A Randomised, Clinical Trial Comparing the Effectiveness of Hospital and Community-Based Reminder Systems for Increasing Uptake of Influenza and Pneumococcal Vaccine in Hospitalised Patients Aged 65 Years and Over

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Key Words
Influenza · Pneumococcus · Vaccination · Hospital · Elderly · Prevention · RCT

Abstract
Hospitalisation represents an opportunity to identify unimmunised people at risk for the complications of influenza and pneumococcal disease. We conducted a randomised controlled trial of two strategies to increase uptake of influenza and pneumococcal vaccines in eligible, hospitalised subjects aged 65 years or more, admitted between May and September 1998 to a Melbourne hospital. Unvaccinated participants were allocated randomly to alert systems for hospital staff or community general practitioners (GPs). Follow-up occurred at 1 and 3 months. The baseline vaccination rates were 70% for influenza (426/606) and 41% (248/606) for pneumococcal disease. For unvaccinated subjects, the hospital alert resulted in 67% uptake compared to 55% following a GP alert for pneumococcal vaccine; and 63% in hospital compared to 53% following a GP alert for influenza vaccine. Although there was a trend toward a higher uptake in hospital, neither of these differences was statistically significant. The majority (75%) of vaccinations following a GP alert occurred within 1 month of discharge. Despite hospital and community-based reminder systems, there are still significant missed opportunities for vaccination. We did not demonstrate significant differences between hospital and GP reminder systems, but there was a trend towards higher uptake with opportunistic vaccination in hospital.

Background

The National Health and Medical Research Council (NHMRC) of Australia recommends that adults aged 65 years and over should be immunised with both influenza and pneumococcal vaccine [1]. Other persons who have medical risk factors are also recommended for immunisation.
Pneumococcus is the most common cause of community-acquired pneumonia. It also causes meningitis, bacteremia, otitis media, and other infections. The mortality rate for pneumococcal disease in the over 60 age group ranges from 5 to 57%, with higher mortality in immunosuppressed groups and people with underlying chronic diseases [2–5]. In addition, rates of penicillin and multidrug-resistant pneumococcus are increasing [6], so that preventive strategies such as vaccination are increasingly important.

Consensus opinion of expert bodies is that pneumococcal vaccination should be offered to the over 65 age group and people with medical risk factors [1–7]. Pneumococcal vaccine is most effective in younger, immunocompetent persons [8], but the antibody response to pneumococcal vaccine in the elderly and in people with preexisting medical conditions is less predictable. However, there is evidence of efficacy [9] and cost-effectiveness of vaccination in these risk groups [10]. Despite this, uptake of pneumococcal vaccine is reported to be between 4 and 20% in the over 65 age group [11, 12]. Despite adequate knowledge of the indications for pneumococcal vaccine, many health providers fail to put this knowledge into practice [13]. One study found that published reviews of the efficacy of the vaccine were biased in favour of studies which showed low efficacy of the vaccine [14].

Influenza is a major cause of morbidity and mortality in the elderly during epidemics [15]. It can cause primary viral pneumonia, or secondary bacterial pneumonia, and causes higher mortality in persons with underlying chronic diseases. The vaccine is proven to be efficacious in preventing influenza, and in reducing the incidence of pneumonia and death in the elderly [16]. Influenza immunisation is a cost-effective intervention [17], and around the world it has been recommended for people over the age of 65 and for those with predisposing medical risk factors [1, 18].

Uptake of influenza vaccine has been varied in Victoria, the second most populous state of Australia. A study in 1993 showed that 45% of people over the age of 65 were vaccinated, but that rates were much lower in other risk groups [19]. Uptake in nursing homes in Victoria was shown to be 52% overall, but there was a wide variation between nursing homes, with some facilities having rates of <25% [19]. These rates have increased to over 70% in recent years, as a result of targeted campaigns to increase uptake of influenza vaccine in the elderly.

Victoria has a long history of commitment to adult immunisation, which has included media campaigns to increase influenza vaccination and comprehensive surveillance. In 1997, in an effort to improve vaccination rates, the Victorian government provided influenza vaccine free of charge to all Victorians aged 65 years and over, and followed this in 1998 with the provision of free pneumococcal vaccine to the same age group. The vaccines are usually given to eligible patients in the community, by their general practitioner, but hospitals may be an important site for opportunistic vaccination of high-risk patients. Although studies have shown that vaccination against pneumococcus is less effective in high-risk groups, such as those with chronic disease [8], illness requiring hospitalisation is not a contraindication to pneumococcal vaccination unless the patient has had recent treatment with immunosuppressants or has had radiation of lymph nodes [1]. Patients with an acute febrile illness or with a history of Guillain-Barre syndrome should not be given influenza vaccine [1]. Otherwise, hospitalisation represents an opportunity to vaccinate eligible patients.

In Victoria in 1996, there were 524,822 persons over the age of 65 [20], and over a 12-month period (excluding readmissions for the same individual), 187,164 persons in this age group were admitted to Victorian Public Hospitals (data obtained from Victorian Inpatient Minimum Database [21], financial year 1995/1996). Thus, up to 36% (187,164/524,822) of the main target group for pneumococcal and influenza vaccination may be accessible as in-patients each year.

We tested the hypothesis that opportunistic immunisation of eligible patients while hospitalised may result in increased uptake compared to a GP reminder letter.

**Aims**

To determine the effectiveness of hospital reminders compared to community general practitioner (GP) reminders on uptake of influenza and pneumococcal vaccination in hospitalised patients aged 65 years or older.

**Methods**

**Study Design**

A randomised clinical trial was conducted of hospitalised patients aged 65 years and over, admitted between May and September 1998 to The Royal Melbourne Hospital to selected medical units. Eligible patients were those who were aged 65 years or older who were not vaccinated against either influenza in the current year and/or pneumococcus in the previous five years. As the benefits of influenza and pneumococcal vaccination are established in the elderly, we felt it would not be ethical to have a control arm. The intervention of interest, opportunistic vaccination of hospitalised patients, was compared with vaccination in response to a GP reminder letter.
Intervention

Patients who were identified as eligible for either pneumococcal or influenza vaccine were randomised to either:

(A) A reminder to hospital staff in the form of a memo left in the patient’s medical notes and a verbal reminder (face to face) to ward staff (nursing and medical). The decision to vaccinate was left to the treating physician.

(B) A reminder to the patient’s usual general practitioner/family doctor. This was posted to the family doctor on the day of discharge from hospital.

These reminders contained the same information – that the patient had been identified as eligible for influenza and/or pneumococcal vaccine, but was unvaccinated, and that vaccination was recommended.

Patients were randomly allocated to receive intervention A or B. Once a patient consented, the research nurse picked a sealed envelope from a randomisation box, which stated which arm the patient would be allocated to. The hospital did not normally stock influenza or pneumococcal vaccine, so for patients allocated to the hospital reminder, vaccine was provided to the ward staff, and usage of vaccine was monitored. The batch number of each vaccine dose allocated per patient was recorded in the study.

Sample Selection

The Victorian state hospital morbidity database was used to determine the proportion of hospitalised patients who were aged 65 years or older in Victoria and at the study hospital. At the Royal Melbourne Hospital, in the financial year 1995–1996, there were 9,304 separations of patients aged 65 years and over who were admitted for at least a stay of one day and night. A total sample size of 100 was required to measure a 10% difference in immunisation uptake rates between the two interventions with 95% confidence and 80% power [22]. To allow for patient ineligibility, refusal and inability to confirm vaccine status, we aimed to identify 600 patients in the target age group.

We selected inpatients over the age of 65, at the Royal Melbourne Hospital from two general medical units and four specialist medical units (Cardiology, Neurology, Infectious Diseases and Respiratory Medicine).

Eligibility Criteria

(1) Age 65 years and over. (2) No contraindication to immunisation [1]. (3) Admitted under the specified medical units, for a stay of greater than one day and one night, between May and September 1998. (4) Not vaccinated against influenza in 1988 and/or not vaccinated against pneumococcus in the past 5 years.

A research nurse identified patients meeting the eligibility criteria by daily liaison with the participating medical units. The research nurse obtained informed, written consent from eligible patients and collected the following descriptive data from the clinical notes and by interviewing the patient:

Demographic data
Principal diagnosis at admission
Current vaccination status for both influenza and pneumococcal vaccine
Past history of influenza and pneumococcal vaccination
Medical risk factors which are listed as indicators for immunisation
Frequency of visits to general practitioner (GP)

Medical risk factors for influenza or pneumococcal disease were defined as follows:
1. Asplenia (anatomical or functional).
2. Immunosuppression (by drugs such as corticosteroids, or diseases such as AIDS or haematological malignancies).
3. Aboriginal or Torres Strait Islanders aged 50 years or over.
4. Chronic illness (such as chronic cardiac, renal or pulmonary disease, diabetes or alcoholism).
5. Cerebrospinal fluid leak.
6. Residents of nursing homes or other chronic care facilities.

Vaccination history was first obtained from patients, and confirmed with a telephone call to the patient’s general practitioner (GP). If the patient had two GPs, both were contacted. These data were used to describe rates of influenza and pneumococcal immunisation before and after the introduction of free vaccines.

Outcomes

The main outcome of interest was vaccination against influenza and/or pneumococcus. For patients who were in arm A (hospital reminder), this was measured on the day of discharge by documentation in the patient records (including the medication chart) and checking for usage of vaccine. For patients in arm B (GP reminder) this was checked by telephoning the relevant GP at 1 month and at 3 months after discharge from hospital. If telephone calls were unsuccessful in contacting the GP, a letter was sent to the GP inviting him/her to call back.

The study was approved by the Royal Melbourne Hospital Clinical Research and Ethics Committee.

Results

There were 244 subjects who were eligible for the study, able to give consent and whose vaccination history could be verified. Of these, 131/244 (54%) consented to the study. The most common reason for refusal was that patients believed that if they needed vaccination, their doctor would give it to them. Figure 1 describes the recruitment of subjects and process of attrition.

Demographics

The mean and median age was 74 years (range of 65–100 years). 56% (73/131) of the study population were female and 44% (58/131) were male. More than half (58%, 69/131) were in general medical units and 42% (62/131) were in specialist medical units. Only 1/131 claimed that they did not have a GP or family doctor, and 16% (21/131) claimed to be current tobacco smokers. A further 41% (54/131) claimed to be ex-smokers. Table 1 describes the differences between the patients who refused and those who consented. The patients who consented were slightly more likely to be female and to have chronic disease, and had a slightly lower mean age than patients who refused.
There were no significant differences in the characteristics of patients randomised to arm A or B (table 2).

**Vaccination Status**

In 4% (15/368) of eligible subjects, there was conflict between patient recall and GP verification of vaccination status. In a further 20 patients, the GP could not be contacted to verify vaccination status. Table 3 shows influenza and pneumococcal vaccination status for various categories, including risk categories. Overall, 70% (426/606) were vaccinated against influenza and 41% (248/606) against pneumococcus. There was one patient with asplenia, and one with a cerebrospinal fluid leak, but neither was vaccinated against pneumococcus or influenza.
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Fig. 2. Number of patients vaccinated against influenza by month of the year, 1998.

Fig. 3. Percent of patients vaccinated against pneumococcal disease by year.

Table 1. Differences between eligible patients who consented and patients who refused

<table>
<thead>
<tr>
<th>Variable</th>
<th>Consented</th>
<th>Refused</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>74</td>
<td>77</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male sex</td>
<td>44% (58/131)</td>
<td>59% (67/113)</td>
<td>0.05</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>3% (4/131)</td>
<td>5% (6/113)</td>
<td>0.3</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>96% (126/131)</td>
<td>89% (101/113)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>General medical unit</td>
<td>58% (69/131)</td>
<td>54% (61/113)</td>
<td>0.8</td>
</tr>
<tr>
<td>Current smoker</td>
<td>16% (21/131)</td>
<td>11% (12/113)</td>
<td>0.2</td>
</tr>
<tr>
<td>English as first language</td>
<td>75% (98/131)</td>
<td>77% (87/26)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Table 2. A comparison of the characteristics of patients in the two study arms

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hospital</th>
<th>GP</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>74</td>
<td>73</td>
<td>0.6</td>
</tr>
<tr>
<td>Male sex</td>
<td>44% (31/70)</td>
<td>44% (27/61)</td>
<td>0.99</td>
</tr>
<tr>
<td>Nursing home resident</td>
<td>3% (2/70)</td>
<td>3% (2/61)</td>
<td>0.9</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>96% (67/70)</td>
<td>95% (58/61)</td>
<td>0.8</td>
</tr>
<tr>
<td>General medical unit</td>
<td>51% (36/70)</td>
<td>54% (35/61)</td>
<td>0.5</td>
</tr>
<tr>
<td>Current smoker</td>
<td>18% (13/70)</td>
<td>13% (8/61)</td>
<td>0.2</td>
</tr>
<tr>
<td>English as first language</td>
<td>76% (53/70)</td>
<td>74% (45/61)</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Table 3. Vaccination rates for influenza and pneumococcal vaccine for various groups (including risk groups)

<table>
<thead>
<tr>
<th>Variable</th>
<th>% of total (n)</th>
<th>% vaccinated for influenza (n)</th>
<th>% vaccinated for pneumococcus (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic disease</td>
<td>93 (564/606)</td>
<td>71 (403/564)</td>
<td>41 (233/564)</td>
</tr>
<tr>
<td>Immunosuppressed</td>
<td>9 (54/606)</td>
<td>69 (37/54)</td>
<td>50 (27/54)</td>
</tr>
<tr>
<td>Nursing home</td>
<td>7 (45/606)</td>
<td>72 (32/45)</td>
<td>31 (14/45)</td>
</tr>
<tr>
<td>Smoker</td>
<td>13 (80/606)</td>
<td>65 (52/80)</td>
<td>40 (32/80)</td>
</tr>
<tr>
<td>Foreign born</td>
<td>51 (307/606)</td>
<td>70 (215/307)</td>
<td>39 (121/307)</td>
</tr>
<tr>
<td>Total</td>
<td>100 (606)</td>
<td>70 (426/606)</td>
<td>41 (248/606)</td>
</tr>
</tbody>
</table>

A total of 67% (402/606) of patients indicated that they had received influenza vaccine in the past (prior to 1998), and 55% (332/606) had received it in 1997. Figure 2 shows influenza vaccination rates by month, and indicated that 42% of vaccinated patients had been vaccinated by March and 70% by April 1998.

A total of 41% (248/606) of patients had received pneumococcal vaccine within the past five years. Of these, 80% (197/248) received the vaccine in 1998. Only 13% (33/248) received vaccine in 1997. Figure 3 shows the rate of pneumococcal vaccination status of patients by recent years. Only 9% (23/248) reported any adverse events associated with the vaccine, all of which were local
reactions and other minor side effects. Of those who were not vaccinated against pneumococcus, only 21% (75/355) had heard about pneumococcal vaccine. Of these, 40% (30/75) said they intended to be vaccinated, but had not yet got around to it.

Differences between Interventions

Influenza Vaccine. For influenza vaccine, 63% (17/27) of patients in arm A (hospital) were vaccinated, compared to 50% (9/18) in arm B (GP). In univariate analysis, this difference was not significant (p = 0.58). The relative risk for vaccination in hospital compared to in the community was 1.26 (95% CI 0.73–2.17). Only one of the 26 patients who received influenza vaccine had an adverse event (local pain and inflammation).

Pneumococcal Vaccine. For pneumococcal vaccine, 67% (47/70) of patients in arm A (hospital) were vaccinated, compared to 55% (32/58) in arm B (GP). This difference was not significant (p = 0.22). The relative risk for vaccination in hospital compared to in the community was 1.22 (95% CI 0.92–1.62). Of all the patients who received pneumococcal vaccine, 18% (14/79) reported adverse events, all of which consisted of minor local reactions.

When all vaccinations were analysed in combination, 67% (47/70) of patients were vaccinated in hospital compared to 54% (33/61) by GPs. This difference was not significant (p = 0.1).

For patients in the hospital arm who consented but did not get vaccinated, the most common reasons for not being vaccinated (in order of frequency) were: the hospital doctor not recommending or prescribing the vaccine (33%); patient refusal at the time vaccination was offered (21%); patient preference to get vaccinated by their own GP (21%), and vaccine order being written up but not given (19%).

Follow-Up

By 1 month of follow-up, 50/131 (38%) of the randomised patients had been readmitted to hospital and 5 patients (3.8%) were reported as deceased by their GPs. Of the readmissions, 2/50 (4%) were for pneumonia. One of these two was unvaccinated. At 3 months of follow-up, 50% (65/131) had been readmitted and 12/131 (9%) were deceased. The causes of death and hospitalisation were not related to immunisation in any of these cases.

Discussion

There was high vaccination coverage for influenza at the start of the study, and as a result we had low numbers of patients who were eligible for this vaccine. Our study found that patient recall of vaccination, when validated against GP records, was fairly accurate, with only 4% disagreement between the two sources.

We were unable to demonstrate a significant difference in effectiveness between hospital and GP reminder systems for adult immunisation, but there was a trend towards hospital vaccination rates being higher. Both strategies increased vaccine uptake in this high-risk group of patients, but there were still significant missed opportunities for vaccination. It is disappointing that our alert system in hospital, which included a written and verbal prompt, as well as provision of the vaccine, still left over 30% of eligible patients unvaccinated. We were able to examine the reasons for not vaccinating patients in the hospital arm, and found that omission by medical and nursing staff, as well as patient refusal, were important factors. Low perceived importance of vaccination by both staff and patients, as well as misinformation about the contraindications for vaccination may play a role. There may also be a lack of faith in the efficacy of the vaccines. We also found that 19% of unvaccinated patients in the hospital arm refused vaccination because they preferred to be vaccinated by their own GP. This highlights the importance of the relationship between patients and their GPs, as well as the role of continuity of care, in delivering vaccination.

There are many effective strategies to improve uptake of adult vaccination, which have been demonstrated in various countries and sites, including educational campaigns (directed at both patients and providers), advertising, reminder letters to GPs or patients, and opportunistic vaccination of eligible people [23–28]. One study found that sending a reminder letter to patients increased the vaccination rate for influenza from 20 to 47% in the 65 and over age group [27]. In another study, reminder letters sent to patients increased influenza vaccination rates from 50 to 66% [29]. It has also been shown that if vaccine is provided free of charge, the supplementary strategy of patient education increases influenza immunisation rates more than offering financial incentives to the patient [28]. Our data show that provision of free pneumococcal vaccine increased coverage in the study population from 13% in 1997 to 41% in 1998. One study showed that the availability of free-of-charge vaccines is not sufficient to ensure a high vaccination rate on its own, and that educational
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programs need to be effected to have an impact [30]. It is important to realise that few of these strategies have worked in isolation.

The rates of pneumococcal vaccination are far lower than the desired rates of 80% or higher, but are a vast improvement on described rates in previous years. Of concern were the particularly low rates (31%) in nursing homes, which are a high risk setting. Unlike influenza vaccination, which has been the subject of annual immunisation campaigns since 1993 in Victoria, pneumococcal vaccine has not been promoted as widely. Only 22% of the unvaccinated subjects had ever heard of pneumococcal vaccine, and the only study subject with asplenia was not vaccinated. Our data suggest that an educational and promotional campaign for consumers and providers would improve pneumococcal vaccination rates. One study showed an increase in pneumococcal vaccination rates from 4 to 33% following a GP-based vaccination campaign [11]. The combination of such a campaign in Victoria, together with provision of free vaccine, may further increase uptake.

Our study is subject to the following caveats: we may not have had the power to describe differences in the two reminder systems. This study describes an in-patient population, and may not reflect the same age group in the community as a whole. However, we calculated that a significant proportion of the 65 and over age group are hospitalised each year, so that studying hospitalised inpatients is important. In addition, hospitalised patients are likely to represent the sickest group and those at most risk for the complications of influenza and pneumococcal disease. This is highlighted by the fact that 50% of patients were readmitted to hospital within 3 months of discharge. Furthermore, the episode of hospitalisation represents a valuable opportunity to vaccinate eligible, high-risk people. We also cannot exclude the possibility of a selection bias caused by the high refusal rate (46%) of eligible, unvaccinated patients. We described some differences in age, sex and chronic disease status between patients who refused and those who consented, suggesting that such a selection bias may have been present. If unvaccinated patients are more likely to have refused vaccination, we would have overestimated the effectiveness of both hospital and GP vaccination. As randomisation was performed after consent, the effects of such bias are likely to be distributed equally between the two arms, and therefore are unlikely to have affected the comparison between the two arms. We only studied selected specialist and generalised medical wards – these may have contained sicker patients than, for example, surgical wards. Any bias introduced by the sampling of only medical wards (whose patients may be different from other wards in terms of severity of illness and number of comorbidities) may tend to overestimate the baseline vaccination rates, but would be unlikely to affect the difference between the two interventions in unvaccinated patients.

Ultimately, the community and the hospital are both important points of contact where eligible patients could be vaccinated, although patients may have a preference for being vaccinated by their GP. The high rate of readmission to hospital that we found indicates that there may be multiple hospital opportunities for vaccination of any one patient. Resident medical staff need reminders of the importance of inquiring about vaccination status of all admitted patients. Nursing homes, which house ‘captive’ populations, are also an important site for vaccination, and should have vaccination policies in place. The effectiveness of reminder systems in any of these settings would be enhanced by educational campaigns directed at both providers and patients.

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References


