

*Research Article*

## Polypharmacy and medication related falls risk in orthogeriatric femoral fracture patients

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**ARTICLE INFO**

Received: 10/09/2021  
Revised: 22/11/2021  
Accepted: 25/05/2022  
Published: 27/05/2022

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**KEYWORDS:**  
polypharmacy; falls risk;  
femoral fractures;  
geriatrics

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**ABSTRACT**

To report polypharmacy rates and identify specific medications that increase falls risk in orthogeriatric femoral fracture patients. A retrospective sub-analysis, using the electronic medical records of patients admitted with a minimal trauma femoral fracture to a tertiary teaching hospital during a 12-month period was undertaken. Specific medications associated with falls risk were classified under three specific groups: benzodiazepines, tricyclic antidepressants (TCAs), and non-benzodiazepine hypnotics. A sample of 131 patients was included in the audit. Of these, 99 patients (75.6%) were reported to be taking five or more medications prior to their falls related admission. From this, 49 patients (37.4%) were taking ten or more medications. One in five patients were found to be taking specified falls risk medications prior to admission, primarily benzodiazepines (75.8%). Orthogeriatric patients admitted to hospital with a femoral fracture following a minimal trauma fall were commonly taking five or more medications prior to admission. Over a third of patients that were reported to take ten or more pre-admission medications were taking specified falls risk medications. This highlights the need for medication-reviews and potential de-prescribing, focusing on falls risk medications, to reduce incidence of falls and minimal trauma fractures in high-risk patients.

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**INTRODUCTION**

Falls are one of the most common mechanisms of injury and endure as a persistent risk to morbidity and mortality across all ages (Patel & Ackermann, 2018). Unintentional falls in older adults impose a significant physical and emotional burden on patients as well as considerable economic burden on national health care systems (Peel, 2011).

Polypharmacy is a growing concern for older adults and the geriatric aging population (Hubbard et al., 2015). It is defined as the use of multiple medications, commonly more than is medically necessary (Page, Falster, Litchfield, Pearson, & Etherton-Ber, 2019). Literature supports that polypharmacy is common in older adults with the highest number of medications

taken by those residing in residential care facilities (Ray, Thapa, & Gideon, 2000). Nearly 50% of older adults take one or more medications that are not medically necessary (Woolcott et al., 2009). Polypharmacy is associated with an increased falls risk in the geriatric population (Hubbard et al., 2015).

Research has clearly established a strong relationship between polypharmacy and negative clinical consequences, including falls and subsequent minimal trauma femoral fractures (Ray et al., 2000). Moreover, well designed inter-professional intervention studies that focus on enrolling high risk older patients with polypharmacy have shown that they can be effective in improving the overall quality of prescribing including rationalisation of medications and de-prescribing (Wimmer et al., 2017).

All patients should have their medication burden reviewed regularly with respect to its propensity to cause falls. Falls can be caused by almost any medication that acts on the central nervous system or on the circulation system (ACSQHC, 2009). Falls may be the consequence of recent medication changes but are usually caused by medicines that have been given for some time. Medications that act on the brain (psychotropic drugs), are known to approximately double the risk of falling (Ray et al., 2000). There is good evidence that stopping these medications can reduce the incidence of falls (Finkle et al., 2011).

This audit focuses on reporting cases of polypharmacy and identifying specific medications that increase falls risk in orthogeriatric femoral fracture patients following a minimal trauma fall.

## MATERIALS AND METHODS

### Study Design

This study was a sub-analysis of a retrospective inpatient file audit of geriatric patients with a femoral fracture who were commenced on anti-osteoporosis therapy by discharge. It was performed at a central site in a major tertiary teaching hospital in Victoria, Australia. All medication therapy data was collected by examining patients' electronic records.

The inclusion criteria encompassed patients admitted for a hip fracture specifically the neck of femur, following minimal trauma fall with a discharge date during the specified 12-month period. The incidence of polypharmacy and specific medications associated with an increased falls risk is reported in this sub-analysis, as part of a subsection of the wider osteoporotic femoral fracture audit.

Between June 1, 2018, and June 30, 2019, a list of potentially eligible patients was retrieved from a central database. Based on the aims of the original audit, patients were screened and excluded if one or more of the following criteria applied: non-minimal trauma fracture; less than 65 years of age during admission; anti-osteoporosis therapy prior to admission; pathological fractured neck of femur; palliative; died during admission.

### Participants

The population chosen were those with minimal trauma fall and femoral fractures as per inclusion

criteria for the original audit. These injuries tend to be associated with longer lengths of hospital stay, providing greater opportunity for prescribers to review and implement changes after a falls assessment.

### Outcome Measures

The primary outcome was to determine the proportion of patients with various degrees of polypharmacy prior to admission in orthogeriatric femoral fracture patients following a minimal trauma fall.

Secondary outcomes were formulated to determine what proportion of polypharmacy had the potential to increase falls risk in this cohort and to identify specific medication usage. A selected group of medications were audited with a specific focus on a group of medications commonly associated with a significant falls risk as well as their potential for deprescribing. These were classified under three specific groups: benzodiazepines, tricyclic antidepressants, and non-benzodiazepine hypnotics. Refer to Table 1.

### Data Collection

Data was obtained through electronic medical systems, including scanned medical records using electronic content manager, pathology results system via clinical information systems, and the hospital prescription dispensing system.

Table 1. Classification of selected drug classes

Drug Class	Drug Name
Benzodiazepines	Alprazolam, Bromazepam Clobazam, Diazepam Flunitrazepam, Lorazepam Nitrazepam, Oxazepam Temazepam
Tricyclic antidepressants	Amitriptyline, Clomipramine Dosulepin (dothiepin), Doxepin Imipramine, Nortriptyline
Non-benzodiazepine hypnotics	Zolpidem, Zopiclone

Data was collected in two sections using a data collection tool: the first section investigated patients who met inclusion criteria and the second section referred to patient parameters such as diagnosis and date of admission. This data was entered into an auditing tool, Research Electronic Data Capture (REDCap®) by two auditors. Data was then extracted

into an excel spreadsheet for analysis. The spreadsheet was then stored on the secure pharmacy shared drive in a folder named for that purpose and all files were password protected, with the intent to be destroyed seven years after completion of the audit.

Pharmacy students were recruited as auditors and allocated to work in pairs to ensure accurate data collection and minimize variability in data interpretation. The pairing of students aided in reducing programmer input error in the setting of manual electronic data entry. The method for monitoring competence between these auditors included attendance and completion of an auditing workshop and supervision by the lead pharmacist investigator throughout the auditing phase of this study.

### Data Analysis

Results from the data collection tool were analysed manually using pivot tables in Microsoft Excel. The data was analysed to obtain the total number of regular and when required medications patients were documented to be taking prior to their falls related admission. All parameter analyses were expressed as percentages and total number of patients.

### Ethics approval

This project was reviewed against the tenets of the National Statement on Ethical Conduct in Research (NHMR, 2007). The ethics application was deemed to have met the criteria for a Quality Assurance project that did not require a full review by the Human Research Ethics Committee (HREC). The Melbourne

Health HREC granted ethics approval (QA Ref. No. QA2019092) to be conducted at the city campus site for this project.

## RESULTS

### Patient Characteristics

A total of 218 patients were screened in this sub-analysis. Of these, 87 patients met exclusion criteria, leaving 131 patients included in the audit. Female gender represented 73.5% of the sample size, and there was a mean age of 82 years. Most of the sample population were identified as non-smokers (69.9%) with few active smokers (5.9%). Smoking status of the remaining 24.3% was unable to be identified from patient notes.

Patients were excluded if they met one palliative management or pathological neck of femur fractures excluded if they met one or more of the following exclusion criteria; preadmission anti-resorptive therapy (n=43), for palliative management or pathological neck of femur fractures (n=26), deceased during admission (n=9), fractures which were not a result of minimal trauma (n=7), non-neck of femur fractures (n=20).

Co-morbidities recorded included gastro-oesophageal reflux disease (GORD) (23, 16.9%), chronic renal impairment (10, 7.4%), cardio- or cerebro-vascular disease (2, 1.5%), past or present embolism (7, 5.1%), anaemia (12, 8.8%), dysphagia/ swallowing difficulties (3, 2.2%), hypercalcaemia (1, 0.7%) and hepatic impairment (3, 2.2%).

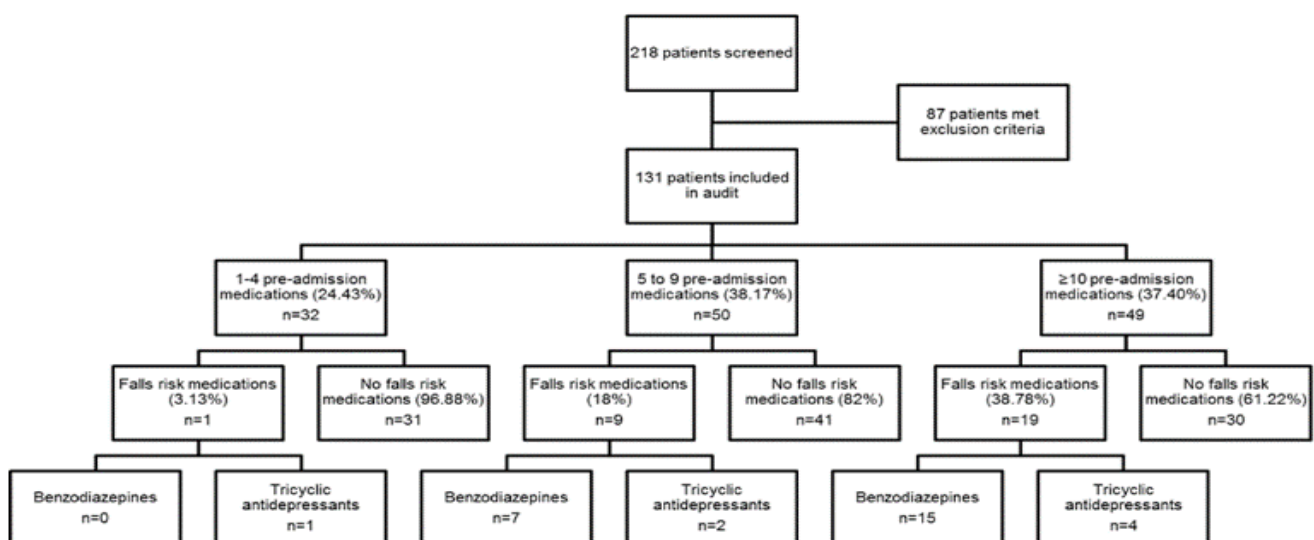


Figure 1. Regular medications prior to admission flowchart

## Polypharmacy

A total of 75.6% of patients audited were reported to be taking five or more medications prior to their falls related admission. Of these, 37.4% of patients were found to be taking ten or more medications prior to admission (Refer to figure 1). Only 24.4% of patients were reported to be on four medications or less.

## Medication associated with falls risk

A total of 22.1% of patients were found to be taking the specified high falls risk medications focused on in our audit prior to admission. Benzodiazepines accounted for 75.8% (n=22) of these and tricyclic antidepressants 19.3% (n=7). One patient was reported to be taking both a benzodiazepine and a tricyclic. There were no patients in this study that were taking non-benzodiazepine hypnotics in the form of zolpidem or zopiclone. Refer to Figure 1.

## DISCUSSION

Polypharmacy greatly affects older patients in both community and hospital settings (Hubbard et al., 2015). According to Australian Pharmaceutical Benefits Scheme (PBS) dispensing data (Page et al., 2019) and an Australian hospital prospective cohort study (Hubbard et al., 2015), 36.1 – 52.7% of patients aged 70 years or older were taking five - nine regular prescription medications, and 6.6% – 23.42% were taking ten or more regular prescription medications. Community polypharmacy rates are likely to be conservative as Page et al. (2019) did not assess non-PBS prescriptions and neither study assessed complementary and alternative medications or over-the-counter products. Upon discharge from hospital, the proportion of patients taking 5-9 prescription medications decreased slightly (50.88%), however, the proportion of patients taking 10 or more prescription medications increased by 4.89% (28.31%) (Hubbard et al., 2015). These figures highlight significantly high rates of geriatric polypharmacy and a need for potential deprescribing during hospital admission.

Review with the intent of potential deprescribing is essential to reduce the risk of drug-drug interactions and potential adverse effects for patients taking five or more medications (Holbeach & Yates, 2010). Medicated related problems are the cause of 30% of all hospital admissions in patients aged over 75

(Holbeach & Yates, 2010), highlighting polypharmacy as a significant risk factor. In some cases, patients are prescribed additional medications to treat adverse effects (Holbeach & Yates, 2010), further increasing their medication burden. This study found that 75.57% of the patient cohort was taking at least five medications pre-admission, similar to Hubbard et al.'s study of multiple Australian hospitals from 2005 to 2010 (76.16%) (Hubbard et al., 2015; Wimmer et al., 2017).

Estimated rates of polypharmacy for those patients taking ten or more medications was much lower in community, 6.6% (Page et al., 2019), than demonstrated in the hospital population. Our study showed 37.4% of patients admitted were taking ten or more medications pre-admission, a higher result when compared to Hubbard et al.'s hospital study (23.42%). These results are consistent with the premise that polypharmacy in geriatrics increases the likelihood of adverse events, such as minimal trauma fractures, and subsequent hospitalisation.

Orthogeriatrics is a subspecialty developed in response to clinical, social and financial needs in the management of patients with fragility fractures, and more specifically hip fractures (Sabharwal & Wilson, 2015). This medical unit commonly accommodates complex frail older patients with multifaceted comorbidities (Roll, Tittel, Schäfer, Burkhardt, & Kinner, 2019) and tends to require multidisciplinary team approach to clinical care. Geriatric patients taking more than five medications should be identified upon admission and flagged for pharmacist review. Those presenting following a fall should be prioritised (Donaldson, Kelley, Dhingra-Kumar, Kieny, & Sheikh, 2017). Pharmacists can then review the patient, obtain a best possible medicines history, and create a medication management plan (ACSQHC, 2019). The goal of pharmacist intervention should be to simplify patient regimens to improve adherence and minimise adverse events. The pharmacist should encourage the patient to ask questions about their medications and convey the risks and benefits of changing or ceasing medications (ACSQHC, 2019).

It is essential to communicate clearly and in a timely manner with the patient's regular general practitioner after discharge to convey any deprescribing

recommendations and changes made to medication regimens to ensure continuity of care. Pharmacists should also provide patients with medication education, including medication lists, and where appropriate consider compliance aids to reduce confusion and improve adherence when managing multiple medications (ACSQHC, 2019).

Causes of falls are often multifactorial, but medications can play a big role and are a modifiable risk factor (Patel & Ackermann, 2018). Many medications can contribute to increasing a patients' falls risk. Medications that contribute to adverse effects such as postural hypotension, drowsiness, dizziness, blurred vision or confusion are thought to increase this risk. Common medication classes that can contribute to these adverse effects include psychotropic medications (antidepressants – including TCAs, antipsychotics, hypnotics – including benzodiazepine and non-benzodiazepine hypnotics), some of which were focussed on in this audit, but anticholinergic medications, antihypertensives, diuretics and other cardiovascular medications are also known to contribute. There is some evidence to suggest that withdrawal of psychotropic and cardiovascular drugs may reduce falls by around 50% (Poly, Islam, Yang & Li, 2020), however the risk/benefit of withdrawal of some medications must be weighed carefully.

The use of sedatives and hypnotics, antidepressants, and benzodiazepines has demonstrated a significant association with falls in elderly individuals (Woolcott et al., 2009). Many studies group psychotropics together so interpretation of the risk of falls for each individual drug class is often difficult to conclude (Poly et al., 2020; Ray et al., 2000). In one meta-analysis, investigating the association between medications and falls, the pooled odds ratio was 1.51 for tricyclic antidepressant use and 1.48 for benzodiazepine use for one or more falls (Leipzig, Cumming, & Tinetti, 1999). An American study showed the rate of falls was increased in a Tennessee nursing home by 44% in those taking benzodiazepines (Ray et al., 2000).

Another meta-analysis of observational studies suggested the relative rate of hip fractures in benzodiazepine users was 1.34 compared with non-

users (Poly et al., 2020). Zolpidem has been demonstrated to increase the risk of hip fractures by 2.55 times after initial prescription in those older than 65 years (Finkle et al., 2011).

Twenty-nine patients in our study were taking either benzodiazepines or tricyclic antidepressants and one patient was taking both. This highlights that this reversible risk factor of patients taking high falls risk medications could have potentially been addressed through a medication review in 22% of patients audited.

In our study, the focus was only placed on three classes of medications, but other patients audited may have been taking different medications that have also been demonstrated to contribute to falls. Review of medications with the aim of de-prescribing or changing to lower falls risk medications where possible, ideally should be done routinely as a preventative measure in all patients. It should also be an integral component of falls reviews and assessments for all patients presenting with a fall and fracture.

The patient characteristics of this audit sample size were heavily swayed towards the female gender (73.5%). In women, the proportion of the hip fractures that occurred at the intertrochanteric site rises significantly with age (Crilly, Kloseck, & Mequanint, 2016). It is reported the rising proportion of intertrochanteric fractures in women may reflect greater trabecular bone loss with age in women (Tanner, Kloseck, Crilly, Chesworth, & Gilliland, 2010). The mean age of this study is also in line with intertrochanteric fractures is significantly older than those with subcapital fractures ( $83.9 \pm 8.03$  SD) (Wimmer et al., 2017). With increasing age, the fall becomes more common and fracturing may be more a reflection of the falling rather than thin bones, although the rising proportion of intertrochanteric fractures speaks to the rising prevalence of osteoporosis, at least in women (Tanner et al., 2010).

## LIMITATIONS

Data was retrieved from scanned medical records. The limitation of collecting data retrospectively meant there was a potential for incomplete data. Omitted

data affects overall results which may mislead conclusions. A relatively small sample (n=131 patients) size will also affect the limited ability to demonstrate statistical significance, leads to a higher variability, which may lead to bias. Larger studies involving patients from multiple specialties is suggested to validate the results found in this study. The study was limited by auditing time constraints. The specified data collection period of 12 months produced a small sample size of 131 patients. The sample size could have been increased by extending the retrospective data collection period.

The authors of this study recognise the potential of other medication groups to increase falls risk which were not audited in this study. The specific focus of three groups (benzodiazepines, tricyclic antidepressants, and non-benzodiazepine hypnotics (zolpidem and zopiclone) were selected for their potential ease of deprescribing. Given the audit time constraints, it was not possible to include all medications which may be associated with increased falls risk. Authors recommend potential audits to include a wider scope of medication groups in future. Furthermore, other falls risk assessments, such as postural blood pressure measurements, blood sugar levels, sedation and vision assessments were not audited by this study and could have provided further information on falls risk.

Auditors did not collect data on the commencement of medications that increase a patient's fall risk during the admission following the minimal trauma fracture. If a patient included in the study was started on a falls risk medication while in hospital, this would highlight a need for further education on these medication classes and their role in increasing the risk of further falls and potential hospitalisation in orthogeriatric patients.

This study did not investigate if patients taking the specified pre-admission falls risk medications had these medications changed during admission. Hospital admissions provide a valuable opportunity for pharmacist interventions through medication reviews and patient education. A patient may have their pre-admission medication ceased, reduced to a lower regular dose, or changed from taking regularly to only when required. These changes contribute to

reducing polypharmacy and lowering risk of future falls, minimal trauma fractures, and consequent hospital admissions.

## CONCLUSIONS

Falls in older adults impose a significant physical and emotional burden on patients. Polypharmacy continues to be an area for review in the orthogeriatric femoral fracture patient cohort. Over three quarters of orthogeriatric patients admitted to hospital with a neck of femur following a minimal trauma fall were taking five or more medications prior to admission. Over thirty percent of these patients were actually on ten or more medications pre-admission and almost 39 percent of those on more than ten medications were taking high falls risk medications. The current best practice encompasses the patient's care from arriving at the hospital through to discharge and involves the whole multidisciplinary team.

All patients should have their medication burden reviewed with respect to its propensity to cause falls at regular intervals. It was found that one in five patients who presented with a femoral fracture following a minimal trauma fall were taking specified medications known to increase falls. This highlights the need for medication review and potential deprescribing in patients aged 65 and older, with a particular focus on falls risk medications, to reduce incidence of falls and minimal trauma fractures.

## ACKNOWLEDGEMENTS

We acknowledge Evelyn Dimopoulos, Kimberly Wadyehwata, Sukhan Kaur pharmacy students, for their role as auditors, Sara Chuang, Monash University Pharmacy Student supervisor, and the pharmacy practice research committee at the Royal Melbourne Hospital, for their contribution in reviewing this report.

Study data was collected and managed using the REDCap electronic data capture tool hosted by the Royal Melbourne Hospital Business Intelligence Unit.

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