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RESEARCH PAPER

The association between STOPPFall medication use and falls and fractures in community-dwelling older people

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Abstract

Introduction: Falls and fractures are common among older people. The Screening Tool of Older Persons Prescriptions in older adults with high fall risk (STOPPFall) provides a comprehensive list of fall-risk-increasing drugs (FRIDs). This study assesses the association between STOPPFall medications and future falls/fractures among a large cohort of community-dwelling people ≥65 years using The Irish Longitudinal Study on Ageing (TILDA) Waves 1–6, collected from 2009 to 2021.
Methods: STOPPFall medications were recorded at Wave 1 and Wave 3. Falls/fractures were self-reported. Logistic regression models reporting odds ratios (ORs) assessed the association between STOPPFall medications and falls (including injurious/unexplained falls) and fractures at follow-up, adjusted for relevant covariates.
Results: Over one in four participants (777/2898, 27%) were prescribed one STOPPFall medication, and 15% (421/2898) were prescribed ≥2 STOPPFall medications. Over half of participants fell during follow-up, with 1/5 sustaining any fracture. Prescription of ≥2 STOPPFall medications was independently associated with all falls [OR 1.67 (95%CI 1.28–2.18); $P < 0.001$], injurious falls [OR 1.53 (95%CI 1.19–1.97); $P = 0.001$], unexplained falls [OR 1.86 (95%CI 1.43–2.42); $P < 0.001$], all fractures [OR 1.59 (95%CI 1.20–2.12); $P = 0.001$] and hip fractures [OR 1.75 (95%CI 1.00–3.05); $P = 0.048$]. Increasing prescription of ≥2 STOPPFall medications at Wave 3 was associated with increased likelihood of all falls and injurious falls.
Conclusion: Prescription of ≥2 STOPPFall medications is independently associated with an increased likelihood of all falls and all fractures. This is a potentially modifiable risk factor for falls, and an increased falls risk should be considered when prescribing these medications.

Keywords: fall-risk-increasing drugs; deprescribing; unexplained falls; hip fracture; older people

Key Points

- The STOPPFall screening tool highlights fall-risk-increasing drugs (FRIDs), a potential modifiable risk factor for falls.
- Prescription of two or more STOPPFall medications is independently associated with all falls, injurious and unexplained falls.
- Prescription of two or more STOPPFall medications is independently associated with all fractures and hip fractures.
- Increasing prescription of two or more STOPPFall medications is independently associated with all falls and injurious falls.
- Proactive medication reviews among older people are essential given the adverse events that can occur after falls/fractures.

Introduction

Falls are a common problem among older people, with approximately one in three community dwelling adults aged ≥65 years sustaining at least one fall per year [1]. Older people frequently sustain unexplained falls, i.e. falls without an identifiable cause, with these accounting for approximately one third of falls presenting to emergency departments [2]; orthostatic hypotension (OH) [3] and cardiac arrhythmias [4] can frequently be contributory. Falls can result in significant negative outcomes, including fall-related injuries, hospitalisation, institutionalisation and mortality [5, 6].

Fractures account for a significant burden of fall-related injuries, with the Irish Hip Fracture Database reporting that low-energy falls from standing height are consistently the main cause of hip fracture in older people in Ireland [7]. Fractures are associated with declining function and mobility [8], increased dependency [9] and increased mortality especially associated with hip fracture [10].

An important aspect of multifactorial falls assessment and prevention strategies is identification of potentially modifiable risk factors for falls [11]. An essential modifiable risk factor to consider is medication use, especially identifying fall-risk-increasing drugs (FRIDs) [12–14], particularly if an appropriate indication is no longer evident for their prescription.

STOPPFall (Screening Tool of Older Persons Prescriptions in older adults with high fall risk) [15] was created through a Delphi consensus process to provide a comprehensive list of FRIDs, and contains fourteen different medication classes. Whilst it was developed by an expert group, there is limited evidence to date demonstrating the association of STOPPFall medications with falls and fractures longitudinally, adjusting for covariates including the indications for these medications.

The aim of this study therefore is to assess the longitudinal association between STOPPFall medications and falls and fractures in a large population-based cohort of community-dwelling older adults over median 8 (range 2–12) year follow-up.

Methods

Study design and participants

This is a longitudinal study utilising data from The Irish Longitudinal Study on Ageing (TILDA). TILDA is a large, population-based nationally representative sample of community-dwelling older adults in Ireland, aged ≥50 years. Waves of data collection are conducted every 2 years, except for Wave 6 which was delayed by one year due to the COVID-19 pandemic. This study used data from Waves 1–6, collected between 2009 and 2021.

The TILDA study design has been outlined previously [16]. Briefly, there are three components to data collection: a computer-assisted personal interview (CAPI) completed by social interviewers in the participants' own home, performed by computer assisted telephone interview (CATI) at Wave 6; a self-completion questionnaire completed and returned by the participant; and comprehensive centre-based health assessment or modified home-based health assessment carried out by trained research nurses. The health assessments used in this study were completed at Waves 1 and 3 only.

Participants in this study were included if they were aged ≥65 years, had a medication list available to assess for medications included in STOPPFall and completed follow-up for at least 2 years i.e. to at least Wave 2 of TILDA. This study examines the longitudinal relationship between STOPPFall medications and incident falls and fractures. Participants were excluded at Wave 1 if a pre-existing diagnosis of dementia was present.

STOPPFall medications

Medication use was recorded by Anatomical Therapeutic Chemical (ATC) Classification System at baseline (Wave 1) and follow-up (Wave 3) assessment. Medication lists were examined for all medications within STOPPFall, identified using the ATC Classification System.

A comprehensive list of ATC codes for the specific medications within thirteen of fourteen medication classes were provided by the creators of STOPPFall, excluding anticholinergic medication, as an international Delphi consensus effort defining medications within this class is pending. The thirteen other STOPPFall medication classes comprise benzodiazepines (identified with ATC codes N03AE, N05BA and N05CD), antipsychotics (ATC code N05A), benzodiazepine-related drugs (N05CF), opioids (N02A, R05DA), antidepressants (N06A, N06CA), antiepileptics (N03), diuretics (C02L, C03, C07B, C07C, C07D, C08GA, C09BA, C09BX01, C09BX03, C10BX13, C09DA, C09DX01, C09DX03, C09DX06, C09DX07, C09XA52, C09XA54), alpha-blockers used as antihypertensives (C02CA), alpha blockers used for prostate hyperplasia (G04CA), centrally-acting antihypertensives (C02A), antihistamines (N07CA02, R06), vasodilators used in cardiac diseases (C01D) and drugs for urinary frequency and incontinence (G04BD, G04CA53). Anticholinergic medications were defined by a comprehensive list of medications with 'definite' anticholinergic effects based on the Anticholinergic Cognitive Burden (ACB) scale [17] (i.e. a score of 3), which has been used in previous studies of anticholinergic medication within TILDA [18]. Only anticholinergics not already classified in other STOPPFall classes were included to avoid duplication and included gastrological agents (A03AA07 A03AB05 A03BA01 A03BA03 A03BB01), Parkinsonian agents (N04AA01 N04AA02 N04AA04 N04AB02 N04AC01), antihistamines (N02BE51) and other medications (M03BA03 M03BC01 N05CM05 N05BB01).

The number of STOPPFall medications prescribed were collected at Wave 1 and Wave 3 to assess for changes between these assessments. This informed whether prescription of STOPPFall medications remained unchanged, increased (divided into increase of one or ≥ 2 medications) or

decreased (one or ≥ 2 medications) at Wave 3 compared to Wave 1.

Falls and fractures

At Waves 2–6, participants were asked 'Have you had any falls since the last interview?', which was used to create the 'Falls' variable. The 'Unexplained Falls' variable was defined by a positive answer to the follow-up question 'Were any of these falls non-accidental, i.e. with no apparent or obvious reason?' The 'Injurious Falls' variable was defined by a positive answer to 'Did you injure yourself seriously enough to need medical treatment?'

Fracture data were obtained by self-report. Previous fracture at Wave 1 was self-reported, and participants were asked about hip, wrist, vertebral and other fractures since the last interview at Waves 2–6. Separate variables for 'Hip Fracture', 'Wrist Fracture' and 'Vertebral Fracture' were generated by positive answer to these questions. These were combined with a positive history of 'Other Fracture' to create the 'Fractures' variable including all fractures.

Other measures

Highest level of educational attainment was collected by self-report (primary, secondary, tertiary). The Cut Down, Angry, Guilty, Eye Opener (CAGE) scale was used to assess for excess alcohol intake [19]. Heart disease was defined as self-reported history of angina, heart attack, congestive cardiac failure, murmur and/or arrhythmia. Epilepsy was self-reported. Pain was defined as answering 'yes' when asked 'Are you often troubled with pain?'. History of depression and anxiety were self-reported. Self-reported sleep problems were collected using two items from the Jenkins Sleep Problems Scale [20], 'How often do you have trouble falling asleep?' and 'How often do you have trouble with waking up too early and not being able to fall asleep again?'; participants were defined as having sleep problems if they responded 'most of the time' or 'sometimes' to either question. Indications for antipsychotic medication use were defined by self-reported history of hallucinations, schizophrenia, psychosis, mood swings or bipolar disorder. Urinary incontinence was defined by self-report. Heel ultrasound was performed to assess bone density, categorised as normal bone density, osteopenia (bone mineral density T score < -2.5 standard deviations), or osteoporosis (bone mineral density T score > -2.5 standard deviations) [21]. Chronic disease burden was assessed by self-report of cancer, liver disease, kidney disease, thyroid disease, arthritis, lung disease, eye conditions and diabetes. Cognitive impairment was defined as self-reporting memory as fair/poor when asked 'How would you rate your day-to-day memory at the present time?' and/or Mini Mental State Examination (MMSE) score ≤ 24.

Statistical analysis

Data were analysed using Stata version 15.1 (Stata®, College Station, TX, USA). Baseline characteristics of the study sample by STOPPFall medication use (one or ≥ 2 STOPPFall medications) were presented descriptively using proportions and mean values with 95% confidence intervals (CIs). Continuous variables were compared using Student's t test and categorical variables were compared using chi-square tests. Logistic regression models were used to report odds ratios (ORs) with 95% CIs for the association between STOPPFall medication use at baseline and falls (all falls, injurious and unexplained falls) and fractures (all fractures, hip, wrist and vertebral fractures) at follow-up. All participants aged ≥65 years at Wave 3 were included in the second analysis, including participants excluded at Wave 1 due to being aged <65 years at initial analysis. Logistic regression models reported ORs with 95% CIs for the association between change in STOPPFall medication prescription at Wave 3 compared to Wave 1 and subsequent falls and fractures at Waves 4–6.

Covariates were chosen a priori to control for medical conditions that STOPPFall medications are prescribed to treat, including heart disease, chronic pain, depression, anxiety, sleep disorders, psychosis and related disorders, and urinary incontinence, together with other relevant covariates including age, sex, educational attainment, CAGE score (representing alcohol excess), bone mineral density status from heel ultrasound, chronic disease burden, cognitive impairment, previous fracture and follow-up duration. Presence of relevant covariates were re-assessed at Wave 3 ensuring participants who had developed these conditions since Wave 1, and therefore may be prescribed STOPPFall medications, were included. Prescription of STOPPFall medications at Wave 1 was also controlled for as a relevant covariate in this second analysis, and previous fracture included fractures reported from Waves 1–3.

Ethics

The TILDA study was approved by the Faculty of Health Sciences Research Ethics Committee at Trinity College Dublin, and all participants provided informed written consent. All experimental procedures adhered to the Declaration of Helsinki.

Results

Baseline characteristics

There were 2898 participants included in this study, with a mean age at baseline of 73.0 years (95% CI 72.7–73.2); 53% were female.

Follow-up from Wave 1–6 was completed in 41% of participants (1180/2898), 20% (573/2898) to Wave 5, 12% to Wave 4 (359/2898), 12% to Wave 3 (337/2898) and 15% completed follow-up to Wave 2 (449/2898); median follow-up was 8 (range 2–12) years.

Over one in four participants (777/2898, 27%) were prescribed one STOPPFall medication at baseline, with a further 15% (421/2898) prescribed ≥2 STOPPFall medications.

Table 1. Baseline characteristics (at Wave 1) of total study sample and grouped by STOPPFall medication use

	Total sample (n = 2898)	One STOPPFall medication (n = 777)	≥2 STOPPFall medications (n = 421)
Mean age (years) with 95% CI	73.0 (72.7–73.2)	73.7 (73.3–74.2) ∗	75.0 (74.4–75.6) ∗ ‡
Age bands (proportions with 95% CI)			
65–69 years	0.36 (0.34–0.38)	0.32 (0.28–0.35) ∗	0.25 (0.21–0.29) ∗ ‡
70–74 years	0.28 (0.27–0.30)	0.27 (0.24–0.31)	0.24 (0.20–0.28) ∗
≥75 years	0.36 (0.34–0.38)	0.41 (0.38–0.45) ∗	0.51 (0.47–0.56) ∗ ‡
Female sex (proportions with 95% CI)	0.53 (0.51–0.55)	0.56 (0.52–0.59) ∗	0.56 (0.51–0.61)
Educational attainment (proportions with 95% CI)			
Primary	0.42 (0.40–0.44)	0.44 (0.41–0.48)	0.50 (0.45–0.55) ∗ ‡
Secondary	0.34 (0.32–0.35)	0.33 (0.30–0.36)	0.33 (0.28–0.37)
Tertiary	0.24 (0.23–0.26)	0.23 (0.20–0.26)	0.17 (0.14–0.21) ∗ ‡
CAGE score (proportions with 95% CI)			
<2	0.80 (0.79–0.82)	0.80 (0.77–0.83)	0.76 (0.72–0.80) ∗
≥2	0.06 (0.05–0.07)	0.06 (0.05–0.08)	0.07 (0.05–0.10)
Did not complete	0.14 (0.12–0.15)	0.14 (0.11–0.16)	0.17 (0.13–0.21)
Heart disease (proportions with 95% CI)	0.26 (0.24–0.27)	0.29 (0.26–0.32) ∗	0.44 (0.39–0.49) ∗ ‡
Chronic pain (proportions with 95% CI)	0.36 (0.35–0.38)	0.42 (0.39–0.45) ∗	0.58 (0.54–0.63) ∗ ‡
Depression (proportions with 95% CI)	0.05 (0.04–0.05)	0.06 (0.04–0.08) ∗	0.13 (0.10–0.17) ∗ ‡
Anxiety (proportions with 95% CI)	0.04 (0.03–0.05)	0.03 (0.02–0.04)	0.12 (0.10–0.16) ∗ ‡
Urinary incontinence (proportions with 95% CI)	0.15 (0.14–0.17)	0.17 (0.15–0.20)	0.29 (0.25–0.34) ∗ ‡
Sleep disorder (proportions with 95% CI)	0.57 (0.55–0.59)	0.59 (0.55–0.62)	0.65 (0.60–0.70) ∗ ‡
Indication for antipsychotic medication (proportions with 95% CI)	0.01 (0.006–0.014)	0.01 (0.003–0.018)	0.04 (0.03–0.07) ∗ ‡
Heel ultrasound osteoporosis status (proportions with 95% CI)			
Normal	0.68 (0.66–0.70)	0.69 (0.65–0.72)	0.73 (0.69–0.77) ∗
Osteopenia	0.24 (0.22–0.25)	0.22 (0.19–0.25)	0.20 (0.16–0.24) ∗
Osteoporosis	0.08 (0.07–0.09)	0.09 (0.08–0.12)	0.07 (0.05–0.10)
Chronic disease number (proportions with 95% CI)			
0	0.37 (0.36–0.39)	0.31 (0.28–0.34) ∗	0.20 (0.17–0.24) ∗ ‡
1	0.37 (0.36–0.39)	0.41 (0.38–0.45) ∗	0.37 (0.33–0.42)
≥2	0.25 (0.24–0.27)	0.28 (0.25–0.31)	0.43 (0.38–0.48) ∗ ‡
Cognitive impairment (proportions with 95% CI)	0.24 (0.23–0.26)	0.26 (0.23–0.29)	0.35 (0.30–0.39) ∗ ‡
Previous fracture (proportions with 95% CI)	0.15 (0.14–0.17)	0.15 (0.13–0.18)	0.17 (0.14–0.21)

Notes: Statistically significant differences between groups using one STOPPFall medication or ≥ 2 STOPPFall medications compared to the total sample ($P < 0.05$) are highlighted with an asterisk (∗). Statistically significant differences between groups using one STOPPFall medication compared to ≥2 STOPPFall medications ($P < 0.05$) are highlighted as (‡). Heart disease was defined as a self-reported history of angina, heart attack, congestive cardiac failure, murmur and/or arrhythmia. Chronic pain was defined as answering 'yes' when asked 'Are you often troubled with pain?'. History of depression, anxiety and urinary incontinence were defined by self-report. Sleep disorder was defined by positive response to two items from the Jenkins Sleep Problems Scale, 'How often do you have trouble falling asleep?' and 'How often do you have trouble with waking up too early and not being able to fall asleep again?'. Indications for antipsychotic medication use were defined by a self-reported history of hallucinations, schizophrenia, psychosis, mood swings or bipolar disorder. T score from heel ultrasound used to define normal bone density (T score > −1.0 standard deviations), osteopenia (bone mineral density T score < −2.5 standard deviations), or osteoporosis (bone mineral density T score > −2.5 standard deviations). Chronic disease burden was assessed by self-report of cancer, liver disease, kidney disease, thyroid disease, arthritis, lung disease, eye conditions and diabetes. Cognitive impairment was defined as self-reporting memory as fair/poor when asked 'How would you rate your day-to-day memory at the present time?' and/or Mini Mental State Examination (MMSE) score ≤ 24. Previous fracture at Wave 1 was defined by self-report. STOPPFall medications were identified with the following ATC codes: benzodiazepines (ATC codes N03AE, N05BA and N05CD), antipsychotics (ATC code N05A), benzodiazepine-related drugs (N05CF), opioids (N02A, R05DA), antidepressants (N06A, N06CA), antiepileptics (N03), diuretics (C02L, C03, C07B, C07C, C07D, C08GA, C09BA, C09BX01, C09BX03, C10BX13, C09DA, C09DX01, C09DX03, C09DX06, C09DX07, C09XA52, C09XA54), alpha-blockers used as antihypertensives (C02CA), alpha blockers used for prostate hyperplasia (G04CA), centrally-acting antihypertensives (C02A), antihistamines (N07CA02, R06), vasodilators used in cardiac diseases (C01D) and drugs for urinary frequency and incontinence (G04BD, G04CA53). Anticholinergic medications not already classified in other STOPPFall medication classes included gastrological agents (A03AA07 A03AB05 A03BA01 A03BA03 A03BB01), Parkinsonian agents (N04AA01 N04AA02 N04AA04 N04AB02 N04AC01), antihistamines (N02BE51) and other medications (M03BA03 M03BC01 N05CM05 N05BB01).

Differences in baseline characteristics between participants by prescription of STOPPFall medication are shown in Table 1. Participants prescribed any STOPPFall medications were older, and those prescribed ≥2 STOPPFall medications were significantly more likely to have a history of heart disease, chronic pain, depression, anxiety, urinary incontinence, sleep disorder, an indication for antipsychotic medication use, higher chronic disease burden, cognitive impairment and lower level of educational attainment.

Over half of participants (1689/2898, 58%) fell during follow-up [median 8 (range 2–12) years]. Over one third of participants (1023/2898, 35%) had an injurious fall, and 24% (692/2898) had an unexplained fall.

One in five participants (588/2898, 20%) reported sustaining any fracture during follow-up [median 8 (range 2–12) years], 4% (103/2898) sustained hip fractures, 5% (157/2898) sustained wrist fractures, 2% (66/2898)

Table 2. Fully adjusted logistic regression model with all falls as dependent variable (n = 2898) by STOPPFall medication use

Falls (Any)	OR (95% CI)	Z	*P*
STOPPFall medications (ref: 0 medications)			
One STOPPFall medication	1.12 (0.93–1.35)	1.18	0.236
≥2 STOPPFall medications	1.67 (1.28–2.18)	3.78	<0.001
Age bands (ref: 65–69 years)			
70–74 years	1.30 (1.07–1.59)	2.59	0.010
≥75 years	1.80 (1.47–2.21)	5.59	<0.001
Female sex	1.57 (1.32–1.86)	5.11	<0.001
Educational attainment (ref: Primary)			
Secondary	1.03 (0.86–1.25)	0.36	0.722
Tertiary	1.31 (1.06–1.62)	2.48	0.013
Heart disease	1.06 (0.88–1.28)	0.62	0.535
Pain	1.41 (1.17–1.69)	3.65	<0.001
Depression	1.65 (1.03–2.66)	2.07	0.038
Anxiety	0.90 (0.54–1.48)	−0.42	0.671
Sleep disorder	1.13 (0.95–1.33)	1.41	0.158
Indication for antipsychotic medication	0.56 (0.22–1.45)	−1.19	0.232
Urinary incontinence	1.20 (0.95–1.53)	1.55	0.121
CAGE Alcohol Scale score (ref: 0–1)			
CAGE ≥2	1.83 (1.29–2.61)	3.37	0.001
Did not complete	1.03 (0.81–1.31)	0.25	0.800
Heel ultrasound osteoporosis status (ref: normal)			
Osteopenia	1.13 (0.93–1.38)	1.19	0.233
Osteoporosis	1.23 (0.90–1.68)	1.30	0.193
Chronic disease number (ref: 0)			
1	1.19 (0.99–1.43)	1.80	0.072
≥2	1.38 (1.11–1.73)	2.84	0.005
Cognitive impairment	1.27 (1.04–1.54)	2.39	0.017
Previous fracture	1.26 (1.00–1.58)	1.98	0.048
Follow up duration (ref: Wave 2)			
Wave 3	2.45 (1.80–3.33)	5.71	<0.01
Wave 4	3.03 (2.23–4.11)	7.13	<0.01
Wave 5	4.87 (3.68–6.45)	11.05	<0.01
Wave 6	6.17 (4.73–8.04)	13.44	<0.01

Notes: Heart disease was defined as a self-reported history of angina, heart attack, congestive cardiac failure, murmur and/or arrhythmia. Chronic pain was defined as answering 'yes' when asked 'Are you often troubled with pain?'. History of depression, anxiety and urinary incontinence were defined by self-report. Sleep disorder was defined by positive response to two items from the Jenkins Sleep Problems Scale, 'How often do you have trouble falling asleep?' and 'How often do you have trouble with waking up too early and not being able to fall asleep again?'. Indications for antipsychotic medication use were defined by a self-reported history of hallucinations, schizophrenia, psychosis, mood swings or bipolar disorder. T score from heel ultrasound used to define normal bone density (T score > −1.0 standard deviations), osteopenia (bone mineral density T score < −2.5 standard deviations), or osteoporosis (bone mineral density T score > −2.5 standard deviations). Chronic disease burden was assessed by self-report of cancer, liver disease, kidney disease, thyroid disease, arthritis, lung disease, eye conditions and diabetes. Cognitive impairment was defined as self-reporting memory as fair/poor when asked 'How would you rate your day-to-day memory at the present time?' and/or Mini Mental State Examination (MMSE) score ≤ 24. Previous fracture at Wave 1 was defined by self-report. STOPPFall medications were identified with the following ATC codes: benzodiazepines (ATC codes N03AE, N05BA and N05CD), antipsychotics (ATC code N05A), benzodiazepine-related drugs (N05CF), opioids (N02A, R05DA), antidepressants (N06A, N06CA), antiepileptics (N03), diuretics (C02L, C03, C07B, C07C, C07D, C08GA, C09BA, C09BX01, C09BX03, C10BX13, C09DA, C09DX01, C09DX03, C09DX06, C09DX07, C09XA52, C09XA54), alpha-blockers used as antihypertensives (C02CA), alpha blockers used for prostate hyperplasia (G04CA), centrally-acting antihypertensives (C02A), antihistamines (N07CA02, R06), vasodilators used in cardiac diseases (C01D) and drugs for urinary frequency and incontinence (G04BD, G04CA53). Anticholinergic medications not already classified in other STOPPFall medication classes included gastrological agents (A03AA07 A03AB05 A03BA01 A03BA03 A03BB01), Parkinsonian agents (N04AA01 N04AA02 N04AA04 N04AB02 N04AC01), antihistamines (N02BE51) and other medications (M03BA03 M03BC01 N05CM05 N05BB01).

sustained vertebral fractures, and 12% (359/2898) sustained other fractures.

STOPPFall medications and falls

After controlling for relevant covariates, logistic regression models showed that prescription of ≥2 STOPPFall medications was independently associated with all falls [OR 1.67 (95%CI 1.28–2.18); $P < 0.001$], injurious falls [OR 1.53 (95%CI 1.19–1.97); $P = 0.001$] and unexplained falls [OR 1.86 (95%CI 1.43–2.42); $P < 0.001$]. Prescription of one STOPPFall medication was not associated with any falls. The full output from the fully adjusted logistic regression model with all falls as the dependent variable is shown in Table 2. Appendix 1 in the Supplementary Data section outlines the fully adjusted logistic regression model with injurious falls as the dependent variable; Appendix 2 reports the fully adjusted logistic regression model with unexplained falls as the dependent variable.

Other significant predictors of all falls, injurious and unexplained falls, apart from prescription of STOPPFall

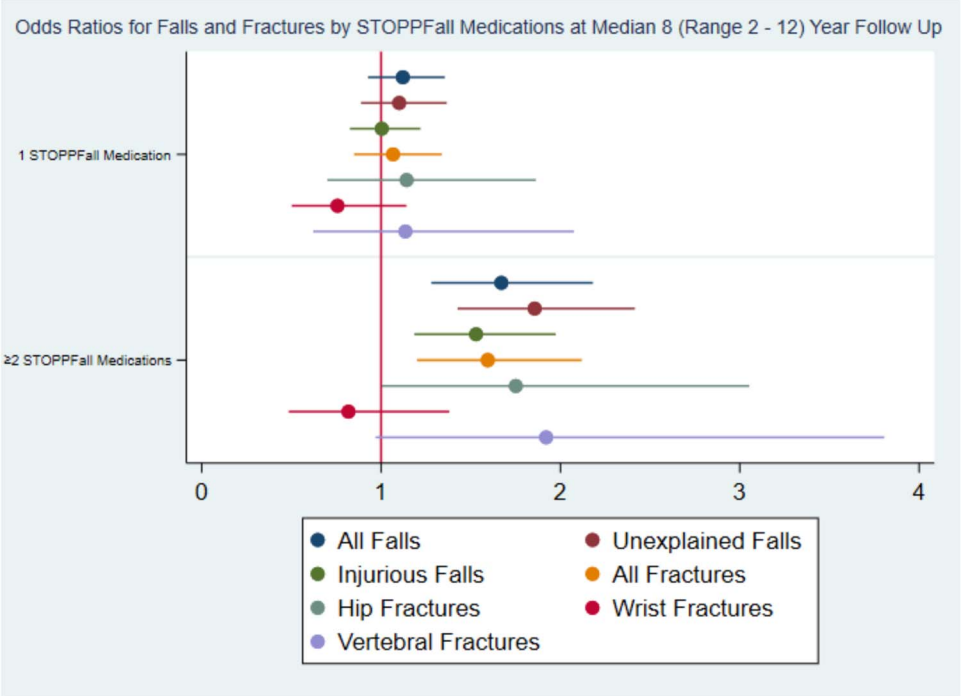

Figure 1. Odds ratios (with 95% confidence intervals) for falls and fractures by STOPPFall Medications (compared to 0 STOPPFall medications) at median 8 (range 2–12) year follow up. Notes: Data presented are odds ratios with 95% confidence intervals from fully adjusted logistic regression models with all falls, unexplained falls, injurious falls, all fractures, hip fractures, wrist fractures and vertebral fractures as dependent variables. Models were adjusted for age, sex, educational attainment, heart disease, pain, depression, anxiety, sleep disorder, indication for antipsychotic medication, urinary incontinence, alcohol excess, osteoporosis status by heel ultrasound, chronic disease burden, cognitive impairment, previous fracture and follow up duration.

medication, were female sex, age ≥75 years, presence of pain, cognitive impairment and previous fracture. See Table 2.

STOPPFall medications and fractures

Prescription of ≥2 STOPPFall medications was a significant predictor of all fractures [OR 1.59 (95%CI 1.20–2.12); $P = 0.001$] and hip fracture [OR 1.75 (95%CI 1.00–3.05); $P = 0.048$] in fully adjusted models. Prescription of ≥2 STOPPFall medications was not associated with increased risk of wrist or vertebral fracture.

Prescription of one STOPPFall medication was not associated with any fractures. Female sex was the only other significant predictor across any fractures. Odds ratios with 95% CIs for falls and fractures by STOPPFall medication use (i.e. 1 or ≥ 2 STOPPFall medications) is shown in Figure 1.

STOPPFall medications and falls and fractures from waves 1–3

A sub-analysis assessed the association of STOPPFall medications at Wave 1 and falls and fractures at follow-up over a shorter time period to Wave 3 only (i.e. 4 years), controlling for relevant covariates as previous. Results were similar, with fully adjusted logistic regression models showing prescription of ≥2 STOPPFall medications was independently associated with all falls [OR 1.53 (95%CI 1.20–1.95); $P < 0.001$], injurious falls [OR 1.57 (95%CI 1.20–2.05); $P = 0.001$], unexplained falls [OR 1.73 (95%CI 1.28–2.35); $P < 0.001$], all fractures [1.54 (95%CI 1.06–2.24); $P = 0.022$] and hip fracture [OR 2.59 (95%CI 1.29–5.22); $P = 0.008$]. Prescription of ≥2 STOPPFall medications was not associated with wrist or vertebral fractures. Prescription of one STOPPFall medication was not associated with any of these outcomes.

Change in STOPPFall medications at Wave 3

There were 2998 participants included in this analysis, with mean age at Wave 3 of 73.4 (95%CI 73.2–73.7); 54% were female (1618/2998). STOPPFall medication prescription remained unchanged in two-thirds of participants (1998/2998, 67%), with 17% (495/2998) increasing by one STOPPFall medication, 5% (148/2998) increasing by ≥2 STOPPFall medications, 10% (300/2998) decreasing by one STOPPFall medication and 2% (57/2998) decreasing by ≥2 STOPPFall medications.

Change in STOPPFall medications and falls

After controlling for relevant covariates present at Wave 3 assessment, there was a significant association between increasing by ≥2 STOPPFall medications and all falls [OR 1.72 (95%CI 1.19–2.48); $P = 0.004$]. The full output from

Table 3. Fully adjusted logistic regression model with all falls as dependent variable (n = 2998) by change in STOPPFall medication at 4 year follow-up

Falls (Any)	OR (95% CI)	Z	*P*
Change in STOPPFall medications (ref: 0 medication changes)			
Increase by 1 STOPPFall medication (n = 495)	1.12 (0.90–1.38)	1.01	0.311
Increase by ≥2 STOPPFall medications (n = 148)	1.72 (1.19–2.48)	2.90	0.004
Decrease by 1 STOPPFall medication (n = 300)	0.91 (0.68–1.21)	−0.64	0.524
Decrease by ≥2 STOPPFall medications (n = 57)	0.66 (0.35–1.25)	−1.27	0.203
Prescription of STOPPFall medications at Wave 1	1.24 (1.10–1.41)	3.44	<0.001
Age bands (ref: 65–69 years)			
70–74 years	1.47 (1.21–1.79)	3.88	<0.001
≥75 years	1.59 (1.31–1.92)	4.73	<0.001
Female sex	1.23 (1.05–1.45)	2.54	0.011
Educational attainment (ref: Primary)			
Secondary	0.85 (0.71–1.02)	−1.70	0.089
Tertiary	1.10 (0.90–1.34)	0.92	0.360
Heart disease	0.95 (0.78–1.15)	−0.55	0.584
Pain	1.27 (1.07–1.51)	2.75	0.006
Depression	1.31 (0.81–2.12)	1.11	0.267
Anxiety	0.87 (0.54–1.42)	−0.55	0.581
Sleep disorder	1.09 (0.93–1.27)	1.07	0.284
Indication for antipsychotic medication	1.61 (0.65–4.00)	1.02	0.306
Urinary incontinence	1.67 (1.35–2.06)	4.72	<0.001
CAGE Alcohol Scale score (ref: 0–1)			
CAGE ≥2	1.19 (0.88–1.62)	1.12	0.262
Did not complete	1.21 (0.98–1.48)	1.80	0.071
Heel ultrasound osteoporosis status (ref: normal)			
Osteopenia	1.17 (0.97–1.43)	1.63	0.104
Osteoporosis	0.94 (0.68–1.29)	−0.38	0.700
Chronic disease number (ref: 0)			
1	1.06 (0.89–1.28)	0.66	0.508
≥2	1.13 (0.91–1.39)	1.12	0.262
Cognitive impairment	1.41 (1.18–1.69)	3.71	<0.001
Previous fracture (Waves 1–3)	1.07 (0.89–1.28)	0.73	0.465
Follow up duration (ref: Wave 4)			
Wave 5	2.24 (1.71–2.93)	5.86	<0.001
Wave 6	3.71 (2.88–4.78)	10.11	<0.001

Notes: Heart disease was defined as a self-reported history of angina, heart attack, congestive cardiac failure, murmur and/or arrhythmia. Chronic pain was defined as answering 'yes' when asked 'Are you often troubled with pain?'. History of depression, anxiety and urinary incontinence were defined by self-report. Sleep disorder was defined by positive response to two items from the Jenkins Sleep Problems Scale, 'How often do you have trouble falling asleep?' and 'How often do you have trouble with waking up too early and not being able to fall asleep again?'. Indications for antipsychotic medication use were defined by a self-reported history of hallucinations, schizophrenia, psychosis, mood swings or bipolar disorder. T score from heel ultrasound used to define normal bone density (T score > −1.0 standard deviations), osteopenia (bone mineral density T score < −2.5 standard deviations), or osteoporosis (bone mineral density T score > −2.5 standard deviations). Chronic disease burden was assessed by self-report of cancer, liver disease, kidney disease, thyroid disease, arthritis, lung disease, eye conditions and diabetes. Cognitive impairment was defined as self-reporting memory as fair/poor when asked 'How would you rate your day-to-day memory at the present time?' and/or Mini Mental State Examination (MMSE) score ≤ 24. Previous fracture from Waves 1–3 was defined by self-report. STOPPFall medications were identified with the following ATC codes: benzodiazepines (ATC codes N03AE, N05BA and N05CD), antipsychotics (ATC code N05A), benzodiazepine-related drugs (N05CF), opioids (N02A, R05DA), antidepressants (N06A, N06CA), antiepileptics (N03), diuretics (C02L, C03, C07B, C07C, C07D, C08GA, C09BA, C09BX01, C09BX03, C10BX13, C09DA, C09DX01, C09DX03, C09DX06, C09DX07, C09XA52, C09XA54), alpha-blockers used as antihypertensives (C02CA), alpha blockers used for prostate hyperplasia (G04CA), centrally-acting antihypertensives (C02A), antihistamines (N07CA02, R06), vasodilators used in cardiac diseases (C01D) and drugs for urinary frequency and incontinence (G04BD, G04CA53). Anticholinergic medications not already classified in other STOPPFall medication classes included gastrological agents (A03AA07 A03AB05 A03BA01 A03BA03 A03BB01), Parkinsonian agents (N04AA01 N04AA02 N04AA04 N04AB02 N04AC01), antihistamines (N02BE51) and other medications (M03BA03 M03BC01 N05CM05 N05BB01).

the fully adjusted logistic regression model with all falls as the dependent variable is shown in Table 3.

There was a significant association between increasing by ≥2 STOPPFall medications and injurious falls [OR 1.49 (95%CI 1.01–2.18); $P = 0.042$]. There was no significant association between increasing by one STOPPFall medication, or decreasing any STOPPFall medications and all falls or injurious falls. There was a significant association between increasing by one STOPPFall medication and unexplained falls [OR 1.43 (95%CI 1.10–1.86); $P = 0.007$], but no association between increasing by ≥2 STOPPFall medications, or decreasing any STOPPFall medications, and unexplained falls. Odds ratios with 95% CIs for all falls, injurious falls, unexplained falls and all fractures, is shown in Figure 2.

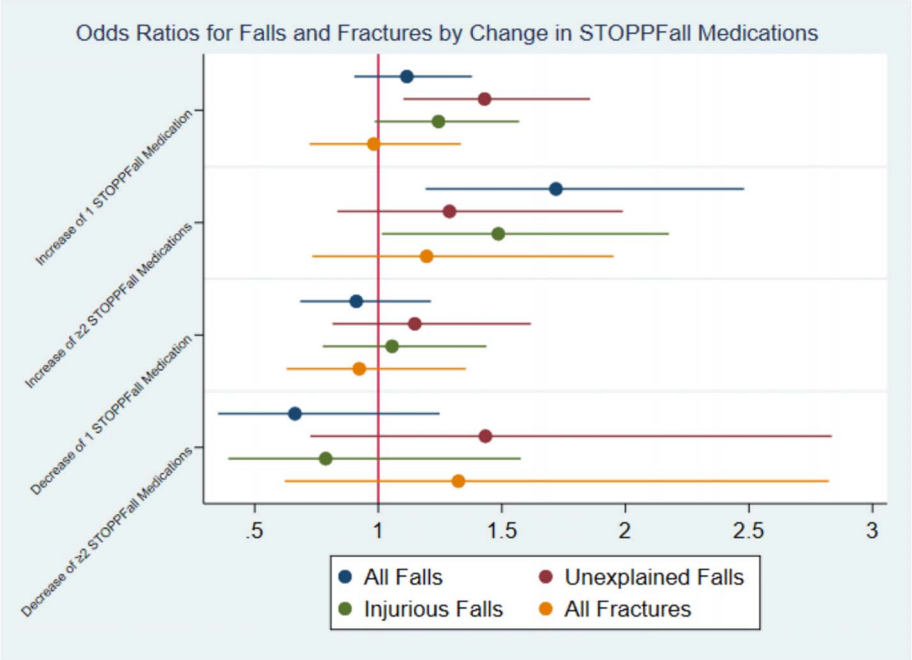

Figure 2. Odds ratios (with 95% confidence intervals) for falls and fractures by increase or decrease in STOPPFall Medications. Notes: Data presented are odds ratios with 95% confidence intervals from fully adjusted logistic regression models with all falls, unexplained falls, injurious falls and all fractures as dependent variables. Models were adjusted for prescription of STOPPFall medications at Wave 1, age, sex, educational attainment, heart disease, pain, depression, anxiety, sleep disorder, indication for antipsychotic medication, urinary incontinence, alcohol excess, osteoporosis status by heel ultrasound, chronic disease burden, cognitive impairment, previous fracture from Waves 1–3 and follow up duration.

Change in STOPPFall medications and fractures

There was no significant association between increasing or decreasing any STOPPFall medications and any fractures, after controlling for relevant covariates.

Discussion

This study demonstrates that prescription of ≥2 STOPPFall medications is independently associated with all falls, unexplained and injurious falls, in a large cohort of community dwelling older people at median 8 (range 2–12) years follow-up. Prescription of ≥2 STOPPFall medications conferred an 86% increased odds of unexplained falls during follow-up. Increasing prescription of ≥2 STOPPFall medications at Wave 3 compared to baseline assessment is associated with increased odds of all falls and injurious falls.

Prescription of ≥2 STOPPFall medications was associated with an increased odds of all fractures and hip fractures, with 75% increased odds of hip fracture in this group compared to participants not prescribed any STOPPFall medication. Changing STOPPFall medication at Wave 3 did not impact odds of future fractures.

Prior studies have explored the relationship between some classes of medication within STOPPFall and increased risk of falls amongst older people [22–27]. Data from TILDA has previously shown that psychotropic medications, especially antidepressants and anticholinergic medications, are independently associated with increased risk of falls and fractures [28]. TILDA data has also shown that antidepressant use is associated with an increased risk of injurious and unexplained falls [29], and those prescribed antidepressants have a twice higher prevalence of OH compared to participants not using antidepressants [30]. This is the first study however to examine the association between the complete list of STOPPFall medication use and falls and fractures longitudinally in older people.

Different medication classes within STOPPFall have also been shown to be associated with increased fracture risk. Risk of fractures is associated with diuretic use especially during the initial weeks after commencing diuretics [22], with reduction in hip bone mineral density in those on long-term diuretic therapy [31]. Benzodiazepine use has been shown to increase fracture risk [32], especially hip fractures [33] and Z-drug use has been shown to confer a >60% increased risk of fracture [34]. Opioid use increases fracture risk especially at higher doses compared to low dose opioids [35] and increase the risk of hip fractures [36] with strong opioids conferring increased risk of hip fracture compared to weak opioids [37]. Antidepressants may accelerate postmenopausal bone loss [38], with selective serotonin reuptake inhibitors (SSRIs) showing a dose-dependent increased bone loss, and SSRIs can increase hip fracture risk [39]. The

findings from this study are in line with these previous studies, with STOPPFall medications especially increasing risk of hip fracture.

These findings are important as FRIDS represent an important modifiable risk factor for falls. Review of these medications is essential in comprehensive multifactorial falls assessments. A prospective cohort study based in the Netherlands has previously shown that withdrawing FRIDs was effective at reducing risk of further falls [40], though in our study it is notable that whilst increasing prescription of ≥2 STOPPFall medications at Wave 3 was associated with increased likelihood of all falls and injurious falls, there was no reduction in the likelihood of future falls with decreased prescription. The possible reasons why deprescribing STOPPFall medications was not associated with reduced falls or fractures is not clear. Deprescribing may occur in response to falls or fractures and the nature of the TILDA study is that it is not possible to determine the exact timing of falls/fractures related to deprescribing. Further, both deprescribing and falls may occur in the context of increasing frailty and functional decline, and despite robust adjustment of covariates in this study there may still exist some residual confounding between the two. The small sample size of participants who had ≥2 STOPPFall medications reduced may also be contributory. Another very relevant possibility is that deprescribing STOPPFall medication as a single intervention may not be effective in preventing falls and fractures and that a multimodal approach is required.

Some limitations of this study should be outlined. Falls and fracture data is collected by self-report. Given assessments are performed every 2 years, these could be subject to recall bias. Medication compliance could not be confirmed, however participants' medication lists were manually checked at the time of assessment. Medication dosages prescribed are not collected during assessment therefore this cannot be accounted for in analysis. Though the gold standard for assessment of bone mineral density is performing dual-energy X-ray absorptiometry (DEXA), performing this on all participants was not feasible, therefore heel ultrasonography was used. Further risk factors for falls may also develop during the follow-up period. The strengths of this study include the large, nationally representative study sample, and the long follow-up period over median 8 (range 2–12) years. We have also robustly adjusted for relevant covariates that may contribute to falls and fractures, including the presence of indications for STOPPFall medications use.

In conclusion, this study shows that prescription of ≥2 STOPPFall medications is independently associated with an increased likelihood of all falls, unexplained and injurious falls, and all fractures and hip fractures in community dwelling older people. Though our study did not demonstrate a reduction in future fall or fracture risk with reduction in STOPPFall medications, it did show an association between increasing prescription of ≥2 STOPPFall medications and increased likelihood of all falls and injurious falls at follow-up. This supports the World Falls Guidelines' recommendation that a history of falls or an increased risk of falls should be considered prior to prescribing potential FRIDs, and tools such as STOPPFall can be useful in highlighting these medications to clinicians [11]. Proactive medication reviews among older people, with an aim towards deprescribing if indicated, are essential given the cascade of adverse events that can occur after falls or fractures in this cohort.

Research data transparency and availability

Researchers interested in using regular waves of TILDA data may access the data for free from the following sites: Irish Social Science Data Archive (ISSDA) at University College Dublin (http://www.ucd.ie/issda/data/tilda/); Interuniversity Consortium for Political and Social Research (ICPSR) at the University of Michigan (http://www.icpsr.umich.edu/icpsrweb/NACDA/studies/34315). Replication of the results reported in this article requires access to the full TILDA dataset. Researchers seeking access to the full TILDA dataset may apply to access the data (tilda.tcd.ie).

Supplementary Data: Supplementary data is available at *Age and Ageing* online.

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