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ORIGINAL ARTICLE

Hospital readmissions, mortality and potentially inappropriate prescribing: a retrospective study of older adults discharged from hospital

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AIMS

Applying version 2 of the STOPP/START criteria to discharge prescriptions of older adults discharged from a general medical unit, the aim of this study is to assess potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs) and their association with hospital readmission and mortality.

METHODS

Discharge medications, co-morbidities and patient demographics were recorded over an 8-month period for consecutive emergency admissions of patients aged ≥65 years. PIMs and PPOs were identified using version 2 of the STOPP/START criteria. Multivariate analysis for association of PIMs and PPOs with re-admissions and mortality during the follow-up period were assessed using binary logistic regression.

RESULTS

Data for 259 patients with a mean age of 77 (65–99, 51% female) were analysed. At discharge, the mean number of co-morbidities and medications per patient were 5.4 (SD: 2.1 range: 0–14) and 9.3 (SD: 4.0 range: 1–31) respectively. During the follow-up period (mean 41.5 months, SD: 2.0 range: 38–46 months), 50.2% of patients had died and the median number of readmissions was two (IQR: 1–4 range: 0–33). Prescription of more than five medications was significantly associated with PIMs and PPOs (OR: 2.75, 95% CI: 1.34–5.62 and OR 3.20, 95% CI: 1.57–6.54 respectively). Presence of a PIM was associated with three or more readmissions (OR: 2.43 95% CI: 1.19–4.98) and PPOs with mortality (OR: 1.88, 95% CI: 1.09–3.27).

CONCLUSIONS

Using version 2 of the STOPP/START criteria, the presence of PIMs and/or PPOs in older adults discharged from hospital is significantly associated with repeated hospital admissions and mortality respectively.

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- PIMs and PPOs identified using STOPP/START version 1 have been associated with adverse drug events, increased morbidity and mortality, and reduced quality of life.

WHAT THIS STUDY ADDS

- Applying STOPP/START version 2 to the discharge prescriptions of older adults, the presence of PIMs and PPOs are associated with increased odds of hospital readmissions and death respectively.
- Interventions applying STOPP/START version 2 to reduce PIMs and PPOs may result in fewer hospital admissions and reduced mortality.

Introduction

In an ageing society, safe and effective prescribing in older adults presents an increasing challenge [1]. The burden of comorbidity, which frequently accompanies advancing age, compounded by the emergence of disease-specific prescribing protocols, has led to an increasing prevalence of polypharmacy in older adults [2]. Additionally, the physiological changes of ageing affect pharmacokinetics and tolerance to drug toxicity and side effects, contributing to the increased risk of adverse drug events (ADEs) [3]. ADEs, many of which are avoidable, are reportedly a major cause of hospitalization, mortality and cost to healthcare systems [4, 5]. Medications which constitute a greater risk than benefit to a patient are termed potentially inappropriate medications (PIMs), while failures to prescribe medications of potential benefit are termed potential prescribing omissions (PPOs). The prevalence of PIMs and PPOs in the older population are reportedly similar for a variety of healthcare settings [6–8].

Numerous explicit criteria have been devised as tools to identify PIMs and PPOs [9–12]. First published in 2008 the STOPP (Screening Tool of Older Person's Prescriptions) START (Screening Tool to Alert doctors to the Right Treatment) criteria have become widely accepted as applicable and appropriate to prescribing practices in Europe [10, 13]. PIMs and PPOs identified using this tool have been associated with increased frequency of adverse drug reactions, increased morbidity and mortality, and reduced quality of life [8, 14–18]. Interventional studies applying these criteria to reduce PIMs and PPOs have been reported to reduce the incidence of ADEs, falls and delirium with reduced duration of hospitalization and healthcare costs [19–23].

In recognition of changes in evidence-based treatment and recognition of the diminished clinical relevance for some criteria, an updated version (version 2) of the STOPP/START criteria were introduced in 2014 [24]. While the updated STOPP criteria have been used extensively to assess PIMs in older adults [25–32], there is limited data using the updated START criteria to assess prevalence of PPOs [33, 34]. Additionally, little is known about the utility of the new criteria to predict clinically meaningful outcomes such as readmission rates and mortality [33].

The aims of this study were to identify PIMs and PPOs and their association with hospital readmission and mortality rates using version 2 of the STOPP/START criteria in older adult emergency admissions to a general medical ward.

Methods

The study population comprised consecutive emergency admissions to a general medical unit of patients aged ≥65 years over an 8-month period (November 2013–June 2014). STOPP/START criteria (version 2) were applied to discharge medications. Two STOPP criteria (category A1: Any drug prescribed without evidence-based clinical indication. A2: Any drug prescribed beyond the recommended duration, where treatment duration is well defined) and two START criteria (I1 and I2 referring to vaccinations) were omitted from the analysis. Demographics and discharge medications were obtained from individual patient immediate discharge letters issued on the day of discharge. For those patients admitted more than once during the study period, the first admission was taken as the index admission. Clinical information relevant to the application of the STOPP/START criteria was obtained from inpatient clinical notes, electronic records of outpatient clinic reviews and GP referral letters. Scoring for PIMs and PPOs for each patient was performed manually by two trainee physicians (J.M. and D.C.) and points of disagreement adjudicated by a consultant clinical pharmacologist (J.S.M.). Follow-up data on mortality and number of readmissions was collected in September 2017 from electronic healthcare records.

Exploratory data analysis and frequency tables were used to describe demographic variables and prevalence of PIMs and PPOs. Chi square analysis was used for univariate analysis and multivariate logistic regression analysis was used to establish the association between PIM/PPO occurrence and both demographic and outcome variables (expressed as odds ratio with 95% confidence intervals). Statistical analysis was conducted using the SPSS software package version 24 (SPSS, Chicago, IL).

This study was conducted as an audit with patient data anonymized at the time of data collection and stored electronically on an encrypted password-protected hard drive.

The clinical audit team confirmed that as this was a clinical audit, an ethics committee review was not required.

Results

Data for 259 consecutive patients [median age 77 years (IQR 71–83 years, range 65–97 years, 51% female), with 35.1% (n = 91) 80 years or older] were analysed. Patients had a mean of 5.4 distinct diagnoses (SD: 2.1 range 0–14). On discharge, patients were prescribed a mean of 9.3 distinct medications

(SD: 4.0, range 1–31), 88.8% (n = 230) were prescribed ≥5 distinct medications and 44% (n = 114) ≥10 distinct medications.

Over a mean follow-up period of 41.5 months (SD: 2.0 range: 38–46 months), the median number of readmissions per patient was two (IQR 1–4, range 0–33) and 50.2% (n = 130) of the study population had died.

PIM and PPO prevalence

At discharge, a total of 2411 medications were prescribed to the study population and 321 PIMs and 405 PPOs were identified. The median number of PIMs per patient was 1.0 (IQR: 0–2, range: 0–7) with 59.1% (n = 153) of patients having at least one PIM. The median number of PPOs per patient was 1.0 (IQR: 0–2, range: 0–8) with 69.1% (n = 179) of patients with at least one PPO. Therefore 83.8% (n = 217) of the study population had at least one potentially inappropriate prescription (PIP): that is presence of PIM and/or PPO.

Association of potentially inappropriate prescribing with demographic and outcome variables

Table 1 reports the unadjusted odds for the occurrence of at least one PIM or PPO according to study variables and outcomes. Patients with at least one PIM or PPO were significantly more likely to be discharged on more than five medications or to have greater than five comorbid conditions. Additionally, those with at least one PIM at discharge were at significantly increased odds of repeated admissions to hospital (three or more over the follow-up period). The presence of at least one PPO was significantly associated with increased odds of death over the follow-up period. There was no significant association between PIMS or PPOs and age or gender.

Multivariate analysis for associations of PIM/PPO occurrence with both demographic and outcome variables are reported in Table 2. Adjusting for co-variables and outcomes, patients prescribed more than five medications at discharge were at significantly increased odds of PIMs and PPOs.

Table 1

Unadjusted association between PIMs or PPOs and study variables and outcomes

		STOPP	START
		Unadjusted OR of at least 1 PIM (95% CI)	**Unadjusted OR of at least 1 PPO (95% CI)**
Sex (ref: male)	Female	1.29 (0.79–2.13)	0.74 (0.44–1.26)
Age (ref: ≥80 years)	65–79 years	1.05 (0.63–1.77)	0.72 (0.41–1.26)
Number of discharge medications (ref: <5)	6–10	2.65 (1.31–5.36)**	3.29 (1.62–6.67)**
	>10	4.42 (2.05–9.53)***	3.13 (1.47–6.66)**
Number of comorbidities (ref: ≤5)	>5	2.21 (1.33–3.68)**	1.96 (1.14–3.39)*
Number of readmissions (ref: 0)	1–2	1.30 (0.67–2.51)	1.00 (0.50–2.01)
	≥3	2.53 (1.26–5.08)**	1.61 (0.77–3.36)
Mortality at follow-up (ref: alive)	Deceased	1.15 (0.70–1.89)	1.96 (1.14–3.35)*

*= $P < 0.05$,
**= $P < .001$,
***= $P < 0.0001$ on univariate analysis

Table 2

Adjusted[a] odds ratios for PIM and PPO occurrence

		STOPP	START
		Adjusted OR of at least 1 PIM (95% CI)	**Adjusted OR of at least 1 PPO (95% CI)**
Sex (ref: male)	Female	1.30 (0.76–2.22) $P = 0.34$	0.92 (0.44–1.91) $P = 0.82$
Age (ref: ≥80 years)	65–79 years	1.18 (0.67–2.05) $P = 0.57$	0.59 (0.26–1.35) $P = 0.21$
Number of discharge medications (ref: <5)	6–10	2.75 (1.34–5.62) $P = 0.006$	3.20 (1.57–6.54) $P = 0.001$
	>10	4.08 (1.87–8.91) $P < 0.001$	2.99 (1.39–6.42) $P = 0.003$
Number of comorbidities (ref: ≤5)	>5	1.48 (0.83–2.63) $P = 0.18$	1.50 (0.63–3.54) $P = 0.36$
Number of readmissions (ref: 0)	1–2	1.40 (0.71–2.76) $P = 0.338$	1.15 (0.45–2.91) $P = 0.77$
	≥3	2.43 (1.19–4.98) $P = 0.015$	1.75 (0.65–4.71) $P = 0.27$
Mortality at follow-up (ref: alive)	Deceased	1.09 (0.63–1.87) $P = 0.77$	1.88 (1.09–3.27) $P = 0.024$

[a]Adjusted for gender, age, number of discharge medications, comorbidities and readmissions and mortality.

Adjusting for variables including number of discharge medications, the presence of one or more PIM at index discharge was significantly associated with three or more further hospital readmissions over the follow-up period (OR 2.43: 1.19–4.98, $P < 0.05$). The presence of at least one PPO was associated with significantly increased odds of death over the follow-up period in the population as a whole (OR 1.88: 1.09–3.27, $P < 0.05$).

After adjusting for co-variables, prescription of more than five medications was significantly associated with presence of at least one PIP (OR: 5.86, 2.56–13.39, $P < 0.001$). Presence of at least one PIP was also significantly associated with death over the follow-up period (OR: 2.51, 1.20–5.28, $P = 0.015$).

Multivariate analysis for associations of PIMs and PPOs from individual categories of the STOPP and START criteria demonstrated that the prescription of at least one PIM in group K of STOPP criteria (drugs associated with falls risk) was associated with an increased risk of death over the follow-up period (OR 2.22: 1.05–4.70, $P < 0.05$).

Discussion

Applying version 2 of the STOPP/START criteria to our study population of older adults discharged from a general medical unit, demonstrated that more than four in five patients were issued a potentially inappropriate prescription (PIP) containing at least one PIM or PPO, a figure similar to the 81.1% reported for older adults presenting to an emergency care centre [35]. Reporting inappropriate prescribing as either PIMs and or PPOs separately underestimates the full extent of inappropriate prescribing in the older adult population and to date published studies have rarely reported the prevalence of PIPs.

Published studies which have applied version 2 of the STOPP criteria report PIM prevalence of between 39.1% and 56.1% in older adults in the community and long-term care setting, and 42.1% to 88.5% in the inpatient setting [25–34]. The higher reported prevalence in the inpatient setting is likely a reflection of greater co-morbidity and prescription medication burden. Our finding that 59.1% of the study population were subject to one or more PIMs is similar to the proportion reported by others applying version 2 of the STOPP criteria in the inpatient setting [27, 30, 31].

Few studies have assessed the prevalence of PPOs using version 2 of the START criteria and to the best of our knowledge this is the first published study to record the prevalence of PPOs using this version in an inpatient setting. Although the proportion of patients over 65 years of age identified as having a PPO has been reported to be 21.8% for community dwelling residents in Spain [33], we obtained a PPO prevalence of 69.1% which is similar to the 67% reported by Wauters *et al*. for community-dwelling residents in Belgium [34].

Consistent with previous studies using both versions 1 and 2 of the STOPP criteria, this study identified a significant association between polypharmacy (>5 medications) and prescription of at least one PIM [25, 30, 32, 33, 35–45]. The association between PPO occurrence and polypharmacy identified in this study has been less consistently reported elsewhere [33, 36, 37, 46]. It is possible that prescribers may regard an increased medication burden and the resulting increased risk of adverse drug reactions as a barrier to the addition of further medication despite the potential for benefit, thus creating a 'treatment-risk paradox' [47].

The presence of PIMs and PPOs has previously been associated with potentially preventable medication-related hospital admissions and visits to the emergency department [8, 18], while reducing PIMs reportedly results in fewer visits to the emergency department [48]. After adjusting for co-variables, we identified a significant association between the presence of at least one PIM and repeated (three or more) hospital readmissions over the follow-up period.

In our study, we observed significantly increased mortality in those who had at least one PPO, a finding similar to that reported by Wauters *et al*. for a community-based population [34]. The reasons for this finding are not clear; however, it is possible that the failure to commence evidence-based therapies may result in increased morbidity and mortality or that in a population with high inherent mortality and poor prognosis, prescribers are less willing to add to their medication burden.

We also observed a significant association between mortality and PIMs in category K of the STOPP criteria. Category K contains medicines likely to increase the risk of falls and the use of drugs from this section, such as benzodiazepines, have been associated with higher mortality in the older adult [49].

Given the association of PIMs with repeated readmissions and PPOs with mortality observed in this study population, one would expect that interventions to reduce PIMs and PPOs would improve these outcomes. There is a dearth of interventional studies applying STOPP/START criteria to older adults, and fewer still that have specifically reported adverse outcomes such as hospital admissions and mortality [19–22, 50]. To the best of our knowledge, no published interventional study has employed version 2 of the STOPP/START criteria. In one analysis of a randomized control trial, medical inpatients aged 80 years and older were randomized to standard care (control) or enhanced pharmacist input (intervention), which included medicines reconciliation and assessment of prescriptions with recommendations of changes to be made [50]. The intervention group had significantly fewer PIMs and PPOs at discharge according to version 1 of STOPP/START compared to controls, and in keeping with our observations, those in the intervention group had a significantly lower adjusted relative risk of drug-related readmissions at 12 months follow-up. These results need to be interpreted with caution, however, as medication review in the trial, for which STOPP/START provided one possible tool, was only one of a number of pharmacist-led measures applied to the intervention group. Clearly, further interventional studies are required to assess what effect applying STOPP/START criteria has on adverse patient outcomes.

There are a number of limitations to our study. The study population comprised patients discharged from a single medical unit in one hospital and therefore results may not be generalizable to other settings. However, the observed prevalence of PIMs and PPOs in our study is comparable to those reported by others in different patient groups [14–18, 27, 30, 31].

Two of the STOPP criteria were not applied in the analysis, one of which was felt to be too implicit to be reliably and consistently applied (section A1) and there was insufficient information from the data sources used to apply the other (section A2). Both START criteria omitted from the analysis referred to administration of vaccinations (category I: influenza and pneumococcal vaccine), which is not recorded on systems accessible to clinicians in secondary care. The omitted criteria comprise only 3.5% of the total number of STOPP/START version 2 criteria and therefore it is unlikely to have had a significant impact on the results. This study only looked at the association of potentially inappropriate prescriptions at one point in time, taking no account of any subsequent changes to patients' prescriptions either in the community or at readmissions. Given that potentially inappropriate prescriptions may have been perpetuated, reduced or even intensified, it is difficult to predict how subsequent medication changes would have influenced the associations observed in this study.

As this is a retrospective observational study, we cannot establish a causal link between inappropriate prescribing and adverse outcomes such as mortality or hospital readmissions. We were unable to ascertain the mortality and readmission status of patients who moved out of the health board, which may have led to an under-recording of these outcomes.

Conclusions

Applying version 2 of the STOPP/START criteria to a population of older adults before discharge from hospital identifies those at high risk of readmission and death who may benefit from interventions to reduce PIMs and PPOs.

Competing Interests

There are no competing interests to declare.

Contributors

D.C. conceptualized and designed the study, collected and analysed data, and wrote the manuscript. J.M. designed the study, collected and analysed data, and wrote the manuscript. J.S.M. was the Principle Investigator, designed the study, analysed data, wrote the manuscript and acts as guarantor for the study.

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