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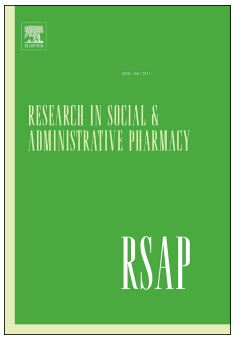

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Abstract

Background

Whilst attention has been paid within the literature to examining potentially inappropriate prescribing (PIP) for older adults in a variety of care settings, less is known about the extent within intermediate care. Furthermore, few studies have examined the utility of clinical pharmacist involvement in this care context.

Objective(s)

Determine the prevalence of PIP in intermediate care (IC) settings in Northern Ireland (NI), explore the utility of a novel pharmacist case management model at reducing PIP and to examine the association with subsequent healthcare utilisation.

Methods

Secondary analysis of prospective data (N = 532) collected during a medicines optimisation pharmacist case management model in three intermediate care sites in NI. Independent prescriber pharmacists delivered the intervention. Variability in Medication Appropriateness Index score change (ΔMAI) from admission to discharge was examined using multivariate linear regression analysis. Multivariate logistic and Poisson regressions were used to examine the association between ΔMAI and likelihood and numbers of unplanned hospital readmissions within 30 and 90 days of IC discharge.

Results

PIP was highly prevalent (89.5%) at baseline with significant reductions in MAI score achieved from admission (*Median* = 14) to discharge (*Median* = 0) (Z = -18.28, $p < .001$). The prevalence of PIP at discharge was 7.8%. No relationship was observed between ΔMAI score and unplanned hospital readmission. Those who received at least one educational intervention were less likely to be readmitted within 30 days of IC discharge (OR = 0.15, 95% CI 0.03, 0.71, $p < .001$). Baseline healthcare utilisation consistently predicted healthcare utilisation post-IC discharge.

Conclusions

Drug-related problems persist for many older adults following acute care discharge and intermediate care may provide an ideal location for medicines optimisation interventions.

Keywords: medicines optimisation; potentially inappropriate prescribing; pharmacist intervention; case management; healthcare utilisation

Highlights

- Potentially inappropriate prescribing is highly prevalent (89.5%) among older adults in intermediate care
- Pharmacist intervention in intermediate care significantly improves prescribing appropriateness
- Improved appropriateness was not directly related to post-discharge healthcare utilisation
- Patient education was associated with lower likelihood of hospital readmission <30 days post discharge

Introduction

Older adults are particularly vulnerable to drug-related problems due to an amalgamation of multiple long term conditions, subsequent polypharmacy and age-related changes in drug metabolism.[1-4] Concerns about the appropriateness of prescribing, and the relative balance between the risks and benefits of prescribed medication,[5-7] have driven a robust research agenda that has not only examined the prevalence of potentially inappropriate prescribing (PIP) among older adults but also evaluated a broad range of interventions to address this issue.[8-13] PIP increases the risk for adverse drug events, hospitalisation and increased healthcare utilisation.[14-16] Hospitalisation may result in a decline in functional status of older adults, which may be particularly pronounced for the oldest old (>90 years of age). [17] If the opportunity for rehabilitation is insufficient, a high proportion of older adults discharged from acute care are at risk for increased dependency and institutionalisation.[18]

However, conflicting trends within the healthcare landscape over recent years have resulted in a reduction in duration of inpatient admissions, a phenomenon that has been observed in Europe between 1985 and 2019.[19] In England for example, the number of acute care beds and beds used for geriatric care has reduced by 35% and 65% respectively, [20] whilst at the same time hospital admissions have continued to rise, particularly for those aged aged ≥60 years.[21-23] Reductions in acute care length of stay present additional challenges for older adults who may require a more comprehensive period of rehabilitation.[24]

In an attempt to address the pressures on the acute hospital sector, intermediate care services were developed in the United Kingdom with the aim of freeing up hospital beds and preventing unwanted hospital admissions.[25-27] However, explicitly defining what intermediate care is has been somewhat of a challenge with varied definitions identified within the literature.[25, 27] Broadly speaking, intermediate care has been defined as "healthcare occurring somewhere between traditional primary (community) and secondary (hospital) care settings" (p.119).[28] Intermediate care is a multidisciplinary service that helps people to remain as independent as possible, providing support and rehabilitation to those at risk of hospital admission or who have experienced a hospital admission.[29] The aim of

intermediate care is to ensure people move from hospital to the community in a timely manner and that unnecessary admissions to hospital and residential care are avoided.[29] Given that 25% of older adults have additional care needs in the post-acute period, [30] intermediate care has become an increasingly important care setting.

Intermediate care may also be an important clinical setting with respect to drug-related problems such as PIP. Hospital admission has also been shown to increase the likelihood of PIP.[31] Poor communication across transitions of care can result in persistence of drug-related problems following hospital discharge. Handwritten communication, illegible writing and omission of medication-related information is commonplace; only one in five changes made to medication during admission are explained in hospital discharge summaries.[32] Three in every five hospital discharge summaries prepared without pharmacist involvement have been shown to contain at least one medication error.[33] Unsurprisingly, transitions of care have been flagged as a critical point for the occurrence of mediation-related harm and have thus been made a global health priority.[34]

However, to date there is a paucity of information on the prevalence of PIP in intermediate care settings. The small number of international studies conducted to date indicate that PIP is likely to be highly prevalent among older adults in intermediate care and may persist or even increase during intermediate care admission. A small study conducted in Northern Ireland (NI) (n = 74), using the STOPP/START criteria, found that 72% of patients received at least one inappropriate medication on admission, with 73% receiving at least one inappropriate medication at discharge.[35] In Norway, the prevalence of PIP, as assessed by the Norwegian General Practice (NORGEP) criteria, was found to increase from 26% on admission to 33% at discharge.[24] More recently, an Italian study of 100 patients in a single intermediate care site reported a prevalence of 88% at admission which significantly decreased to 79% at discharge.[36] Nevertheless, the samples examined in these studies are small and so there is a need to examine PIP using larger intermediate care samples, including multiple sites.

Nevertheless, whilst previously published studies serve to highlight the occurrence of PIP among older adults in intermediate care, little work has been conducted to examine clinical pharmacy services or interventions to improve prescribing appropriateness within this care context. A recent

study found that the inclusion of a pharmacist within the multidisciplinary team resulted in the identification of a high prevalence of drug-related problems (99% patients) and there was high implementation rate by physicians (89.2%) of the recommendations made by the pharmacist to address these drug-related problems.[37] Recent healthcare transformation in NI, aimed at integrating primary and secondary care services for older adults,[38, 39] has provided an opportunity to examine the impact of clinical pharmacy services within intermediate care. Prior to this transformational period, the extent of pharmacy input into intermediate care would have focused solely on the delivery and supply of medication for patients.

A novel care pathway providing medicines optimisation pharmacist case management was piloted in the Western Health and Social Care Trust (Western HSCT) in NI in 2012-2014.[40-42] Within this care pathway intermediate care patients receive a continuum of pharmaceutical care throughout their stay delivered by a case management pharmacist who is an independent prescriber; a baseline medication review on admission informs the content of their personalised pharmaceutical care plan and directs the case management pharmacist on which clinical interventions to deliver. Case management then continues after the patient has been discharged from intermediate care, with additional clinical interventions delivered, if necessary. This pathway is in stark contrast to the supply of medication only service which was in existence prior to this. Following the success of this pilot, additional funding was made available to examine the reproducibility of the care pathway in a second Trust area, the Northern Health and Social Care Trust (Northern HSCT).[41]Accordingly, there is a need to evaluate the clinical impact of a case management medicines optimisation pharmacist in the intermediate care setting.

Aims

This study aimed to i) describe the baseline prevalence of PIP in intermediate care in NI; ii) establish the degree of improvement in prescribing appropriateness achieved by a medicines optimisation pharmacist case management model between intermediate care admission and discharge; iii) establish the proportion of variability in improvements in prescribing appropriateness that is explained by demographic and medication-related factors; and iv) examine the relationship between

improvements in prescribing appropriateness and healthcare utilisation post-discharge from intermediate care.

Methods

Design

This study involved secondary analysis of prospective data collected by the Medicines Optimisation in Older People (MOOP) team in NI between 2015 and 2016. The care model (Figure 1) was delivered by band 8a case management pharmacists, all of whom were independent prescribers, whilst being led and mentored by a consultant pharmacist. In the NHS, roles are graded based on experience and advanced practice training. Newly qualified pharmacists commence at band 6, whilst independent prescriber pharmacists commonly occupy band 7 posts. Band 8a indicates advanced clinical experience and practice and may include supervision of clinical pharmacists as part of the post. The model of care was delivered in three sites across the Western HSCT and Northern HSCTs. Data collection by the MOOP pharmacists adopted a prospective design, with data collected upon admission into intermediate care (baseline) and at discharge (Figure 1).

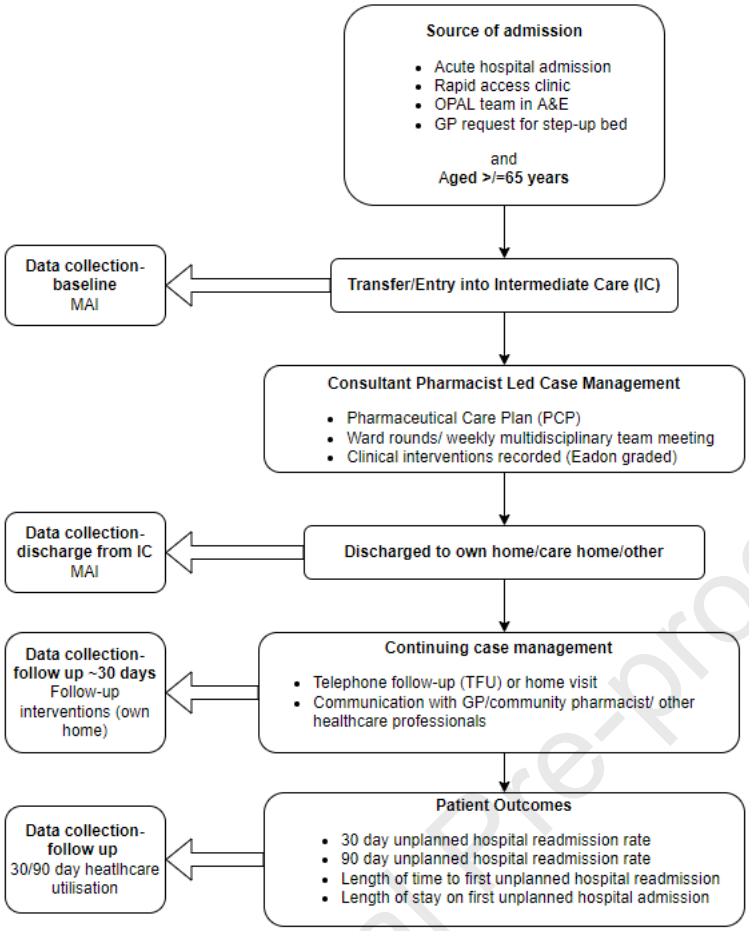

Figure 1: MOOP model of pharmacist case management in intermediate care, where OPAL indicates Older Persons Assessment and Liaison. A&E indicates Accident and Emergency and GP indicates General Practitioner

Medicines Optimisation in Older People Case Management Model

On admission into intermediate care, the MOOP case management pharmacist made an initial assessment. Medication reviews were informed by the appropriateness of prescribing, scored using the Medication Appropriateness Index (MAI).[43] Personalised pharmaceutical care plans (PCPs) were developed for each inpatient, with the MAI scoring of each medication influencing the interventions conducted to rectify this PIP. Clinical interventions were delivered where required and included medication cessation, medication initiation, dosage changes, patient education, addressing Kardex issues, referral to other healthcare professionals, laboratory blood test requests, and medical information to the prescriber. The number and type of clinical interventions by the case management pharmacists were recorded and the clinical significance of each intervention assessed using the Eadon

criteria.[44] Further detail on the Eadon scoring criteria is provided in the Appendix (Table 1A). The MOOP pharmacists provided a continuum of care throughout the inpatient admission, liaising with other members of the multidisciplinary team during ward rounds and weekly meetings. At discharge from intermediate care, the MOOP pharmacists recalculated the MAI score for each medication.

Pharmacist case management continued for approximately 30 days post discharge from intermediate care, with patient follow-up conducted by telephone or home visit, where required. Where necessary, additional interventions were conducted by the case management pharmacists during this follow-up period. Healthcare utilisation data in the 30 and 90 days following intermediate care discharge were collected including the number of unplanned hospital admissions, length of stay on hospital admission and time to first unplanned hospital readmission.

Population

The sample comprised of 532 participants with an age range of 65-99 years (*Mean [M]* = 82, *Standard Deviation [SD]* = 7.6 years). Two-thirds of the sample were female (66.4%). Approximately three-fifths of the sample were from the Northern HCST (*n* = 322) with the remainder (*n* = 210) from the Western HSCT. The model of care was delivered to all inpatients in the intermediate care sites, irrespective of age, as it was deemed unethical to not deliver the same standard of care to all inpatients. For the purposes of this study, data pertaining to those aged <65 years has been excluded.

Variables

Demographic variables including age, sex and residential status were examined. The ability of participants to manage their medicines independently was assessed by the MOOP pharmacists and examined as a categorical variable, coded 1 = completely independent, 2 =some occasional assistance or prompting, 3 = regular informal assistance from a relative/carer/friend, and 4 = formal health/social care package providing assistance with medicines administration. The source of admission into intermediate care was examined using a binary variable 'acute inpatient', coded as follows 1 = admitted from acute care and 0 = admitted following a GP step-up request; via the Western HSCT Older Persons Assessment and Liaison (OPAL); or Rapid Response teams. Normal place of residence

was captured using a binary variable 'origin' such that 0 = private nursing home, residential home, supported living accommodation or other and 1 = own home. The number of acute care admissions in the preceding 12 months, prior to the index intermediate care admission, was captured using a continuous variable and included within the analyses to control for previous healthcare resource utilisation.

Appropriateness of prescribing was calculated using MAI, which is a ten-item weighted questionnaire where each medication is scored on a scale of 0-18, with higher scores indicating greater levels of inappropriateness. The severity of PIP across the entire drug regimen was captured by the total MAI score, calculated by summating the MAI scores for each medication. Change in total MAI score from admission to discharge (Δ MAI) was calculated by subtracting the participant total MAI score at discharge from the total MAI score on admission, such that positive change scores indicated improvement in MAI score over time. The change in the number of medications from admission to discharge (Δ medications) was calculated in the same manner, such that positive change scores indicated reductions in medication prescribing over time. Additional intervention variables were also included within the analysis in order to examine the differential impact of various aspects of care delivered by the case management pharmacists. These binary variables indicated the receipt of at least one of the following interventions: medication stopped; medication started; dosage changed; blood tests requested; Kardex issue addressed; patient education; medicines information to prescriber; referral to another healthcare professional (HCP). Examples of Kardex issues commonly addressed by the case management pharmacists include switching the timing of a medicine e.g. to avoid an interaction or to accommodate a patient's preference, adding an annotation to clarify appropriate formulations e.g. modified release preparation or adding an annotation to indicate the cost-effective hospital formulary choice etc. A further intervention category 'other' captured those less common interventions not captured by the preceding categories, an example of which included communication with the GP to align renewal cycles for prescriptions.

Healthcare utilisation following intermediate care discharge was examined using several binary and continuous variables: unplanned (all-cause) hospital readmission <30 days (Y/N);

unplanned (all-cause) hospital readmission <90 days (Y/N), number of all-cause hospital readmissions <30 days; number of all-cause hospital readmissions <90 days; length of stay on first unplanned (all-cause) hospital readmission; time to hospital readmission.

Ethical approval

Ethical approval for the study was granted by the Office for Research Ethics Committees Northern Ireland (ORECNI) under protocol number 14/NI/0052.

Statistical analyses

Demographic and clinical characteristics are expressed in terms of counts, mean (with standard deviation), median and proportions, as appropriate. Frequency of endorsement for previous medical history diagnoses and medication sub-classifications were consolidated within Microsoft Excel® for ease of tabulation. Descriptive statistics were completed using IBM SPSS Statistics for Windows 24.[45] Baseline differences in mean total MAI score were examined using Mann-Whitney U test for continuous variables and Chi-square test of independence for categorical variables.

The change in mean total MAI score between admission and discharge was examined using the Wilcoxon-Signed Rank test due to the non-normal distribution of data. Linear regression analyses, robust to data non-normality were conducted in Mplus 8.1[46] using the maximum likelihood robust (MLR) estimator. Demographic and clinical variables were entered into a predictive model to determine the association with MAI score change during the intervention. The association between MAI score change and healthcare utilisation outcome variables were examined using multivariate linear regression using Mplus 8.1[46] and logistic regression, Poisson regression and Kaplan-Meier analyses using SPSS version 26.[45]

Results

Sample characteristics

For the 12-month period prior to the index admission the number of unplanned hospital admissions for the cohort ranged from 0 to 11 ($M = 0.90$, $SD = 1.49$). Just over half of the sample (55.8%) did not experience an unplanned hospital admission in the preceding 12 months.

233 Approximately two-thirds of the sample had an intermediate care stay of >2 weeks but <2 months. Of
234 those participants who entered intermediate care from an acute care setting, almost three-quarters
235 (71.2%) spent up to three weeks in acute care. Sample characteristics can be observed in Table 1.

236 *Table 1: Participant demographic characteristics on admission to intermediate care (N = 532)*

Characteristic		***n* (%)**
Marital status (*n* = 440)	Married/cohabiting	181 (34.0)
	Widowed	178 (33.5)
	Single, never married	68 (12.8)
	Divorced/separated	13 (2.4)
Type of residence (*n* = 532)	Own home	484 (91.0)
	Other	48 (9.0)
Admitted from (*n* = 498)	Acute care	462 (86.8)
	GP step up request	57 (10.7)
	Older people assessment and liaison (OPAL)	7 (1.3)
	Rapid access	1 (0.2)
	Other	5 (0.9)
Medicines management (*n* = 527)		
	Completely independent	286 (53.8)
	Some assistance or prompting	18 (3.4)
	Informal assistance from carer/friend/relative	166 (31.2)
	Formal care package	57 (10.7)
Acute care length of stay (*n* = 475)	0-7 days	134 (25.2)
	8-14 days	171 (32.1)
	15-21 days	74 (13.9)
	22-28 days	37 (7.0)
	>28 days	59 (11.1)

Intermediate care length of stay (*n*=498)	0-7 days	16 (3.0)
	8-14 days	58 (10.9)
	15-28 days	177 (33.3)
	29-56 days	174 (32.7)
	57-84 days	50 (9.4)
	>84 days	23 (4.3)
Hospital admissions previous 12 months (*n* = 532)	0	297 (55.8)
	1	119 (22.4)
	2	62 (11.7)
	3	25 (4.7)
	≥4	29 (5.4)

Prescribing at admission

The total number of medications at admission ranged from 1 to 24 (*M* = 10.68, *SD* = 4.14). The majority of participants (89.5%) had some degree of PIP upon admission into intermediate care, as indicated by a total MAI score >0. At admission, total MAI scores ranged from 0 to 63 (*M* = 15.51, *SD* = 11.88). The Mann-Whitney test of differences indicated that the mean ranks for baseline total MAI score was significantly higher for participants who were in the NHSCT (*Median* = 16) than for participants in the WHSCT (*Median* = 13), *U* = 29092.0, *p* =.006, *r* = .12. No significant difference was observed in the mean ranks of baseline MAI total scores for males (*Median* = 13) and females (*Median* = 15, *U* = 28648.5, *p* = .078). Similarly, no significant difference was observed in the mean ranks of baseline MAI total scores between those who had previously been an acute inpatient (*Median* = 14) and those that had not (*Median* = 16, *U* = 13383, *p* = .155). Furthermore, there was no difference in baseline total MAI scores for those who were ordinarily resident in their own home (*Median* = 14) compared with those who were not (*Median* = 10.5, *U* = 10747, *p* = .392). A

significant positive association was observed between the number of prescribed medications and total MAI score at baseline $r_s = .419$, $p < .001$.

Interventions by the case management pharmacists

A total of 2377 clinical interventions were conducted for the cohort, with an average number of 4.48 interventions per participant (SD = 2.56, range 0-12). In total 948 medications were stopped, 432 medications were started and 435 dosage changes were recorded for the cohort. In addition, 313 Kardex issues were addressed, 72 referrals were made to another HCP, 65 blood test requests were completed and 54 patient education interventions were delivered. The proportion of participants who experienced at least one of each intervention type was as follows: medication stopped 77.3%; dosage changed 54.9%; medication started 50.2%; Kardex issue addressed 37%; referral to another HCP 13%; blood test requested 11.7%; patient education 10%. A small number of interventions classified as 'other' (47) were delivered to 8.3% of the sample. Eleven instances of medicines information provided to a prescriber were delivered for 2.1% of the sample.

The clinical interventions enacted by the case management pharmacists were self-rated using the Eadon six-point scale, where higher ratings indicate more clinically significant interventions. The numbers of interventions for each level of the Eadon grading system were as follows: Eadon 1: two (0.08%); Eadon 2: zero (0%); Eadon 3: 40 (1.68%); Eadon 4: 1925 (80.98%); Eadon 5: 404 (17.0%); Eadon 6: six (0.25%). The majority (89.1%) of participants received a clinical intervention that was assessed as 'significant and improved the standard of care' (Eadon score=4). Almost two-fifths (39.9%) of the sample received an intervention that was assessed as 'very significant and prevent major organ failure or adverse reaction of similar importance' (Eadon score=5) and five participants received an intervention rated as 'potentially lifesaving' (Eadon score=6).

Prescribing at discharge

The majority of participants (83.6%) experienced a change in total MAI score from admission to discharge. The prevalence of PIP at discharge was 7.8% (MAI score >0). A Wilcoxon Signed-rank

test showed that pharmacist intervention significantly reduced MAI total scores from admission (*Median* = 14) to discharge (*Median* = 0) (Z = -18.28, $p < .001$). Furthermore, the number of medications prescribed for intermediate care participants was also significantly reduced from admission (*Median* = 10) to discharge (*Median* = 9, Z = -8.30, $p < .001$).

A linear regression model explained 44.2% of the variance in MAI score change (Δ MAI) from admission to discharge (Table 1). Of the demographic variables, only the HSCT location was a significant predictor of variability in MAI score change (ß = .191, p < .001); those in the Northern HSCT experienced a greater reduction in MAI score compared with those in the Western HSCT. Length of stay in IC was a statistically significant weak predictor of MAI score change (ß = .087, p = .029). The change in the number of prescribed medications from admission to discharge was the strongest predictor of MAI score change. Each additional medication discontinued was associated with a 2.805 point reduction in MAI score. Having at least one medication changed or at least one Kardex issue addressed also explained the variability in MAI score change from admission to discharge. Providing medicines information to a prescriber was a significant negative predictor of MAI score change (ß = -.080, p =.001) with those participants who experienced a medicines information intervention experiencing an increase MAI score change.

Table 2: Linear regression model with MAI score change as the dependent variable (N = 442)

Predictor	**Unstandardised estimate**	**Standardised estimate**	***P***
Demographics			
Age	-.007	-.004	.905
Female sex	1.601	.064	.059
Northern HSC Trust‡	4.451	.191	<.001**
Original residence†: *own home*	1.303	.032	.317
Clinical history			
Number of hospital admissions in previous 12 months	.257	.031	.320
Length of stay in acute care	.023	.028	.491

Length of stay in intermediate care	.043	.087	. 029*
Pharmacist intervention			
Δ medications	2.805	.584	<.001**
Blood tests completed	-.038	-.001	.981
Medicines information	-5.948	-.080	.001*
Medication dosage change	4.813	.206	<.001**
Referral to another healthcare professional	.051	.002	.969
Kardex issue addressed	1.916	.079	.032*
Education	1.237	.033	.347
Other	.885	.020	.488

Note. * $p < .05$; ** $p < .001$; ‡ reference group: Western HSCT; † = reference group: other; Δ medications = number of medications at discharge subtracted from number of medications on admission

Healthcare utilisation following intermediate care discharge

Following discharge from intermediate care, a total of 115 participants (21.6%) experienced an unplanned (all-cause) hospital readmission <90 days, with a greater number of participants experiencing this readmission in the 31-90 day period (81 participants) in comparison to <30 days (63 participants). Twenty-nine participants experienced an unplanned hospital readmission within both time periods. The duration of these unplanned readmissions ranged between 1 and 76 days (M = 13.85, SD = 15.30, n = 101), with time to readmission found to range between 1 and 89 days (M = 33.56, SD = 25.71, n = 113).

Variability in healthcare utilisation post-discharge

The degree of MAI total score change was not associated with the likelihood of experiencing an unplanned hospital readmission (all-cause readmission) in either time period (Table 3). Those participants who received at least one educational intervention from the case management pharmacists were less likely to be readmitted to acute care within 30 days of intermediate care discharge (OR = 0.21, 95% CI 0.05, 0.83), p = 0.026). Those who received a medicines information to the prescriber or 'other' intervention were more likely to be readmitted within both 30 and 90 days.

313 The strongest predictor of likelihood of hospital readmission was the number of acute care
314 admissions in the preceding 12-month period; each additional acute care admission in the preceding
315 12 months increased the risk of unplanned hospital readmission <30 days 1.41-fold. When examined
316 over the longer term (<90 days of intermediate care discharge), the number of hospital admissions in
317 the 12 months prior to the index admission remained a significant predictor of increased likelihood for
318 unplanned readmission (Table 2). Each additional admission in the preceding 12 months increased the
319 risk for unplanned hospital readmission 1.43-fold (95% CI 1.22, 1.68).

320 *Table 3: Multivariate logistic regression of likelihood for unplanned hospital readmission <30 and <90 days of intermediate care discharge (N = 483)*

	Likelihood for unplanned readmission < 30 days		Likelihood for unplanned readmission < 90 days	
Variables	**OR (95% CI)**	***p***	**OR (95% CI)**	***p***
Δ MAI score	1.01 (0.98, 1.04)	0.635	1.01 (0.99, 1.03)	0.366
Age	0.97 (0.93, 1.01)	0.138	0.98 (0.94, 1.01)	0.142
Female sex†	1.62 (0.82, 3.20)	0.165	1.07 (0.65, 1.77)	0.775
Medicines management‡				
Completely independent	4.88 (0.94, 25.28)	0.059	1.78 (0.68, 4.65)	0.239
Some assistance/prompting	4.08 (0.46, 35.84)	0.205	1.63 (0.39, 6.82)	0.505
Informal assistance from relative/friend/carer	3.71 (0.70, 19.59)	0.122	1.30 (0.48, 3.50)	0.604
Intermediate care length of stay (days)	0.99 (0.98, 1.01)	0.460	1.00 (0.99, 1.01)	0.495
Northern HSCT^	0.77 (0.37, 1.60)	0.482	0.69 (0.40, 1.19)	0.179
Acute care inpatient~: yes	0.60 (0.24, 1.45)	0.250	0.73 (0.36, 1.48)	0.382
Number of acute admissions in the previous 12 months	1.41 (1.18, 1.69)	<0.001**	1.43 (1.22, 1.68)	<0.001**
Original residence¶: own home	1.04 (0.23, 4.74)	0.955	0.63 (0.25, 1.60)	0.330
Medication stopped	0.89 (0.40, 2.00)	.779	0.84 (0.45, 1.56)	0.583
Medication initiated	1.93 (0.99, 3.78)	.055	1.38 (0.84, 2.29)	0.205
Blood tests requested	0.79 (0.28, 2.22)	.651	1.61 (0.79, 3.30)	0.191
Medicines information service	18.51 (3.91, 87.59)	<.001**	4.67 (1.18, 18.47)	0.028*
Dose changed	1.13 (0.61, 2.12)	.699	0.79 (0.49, 1.27)	0.333
Referred to another healthcare professional	0.89 (036, 2.17)	.792	0.86 (0.43, 1.71)	0.670
Kardex issue addressed	0.95 (0.49, 1.83)	.881	0.97 (0.59, 1.58)	0.903
Education	0.21 (0.05, 0.83)	.026*	0.56 (0.24, 1.28)	0.168
Other intervention	4.49 (1.87, 10.80)	.001*	2.22 (1.05, 4.72)	0.037*

321 *Note.* * $p < .05$; ** $p < .001$; Δ MAI = change in Medication Appropriateness Index score from admission to discharge; †: reference group: male; ‡: reference group: formal assistance package;
322 HSCT= Health and Social Care Trust; ^: reference group: Western HSCT; ~:reference group: no; ¶: reference group: other

No significant predictive relationship was observed between MAI score change and the number of unplanned hospital readmissions <30 or <90 days of intermediate care discharge (Table 3). Patient education resulted in significantly fewer unplanned readmissions (OR = 0.27, 95% CI 0.09, 0.82, $p = 0.021$) <30 days. A medicines information intervention resulted in five times more unplanned hospital readmissions (OR = 5.51, 95% CI, 2.62, 11.56, $p < 0.001$) within 30 days of discharge. Those who received at least one intervention categorised as 'other' experienced twice the number of unplanned hospital readmissions <30 days of discharge than those who did not receive this intervention type (OR = 2.76, 95% CI 1.50, 5.06, $p = .001$). Baseline levels of hospitalisation were again found to positively predict the number of unplanned hospital readmissions following intermediate care discharge. Each additional hospital admission in the 12 months preceding the index intermediate care admission resulted in 1.24 times more unplanned hospital readmissions <30 days (95% CI 1.04, 1.42, $p <0.001$) and < 90 days (95% CI 1.15, 1.34, $p <0.001$).

335 *Table 4: Poisson regression of number of unplanned hospital readmissions <30 days and <90 days of intermediate care discharge (N = 424)*

	Number of unplanned readmissions < 30 days				Number of unplanned readmissions < 90 days			
Variables	**Estimate**	**SE**	**OR (95% CI)**	***p***	**Estimate**	**SE**	**OR (95% CI)**	***p***
ΔMAI score	0.001	0.133	1.00 (0.97, 1.03)	0.957	0.001	0.010	1.00 (0.98, 1.02)	0.889
Age	-0.022	0.018	0.98 (0.94, 1.01)	0.222	0.003	0.013	1.00 (0.98, 1.03)	0.800
Female sex†	0.432	0.292	1.54 (0.87, 2.73)	0.138	0.044	0.193	1.04 (0.72, 1.52)	0.819
Medicines management‡								
Some assistance or prompting	0.051	0.735	1.05 (0.25, 4.45)	0.945	0.030	0.491	1.03 (0.39, 2.70)	0.952
Informal assistance from relative/friend/carer	-0.127	0.276	0.88 (0.51, 1.51)	0.644	-0.108	0.218	0.90 (0.58, 1.38)	0.619
Formal care package	-1.344	0.648	0.26 (0.07, 0.93)	0.038*	-0.683	0.377	0.50 (0.24, 1.06)	0.070
Intermediate care length of stay (days)	-0.004	0.005	1.00 (0.99, 1.01)	0.493	-0.001	0.004	1.00 (0.92, 1.01)	0.895
Northern HSCT^	0.086	0.310	1.09 (0.59, 2.00)	0.782	0.058	0.225	1.06 (0.68, 1.65)	0.796
Acute care inpatient~: yes	-0.299	0.315	0.74 (0.40, 1.37)	0.342	-0.163	0.268	0.85 (0.50, 1.43)	0.542
Number of hospital admissions in previous 12 months	0.216	0.067	1.24 (1.09, 1.42)	0.001*	0.215	0.041	1.24 (1.15, 1.34)	<0.001*
Original residence¶: own home	0.013	0.614	1.01 (0.30, 3.37)	0.983	-0.080	0.393	0.92 (0.43, 2.00)	0.839
Medication stopped	-0.051	0.325	0.95 (0.50, 1.80)	0.875	-0.023	0.243	0.98 (0.61, 1.57)	0.923
Medication initiated	0.373	0.263	1.45 (0.87, 2.43)	0.157	0.292	0.211	1.34 (0.89, 2.02)	0.165
Blood tests requested	-0.117	0.401	0.89 (0.40, 1.95)	0.770	0.267	0.231	1.31 (0.83, 2.05)	0.248
Medicines information	1.706	0.378	5.51 (2.62, 11.56)	<0.001**	0.773	0.440	2.17 (0.91, 5.14)	0.079
Dose changed	0.085	0.262	1.09 (0.65, 1.82)	0.745	-0.193	0.183	0.82 (0.58, 1.18)	0.291
Referred to another healthcare professional	-0.200	0.376	0.82 (0.39, 1.71)	0.594	-0.071	0.271	0.93 (0.55, 1.59)	0.794
Kardex issue addressed	-0.139	0.265	0.87 (0.52, 1.46)	0.600	0.097	0.204	1.10 (0.74, 1.64)	0.637
Education	-1.295	0.562	0.27 (0.09, 0.82)	0.021*	-0.543	0.362	0.58 (0.29, 1.18)	0.134
Other intervention	1.015	0.310	2.76 (1.50, 5.06)	0.001*	0.542	0.274	1.72 (1.00, 2.94)	0.048*

336 *Note.* * $p < .05$; ** $p < .001$; ΔMAI = Medication Appropriateness Index score change from admission to discharge; †: reference group: male; ‡: reference group: completely independent;
337 HSCT= Health and Social Care Trust; ^: reference group: Western HSCT; ~:reference group: no; ¶: reference group: other

The survival distributions for time to first unplanned readmission (days) are shown in Figure 2. A log-rank test of differences indicated that the survival distributions for those who had experienced a change (either increase or decrease) in total MAI score (*Median* = 25) and those who did not (*Median* = 28) were not statistically significantly different, X^2 (1) = .468, *p* = .494.

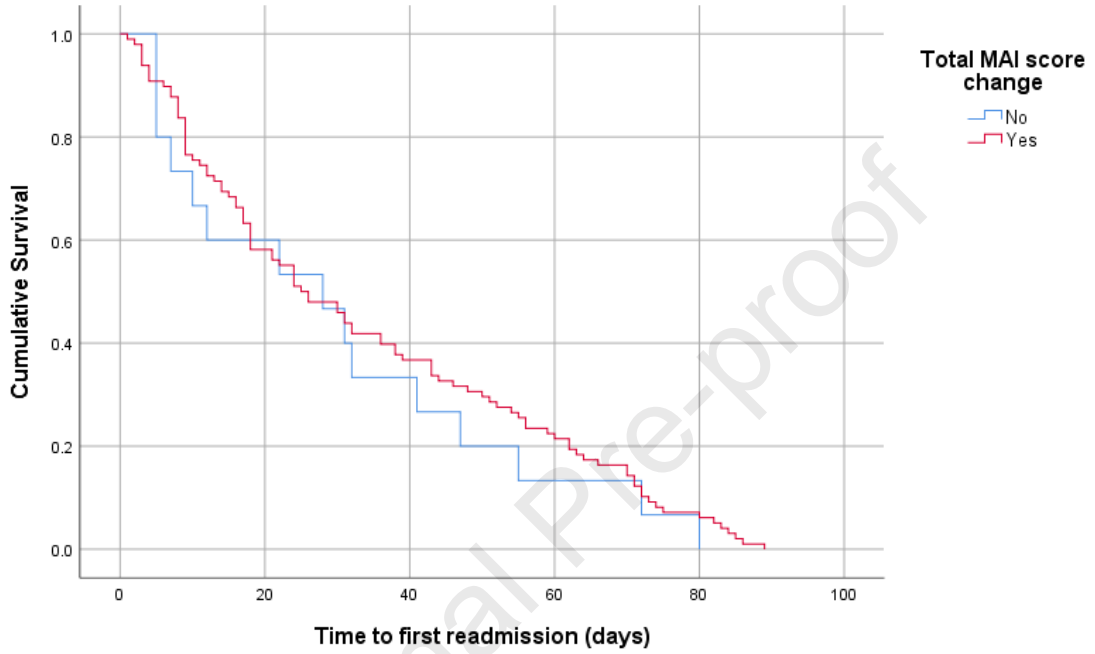

Figure 2: Kaplan-Meier survival plot for time to first unplanned readmission (N = 113), where a change in total MAI score reflected those who had either an increase or decrease in MAI score from admission to discharge

The degree of change in total MAI score was not a significant predictor of length of stay during the first unplanned hospital admission (Table 4).

Table 5: Predictors of length of stay (days) on first unplanned readmission (N = 97)

Variables	**Unstandardised Estimate**	**Standardised Estimate**	**Standard Error**	***p***
ΔMAI score	-0.042	-0.036	0.100	0.721
Age	-0.048	-0.025	0.119	0.834
Female sex†	0.893	0.029	0.121	0.813
Medicines management‡				
Completely independent	-4.152	-0.140	0.262	0.595
Some assistance or prompting	-10.151	-0.137	0.104	0.186
Informal assistance from relative/friend/carer	-2.715	-0.085	0.237	0.721
Intermediate care length of stay (days)	0.019	0.025	0.071	0.722

Northern HSCT^	0.042	0.001	0.113	0.990
Acute care inpatient~: yes	-6.965	-0.162	0.128	0.206
Number of acute admissions in the previous 12 months	0.216	0.032	0.092	0.732
Original residence¶: own home	-16.019	-0.332	0.169	0.050
Had a medication stopped	-0.247	-0.007	0.098	0.944
Had a medication initiated	2.001	0.068	0.103	0.509
Blood tests requested	-0.885	-0.021	0.082	0.803
Medicines information service	4.922	0.081	0.089	0.367
Dose changed	-3.177	-0.108	0.082	0.188
Referred to another healthcare professional	4.481	0.110	0.100	0.269
Kardex issue addressed	-2.691	-0.085	0.092	0.353
Education	-4.054	-0.080	0.104	0.439
Other intervention	-7.063	-0.152	0.083	0.067

Note. * $p < .05$; ** $p < .001$; ΔMAI = Medication Appropriateness Index score change from admission to discharge; †: reference group: male; ‡: reference group: formal assistance package; HSCT= Health and Social Care Trust; ^: reference group: Western HSCT; ~:reference group: no; ¶: reference group: other

Discussion

Principal findings

The present study extends the literature on PIP among older adults in intermediate care by evaluating a novel medicines optimisation pharmacist case management model in this care setting. Previous studies have shown that suboptimal prescribing is prevalent in this care context.[24, 35, 37] A very high baseline prevalence of PIP was found (89.5%) when examined using MAI. The high prevalence identified highlights the need for pharmaceutical care services in this setting beyond a traditional 'supply only' function. Furthermore, the inclusion of a medicines optimisation independent prescriber pharmacist, operating via a case management approach, led to a significant improvement in prescribing appropriateness. Whilst the degree of MAI score improvement was not associated with variation in healthcare utilisation individual aspects of pharmacist intervention showed some significant associations with reduced healthcare utilisation.

Results in the context of other studies

The baseline PIP prevalence reported here is higher than that reported in an earlier study conducted in three intermediate care sites in NI (n=74). [35] Millar and colleagues, using the STOPP/START criteria, found 72% of inpatients had at least one potentially inappropriate medication on admission.[35] The higher PIP prevalence reported here may relate to differences in the screening tool applied (MAI versus STOPP/START). The STOPP/START criteria are explicit lists of medications considered to be inappropriate in older people. Thus, PIP prevalence estimates determined using such criteria are based on the mere presence of the inappropriate medication. In contrast, MAI assesses appropriateness across ten domains, some of which are not captured by explicit list-based criteria. Thus, the higher prevalence identified in present study may relate to the greater sensitivity of MAI as an instrument. Alternatively, MAI is subject to greater bias given its implicit nature as ratings are predicated on the clinical judgement of the rater.

The few studies conducted in intermediate care to date have failed to inform of the patient and environmental factors associated with PIP in this setting. No sex differences in baseline prevalence of PIP were observed which contrasts with the literature that indicates that PIP is more likely to occur in females. [47-51] Hospital admission is independently associated with likelihood of experiencing PIP[31], however no baselined differences were observed between those admitted to intermediate care from hospital versus those admitted following a GP step up request. Higher baseline MAI scores were observed in the Northern HSCT versus the Western HSCT which may point to geographical variation in prescribing culture. Variation in high-risk prescribing has been shown to be influenced by the size, location and accessibility of GP practices.[52, 53] However, cautious interpretation of this geographical variation is required given that no independent assessment of MAI scores was conducted.

Significant improvements in PIP were observed with a large proportion of participants (>80%) showing some degree of improvement. Previous studies have shown that clinical pharmacist interventions targeting hospitalised older adults either increase the likelihood for MAI score reduction or significantly reduce MAI scores. [54-56] In contrast to the present study, the pharmacists who led the interventions in these studies were not independent prescribers.

Gillespie and colleagues (2013) examined the role of a clinical pharmacist providing enhanced pharmacy services to hospitalised older adults aged ≥80 years compared with standard (non-pharmacist) care.[56] The intervention comprised of medication reconciliation on admission and discharge, medication review, communication of drug-related problems to physicians, patient education and post-discharge follow-up telephone calls, which could be considered somewhat similar to the intervention examined here. The pharmacist intervention was standardised but the medication review element did not consistently use any review instrument. In the present study, MAI was used to structure the medication review and direct the development of individualised pharmaceutical care plans. However, in the Gillespie et al study, MAI was used retrospectively to assess PIP. [56] MAI scores improved in 60% of intervention participants compared to 11% of controls. [56] Greater MAI score improvement rates reported here may be a consequence of higher baseline MAI scores (M=15.5 versus M=8.5), the medication review being structured around MAI, the longer duration of admission in intermediate care, or as a consequence of the presence of independent prescriber pharmacist. Assessing PIP using MAI in an acute hospital setting in NI led to a significant reduction in PIP when compared to standard pharmaceutical care. [57] The present findings extend those of previous studies by reporting evidence that a pharmacist case management model, delivered by independent prescriber pharmacists, significantly reduces MAI scores care settings beyond acute care hospitals such as intermediate care.

The present study also extends the literature on PIP by examining factors which drive MAI score reduction in intermediate care and thus, by proxy, factors which may contribute to PIP in the first instance. Unsurprisingly, medication cessation was the strongest contributor to MAI score change. Nevertheless, having at least one medication dosage changed was associated with an almost five point reduction in MAI score and having at least one Kardex issue addressed was associated with an almost two point reduction in MAI score. This underscores the importance of considering medicines optimisation as a response to sub-optimal prescribing in broader terms than merely deprescribing medications. The findings reported here also highlight the importance of active intervention to improve PIP. More passive intervention, such as the provision of a medicines

information service to the clinical team, is reinforced by the identified association of an increase in MAI score. It must be noted that no information was recorded as to the implementation actions of the clinical team following receipt of this medicines information. A recent study examining implementation rates for pharmacist recommendations in intermediate care found that almost 11% of recommendations were not implemented, with inappropriate time to review and discharge prior to review as some reasons for non-implementation. [37]

The study findings also underscore the fallacy of assuming that existing pharmacotherapy has already been optimised in previous care settings, given the high proportion of participants who required some medication adjustment within intermediate care. The cohort examined had predominately been acute care inpatients prior to intermediate care admission (~87%), indicating that drug-related problems persist for a high proportion of older adults in NI following hospital discharge. Furthermore, more than one-third of the sample had a Kardex issue addressed by the intervention pharmacists, with some requiring more than one Kardex intervention. It has been reported that over 90% of Australian patients have at least one medication-related problem following discharge from acute care.[58, 59] A longitudinal study of over 38,000 primary care patients aged ≥65 years found hospital admission was independently associated with PIP, with the likelihood of PIP after admission higher than before admission among those who had experienced a hospital admission.[31]

Overall, MAI score improvement did not predict subsequent healthcare utilisation following intermediate care discharge. Similar findings have previously been reported in a hospital-based study, which failed to find an association between significant reductions in MAI score and Emergency Department visits or mortality.[55] The absence of an association between MAI score reduction and subsequent healthcare utilisation is somewhat surprising given the high degree MAI score improvement reported here. This may relate to the selection of all-cause hospital readmissions as an outcome as opposed to drug-related hospital admissions. A previous hospital-based study, comprised of medication reconciliation and review, found MAI scores at discharge to be significantly related to drug-related hospitalisations but not with all-cause hospitalisations in the year following the intervention. [56] Alternatively, whilst the magnitude of MAI score change indicates an improvement in

prescribing it may not be sufficiently sensitive to adequately capture the clinical significance of the intervention.

The constituent parts of the pharmacist intervention, such as patient education, may be more appropriate indicators of clinical significance. Those who received at least one educational intervention were less likely to experience a hospital readmission and fewer numbers of hospital readmissions within 30 days of intermediate care discharge. A previous systematic review reported mixed evidence on educational interventions among older adults.[60] Many studies examined post-discharge education, whether alone or in combination with medication reconciliation before discharge. Two studies reported a reduction in readmissions, [61, 62] two reported no impact,[63, 64] and one reported evidence of an increase in readmissions. [65] In contrast, more passive interventions, such as providing medicines information to a prescriber, resulted in significantly greater readmissions within 30 days of intermediate care discharge. This may indicated an element of clinical inertia regarding some PIP which may result in further hospitalisation at a later date. Alternatively, it may also reflect a more clinically complex individual with a higher level of healthcare need whereby a more gradual approach to medication optimisation is required.

Strengths and limitations

Several limitations must be considered when interpreting the present study's findings. The absence of a matched control group prevents a comparison with usual care. The lack of a standardised framework to classify the identified drug-related problems that required clinical intervention limits the transferability of the findings. This is further compounded by the high proportion of participants who experienced a change in total MAI score. Maintaining adequate statistical power to examine outcomes such as healthcare resource usage in the post-intervention period is a challenge when most participants have experienced some degree of MAI score change. The implicit nature of MAI scoring means that the impact of clinical experience on the calculation of MAI scores cannot be eliminated. The possibility remains that regional differences in baseline MAI score may occur because of inter-individual differences among the case management pharmacists.

Furthermore, no independent assessment of MAI score was conducted thereby introducing further bias. A previous study conducted in primary care reported moderate inter-group agreement for MAI ratings, with variation in agreement for scores for the individual elements of the overall score.[66] Future research should seek to examine the impact of pharmacist experience, as well as investigating regional differences using multi-level modelling, whilst also including an independent rating of MAI scores. Similarly, future studies should incorporate independent assessments of the clinical significance of pharmacist interventions beyond the self-rated nature of Eadon ratings reported here. Furthermore, future studies should incorporate a standardised assessment of the patient's ability to manage their medication.

An additional limitation of MAI as an assessment tool is that it is time consuming to apply. [67, 68] The time taken to conduct the MAI assessments at admission and discharge was not collected in the present study and so no assessment of cost-effectiveness was possible. However, it has been estimated that it requires 10 minutes to score one medication using MAI. [43] For the person with polypharmacy the time required to assess the entire medication regimen is an important consideration for intervention feasibility; the relative costs in terms of pharmacist time must be balanced with the clinical benefits of the intervention. Nevertheless, the absence of an impact on clinical outcomes such as hospital readmission does not remove one from the ethical argument regarding patient autonomy. [8] Just because it is time-consuming to conduct a thorough assessment of PIP for those with considerable polypharmacy should not mean that patients should continue with medications that increase their risk for adverse outcomes. It has been argued that the absence of impact of deprescribing initiatives on clinical outcomes has not devalued deprescribing as an intervention but that it should be done in collaboration with patients who are living burdensome polypharmacy. [8] If the intervention's purpose is to improve patient care, then the patient must remain central to the evaluation and not be considered as secondary to the impact of overall service efficiency. Future studies should seek to incorporate patient-reported outcome measures within their evaluation.

Reducing pill burden and the risk for adverse drug reactions (ADRs) by reducing PIP will likely confer benefits to healthcare systems also. Reduced medication expenditure should allow those

499 jurisdictions which reimburse the costs of dispensed medications to redirect funding elsewhere. Given
500 that ADRs increase the likelihood for hospital admission[69-73], future costs may also be averted by
501 reducing the likelihood of ADR occurrence. The costs of ADR-related hospitalisations to the United
502 Kingdom National Health Service have been estimated to be £466 million per annum[73], with a further
503 study reporting ADRs to be responsible for 9.5% of all direct healthcare costs.[74] Thus, assessing the
504 cost-effectiveness of medicines optimisation interventions must consider the broader health service
505 impact on the health service and potential future cost savings, and may require a longer follow-up
506 period than examined in the present study.

507 Notwithstanding these limitations, the present study has a number of strengths that must be
508 acknowledged. The evidence base around intermediate care as a key location for addressing PIP has
509 been augmented through an examination of a care model comprised of active pharmacist engagement
510 with clinical care in this setting. The extent of activities conducted by the intervention pharmacists
511 have been explored and the relationship with MAI score improvements and subsequent healthcare
512 utilisation have been delineated. Some inferences on the prescribing culture within acute care settings
513 can be inferred from the improvements made during intermediate care admission. The large sample
514 size and multivariate nature of the analysis, including adjustment for baseline healthcare utilisation
515 levels, adds further weight to the robustness of the findings reported. Furthermore, the examination of
516 follow-up healthcare utilisation post-discharge from intermediate care extends the literature regarding
517 this care context. The results presented indicate the successful reproduction of the care model in a
518 second healthcare trust area, with significant improvements in MAI score achieved in both healthcare
519 areas. The care model has subsequently been rolled out across the entire region, with some minor
520 local variation reflective of the varied provision of IC beds at local level. The care model has also
521 been used as a shared learning exemplar by the National Institute for Health and Care Excellence.[75]

522 **Conclusions**

523 The findings presented here outline that PIP persists following acute care discharge and that
524 intermediate care may serve as an ideal opportunity to further optimise the medication regimens of
525 older adults. In the present study, a high prevalence of PIP was identified in a cohort that was

predominately recently discharged from acute care and was successfully and significantly reduced by a novel pharmacist case management model. As a care context, intermediate care has received less attention within the literature. Whilst there is considerable variation in the provision of intermediate care services consideration should be given to the inclusion of clinical pharmacy services in this setting. The pharmacist-led medicines optimisation case management model examined led to significant improvements in appropriateness of pharmacotherapy, with some aspects of pharmacist intervention shown to be related to a lower post-discharge healthcare utilisation. The findings promote the need to consider more than deprescribing of inappropriate medications but rather a focus on medicines optimisation that allows for person-centred flexibility. As health and social care systems recover from the challenges presented by the COVID-19 pandemic, opportunity for rehabilitation will become an increasingly important public health priority. Against a backdrop of increasing prevalence of multiple long-term conditions and polypharmacy among older persons the inclusion of clinical pharmacy services aimed at improving medication regimens will become increasingly relevant.

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763 **Appendix**

764 *Table 1A: Eadon grading of clinical pharmacist interventions (Eadon, 1992)*

Score	Clinical significance
1	Intervention which is detrimental to a patient's well-being
2	Intervention that is of no significance to patient care
3	Intervention is significant but does not lead to improvement in patient care
4	Intervention is significant and results in improvement in the standards of care
5	Intervention is very significant and prevents major organ failure or adverse reaction of similar importance
6	Intervention is potentially lifesaving

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Minding the gap-an examination of a pharmacist case management medicines optimisation intervention for older people in intermediate care settings.

Highlights

- Potentially inappropriate prescribing is highly prevalent (89.5%) among older adults in intermediate care
- Pharmacist intervention in intermediate care significantly improves prescribing appropriateness
- Improved appropriateness was not directly related to post-discharge healthcare utilisation
- Patient education was associated with lower likelihood of hospital readmission <30 days post discharge