A Comprehensive Pharmacist Intervention to Reduce Morbidity in Patients 80 Years or Older

A Randomized Controlled Trial

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Background: Patients 80 years or older are underrepresented in scientific studies. The objective of this study was to investigate the effectiveness of interventions performed by ward-based pharmacists in reducing morbidity and use of hospital care among older patients.

Methods: A randomized controlled study of patients 80 years or older was conducted at the University Hospital of Uppsala, Uppsala, Sweden. Four hundred patients were recruited consecutively between October 1, 2005, and June 30, 2006, and were randomized to control (n = 201) and intervention (n = 199) groups. The interventions were performed by ward-based pharmacists. The control group received standard care without direct involvement of pharmacists at the ward level. The primary outcome measure was the frequency of hospital visits (emergency department and readmissions [total and drug-related]) during the 12-month follow-up period.

Results: Three hundred sixty-eight patients (182 in the intervention group and 186 in the control group) were analyzed. For the intervention group, there was a 16% reduction in all visits to the hospital (quotient, 1.88 vs 2.24; estimate, 0.84; 95% confidence interval [CI], 0.72-0.99) and a 47% reduction in visits to the emergency department (quotient, 0.35 vs 0.66; estimate, 0.53; 95% CI, 0.37-0.75). Drug-related readmissions were reduced by 80% (quotient, 0.06 vs 0.32; estimate, 0.20; 95% CI, 0.10-0.41). After inclusion of the intervention costs, the total cost per patient in the intervention group was $230 lower than that in the control group.

Conclusion: If implemented on a population basis, the addition of pharmacists to health care teams would lead to major reductions in morbidity and health care costs.

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of all prescribed drugs. A national initiative has focused on this patient group, with the aim of investigating the extent of drug-related morbidity and mortality as a means of increasing patient safety. Our study was initiated in this context at the University Hospital of Uppsala, Uppsala, Sweden, in 2005.

The objectives of our study were to assess the effectiveness of interventions performed by ward-based pharmacists on morbidity and overall use of secondary (hospital) care. The primary prespecified outcome measure was the frequency of hospital visits (emergency department [ED] visits and readmissions [total and drug-related]) during the 12-month follow-up period. The secondary exploratory outcome measure was the cost of hospital care.

**METHODS**

**STUDY DESIGN**

The study was a randomized controlled trial. We compared hospitalized patients receiving standard (nonpharmacist) care with those receiving more comprehensive enhanced services in which a pharmacist was part of the health care team.

**PARTICIPANTS**

From October 1, 2005, to June 30, 2006, 400 patients 80 years or older were included from 2 acute internal medicine wards at the University Hospital of Uppsala. Patients from both wards were randomly assigned to intervention or control groups using block randomization with a closed-envelope technique. Randomization was performed in blocks of 20 (each block contained 10 intervention and 10 control allocations). Patients were excluded if they had previously been admitted to the study wards during the study period or had scheduled admissions. Each participant gave written informed consent, and the study protocol was approved by the regional ethics committee.

**PHARMACIST INTERVENTION**

The main elements of the enhanced service provided by clinical pharmacists (U.G. and A.A.) to patients in the intervention group were as follows: A comprehensive list of current medications was compiled on admission to complement that obtained in the ED, ensuring that the medication list received by the ward was correct. A drug review was performed, and advice was given to the patient’s physician on drug selection, dosages, and monitoring needs, with the final decision made by the physician in charge. Patients were educated and monitored throughout the admission process, and received discharge counseling. Information about discharge medications (eg, rationale for changes, therapeutic goals, and monitoring needs for newly commenced drugs) was communicated to the primary care physicians by the pharmacists (U.G. and A.A.). A follow-up telephone call to patients 2 months after discharge was conducted.

Patients in the control group received standard care without pharmacist involvement in the health care team at the ward level. Standard care usually included the same elements as those of the enhanced service but was less extensive, focusing mainly on the cause of admission, and was performed by physicians and nurses. Patients were informed of the group to which they had been randomly allocated.

Standard operating procedures for the enhanced service were prepared by the study pharmacists (U.G. and A.A.) during the preceding pilot study and were peer reviewed in an open forum multiprofessional discussion and revised accordingly. Three clinical pharmacists (U.G., A.A., and Anna Finquist, MSc Pharm) who had taken postgraduate courses in clinical pharmacy (1 had an MSc in clinical pharmacy [U.G.] and the other 2 had completed a 10-week course on the subject [A.A. and Finquist]) and had hospital work experience to various degrees were involved in the care of the intervention group, which took place on weekdays between 8 AM and 4 PM. Throughout the study period, a multiprofessional reference group (U.G., A.A., D.H., H.T., H.M., and C.M. and Agnete Eklund, RN, Astrid Forsstrom, MSc Pharm, and Ann-Sophie Norrman-Lawasani, RN) conducted regular meetings to assess the study process and to monitor patient safety.

**ADMISSIONS**

Relevant demographic and medical data were collected from all patients in the intervention group and summarized on a patient registration form. Data included age, sex, medical history, reason for admission, and drug history. A comprehensive list of current medications was compiled by the pharmacist (U.G. or A.A.) from various information sources, including interviews with the patient, prescriptions and drug lists from primary care centers, and the patient’s computerized hospital medical record. Identified transcription errors and faulty omission or addition of drugs owing to incomplete drug history were reported to the patient’s physician and corrected.

A semistructured interview was undertaken with all patients (or their next of kin or caregiver). The interview involved questions about adherence to and understanding of the drug therapy regimen, perceived problems and adverse effects, use of over-the-counter drugs, complementary and alternative medicines, and other topics. Advice was given in a patient-centered manner (ie, the patient’s viewpoint was actively sought).

**INPATIENT STAY**

The pharmacist (U.G. or A.A.) performed a comprehensive review of factors associated with the patient’s drug therapy, which addressed issues of indication, effectiveness, safety, and adherence and followed the well-defined procedure developed by Cipolle et al. Information sources included admission files, the patient’s medical record, and clinical chemistry, urinalysis, and hematologic findings. All data were recorded on a patientspecific documentation sheet. Relevant DRPs for the patient were discussed among the health care team during ward rounds. Necessary adjustments to the drug treatment were then made by the patient’s physician. The patient’s response to drug treatment was monitored throughout the hospital stay. Counseling was provided to individual patients regarding newly commenced or newly discontinued drugs. The counseling sessions were not standardized or recorded in the patient documentation sheets. Patients received counseling to the extent that the pharmacist thought appropriate for each individual.

The DRPs identified by the pharmacist were recorded in a database. Also recorded were suggested actions and outcomes (ie, whether the action was performed).

**DISCHARGE**

Patients in the intervention group received counseling about their medications from the pharmacist as a complement to the physician’s discharge information. On the study wards, a discharge letter summarizing the patient’s hospital experience is
readmissions and visits to the ED were collected, along with care use during the follow-up year. Data such as numbers of patients’ national identification numbers were entered into the hospital’s patient administrative system to explore secondary admissions. After the study had been closed, all patients during the 12-month follow-up period received the enhanced service again. The study was closed 12 months after the last patient had been admitted. The patients who were unable to communicate coherently. The pharmacist contacted the next of kin or caregiver of the ward was required to approve the contents of the pharmacist’s discharge letter before it was sent to the patient’s general practitioner with the original discharge letter. The pharmacist provided a comprehensive account of all changes in drug therapy during the hospital stay, including the rationale behind medication decisions, monitoring needs, and expected therapeutic goals. Any DRPs not yet dealt with were listed, with suggested actions. The physician responsible for the patient on the ward was required to approve the contents of the pharmacist’s discharge letter before it was sent to the patient’s general practitioner with the original discharge letter. The pharmacists’ discharge letters were not given to the patients.

2-MONTH FOLLOW-UP

Pharmacists contacted the intervention group patients by telephone 2 months after discharge to ensure adequate home management of medications. The rationale for choosing 2 months was that the patient would then have had time to see his or her general practitioner after discharge. Another assumption was that adherence decreased with time and that the intervention group should get a motivational “boost” after a reasonable amount of time. Any additional changes in drug therapy made after discharge were recorded, and patients were encouraged to ask questions. The pharmacist contacted the next of kin or caregiver of patients who were unable to communicate coherently.

OUTCOMES

The study was closed 12 months after the last patient had been discharged. Intervention group patients who had been readmitted during the 12-month follow-up period received the enhanced service again. After the study had been closed, all patients’ national identification numbers were entered into the hospital’s patient administrative system to explore secondary care use during the follow-up year. Data such as numbers of readmissions and visits to the ED were collected, along with the costs associated with each visit or admission. A patient administrative system was used (IMX; TietoEnator, Kista, Sweden) that is based on International Statistical Classification of Diseases, 10th Revision codes and on diagnosis related groups. The electronic medical records were used to establish the reasons for readmission and the current medication list for each readmission. The physician in charge of the patient was required to document in the medical record if readmissions were drug related. The physicians making this decision were blinded as to whether the patients were study participants. The researchers (U.G. and A.A.) responsible for analyzing readmission data were blinded regarding the group to which the patients had been randomized.

STATISTICAL ANALYSIS

The sample size calculations were based on results from a previously performed pilot investigation and from a study conducted by Scullin et al. To detect a 15% reduction in hospital visits with 80% power, we needed to enroll 162 patients in each group. To compensate for dropouts, the number was increased to 200 patients in each group. Comparisons between the intervention and control groups were made by logistic regression analysis for binary responses using odds ratios, by Cox proportional hazards model for survival data using relative risks, by linear regression analysis for continuous responses using differences, and by Poisson regression analysis for incidences using the log of time spent by patients outside of the hospital as offset and using fractions for comparisons. The choice of comparison measure was made to enable use of simple statistical tools. All statistical analyses were performed using the statistical program package R (R Project for Statistical Computing, Department of Statistics and Mathematics, Wirtschaftsuniversität Wien, Vienna, Austria).

RESULTS

Consecutive patients were asked to participate in the study based on the inclusion and exclusion criteria. Of 482 patients invited to participate in the study, 82 declined. The most common reason for declining was that patients thought it was unnecessary because they expected to be discharged soon. Of 400 randomized patients (199 intervention and 201 control), 5 patients (4 intervention and 1 control) asked to be excluded from the study soon after randomization, and 27 patients (13 intervention and 14 control) died during their first (index) admission and were excluded from further analyses. This left 368 evaluable patients. Figure shows the flow of patients through the study. All 368 patients were followed up for the predefined period of 12 months, and costs, details of visits to the ED, and readmissions were monitored for all patients.

The groups were well balanced except in 2 respects (Table 1). First, more patients in the intervention group had a history of cerebral vascular lesions (20.9% vs 10.2%, P = .006). Second, the intervention group patients were taking more prescription drugs (8.7 vs 7.3, P = .004). The inclusion of 27 patients who died during their index admission did not alter these differences. The mean age of the patients was 86.6 years, 58.7% were female, and 46.5% received help with their medications and daily activities from a spouse or nursing staff member at a residential home. The pharmacists identified a need for increased
support for 30% of the self-medicating patients in the intervention group.

The mean duration of the index hospitalization was 11.2 days (range, 1-98 days); however, the last part often took place in a rehabilitation ward, which was excluded from the study. The mean time that the pharmacist spent on each patient was 2 hours and 20 minutes.

In total, 476 DRPs (as defined by Cipolle et al30) were identified by the pharmacists for the intervention group patients during their index admission. The most common DRPs were adverse drug reaction (n=119), need for additional drug therapy (n=90), unnecessary drug therapy (n=86), dosage too high (n=78), noncompliance (n=41), and dosage too low (n=39).

All DRPs were communicated to the physician in charge of the patient, and suggested actions were presented. The most frequent suggestions were discontinuation of drug therapy (n=150), initiation of drug therapy (n=86), reduction in dosage (n=78), and change of drug or drug formulation (n=45). Suggested actions were carried out in 75% of the cases (69% in the hospital by the physician in charge of the patient and 6% after discharge by the general practitioner). Twenty-three percent of the suggested actions were rejected, and for 2% the result was unknown. Transcription errors and faulty omission or addition of drugs were frequently detected by the pharmacists.

**HOSPITALIZATIONS AND DEATHS**

The numbers of hospitalizations and deaths during the study are summarized in Table 2. Of 368 analyzed patients, 32.1% (118 patients [37 intervention and 61 control]; P=.82, Fisher exact test) died before the end of the 12-month follow-up period. Of 230 surviving patients, 34.8% (87 patients [48 intervention and 39 control]; P=.29, Fisher exact test) did not revisit the hospital. For the intervention group, there was a 16% reduction in all visits to the hospital (ED visits plus readmissions; quotient, 1.88 vs 2.24; estimate, 0.84; 95% confidence interval [CI], 0.72-0.99) and a 47% reduction in visits to the ED (quotient, 0.35 vs 0.66; estimate, 0.53; 95% CI, 0.37-0.75). There were no significant differences between groups in the number of patients readmitted to hospital or the total number of readmissions.

**DRUG-RELATED READMISSIONS**

There was limited information in the case notes about reasons for visits and patients’ medication use before visits. Therefore, analyses of drug-related ED visits were not possible.

Fifty-four of 440 readmissions (12.3%) were considered directly due to suboptimal drug therapy (Table 3). Of 54 drug-related readmissions, 9 were in the intervention group, and 45 were in the control group (quotient, 0.06 vs 0.32; estimate, 0.20; 95% confidence interval [CI], 0.10-0.41). The most common reason for drug-related readmission was over-prescribing of psychotropic drugs (eg, sedatives, opioids, and anticholinergic agents) resulting in confusion, falling, and sedation, followed by overprescribing of antihypertensive and diuretic agents resulting in bradycardia, hypotension, and dehydration. Of 9 drug-related readmissions in the intervention group, 4 could have been avoided, as the pharmacist had suggested alterations in drug therapy (dosage reductions for digoxin, furosemide, and 2 antihypertensive agents) that had not been acted on.
The cost of implementation of this intervention in everyday practice would be approximately $170 per patient, based on the salary of 1 clinically trained, experienced pharmacist working at 0.5 full-time equivalents for 9 months with 182 patients (Table 4). Cost savings balanced against the cost of the intervention was $230 per patient.

### COST OF INTERVENTION

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**Table 3. Drug-Related Readmissions**

<table>
<thead>
<tr>
<th>Drug-Related Cause for Readmission</th>
<th>Intervention Group (n=9)</th>
<th>Control Group (n=45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dipoxin intoxication</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Overprescribing of antihypertensive agents</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>Suboptimal drug therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Dehydration due to overprescribing of diuretics</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Anemia due to aspirin or nonsteroidal anti-inflammatory drugs</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Confusion and/or fall due to sedatives, opioids, or anticholinergic drugs</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Diarrhea due to antibiotic treatment</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Hyperkalemia</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Hyponatremia due to diuretics and selective serotonin reuptake inhibitor therapy</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Lack of drug treatment for atrial fibrillation (embolism)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding (hematoma) due to warfarin sodium</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 4. Direct Costs per Patient for Visits to the Emergency Department and for Readmissions**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention Group, $</th>
<th>Control Group, $</th>
<th>Estimate, $ (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>12 100</td>
<td>12 500</td>
<td>−400 (−4000 to 3200)</td>
</tr>
<tr>
<td>Visits to the emergency department</td>
<td>160</td>
<td>260</td>
<td>−100 (−220 to −10)</td>
</tr>
<tr>
<td>Readmissions</td>
<td>12 000</td>
<td>12 300</td>
<td>−300 (−3900 to 3300)</td>
</tr>
<tr>
<td>Cost of interventionb</td>
<td>170</td>
<td>170</td>
<td></td>
</tr>
</tbody>
</table>

a Comparison using difference.
b Calculated salary for 1 clinical pharmacist for 9 months at 0.5 full-time equivalents.

To our knowledge, this is the only randomized controlled study of the effectiveness of pharmacist interventions in reducing drug-related morbidity and use of secondary care in patients 80 years or older. The inclusion of study participants in this age group who have been acutely admitted to the hospital selects for individuals who are generally frail with a high risk of mortality. Despite this, we demonstrated a 16% reduction in all visits to the hospital and a 47% reduction in visits to the ED. The study did not have sufficient power to detect a reduction in readmissions alone, possibly due to the high morbidity and mortality in the population.

Pharmacists directly involved in patient care are scarce in hospitals and other health care settings in Sweden. The past few years have seen an increase in the number of clinical pharmacists, but debate continues about which profession is best suited to perform drug reviews and carry out other methods of improving drug therapy.

Holland et al32 determined the effects of pharmacist-led medication review in older patients (mean age across the studies, 71 years) by means of a systematic review and meta-analysis. Thirty-two studies were included, and the researchers concluded that there was no evidence of beneficial effects on hospital admissions and deaths, although positive effects were seen on other end points such as knowledge and adherence. However, only 8 of 32 studies were hospital based; furthermore, there was no direct communication between the pharmacist and the prescriber in half of the studies, and the pharmacist did not have access to medical records in a third of the studies. Therefore, the lack of evidence from the meta-analysis could be partly explained by the suboptimal design of many of the studies.

In contrast to the findings by Holland et al,32 a systematic review performed by Koshman et al33 of 12 randomized controlled studies showed that the addition of a pharmacist to a multidisciplinary heart failure team reduces the rates of all-cause hospitalization and heart failure hospitalization by almost one-third (mean age across the studies, 70 years). However, this effect was not seen if care was directed by and provided by the pharmacist alone.33 Similarly, a recent hospital-based study21 from Northern Ireland showed that pharmacist intervention was associated with significantly fewer readmissions and shorter durations of stay. However, participants in Northern Ireland were significantly younger than those in our study (mean age, 70.1 vs 86.6 years).

In our opinion, hospital pharmacists with postgraduate clinical knowledge and training are best suited to perform the tasks in the setting described herein. However, for pharmacists to make a difference in patient care and medication management, we believe that physicians, pharmacists, and nurses should work together as a team, which is usually easier to accomplish in a hospital setting than in community or primary care. To achieve this, pharmacists need access to all information sources that are available to physicians and nurses, and, perhaps most important, pharmacists need to be able to meet the patient. Patients provide pertinent information about their medication use, and preliminary evidence shows that patient
involvement has a positive effect on compliance with treatment regimens.34

There are some important potential drawbacks associated with our study. For example, only 3 pharmacists were involved, which limits the generalizability of the results. Also, the number of included patients could have been higher to compensate for the high mortality rate. We also had limited information about the extent of visits to primary care facilities during the follow-up year. However, the mean cost of a primary care visit is only about one-fifth of the cost of a visit to the ED. Therefore, the total direct costs would be affected by group differences to only a minor extent.

The randomization of patients from both wards to the control and intervention groups may have increased the risk of contamination bias. The physicians on each ward treated patients from both groups in that ward, and the presence of pharmacists on the wards may have resulted in increased efforts from physicians to optimize drug therapy for control group patients. Therefore, the difference in the number of visits to the hospital may have been greater had the intervention been carried out on one ward and the results compared with standard care on a separate ward. However, doing so would mean a higher risk of achieving nonequivalent patient groups.

The findings of more prescribed medications and greater incidence of cerebral vascular lesions in the intervention group suggest that the risk of drug-related morbidity and subsequent hospital visits was potentially higher in this group than in the control group. However, despite this, the results for these outcome measures were not in favor of the intervention group. Another viewpoint is that these group differences represent specific scopes for the pharmacists’ interventions on the grounds that certain diseases are more positively sensitive to pharmacist contributions.

Individualized patient counseling during the hospital stay, the follow-up telephone call 2 months after discharge, and communication with practitioners in primary care seem to be important factors in reducing hospital visits. Patients’ sense of security and motivation is increased, and risk of medication errors and adverse drug events is reduced. In an earlier study33 that evaluated a medication counseling service from a patient perspective, patients stated that their perceptions of greater control of their drug treatment and increased safety were the most tangible effects of the service.

The number of drug-related readmissions differed greatly between the groups, with 5 times as many in the control group compared with the intervention group (45 vs 9 readmissions). This was not an absolute outcome measure, as results were based on the (albeit blinded) judgment of the physician in charge at the ED, which was documented in the medical record as the reason for admission. Most of the 54 readmissions were clearly drug related, with drug concentrations and clinical chemistry results as supporting evidence. The specific factors and agents responsible for these drug-related readmissions underscore the strong need for close dosage monitoring in this older population. Overvigorously reduction of blood pressure or heart rate, ordering of high-dosage diuretics, and overprescription of medications with negative effects on the central nervous system were the most common causes of adverse drug events leading to acute admissions. In contrast, treatment of heart failure and diabetes mellitus commonly resulted in suboptimal dosages and underuse of medication because of poor adherence.

Balanced cost savings (actual costs of hospital care minus estimated costs of the intervention) were $230 per patient in our study. Extrapolated over a 12-month period when 2538 medical patients in the age group of 80 years or older visited the University Hospital of Uppsala (ED visits and admissions) and 877 patients in the age group 80 years and older visited the ED, the cost savings based on our results would be $1,060,000 for total visits and $92,000 for ED visits. On a population basis, our results suggest that the addition of pharmacists to health care teams would lead to major reductions in morbidity and health care costs.

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Author Contributions: Mss Gillespie and Alassaad contributed equally to this work and should be considered as equal first authors, and Drs Melhus and Mörlin contributed equally to this work and share the last authorship. Mss Gillespie and Alassaad had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Gillespie, Alassaad, Henrohn, Toss, and Mörlin. Acquisition of data: Gillespie and Alassaad. Analysis and interpretation of data: Gillespie, Alassaad, Henrohn, Garmo, Hammarlund-Udenaes, Kettis-Lindblad, Melhus, and Mörlin. Drafting of the manuscript: Gillespie, Alassaad, Henrohn, and Mörlin. Critical revision of the manuscript for important intellectual content: Gillespie, Alassaad, Henrohn, Garmo, Hammarlund-Udenaes, Toss, Kettis-Lindblad, Melhus, and Mörlin. Financial Disclosure: None reported.

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