Reducing Medical Admissions and Presentations Into Hospital through Optimising Medicines (REMAIN HOME): a stepped wedge, cluster randomised controlled trial

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The known: Pharmacists integrated into general practice teams improve a number of clinical and non-clinical patient outcomes, but the impact on hospital re-admissions and emergency department presentations by recently hospitalised patients is unknown.

The new: Integrating pharmacists into 14 general practices to review medicine management of patients recently discharged from hospital was associated with significantly lower incidence of emergency department presentations and a statistically non-significant lower incidence of re-admission during the 12 months after discharge.

The implications: Given the potentially significant cost savings to the health system, this model should be adopted as routine care for patients after their discharge from hospital.

Abstract

Objective: To investigate whether integrating pharmacists into general practices reduces the number of unplanned re-admissions of patients recently discharged from hospital.

Design, setting: Stepped wedge, cluster randomised trial in 14 general practices in southeast Queensland.

Participants: Adults discharged from one of seven study hospitals during the seven days preceding recruitment (22 May 2017 – 14 March 2018) and prescribed five or more long term medicines, or having a primary discharge diagnosis of congestive heart failure or exacerbation of chronic obstructive pulmonary disease.

Intervention: Comprehensive face-to-face medicine management consultation with an integrated practice pharmacist within seven days of discharge, followed by a consultation with their general practitioner and further pharmacist consultations as needed.

Major outcomes: Rates of unplanned, all-cause hospital re-admissions and emergency department (ED) presentations 12 months after hospital discharge; incremental net difference in overall costs.

Results: By 12 months, there had been 282 re-admissions among 177 control patients (incidence rate [IR], 1.65 per person-year) and 136 among 129 intervention patients (IR, 1.09 per person-year; fully adjusted IR ratio [IRR], 0.79; 95% CI, 0.52–1.18). ED presentation incidence (fully adjusted IRR, 0.46; 95% CI, 0.22–0.94) and combined re-admission and ED presentation incidence (fully adjusted IRR, 0.69; 95% CI, 0.48–0.99) were significantly lower for intervention patients. The estimated incremental net cost benefit of the intervention was $5072 per patient, with a benefit–cost ratio of 31:1.

Conclusion: A collaborative pharmacist–GP model of post-hospital discharge medicines management can reduce the incidence of hospital re-admissions and ED presentations, achieving substantial cost savings to the health system.

Trial registration: Australian New Zealand Clinical Trials Registry, ACTRN12616001627448 (prospective).

Patients recently discharged from hospital after an acute illness are at high risk of renewed hospitalisation.[1] A major contributory factor is that as many as 44% of patients[2] do not follow medication changes initiated in hospital; that is, they continue using a discontinued medicine, do not take a newly prescribed medicine, or do not implement dose changes.[3,4] Patients with chronic conditions and those receiving five or more medicines (polypharmacy) are most likely to be re-admitted.[1,3]

Several pharmacist-led interventions with the aim of averting re-admissions by improving medicine management during the transition from hospital to primary care have been described.[3,5-11] In most studies, hospital-based pharmacists conducted medicine reviews and reconciliations within 14 days of hospital discharge, whether in patients' homes,[5-7] in an outpatient clinic,[8] or by telephone.[9] While pharmacists were purported to have communicated with patients' primary care providers, contact was usually *ad hoc* and rarely involved close, formalised relationships. One United States study reported fewer re-admissions (at 30 and 180 days) of patients reviewed by a pharmacist in a primary care clinic shortly after discharge than of patients who were not reviewed.[11] However, the impact of interventions on re-admission rates differs between reports, and few studies have involved primary care-based pharmacists.

In Australia, pharmacists working in general practices to provide medicine management services in a collaborative and integrated manner is a model that is slowly gaining ground.[12,13] A 2013 survey found that only 26 pharmacists worked in this setting,[13] but the number continues to grow as a result of the activities of Primary Health Networks (PHNs); in 2020, 13% of GPs reported they worked in practices employing pharmacists.[14] This model can optimise the management of hypertension[15] and improve implementation of post-discharge treatment plans,[16] but whether it averts hospital re-admissions and emergency department (ED) presentations has not been examined. The Reducing Medical Admissions into Hospital through Optimising Medicines (REMAIN HOME) trial assessed the effects of integrating pharmacists into general practices on hospital use by recently discharged patients.

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Methods

REMAIN HOME was a stepped wedge, cluster randomised controlled trial (RCT) involving patients at 14 general practices who had recently been discharged from seven public hospitals in southeast Queensland (Royal Brisbane and Women's, Caboolture, Redcliffe, The Prince Charles, Princess Alexandra, Logan, Queen Elizabeth II). The primary outcome of the study was the rate of unplanned, all-cause, hospital re-admissions during the 12 months following discharge from the index admission. Secondary outcomes were re-admissions at 30 days, three months, and six months; ED presentations; and differences in costs between the intervention and normal care. The protocol has been published[17] and the trial was conducted and reported according to the CONSORT statement extension for stepped wedge RCTs.[18] The study was prospectively registered with the Australian New Zealand Clinical Trials Registry (ACTRN12616001627448, 24 November 2016).

Trial design and context

General practices (clusters of two) were randomised to one of seven steps in the stepped wedge design (Supporting Information, table 1). Control phase data were collected in each practice for at least one month. Each month thereafter, two practices were switched to a one-month lead-in phase, during which the intervention was embedded into the practice; a pharmacist began working in the practice and conducted the intervention with recruited patients. Following the lead-in phase, practices entered the intervention phase; data collected during the lead-in phase were not included in our analysis. All participating intervention and control patients were followed up 30 days and three, six, and 12 months after discharge from their index hospitalisations.

Recruitment of general practices and patients

Regions of southeast Queensland with high rates of potentially preventable hospitalisations were identified in publicly available datasets.[19] With the assistance of the local PHNs (Brisbane North and South), general practices in these areas without co-located pharmacists were invited by email to express their interest in participating in our study. The trial coordinator visited interested practices; if accepted, consent for participation was obtained from the practice principals. Practice pharmacists were recruited through online advertising by national pharmacy organisations (Pharmaceutical Society of Australia, Australian Association of Consultant Pharmacy); each practice was allocated a pharmacist to provide 12 hours of remunerated consultation time per week. Pharmacists received one day of training in intervention processes, procedures for documenting drug-related problems, and data collection.

Patients were recruited during the period 22 May 2017 – 14 March 2018. Adults (18 years or older) who had been discharged during the preceding seven days from a study hospital were eligible if they had nominated a general practitioner in a participating general practice as their regular GP, and had been prescribed five or more long term regular medicines on discharge or had received a primary discharge diagnosis of congestive heart failure or exacerbation (infective or non-infective) of chronic obstructive pulmonary disease (conditions associated with high re-admission rates). Patients were excluded if they were receiving active radiation therapy or chemotherapy for malignant conditions, renal dialysis, or palliative care.

Randomisation and blinding

After practice recruitment was completed, each practice was randomised to a study cluster by the study statistician using a computer-generated list of random numbers. The personnel who recruited patients were blinded to the practice randomisation schedule and had no contact with practice pharmacists or other care providers. Blinding of general practice staff and patients to the intervention was not possible.

Intervention phase

The intervention consisted of a face-to-face medicine management consultation between the patient and practice pharmacist, followed by a consultation between the patient and their GP, within one week of hospital discharge when possible. The pharmacist–patient consultation included a comprehensive medicine review to identify drug-related problems, review of discharge medicines lists and their reconciliation with practice records, and discussion of any changes to usual medicines during the hospital admission.

The pharmacist discussed the outcomes of the consultation with the patient's regular GP. The patient then had a consultation with their GP, on the same day when possible.

Pharmacists followed up patients in person or by telephone, and also liaised with patients' community and hospital pharmacists, as well as other prescribers if appropriate, to clarify medicine-related problems or discrepancies, and to communicate medicine changes made during the hospital admission.

Control phase

Patients recruited during control phases received usual care at their general practice; that is, they received no practice pharmacist review or routinely scheduled GP appointments.

Statistical analysis

The primary outcome was the hospital re-admission rate at 12 months; control and intervention group rates were compared in incidence rate ratios (IRRs). Assuming an individual patient drop-out rate of 20% and intra-cluster coefficients (ICCs) of 0.05–0.15, the sample size required to detect a 10% absolute reduction in the number of unplanned re-admissions (power, 80%; $\alpha = 0.05$) was estimated to be 2240 patients.[17] Secondary outcomes were re-admissions at 30 days, three months, and six months; ED presentations; re-admissions and ED presentations combined; time to first re-admission (median with interquartile range [IQR]); and differences in costs associated with the intervention.

Analyses were intention-to-treat analyses and included all participants except those recruited during the lead-in phase. In a per protocol analysis, participants who did not receive the full intervention were excluded.

The planned analysis involved fitting generalised mixed models adjusted for clustering of data and secular trends. However, mixed effects models often failed to converge, as variance in the random effects components was close to zero because of the very small numbers of events during many cluster periods. In such cases, we instead fitted generalised linear models. All models include fixed effects for time period (time-adjusted models); fully adjusted models were also adjusted for age, sex, days to GP visit, length of stay, planned or unplanned admission, number of medications, and number of comorbid conditions. Models were fitted with log links and using the

Poisson distribution offset for number of person-months at risk. Variance components are reported for mixed models that converged.

Post hoc analyses of re-admissions at 12 months assessed sensitivity to the exchangeability assumption for clustering by additionally including cluster by period random effects and identifying whether mixed models converged. We also assessed sensitivity to the Poisson distribution assumption by additionally fitting models with negative binomial, zero-inflated negative binomial, and zero-inflated Poisson distributions. Most analyses were conducted in Stata 16; some sensitivity analyses were conducted in SAS 9.4.

Economic evaluation

We undertook a cost–benefit analysis from the perspective of the Australian health care system. Intervention costs (pharmacist and Medicare Benefits Schedule [MBS] use) and changes in costs for hospital and ED utilisation during the 12-month follow-up period were estimated.

Ethics approval

Ethics approval for the study was granted by the Royal Brisbane and Women's Hospital Human Research Ethics Committee (reference, HREC/16/QRBW/410). All patients provided written consent to participation.

Results

Patient recruitment at each practice is depicted in the Supporting Information, table 1. The target sample size was not achieved. Of 561 patients referred to on-site research assistants, 477 met eligibility criteria, and 353 provided consent. After excluding 47 patients recruited during the lead-in phase, 177 control and 129 intervention patients were included in our analysis. Patient characteristics were similar in the two groups (Box 1).

Each of the fourteen recruited general practices (Supporting Information, table 2) achieved crossover from the control to the intervention phase as scheduled (Supporting Information, table 1). The recruited pharmacists were experienced and many had postgraduate qualifications and accreditation (Supporting Information, table 3).

The proportions of patients who consulted their GPs within a week of discharge were similar for the two groups: 103 control (58%) and 79 intervention patients (61%).

In the intervention group, 28 patients (22%) dropped out of the study without receiving the full intervention (they did not attend appointments, or changed their minds after consenting); their baseline characteristics were similar to those of people who completed the intervention (data not shown). For the 101 patients who completed the intervention, the first pharmacist consultation took place a median of 8.0 days (IQR, 5.0–12.3 days) after discharge, took place at the practice (84 patients) or at the patient's home (17 patients), and lasted a median of 45 minutes (IQR, 30–60 min). After the first pharmacist consultation, 48 patients had GP consultations on the same day, 36 within one week, and 17 more than one week later.

Pharmacists identified a mean of four (standard deviation [SD], 2.5) drug-related problems during the initial consultation, most related to medication choices (eg, duplication), medication adherence, or problems related to conditions requiring additional management or prevention. For 81 patients, GPs implemented at least one pharmacist recommendation, with a mean of 1.5 (SD, 1.2) recommendations implemented per patient within one week of the initial pharmacist consultation.

By 12 months, there had been 282 re-admissions of control patients to hospital (incidence rate [IR], 1.65 per person-year) and 136 of intervention patients (IR, 1.09 per person-year). The time-adjusted IRR for all-cause hospital re-admissions was 0.74 (95% confidence interval [CI], 0.50–1.08), and the fully adjusted IRR 0.79 (95% CI, 0.52–1.18) (Box 2).

At 12 months, ED presentation incidence was 54% lower for intervention than control patients (fully adjusted IRR, 0.46; 95% CI, 0.22–0.94), and the composite measure of re-admission and ED presentation incidence was 31% lower (fully adjusted IRR, 0.69; 95% CI, 0.48–0.99).

At 30 days, the re-admission incidence rate for intervention patients was 0.1 per person-months, and 0.3 per person-months for control patients (fully adjusted IRR, 0.35; 95% CI, 0.14–0.90).

The results of sensitivity analyses using the best fitting random effects models were consistent with our main results (Supporting Information, table 4). Several models with random effects (Poisson, negative binomial, zero-inflated negative binomial, zero-inflated Poisson distributions with and without robust standard errors) did not converge, but fixed effect models for cluster and fixed period effects each yielded similar results (Supporting Information, table 5). Variance components for the random effects that did converge are provided (Supporting Information, table 6).

Per protocol analysis of data for patients receiving the full intervention yielded similar results to the main analysis of 12-month hospital re-admissions: IRR, 0.71 (95% CI, 0.50–1.01); ED presentations: IRR, 0.45 (95% CI, 0.23–0.87);

1 Baseline characteristics of the participating patients

Characteristic	Control group	Intervention group
	177	129
Sex (women)	98 (55%)	69 (53%)
Age (years), mean (SD)	69.3 (13.7)	70.8 (12.4)
Comorbid conditions, median (IQR)	5 (3–8)	5 (4–7)
Regular medicines, median (IQR)	9 (6–11)	8 (6–11)
Index admission unplanned	138 (78%)	98 (76%)
Length of stay for index admission (days), median (IQR)	5 (3–8)	4 (3–8)
Most frequent primary diagnoses (DRGs) for index admission		
I04B: Knee replacement, minor complexity	9 (5%)	3 (2%)
F62A: Heart failure and shock, major complexity	6 (3%)	2 (2%)
D63A: Otitis media and upper respiratory infections, major complexity	4 (2%)	2 (2%)
G70A: Other digestive system disorders, major complexity	4 (2%)	2 (2%)
J64A: Cellulitis, major complexity	3 (2%)	3 (3%)

DRG = diagnostic-related group; IQR = interquartile ranges; SD = standard deviation.

2 Primary and secondary outcomes, by study group and time period

Exposure and outcomes	Events (incidence rate)		Incidence rate ratio (95% CI)	
	Control	Intervention	Time-adjusted	Fully adjusted*
30 days				
Exposure time (person-months)	176.1	129.0		
Hospital re-admissions	59 (0.33)	15 (0.12)	0.30 (0.12–0.72)†	0.35 (0.14–0.90)†
Non-admitted ED presentations	15 (0.09)	5 (0.04)	0.43 (0.05–3.68)†	0.43 (0.03–6.64)†
Hospital re-admission or ED presentation	74 (0.42)	20 (0.16)	0.31 (0.14–0.71)†	0.36 (0.15–0.87)†
90 days				
Exposure time (person-years)	43.0	31.6		
Hospital re-admissions	105 (2.4)	38 (1.2)	0.53 (0.27–1.01)	0.57 (0.31–1.06)†
Non-admitted ED presentations	27 (0.63)	12 (0.38)	0.40 (0.15–1.09)†	0.54 (0.18–1.59)†
Hospital re-admission or ED presentation	132 (3.07)	50 (1.58)	0.51 (0.29–0.90)	0.57 (0.33–0.96)†
180 days				
Exposure time (person-years)	85.4	62.7		
Hospital re-admissions	156 (1.83)	72 (1.15)	0.73 (0.44–1.23)	0.76 (0.47–1.23)†
Non-admitted ED presentations	52 (0.56)	22 (0.35)	0.26 (0.11–0.61)†	0.32 (0.13–0.80)†
Hospital re-admission or ED presentation	208 (2.44)	94 (1.50)	0.58 (0.38–0.91)	0.63 (0.42–0.97)†
12 months				
Exposure time (person-years)	170.6	125.1		
Hospital re-admissions	282 (1.65)	136 (1.09)	0.74 (0.50–1.08)	0.79 (0.52–1.18)
Non-admitted ED presentations	88 (0.52)	45 (0.36)	0.37 (0.19–0.73)	0.46 (0.22–0.94)
Hospital re-admission or ED presentation	370 (2.17)	181 (1.45)	0.63 (0.45–0.90)	0.69 (0.48–0.99)

CI = confidence interval; ED = emergency department.
All models were adjusted for time period. * Adjusted for age, sex, days to GP visit, length of stay, planned or unplanned admission, number of medications, and number of comorbid conditions. † Not adjusted for clustering of observations because of convergence problems (see "Statistical analysis" in Methods).

re-admissions and ED presentations: IRR, 0.64 (95% CI, 0.47–0.87) (Supporting Information, table 7).

The median time from discharge to first re-admission (re-admitted patients only) was 46 days (IQR, 16–158 days) for control patients and 98 days (IQR, 39–236 days) for intervention patients. The median length of hospital stay was the same for both groups (three days; IQR, 1–7 days).

The most frequent reason for re-admission (by Australian Refined Diagnosis Related Group) was "chronic obstructive airways disease, major complexity" (Box 3).

3 Most frequent reasons for re-admission, by Australian Refined Diagnosis Related Groups (AR-DRG) code

AR-DRG code	Control patients	Intervention patients
Total number of re-admissions (by 12 months)	282	136
E65A: Chronic obstructive airway disease, major complexity	13 (5%)	10 (7%)
G70A: Other digestive system disorders, major complexity	—	5 (4%)
E62A: Respiratory infections and inflammations, major complexity	11 (4%)	4 (3%)
F62A: Heart failure and shock, major complexity	10 (4%)	4 (3%)
F62B: Heart failure and shock, minor complexity	9 (3%)	—
F65A: Peripheral vascular disorders, major complexity	7 (2%)	—

Economic evaluation

Pharmacists spent a total of 101 hours, 3 minutes with intervention patients, for a total cost of $6678 ($51.77 per patient). MBS costs per patient were similar for both groups. The total costs of hospital re-admissions and ED presentations were estimated to be $8138 per patient for intervention patients and $13 374 per patient receiving usual care. The estimated incremental net benefit (overall health service cost saving) achieved by the intervention at 12 months was therefore $5072 per patient (Box 4). As the estimated incremental cost per patient of the intervention was $164, the benefit–cost ratio was about 31:1. In a sensitivity analysis assuming higher pharmacist wages in 2023 ($69 per hour, including on-costs[20]), the estimated total intervention cost was $1666 per patient, or an incremental cost of $182 per patient, and the estimated incremental net benefit $5054 per patient, yielding a benefit–cost ratio of 28:1.

Discussion

In the REMAIN HOME trial, pharmacists integrated into general practice teams provided medicines management for patients recently discharged from hospital. This care model was associated with a 21% lower incidence of

4 Treatment- and hospital-associated costs at 12 months, by treatment group

	Control patients	Intervention patients
Number of patients	177	129
Treatment model-associated costs		
Medical Benefits Scheme*	$262 678	$206 017
Pharmacist consultations†		
Initial	—	$5107
Follow-up	—	$1571
Total	$262 678	$212 695
Per patient	$1484	$1648
Hospital-associated costs		
Hospital re-admissions‡	$2 321 084	$1 026 243
Emergency department presentations	$46 112	$23 580
Total	$2 367 196	$1 049 823
Per patient	$13 374	$8138
Total costs	$2 629 874	$1 255 840
Per patient	$14 858	$9786

* Data were unavailable for 30 control patients and 23 intervention patients; costs were imputed as the mean cost for other patients in their group.
† Costs for 28 patients who were allocated to the intervention group but did not receive the intervention were imputed as the mean cost for other patients in the group.
‡ Data were unavailable for nine control patients and seven intervention patients; costs were imputed as the mean cost for other patients in their group.

all-cause, unplanned hospital re-admissions within 12 months of discharge from hospital. This difference was not statistically significant, but the incidence of ED presentations (54% lower) and the combined incidence of hospital re-admissions and ED presentations (31% lower) were each statistically significantly lower during the intervention. As the incidence of re-admissions was significantly lower at 30 days, additional intervention by pharmacists and GP teams may be required after the initial intervention.

Findings by other authors regarding medication review and reconciliation involving collaboration between pharmacists and GPs have been mixed.[21] The benefits of our intervention may be related to the timely and coordinated care provided by the pharmacist consultation, linked closely with GP review and engagement, whereby the clinical rapport and trust between the co-located practitioners, not a feature of some studies,[22] encourages implementation of pharmacists' recommendations.[23-25] Our intervention also enabled pharmacists to reconcile accessible general practice records with the hospital discharge medicine list; most other studies have relied on these lists being forwarded to GPs for reconciliation. Drug-related problems identified by pharmacists during the intervention, particularly poor adherence, are a common reason for patients returning to hospital.[2-4] GPs having additional clinical information and tacit knowledge about their patients may also be beneficial.

As the proportions of patients who saw their GP within a week of discharge were similar for both groups (about 60%), lower hospital use was probably more attributable to the consultation with the pharmacist than early GP review.

A substantial net benefit to the health care system was associated with the intervention, with a return over 12 months of $31 per dollar invested. A return of $1.56 per dollar was reported for a similar intervention, but the study had examined only adverse drug event-related hospitalisations;[26] our figure was also higher than the return of $23 per dollar invested in pharmacist-initiated changes in drug therapy or management in eight Australian public hospitals.[27]

Limitations

We were unable to ascertain how many hospital re-admissions were attributable to medicine-related adverse events because of limitations in retrospectively identifying preventable or medicine-related re-admissions, insensitive hospital coding, and limited researcher time.[28] The patient sample size target was not achieved for several reasons, including delays in obtaining ethics and governance approvals from several hospitals,[29] inconsistent identification and referral to researchers of potentially eligible patients, rapid patient turnover linked with limited bed numbers (leading to discharge of patients before they could be recruited), patients having no recorded regular GP, and not recruiting patients discharged outside research assistants' work hours (9 am – 5 pm). The proportion of intervention patients who did not receive the full intervention was 22%, similar to the reported fail-to-attend rate for a general medical outpatient clinic providing a pharmacist review service,[30] and reflecting the real world conditions in which the study was conducted. The baseline characteristics of patients who dropped out and those who completed the intervention were similar, as were the results of our intention-to-treat and per protocol analyses.

Conclusion

Integrating pharmacists into general practice teams to review the medicines management of patients shortly after their discharge from hospital and provide recommendations to GPs can reduce hospital use, resulting in significant cost savings to the health system. Larger scale studies of this model of care, assessing different clinical and non-clinical outcomes, are warranted.

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Supporting Information

Additional Supporting Information is included with the online version of this article.