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A pilot cohort study of deprescribing for nursing home patients acutely admitted to hospital

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Abstract

Background: Patients from residential aged care facilities are commonly exposed to inappropriate polypharmacy. Unplanned inpatient admissions can provide an opportunity for review of complex medical regimens and deprescribing of inappropriate or nonbeneficial medications. The aim of this study was to assess the efficacy, safety and sustainability of in-hospital deprescribing.

Methods: We followed a prospective, multi-centre, cohort study design, with enrolment of 106 medical inpatients age 75 years and older (mean age was 88.8 years) who were exposed to polypharmacy prior to admission and with a planned discharge to a nursing home for permanent placement. Descriptive statistics were calculated for relevant variables. The Short Form-8 (SF-8) health survey was used to assess changes in health-related quality of life (HRQOL) at 90-day follow up, in comparison with SF-8 results at day 30.

Results: Deprescribing occurred in most, but not all patients. There were no differences between the groups in principal diagnosis, Charlson index, number of medications on admission or number of Beers list medications on admission. At 90 days, mortality and readmissions were similar, though the deprescribed group had significantly higher odds of better emotional wellbeing than the nondeprescribed group [odds ratio (OR) = 5.08, 95% confidence interval (CI): 1.93, 13.39; $p = 0.001$]. In the deprescribing group, 31% of the patients still alive at 90 days had medications restarted in primary care. One-year mortality rates were similar.

Conclusions: Deprescribing medications during an unplanned hospital admission was not associated with mortality, readmissions, or overall HRQOL.

Keywords: deprescribing, health-related quality of life, hospital medicine, mortality, nursing homes

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Introduction

Inappropriate polypharmacy is typically a result of the perfect storm of patient age and comorbidities meeting the widening array of medications and clinical practice guidelines available to treat them. By some estimates, over 95% of older consumers residing permanently in residential aged care facilities (RACF) are exposed to polypharmacy and its potential adverse consequences such as falls, increased mortality, and cognitive decline.[1] It is no surprise, then, that as many as 30% of admissions to hospital for this age group are for an adverse drug event.[2]

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Ceasing or reducing inappropriate medications to prevent harm in this patient group – a process referred to as deprescribing – has significant, though surmountable, barriers, including access to expert opinion from pharmacists as well as staff time at the RACF to monitor for recurrence of symptoms.[3–5] If these barriers can be overcome, and deprescribing is sustained, potential benefits to a consumer include improved mortality rate and quality of life.[6] However, evidence addressing deprescribing in this patient cohort is scant compared with evidence supporting medication use in younger patients. Further, ceasing medications can be associated with withdrawal syndromes or relapse of disease,[7] resulting in adverse patient outcomes or hospital readmission.

Many things, such as an adverse drug event, identification of a drug-disease interaction, or clinical changes like cognitive decline or falls, can trigger consideration of deprescribing. An unplanned hospital admission can signal a significant change in prognosis, and, because of this, render some medications inappropriate by reducing the likelihood of a patient living long enough to reach the point of benefit. Thus, inpatient medical admissions might be an ideal place to deprescribe potentially inappropriate medications. An inpatient admission can provide an opportunity to observe closely for a recurrence of symptoms after deprescribing; provide timely access to expert opinion and information at the point of decision making; and provide the time to discuss an individual patient's prognosis with both patient and family.

The aim of this study was to assess the short-term efficacy, safety, and sustainability of in-hospital deprescribing.

Materials and methods

This was a prospective cohort study of older medical inpatients on five or more regular medications before admission. Our study was approved by the Royal Adelaide Hospital Ethics Committee (HREC/15/RAH/302) with mutual recognition at participating sites. We assessed for a change in outcomes associated with any reduction in medication burden. Hospital pharmacists enrolled patients from acute care in seven hospitals. We included medical inpatients aged at least 75 years, exposed to polypharmacy (defined as five or more regularly scheduled medications) before an unplanned admission between March 2016 and November 2016. All patients were discharged to permanent placement in a RACF. Patients consented to ongoing follow up only; deprescribing that occurred whilst in hospital was not on a voluntary basis, but in line with best practice that medications be reviewed and nonbeneficial medications ceased. Patients were categorised, then analysed, according to those who had medication deprescribed or not. Patients were excluded if admitted for less than 48 h or expected to die in less than 30 days. Evidence published in 2007 by Garfinkeland colleagues from a nonrandomised group of older institutionalised people in Israel suggested that a 50% relative reduction in mortality was possible through deprescribing.[8] The sample size needed to detect a difference in mortality was estimated based on this latter study and on our own pilot data,[9] assuming a 1-year mortality of 50%. A power procedure using a Pearson Chi-square test for two proportions was performed. A clinically significant difference of 30% in mortality between the deprescribing and nondeprescribing groups was assumed. Group weighting was approximately 7:3, the alpha value was 0.05, and a 2-sided test was performed. For a power of 80% to detect a clinically significant difference in mortality, a sample size of 100 was needed. We did not record the number of patients who declined to participate or the number who met exclusion criteria.

All patients received routine care consisting of a multi-disciplinary assessment of medications involving a clinical pharmacist and specialist physician (clinical pharmacologist, geriatrician, palliative care physician, or general physician). The multi-disciplinary team used the patient's medication list at the time of admission, which was provided by the RACF or confirmed with the community pharmacist. Decisions about medication changes were at the discretion of the treating physician and involved the patient and carer, as well as the patient's general practitioner whenever possible. Investigators were not engaged collectively in prescribing or deprescribing actions. All deprescribing decisions were made by the multidisciplinary team members involved in the care of that patient. In addition, the team could employ any available deprescribing guideline to identify potentially inappropriate medications. Teams were not required to adhere to a specific guideline for deprescribing. Most specialist physicians practised within a general medical team, rather than within a specialty team.

The admission medication list was compared with the discharge medication list for regularly scheduled medications. Medications were categorised as ceased; unchanged; total daily dose increased; or total daily dose decreased; we did not record the indications for medication changes. In line with a previously published definition, a medication was considered deprescribed if it was either ceased or its dose reduced. Only medications given regularly were counted; pro re nata (PRN) medications, topical creams, and eye drops were excluded from analysis.[10,11] PRN medications were considered regularly scheduled if given more than once weekly, as defined in a previous study.[10] Short-term antibiotics and glucocorticoids were excluded if ceased before the 30-day follow up. Combination medications (e.g. aspirin/dipyridamole) were counted as two medications. To address the possibility of a selection bias, we used Beers 2015 list of potentially inappropriate medications to compare the number of potentially inappropriate medications being taken before admission and at the time of discharge.[12] The patient's age, sex, and Charlson comorbidity index were also recorded. Because all patients were living permanently in nursing homes, we assumed a 100% compliance to medication regimens.

Using hospital administrative databases, mortality and readmissions were assessed 30 and 90 days after hospital discharge. Nursing staff at the RACF were contacted by phone at 30 and 90 days to review the current medication list and evaluate the restarting or increasing of medications deprescribed. Because of limitations in death certification at RACF, only all-cause mortality is reported. Readmission data was extracted from the hospital database.

Secondary outcomes included self-reported health-related quality of life (HRQOL) at 30 and 90 days, as well as economic impact to RACF. For HRQOL, patients served as their own controls. The Short Form 8-item (SF-8) health survey was administered 30 days after discharge to establish a baseline after recovery from acute hospitalisation and compared with the same assessment 90 days after discharge.[13] The authors were concerned that an earlier baseline measurement would be confounded by recovery from an acute illness. If the participant was unable to answer, a substitute was sought from RACF staff or family. The economic impact of the decreased need for medication administration at the RACF was based on a time-motion study in North America assuming mid-level nursing personnel ($0.52 AUD per medication administration)[14]; the authors felt the administration practices in both continents were suitably similar to support this estimate. For those patients who died, the most recent medication list was used, including administrations on the day of death. Written informed consent was obtained from all participants, or next of kin in the case of cognitive impairment or language barriers. Statistical software used was SAS 9.4 (SAS Institute, Inc., Cary, NC, USA). Descriptive statistics were calculated for variables across deprescribed and nondeprescribed groups; comparisons were made using Chi-square tests (categorical variables), independent *t* tests (normally distributed continuous variables), Wilcoxon rank sum test (non-normally distributed continuous variable) and Fisher's exact test. Assessment of the association between HRQOL and deprescribing practice was investigated using ordinal logistic generalised estimating equation (GEE) models, with each HRQOL question as the dependent variable. This model allowed for clustering within hospitals (seven centres) and within subjects (repeated measures at 30 and 90 days). An interaction term between time and deprescribing was included in each model. For each of the eight questions, we assessed for a time-deprescribing interaction indicating a change in the mean Likert scale response between day 30 and day 90 due to a medication being ceased or dose-reduced at discharge from hospital, or not. A Bonferroni correction was applied to the time-deprescribing interaction *p* values (cut-off *p* value for significance = 0.0063), to reduce false-positives associated with multiple significance testing.[15]

Results

A total of 106 patients were enrolled; cluster sizes ranged from 1 patient to 32 patients. In addition to mortality, patient drop-out included 6 patients who either withdrew, did not meet inclusion criteria or had an invalid consent. This left 100 patients for analysis, 73 of whom had medications deprescribed (median 2.0, interquartile range 1.0, 3.0). Table 1 gives descriptive statistics for relevant variables across deprescribed and nondeprescribed groups. Across the 100 patients, the mean (SD) age was 88.8 (5.6) years (range 75–102), 55% were female and 62% required third-party

Table 1. Patient groups separated by whether or not medications were deprescribed during unplanned hospital admission.

	Patients whose medications were deprescribed (either ceased or dose reduced) (*n* = 73)	Patients for whom no medications were deprescribed (*n* = 27)	*p* value
Age, mean (SD)	87.8 (5.6)	91.0 (4.7)	0.009*
Gender: male, *N* (%)	34 (46.6)	11 (40.7)	0.603$
Charlson index: mean (SD)	2.5 (2.1)	2.9 (2.2)	0.41*
Medications at admission			
N	702	244	
Median (IQR)	10.0 (7.0,11.0)	8.0 (6.0,12.0)	0.488*
Medications ceased (does not include those dose-reduced) (*N* = Median) (IQR)	145 2.0 (1.0, 3.0)	0 0 (0,0)	<0.001‡
30-day mortality [*N* (%)]‖	13 (17.8)	4 (14.8)	1.000§
90-day mortality [*N* (%)]‖	24 (32.9)	5 (18.5)	0.16$
30-day readmission [*N* (%)]‖	18 (24.7)	4 (14.8)	0.416§
90-day readmission [*N* (%)]‖	28 (38.4)	9 (33.3)	0.639$
Single readmission [*N* (%)]	21 (28.8)	5 (18.5)	0.647$
Multiple admissions [*N* (%)]	7 (9.6)	4 (14.8)	0.804$
Length of stay [days, median (IQR)]	14 (8,21)	11 (6,20)	0.423‡
New medications at discharge	107	37	
N = mean (SD)	1.5 (1.7)	1.4 (1.8)	0.597$
Number of medications at discharge (including those dose-reduced) *N* = mean (SD)	9.0 (3.4)	10.4 (4.1)	0.0800*
Number of medications at 90 days *N* = mean (SD)	6.6 (4.9)	8.4 (5.5)	0.1025*

*Independent *t* test *p* value.
$Chi square *p* value.
‡Wilcoxon rank sum test *p* value.
§Fisher's exact test *p* value.
‖Adjusted for age and Charlson index.
SD, standard deviation; IQR, interquartile range.

consent. Patients for whom medications were ceased were significantly younger than those with no medications deprescribed [years (SD) = 87.8 (5.6) and 91.0 (4.7), respectively, $p = 0.009$], and had a higher rate of third party consent [52 of 73 (71%) and 10 of 27 (37%) respectively, $p = 0.003$]. There were no differences between the two groups in frequency of principal diagnosis ($p = 0.75$), or number of Beers list medications on admission or at discharge ($p = 0.9454$); 79% of patients in the deprescribing group had one or more Beers list medications at discharge, and 81% of patients in

Table 2. Medications at admission, deprescribed before discharge, represcribed by 90-day follow up [N (%)].

Drug class (ATC code)	Total number of medications in this class prescribed at point of admission	Meds deprescribed (% of prescribed)	Meds represcribed (% of deprescribed)
Acid suppression meds (A02)	53	11 (21)	3 (27)
Antihypertensives (C02, C07, C08, C09)	109	25 (23)	2 (8)
Diuretics (C03)	52	19 (37)	0 (0)
Antiplatelet agents (B01)	78	17 (22)	0 (0)
Benzodiazepines (N05C, N05B)	22	12 (55)	1 (8)
Antipsychotics (N05AH, N05AX)	14	5 (36)	0 (0)
Antiresorptive treatment (M05B)	13	3 (23)	0 (0)
Statins (C10)	49	11 (23)	2 (18)
Long acting nitrates (C01)	22	5 (23)	0 (0)
Other	534	91 (17)	11 (12)
Total	946	199 (21)	19 (10)

ATC, Anatomical Therapeutic chemical classification system.

the nondeprescribing group had one or more Beers list medications at discharge. Of the 100 patients, 8 left the RACF by the end of the study: 5 returned home with extra support, while 3 went to independent living in a retirement home.

Quality of life

All patients, whether medications were deprescribed or not, either enjoyed improved HRQOL or reported no change in each HRQOL question between 30 and 90 days (Appendix, Table 1). At 90 days, the deprescribed group had significantly higher odds of better emotional well-being than the nondeprescribed group [odds ratio (OR) = 2.43, 95% confidence interval (CI) = 1.94, 3.05; $p < 0.001$]. After adjustment for the number of Beers list medications at discharge, including only patient as respondent and adjusting for clustering on hospital, there was still a statistically significant difference in the HRQOL between deprescribing group and the nondeprescribing groups at 90 days (OR = 5.08, 95% CI: 1.93, 13.39; $p = 0.001$). The deprescribed group had significantly higher odds of better emotional well-being than the nondeprescribed group.

Prescribing patterns

After routine medication review, 19 (26%) of the deprescribed patient group had 4 or more medications deprescribed; 145 medications were ceased (median 2.0, range 1–7) in 64 patients, while 54 medications were dose-reduced in 37 patients (mean 1.5 medications per patient, range 1–2); 144 new, regularly scheduled long-term medications were started for 58 patients (107 new medications in 44 patients who had other medications deprescribed, 37 in 14 patients who had no medications deprescribed). At 90-day follow up, of the 49 patients still alive in the deprescribing group, a further 126 medications had been deprescribed, (87 ceased, 39 decreased), 19 medications (10% of those that had been deprescribed) were restarted in 15 patients (31% of the remaining patients) (see Table 2). There was no association between deprescribing and medication class (Fisher's exact test, p value = 0.20).

Mortality

The 90-day mortality rate was 29% ($p = 0.16$), while 1-year mortality was 42% ($p = 0.23$), with no difference between patients for whom medications

had been deprescribed and those for whom medications were not deprescribed (Table 1).

Readmissions

The readmission rate within 90 days was 38%, with no difference between those patients who had medications deprescribed or not (33% *versus* 38%; $p = 0.64$). A total of 37 patients were readmitted over a total of 48 episodes. Of the 11 patients with multiple readmissions, 7 were in the deprescribed group.

Economic analysis

The total number of drug administrations saved in RACFs over the 90-day period was 8462, with an estimated savings in drug administration cost of $4400.24 AUD.

Discussion

Doctors prescribe medications on the basis of perceived patient benefit, and the understanding that little harm is likely; however, numerous publications demonstrate the dangers associated with polypharmacy in older patients. Polypharmacy remains prevalent in hospitalised patients and poses a significant problem in the community, where general practitioners are frequently left to manage multiple comorbidities.[5,16] Many factors might prompt a clinician to consider deprescribing medications, such as the time-to-benefit of a medication being longer than life expectancy (e.g. statins); perceived anticholinergic burden; or a change in clinical condition of a patient (e.g. falls, cognitive impairment). Deprescribing guidelines support clinical judgment in the context of an individual patient's goals and prognosis, though the evidence underpinning deprescribing guidelines is not robust.

First, our study found no difference in mortality or readmissions – even after adjustment for age and Charlson index – in those patients who had medications ceased or doses reduced. There was no difference in length of stay between the two groups. The two groups were also similar in principal diagnosis and number of Beers list medications on admission. We used Beers list of potentially inappropriate medications to demonstrate that there was no significant difference in the number of potentially inappropriate medications in each group – a potential confounder. This also shows that inpatient deprescribing opportunities might have been missed in the nondeprescribed group. We initially powered our study for a 30% mortality benefit in the setting of high 1-year mortality, based on early positive publications. After we began enrolment, several systematic reviews were published that suggested no mortality benefit from deprescribing. Page and colleagues published a systematic review in 2016 combining results of 132 studies of deprescribing that included an aggregate of 34,000 patients (inpatient and outpatient) and found no difference in mortality, consistent with our study.[17] A 2018 systematic review of hospital deprescribing also found little difference in clinical outcomes.[18] Our study highlights the importance of ongoing randomised, controlled trials (RCT) in building the evidence base that will define practice for clinicians providing care to this group of patients in years to come.

Second, to our knowledge, our study is one of few to describe explicit represcribing rates and give insight into the sustainability of inpatient deprescribing. Garfinkel and colleagues reported a nonrandomised study of deprescribing in 2007, with an overall 'discontinuation failure' of 18% at 12 months. In a sample of 95 nursing home patients recruited to a randomised study in the community, Potter and coworkers listed 20% withdrawal failure 12 months after initial medication withdrawal for the 47 patients randomised to the intervention.[11] Dalleur and colleagues reported a similar study, but with a rate of represcribing potentially inappropriate medications 12 months after discharge from hospital of 39%.[19] An inpatient admission might give an excellent opportunity to reduce medication burden, but any benefits might be mitigated by represcribing after discharge. Indeed, by 90-day follow up, 30% of the remaining patients in our study had medications restarted. The most commonly restarted medications included gastric acid suppression medications, benzodiazepines, statins and antihypertensives. Medications not restarted included long-acting nitrates, antipsychotics, antiplatelet agents and diuretics. Without a clear understanding of represcribing rates, it could prove difficult to judge the long-term risk or benefit of deprescribing. Future studies could likewise drill down to specific drugs or drug classes so that interventions can be devised to reduce unnecessary restarting of nonbeneficial medications. It is

difficult to surmise the reasons for represcribing medications after in-hospital cessation by a specialist physician. The represcription of statins in a cohort of patients with poor life expectancy might reflect the difficulty in rendering an accurate prognosis in older frail patients without a clear terminal diagnosis; the limited time-to-benefit might not be apparent. Restarting antihypertensives might be a response to dietary sodium changes from hospital to RACF that lead to increases in blood pressure or it could be due to residual guideline-based prescribing practices that often view frail older people the same as younger, robust patients with much longer to live.

Third, applying a formula derived in a North American study of medication administration time gives a glimpse of the potential savings to RACFs if ceasing medications becomes more commonplace; this can serve as an estimate only.

Lastly, our study demonstrated a greater improvement in emotional wellbeing, one domain within the SF-8, for those patients who had medications ceased. Question 7, of the 8 questions in the SF-8, asked, 'During the past 4 weeks, how much have you been bothered by emotional problems (such as feeling anxious, depressed or irritable)?' Understanding medication factors that enhance or diminish HRQOL could be of greatest importance to a group of people who often place more value on quality of life than longevity,[20] and whose 1-year mortality is high. In the other domains measured by SF-8, our study found no association between deprescribing and changes in HRQOL measured between 30 and 90 days after discharge; patients seemed to improve regardless.

Admission to hospital is an opportunity for multi-disciplinary opinion to address rational use of medications.[21] An unplanned admission to hospital could provide easier passage through the barriers to deprescribing identified by General Practitioners including access to expert opinion.[5,22]

Our study had a number of limitations. A larger sample size might show a mortality difference missed by our estimate; our estimate of a 30% mortality reduction is extreme and was based on early, perhaps exuberant, hopes for deprescribing. This is a significant limitation, and highlights the importance of ongoing RCTs to address the question of mortality. Additionally, recruitment was nonconsecutive and nonrandomised, which could allow hidden selection bias. Hidden bias might have led to two different cohorts instead of one: those on too many nonbeneficial medications and those who were not. Deprescribing medications in the first group might have made them more similar at the point of discharge, accounting for similarities in outcomes; however, our group of older medical inpatients were similar in principal diagnosis, Charlson index, number of medications on admission, and length of stay, implying more similarities than differences. Analysis using Beers list as a lens also did not find any statistical difference in the groups before deprescribing. Medications were stopped, started, and stopped again as clinical conditions changed, patients moved from inpatient to community settings and were attended by different clinicians and pharmacists. Deprescribing is a moving target. This might explain best the lack of visible mortality benefit noted in recent systematic reviews and meta-analyses.[18,19]

Conclusion

Patients from RACFs have medications deprescribed while in hospital without apparent harm. We observed no increase in the rate of readmission to hospital or impact on HRQOL related to deprescribing. A larger RCT using an explicit deprescribing algorithm is required to better clarify the risks and benefits of deprescribing in this patient group and better clarify potential improvements in HRQOL.

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Author contributions

Study concept and design: PR, GR, AM, IH, UD, DH, RM, SS, CT; acquisition of subjects and data: PR, SL, GR, CM, IH, SM, LT, GC, JM; analysis and interpretation of data: PR, SL, GR, AM, CM, IH, UH, DH, SM, LT, RM, SS, GC, JM, CT; preparation of manuscript: PR, SL, GR, AM, CM, IH, UH, DH, SM, LT, RM, SS, GC, JM, CT.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

Supplemental material

Supplemental material for this article is available online.

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