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Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care

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Abstract

Background: regular medication review has been recommended for those over 75 and those on multiple drug therapy. Pharmacists are a potential source of assistance in reviewing medication. Evidence of the benefits of this process is needed.
Objective: to study the effect of medication review led by a pharmacist on resolution of pharmaceutical care issues, medicine costs, use of health and social services and health-related quality of life.
Design: randomized, controlled trial.
Setting: general medical practices in the Grampian region of Scotland.
Subjects: patients aged at least 65 years, with at least two chronic disease states who were taking at least four prescribed medicines regularly.
Methods: pharmacists reviewed the drug therapy of 332 patients, using information obtained from the practice computer, medical records and patient interviews. In 168 patients, a pharmaceutical care plan was then drawn up and implemented. The 164 control patients continued to receive normal care. All outcome measures were assessed at baseline and after 3 months.
Results: all patients had at least two pharmaceutical care issues at baseline. Half of these were identified from the prescription record, the rest from notes and patient interview. Of all the issues, 21% were resolved by information found in notes and 8.5% by patient interview. General practitioners agreed with 96% of all care issues documented on the care plans in the intervention group. At the time of follow-up, 70% of the remaining care issues had been resolved in the intervention group, while only 14% had been resolved in the control group. There were no changes in medicine costs or health-related quality of life in either group. There were small increases in contacts with health-care professionals and slightly fewer hospital admissions among the intervention group than the control group.
Conclusions: pharmacist-led medication review has the capacity to identify and resolve pharmaceutical care issues and may have some impact on the use of other health services.

Keywords: *medication-related problems, medication review, pharmaceutical care, pharmacist*

Introduction

Medication-related problems, particularly adverse drug reactions, poor compliance with therapy and inappropriate drug selection, are present in 12–14% of patients over 65 admitted to hospital in Scotland [1, 2]. Regular medication review can reduce the risk of medication-related problems and has been recommended for those over 75 [3, 4] and those on multiple drug therapy [5]. Pharmacists can assist in reviewing medication [6] and are increasingly doing so [7].

Medication review involves: (i) assessment of medicines prescribed regularly, (ii) extraction of information from the medical records and (iii) interview with the

patient. Pharmaceutical care issues (PCIs) such as potential or actual medication-related problems [8] can be identified or resolved at any stage of this process, therefore all three stages are required. Following this, the pharmacist, in collaboration with the general practitioner (GP) and the patient, formulates a care plan, which documents all PCIs and agrees goals and necessary actions [8].

Many problems can be identified in patients taking multiple medicines from the first two stages of this process: review of the prescription and records [9–11]. Collaboration between pharmacists and GPs can reduce these problems [9, 11]. The proportion of elderly patients whom pharmacists have identified as requiring changes to their medication varies between studies from around 50% [12, 13] to 85% [14].

Pharmacists in the USA increasingly take responsibility for patients' medicine-related needs and include medication review as part of their pharmaceutical care service [15]. In a randomized, controlled study in patients over 65 taking at least five medicines, inappropriate prescribing showed a significantly greater decline in the intervention group than in the control group [16].

Medication review involves a significant time commitment and further evidence of potential benefits is needed. This study aimed to evaluate the effect of pharmacist-led medication review on outcomes such as presence of PCIs, hospitalization, medication costs and health-related quality of life. Elderly patients taking multiple drug therapy were selected for study, since they may be at greatest risk of medication-related problems [17]. The study was sufficiently powered to detect a 25% reduction in the number of patients with PCIs, based on an uncontrolled before and after study [14].

Methods

Selection of practices and patients

Following ethical committee approval, all Grampian medical practices that had at least 500 patients aged 65 years or over were stratified into three levels by the deprivation status (Jarman index) of their practice population and by fundholding status (yes/no). Using random number tables, one practice from each of the six resultant categories was selected and invited to participate. One practice refused and a further practice was randomly selected. None of the practices had previously received input directly from a pharmacist.

The inclusion criteria for subjects were age at least 65 years, regular request for at least four medicines via the computerized repeat prescribing system and at least two chronic diseases. Exclusion criteria were dementia and being considered by the GP to be unable to cope with the study. A maximum of 70 patients from each practice was invited to participate by letter, then telephoned after several days to provide further information and seek verbal consent. Written consent was obtained from those who agreed to proceed during a home visit.

Following stratification by number of drugs, number of cardiovascular drugs and the presence of a non-steroid anti-inflammatory drug other than low-dose aspirin on the repeat prescription, patients were allocated randomly to intervention or control.

Medication review

Clinically-trained pharmacists completed a detailed profile for each patient using medical notes and practice computer records. All patients were then interviewed in their own home about their use of and responses to medication, and their use of health and social services (particularly in relation to medicines) and were asked to complete the SF-36 questionnaire [18]. The cost of 1 month's supply of each patient's prescribed medicines at the time of interview was calculated, incorporating information from the patient on actual use.

A pharmaceutical care plan was drawn up for each intervention group patient, listing all potential and actual PCIs, together with the desired output(s), the action(s) planned to achieve the output(s) and the outcomes of any potential PCIs already resolved by the pharmacist. Copies of the plan were inserted in the patients' medical notes and given to their GP, who was asked to indicate their level of agreement with each PCI identified and with the actions. The pharmacist then implemented all remaining agreed actions, assisted by other practice staff where appropriate.

Control patients were similarly interviewed and PCIs identified, although no pharmaceutical care plan was implemented. Patients were advised to consult any usual carers or health-care professionals in response to direct queries during interview. However, where the pharmacist considered a PCI to be potentially serious, an independent medical assessor decided on the need to withdraw the patient from the study on clinical grounds.

Follow-up

Patients in both groups were followed up after 3 months, their use of medicines re-assessed and new or pre-existing PCIs determined. The health and social services and SF-36 questionnaires were also re-administered, and medicine costs at the time of interview calculated as before. Any outstanding care issues in both groups were communicated to the patient's GP.

Data analysis

Data on use of services were analysed manually. All other data were analysed using SPSS version 6.0 and Excel version 6.0. Medicines used were classified using the *British National Formulary* [19]. Data from the SF-36 questionnaire were analysed by Ware's method [18].

A previously developed classification system for PCIs [10] was modified for the study. The points at which PCIs were identified and resolved were noted, and actions needed to address PCIs classified both by their purpose and by the personnel involved.

Differences between intervention and control groups were studied using χ^2 tests and relationships between variables studied using Pearson's correlation coefficient, both at a probability level of 95%.

Results

Demographic data

A total of 381 patients agreed to participate, of whom 332 completed the study: 168 in the intervention group and 164 in the control group. Twenty-four patients in the intervention group and 25 in the control group withdrew after randomization, mainly because of hospital admission, ill health or holidays at the time of interview. One control patient was withdrawn from the study after consultation with the independent assessor. There were no differences in demography or medicine use between groups (Table 1).

The number of medicines being taken by the 332 patients was not related to age ($r = 0.04$, $P = 0.42$), but was significantly positively correlated with the number of chronic disease states present ($r = 0.364$, $P < 0.001$). A total of 196 patients (59%) were taking a different number of prescribed medicines from those listed on the practice computer as regular medication. This included 117 who were taking medicines purchased themselves, most commonly analgesics (36 out of 145 products).

Pharmaceutical care issues

Pharmacists identified 2586 PCIs, 1380 in control patients (median 8, range 2–21) and 1206 in the intervention group (median 7, range 2–17). While there were significantly more PCIs in the control group than in the intervention group at baseline, the frequency of different types of care issues was similar in both groups (Table 3).

The number of PCIs present was positively correlated with both the number of medicines being taken ($r = 0.552$, $P < 0.001$) and with the number of chronic diseases ($r = 0.304$, $P < 0.001$). PCIs were identified from the prescription in 52.4% of cases, medical note review in 18.2% and patient interview in 29.4%; this did not differ between intervention and control groups.

Overall, PCIs were associated most frequently with cardiovascular drugs, in particular diuretics (26.1% of total care issues), nitrates, calcium channel blockers and potassium channel activators (10.9%), and angiotensin-converting enzyme inhibitors and other antihypertensives (6.6%; Table 2). For most drug groups, the frequency of associated PCIs was in line with their prescription frequency, but diuretics and angiotensin-converting enzyme inhibitors resulted in disproportionately more PCIs per prescription. Most issues associated with these drugs involved a potential for biochemical abnormalities, for which there was no previous monitoring. These were classed as 'potential adverse drug reactions'. Diuretics were also frequently associated with 'inadequate monitoring' for disease progress and 'use with no indication'. Inhaled bronchodilators and corticosteroids were commonly associated with the 'need for education'. 'Inappropriate doses' and 'discrepancies in dose' were common with antiplatelet drugs, notably aspirin.

Some potential PCIs identified from prescriptions were resolvable by review of medical records (Figure 1) and others were resolved by interview with the patient, with no difference in frequency between intervention and control groups. Overall, 320 patients (96.4%) had PCIs remaining, which required GP referral, again with no difference between groups. Of the 1206 PCIs originally identified in intervention patients, 843 (69.9%) required further action. GPs agreed with 1155 (95.8%) of the PCIs documented on care plans in the intervention group and with the actions for resolving 1053 (87.3%) of them.

Table 1. Demographic details and medicines used in 332 patients completing the study

Variable	Group: Intervention (n=168)	Group: Control (n=164)	P
Age in years, mean ± SD (and range)	74.8 ± 6.2 (65–90)	75.2 ± 6.6 (65–93)	0.972
No. of women (and %)	95 (56.5%)	106 (64.6%)	0.132
Mean no. ± SD (and range)			
Chronic diseases	3.9 ± 1.4 (2–8)	3.8 ± 1.4 (2–9)	0.968
Repeat medicines on computer records	7.4 ± 2.7 (4–16)	7.7 ± 2.8 (4–18)	0.951
Non-prescription medicines in use	0.4 ± 0.7 (0–3)	0.5 ± 0.7 (0–3)	0.936
Medicines actually being taken[a]	7.3 ± 2.7 (3–16)	7.6 ± 2.7 (3–17)	0.950

[a]Many patients were not taking all the medicines listed on their repeat prescription record.

Table 2. Association between drugs taken and pharmaceutical care issues in 332 patients

Drug class (BNF category)	No. (and %) of drugs taken	No. of care issues	
		Associated with drugs	Per prescribed drug
Diuretics (2.2)	276 (11.2%)	676	2.45
Angiotensin-converting enzyme inhibitors and other antihypertensives (2.5)	71 (2.9%)	171	2.41
Lipid-regulating drugs (2.12)	51 (2.1%)	103	2.02
Inhaled corticosteroids (3.2)	66 (2.7%)	101	1.53
β-adrenoceptor blocking drugs (2.4)	70 (2.8%)	105	1.50
Drugs used in diabetes (6.1)	61 (2.5%)	91	1.49
Non-steroidal anti-inflammatory drugs (10.1.1)	80 (3.2%)	106	1.32
Bronchodilators (3.1)	141 (5.7%)	178	1.26
Nitrates, calcium channel blockers, potassium channel activators (2.6)	271 (11.0%)	281	1.04
Ulcer-healing drugs (1.3)	131 (5.3%)	125	0.95
Antiplatelet drugs (2.9)	139 (5.6%)	107	0.77
Analgesics[a] (4.7)	258 (10.4%)	177	0.68

[a]Since aspirin was not used as an analgesic in any patient in this study, it was classed as an antiplatelet agent (2.9).
BNF, *British National Formulary*, 1998 [19].

Table 3. Pharmaceutical care issues identified in 332 patients over 65 who were taking four or more medicines and their resolution 3 months after pharmacist review

Issue	No. of pharmaceutical care issues				
	Intervention (n=168)		Control (n=164)		
	Total (%)[a]	Resolved (%)[b]	Total (%)[a]	Resolved (%)[b]	P value
Potential/suspected adverse drug reaction	300 (24.9)	253 (84.3)	327 (23.7)	189 (57.8)	<0.0001
Monitoring issues	185 (15.3)	175 (94.6)	199 (14.4)	156 (78.4)	<0.0001
Potential ineffective therapy	140 (11.6)	80 (57.1)	169 (12.3)	41 (24.3)	<0.0001
Education required	135 (11.2)	109 (80.7)	163 (11.8)	30 (18.4)	<0.0001
Inappropriate dosage regime	69 (5.7)	54 (78.3)	95 (6.5)	17 (17.9)	<0.0001
Potential/actual compliance	74 (6.2)	51 (68.9)	69 (5.0)	21 (30.4)	<0.0001
Untreated indication	66 (5.5)	44 (66.7)	69 (5.0)	19 (27.5)	<0.0001
Drug with no indication	59 (4.9)	32 (54.2)	80 (5.8)	15 (18.8)	<0.0001
Repeat prescription no longer required	55 (4.6)	53 (96.4)	66 (4.7)	4 (5.9)	<0.0001
Inappropriate duration of therapy	43 (3.6)	31 (72.1)	64 (4.6)	25 (29.1)	<0.0001
Discrepancy between doses prescribed and used	28 (2.3)	27 (96.4)	33 (2.4)	1 (3.0)	<0.0001
Potential drug-disease interaction	18 (1.5)	13 (72.2)	17 (1.2)	8 (47.1)	0.1302
Others[c]	34 (2.8)	28 (82.3)	27 (2.0)	16 (59.2)	<0.05
Total	1206 (100)	950 (78.8)	1380 (100)	542 (39.3)	

[a]Of all in group.
[b]Excludes issues partially or spontaneously resolved; % is of total number of pharmaceutical care issues.
[c]Including out-of-date medicine use, duplication of therapy, cost issues and potential drug–drug interactions.

Significantly more PCIs of virtually all types (Table 3) were resolved at 3-month follow-up in the intervention group than in the control group. There were no differences between groups in either the number of PCIs which resolved spontaneously or in the number of new issues identified at follow-up (Figure 1). The total number of PCIs wholly or partially resolved at follow-up was 998 (82.7%) in the intervention group and 569 (41.2%) in the control group. Fifty-two (31%) of the intervention group had no outstanding PCIs at follow-up, compared with only one (0.6%) of the control group.

Medication costs

There were no significant differences in the average monthly costs of prescribed medication per patient between groups, either at initial interview or after intervention (Table 4). The costs of all prescribed medicines not being taken by patients were excluded from these calculations.

Health-related quality of life

The SF-36 questionnaire provided information about patients' perceptions of health-related quality of life

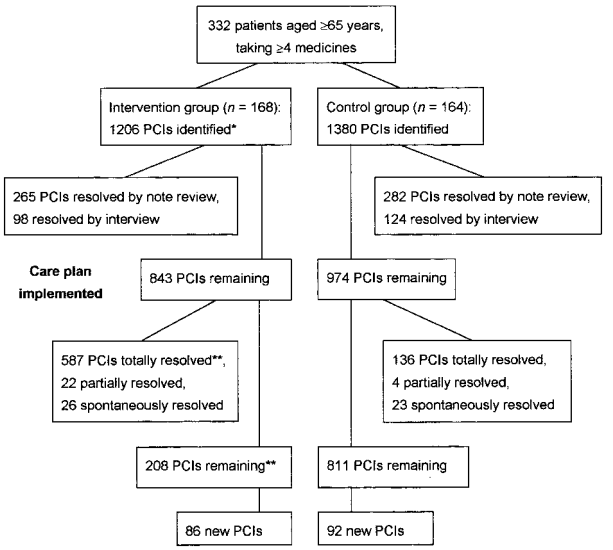

Figure 1. Resolution of pharmaceutical care issues (PCIs)—comparison between intervention and control patients. $^{*}P<0.05$; $^{**}P<0.0001$, χ^2.

Table 4. Changes in medication costs (£ per month) in intervention and control groups

	Group	
	Intervention	Control
Medicine costs (£), mean ± SD		
At initial interview	39.29 ± 29.07	42.80 ± 33.50
At follow-up	38.83 ± 29.60	42.61 ± 31.84
Patients in whom costs increased		
No. (and %)	58 (34.5)	41 (25.0)
Range of increase (£)	0.06–38.93	0.06–68.12
Patients in whom costs decreased		
No. (and %)	75 (44.6)	57 (34.7)
Range of decrease (£)	0.38–57.92	0.16–60.79

in eight different domains. There were no significant differences in any of the scores at baseline between groups. None of the domains showed any significant changes in either group at follow-up.

Use of health and social services

There were no differences in hospital clinic attendance, use of social services or contacts with district nurses and health visitors before and after the pharmacist review. There were slight increases in contacts with both practice nurses (from 15 to 28) and GPs (from eight to 22) for drug-related or therapy monitoring purposes in the intervention group, which was not seen in the control group. Thirty-seven control patients and 35 in the intervention group received help with collecting or taking their medicines, with no changes after review in either group.

Despite the randomization process, intervention group patients had experienced both more elective (13) and emergency admissions (23) prior to intervention than the control group (five elective and 11 emergency admissions). During the 3-month period between interviews, intervention patients had undergone six emergency admissions, while control patients had undergone eight. Numbers of elective admissions were similar in both groups (six intervention, five control). Whilst the decrease in emergency admissions was 74% in the intervention group compared with 27% in the control group, the numbers were too small for statistics to be meaningful.

Discussion

PCIs were identified by pharmacists in all patients who had their medication reviewed. Patients were recruited from randomly selected general practices, stratified for deprivation and fundholding status. The frequency of PCIs was related to the number of medicines actually being taken, which in turn was related to the number of chronic diseases present. Compared with patients continuing to receive standard care, patients who had a pharmaceutical care plan implemented had significantly fewer PCIs. No reduction in medicine costs, health-related quality of life or contacts with health and social services was found as a result of this review, although the data suggest that the potential of medication review to reduce hospital admissions warrants further investigation.

The size of the study was sufficient to demonstrate a reduction in the proportion of patients who had PCIs, but not to demonstrate any clear effect of medication review on hospital admissions or use of other health and social services. While patient groups were matched for a number of important factors, there were differences between the groups in both the number of PCIs and recent hospital admissions. These may have been related, since the higher number of recent hospital admissions in intervention group patients could have contributed to resolution of issues prior to the medication review.

The practicalities of such a study result in a number of limitations. The pharmacists undertaking the medication review also administered the SF-36 questionnaire and identified all care issues. There is also potential for GPs receiving recommendations for some patients to increase their tendency to note similar issues in control patients. However, there is likely to be a greater potential confounding effect of different prescribing behaviour from the use of different intervention and control practices. As in any longitudinal study, there is considerable potential for other factors to influence outcomes, which may have occurred within the 3-month follow-up period. In some cases, however, the care plan was not fully implemented by 3 months.

Pharmacist intervention clearly increased the number of various types of issues resolved, particularly those

related to patients' information needs, dosage, prescription problems and monitoring to prevent adverse drug reactions. These are areas where pharmacists' expertise is acknowledged, and all could be regarded as important in improving the quality of care as evidenced by the extent of GPs' agreement with PCIs and actions. All GPs involved in the study welcomed the process. The lack of any discernible effect on health-related quality of life has been found elsewhere [16]. This may be attributed to the heterogeneous nature of the patients, the generic tool used and a minimal effect of modifications to medicine use on quality of life.

The reduction in problems after pharmacist intervention confirms previous reports in both controlled [16, 20] and uncontrolled studies [10, 11, 14]. While there was no clear effect on hospital admissions in this study, a different approach has suggested that pharmacists may be able to prevent hospital admissions merely by reviewing prescriptions [21]. In the reviews expensive medicines were often recommended in line with latest evidence-based practice, which may explain the lack of effect on medication costs. Reduction in drug costs has been reported elsewhere as a result of medication review [14, 22], particularly when targeted towards patients with specific disease states [23].

This study did not set out to reduce medication costs, but to evaluate the implementation of pharmaceutical care plans. Consequently, opportunities for reduction in medication cost were not always taken and warrant further investigation. In addition, potential cost savings generated by the removal of medicines not being taken from the repeat prescribing record were not included. Future work should focus on measuring the comparative cost-effectiveness of pharmacists reviewing medication, which will require work on appropriate economic, clinical and other patient outcome measures. This may be assisted by the development of agreed indicators of prescribing quality [24].

Key points

- All patients aged 65 years or over taking multiple medicines may have pharmaceutical care issues.
- Although many pharmaceutical care issues can be identified from prescriptions, about half require access to medical records and the patient.
- Diuretics and other drugs used in cardiovascular disorders were commonly associated with pharmaceutical care issues.
- Pharmacist-led medication review can reduce the number of pharmaceutical care issues, decreasing the potential for medication-related problems.

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