Modification of Potentially Inappropriate Prescribing Following Fall-Related Hospitalizations in Older Adults.

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ABSTRACT

Background: There is strong evidence that potentially inappropriate prescribing is associated with falls in older adults. Fall-related hospitalizations should trigger medication review.

Objectives: The aim of this before-and-after cohort study was to explore patterns of relevant potentially inappropriate prescribing in older people with fall-related hospitalizations.

Methods: Data on older adults with hospitalizations for falls, fractures and syncope between 2012 and 2016 were collected from 44 General Practices in Ireland. Fall-related prescribing was defined from the Screening Tool for Older Persons' Prescriptions (sedatives and vasodilators) and the Screening Tool to Alert to Right Treatment (vitamin D). Prevalence of prescriptions were estimated from general practice and hospital discharge records. Mixed-effects logistic regression was conducted to compare the 12-month pre- and post-hospitalization periods.

Results: Overall, 927 individuals (68% female, average age 81.2 (SD=8.6)) were included. The diagnosis for 45% was a fracture, 28% had syncope, and 27% had a fall without fracture/ syncope. After adjustment for covariates and practice clustering effects, both vitamin D and sedatives had higher odds of prescription post-hospitalization (adjusted Odds Ratio (aOR)=4.47 (95% confidence interval (CI)=2.09-9.54) and aOR=1.75 (95% CI=1.29- 2.39), respectively. With adjustments for age and sex, having a fracture was associated with new initiation of vitamin D (aOR=2.81 (95% CI=1.76-4.46)) and having syncope was associated with continuing on vasodilators (aOR=1.99 (95% CI=1.06-3.74)). No factors were associated with new sedative initiation.

Conclusion: Fall-related potentially inappropriate prescribing is prevalent in older adults who have a history of falls and continues after discharge from hospital. Future studies should investigate why such prescribing is initiated after a fall-related hospitalization and explore interventions that could reduce such hazardous prescribing.

KEY POINTS

- Our study highlights that prescription of sedative medications is prevalent in older adults and increases after hospitalization for a fall event. This contrasts with the advice of prescribing guidelines.
- New initiation of vitamin D was also frequent after a fall-related admission
- New initiation of sedatives was not found to be associated with demographic factors or type of fall experienced
- Future studies should investigate why new initiation of falls-related potentially inappropriate prescribing may occur in this population to inform and improve deprescribing interventions

MAIN MANUSCRIPT

1. INTRODUCTION

Falls among older adults are a growing problem globally. In Ireland and the UK, falls from a low height are now the leading cause of major trauma, surpassing road traffic accidents [1, 2]. One third of older adults fall each year, with approximately 5% of these events resulting in serious consequences including fractures [3]. Of community-dwellers hospitalized with a fall, around 10% will not return home [4]. Guidelines recommend that falls that require hospitalization should trigger a multi-factorial risk assessment, including medication review [5, 6]. Psychotropic medication including benzodiazepines, antipsychotics, neuroleptics and antidepressants have been consistently found to be associated with a higher risk of falls in large meta-analyses [7, 8]. Non-benzodiazepine hypnotics (often called 'z-drugs') were previously thought to be a safer alternative to benzodiazepines but are now recognized to have similar adverse events [9, 10]. Some cardiovascular medications, including vasodilators, can increase the risk of falls related to balance and gait impairment, dizziness and postural hypotension and they are recommended to be used with caution in specific groups [9-11]. Fractures disproportionately affect older adults due to the higher incidence of osteoporosis in this population [5]. Dietary supplements of vitamin D are often prescribed in patients prone to deficiency to improve calcium absorption as part of osteoporosis treatment and to prevent proximal muscle weakness which can lead to falls [12].

Several guidelines have been developed to assist clinicians to improve prescribing in older adults [9, 10]. The Screening Tool for Older Person's Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START) are tools for identifying medications that may be prescribed inappropriately and medications that may have been omitted, respectively [10, 13]. These Potentially Inappropriate Prescribing (PIP) measures have been validated and used widely in Ireland and other European settings [14]. The STOPP/ START criteria include a specific section of recommendations for patients prone to falls [10, 13]. In 2015, the 2008 STOPP/ START criteria were updated based on literature review and expert consensus [10]. A recommendation to start vitamin D supplementation in those who are experiencing falls was added and z-drugs were listed under STOPP criteria separately from benzodiazepines. The other retained STOPP criteria in relation to fall-risk were benzodiazepines and neuroleptics in those prone to falls, and vasodilator agents for those with persistent postural hypotension [10].

Previous studies have examined prescription modification based on 2008 STOPP/ START criteria in patients hospitalized with falls. A Canadian study [15], found that benzodiazepines and z-drug use continued in 74% of patients following discharge, whilst in an Irish study of 1,016 fall presentations

to a single hospital between 2007 and 2010, McMahon et al [16] identified a significant decrease in the prevalence of neuroleptic but not benzodiazepine prescription in the year post discharge. They also identified new initiation of anxiolytics and hypnosedatives occurring in 9% and 15% of individuals, respectively. These findings were based on dispensed medications for those eligible for the means-tested General Medical Services scheme [16]. It is unknown if these findings reflect actual prescribing patterns. As hospitalization itself can be associated with PIP it is important to identify factors that may be related to continuation and new initiation of PIP in this vulnerable group [17].

This study aimed to estimate the prevalence of PIP based on relevant updated STOPP/ START criteria in older people with fall-related hospitalizations and to compare pre- and post-hospitalization prescribing. A secondary objective was to explore whether demographic and clinical factors were associated with post-hospitalization prescription modification.

2. METHODS

2.1. Study Design

A before-and-after study design was used with admission to hospital with a fall, fracture or syncope/ collapse as the index event. The STROBE (STrengthening the Reporting of OBservational studies in Epidemiology) statement was used in the conduct and reporting of this study [18].

2.2. Setting and Data Source

Data were collected from 44 general practices in the Republic of Ireland using the patient management software *Socrates* (www.socrates.ie) between January 2011 and 2016 [19]. They were collected as part of a larger study that aimed to examine the continuation of long term medication at the primary/ secondary care interface. Participating practices (in the catchment areas of Dublin (n=30), Galway (n=11), and Cork (n=3) hospitals) represented 91% of those contacted. Data included demographic, clinical, prescribing and hospitalization records of patients 65 years and older. Ethical approval was obtained from the Irish College of General Practitioners.

2.3. Participant Selection

Hospitalizations that recorded a diagnosis of a fall, fracture or syncope were selected for the current study based on a combination of ICD-10-AM codes [20] and free-text diagnosis descriptions. Definitions are detailed in the Online Resource (Supplemental Table 1). For participants who experienced more than one fall-related hospitalization, the first eligible record was selected to avoid overlapping and interdependence of observations. Hospitalizations prior to April 2011 or within three months of the data extraction date were excluded to ensure that at least a three-month observation period would be available either side of the index hospitalization.

2.4. Prescription Data

2.4.1 Medication prescription at discharge

Medications listed at the point of discharge from hospital for each participant were analyzed to identify five categories relevant to falls-risk as defined by the STOPP/ START criteria (benzodiazepines, neuroleptics, z-drugs, vasodilators and vitamin D) [10]. Specific definitions of these categories (Online Resource, Supplemental Table 2) have been validated in previous literature [21, 22]. A manual search was conducted to establish context (i.e. continued, discontinued or changed).

2.4.2 General Practice (GP) prescription records

GP prescription records were selected for each participant for up to 12 months prior to the index hospitalization and up to 12 months post hospital discharge. For this study, a single "prescription record" is defined as all medications prescribed on the same date. Five categories of medication were identified (Online Resource, Supplemental Table 2). The following variables were also calculated separately for observation periods pre hospital admission and post hospital discharge: total number of prescription records, total number of medications (defined as unique WHO Anatomical Therapeutic Chemical classification codes) [23], and mean number of medications per prescription record.

2.5 Analysis

2.5.1. Comparison of prescription prevalence pre and post hospitalization

The overall prevalence of prescriptions for benzodiazepines, neuroleptics, z-drugs, vasodilators and vitamin D were estimated prior to the index hospitalization based on GP prescription records. The prevalence of prescriptions post discharge were estimated using a combination of medication prescription at discharge and GP prescription records (i.e. if a prescription was present through either source it was recorded as present during the post-hospitalization period). Prevalence of these medications pre and post hospitalization were compared using McNemar's test.

Mixed-effects logistic regression models were fitted that allow the modelling of correlated data (multiple observations per patient), and include a random intercept for each patient to allow between-patient variability in the outcome. A random effect to account for clustering within GP practice was also included in the model. The GLIMMIX procedure in SAS 9.4 (SAS Institute Inc., Cary, NC, USA) was used to run all models. Three outcomes were considered separately in regression analyses: sedatives (benzodiazepines, z-drugs or neuroleptics), vasodilators and vitamin D. For each of the outcomes, whether they were prescribed or not was recorded. Time period was the

independent variable (post hospitalization, relative to pre hospitalization). In multivariable analysis, adjustments were made for the following covariates: age, sex, fall-related diagnosis category (with three categories: fall, fracture or syncope), number of prescription records, mean number of medications per prescription record, number of other hospitalizations before and after the event, hospital and health cover type. Length of total observation time in days was also included to account for those that had less than 12 months of prescriptions available before or after hospitalization. Health cover type was grouped into three categories relevant to the Irish Healthcare System based on whether patients are required to pay at the point of care: "General Medical Services scheme" (covering GP care, hospital care and medications), Doctor Visit Card (covering GP care only), and Private. As Health cover is means-tested, it can be considered to be a marker of socioeconomic status [17]. A planned subgroup analysis explored the prescription of vasodilators among those with a syncope diagnosis only. In all analyses $p<0.05$ was defined as statistically significant.

2.5.2. Exploration of factors associated with prescription continuation and new initiation

To explore prescription modification, we evaluated whether individuals with PIP prior to hospitalization (on sedatives, on vasodilators or not on vitamin D) had PIP post hospitalization. We explored if demographic or clinical factors (specifically age, sex and diagnosis category) were associated with continuation on sedatives and vasodilators and initiation of vitamin D. This was conducted through multivariable logistic regression analysis. This analysis was repeated for participants who did not have PIP pre hospitalization to explore if demographic or clinical factors were associated with continuation on vitamin D and initiation of sedatives and vasodilators.

All analyses were conducted in Stata 15 (StataCorp 2017. College Station, TX) and SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

3. RESULTS

3.1. Participant characteristics

A total of 1,047 patients were identified as having a fall-related hospitalization within the study timeframe. Of these, 927 individuals (626 women and 301 men, mean age 81 years) had prescription data available and an observation period of at least three months both pre and post hospitalization. The majority, 81% (n=707) had 12 months of data either side of hospitalization. Hospitalizations identified were to 29 different sites, although the majority of patients (79%) were admitted to large teaching hospitals in three cities in Ireland. Figure 1 shows a flow diagram of participant eligibility. Table 1 shows participant demographics and clinical characteristics pre and post hospitalization. The largest diagnosis category was those admitted with a fracture (45%). A large proportion of

participants could be considered to have polypharmacy with 46% and 51% having a mean of ≥5 medications per GP prescription pre and post hospitalization, respectively.

3.2. Descriptive statistics of prescriptions pre and post hospitalization

Overall, a large proportion of patients received fall-related potentially inappropriate prescriptions as defined by STOPP criteria (Table 2) [10]. No significant decrease in these medications was found post hospitalization. In fact, there was a significant increase in the proportion with sedative prescriptions, specifically those with z-drug and neuroleptic prescriptions ($p<0.01$). There was also a significant increase in the proportion prescribed vitamin D ($p<0.01$) as recommended by START criteria [10].

Figure 2 shows univariable and multivariable results of mixed-effect logistic regression with PIP as the outcome and time period as an independent variable. After adjustment for relevant covariates and clustering effects, both vitamin D and sedatives had a higher odds of being prescribed in the post-hospitalization period (adjusted Odds Ratio (aOR)=4.47 (95% Confidence Interval (CI) 2.09-9.54) and aOR=1.75 (95% CI 1.29-2.39), respectively). The prevalence of the prescription of vasodilators did not differ significantly pre and post hospitalization even when considering only those patients with a syncope admission type.

3.3. Exploration of factors associated with prescription continuation and initiation

The factors associated with post-hospitalization prescription of vitamin D in those with and without vitamin D prescription prior to hospitalization is shown in Table 3. The majority of those on vitamin D prior to hospitalization continued to be prescribed post hospitalization (88%), while only 30% of patients were newly prescribed vitamin D after hospitalization as recommended by the START criteria [10]. With adjustments for age and sex, in comparison to a simple fall diagnosis, having a fracture diagnosis was associated with new initiation of vitamin D (aOR=2.81 (95% CI 1.76 to 4.46)).

The factors associated with post-hospitalization prescription of sedatives in those with and without sedative prescription prior to hospitalization is shown in Table 4. While 16% of those on sedatives had discontinuation of their PIP post hospitalization, almost one-fifth of the remaining participants had new sedative initiation after hospitalization. No factors were identified as being associated with initiation of sedatives. Similarly, Table 5 demonstrates that while 16% of those on vasodilators had discontinuation of their PIP post hospitalization, 20% received a new initiation of these medications. With adjustments for age and sex, in comparison to a simple fall diagnosis, having a syncope diagnosis was associated with continuing on vasodilators (aOR=1.99 (95% CI 1.06 to 3.74)).

4. DISCUSSION

4.1. Summary of findings

This study of 927 individuals with a hospitalization for a fracture, fall or syncopal episode over five years in the Republic of Ireland, shows that treatment burden is high with over 11 medicines being prescribed per participant in the year prior to hospital admission, increasing to 13 medicines in the post-discharge year. Prescription of medications that "predictably increase the risk of falls" according to the STOPP criteria [10], including z-drugs and neuroleptic medications, increased after discharge. The prescription of vasodilators is common with over 50% of participants taking these medicines and this remained unchanged after discharge from hospital. Prescription of vitamin D, in accordance with recommendations from the START criteria [10], increased after a fall-related admission. With adjustments for age and sex, having a fracture diagnosis is associated with positive modification of vitamin D and having a syncope diagnosis is associated with maintenance on vasodilators.

4.2. This research in the context of other studies

Despite a large body of evidence and guidelines supporting the link between sedative medication and falls [7-10], our results show no decrease in their prescription after a relevant hospitalization. While previous Irish findings did suggest some decrease in neuroleptic prescriptions, this was not replicated in our study [16]. In addition, we explored z-drug prescription and identified an increase post-hospitalization. While this may point to clinical decisions to prescribe z-drugs in place of benzodiazepines [9], this practice is no longer supported by guidelines [9, 10]. Interventions that target deprescribing of sedative medications have not yet shown to reduce numbers of fallers [24]. It must be acknowledged however, that successful implementation of these interventions is challenging in practice. Several studies have shown low rates of prescribing modification even when it is deemed to be appropriate in the majority of patients [25-28]. Where it is attempted, rates of successful withdrawal have been found to be as low as 33% at long-term follow-up [26]. This may be explained in part by GPs' and older adults' concerns about the potential return of symptoms, especially insomnia, if medications are withdrawn [25, 28-31]. Deprescribing interventions found to be most effective are those that combine supervised gradual withdrawal schedules with psychotherapy to assist coping with both original and withdrawal symptoms [30]. Insufficient access to psychotherapy services could be a barrier to GPs implementing these interventions in Ireland as it is elsewhere [29]. Appropriate management of psychological symptoms could be particularly relevant in those who experience falls and subsequent fear and anxiety [32, 33]. Future studies should explore the reasons for the observed increase in sedative prescriptions in this study and

whether psychological consequences of falls are being managed pharmacologically rather than with other evidence-based interventions [32, 33].

Our study showed an increase in vitamin D prescription, specifically after fracture. While evidence from recent large meta-analyses does not support vitamin D supplementation to prevent falls or fractures or improve bone mineral density in the general older population, targeted prescription as observed in this study is supported by several current guidelines and the STOPP/ START criteria [5, 6, 10, 24, 34, 35]. A Cochrane meta-analysis conducted in 2012 of trials that included only those with vitamin D deficiency at baseline (4 trials, n=804), suggested a reduction in fallers [24]. It is unknown whether participants in the current study were tested for vitamin D deficiency but the observed rate of post-discharge vitamin D prescription (52%) is lower than the proportion that may have been expected to be deficient (<20 ng/mL) based on previous studies among the general older community-dwelling population and those admitted to hospital with fracture [36, 37]. One problem with vitamin D supplementation is poor adherence, with one post-hip fracture intervention achieving only 26% continuation twelve months after discharge [38]. As our analysis focused on prescribed rather that dispensed medication, we are unable to assess whether participants continued to take vitamin D. Furthermore, as vitamin D is available without prescription in Ireland, it is also possible that additional patients were taking this supplement that were not recorded in the dataset.

Overall, the evidence for an association between cardiovascular medications and falls is conflicting and likely dependent on specific pharmacological properties and drug-disease interactions [11]. Qualitative research among GPs however, suggests that primary care practitioners perceive orthostatic hypotension to be a greater contributor to falls than psychotropic drugs and are more likely to deprescribe them [31]. The current study found no significant difference in the proportion prescribed vasodilators before and after hospitalization. We did however note that 20% of those who were not on vasodilators at baseline had a new initiation after hospitalization. From data available we are unable to explore if this was due to new diagnosis of cardiovascular conditions. A previous large case-crossover study (n= 90,127) found an increased risk of serious fall injury in the 15 days after antihypertensive medication initiation [39]. This could have further implications for those already prone to falls. It must be noted that although we conducted a subgroup analysis of those with syncope, it was not possible to determine whether participants had “persistent postural hypotension” as defined by STOPP criteria [10] or if prescription modification would have been appropriate. Furthermore, it is unknown if some of those in other diagnosis categories experienced postural hypotension that was not recorded in available data.

4.3. Limitations

The use of routinely recorded data in this study has several limitations. We were unable to assess details of care, services or procedures received by patients in hospital or after discharge that could have influenced prescribing practices. The majority of participants were admitted to large teaching hospitals and it is expected that those with fractures would have been admitted under the care of orthopedic surgeons, while those with syncope and other causes of falls would have been cared for by medical and geriatric medicine specialties [40]. In Ireland, the majority of hospital pharmacists have no formal involvement in the discharge prescribing process and only half of patients with hip fracture are assessed by a consultant geriatrician during their hospital stay [40, 41]. In this setting, the focus may have been on immediate falls-management with long-term falls prevention not being considered a priority.[42] We also have no information on non-pharmacological interventions for fall-risk that may have been received in hospital or in primary care. The causes of falls are complex and, in addition to medication review, balance training and home hazard assessment play important roles in prevention [5, 6]. General Practitioners may provide referrals to physiotherapy and occupational therapy services even if they do not titrate medications [27, 31, 42]. Ideally, secondary falls prevention after hospital admission should be individualized and span the responsibility of different professionals across hospital to the community settings [5]. In Ireland, a national initiative to improve cohesiveness of care for older adults is in development [43]. This includes the piloting of falls services whereby hospital and primary care practitioners can refer to a single point of triage from where Consultant Geriatricians lead medical investigations and interventions [43]. This has the potential to improve prescribing for patients in which there is an indication. The effect of these interventions on prescribing patterns and falls requires further investigation.

The primary aim of this study was to estimate the prevalence of PIP based on relevant updated STOPP/ START criteria in older people with fall-related hospitalizations and to compare pre- and post-hospitalization prescribing. We explored whether demographic variables and the category of fall experienced were associated with post-hospitalization prescription modification. As the quality of co-morbidity coding was variable across practices in the dataset, we were not able to explore other potential risk factors for falls or factors that may influence medication prescription including diagnoses of anxiety, insomnia, dementia, mobility limitations or cardiovascular conditions [11, 24, 29, 44]. In addition, a minority of patients (n=69, 7%) had a subsequent fall-related admission in the year after the event included in the analysis and this may also have influenced prescribing patterns. Future work is planned to explore further details of prescription among a subset of patients with sufficient available data. As the identification hospitalizations relied on General Practice records,

some patients with fall-related diagnoses may not have been included if they did not attend their GP within the observation period or if the diagnosis was not recorded. Participants in this study were receiving prescriptions from a General Practice and were primarily community-dwelling. This study may not therefore be representative of older adults in residential care settings. There is also a risk of misclassification of exposure to particular medications as prescriptions could have been received from another source or Vitamin D could have been purchased without prescription. Furthermore, it was not possible to evaluate dosing regimens, routes of administration, or subtle changes in prescription patterns that may have been relevant to medications under study [5, 6, 24, 45].

Several commonly prescribed medications relevant to falls, fractures and syncope were not investigated in this study. STOPP/START and Beer's criteria are two very commonly cited tools for identifying potentially inappropriate prescribing in older adults. We chose to focus on STOPP/START as it is particularly relevant and extensively validated in the Irish setting, and it has a specific section dedicated to falls-risk [10, 46]. In a previous analysis of the larger dataset from which participants for this study were selected (n=40,816), long-term use of Proton Pump Inhibitors was found to be present in approximately a quarter of the sample [17]. These medications, that can effect bone density and increase risk of fractures and potentially falls, should be studied further in this population [9, 47]. Opioid use, particularly during the initiation phase, has been found to significantly increase fall-risk but prescribing guidelines allow for their use to manage early fracture-related pain [9, 47]. Future research is needed to provide recommendations about optimal duration of post-fracture pain relief and safe withdrawal in this group who are prone to falls. In addition, a series of three recent meta-analyses from the EuGMS Task and Finish Group on Fall-Risk-Increasing Drugs found associations between falls and loop diuretics, digoxin, anti-convulsants and certain classes of anti-depressants [8, 11, 47]. These studies could provide the basis for future adaptions of prescribing guidelines relevant to falls, which would require validation in clinical settings.

5. Conclusion

This study shows that fall-related PIP, particularly in relation to sedative medication is prevalent in older adults with falls and continues even after fall-related hospitalization episodes. Future detailed work in Ireland is needed to explore specific prescribing practices during hospitalizations for fractures, falls and syncope to identify areas for improvement. Studies should investigate why sedative prescriptions may be initiated after fall and fracture related hospitalizations and whether deprescribing interventions should be adapted for this population to address specific psychological consequences of falls. Further research is also required to assess whether improvements in

integration of fall-related primary and secondary care can alter long-term prescribing patterns and prevent subsequent falls in this population.

COMPLIANCE WITH ETHICAL STANDARDS

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Conflicts of interest

MEW, FB, FM and TF declare that they have no conflict of interest.

Ethical approval

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

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Table 1. Participant demographics and clinical characteristics (n=927)

Overall demographics		
Mean age at admission in years (SD)		81.2 (SD=8.6)
Sex (% Female)		67.5%
Hospitalisation diagnosis category (n (%)):		
• Fall without Fracture or Syncope		252 (27%)
• Fracture		413 (45%)
• Syncope		262 (28%)
Median length of hospital stay in days (IQR)*		7 (2-17)
Characteristics during each observation period	**Prior to hospitalisation**	**Post hospitalisation**
Mean observation period in days (SD)	347 (56)	349 (53)
No. of participants with other hospitalisation (%)	251 (27%)	317 (34%)
Mean no. of total GP prescription records per participant**	10.1 (7.0)	10.6 (7.0)
Mean no. of total medications per participant (SD)**	11.6 (6.9)	13.4 (7.2)
Mean no. of medications per prescription per participant**	4.8 (2.6)	5.5 (2.9)
No. of participants with mean no. of medications per prescription ≥5 (%)**	398 (46%)	441 (51%)

*n=105 participants were missing length of stay data. Post-hospitalisation observation period for these participants was calculated as a) *12 months post admission + median length of stay* or b) *12 months post the first prescription record,* whichever was sooner

**Based on GP prescription records for n=862 with this data available pre and post hospitalisation

Table 2. Comparison of medications pre and post hospitalisation (n=927)

	Prior to hospitalisation	Post hospitalisation	Mc Nemar's test p-value
Proportion on specific medications	**N (%)**	**N (%)**	
Sedatives	369 (40%)	421 (45%)	<0.01*
• Benzodiazepines	190 (21%)	210 (23%)	0.06
• Z-drugs	171 (18%)	207 (22%)	<0.01*
• Neuroleptics	108 (12%)	135 (15%)	<0.01*
Vasodilators	498 (54%)	503 (54%)	0.70
Vitamin D	342 (37%)	478 (52%)	<0.01*

*Significant at p<0.05 level

Table 3. Factors associated with post-hospitalisation Vitamin D prescription in those with and without prescription pre-hospitalisation (n=927)

	On vitamin D prior to hospital admission (n=342)				NOT on vitamin D prior to hospital admission (n=585)			
Post Hospitalisation	**Prescription continued**	**Prescription not continued**	**Adjusted OR* (95% CI)**		**New initiation of prescription**	**No initiation of prescription**	**Adjusted OR* (95% CI)**	
N (% of group)	301 (88%)	41 (12%)			177 (30%)	408 (70%)		
Mean Age (SD)	82.6 (7.7)	81.9 (7.2)	1.02	(0.97-1.06)	81.7 (8.4)	80.0 (9.3)	1.02	(1.00-1.04)
Sex (% Female)	81%	88%	1.84	(0.68-4.97)	69%	55%	1.44	(0.97-2.14)
Diagnosis category (% of group):								
Fall without Fracture or Syncope	32%	37%			19%	26%		
Fracture	48%	44%	1.39	(0.66-2.94)	66%	33%	2.81	(1.76-4.46)**
Syncope	21%	20%	1.32	(0.52-3.32)	15%	40%	0.57	(0.32-1.01)

*Adjusted OR represents Odds of prescription of the medication of interest in the post-hospitalisation period. Adjustments made for age in single years, sex (with male as reference category) and diagnosis (with fall without fracture or syncope as reference category)
** Significant at $p<0.05$

Table 4. Factors associated with post-hospitalisation Sedative prescription in those with and without prescription pre-hospitalisation (n=927)

	On sedatives prior to hospital admission (n=369)				NOT on sedatives prior to hospital admission (n=558)			
Post Hospitalisation	**Prescription continued**	**Prescription not continued**	**Adjusted OR* (95% CI)**		**New initiation of prescription**	**No initiation of prescription**	**Adjusted OR* (95% CI)**	
N (% of group)	310 (84%)	59 (16%)			111 (20%)	447 (80%)		
Mean Age (SD)	81.4 (8.5)	81.4 (8.4)	1.00	(0.97-1.03)	81.7 (9.8)	81.0 (8.4)	1.01	(0.99-1.04)
Sex (% Female)	74%	78%	0.83	(0.42-1.64)	63%	63%	0.97	(0.62-1.51)
Diagnosis category (% of group):								
Fall without Fracture or Syncope	31%	31%			23%	25%		
Fracture	45%	51%	0.89	(0.47-1.70)	47%	43%	1.26	(0.74-2.16)
Syncope	24%	19%	1.28	(0.57-2.87)	34%	32%	1.12	(0.62-2.00)

*Adjusted OR represents Odds of prescription of the medication of interest in the post-hospitalisation period. Adjustments made for age in single years, sex (with male as reference category) and diagnosis (with fall without fracture or syncope as reference category)

Table 5. Factors associated with post-hospitalisation Vasodilator prescription in those with and without prescription pre-hospitalisation (n=927)

	On vasodilators prior to hospital admission (n=498)				NOT on vasodilators prior to hospital admission (n=429)			
Post Hospitalisation	**Prescription continued**	**Prescription not continued**	**Adjusted OR* (95% CI)**		**New initiation of prescription**	**No initiation of prescription**	**Adjusted OR* (95% CI)**	
N (% of group)	419 (84%)	79 (16%)			84 (20%)	345 (80%)		
Mean Age (SD)	81.8 (8.5)	83.4 (7.4)	0.98	(0.95-1.01)	80.5 (9.3)	80.3 (8.7)	1.00	(0.97-1.03)
Sex (% Female)	65%	66%	1.08	(0.63-1.83)	69%	71%	0.97	(0.57-1.65)
Diagnosis category (% of group):								
Fall without Fracture or Syncope	27%	41%			28%	24%		
Fracture	40%	35%	1.65	(0.94-2.90)	42%	53%	0.68	(0.38-1.21)
Syncope	33%	24%	1.99	(1.06-3.74)**	30%	23%	1.11	(0.58-2.1)

*Adjusted OR represents Odds of prescription of the medication of interest in the post-hospitalisation period. Adjustments made for age in single years, sex (with male as reference category) and diagnosis (with fall without fracture or syncope as reference category)
** Significant at $p<0.05$

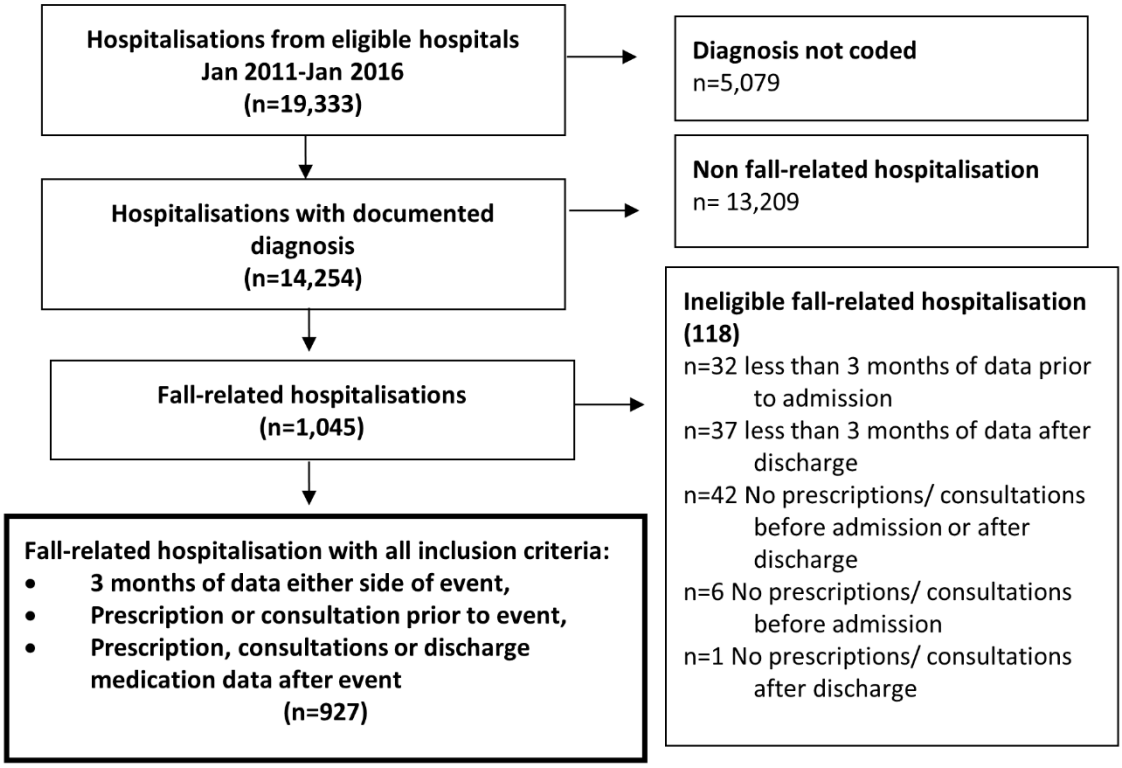
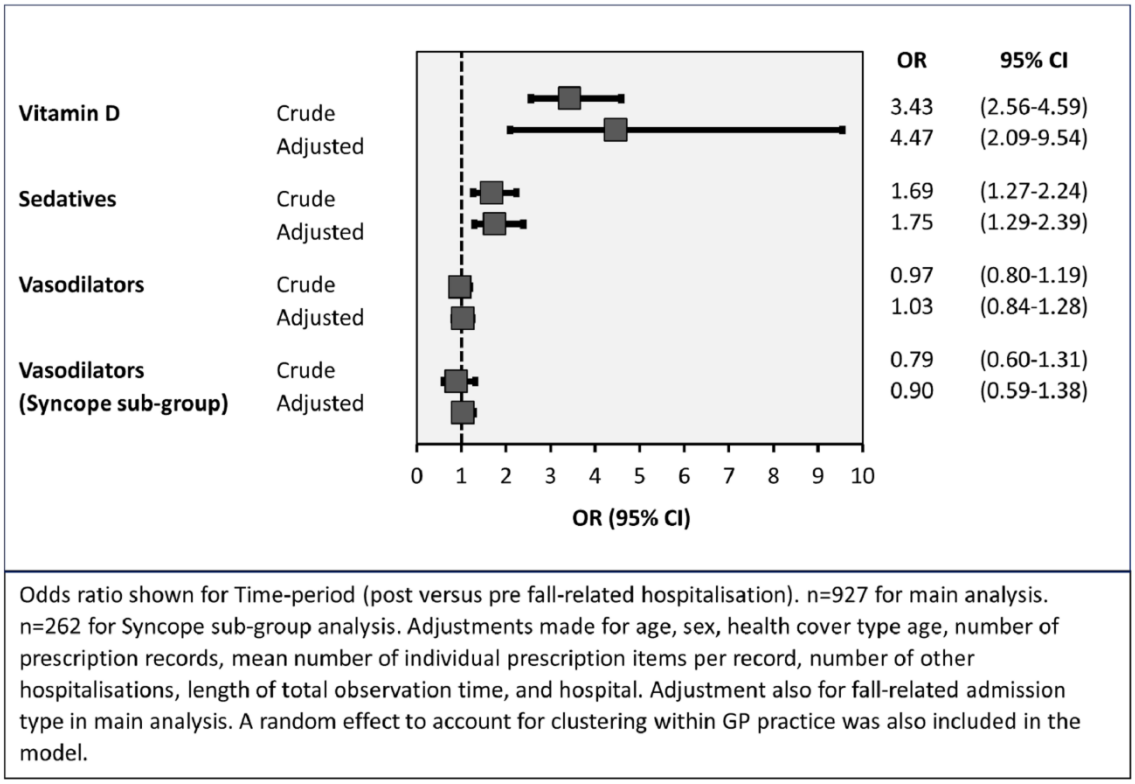


Fig 1 Flow-diagram of participants



Odds ratio shown for Time-period (post versus pre fall-related hospitalisation). n=927 for main analysis. n=262 for Syncope sub-group analysis. Adjustments made for age, sex, health cover type age, number of prescription records, mean number of individual prescription items per record, number of other hospitalisations, length of total observation time, and hospital. Adjustment also for fall-related admission type in main analysis. A random effect to account for clustering within GP practice was also included in the model.

Fig 2 Mixed-effect logistic regression with prescription of medication categories as the outcome and time-period as an independent variable

SUPPLEMENTAL MATERIAL

Supplemental Table 1: Selection of Hospitalisations

Three categories of hospitalisations were selected for the purpose of this study: falls, fractures and syncope/collapse. They were defined as follows:

- Falls: ICD-10-AM diagnosis code= W00-W19 OR R29.81 OR R29.6 OR diagnosis description contains text “fall” or “fell”
- Fractures: ICD-10-AM diagnosis code= S02, S12, S22, S32, S42, S52, S62, S72, S82, S92 OR diagnosis description contains text “fracture” or “#”
- Syncope and Collapse: ICD-10-AM diagnosis code= R55 OR diagnosis description contains text “vasovag” “syncope” “collapse”

Admission diagnoses were reviewed by hand for context. Hospitalisations were excluded if clearly irrelevant (“lobar collapse”, “vertebral collapse” or “pre-syncope” (ICD-10-AM= R42) without fall).

Supplemental Table 2: Fall-risk medications ATC codes according to STOPP/ START 2 Criteria

STOPP Version 2, Section K: Drugs that predictably increase the risk of falls in older people (O'Mahony et al 2015)	**ATC Codes adapted from De Groot et al (2014) and Nauta et al (2017)**
1. Sedatives	
1a. Benzodiazepines (sedative, may cause reduced sensorium, impair balance).	N05BA (benzodiazepines) N03AE (benzodiazepine derivatives) N05CD (benzodiazepine derivatives)
1b. Neuroleptic drugs (may cause gait dyspraxia, Parkinsonism)	N05A (antipsychotics) Excluding N05AN (lithium)
1c. Hypnotic Z-drugs e.g. zopiclone, zolpidem, zaleplon (may cause protracted daytime sedation, ataxia).	N05CF (benzodiazepine related agents)
2. Vasodilator drugs (e.g. alpha-1 receptor blockers, calcium channel blockers, long-acting nitrates, ACE inhibitors, angiotensin I receptor blockers) with persistent postural hypotension i.e. recurrent drop in systolic blood pressure ≥ 20mmHg (risk of syncope, falls).	C01D (vasodilator agents) C02DB01, C02LG01, C02LG51, C02DB02 C02LG02, C02DC01 direct vasodilators) G04CA, C02CA04, C02CA06, C02KD01 selective alpha-receptor blockers) C08 (calcium channel blockers) C09A, C09B (ACE-inhibitor and combinations) C09C, C09D (angiotensin II receptor blocker and combinations)
Screening Tool to Alert to Right Treatment (START), version 2, Section E: Musculoskeletal System (O'Mahony et al 2015)	**ATC Codes adapted from De Groot et al (2014) and Nauta et al (2017)**
3. Vitamin D supplement in older people who are housebound or experiencing falls or with osteopenia	A12AX (calcium carbonate + cholecalciferol) A11JB (calcium carbonate + vitamins) A11CC (vitamin D and analogues) A11CB (vitamin D + vitamin A)

Supplementary material references

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