ORIGINAl RESEARCH

Clinical pharmacist review: A randomised controlled trial

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Abstract

Objectives: To determine if medication review by a clinical pharmacist of older patients in the ED impacted on admission to hospital and other outcomes.

Methods: A stratified, randomised controlled study comparing the intervention to current practice. A tertiary referral ED in New South Wales, Australia. Older people (>70 years) living at home who initially reported taking greater than five medications. Medication review by an experienced hospital pharmacist within the ED. Rate of admission, rate of readmission, length of stay and admission to an aged care facility at 4 months post presentation, and rate of general practitioner acceptance of pharmacist recommendations.

Results: The odds of admission decreased for those receiving the intervention (odds ratio [OR] = 0.68, 95% confidence interval [CI]: 0.53, 0.87; \( P = 0.002 \)). There was no evidence that the intervention affected hospital length of stay for admitted patients (0.09 days change, 95% CI −0.08, 0.25; \( P = 0.31 \)), the rate of re-presentation (0.08% change, 95% CI −0.12, 0.28; \( P = 0.44 \)) or admission to an aged care facility. The odds of admission to an aged care facility increased with the Identification of Seniors at Risk score. General practitioners adopted 49% of pharmacists’ recommendations.

Conclusions: The presence of an experienced pharmacist in the ED reduced hospital admissions. Further study is required to determine longer term impacts of General Medical Practitioner acceptance of pharmacists’ recommendations.

Key words: aged, emergency service, hospital, medication reconciliation, pharmacy service, polypharmacy.

Introduction

Many older patients, because of a range of chronic and often complex conditions, are prescribed multiple medications to manage these conditions. Polypharmacy is defined as ‘the use of five or more drugs, including prescribed, over-the-counter, and complementary medicines’.1 Polypharmacy places older patients at increased risk of adverse drug reactions and interactions, as well as problems with compliance and the financial burden of their medication costs. Adverse events associated with polypharmacy are common reasons for older people presenting to the ED that might also lead to hospital admission.2,3

There are a number of methods for reviewing medications. Beers4 criteria for the use of inappropriate medication in older people comprises a list of medications for which the risks are thought to outweigh the benefits in this population.

Home Medicines Reviews in the Community5 by pharmacists and pharmacist-led documentation of patients’ medications on admission to hospital to avoid medication errors6,7 are not new or novel concepts. However, combining the two approaches to older patients (>70 years) presenting to an ED might assist with accurately documenting pre-admission medications early, alert hospital doctors to potential concerns and allow for the provision of an ED clinical pharmacist medication review (EDMR).

Key findings

- Adverse events related to polypharmacy are a common reason for older people to present to EDs.
- Admission rate was lower for patients who had their medication reviewed by the clinical pharmacist.
- On average, patients were taking 3.8 more medications than they self-reported.
- Clinical pharmacist recommendations were generally accepted by the general practitioner.

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for patients who might not require hospitalisation. There have been limited numbers of related studies in Australia, some prospective but none randomised.1–11 Specifically, there was no information regarding the attitude of general practitioners (GPs) to having advice provided by hospital pharmacists. Relevant studies were found in overseas settings.7,13,14

The Identification of Seniors at Risk (ISAR)15 (Appendix S1) screening tool improves detection of older people who present to the ED who are likely to have an increased need for health services.15–17 By identifying patients with the greatest needs, the clinical pharmacist is well positioned to direct their review to those older people who are most likely to benefit.

The aim of the present study was to determine whether an experienced clinical pharmacist reviewing the medications of older patients in an ED setting could reduce hospital admissions. Secondary outcomes included readmissions, length of stay, admission to an aged care facility and improved medication management via the use of an EDMR with feedback faxed to the patients’ local GPs.

Methods

The present study used a single site, randomised controlled trial design that was stratified on ISAR score. Block randomisation by strata was performed with block sizes of 4 or 6 by an independent statistical unit (Clinical Research Design, Information Technology, and Statistical Support [CReDITSS] Unit) at Hunter Medical Research Institute, using a random number generator with a seed.18 The randomisation list was held by the study co-ordinator and assigned sequentially to the next participant referred by the ED clinicians. Older people aged over 70 years presenting to the study ED were randomised to either the intervention EDMR group or to the control group (usual care).

Participants

Patients were included if they lived at home and reported taking more than five medications daily, and excluded if they lived in a residential aged care facility (RACF). The ISAR screening tool11 was used to stratify patients into two groups: those more likely to represent to an ED or be admitted (ISAR positive = score of 3 or more) and those less likely (ISAR negative = score of 2 or less).

Study setting

The setting for the study was the ED of a large tertiary referral hospital in NSW, Australia, from October 2011 to June 2012. In 2012, the tertiary referral hospital ED had 70 000 ED presentations, 16% of whom were over 70 years of age. As a tertiary referral hospital with over 550 adult beds, it serves a population of 850 000 people from metropolitan to rural and remote communities across a geographic area of 130 000 square kilometres.

The intervention

The pharmacist was in the ED Monday to Friday 8:30am–5pm. People over the age of 70 years who presented to the ED were identified and referred by the Aged Services Emergency Team Registered Nurse (ASET) to the trial pharmacist who provided information about the study and obtained informed consent to participate in the trial. The pharmacist undertook initial data collection and stratification of the older person by completing the ISAR questionnaire. The older person was then randomised to receive an EDMR or not; therefore, allocation was randomised but not concealed.

An EDMR involved a clinical pharmacist obtaining a medication list from the patient’s GP, a 6–12 month dispensing history from their community retail pharmacy and interviewing the patient about their medication use. Concerns about medication overdose; non-compliance; duplication of therapy; missing therapy; drug interactions; doses in older people; drug-condition precautions; drugs without clear indications; suspected adverse reactions; and/or drug selection were documented.19–21 Medications were also assessed in terms of the Anticholinergic Burden Scale22 and the Beers criteria.4

The study was approved by the Local Health District Research Ethics Committee.

Outcomes

Four months after discharge from the ED, the older patient, their GP and community retail pharmacy were contacted to obtain a medication history at that time. Data collected included medications, if the patients had been admitted to an RACF and if the patient had re-presented to the ED. The person making the call was blinded to the individual’s group allocation.

Statistical methods

Continuous variables were summarised using means and standard deviations. Categorical variables were summarised using counts and percentages of each category. P-values resulting from t-tests and χ²-test are given to examine changes in the variables between each intervention and ISAR group.

For hospital admission, a logistic regression model was fitted with age, intervention group and ISAR score as the predictors; these were judged to be the most important confounders indicated by the literature. Crude and adjusted odds ratios and P-values are reported for completion. However, given that allocation was randomised and baseline characteristics were evenly distributed, we believe that randomisation was achieved and that the unadjusted outcomes are not confounded. For the outcome ‘Transfer to RACF’, a multinomial logistic regression was fitted comparing the outcomes ‘No’, ‘Yes’ and ‘Deceased’. Separate models were also given for each ISAR group (positive and negative). A P-value of 0.05 was used to determine statistical significance.

A sample size calculation was based on the assumption of a 50% admission rate in the control group, decreasing to 40% in the intervention group, with a power of 80% and P = 0.05; this led to a minimum target recruitment of 410 per group over the 8 month period of the trial.
Results

One thousand and ninety-four patients were referred by ASET nursing staff to the pharmacist over this period. Thirteen reviewed patients were deemed ‘Not eligible’ for the study as they were residents of aged care facilities or were unable to answer the ISAR questions. Of the remaining 1081 patients, 604 patients were ISAR positive (ISAR score 3 to 6) and 477 patients were ISAR negative (ISAR score 0 to 2). Sixty of these patients were missing data on admission status or group assignment and were excluded. Reasons for exclusion included: older patient who initially said they took >5 meds but did not; or who were discharged before being approached (total n = 60, Fig. 1).

Three hundred and seven ISAR positive patients were randomised to the intervention group. One hundred and twenty-four of these patients were discharged from the ED with resulting recommendations being relayed by fax to their GPs.

Two hundred and eighteen ISAR negative patients were randomised to the intervention group. One hundred and twenty-four of these patients were

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discharged from the ED, resulting in any recommendations being relayed by fax to their GPs.

Across the ISAR groups, there were 525 in the intervention arms and 496 in the control arms, exceeding the target sample size. The baseline demographics were evenly distributed across the intervention and control arms and are listed in Table 1.

The raw event numbers are listed in Table 2, by intervention group and by ISAR subgroup.

**Risk of admission**

The absolute crude admission rate was 9% lower in the intervention group compared with the control group (53% vs 62%, respectively, \( P = 0.003 \)). This equates to an adjusted odds ratio for admission of 0.67, that is the odds of admission decreased by 33% for those receiving the intervention (Table 3, \( P \)-value = 0.0017). This effect was similar and statistically significant within the ISAR positive and negative groups separately.

**Length of stay**

There was no evidence that the intervention had an effect on the length of stay for admitted patients (Tables 2,3) with a point estimate of 0.09 days difference between the groups (\( P = 0.31 \)).

**Re-presentation to ED**

There was no evidence that the intervention had an effect on the rate of re-presentation (Tables 2,3) with an estimated difference of 8% between groups (\( P = 0.44 \)). We also investigated whether those with a significant anticholinergic burden (score of 3 or more) or those taking medications listed in the Beers criteria (41 out of 526 patients) were at greater risk of re-presentations or mortality, but no association was seen.

**Admission to an aged care facility**

There was no evidence that the intervention had an effect on admission to an RACF.

**Reported versus actual number of medications**

The number of medications patients were taking was first self-reported and then verified by the pharmacist. On average patients were taking 3.8 more medications than they self-reported. The greatest difference was 14 medications (two reported vs actually taking 16). Only 6% of patients reported the exact number of medications they had been taking. Non-compliance was observed and recorded for 161 patients out of 526 (31%).

**Uptake of clinical pharmacist recommendations**

Of the 525 patients reviewed, 248 were sent home directly from the ED and 641 recommendations or concerns were raised with their GPs. Forty-nine per cent of total recommendations were adopted by the GPs, and 45% were not accepted. The remaining 6% were either being considered (1%), the GP was attempting the change (1%) or it was not changed because of patient apprehension (4%).

**Discussion**

Clinical pharmacists work directly with doctors, nurses as well as other members of the clinical team and patients to ensure that the medications prescribed for patients contribute to the best possible health outcomes by reviewing appropriateness, effectiveness and safety of medication. The clinicians in the study were not blinded so it is difficult to separate what benefit is a result of this structured intervention and what would have occurred from the presence of a pharmacist in the ED and from ongoing unstructured discussion, intervention and advice.

Our results support the view that pharmacist review of older patients in ED reduces hospital admissions. This is consistent with overseas research.7 Research estimates show that between 7% and 10% of patients in acute care settings experience an adverse drug event of which 28–56% are preventable. Hospital admissions because of adverse drug reactions might be more

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**TABLE 1.** Descriptive statistics by intervention and ISAR group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Summary</th>
<th>ISAR positive</th>
<th>ISAR negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD)</td>
<td>Mean</td>
<td>82 (6)</td>
<td>81 (6)</td>
<td>81.6</td>
</tr>
<tr>
<td>Age (SD)</td>
<td>Mean</td>
<td>3 (1)</td>
<td>3 (1)</td>
<td>3</td>
</tr>
<tr>
<td>ISAR score</td>
<td>Mean</td>
<td>0.66</td>
<td>0.66</td>
<td>0.66</td>
</tr>
<tr>
<td>ISAR score</td>
<td>Mean</td>
<td>3 (1)</td>
<td>3 (1)</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>1081</td>
<td>496</td>
<td>525</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>248</td>
<td>122</td>
<td>126</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>248</td>
<td>122</td>
<td>126</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.0004</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.0004</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.0004</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### TABLE 2. Outcomes by intervention and ISAR groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Summary</th>
<th>Both ISAR groups</th>
<th>ISAR positive</th>
<th>ISAR negative</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treatment</td>
<td>Control</td>
<td>Total</td>
<td>P-value</td>
</tr>
<tr>
<td>Admitted or discharged</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>from ED</td>
<td>Admitted</td>
<td>277 (53%)</td>
<td>308 (62%)</td>
<td>620 (57%)</td>
</tr>
<tr>
<td></td>
<td>Discharged</td>
<td>248 (47%)</td>
<td>188 (38%)</td>
<td>461 (43%)</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>Mean (SD)</td>
<td>6 (12)</td>
<td>6 (11)</td>
<td>12 (11)</td>
</tr>
<tr>
<td>No. of representations to ED</td>
<td>Mean (SD)</td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transfer to RACF at 4 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>31 (5.9%)</td>
<td>25 (5.0%)</td>
<td>61 (5.6%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>441 (84%)</td>
<td>408 (82%)</td>
<td>897 (83%)</td>
</tr>
<tr>
<td></td>
<td>Deceased</td>
<td>53 (10%)</td>
<td>63 (13%)</td>
<td>123 (11%)</td>
</tr>
<tr>
<td>Beers criteria medication</td>
<td>Yes</td>
<td>40 (7.8%)</td>
<td>40 (7.7%)</td>
<td>19 (6.4%)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>466 (91%)</td>
<td>4 (100%)</td>
<td>477 (92%)</td>
</tr>
<tr>
<td></td>
<td>applicable or not specified</td>
<td>4 (0.8%)</td>
<td>4 (0.8%)</td>
<td>3 (1.0%)</td>
</tr>
</tbody>
</table>

### TABLE 3. Odds ratio (95% CI) and P-values for admitted patients only

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Both ISAR groups</th>
<th>ISAR positive only</th>
<th>ISAR negative only</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude odds ratio</td>
<td>Adjusted odds ratio</td>
<td>Adjusted P-value</td>
</tr>
<tr>
<td>Risk of admission</td>
<td>0.68 (0.53, 0.87)</td>
<td>0.67 (0.52, 0.86)</td>
<td>0.002</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>Estimated change</td>
<td>Adjusted P-value</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.09 (−0.08, 0.25)</td>
<td>0.31</td>
<td>0.01 (−0.19, 0.21)</td>
</tr>
<tr>
<td>Re-presentation to ED (%)</td>
<td>Estimated change</td>
<td>Adjusted P-value</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.08 (−0.12, 0.28)</td>
<td>0.44</td>
<td>0.14 (−0.12, 0.40)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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than 10% of total admissions in some countries.23

An Australian review has found that medication-related issues were assessed as a primary cause in 15–22% of unplanned hospital admissions involving older people.24 It rated the most common cause of drug-related hospital admissions as adverse drug reactions.24 Another study found that omission or cessation of indicated treatment and non-adherence contributes to approximately 26% of drug-related admissions.25 Unintentional over-consumption of prescribed medication and drug interactions have also been associated with hospital admissions.26,27 The 25 year risk of a significant adverse drug reaction causing hospital admission or occurring during a hospital stay, for a 60-year-old Australian is estimated to be around 35%.

Patients often do not give an accurate recount of their current medication use on presentation to an ED, with patients taking on average 3.8 more medications than they self-reported. This can hinder timely diagnoses and treatment. Research has also shown pharmacists are able to improve medication reconciliation.14 In our study only 6% of patients reported the number of medications that were taking accurately. Pharmacists’ EDMRs were also able to identify non-compliance with prescribed medications; in the present study, this was 31% of older patients. This is important information for emergency physicians in deciding further management. Having a pharmacist available in the ED also facilitated early detection of potential adverse drug effects. Medications without clear indication were also found on occasion. Bradycardia in elderly patients taking beta-blockers was another common finding (Table 4), with dose review suggested to minimise the patients’ long-term risk of syncope and falls.

This intervention allowed medication-related admissions to be identified early in the ED assessment, improving the opportunity for discharge home. For example, a patient was identified as needing admission for an exacerbation of chronic obstructive pulmonary disease. The patient’s carer had been away on holiday and another carer was ‘looking after my medicine’. Her Seretide® puffer was empty and not been replaced. Without the pharmacist physically checking the doses left in the puffer, the patient would have been admitted. With the pharmacist intervention she was prescribed oral prednisone, dispensed a new puffer, an explanation provided to her current carer and she was discharged from the ED.

Another conclusion from our study is that GPs appear generally willing to accept pharmacist recommendations; 49% of recommendations were accepted. This is consistent with research from the USA,29 which has shown an uptake rate of 47%. The rate of acceptance varied greatly with the type of medication involved. We did not have sufficient power to detect whether outcomes were different for those who followed recommendations versus those who did not but future research could focus on these outcomes.

**Limitations**

The trial has some caveats. There was only one pharmacist employed on the study, who is an experienced pharmacist; these results might not be seen with less experienced pharmacists. Our ED is one of the busiest in NSW and potentially this intervention might be even more effective and translate into shortened ED length of stay if other factors, such as bed block were not also at play. The impact of our intervention will presumably be greatest in the most medically complex patients. Future analysis on the actual cost versus benefits would be useful. The trial was funded as a Local Health District Innovation and Reform initiative. It became apparent after the initial

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**TABLE 4. Examples of pharmacist interventions**

<table>
<thead>
<tr>
<th>Medication involved</th>
<th>Pharmacist intervention</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitor (ACE-I) induced angioedema</td>
<td>Recognised medication side-effect, medication ceased</td>
<td>Patient had presented to three different EDs with the same problem. Patient's cognition meant that his capacity to report his own medication history was very limited. Drs were unaware of the ACE-I.</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Therapeutic drug monitoring</td>
<td>Serum sample taken to early and dose doubled, resulting in toxicity</td>
</tr>
<tr>
<td>Oxpentifylline</td>
<td>Recognised medication side-effect, medication ceased</td>
<td>Acute angina secondary to newly started oxpentifylline</td>
</tr>
<tr>
<td>Seretide® inhaler</td>
<td>Checking of doses remaining</td>
<td>Practical intervention. Patients’ carer had not replaced an empty inhaler, so patient was not receiving their dose of steroids</td>
</tr>
<tr>
<td>Metoprolol</td>
<td>Recommended dose reduction in an elderly patient</td>
<td>Seventeen recommendations were made. Nine were accepted.</td>
</tr>
<tr>
<td>Amiodarone</td>
<td>Recognised medication side-effect, medication ceased</td>
<td>Prolonged QT interval secondary to amiodarone</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Therapeutic drug monitoring</td>
<td>Toxic digoxin level was reported back to emergency physicians for management (as GP was on holidays for an extended period)</td>
</tr>
</tbody>
</table>
engagement of clinicians and consideration of the processes that it would be suitable as a trial. As a result the trial was not registered. This lack of early planning prevented us from collecting data on patients that presented after hours, and these patients might have significantly different patient characteristics. Patient demographics triage category, comorbidity and presenting problem for all patients presenting over the study period would be useful to capture in future studies to assess the effect by level of patient complexity.

Conclusions
The intervention reduced the odds of an admission to hospital for both ISAR positive and negative patients. Pharmacists’ EDMRs were able to identify errors and non-compliance with prescribed medications; this can be important information for emergency physicians’ in deciding whether to admit or refer a patient back to their GP for further management. The clinical pharmacist was a respected senior member of the ED team. Medical and nursing staff valued the professional input made into safe management of medications and largely followed the advice given. Having a pharmacist available in the ED also allowed for the provision of early detection of potential adverse drug effects. Provision of a clinical pharmacy service to the ED can be one tool in the arsenal to maximise effective use of hospital resources.

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Competing interests
None declared.

References


Supporting information
Additional Supporting Information may be found in the online version of this article at the publisher’s web-site:

Appendix S1. On-line appendix.