

Exploring the prevalence and types of fall-risk-increasing drugs among older people with upper limb fractures

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Abstract

Objectives Medications and specifically fall-risk-increasing drugs (FRIDs) are associated with increased risk of falls: reducing their prescription may improve this risk. This study explored patient characteristics associated with FRID use, prevalence and type of FRIDs and changes in their prescriptions among older people with arm fractures over 6 months.

Methods Observational prospective study in three fracture clinics in England. Patients aged ≥ 65 years with a single upper limb fragility fracture were recruited. The STOPPFall tool identified the number and type of FRIDs prescribed at baseline, 3- and 6-month follow-ups. Changes in FRID prescription were categorised as discontinued, new or exchanged.

Key findings 100 patients (median age 73 years; 80% female) were recruited. At baseline, 73% used ≥ 1 FRID daily (median = 2), reducing to 64% and 59% at 3 and 6 months, respectively. Those with >1 FRID prescription had a significantly higher number of co-morbidities and medications and higher rates of male gender, polypharmacy, frailty and sarcopenia. The most frequently prescribed FRIDs were antihypertensives, opioids and antidepressants. Between 0 and 3 months, 44 (60%) participants had changes to FRID prescription: 20 discontinued (opioids and antihistamines), 13 started (antidepressants) and 11 exchanged for another. Similar trends were observed at 6 months.

Conclusion Use of FRIDs among older people with upper limb fragility fractures was high. Although overall use decreased over time, 59% were still on ≥ 1 FRID at the 6-month follow-up, with trends to stop opioids and start antidepressants. Older people presenting with upper limb fractures should be offered a structured medication review to identify FRIDs for targeted deprescribing.

Keywords: FRID; deprescribing; fall; fracture; older people

Introduction

Falls are a common problem for older people. One-third of those aged 65+ years worldwide fall at least once annually increasing to 50% among those aged 80+. [1] The most common fall-related injuries that lead to emergency department visits are fragility fractures, and 25% suffer a subsequent fracture, often of the hip, within 10 years. [2, 3] Fragility fractures lead to reduced patients' quality of life with an annual estimated cost of £4.4 billion in the UK. [4]

Polypharmacy (the use of five or more regular medications daily) is also common and increases the risk of falls in older people and is recognised as a potentially modifiable contributing factor. [5] A recent study showed that among patients aged ≥ 65 years who fell in the past year each additional medication above four increased their fall risk by 14%. [6] Some researchers suggest a stronger link between the types of medications taken and falling beyond polypharmacy alone. [7] Common fall-risk-increasing drugs (FRIDs) include antihypertensives, antihistamines, sedatives-hypnotics, antipsychotics, antidepressants, opioids and non-steroidal

anti-inflammatory drugs. [8] Although the mechanisms are not fully understood, these drugs may influence falls risk by adversely affecting the cardiovascular or central nervous system (e.g. orthostatic hypotension, bradycardia, sedation, sleep disturbance, confusion, dizziness). [8]

Frailty and sarcopenia are also recognised risk factors for falling in older age. [9] A prospective observational study of 204 patients (mean age 80.5 ± 8.3 years, with 101 robust and 103 frail) found that frail participants had significantly higher mean number of FRIDs, total number of medications, and drug-drug interaction exposure compared to their robust counterparts. [10] A recent review reported that sarcopenia and the risk of sarcopenia are associated with polypharmacy or a greater number of medications in community-dwelling older adults, regardless of diagnostic criteria used for sarcopenia. [11] However, the association between FRIDs specifically and sarcopenia has not yet been investigated.

Some observational studies and randomised controlled trials have shown that medication management interventions (including those with a broader focus of reducing polypharmacy

and/or potentially inappropriate prescribing) in different settings may reduce the risk of falls.^[12] It has also been reported that deprescribing, the process of tapering/dose reduction, stopping, or switching drugs, with the goal of improving outcomes,^[13] is feasible and can be performed safely in older people.^[14] Yet, deprescribing FRIDs specifically was reported to be difficult and infrequently performed even when supported by decision-making tools such as the STOPPFall tool.^[15–17] Difficulties relating to deprescribing FRIDs have been reported as a lack of awareness among physicians, older people and their caregivers and limited physician knowledge and skills in FRIDs withdrawal and uncertainty about the consequences of withdrawing FRIDs.^[18] Older patients also have concerns about deprescribing, such as fearing a relapse of their condition, and concerns about adverse drug withdrawal reactions.^[19]

Most previous studies have focused on hospital settings with limited research on the prevalence and patterns of FRIDs prescribing among older patients presenting with a fall to fracture clinics. A total of 25% of patients with upper limb fragility fractures will suffer a subsequent fracture, often of the hip, within 10 years. It is estimated that by identifying and managing these patients systematically, future hip fractures (approximately 20,000 a year in the UK) can be prevented.^[2, 20] NICE clinical guideline 161 recommends that future research studies focus on identifying the risk factors for falling that are most prevalent in the current UK older people to underpin the development of more effective and better-targeted multifactorial assessments and interventions.^[21] Screening and identifying FRIDs among those presenting with upper limb fractures caused by an accidental fall could enable a targeted medication review and deprescribing intervention.

The aims of this study were to: (1) describe the characteristics associated with FRIDs use among older people with upper limb fragility fracture resulting from a fall, (2) explore the prevalence and types of FRIDs using the STOPPFall screening tool and (3) observe any modifications in FRIDs prescription through routine care over 6-month follow-up.

Methods

Setting and participants

This study was a secondary analysis of data collected from an observational prospective study conducted in three outpatient fracture clinics in (blinded for reviewers). Ethical approval was given (REC Number: 18/NE/0377). Informed written consent was obtained from participants.

Participants aged ≥ 65 years attending a fracture clinic with a single upper limb fragility fracture from a low-trauma fall were recruited over a period of 12 months (March 2019 to March 2020) and were followed up for 6 months. Exclusion criteria included care home residents, active cancer diagnosis, multiple or lower limb fractures and inability to provide informed consent. Eligible patients were identified by the fracture clinic team using electronic records and sent an invitation letter and study information sheet before their clinic appointment. Informed written consent was obtained from all participants. A total of 375 patients were identified to be potentially eligible; 117 declined, 153 were not approached as only one researcher was recruiting during the fracture visits, one was identified to be on end-of-life care and four had no confirmed fractures (see [Supplementary File 1](#)). Therefore, the recruitment rate was 100/217 (46%).

Data collection

Baseline sociodemographic variables including gender, age, marital status, usual residence, the number of falls in the previous year, and the number of co-morbidities were collected from participants in person by a researcher. All prescribed medications (excluding topical medications) at baseline and 3- and 6-month follow-ups, reported by participants were recorded. Polypharmacy was defined by the presence of 5–9 regular medications and hyperpolypharmacy as the prescription of 10 or more regular medications.

Frailty was assessed according to the Fried Frailty Phenotype (FFP).^[22] This was operationalised as self-reported weight loss, exhaustion or low physical activity, measured slow gait speed (<0.8 m/s) and weak grip strength (maximum measurement with only unfractured arm <16 kg for women and <27 kg for men)^[23] measured using hand dynamometer (JAMAR). The presence of one or two criteria indicated pre-frailty and three or more represented frailty. The risk of sarcopenia was assessed using the SARC-F questionnaire.^[22]

Participants were asked to complete a prospective fall diary recording the date, suspected cause, location and the consequences of any further falls. They were telephoned by a researcher at 3 and 6 months after recruitment to collect self-reported information on falls and fractures within the previous 3 months and obtain a current list of medications. Participants' electronic primary care and hospital records were also reviewed to abstract details of medications and any documented falls or fractures.

Fall-risk-increasing drugs

The number and type of FRIDs prescribed for each participant were identified by a researcher at baseline, 3- and 6-month follow-up using the STOPPFall tool which includes 14 different classes of FRID and has been developed to help prescribers identify FRIDs that could be suitable for deprescribing.^[17] Prevalence of FRIDs was defined as the proportion of patients who had at least one FRID prescribed.^[24]

All changes in FRIDs prescription from baseline to 3-month follow-up, and from 3-month to 6-month follow-up, were defined as: (1) a FRID(s) discontinued, (2) a new FRID(s) prescribed or (3) FRIDs exchanged (i.e. one FRID being changed for another).

Data analysis

Data were analysed using SPSS (SPSS IBM Corp version 24). Participant characteristics were described for the whole group and subgroups were categorised according to FRID use: no FRIDs, one FRID, and >1 FRID prescribed. Median values with interquartile range (IQR) were reported for continuous variables with a skewed distribution and counts and percentages for categorical variables. Differences between characteristics of participants with no FRIDs, 1 FRID or >1 FRIDs were calculated using Kruskal–Wallis tests for continuous skewed data and chi-squared tests for categorical data. The prevalence of FRIDs and the most common FRID pharmacological subgroups were calculated for each time interval using descriptive statistics (numbers, percentages). The changes in the number or type of FRIDs between baseline and 3 months and between 3- and 6-month follow-ups were recorded using descriptive summaries.

Results

Participant characteristics

One hundred participants were included in the study (Table 1). Their median age was 73 years, (IQR 70–80), 80% were women and 99% lived in private housing either alone (44%) or with relatives or friends (55%). The median number of co-morbidities was 5 (IQR 3–7) and the median number of medications was 5 (IQR 3–8). At baseline, 42% had polypharmacy and an additional 14% were on hyperpolypharmacy. Fifteen percent of the participants were living with frailty and 18% were at risk of sarcopenia. The median number of falls within the previous year was 1 (IQR 1–2).

Participants prescribed 1 FRID were of similar age and female predominance compared with those not prescribed FRIDs and had similar rates of frailty and risk of sarcopenia. Significant differences were observed for participants prescribed > 1 FRIDs, with higher prevalence of men (85% of men >1 FRIDs compared to 5% without FRID and 10% on 1 FRID; $P = .001$). Those with >1 FRIDs had a higher number of co-morbidities (median 6 versus 3 without FRIDs, 4 with 1 FRID; $P \leq .001$), and a total number of medications (median 6 versus 2 without FRIDs, 4 with 1FRID; $P < .001$).

Most cases of polypharmacy were among those prescribed >1 FRID ($P < .001$). There were also increased rates of frailty and risk of sarcopenia observed for those with >1 FRID prescribed (27% Frail versus 4% and 4%; $P < .001$, and 30% sarcopenia versus 7% and 8%; $P = .015$).

A total of 87% and 80% of patients had follow-up interviews at 3 and 6 months, respectively, to collect self-reported data on falls and medications, supplemented by reviewing their clinical records. For those who did not have a follow-up interview, data on medications and falls were obtained solely from their primary care and hospital clinical records. Over the 6-month follow-up, 14 (14%) participants had at least one further fall but no significant differences were found in the number of participants who had further falls between those who had 1 or >1 FRIDs compared to those without FRID (15% and 11%, respectively; $P = 0.878$).

Prevalence and type of FRIDs at baseline, 3-month and 6-month follow-up

At baseline, 73% of participants were prescribed ≥ 1 FRID (median 2 (IQR 1–3). This decreased to 64% at 3-month and 59% at 6-month follow-up. The most common pharmacological

Table 1 Characteristics of study population based on FRID prescription

Characteristic		Total N = 100	No FRIDs N = 27	1 FRID N = 26	>1 FRIDs N = 47	P
		Median (IQR)				
Age		73 (70–80)	73 (70–78)	73 (71–78)	75 (71–82)	0.427
Number of co-morbidities		5 (3–7)	3 (2–6)	4 (3–5)	6 (5–9)	<.001
Number of medications		5 (3–8)	2 (0–4)	4 (2–7)	6 (5–10)	<.001
Number of falls within the past year		1 (1–2)	1 (1–2)	1 (1–2)	2 (1–2)	0.305
		Frequency (%)				
Gender	Female	80 (80%)	26 (96%)	24 (92%)	30 (64%)	0.001
	Male	20 (20%)	1 (4%)	2 (8%)	17 (36%)	
Marital status	Single	13 (13%)	5 (19%)	4 (15%)	4 (9%)	0.707
	Married	55 (55%)	12 (44%)	13 (50%)	30 (64%)	
	Divorced or separated	6 (6%)	1 (4%)	2 (8%)	3 (6%)	
	Widowed	24 (24%)	8 (30%)	6 (23%)	10 (21%)	
	Cohabiting	2 (2%)	1 (4%)	1 (4%)	0 (0%)	
Residence	Private home living alone	44 (44%)	14 (52%)	11 (42%)	19 (40%)	0.435
	Private home with friends/relatives	55 (55%)	13 (48%)	14 (54%)	28 (60%)	
	Sheltered accommodation	1 (1%)	0 (0%)	1 (4%)	0 (0%)	
Fried frailty phenotype	Robust	39 (39%)	14 (52%)	16 (62%)	9 (19%)	<.001
	Pre-frail	46 (46%)	12 (44%)	9 (35%)	25 (53%)	
	Frail	15 (15%)	1 (4%)	1 (4%)	13 (27%)	
Sarcopenia (SARC-F)	No sarcopenia	82 (82%)	25 (93%)	24 (92%)	33 (70%)	0.015
	sarcopenia	18 (18%)	2 (7%)	2 (8%)	14 (30%)	
Polypharmacy	0–4 (no polypharmacy)	44 (44%)	21 (78%)	14 (54%)	9 (19%)	<.001
	5–9 (polypharmacy)	42 (42%)	6 (22%)	11 (42%)	25 (53%)	
	>10	14 (14%)	0 (0%)	1 (4%)	13 (28%)	
	(hyperpolypharmacy)					
Number of participants with ≥ 1 fall during the 6-month follow-up		14 (14%)	3 (11%)	4 (15%)	7 (15%)	0.878

Table 2 Prevalence of FRID subgroups among those prescribed FRIDs at baseline and 3- and 6-month follow-ups. Listed by greatest baseline prevalence

FRID pharmacological classes	Baseline	3-month follow-up	6-month follow-up
	N = 73	N = 64	N = 59
Antihypertensives	45 (62%)	45 (70%)	42 (71%)
Opioids	28 (38%)	18 (28%)	12 (20%)
Antidepressants	16 (22%)	19 (30%)	18 (31%)
Antihistamines	12 (16%)	10 (16%)	8 (14%)
Diuretics	12 (16%)	10 (16%)	10 (17%)
Antiepileptics	7 (10%)	5 (8%)	4 (7%)
Oral hypoglycaemics	8 (10%)	7 (11%)	7 (12%)
Benzodiazepines and related drugs	4 (5%)	4 (8%)	2 (3%)
Antipsychotics	2 (3%)	2 (3%)	3 (5%)
Anticholinergics	4 (5%)	4 (6%)	4 (7%)
Alpha blockers for benign prostatic hyperplasia	3 (4%)	3 (5%)	2 (3%)
Alpha blockers as antihypertensives	1 (1%)	1 (2%)	2 (3%)
Vasodilators	1 (1%)	3 (5%)	2 (3%)
Medicines for overactive bladder	0 (0%)	0 (0%)	0 (0%)

Table 3 Types of prescription change to FRIDs during follow-up period

Type of prescription change	Baseline–3 months	3–6 months
	(N = 44)	(N = 31)
FRIDs discontinued	20 (45%)	20 (65%)
New FRIDs	13 (30%)	7 (23%)
FRIDs swapped	11 (25%)	4 (13%)

class of FRIDs prescribed at baseline, 3- and 6-month follow-ups were antihypertensives, opioids and antidepressants (Table 2). The total number of medications prescribed at 3- and 6-month follow-ups reduced from 6 (IQR 4–9) to 5 (IQR 2–8) but the median number of FRIDs at 3- and 6-month follow-ups remained the same with 2 (IQR 1–3) prescribed. The prevalence of polypharmacy among those who were prescribed at least one FRID decreased from 49% at baseline to 38% at 3 months then increased slightly at 6 months (40%).

A total of 44 (60%) of 73 participants with at least one FRID at baseline had changes made to their prescribed FRIDs during 3-month follow-up: discontinuation ($n = 20$, 45%), new prescription (13), and 11 had one FRID exchanged for another type of FRID (Table 3). Between 3- and 6-month follow-ups, 31 (48%) patients had changes to their FRIDs prescription. Similarly, discontinuation was the most common change (20; 65%), 7 participants were prescribed new FRIDs and 4 had one FRID exchanged for another type of FRID. Overall, the FRID pharmacological class with the greatest increase in use over 3- and 6-month follow-ups were antihypertensives (baseline users 62%, 3 months 70%, 6 months 71%) and antidepressants (baseline users 22%, 3 months 30%, 6 months 31%). The FRID pharmacological class with the greatest decrease at follow-up intervals was opioids, which decreased from 38% at baseline to 20% at 6 months.

Discussion

This observational, descriptive, prospective study of participants aged ≥ 65 years with a recent upper limb fragility fracture found that three-quarter of participants was

prescribed at least one FRID at baseline and 59% were still prescribed at least one FRID 6 months later. The most common classes of FRIDs prescribed were antihypertensives, opioids and antidepressants. Most changes to FRID prescription occurred during the first 3 months of follow-up, with opioid discontinuation and antidepressants commencement most common. Male gender, high levels of co-morbidity, total number of medications, polypharmacy, frailty and risk of sarcopenia were all associated with increased use of FRIDs.

This study was able to show the prevalence of FRIDs prescription among a sample of older people who sustained a fracture following a fall and to report when most changes in FRIDs prescription occurred during 6-month follow-up. However, the study was small and took place in one city, with a convenience sample of participants limited to those with a previous history of fall, single upper limb fracture and able to provide informed consent. This may limit generalisability, particularly given the high rates of falls among individuals with dementia or those with hip fractures and so potentially underestimates FRID usage. On the other hand, FRIDs prescription might be higher in this study population of patients who have all fallen, compared to the general population of frail people who have not fallen. Data collection of the number and type of FRIDs did not include the daily dosage of each drug and more detailed drug information might have improved understanding of the association between drug dosage and fall risk. There was also no information regarding where medication changes took place and by whom. This study utilised descriptive statistics comparing participants without FRIDs to those on 1 FRID or >1 FRID, while this has highlighted interesting observed differences between the groups, it does not deeply assess associations with FRID use and how these may be impacted by other characteristics. Further observational studies on larger cohorts of older adults, with wider inclusion criteria, would be of benefit.

The high prevalence of FRID prescription (73%) found among older people attending outpatient clinics for fall-related fragility fractures in this study is similar to figures reported in hospital settings. For example, one study in the UK found that 65% of older patients admitted to the hospital following

a fall took at least one FRID.^[24] Another retrospective study in the US found that over 75% of older people admitted to the hospital with fragility fractures (wrist, shoulder and hip fractures) were prescribed at least one FRID both before and after the fracture.^[25] This might be due to the characteristics of the target populations, as high co-morbidity and polypharmacy rates were associated with increased FRIDs prescription in this study. Interestingly, in this study those individuals on >1 FRIDs had higher rates of frailty and sarcopenia, perhaps suggesting that those prescribed more than 1 FRID should be given priority as a group for a medication review.

Prescription of antihypertensives remained high throughout the 6-month study period with some participants using multiple antihypertensives in combination. This may be due to recognised common barriers to deprescribing antihypertensives including automatic repeat-prescription algorithms, time constraints, clinicians' fear of subsequent hypertension with risk of stroke, and unclear guidance for treatment of hypertension in the older population.^[26] A more pragmatic approach to current stringent blood pressure regulation guidance for older people might help reduce the adverse effects of orthostatic hypotension and the associated risk of falls and fracture,^[27] but a better understanding of the effects of ageing syndromes, such as frailty, on the management of hypertension is needed.^[28] Antidepressant prescription also increased during the 6 months after the fracture. A similar trend (9% increase in antidepressant prescription) was observed in a Spanish study which investigated the prevalence of FRIDs in older people before and after a fracture.^[7] An increase in antidepressant prescribing among older adults following fractures was associated with reduced mobility and mood.^[29] Studies with a longer follow-up would be of use to investigate whether antidepressants are continued to be prescribed long-term.

There are recognised challenges for deprescribing opioids due to the lack of specific guidelines or alternative treatments, and patients' fears of stopping medication and pain recurrence.^[30] However, in this study opioids were the most common FRID class to be discontinued. This may reflect the short-term use for acute pain due to fractures and/or clinician awareness of the association between opioids and falls/fractures in older people.^[31] Whereas the literature focuses on the long-term use of opioids for pain management with few studies investigating the feasibility and impact of deprescribing opioids.^[32]

In this study, 14% of participants had another fall within 6 months with no significant differences between those who were prescribed FRIDs compared to those who were not. This is consistent with a systematic review that was inconclusive regarding the impact of deprescribing on fall rates or incidents.^[8] This may be due to the small sample sizes of the included studies as well as the likely multifactorial nature of falls and the varying risk of different FRIDs. It is unclear to what degree a particular risk factor or combination of risk factors (e.g. specific FRIDs) must be reduced to produce an appreciable change in falls. Therefore, it has been suggested that medication review/deprescribing interventions work best in combination with other interventions. For example, deprescribing antihypertensives in older people and taking non-pharmacological approaches, such as regular exercise and reduced dietary sodium, is beneficial in reducing falls risk.^[33, 34] Recently, the Department of Health and Social Care in the UK published the national overprescribing review report which

suggests exploring the evidence of social prescribing and non-pharmacological treatments in conjunction with medicine optimisation and deprescribing on patient outcomes.^[35] Future research should focus on understanding the effectiveness of multifactorial person-centred interventions that integrate a fall risk assessment tool including FRIDs in preventing further falls and fractures.

The European Geriatric Medicine Society (EuGMS) recommends taking a history of falls and use of the STOPPFall screening tool to identify FRIDs when performing a medication review in older people.^[17] The STOPPFall tool should not be used as a stand-alone strategy to reduce fall incidents but should be implemented in a multifactorial strategy to achieve the best chance of success.^[17] Several evidence-based algorithms and guidelines have been developed by the Bruyère Research Institute Deprescribing Guidelines Research Team that could be used by clinicians to guide them in the deprescribing process <https://deprescribing.org/resources/deprescribing-guidelines-algorithms/>. Patients should be engaged throughout the process with their personalised needs and concerns taken into account as there is a mounting evidence that patient-centred care and shared decision-making could improve patient satisfaction, adherence, quality of life and overall health outcomes.^[36]

Policy and practice implications

The study findings support the recommendations and suggestions made by the EuGMS Task and Finnish Group on FRIDs for systematically checking for a history of falls and a high risk of falling before prescribing FRIDs. Taking into account the high proportion of older people with arm fractures who are prescribed at least one FRID, a structured medication review should be conducted for all patients with an acute fall, recurrent falls in the past year. Clinicians and commissioners should use appropriate tools and processes to identify and reduce FRIDs prescriptions in their older population, especially those with a fall history. STOPPFall is useful in a research context but future studies should explore the feasibility and practicality of using and implementing the tool by clinicians in clinical practice and the barriers and facilitators for integration in different inpatient and outpatient settings.

Conclusions

This study has shown that FRIDs prescription in older people with upper limb fragility fractures was high, with 73% of participants prescribed ≥ 1 FRID at baseline. Although overall use decreased over time, 59% of participants were still on at least one FRID at the 6-month follow-up, with trends to stop opioids and start antidepressants during the follow-up period. Male gender, number of co-morbidities, total number of medications, polypharmacy, frailty and risk of sarcopenia were associated with the use of > 1 FRID. The findings from this study highlight the high prevalence of FRID prescription at or following upper limb fragility fracture and also indicate individual characteristics associated with greater amounts of FRIDs prescribed. Future studies should focus on exploring the impact of a structured medication review to identify FRIDs for targeted deprescribing as part of a multifactorial person-centred intervention targeting older people presenting with upper limb fractures on preventing future falls and fractures.

Supplementary Material

Supplementary data are available at *International Journal of Pharmacy Practice* online.

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Author Contributions

All authors contributed to the conception and design of the study. KI completed the day-to-day research activity, recruitment, data collection and data entry. NC and II completed the quantitative data analysis. KI, NC and HCR drafted the manuscript and all authors read and approved the final manuscript.

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Declaration of Interest

All authors declare that they have no competing interests.

Data Access

The authors confirm had complete access to the study data, with an explanation of the nature and extent of access, including whether access is ongoing.

Data Availability

The data underlying this article cannot be shared publicly due to the privacy of individuals that participated in the study. The data will be shared upon reasonable request to the corresponding author.

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