduced between 2.87% and 7.65% and were fewer than shown in previous literature. Another logical limitation is that this study assumes that the influenza mailing intervention only impacted influenza-related utilization as defined in previous literature. Furthermore, these results may not be able to be generalized to the entire Medicare population. The study states included in this analysis were compared against the 5% Centers for Medicare & Medicaid Services (CMS) Limited Data Set sample. This comparison revealed that the study population was on average older (78 years for the study group vs 71 years for the CMS sample data set) and was less likely to be male (40% male for the study group vs 45% for the CMS sample data). Results may be dependent upon the particular flu strain in a given year, as regional variation was noted. Lastly, the predominant influenza virus strain circulating during the 2002-2003 influenza season caused relatively mild illness, and the vaccine-virus match was very close. Our results might have been different had the viral strain been more virulent or the vaccine match less close.

The health plan was interested in whether or not mailings to members resulted in behavior change. These results show that a commercial health plan can have positive and cost-saving impacts on medical service utilization as a result of mailing information to their members. Both interventions provided a favorable ROI as measured by both methods to calculate costs. As such, both interventions are recommended for health plans to consider. Additional studies to investigate the utility of this type of intervention in noncommercial health plan populations would be of interest.
Take-away Points

This study provides convincing evidence that a relatively simple mail-delivered prompt to encourage flu vaccination or to encourage the use of a nurse advice line can have measurable effects on health services utilization rates and generate cost savings.

- Mailing information to their members is a cost-effective way for health plans to affect condition-related medical service utilization with a positive return on investment.
- This study tested an intervention designed to support the Advisory Committee of Immunization Practices recommendation to increase vaccination levels and an intervention designed to measure the effect of a nurse advice service.

Author Affiliations: From the McKesson Corporation (GDb, SS), Broomfield, CO; and the Blue Cross Blue Shield Association (AMK), Chicago, IL.

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Authorship Information: Concept and design (GDb, SS, ET); acquisition of data (ET); analysis and interpretation of data (GDb, SS); drafting of the manuscript (GDb, SS, AMK); critical revision of the manuscript for important intellectual content (GDb, SS, ET, AMK); statistical analysis (GDb); obtaining funding (ET, AMK); and supervision (ET).

Address correspondence to: Gregory D. Berg, PhD, McKesson Corporation, 335 Interlocken Pky, Broomfield, CO 80021. E-mail: greg.berg@mckesson.com.

REFERENCES

33. CDC. Influenza and pneumococcal vaccination coverage among persons aged ≥65 years and persons aged 18-64 years with diabetes or asthma—United States, 2003. MMWR. 2004;53(43):1008-1012.