### Medications and Falls

This document contains all abstracts for publications relating to medications and falls from 2021 so far and will be updated quarterly. These abstracts have been sourced from <u>SafetyLit.org</u> and include only those relevant to falls prevention.

SafetyLit provides weekly abstracts of peer reviewed articles from researchers who work in the more than 30 distinct professional disciplines relevant to preventing and researching unintentional injuries, violence, and self-harm. Each week citations and summaries of about 400 articles and reports are included in a PDF document or through an RSS subscription.







### Deprescribing fall-risk increasing drugs (FRIDs) for the prevention of falls and fall-related complications: a systematic review and meta-analysis

Lee J, Negm A, Peters R, Wong EKC, Holbrook A. BMJ Open 2021; 11(2): e035978.

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DOI 10.1136/bmjopen-2019-035978 PMID unavailable

### Abstract

OBJECTIVES: Prevention of falls and fall-related injuries is a priority due to the substantial health and financial burden of falls on patients and healthcare systems. Deprescribing medications known as 'fall-risk increasing drugs' (FRIDs) is a common strategy to prevent falls. We conducted a systematic review to determine its efficacy for the prevention of falls and fall-related complications.

DESIGN: Systematic review and meta-analysis. DATA SOURCES: MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, CINAHL and grey literature from inception to 1 August 2020. ELIGIBILITY CRITERIA FOR SELECTING STUDIES: Randomised controlled trials of FRID withdrawal compared with usual care evaluating the rate of falls, incidence of falls, fall-related injuries, fall-related fractures, fall-related hospitalisations or adverse effects related to the intervention in adults aged ≥65 years. DATA EXTRACTION AND SYNTHESIS: Two reviewers independently performed citation screening, data abstraction, risk of bias assessment and certainty of evidence grading. Random-effects models were used for metaanalyses.

RESULTS: Five trials involving 1305 participants met eligibility criteria. Deprescribing FRIDs did not change the rate of falls (rate ratio (RaR) 0.98, 95% CI 0.63 to 1.51), the incidence of falls (risk difference 0.01, 95% CI -0.06 to 0.09; relative risk 1.04, 95% CI 0.86 to 1.26) or rate of fall-related injuries (RaR 0.89, 95% CI 0.57 to 1.39) over a follow-up period of 6-12 months. No trials evaluated the impact of deprescribing FRIDs on fall-related fractures or hospitalisations.

CONCLUSION: There is a paucity of robust high-quality evidence to support or refute that a FRID deprescribing strategy alone is effective at preventing falls or fall-related injury in older adults. Although there may be other reasons to deprescribe FRIDs, our systematic review found that it may result in little to no difference in the rate or risk of falls as a sole falls reduction strategy. PROSPERO REGISTRATION NUMBER: CRD42016040203.

Language: en

### Keywords

primary care; clinical pharmacology; geriatric medicine; internal medicine







### Association of baclofen with falls and fractures in patients with CKD

Muanda FT, Blake PG, Weir MA, Bathini L, Chauvin K, Dixon SN, McArthur E, Sontrop JM, Moist L, Kim RB, Garg AX. Am. J. Kidney Dis. 2021; ePub(ePub): ePub.

(Copyright © 2021, National Kidney Foundation, Publisher Elsevier Publishing)

DOI 10.1053/j.ajkd.2020.12.017 PMID unavailable

#### Abstract

Baclofen is a popular muscle relaxant that is eliminated primarily unchanged in the urine. We recently reported a higher risk of encephalopathy in a cohort of 15,942 older adults with chronic kidney disease (CKD) who started baclofen at ≥20 mg/day vs. <20 mg/day; a higher risk was also observed in all baclofen users vs. non-users. In another study of patients receiving dialysis, 1 in 14 were hospitalized with encephalopathy within 3 days of starting baclofen...







### The extent of polypharmacy and use of 'fall risk increasing drugs' in the oldest old admitted to a regional New South Wales hospital

Bemand TJ, Thomas S, Finucane P. Australas. J. Ageing 2021; ePub(ePub): ePub.

(Copyright © 2021, Australian Council on the Ageing, Publisher John Wiley and Sons)

DOI 10.1111/ajag.12909 PMID unavailable

#### Abstract

OBJECTIVE(S): Polypharmacy is associated with significant morbidity including cognitive decline and falls. We sought to quantify the extent of polypharmacy and use of medications associated with fall risk in the very old admitted to a regional NSW hospital.

METHODS: Cross-sectional study of patients aged over 80 years admitted to a regional NSW hospital from September to October 2019. Demographic data and medication usage on admission were collected. Polypharmacy was defined as regular use of five or more medications.

RESULTS: A total of 401 patients were included: mean age was 87.2 (±4.6) years and 56.9% were female. Of the participations, 82.9% experienced polypharmacy, and the mean number of medications was 8.2 (±4.2). Of the patients, 91.6% utilised medications associated with risk of falls. There was no association between age and number of preadmission regular medications.

CONCLUSION: Polypharmacy is extremely common prior to acute hospitalisation for regional older individuals. This highlights the importance of medication rationalisation to reduce medication-related harm.

Language: en

### Keywords

Australia; polypharmacy; aged 80 and over; drug prescriptions; rural health







## Fall risk-increasing drugs, polypharmacy, and falls among low-income community-dwelling older adults

Ie K, Chou E, Boyce RD, Albert SM. Innov. Aging 2021; 5(1): igab001.

(Copyright © 2021, Oxford University Press)

DOI 10.1093/geroni/igab001 PMID 33644415

#### Abstract

BACKGROUND AND OBJECTIVES: Medication exposure is a potential risk factor for falls and subsequent death and functional decline among older adults. However, controversy remains on the best way to assess medication exposure and which approach best predicts falls. The objective of the current study was to examine the association between different measures of medication exposure and falls risk among community-dwelling older adults. RESEARCH DESIGN AND METHODS: This retrospective cohort study was conducted using Falls Free PA program data and a linked prescription claims data from Pennsylvania's Pharmaceutical Assistance Contract for the Elderly program. Participants were community-dwelling older adults living in Pennsylvania, United States. Three measures of medication exposure were assessed: (a) total number of regular medications (polypharmacy); (b) counts of potentially inappropriate medications derived from current prescription guidance tools (Fall Risk-Increasing Drugs [FRIDs], Beers Criteria); and (c) medication burden indices based on pharmacologic mechanisms (Anticholinergic Cognitive Burden, Drug Burden Index) all derived from claims data. The associations between the different medication risk measures and self-reported falls incidence were examined with univariate and multivariable negative binomial regression models to estimate incidence rate ratios (IRRs).

RESULTS: Overall 343 older adults were included and there were 236 months with falls during 2,316 activity-adjusted person-months (10.2 falls per 100 activity-adjusted person-months). Of the 6 measures of medication risk assessed in multivariate models, only the use of 2 or more FRIDs (adjusted IRR 1.67 [95% CI: 1.04-2.68]) independently predicted falls risk. Among the 13 FRID drug classes, the only FRID class associated with an increased fall risk was antidepressants.

DISCUSSION AND IMPLICATIONS: The presence of multiple FRIDs in a prescription is an independent risk factor for falls, even in older adults with few medications. Further investigation is required to examine whether deprescribing focused on FRIDs effectively prevents falls among this population.

Language: en

#### Keywords

Falls risk; Medication exposure; Pharmacoepidemiology; Prescription guidance







### Special Report from the CDC: Antidepressant subclass use and fall risk in communitydwelling older Americans

Haddad YK, Luo F, Bergen G, Legha JK, Atherly A. J. Saf. Res. 2021; 76: 332-340.

(Copyright © 2021, U.S. National Safety Council, Publisher Elsevier Publishing)

DOI 10.1016/j.jsr.2020.11.008 PMID unavailable

#### Abstract

INTRODUCTION: Falls among older adults are a significant health concern affecting more than a quarter of older adults (age 65+). Certain fall risk factors, such as medication use, increase fall risk among older adults (age 65+).

AIM: The aim of this study is to examine the association between antidepressantmedication subclass use and self-reported falls in community-dwelling older adults.

METHODS: This analysis used the 2009-2013 Medicare Current Beneficiary Survey, a nationally representative panel survey. A total of 8,742 community-dwelling older adults, representing 40,639,884 older Medicare beneficiaries, were included. We compared self-reported falls and psychoactive medication use, including antidepressant subclasses. These data are controlled for demographic, functional, and health characteristics associated with increased fall risk. Descriptive analyses and multivariate logistic regression analyses were conducted using SAS 9.4 and Stata 15 software.

RESULTS: The most commonly used antidepressant subclass were selective serotonin reuptake inhibitors (SSRI) antidepressants (13.1%). After controlling for characteristics associated with increased fall risk (including depression and concurrent psychoactive medication use), the risk of falling among older adults increased by approximately 30% among those who used a SSRI or a serotonin-norepinephrine reuptake inhibitors (SNRI) compared to non-users. The adjusted risk ratio (aRR) for SSRI was 1.29 (95% CI = 1.13, 1.47) and for SNRI was 1.32 (95% CI = 1.07, 1.62).

CONCLUSION: SSRI and SNRI are associated with increased risk of falling after adjusting for important confounders. Medication use is a modifiable fall risk factor in older adults and can be targeted to reduce risk of falls. Practical Applications: Use of selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors increased the risk of falling in older adults by approximately 30%, even after controlling for demographic, functional, and health characteristics, including depression. Health care providers can work towards reducing fall risk among their older patients by minimizing the use of certain medications when potential risks outweigh the benefits.

Language: en

#### Keywords

Depression; Falls; Elderly; Older adults; Antidepressants; Psychoactive medications







### Depression, antidepressants and fall risk: therapeutic dilemmas-a clinical review

van Poelgeest EP, Pronk AC, Rhebergen D, van der Velde N. Eur. Geriatr. Med. 2021; ePub(ePub): ePub.

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DOI 10.1007/s41999-021-00475-7 PMID unavailable

#### Abstract

PURPOSE: The aim of this clinical review was to summarize the existing knowledge on fall risk associated with antidepressant use in older adults, describe underlying mechanisms, and assist clinicians in decision-making with regard to (de-) prescribing antidepressants in older persons.

METHODOLOGY: We comprehensively examined the literature based on a literature search in Pubmed and Google Scholar, and identified additional relevant articles from reference lists, with an emphasis on the most commonly prescribed drugs in depression in geriatric patients. We discuss use of antidepressants, potential fall-related side effects, and deprescribing of antidepressants in older persons.

RESULTS: Untreated depression and antidepressant use both contribute to fall risk. Antidepressants are equally effective, but differ in fall-related side effect profile. They contribute to (or cause) falling through orthostatic hypotension, sedation/impaired attention, hyponatremia, movement disorder and cardiac toxicity. Falling is an important driver of morbidity and mortality and, therefore, requires prevention. If clinical condition allows, withdrawal of antidepressants is recommended in fall-prone elderly persons. An important barrier is reluctance of prescribers to deprescribe antidepressants resulting from fear of withdrawal symptoms or disease relapse/recurrence, and the level of complexity of deprescribing antidepressants in older persons with multiple comorbidities and medications. Practical resources and algorithms are available that guide and assist clinicians in deprescribing antidepressants.

CONCLUSIONS: (De-) prescribing antidepressants in fall-prone older adults is often challenging, but detailed insight in fall-related side effect profile of the different antidepressants and a recently developed expert-based decision aid STOPPFalls assists prescribers in clinical decision-making.

Language: en

#### Keywords

Falls; Antidepressants; Deprescribing; FRIDs; Geriatric; Orthostatic hypotension







## CYP2D6-inhibiting drugs and risk of fall injuries after newly initiated antidepressant and antipsychotic therapy in a Swedish, register-based case-crossover study

Dahl ML, Leander K, Vikström M, Frumerie C, Nordenmalm S, Moller J, Söderberg-Löfdal K. Sci. Rep. 2021; 11(1): e5796.

(Copyright © 2021, Nature Publishing Group)

DOI 10.1038/s41598-021-85022-x PMID unavailable

### Abstract

Drug-drug interactions have been shown to affect the risk of fall injuries when opioids are used concomitantly with drugs inhibiting the cytochrome P450 2D6 (CYP2D6) enzyme in a previous pharmacoepidemiological study. The aim of this study was to determine whether CYP2D6-inhibiting drugs reinforce the risk of fall injuries when used concomitantly with antidepressants or antipsychotics. We identified all 252,704 adults with a first fall injury leading to hospitalisation from the National Patient Register in Sweden 2006-2013. Data on dispensed drugs was linked from the Swedish Prescribed Drug Register. We applied a casecrossover design to analyse newly dispensed (28 days preceding the fall injury, preceded by a 12-week washout period) antidepressants and antipsychotics, respectively, in relation to risk of a fall injury and according to concomitant use of CYP2D6-inhibiting drugs. Newly dispensed drugs were assessed correspondingly in a control period of equal length, 28 days prior to the 12-week washout period. Overall, the risk of fall injury was increased after newly initiated antidepressant and antipsychotic treatment. For antidepressants, concomitant CYP2D6 inhibitor use further elevated the risk estimates compared to non-use, most pronounced for the groups selective serotonin reuptake inhibitors (sertraline excluded) [OR = 1.47 (95% CI 1.19-1.80) vs. OR = 1.19 (95% CI 1.13-1.26)], and tricyclic antidepressants [OR = 1.71 (95% CI 1.17-2.51) vs. 1.27 (95% CI 1.11-1.47)] as well as for sertraline [OR = 1.61 (95% CI 1.05-2.38) vs. 1.12 (95% CI 1.00-1.26)]. For antipsychotics, the risk of fall injury was not altered by concomitant use of CYP2D6-inhibiting drugs. In conclusion, concomitant use of CYP2D6 inhibiting drugs tends to further increase the risk of fall injury in newly initiated antidepressant treatment, but not in antipsychotic treatment.







### Association of drugs with special caution in the guidelines with falls: a case-control and case-crossover study in Japan

Ishibashi Y, Nishitani R, Kato T, Chiba S, Ashidate K, Ishiwata N, Ichijo T, Sasabe M. Geriatr. Gerontol. Int. 2021; ePub(ePub): ePub.

(Copyright © 2021, Japan Geriatrics Society, Publisher John Wiley and Sons)

DOI 10.1111/ggi.14127 PMID unavailable

#### Abstract

AIM: To determine the relationship between multiple medications and falls.

METHODS: This case-control and case-crossover study was carried out at Kudanzaka Hospital in Chiyoda, Tokyo, Japan. A total of 325 patients who experienced their first falls when hospitalized between January 2016 and November 2018, and 1285 controls matched by sex, age and clinical departments were included in this study. Hospitalization duration and fall risk score were adjusted for in the analyses.

RESULTS: In the case-control study, multivariable logistic regression showed that increasing the intake of oral medications was not significantly associated with the incidence of falls (odds ratio 1.02, 95% confidence interval 0.998-1.049). In contrast, drugs prescribed with special caution in accordance with the Elderly Oral Medication Guidelines were significantly associated with falls (odds ratio 1.17, 95% confidence interval 1.09-1.26). A similar pattern was observed in the case-crossover analysis. Among the drugs to be prescribed with special caution according to the guidelines, atypical antipsychotics, non-benzodiazepine hypnotics and magnesium oxide were significantly associated with the risk of falls.

CONCLUSION: The drugs to be prescribed with special caution according to the guidelines were associated with an increased fall risk. The risk of falls in hospitalized older people due to multiple medications varies among medications. Geriatr Gerontol Int

Language: en

### Keywords

risk factors; polypharmacy; fall; guidelines; older patients







### Fall-related hospitalizations in nursing home residents co-prescribed a cholinesterase inhibitor and beta-blocker

Watt JA, Campitelli MA, Maxwell CJ, Guan J, Maclagan LC, Gomes T, Bokhari M, Straus SE, Bronskill SE. J. Am. Geriatr. Soc. 2020; 68(11): 2516-2524.

(Copyright © 2020, John Wiley and Sons)

DOI 10.1111/jgs.16710 PMID unavailable

### Abstract

BACKGROUND/OBJECTIVES: To examine the association between hospitalization for a fallrelated injury and the co-prescription of a cholinesterase inhibitor (ChEI) among persons with dementia receiving a beta-blocker, and whether this potential drug-drug interaction is modified by frailty.

DESIGN: Nested case-control study using population-based administrative databases. SETTING: All nursing homes in Ontario, Canada. PARTICIPANTS: Persons with dementia aged 66 and older who received at least one beta-blocker between April 2013 and March 2018 following nursing home admission (n = 19,060). MEASUREMENTS: Cases were persons with dementia with a hospitalization (emergency department visit or acute care admission) for a fall-related injury with concurrent beta-blocker use. Each case (n = 3,038) was matched 1:1 to a control by age (±1 year), sex, cohort entry year, frailty, and history of fall-related injuries. The association between fall-related injury and exposure to a ChEI in the 90 days prior was examined using multivariable conditional logistic regression. Secondary exposures included ChEI type, daily dose, incident versus prevalent use, and use in the prior 30 days. Subgroup analyses considered frailty, age group, sex, and history of hospitalization for fallrelated injuries.

RESULTS: Exposure to a ChEI in the prior 90 days occurred among 947 (31.2%) cases and 940 (30.9%) controls. In multivariable models, no association was found between hospitalization for a fall-related injury and prior exposure to a ChEI in persons with dementia dispensed beta-blockers (adjusted odds ratio =.96, 95% confidence interval =.85-1.08).

FINDINGS were consistent across secondary exposures and subgroup analyses.

CONCLUSION: Among nursing home residents with dementia receiving beta-blockers, coprescription of a ChEI was not associated with an increased risk of hospitalization for a fallrelated injury. However, we did not assess for its association with falls not leading to hospitalization. This finding could inform clinical guidelines and shared decision making between persons with dementia, caregivers, and clinicians concerning ChEI initiation and/or discontinuation.

Language: en

### Keywords

dementia; nursing home; beta-blocker; cholinesterase inhibitor; fall-related injuries; frailty







## Patient and physician perspectives of deprescribing potentially inappropriate medications in older adults with a history of falls: a qualitative study

Hahn EE, Munoz-Plaza CE, Lee EA, Luong TQ, Mittman BS, Kanter MH, Singh H, Danforth KN. J. Gen. Intern Med. 2021; ePub(ePub): ePub.

(Copyright © 2021, Holtzbrinck Springer Nature Publishing Group)

DOI 10.1007/s11606-020-06493-8 PMID unavailable

### Abstract

BACKGROUND: High-risk medications pose serious safety risks to older adults, including increasing the risk of falls. Deprescribing potentially inappropriate medications (PIMs) in older adults who have experienced a fall is a key element of fall reduction strategies. However, continued use of PIMs in older adults is common, and clinicians may face substantial deprescribing barriers.

OBJECTIVE: Explore patient and clinician experiences with and perceptions of deprescribing PIMs in patients with a history of falls.

DESIGN: We led guided patient feedback sessions to explore deprescribing scenarios with patient stakeholders and conducted semi-structured interviews with primary care physicians (PCPs) to explore knowledge and awareness of fall risk guidelines, deprescribing experiences, and barriers and facilitators to deprescribing. PARTICIPANTS: PCPs from Kaiser Permanente Southern California (KPSC) and patient members of the KPSC Regional Patient Advisory Committee. APPROACH: We used maximum variation sampling to identify PCPs with patients who had a fall, then categorized the resulting PIM dispense distribution for those patients into high and low frequency. We analyzed the data using a hybrid deductiveinductive approach. Coders applied initial deductively derived codes to the data, simultaneously using an open-code inductive approach to capture emergent themes. KEY RESULTS: Physicians perceived deprescribing discussions as potentially contentious, even among patients with falls. Physicians reported varying comfort levels with deprescribing strategies: some felt that the conversations might be better suited to others (e.g., pharmacists), while others had well-planned negotiation strategies. Patients reported lack of clarity as to the reasons and goals of deprescribing and poor understanding of the seriousness of falls.

CONCLUSIONS: Our study suggests that key barriers to deprescribing include PCP trepidation about raising a contentious topic and insufficient patient awareness of the potential seriousness of falls.

FINDINGS suggest the need for multifaceted, multilevel deprescribing approaches with clinician training strategies, patient educational resources, and a focus on building trusting patient-clinician relationships.

Language: en

Keywords falls; older adults; deprescribing; potentially inappropriate medications







## Hospitalisations for falls and hip fractures attributable to vitamin D deficiency in older Australians

Neale RE, Wilson LF, Black LJ, Waterhouse M, Lucas RM, Gordon LG. <u>Br. J. Nutr.</u> 2021; ePub(ePub): ePub.

(Copyright © 2021, Nutrition Society, Publisher CABI Publishing)

### DOI 10.1017/S0007114521000416 PMID unavailable

### Abstract

Vitamin D deficiency is associated with increased risk of falls and fractures. Assuming this association is causal, we aimed to identify the number and proportion of hospitalisations for falls and hip fractures attributable to vitamin D deficiency [25 hydroxy D (25(OH)D) <50 nmol/L] in Australians aged 65 years and over. We used 25(OH)D data from the 2011/12 Australian Health Survey and relative risks from published meta-analyses to calculate population attributable fractions for falls and hip fracture. We applied these to data published by the Australian Institute of Health and Welfare to calculate the number of events each year attributable to vitamin D deficiency. In men and women combined, 8.3% of hospitalisations for falls (7991 events) and almost 8% of hospitalisations for hip fractures (1315 events) were attributable to vitamin D deficiency. These findings suggest that even in a sunny country such as Australia vitamin D deficiency contributes to a considerable number of hospitalisations as a consequence of falls and for treatment of hip fracture in older Australians; in countries where the prevalence of vitamin D deficiency is higher the impact will be even greater. It is important to mitigate vitamin D deficiency but whether this should occur through supplementation or increased sun exposure needs consideration of the benefits, harms, practicalities, and costs of both approaches.

Language: en

### Keywords

Australia; falls; vitamin D; hip fractures; population attributable fraction







### Are anticholinergic symptoms a risk factor for falls in older general practice patients with polypharmacy? Study protocol for the development and validation of a prognostic model

Dinh TS, González-González AI, Meid AD, Snell KIE, Rudolf H, Brueckle MS, Blom JW, Thiem U, Trampisch HJ, Elders PJM, Donner-Banzhoff N, Gerlach FM, Harder S, van den Akker M, Glasziou PP, Haefeli WE, Muth C. Front. Pharmacol. 2020; 11: e577747.

(Copyright © 2020, Frontiers Media)

DOI 10.3389/fphar.2020.577747 PMID 33519441

### Abstract

BACKGROUND: Cumulative anticholinergic exposure, also known as anticholinergic burden, is associated with a variety of adverse outcomes. However, studies show that anticholinergic effects tend to be underestimated by prescribers, and anticholinergics are the most frequently prescribed potentially inappropriate medication in older patients. The grading systems and drugs included in existing scales to quantify anticholinergic burden differ considerably and do not adequately account for patients' susceptibility to medications. Furthermore, their ability to link anticholinergic burden with adverse outcomes such as falls is unclear. This study aims to develop a prognostic model that predicts falls in older general practice patients, to assess the performance of several anticholinergic burden scales, and to quantify the added predictive value of anticholinergic symptoms in this context.

METHODS: Data from two cluster-randomized controlled trials investigating medication optimization in older general practice patients in Germany will be used. One trial (RIME, n = 1,197) will be used for the model development and the other trial (PRIMUM, n = 502) will be used to externally validate the model. A priori, candidate predictors will be selected based on a literature search, predictor availability, and clinical reasoning. Candidate predictors will include socio-demographics (e.g. age, sex), morbidity (e.g. single conditions), medication (e.g. polypharmacy, anticholinergic burden as defined by scales), and well-being (e.g. quality of life, physical function). A prognostic model including sociodemographic and lifestyle-related factors, as well as variables on morbidity, medication, health status, and well-being, will be developed, whereby the prognostic value of extending the model to include additional patient-reported symptoms will be also assessed. Logistic regression will be used for the binary outcome, which will be defined as "no falls" vs. "≥1 fall" within six months of baseline, as reported in patient interviews.

DISCUSSION: As the ability of different anticholinergic burden scales to predict falls in older patients is unclear, this study may provide insights into their relative importance as well as into the overall contribution of anticholinergic symptoms and other patient characteristics. The results may support general practitioners in their clinical decision-making and in prescribing fewer medications with anticholinergic properties.







**Keywords:** polypharmacy; general practice; accidental falls [MeSH]; aged [MesH]; anticholinergic burden; multimorbidity [MeSH]; prediction model; prognosis research







### Falls in young adults: the effect of sex, physical activity, and prescription medications

Cho HY, Heijnen MJH, Craig BA, Rietdyk S. PLoS One 2021; 16(4): e0250360.

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DOI 10.1371/journal.pone.0250360 PMID unavailable

### Abstract

Falls are a major public health issue not only for older adults but also young adults, with fallrelated injuries occurring more frequently in adult females than males. However, the sex differences in the frequency and circumstances of falls in young adults are understudied. This research quantified the frequency and circumstances of falls as a function of sex, physical activity, and prescription medications in young adults. For 16 weeks, young adult participants  $(N = 325; 89 \text{ males}; 19.9 \pm 1.1 \text{ years})$  responded to a daily email asking if they had slipped, tripped, or fallen in the past 24 hours. Falls and fall-related injuries were not uncommon in young adults: 48% fell at least once, 25% fell more than once, and 10% reported an injury. The most common activities at the time of the fall for females were walking (44%) and sports (33%), and for males, sports (49%) and walking (37%). A zero-inflated Poisson model revealed that higher number of falls were associated with the following: higher levels of physical activity (p = 0.025), higher numbers of medications (p < 0.0001), and being male (p = 0.025) 0.008). Regarding circumstances of falling, females were more likely to be talking to a friend at the time of the fall (OR (95% CI): 0.35 (0.14-0.73); p = 0.01). For slips and trips without a fall, males and females reported the same number of slips (OR (95% CI): 0.885 (0.638-1.227) p = 0.46), but females reported more trips (OR (95% CI): 0.45 (0.30-0.67); p<0.01). Only females reported serious injuries such as concussion and fracture. In conclusion, the rate of falls in young adults was affected by physical activity levels, number of medications, and sex. Quantifying and understanding these differences leads to increased knowledge of falls across the lifespan and is instrumental in developing interventions to prevent falls.







### Risk of electrolyte disorders, syncope and falls in patients taking thiazide diuretics: results of a cross-sectional study

Ravioli S, Bahmad S, Funk GC, Schwarz C, Exadaktylos A, Lindner G. Am. J. Med. 2021; ePub(ePub): ePub.

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DOI 10.1016/j.amjmed.2021.04.007 PMID unavailable

### Abstract

BACKGROUND: Thiazide diuretics are a mainstay in the management of hypertension and often associated with dyselectrolytemias. We investigated prevalence of and risk factors for hyponatremia and hypokalemia in thiazide users, substance-specific differences and the association of thiazides with syncope and falls.

METHODS: In this cross-sectional analysis all patients admitted to an interdisciplinary emergency department in Switzerland between January 1(st) 2017 and December 31(st) 2018 with measurements of serum sodium and potassium were included. Data regarding serum electrolytes and creatinine were analyzed to classify for dysnatremias, dyskalemias and acute kidney injury. Chart reviews were performed to screen for syncope or falls.

RESULTS: A total of 1,604 patients (7.9%) took thiazides. Acute kidney injury was significantly more common in thiazide users (22.1 vs. 7%, p<0.0001). Hyponatremia (22.1 vs. 9.8%, p<0.0001) and hypokalemia (19 vs. 11%, p<0.0001) were more frequent with thiazides. Thiazide use together with higher age and female sex were independent predictors of hyponatremia and hypokalemia. A dose-dependent effect was found for electrolyte disorders and there was a variance in risk between the investigated substances with chlorthalidone bearing the highest and hydrochlorothiazide the lowest risk. Patients taking thiazide diuretics had significantly more episodes of syncope and falls.

CONCLUSIONS: Thiazide use is a clear risk factor for hyponatremia and hypokalemia. The effect appears to be dose-dependent and highly variable depending on the substance. Syncope and falls seem to be causally related to thiazide use. Especially in elderly, female and patients prone to falls, the use of thiazide diuretics should therefore be thoroughly questioned.

Language: en

### Keywords

falls; syncope; electrolyte disorders; hypokalemia; hyponatremia; Thiazide diuretics







### Cardiovascular outcomes and rates of fractures and falls among patients with brandname versus generic L-thyroxine use

Brito JP, Ross JS, Deng Y, Sangaralingham L, Graham DJ, Qiang Y, Wang Z, Yao X, Zhao L, Smallridge RC, Bernet V, Shah ND, Lipska KJ. Endocrine 2021; ePub(ePub): ePub.

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DOI 10.1007/s12020-021-02779-x PMID unavailable

### Abstract

PURPOSE: To compare cardiovascular outcomes and rates of fractures and falls among patients with persistent brand-name versus generic L-thyroxine use.

METHODS: Retrospective, 1:1 propensity-matched longitudinal study using a national administrative claims database to examine adults ( $\geq$ 18 years) who initiated either brand or generic L-thyroxine between 2008 and 2018, censored at switch or discontinuation of L-thyroxine formulation or disenrollment from the health plan. Main outcome measures included rates of hospitalization for atrial fibrillation, myocardial infarction, congestive heart failure, stroke, spine and hip fractures, and rate of falls in the outpatient or inpatient setting. Hospitalizations for pneumonia were used as a negative control.

RESULTS: 195,046 adults initiated treatment with L-thyroxine between 2008 and 2017: 87% generic and 13% brand formulations. They were mostly women (76%), young (94.6% under age 65), white (66%), and 47% had baseline thyroid stimulating hormone levels between 4.5 and 9.9 mIU/L. Among 35,667 propensity-matched patients, there were no significant differences between patients treated with brand versus generic L-thyroxine in atrial fibrillation (HR 0.96, 0.58-1.60), myocardial infarction (HR 0.66, 0.39-1.14), congestive heart failure (HR 1.30, 0.78-2.16), stroke (0.72, 0.49-1.06), spine (HR 0.87, 0.38-1.99) and hip fractures (HR 0.86, 0.26-2.82), or fall outcomes (HR 1.02, 0.14-7.32). Hospitalization rates for pneumonia (used as negative control) did not differ between groups (HR 0.85, 0.61-1.19). There were no interactions between brand versus generic L-thyroxine, these outcomes, and thyroid cancer, age, or L-thyroxine dose subgroups.

CONCLUSIONS: We found no significant differences in cardiovascular outcomes and rates of falls and fractures for patients who filled brand versus generic L-thyroxine.

Language: en

### Keywords

Brand; Generic; Hypothyroidism; Levothyroxine







### The effects of vitamin D supplementation on types of falls

Wanigatunga AA, Sternberg AL, Blackford AL, Cai Y, Mitchell CM, Roth DL, Miller ER, Szanton SL, Juraschek SP, Michos ED, Schrack JA, Appel LJ. J. Am. Geriatr. Soc. 2021; ePub(ePub): ePub.

(Copyright © 2021, John Wiley and Sons)

DOI 10.1111/jgs.17290 PMID unavailable

### Abstract

BACKGROUND/OBJECTIVES: To assess whether vitamin D supplementation prevents specific fall subtypes and sequelae (e.g., fracture).

DESIGN: Secondary analyses of STURDY (Study to Understand Fall Reduction and Vitamin D in You)-a response-adaptive, randomized clinical trial. SETTING: Two community-based research units. PARTICIPANTS: Six hundred and eighty-eight participants ≥70 years old with elevated fall risk and baseline serum 25-hydroxyvitamin D levels of 10-29 ng/ml. INTERVENTION: 200 IU/day (control), 1000 IU/day, 2000 IU/day, or 4000 IU/day of vitamin D3. MEASUREMENTS: Outcomes included repeat falls and falls that were consequential, were injurious, resulted in emergency care, resulted in fracture, and occurred either indoors or outdoors.

RESULTS: After adjustment for multiple comparisons, the risk of fall-related fracture was greater in the pooled higher doses ( $\geq 1000 \text{ IU/day}$ ) group compared with the control (hazard ratio [HR] = 2.66; 95% confidence interval [CI]:1.18-6.00). Although not statistically significant after multiple comparisons adjustment, time to first outdoor fall appeared to differ between the four dose groups (unadjusted p for overall difference = 0.013; adjusted p = 0.222), with risk of a first-time outdoor fall 39% lower in the 1000 IU/day group (HR = 0.61; 95% CI: 0.38-0.97; unadjusted p = 0.036; adjusted p = 0.222) and 40% lower in the 2000 IU/day group (HR = 0.60; 95%CI 0.38-0.97; p = 0.037; adjusted p = 0.222), each versus control.

CONCLUSION: Vitamin D supplementation doses  $\geq 1000$  IU/day might have differential effects on fall risk based on fall location and fracture risk, with the most robust finding that vitamin D doses between 1000 and 4000 IU/day might increase the risk of first time falls with fractures. Replication is warranted, given the possibility of type 1 error.

Language: en

### Keywords

fall reoccurrence; indoor; outdoor; randomized clinical trial; vitamin D dose







### Effects of bedtime dosing with suvorexant and zolpidem on balance and psychomotor performance in healthy elderly participants during the night and in the morning

Bland H, Li X, Mangin E, Yee KL, Lines C, Herring WJ, Gillespie G. J. Clin. Psychopharmacol. 2021; 41(4): 414-420.

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### Abstract

PURPOSE/BACKGROUND: This study was designed as an early assessment of the safety of the orexin receptor antagonist suvorexant, but also included exploratory assessments of balance and psychomotor performance that are the focus of this report.

METHODS/PROCEDURES: This was a double-blind, randomized, 3-period, crossover, phase 1 study. Balance and psychomotor performance were evaluated during the night in 12 healthy elderly participants after bedtime administration of suvorexant 30 mg (a supratherapeutic dose), the GABAergic agonist zolpidem 5 mg (the recommended dose in the elderly), or placebo. Balance (body sway measured by platform stability) and psychomotor performance (measured by choice reaction time) were assessed predose and at 1.5, 4, and 8 hours postdose in each period. Memory (measured by word recall) was assessed predose and at 4 hours postdose.

FINDINGS/RESULTS: At 1.5 hours after nighttime administration of each drug (the approximate time of their anticipated maximal plasma concentrations), both zolpidem and suvorexant increased body sway versus placebo, with a greater increase for zolpidem than suvorexant. Suvorexant increased choice reaction time compared with placebo or zolpidem at 1.5 hours. There were no treatment differences on body sway or choice reaction time at 4 or 8 hours, or on word recall at 4 hours. IMPLICATIONS/CONCLUSIONS: These exploratory data suggest that a 30-mg dose of suvorexant (supratherapeutic) and a 5-mg dose of zolpidem (recommended dose in the elderly) impaired balance at 1.5 hours in healthy elderly people, with potentially less impairment for suvorexant relative to zolpidem, but no treatment differences on body sway or psychomotor performance at 4 and 8 hours. Because of their exploratory nature, these findings and their clinical relevance, if any, require confirmation in a prospective study.







### Relationship between number of medications and incidence of falls or bone fracture in elderly patients with non-valvular atrial fibrillation: Shinken database analysis

Fujisawa T, Arita T, Suzuki S, Yagi N, Otsuka T, Kishi M, Kano H, Matsuno S, Kato Y, Uejima T, Oikawa Y, Matsuhama M, Iida M, Yajima J, Yamashita T. Geriatr. Gerontol. Int. 2021; ePub(ePub): ePub.

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### Abstract

AIM: Polypharmacy is known to be a risk factor for falls or bone fracture (F/F) in elderly patients. However, this relationship is not fully described in patients with non-valvular atrial fibrillation (NVAF), for which F/F may lead to serious clinical outcomes, including major bleeding.

METHODS: We analyzed 509 elderly (aged  $\geq$ 75 years) patients with NVAF who had recently visited a hospital specializing in cardiology, of which 272 patients had paroxysmal atrial fibrillation (PAF) and 237 had persistent/permanent atrial fibrillation (PeAF). Patients were divided into four groups according to the number of medications:  $\leq$ 3, 4-6, 7-9, and  $\geq$ 10. The relationship between the number of medications and incidence rate of F/F in AF patients was analyzed. In addition, this relationship was analyzed in patients with each AF type.

RESULTS: Cumulative incidence of F/F at 3 years in the respective categories was 3.7%, 5.4%, 4.3% and 5.7% for PAF, and 5.2%, 7.5%, 7.8% and 25.0% for PeAF (log-rank test, P = 0.930 and 0.003, respectively). In a multivariable model, patients with  $\geq$ 10 medications showed a significantly higher risk for F/F compared with those with  $\leq$ 3 medications as reference only in PeAF (adjusted hazard ratio 4.82, 95%CI 1.42-16.33), without significant interaction (P = 0.081).

CONCLUSIONS: Elderly NVAF patients using  $\geq 10$  medications showed a higher risk for F/F. In subgroup analysis, this association was observed only in patients with PeAF, although there was no significant interaction between number of medications and AF type. Geriatr Gerontol Int 2021; ••: ••-••.

Language: en

### Keywords

elderly; polypharmacy; atrial fibrillation; accidental falls; bone fracture







### Association of polypharmacy with falls among older Chinese inpatients: a nationwide cohort study

Zhang XM, Jiao J, Guo N, Bo HX, Xu T, Wu XJ. Geriatr. Gerontol. Int. 2021; ePub(ePub): ePub.

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### Abstract

AIM: Polypharmacy is prevalent among older adults and has been mainly reported to be associated with falls among community-dwelling or nursing home residents. Our study aimed to investigate the relationship between polypharmacy and falls among older Chinese hospitalized patients.

METHODS: A nationwide prospective cohort study included 9062 participants in six hospitals from China aged  $\geq 65$  years, with a 1-year follow-up period. Baseline polypharmacy and other health-related variables were collected when older inpatients were recruited on hospital admission. Polypharmacy was defined as patients who have taken five medications or more. Well-trained nurses assessed falls by telephone at follow up. We used multivariate logistic regression analysis to examine the association between polypharmacy and the risk of falls based on cross-sectional analyses and longitudinal analyses.

RESULTS: Of 9062 participants, the mean age was 72.42 years (SD= 5.69), and 5228 (57.69%) were men. After fully adjusted for age, sex, education, depression, cognitive impairment, low handgrip strength, frailty, various hospitals, and nutritional status, the cross-sectional and longitudinal analyses showed that inpatients with polypharmacy had an increased risk of falls (OR 1.37, 95%CI 1.17-1.56 for the cross-sectional association; OR 1.43, 95% CI 1.01-2.03 for the longitudinal association, respectively), compared with those without polypharmacy. In addition, subgroup analyses of the association between polypharmacy and 1-year falls, or history of falls was unchanged.

CONCLUSIONS: Polypharmacy was prevalent among older Chinese hospitalized patients and was an independent risk factor of 1-year falls, suggesting that clinicians should make a comprehensive assessment of medications, and deprescribing strategies should be implemented to reduce unnecessary medications for decreasing the rate of falls. Geriatr Gerontol Int 2021; ••: ••-••.

Language: en

### Keywords

polypharmacy; falls; older adults; hospital; inpatients







### Polypharmacy: an unignorable factor for fall injury in the elderly

Sugitani K, Ito H. Am. J. Med. 2021; 134(8): e474.

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### Abstract

We read with great interest the article by Sherer et al entitled "Atrial Fibrillation and the Risk of Subsequent Fracture." This study showed the association between atrial fibrillation and increased risk of incident fracture. The relationship between atrial fibrillation and subsequent fracture has been inconclusive, and this study will add insights into that relationship. However, there is a concern that should be pointed out.

Although this article referred to some potential confounding factors such as decreased brain perfusion, reduced bone density, and heart failure, it did not refer to the effect of polypharmacy. About 70%-80% of patients with atrial fibrillation have other comorbidities such as hypertension and diabetes mellitus.

Due to these multimorbidities, polypharmacy is a major long-time issue facing patients with atrial fibrillation.

Polypharmacy is an established risk factor for falls in the elderly. Medications such as antihypertensive agents and diuretics, in particular, have been regarded as fall risk-increasing drugs. Thus, the effect of polypharmacy cannot be ignored...







# Risk of fall-related injury and all-cause hospitalization of select concomitant central nervous system medication prescribing in older adult persistent opioid users: a case-time-control analysis

Moran KM, Calip GS, Lee TA, Koronkowski MJ, Lau DT, Schumock GT. Pharmacotherapy 2021; ePub(ePub): ePub.

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### Abstract

BACKGROUND: Concomitant use of central nervous system (CNS) medications frequently occurs in older adults with persistent opioid use. The risks of adverse outcomes associated with combinations of opioids, sedative-hypnotics, or skeletal muscle relaxants have not been sufficiently described in this population.

OBJECTIVE: To compare the overall and incremental risk of 1) fall-related injury and 2) allcause hospitalization associated with sedative hypnotics and skeletal muscle relaxants among older persistent opioid users.

METHODS: A case-time-control study was conducted using administrative claims of adults ages  $\geq 66$  years with a history of persistent ( $\geq 90$  days) opioid use. Cases included those with first 1) emergency department, hospital, or outpatient visit for a fall-related injury, or 2) all-cause hospitalization. Exposure to CNS medications prior to the case event versus earlier periods, and the risk associated with CNS drug class combinations and sequence of use, was estimated using conditional logistic regression, adjusted for time trends and time-varying covariates.

RESULTS: Among 140,101 older persistent opioid users, 20,723 experienced fall-related injury and 39,444 were hospitalized during follow-up. Skeletal muscle relaxant use was associated with an increased risk of fall-related injury (Odds ratio [OR] 1.28) and all-cause hospitalization (OR 1.11). Statistically significant associations were observed for the joint effects of interactions involving skeletal muscle relaxants on fall-related injury (with opioid: OR 1.25; with sedative hypnotic: OR 1.24), and interactions involving opioids on all-cause hospitalization (with sedative hypnotic: OR 1.10; with skeletal muscle relaxant: OR 1.17). The addition of a skeletal muscle relaxant to an opioid regimen was associated with a 25% increased risk of fall-related injury. Additions of other CNS medications did not have apparent incremental effects on the risk of all-cause hospitalization.

CONCLUSION: The excess risks of fall-related injury and hospitalization associated with various combinations of CNS medications among older persistent opioid users should be considered in therapeutic decision-making. Further research is needed to confirm these findings.

Language: en

### Keywords

Accidental Falls; Drug Interactions; Analgesics; Opioid; Adverse Drug Events; Hypnotics and Sedatives; Older Adults; Polypharmacy







## Medication review in preventing older adults' fall-related injury: a systematic review & meta-analysis

Ming Y, Zecevic AA, Hunter SW, Miao W, Tirona RG. Can. Geriatr. J. 2021; 24(3): 237-250.

(Copyright © 2021, Canadian Geriatrics Society)

DOI 10.5770/cgj.24.478 PMID 34484506

### Abstract

BACKGROUND: Medication review is essential in managing adverse drug reactions and improving drug safety in older adults. This systematic review evaluated medication review's role as a single intervention or combined with other interventions in preventing fall-related injuries in older adults.

METHODS: Electronic databases search was conducted in PubMed, EMBASE, Scopus, and CINAHL. Two reviewers screened titles and abstracts, reviewed full texts, and performed data extraction and risk of bias assessment. Meta-analyses were conducted on studies with similar participants, interventions, outcomes or settings.

RESULTS: Fourteen randomized, controlled studies were included. The pooled results indicated that medication review as a stand-alone intervention was effective in preventing fall-related injuries in community-dwelling older adults (Risk Difference [RD] = -0.06, 95% CI: [-0.11, -0.00], I(2) = 61%, p =.04). Medication review also had a positive impact on decreasing the risk of fall-related fractures (RD = -0.02, 95% CI: [-0.04, -0.01], I(2) = 0%, p =.01).

DISCUSSION: This systematic review and meta-analysis has demonstrated that medication review is effective in preventing fall-related injuries in general, and fractures specifically, in community-dwelling older adults. Future investigations focusing on the process of performing medication review will further inform fall-related injury prevention for older adults.

Language: en

### Keywords

prevention; falls; older adults; fall-related injuries; medication review







### Does the association of therapeutic exercise and supplementation with sucrosomial magnesium improve posture and balance and prevent the risk of new falls?

Scaturro D, Vitagliani F, Terrana P, Tomasello S, Camarda L, Letizia Mauro G. Aging Clin. Exp. Res. 2021; ePub(ePub): ePub.

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### Abstract

BACKGROUND: Fracture of the proximal femur is the most feared complication of osteoporosis. Given the numerous physiological functions that magnesium performs in our body, in the literature there is a correlation between osteoporosis and low serum levels of magnesium.

AIM: Evaluate the incidence of hypomagnesemia in patients with lateral fragility fracture of the proximal femur, the possible correlation between serum magnesium levels and fractures, and the effectiveness of supplementing Sucrosomial(®) magnesium associated with therapeutic exercise on the outcome of these patients.

METHODS: We divided the study into two parts. In the first part, we assessed the preoperative incidence of hypomagnesemia in patients using a blood test. In the second part, patients with hypomagnesemia were divided, in the post-operative period, into two groups, who received, respectively, only therapeutic exercise or oral supplementation with sucrosomial magnesium associated with therapeutic exercise.

RESULTS: Half of the patients with fragility femoral fracture had hypomagnesemia, with a higher incidence of the subclinical form. From the comparison between the two groups, the T1 treatment group showed a significant improvement in blood levels of magnesium  $(2.11 \pm 0.15 \text{ vs. } 1.94 \pm 0.11; \text{ p} < 0.05)$ , on the NRS scale  $(5.7 \pm 0.81 \text{ vs. } 6.6 \pm 1.18; \text{ p} < 0.05)$ , the Tinetti scale  $(17.3 \pm 1.15 \text{ vs. } 15.2 \pm 2.98; \text{ p} < 0.05)$  and the SarQoL questionnaire  $(47.3 \pm 5.21 \text{ vs. } 44.9 \pm 5.54; \text{ p} < 0.05)$ .

CONCLUSIONS: More attention would be needed in the diagnosis and correction of subclinical hypomagnesemia and not just the simple and clinically evident one, including hypomagnesemia among the modifiable risk factors for osteoporosis.

Language: en

### Keywords

Rehabilitation; Balance; Magnesium deficiency; Posture; Senile osteoporosis







### Use of antipsychotic drugs and cholinesterase inhibitors and risk of falls and fractures: self-controlled case series

Wang GHM, Man KKC, Chang WH, Liao TC, Lai ECC. BMJ 2021; 374: n1925.

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#### Abstract

OBJECTIVE: To evaluate the association between the use of antipsychotic drugs and cholinesterase inhibitors and the risk of falls and fractures in elderly patients with major neurocognitive disorders.

DESIGN: Self-controlled case series. SETTING: Taiwan's National Health Insurance Database. PARTICIPANTS: 15 278 adults, aged ≥65, with newly prescribed antipsychotic drugs and cholinesterase inhibitors, who had an incident fall or fracture between 2006 and 2017. Prescription records of cholinesterase inhibitors confirmed the diagnosis of major neurocognitive disorders; all use of cholinesterase inhibitors was reviewed by experts. MAIN OUTCOME MEASURES: Conditional Poisson regression was used to derive incidence rate ratios and 95% confidence intervals for evaluating the risk of falls and fractures for different treatment periods: use of cholinesterase inhibitors alone, antipsychotic drugs alone, and a combination of cholinesterase inhibitors and antipsychotic drugs, compared with the nontreatment period in the same individual. A 14 day pretreatment period was defined before starting the study drugs because of concerns about confounding by indication.

RESULTS: The incidence of falls and fractures per 100 person years was 8.30 (95% confidence interval 8.14 to 8.46) for the non-treatment period, 52.35 (48.46 to 56.47) for the pretreatment period, and 10.55 (9.98 to 11.14), 10.34 (9.80 to 10.89), and 9.41 (8.98 to 9.86) for use of a combination of cholinesterase inhibitors and antipsychotic drugs, antipsychotic drugs alone, and cholinesterase inhibitors alone, respectively. Compared with the non-treatment period, the highest risk of falls and fractures was during the pretreatment period (adjusted incidence rate ratio 6.17, 95% confidence interval 5.69 to 6.69), followed by treatment with the combination of cholinesterase inhibitors and antipsychotic drugs (1.35, 1.26 to 1.45), antipsychotic drugs alone (1.33, 1.24 to 1.43), and cholinesterase inhibitors alone (1.17, 1.10 to 1.24).

CONCLUSIONS: The incidence of falls and fractures was high in the pretreatment period, suggesting that factors other than the study drugs, such as underlying diseases, should be taken into consideration when evaluating the association between the risk of falls and fractures and use of cholinesterase inhibitors and antipsychotic drugs. The treatment periods were also associated with a higher risk of falls and fractures compared with the non-treatment period, although the magnitude was much lower than during the pretreatment period. Strategies for prevention and close monitoring of the risk of falls are still necessary until patients regain a more stable physical and mental state.





