Inclusion of medication-related fall risk in fall risk assessment tool in geriatric care units

Jana Michalcova1,2*, Karel Vasut1, Marja Airaksinen2 and Katarina Bielakova3

Abstract

Background: Falls are common undesirable events for older adults in institutions. Even though the patient’s fall risk may be scored on admission, the medication-induced fall risk may be ignored. This study developed a preliminary categorization of fall-risk-increasing drugs (FRIDs) to be added as a risk factor to the existing fall risk assessment tool routinely used in geriatric care units.

Methods: Medication use data of older adults who had experienced at least one fall during a hospital ward or a nursing home stay within a 2-year study period were retrospectively collected from patient records. Medicines used were classified into three risk categories (high, moderate and none) according to the fall risk information in statutory summaries of product characteristics (SmPCs). The fall risk categorization incorporated the relative frequency of such adverse drug effects (ADEs) in SmPCs that were known to be connected to fall risk (sedation, orthostatic hypotension, syncope, dizziness, drowsiness, changes in blood pressure or impaired balance). Also, distribution of fall risk scores assessed on admission without considering medications was counted.

Results: The fall-experienced patients (n = 188, 128 from the hospital and 60 from nursing home records) used altogether 1748 medicaments, including 216 different active substances. Of the active substances, 102 (47%) were categorized as high risk (category A) for increasing fall risk. Fall-experienced patients (n = 188) received a mean of 3.8 category A medicines (n = 710), 53% (n = 375) of which affected the nervous and 40% (n = 281) the cardiovascular system. Without considering medication-related fall risk, 53% (n = 100) of the patients were scored having a high fall risk (3 or 4 risk scores).

Conclusion: It was possible to develop a preliminary categorization of FRIDs basing on their adverse drug effect profile in SmPCs and frequency of use in older patients who had experienced at least one documented fall in a geriatric care unit. Even though more than half of the fall-experienced study participants had high fall risk scores on admission, their fall risk might have been underestimated as use of high fall risk medicines was common, even concomitant use. Further studies are needed to develop the FRID categorization and assess its impact on fall risk.

Keywords: Older adults, Fall risk, Medication, Hospital, Nursing home, Preventive risk management
Background

Falls constitute a leading preventable cause of geriatric injuries and hospitalization, prolonged recovery times and deaths [1, 2]. More than a third of older adults fall each year, meaning worldwide a high number of patients [3]. Fall-related injuries can be serious, occurring approximately in 10% of all falls, and conserving an urgent hospitalization [3, 4]. Furthermore, falls decrease self-sufficiency and quality of life among older adults, because falls can result in fear of falling, loss of confidence, mobility and ability to live independently [5].

Fall risk is a multifactorial problem associated with numerous intrinsic and extrinsic factors [6, 7]. Intrinsic factors are related to ageing, including age-related changes to the pharmacokinetic and pharmacodynamic effects of pharmacotherapies. Age-related pharmacokinetic changes are represented by drug absorption, distribution, metabolism and elimination route. The drug absorption is usually decreased due to changes in the gastrointestinal tract, e.g., reduced gastric secretion, loss of mucosal intestinal surface and decreased blood flow in splanchnic area. The drug distribution is affected by many factors, e.g., increase in fat compartment, decrease in total body water, muscle mass and serum albumin level. The distribution volume of water soluble drugs is decreased leading to their potential toxicity, while the distribution volume of lipid soluble drugs is increased leading to prolongation of elimination half-life and accumulation of the drug in fatty tissues. The drug metabolism is influenced by decreased hepatic blood flow and low activity of liver enzymes. The elimination route is limited due to reduction in renal clearance [7, 8]. Pharmacodynamic changes involve altered sensitivity to many pharmacological agents, increased sensitivity in psychotropic or cardiovascular drugs, in contrast with decreased capacity to respond to physiological challenges and side effects of the drug therapy, e.g., orthostatic hypotension [1, 9].

Extrinsic factors include fall risks related to the environment where individuals live, e.g., how medicines are taken at home [6, 10]. Prescribed medication is an important and potentially underappreciated contributor to falls [11, 12]. The older adults are susceptible to polypharmacy and higher risk of falls [13]. Polypharmacy can increase the risk of medication-related falls, especially when at least one established fall risk-increasing drug is part of the patient's daily regimen [14]. A leading mechanism for increased risk can be sedation which slows reaction time, orthostatic hypotension, syncope, dizziness, drowsiness, and blood pressure change or impaired balance [15]. Normally, long-acting medications pose a higher risk, but the metabolism and half-life of otherwise short-acting drugs can be also prolonged in older adults [16, 17]. Previous studies have presented various methods reducing fall risks in older adults, such as supplementation of vitamin D and calcium, cataract surgery, hip protectors, modification of hazard environment and adjustment of medications [18, 19]. In addition, stability of the human body is a crucial factor for reducing falls [20]. Recommended actions to improve stability include exercise programs focusing on balance and muscle strength [21]. There is a good evidence for reducing medication-induced falls. In psychotropics, the fall risk can be reduced by prospective management of adverse effects such as drowsiness, dizziness, slow reaction time and orthostatic hypotension [22, 23]. Drugs reducing blood pressure are associated with fall risk because of their hypotension effect. Thus, adjusting anti-hypertensive medication may reduce syncope and falls [24, 25]. The fall risk prevention with anticoagulants should focus on bleeding events such as a cerebral hemorrhage and associated falls [26]. Many drugs disturb vision and vestibular system, which exacerbate gait disturbance in older adults [27, 28].

In case of falls, reduced bone mineral density and osteoporosis can increase risk of fracture and more severe consequences [29].

Evidence on medication-related fall risks is not always integrated into multifactorial risk assessments which contribute to preventive programmes for reducing falls [30, 31]. Incorporating these risks could improve accuracy of existing tools routinely used in geriatric care units as many of the current workflows do not contain medication as a risk factor [32]. This study aimed to provide a better screen on falls in institutions by developing a preliminary categorization of fall-risk-increasing drugs (F RIDs) that could be added as a risk factor to the existing fall risk assessment tool routinely used in geriatric care units.

Methods

Patient data

The patient data used in this study were retrospectively derived from two different types of health care institutions, i.e., a hospital and a nursing home in Brno, Czech Republic. Medication data on all patients who had fallen at least once during their stay at a health care institution (hospital or nursing home) within a 2-year observational period were derived from patient records. The falls are defined by World Health Organization as an event which results in a person coming to rest inadvertently on the ground or floor or other lower level [31]. The falls during a stay at a health care institution were documented as undesirable events in a protocol, which contained information about circumstances of the fall such as a description of fall, exact time and place, and consequences, e.g., severe injuries, bone fracture or head injury, bruises or bleeding risk. Descriptive and demographic information on patients (sex, age, length of stay, MMSE score and medication use) were collected from the patient records.
records. Inclusion criteria of the study participants were 1) age ≥ 60 years old, 2) evidence of at least one fall during their stay in a geriatric care unit, 3) evidence of fall documented by health care professionals (nurses, physicians). Exclusion criteria were 1) age < 60 years old, 2) absence of falls during their stay in a geriatric care unit, 3) no evidence of falls documented by health care professionals. The nursing home had less descriptive records of their residents, e.g., they missed a cognitive impairment scale.

Developing categorization of medicines increasing fall risk (FRIDs)
The medication-related fall risk was determined by categorizing all medicines patients used according to each medicine’s fall risk. The criteria for this categorization was derived from the statutory summaries of product characteristics (SmPCs) approved by authorities as part of marketing authorization within European Union countries [33]. The SmPC information of each medicine was systematically reviewed by two researchers (JM, KV) to derive the fall risk. We applied information on a direct connection between the fall risk and adverse drug effects (ADEs) disturbing the patient’s balance as presented in SmPCs. This information was used to create an A, B, C medication-related fall risk categorization. Usually the mechanism leading to medication-related fall risk is one or more of the following adverse drug effects: sedation, orthostatic hypotension, syncope, dizziness, drowsiness, changes in blood pressure or impaired balance [34, 35]. All these adverse drug effects have a negative influence on a patient’s balance, which can then predispose the patient to falls [36].

Adverse drug effects posing fall risk are classified in the SmPC as very common (≥1/10), common (≥ 1/100), uncommon (≥ 1/1000), rare (≥ 1/10000) and very rare (<1/10000) (Table 1). Medicines with at least one of the above-mentioned adverse drug effect frequencies of “very common” or “common” in the SmPC were categorized as high fall risk medicines (category A). Similarly, the medicines with an adverse drug effect frequency “uncommon” were categorized as moderate fall risk medicines (risk level B) and those with rare or very rare frequency as no fall risk medicines (risk level C). The high-risk category A medicines are considered as a predisposition factor to fall, because the occurrence of adverse drug effects connected to falls is documented by at least one patient per each 100 patients using the same active substance. The risk information provided in the SmPC of the brand product used by the patients involved in the study was validated by comparing the information with the SmPC information of another similar product on the market.

Frequency of use of high fall risk medicines in study participants with a fall history
The second phase of the study focused on counting the frequency of use of high fall risk medicines in study participants with a fall history in institutions. This phase made use of the existing routine practice at the time of the study of assessing and scoring all patients for fall risk by nurses in the routine admission procedure. Both institutions used the same set of 4 risk items other than medications to estimate fall risk (Table 2). The original Morse Fall Score [37] had been shortened to a time-saving procedure of 4 items suitable for clinical practice. Each fall risk item yielded 1 point and they assessed 1) history of falls, 2) mental condition, 3) physical condition, and 4) occurrence of dizziness or drowsiness in older patients. The estimation was based on patient interviews on admission or notes from patient records. Direct questions to the patient were dependent on the patient’s health condition. As this fall risk estimation did not consider patient’s medication as a contributor to the fall risk, the patient data on medication use were retrospectively collected from the patient records by the researcher (JM). All the medicines were classified into three risk categories (high, moderate and none) using the new categorization based on the fall risk information in the SmPCs. For the descriptive feasibility testing, the medication data of the patients in the hospital and nursing home were combined to provide the widest possible coverage of medicines used by older adults in institutions.

Table 1 Fall risk level criteria: categorization according to information derived from the summaries of product characteristics (SmPC) on the frequency of adverse drug effects (ADEs) contributing to fall risk (sedation, orthostatic hypotension, syncope, dizziness, drowsiness, changes in blood pressure or impaired balance).

| Frequency of ADEs | Number of patients experiencing ADEs | Fall risk level |
|-------------------|--------------------------------------|----------------|
| Very common       | ≥ 1/10                               | A              |
| Common            | ≥ 1/100 to < 1/10                    | A              |
| Uncommon          | ≥ 1/1000 to < 1/100                  | B              |
| Rare              | ≥ 1/10000 to < 1/10000               | C              |
| Very rare         | < 1/10000                            | C              |
Statistical analysis

Descriptive statistics were used in both study phases to categorize active substances according to their fall risk, and to test the categorizations with a retrospective sample of patients from a secondary care hospital and a nursing home. All patients were grouped together for the analysis. Data were processed in Microsoft Excel, version 2016. A pivot table was created to analyze worksheet data. Descriptive statistics were used for patient data to count metric items such as frequencies, means, ranges, and standard deviations. The categorization of medicines according to their fall risk used ATC codes, specified in levels of anatomical main group, therapeutic subgroup, and pharmacological subgroup [38]. The commonly used active substances in the high fall risk category A were processed from the retrospective patient data as the frequency of use.

Results

Study participants

In total 188 fall-experienced older patients were retrospectively drawn from the patient registers of both institutions included in this study covering the 2-year period from January 2016 to December 2017 (Table 3). Of the patients, 128 (68%) were from the geriatric department of a secondary care hospital and 60 (32%) from a nursing home. Of them, 103 were females and 85 males with the mean age of 79 years (range: 60–97 years, standard deviation ±18.5). They used on average 9.3 medicaments (range: 2–17, standard deviation ±7.5) during a stay in a health care institution. The mean length of stay of the study patients in the secondary care hospital (n = 128) was 15.8 days (range: 1–56 days, standard deviation ±27.5). The most common causes of hospitalization were cardiovascular problems, and/or respiratory and urogenital tract infections. The half (52%) of the patients had at least a mild cognitive impairment (≤ 23 points), the mean score in the Mini Mental State Exam (MMSE) being 21.7 points (range: 5–30 points, standard deviation ±12.5). The stay for nursing home residents (n = 60) was permanent. Data about their cognitive function was not available. They suffered from many chronic diseases (cardiac, neurologic) and used chronic long-term medications.

Table 3 Characteristics of the participants from two health care institutions included in the study (n = 188, of which hospital inpatients, n = 128; nursing home residents, n = 60)

| Characteristics                      | Hospital | Nursing home | Total |
|---------------------------------------|----------|--------------|-------|
| Sex n (%)                             | Male     | Female       |       |
|                                       | 67 (52)  | 61 (48)      | 128 (100) |
|                                       | 18 (30)  | 42 (70)      | 60 (50)  |
| Age, years, mean (range)              | 80 (60–97) | 77 (63–95) | 79 (60–97) |
| MMSE, mean (range)                    | 21.7 (5–30) | unknown     | –      |
| Length of stay, days, mean (range)    | 15.8 (1–56) | permanent   | –      |
| Number of drugs in use, mean (range)  | 10.0 (3–17) | 7.8 (2–15) | 9.3 (2–17) |
for the nervous system (53%, \( n = 375 \)) and the cardiovascular system (40%, \( n = 281 \)) (Fig. 1). The nervous system medicines in use were mainly psychotropic medications (73% of the medicines in use in this category), while analgesics (16%), antiepileptics (8%) and antiparkinson drugs (3%) represented a minority. Psychotropic medications (\( n = 274 \)) consisted of 1) psycholeptics (\( n = 179 \), representing 65% of the medicines in this category) such as antipsychotics (\( n = 109 \), 40%), anxiolytics (\( n = 55 \), 20%), hypnotics and sedatives (\( n = 15 \), 5%), and 2) psychopathics (\( n = 95 \), representing 35% of the medicines in this category) such as antidepressants (\( n = 65 \), 24%) and anti-dementia drugs (\( n = 30 \), 11%). The high fall risk cardiovascular medications (\( n = 281 \)) included agents acting on the renin-angiotension system (RAS) (\( n = 92 \), 33% of the medicines in use in this category), beta blocking

![Table 4 Distribution of fall risk scores in fall-experienced patients (n = 188) using 4 fall risk items routinely assessed by nurses on admission (each item yielding 1 point, score range 0–4). Medications were not included in the assessment](image)

| Scores | Fall risk level | Number of patients | Proportion (%) of patients |
|--------|----------------|--------------------|----------------------------|
| 0      | No risk        | 5                  | 3                          |
| 1      | Low risk       | 17                 | 9                          |
| 2      | Medium risk    | 66                 | 35                         |
| 3      | High risk      | 69                 | 37                         |
| 4      | Full risk      | 31                 | 16                         |

![Fig. 1 Categorization of high fall-risk Category A medicines (n = 710) according to therapeutic group and number of users. The medicines are organized according to the ATC Classification [38]. Anatomical main group (1st level, dark grey), Therapeutic subgroup (2nd level, blue), Pharmacological subgroup (3rd level, grey)](image)
agents \( (n = 85, 30\%) \), cardiac therapy \( (n = 54, 19\%) \), calcium channel blockers \( (n = 27, 10\%) \) and other therapeutic subgroups \( (n = 23, 8\%) \).

Of the 216 active substances used by the patients, 102 (47\%) were classified in the high-risk category (fall risk level A), 29 (13\%) in the moderate risk category (fall risk level B) and 85 (40\%) in no risk category (fall risk level C). The leading mechanisms of ADEs consequing in high fall risk of most commonly used active ingredients by study participants are presented in Table 5. The most commonly used active ingredients in the high fall risk category A \( (n = 710) \) are presented in Table 6, included metoprolol \( (n = 49, \) beta blocking agents), tiapride \( (n = 36, \) antipsychotics), quetiapine \( (n = 24, \) antipsychotics), tramadol \( (n = 24, \) opioids), citalopram \( (n = 23, \) calcium channel blockers), melperone \( (n = 23, \) antipsychotics), bromazepam \( (n = 20, \) anxiolytics), digoxin \( (n = 18, \) cardiac glycosides), and ramipril \( (n = 18, \) ACE inhibitors).

Discussion
This study developed a preliminary categorization to identify medicines that may increase a fall risk in older adults in institutions, by using evidence derived from statutory medicines information and retrospective patient records. Our results indicate that numerous medicines have such an ADE profile that can lead to an increased fall risk and that the use of these high fall-risk medicines, even concomitant use of several active ingredients, is common in older adults during a hospital stay or while living in a nursing home. These findings suggest incorporating a medication-related fall risk indicator in a routine fall risk assessment on admission to geriatric care units. In long-term care units such as nursing homes, it may be useful to repeat the fall risk assessment regularly, e.g., at least once a year.

The high-fall risk categorization presented in this study considered also patient data which gives an idea of the prevalence of clinical use of different medicines. By this way it was possible to identify a few widely used medicines with a high fall risk. The top three clearly most commonly used high fall risk active substances were metoprolol (beta blocking agent), perindopril (ACE inhibitor) and tiapride (antipsychotic agent). Of the top ten active ingredients, 6/10 were psychotropics (3 of them antipsychotics) and 4/10 cardiovascular agents. Optimizing the use of these few medicines in terms of prospectively managing fall risk could make a remarkable change in the incidence of actual falls in geriatric care units.

Our findings concerning the “ranking” of drugs with a high fall risk are in line with previous research. The association with falls has been consistently reported for psychotropic and cardiovascular medicines [39–45]. The recent systematic reviews and meta-analyses (Seppala [43] and de Vries [44]) confirmed the association between certain drug classes and fall risk from psychotropics, i.e., antidepressants \( (OR = 1.57) \), antipsychotics \( (OR = 1.54) \), and benzodiazepines \( (OR = 1.42) \), and cardiovascular drugs, i.e., cardiac glycosides \( (OR = 1.6) \), antiarrhythmics \( (OR = 1.27) \), vasodilators \( (OR = 1.03) \), and ACE inhibitors \( (OR = 1.03) \). The increased fall risk is also evidenced in patients using opioids \( (OR = 1.61) \), antiepileptics \( (OR = 1.55) \), anti-Parkinson drugs \( (OR = 1.54) \), and NSAIDs \( (OR = 1.09) \).

Table 5 The most commonly used fall risk increasing drugs (Category A) having very common (≥1/10) or common (≥1/100) frequency of ADEs connected to fall risk according to statutory summary of product characteristics (SmPCs)

| Active ingredient (number of users) | Drug class (ATC) | Frequency of ADEs according to SmPCs |
|-----------------------------------|-----------------|--------------------------------------|
| Metoprolol \( (n = 49) \) | Beta blocking agents (C07A) | Common: dizziness, bradycardia |
| Perindopril \( (n = 38) \) | ACE inhibitors (C09A) | Common: dizziness, orthostatic hypotension, syncope |
| Tiapride \( (n = 36) \) | Antipsychotics (N05A) | Common: dizziness, drowsiness |
| Quetiapine \( (n = 24) \) | Antipsychotics (N05A) | Very common: dizziness, drowsiness |
| Tramadol \( (n = 24) \) | Opioids (N02A) | Very common: dizziness |
| Citalopram \( (n = 23) \) | Antidepressants (N06A) | Very common: drowsiness |
| Amlodipine \( (n = 23) \) | Calcium channel blockers (C08C) | Common: dizziness, drowsiness |
| Melperon \( (n = 23) \) | Antipsychotics (N05A) | Very common: sedation |
| Bromazepam \( (n = 20) \) | Anxiolytics (N05B) | Common: drowsiness, falls* |
| Digoxin \( (n = 18) \) | Cardiac glycosides (C01A) | Common: bradycardia, dizziness |
| Ramipril \( (n = 18) \) | ACE inhibitors (C09A) | Common: dizziness, orthostatic hypotension, syncope |

*unknown frequency of ADE
Table 6 The preliminary categorization of high fall risk medicines (Category A) basing on their adverse drug effect (ADE) profiles in statutory summaries of product characteristics (SmPCs) and frequency of use in older patients who had experienced at least one documented fall in a geriatric care unit (n = 188). The medicines are organized according to the ATC Classification [38].

| High fall risk (A) | ATC Code | ATC classification | Users of the medicines n (%) |
|--------------------|----------|--------------------|------------------------------|
| Metoprolol         | C07AB02  | Beta blocking agents | 49 (26.1)                   |
| Perindopril        | C09AA04  | ACE inhibitors      | 38 (20.2)                   |
| Tiapride           | N05AL03  | Antipsychotics      | 36 (19.1)                   |
| Quetiapine         | N05AH04  | Antipsychotics      | 24 (12.8)                   |
| Tramadol           | N02AX02  | Opioids             | 24 (12.8)                   |
| Citalopram         | N06AB04  | Antidepressants     | 23 (12.2)                   |
| Amlodipine         | C08CA01  | Calcium channel blockers | 23 (12.2)               |
| Melperone          | N05AD03  | Antipsychotics      | 23 (12.2)                   |
| Bromazepam         | N05BA08  | Anxiolytics         | 20 (10.6)                   |
| Ramipril           | C09AA04  | ACE inhibitors      | 18 (9.6)                    |
| Digoxin            | N05AA05  | Cardiac glycosides  | 18 (9.6)                    |
| Tramadol combination | N02AJ13 | Opioids             | 16 (8.5)                    |
| Bisoprolol         | C07AB07  | Beta blocking agents | 16 (8.5)                    |
| Zolpidem           | N05CF02  | Hypnotics and Sedatives | 15 (8.0)                  |
| Donepezil          | N06DA02  | Anti-dementia drugs | 14 (7.4)                    |
| Mirtazapine        | N06AX11  | Antidepressants     | 14 (7.4)                    |
| Amiodarone         | C01BD01  | Antiarrhythmics     | 14 (7.4)                    |
| Oxazepam           | N05BA04  | Anxiolytics         | 14 (7.4)                    |
| Tamsulosin         | G04CA02  | Urologicals         | 14 (7.4)                    |
| Memantine          | N06DX01  | Anti-dementia drugs | 12 (6.4)                    |
| Diazepam           | N05BA01  | Anxiolytics         | 11 (5.9)                    |
| Gabapentin         | N03AX12  | Antiepileptics      | 11 (5.9)                    |
| Trazodone          | N06AX05  | Antidepressants     | 10 (5.3)                    |
| Isosorbide mononitrate | C01DA14 | Vasodilatators      | 10 (5.3)                    |
| Clonazepam         | N03AE01  | Antiepileptics      | 10 (5.3)                    |
| Codein combination | N02AJ06  | Opioids             | 9 (4.8)                     |
| Risperidone        | N05AX08  | Antipsychotics      | 8 (4.3)                     |
| Losartan           | C09CA01  | AT II receptor blockers | 8 (4.3)                  |
| Sertraline         | N06AB06  | Antidepressants     | 7 (3.7)                     |
| Levodopa           | N04BA01  | Dopaminergic agents | 7 (3.7)                     |
| Aminophylline      | R03DA05  | Drugs for obstructive airway diseases | 7 (3.7)             |
| Carvedilol         | C07AG02  | Beta blocking agents | 7 (3.7)                     |
| Fentanyl           | N02AB03  | Opioids             | 6 (3.2)                     |
| Rosuvastatin       | C10AA07  | Lipid modifying agents | 6 (3.2)                  |
| Betaxolol          | C07AB05  | Beta blocking agents | 6 (3.2)                     |
| Haloperidol        | N05AD01  | Antipsychotics      | 6 (3.2)                     |
| Levomepromazine    | N05AA02  | Antipsychotics      | 6 (3.2)                     |
| Pregabalin         | N03AX16  | Antiepileptics      | 6 (3.2)                     |
| Nitrofurantoin     | J01XE01  | Antibacterials for systemic use | 6 (3.2)               |
| Urapidil           | C02CA06  | Antiadrenergic agents | 5 (2.7)                  |
| Rilmenidine        | C02AC06  | Antiadrenergic agents | 5 (2.7)                  |
| Nebivolol          | C07AB12  | Beta blocking agents | 5 (2.7)                     |
Table 6 The preliminary categorization of high fall risk medicines (Category A) basing on their adverse drug effect (ADE) profiles in statutory summaries of product characteristics (SmPCs) and frequency of use in older patients who had experienced at least one documented fall in a geriatric care unit (n = 188). The medicines are organized according to the ATC Classification [38] (Continued).

| High fall risk (A)                                      | ATC Code  | ATC classification          | Users of the medicines n (%) |
|--------------------------------------------------------|-----------|-----------------------------|-----------------------------|
| Escitalopram                                           | N06AB10   | Antidepressants             | 5 (2.7)                     |
| Telmisartan                                            | C09CA07   | AT II receptor blockers     | 5 (2.7)                     |
| Midazolam                                              | N05CD08   | Hypnotics and Sedatives     | 5 (2.7)                     |
| Alprazolam                                             | N05BA12   | Anxiolytics                 | 5 (2.7)                     |
| Perindopril/Indapamide                                  | C09BA04   | ACE inhibitors combination  | 5 (2.7)                     |
| Verapamil                                              | C08DA01   | Calcium channel blockers    | 4 (2.1)                     |
| Amiloride/Hydrochlorothiazide                           | C03EA01   | Diuretics                   | 4 (2.1)                     |
| Rivastigmine                                            | N06DA03   | Anti-dementia drugs         | 4 (2.1)                     |
| Olanzapine                                             | N05AH03   | Antipsychotics              | 4 (2.1)                     |
| Dutasteride/Tamsulosin                                 | G04CA52   | Urologicals                 | 4 (2.1)                     |
| Trimetazidine                                           | C01EB15   | Other cardiac preparations  | 4 (2.1)                     |
| Fosinopril                                             | C09AA09   | ACE inhibitors              | 3 (1.6)                     |
| Isosorbide dinitrate                                    | C01DA08   | Vasodilators                | 3 (1.6)                     |
| Aceclofenacin                                           | M01AB16   | Anti-inflammatory drugs     | 3 (1.6)                     |
| Captopril                                              | C09AA01   | ACE inhibitors              | 3 (1.6)                     |
| Baclofen                                                | M03B01    | Muscle relaxants            | 3 (1.6)                     |
| Lansoprazole                                            | A02BC03   | Drug for peptic ulcer and reflux | 3 (1.6)                   |
| Cefuroxime                                              | J01DC02   | Antibacterials for systemic use | 3 (1.6)                |
| Levetiracetam                                           | N03AX14   | Antiepileptics              | 2 (1.1)                     |
| Propafenone                                             | C01BC03   | Antiarrhythmics             | 2 (1.1)                     |
| Carbamazepine                                           | N03AF01   | Antiepileptics              | 2 (1.1)                     |
| Diclofenac                                              | M01AB01   | Anti-inflammatory drugs     | 2 (1.1)                     |
| Solifenacin/Tamsulosin                                 | G04CA53   | Urologicals                 | 2 (1.1)                     |
| Oxycodone                                               | N02AA05   | Opioids                     | 2 (1.1)                     |
| Trandolapril                                            | C09AA10   | ACE inhibitors              | 2 (1.1)                     |
| Levodopa/Carbidopa                                      | N04BA02   | Dopaminergic agents         | 2 (1.1)                     |
| Perindopril/Amlodipine/Indapamide                       | C09BX01   | ACE inhibitors combination  | 2 (1.1)                     |
| Bicalutamide                                            | L02BB03   | Hormone antagonists         | 2 (1.1)                     |
| Glyceryl trinitrate                                     | C01DA02   | Vasodilators                | 2 (1.1)                     |
| Fluoxetine                                              | N06AB03   | Antidepressants             | 1 (0.5)                     |
| Dosulepin                                               | N06AA16   | Antidepressants             | 1 (0.5)                     |
| Mianserin                                               | N06AX03   | Antidepressants             | 1 (0.5)                     |
| Candesartan                                             | C09CA06   | AT II receptor blockers     | 1 (0.5)                     |
| Venlafaxine                                             | N06AX16   | Antidepressants             | 1 (0.5)                     |
| Telmisartan/Hydrochlorothiazide                         | C09DA07   | AT II receptor blockers     | 1 (0.5)                     |
| Tizanidine                                              | M03BX02   | Muscle relaxants            | 1 (0.5)                     |
| Lisinopril                                              | C09AA03   | ACE inhibitors              | 1 (0.5)                     |
| Famotidine                                              | A02BA03   | Drug for peptic ulcer and reflux | 1 (0.5)                |
| Quinapril/Hydrochlorothiazide                           | C09BA06   | ACE inhibitors combination  | 1 (0.5)                     |
| Nafldrofuryl                                            | C04AX21   | Peripheral vasodilators     | 1 (0.5)                     |
| Celiprolol                                              | C07AB08   | Beta blocking agents        | 1 (0.5)                     |
| Paroxetine                                              | N06AB05   | Antidepressants             | 1 (0.5)                     |
[46, 47]. Furthermore, the previous study from Czech Republic (Maly et al. [48]) classified drugs that affected to the nervous system (antipsychotics, antidepressants, analgesics) and to the cardiovascular system (diuretics, beta blocking agents, agents acting on the renin-angiotensin system) as the most frequently used fall risk-increasing drugs in hospitals. Thus, many studies have reached similar conclusions, although the fall-increasing medicines have been presented slightly in different order. The identification of increased risk of falls in different drug classes might be a crucial risk factor for falls. The European Geriatric Medicine Society and Finnish Expert Group on Fall-Risk-Increasing Drugs (FRIDs) have concluded that the knowledge about the risk of falls associated with therapeutic classes and individual medications can help in fall prevention [49].

According to our findings, the fall risk assessment tool presented in this study could be helpful to prevent medication-related falls and increase quality of geriatric care in health care institutions. This is supported by the findings of previous studies that have reported the medication use as a remarkable but modifiable fall risk factor [48, 50]. Therefore, it is reasonable to implement a strategy to avoid use of fall risk-increasing drugs in the routine practice in geriatric care units. Nevertheless, many of developed fall risk assessment tools do not consider medication as a risk factor included in the tool. A review of twenty fall risk assessment tools found that only seven of the tools consider medication use as a risk factor [32]. More recent tools include medication use in a fall risk assessment, e.g., The Johns Hopkins Fall Risk Assessment Tool: it ranks opiates, anticonvulsants, antihypertensives, diuretics, hypnotics, laxatives, sedatives, and psychotropics among high fall risk drugs [51]. The Johns Hopkins Fall Risk Assessment Tool is well structured and validated, but the total number of risk points to evaluate is high (maximum 28). This makes it more time consuming for health care providers to assess the fall risk than by using a tool with fewer risk points, such as the five items suggested to be used in our updated fall risk assessment tool. Our tool is also unique in the way that the list of fall risk medicines was created basing on statutory medicines information presented in the summaries of product characteristics approved by European Union (EU) authorities.

This study indicates that the current practice of fall risk estimation in geriatric care units without including medications understimates the actual fall risk. More than half (53%, n = 100) of the patients included in our study scored at least a high fall risk, but the remaining 46% (n = 88) of these fall-experienced patients scored a medium risk (35%), a low risk (9%) or no risk (3%). The addition of a new item scoring the exposure to the high fall risk medication could refine the prospective risk assessments. This new risk item represented by high fall risk medicines (FRIDs) should

### Table 6

The preliminary categorization of high fall risk medicines (Category A) basing on their adverse drug effect (ADE) profiles in statutory summaries of product characteristics (SmPCs) and frequency of use in older patients who had experienced at least one documented fall in a geriatric care unit (n = 188). The medicines are organized according to the ATC Classification [38] (Continued)

| High fall risk (A) | ATC Code   | ATC classification          | Users of the medicines n (%) |
|-------------------|------------|-----------------------------|-----------------------------|
| Methyldopa        | C02AB01    | Antiadrenergic agents       | 1 (0.5)                     |
| Tianeptine        | N06AX14    | Antidepressants             | 1 (0.5)                     |
| Doxazosin         | C02CA04    | Antiadrenergic agents       | 1 (0.5)                     |
| Ticagrelor        | B01AC24    | Antithrombotic agents       | 1 (0.5)                     |
| Losartan/Hydrochlorothiazide | C09DA01 | ACE inhibitors combination | 1 (0.5)                     |
| Codeline          | R05DA04    | Cough suppressants          | 1 (0.5)                     |
| Acebutolol        | C07AB04    | Beta blocking agents        | 1 (0.5)                     |
| Mirabegron        | G04BD12    | Urologicals                 | 1 (0.5)                     |
| Ibandron acid     | M05BA06    | Drugs affecting bone        | 1 (0.5)                     |
| Levodopa/Benserazide | N04BA02 | Dopaminergic agents        | 1 (0.5)                     |
| Selegiline        | N04BD01    | Dopaminergic agents         | 1 (0.5)                     |
| Moxonidine        | C02AC05    | Antiadrenergic agents       | 1 (0.5)                     |
| Irbesartan        | C09CA04    | ACE inhibitors              | 1 (0.5)                     |
| Perindopril/Amlodipine | C09BB04 | ACE inhibitors combination | 1 (0.5)                     |
| Cilazapril        | C09AA08    | ACE inhibitors              | 1 (0.5)                     |
| Fluphenazine      | N05AB02    | Antipsychotics              | 1 (0.5)                     |
| Ropinirole        | N04BC04    | Dopaminergic agents         | 1 (0.5)                     |
| Chlorprothixene   | N05AF03    | Antipsychotics              | 1 (0.5)                     |
be considered in each patient admission or medication change and periodically assessed in the existing fall risk assessment tool by health care experts.

Fine-tuning the fall risk scoring system requires further research and comparisons with the contents of other existing tools. Further research should compare how much adding high risk medicines to the fall risk assessment tool changes the risk score and makes the risk score more accurate in terms of predicting and preventing actual falls. It also might be useful to assess whether concomitant use of more than one FRID medicines will elevate the fall risk. Determining this in future studies may be necessary because the concomitant use of several drugs that increase the risk of falls was common in our data (on average 3.8 high risk medicaments per patient). In addition to this kind of risk verification research, more generalizable results are needed by testing the fall risk assessment tool with a larger number of geriatric patients from a larger number of hospital wards and nursing homes. These studies should be based on prospective patient data. Furthermore, the fall risk profiles and patterns of the high fall risk medicines should be further investigated in older adults in hospital and home care settings.

Study limitations
When interpreting the results of this study it is important to keep in mind that the study does not cover the complete spectrum of medicines used by older adults, only the medicines used by the 188 study patients. Furthermore, the retrospective patient and medication data from the patient records may perform as a source of bias. The data related to the nursing home residents were not documented in such detail compared to that of hospital patients. The differences in the detailed-ness of documentation concern e.g., information on cognitive impairment or changes made to medications of individual patients. Documentation may have missed minor falls which were not reported to the staff by the patients.

Conclusion
It was possible to develop a preliminary categorization of FRIDs basing on their adverse drug effect profile in SmPCs and frequency of use in older patients who had experienced at least one documented fall in a geriatric care unit. Even though more than half of the fall-experienced older adults had at least high fall risk scores on admission according to the fall risk items routinely assessed, their fall risk might have been underestimated as use of high fall risk medicaments was common, even concomitant use. Further studies are needed to develop the FRID categorization and assess its impact on fall risk.

Abbreviations
ADE: Adverse Drug Effect; ATC Classification: Anatomical Therapeutic Chemical Classification; EU: European Union; FRID: Fall Risk Increasing Drug; MMSE: Mini Mental State Exam; OR: Odds Ratio; SmPC: Summary of Product Characteristic

Acknowledgements
The authors would like to thank Professor Charles Alan Lyles from the University of Baltimore, USA for his valuable comments in preparing the manuscript.

Authors’ contributions
Study concept and design: JM, KV. Interpretation of data: JM, KV, MA. Drafting of manuscript: JM, MA. Revision of manuscript: JM, MA, KB. All authors have read and approved the final manuscript.

Funding
Not applicable.

Availability of data and materials
The datasets derived from summaries of product characteristics during the current study are available from the corresponding author on reasonable request. The datasets generated and analysed during this study that were derived from retrospective patient records are not publicly available due to regulations on secondary use of patient data and subsequent agreements with the institutions to perform the study.

Ethics approval and consent to participate
The study protocol was approved by the University Hospital Brno, Jihlavská 20, Brno, Czech Republic with an authorization by Head of Geriatric Clinic and Assistant Director for Health Care. No ethics approval was required for this retrospective study (Ethics Committee of University Hospital Brno). An informed written consent was voluntarily signed by all study participants to use their anonymous data for education and research purposes.

Consent for publication
Not applicable.

Competing interests
All authors declare that there are no conflicts of interest.

Author details
1Faculty of Pharmacy, Department of Applied Pharmacy, Masaryk University, Palackého 1946/1, 612 42 Brno, Czech Republic. 2 Faculty of Pharmacy, Division of Pharmacology and Pharmacotherapy, Clinical Pharmacy Group, University of Helsinki, Viikinkaari 5E, 00014 Helsinki, Finland. 3 Clinic of Internal Medicine, Geriatrics and Practical Medicine, University Hospital Brno, Jihlávská 20, 625 00 Brno, Czech Republic.

Received: 15 January 2020 Accepted: 22 October 2020
Published online: 06 November 2020

References
1. Huang AR, Mallet L, Rochefort CM, Eguale T, Buckeridge DL, Tamblyn R. Medication-related falls in the elderly: causative factors and preventive strategies. Drugs Aging. 2012;29(1):359–76.
2. Weil TP. Patient falls in hospitals. An increasing problem. Geriatr Nurs. 2015; 36(5):342–7.
3. Tinetti ME, Kumar C. The patient who falls: it is always a trade-off. JAMA. 2010;303(5):258–66.
4. Burns Z, Khasnabish S, Hurley AC, et al. Classification of injurious fall severity in hospitalized adults. J Gerontol A Biol Sci Med Sci. 2020. https://doi.org/10.1093/gerona/glaa014.
5. Vaapio SS, Salminen MJ, Ojanlatva A, Kivelä SL. Quality of life as an outcome of fall prevention interventions among the aged: a systematic review. Eur J Pub Health. 2009;19(1):7–15.
6. Ambrose AF, Paul G, Haudsoff JM. Risk factors for falls among older adults: a review of the literature. Maturitas. 2013;75(1):51–61.
7. Mangoni AA, Jackson SHD. Age-related changes in pharmacokinetics and pharmacodynamics: basic principles and practical application. Br J Clin Pharmacol. 2003;57(1):6–14.
8. Turnheim K. When drug therapy gets old. Pharmacokinetics and pharmacodynamics in the elderly. Exp Gerontol. 2003;38(8):843–53.
9. Wooten JM. Pharmacotherapy considerations in elderly adults. South Med J. 2012;105(8):437–45.
10. Jung D, Shin S, Kim H. A fall prevention guideline for older adults living in long-term care facilities. Int Nurs Rev. 2014;61(4):525–33.
11. Lawlor DA, Patel R, Ebrahim S. Association between falls in elderly woman and chronic diseases and drug use: cross sectional study. BMJ. 2003; 327(7417):712–7.
12. Neutel CJ, Perry S, Maxwell C. Medication use and risk of falls. Pharmacoepidemiol and Drug Saf. 2002;11(2):97–104.
13. World Health Organization. Medication Safety in Polypharmacy: Technical Report. 2019. Available at: https://apps.who.int/iris/handle/10665/295454. Accessed Sep 2020.
14. Ziere G, Dieleman JP, Hofman A, Pols HA, van der Cammen TJ, Stricker BH. Psychiatric symptoms and use of psychotropic medication in elderly fall and syncope patients. Eur Geriatr Med. 2017;8(2):5–419–23.
15. Ensrud KE, Blackwell TL, Mangione CM, Bowman PJ, WHOley MA, Bauer DC, Schwartz AV, Hanlon JT, Nevitt MC. Central nervous system-active medications and risk for falls in older women. J Am Geriatr Soc. 2002;50(10): 1629–37.
16. McLean AJ, Le Couteur DG. Aging biology and geriatric clinical pharmacology. Pharmaco Rev. 2004;56(2):163–84.
17. Kannus P, Seppala LJ, Palvanen M, Jarvinen T, Parkkari J. Prevention of falls and consequent injuries in elderly people. Lancet. 2005;366:1885–93.
18. Kenny RA, Rubenstein LZ, Tinetti ME, et al. Summary of the updated American Geriatrics Society/British geriatrics society clinical practice guideline for prevention of falls in older persons. J Am Geriatr Soc. 2011; 59(11):148–57.
19. Tinetti ME. Preventing falls in elderly persons. N Engl J Med. 2003;348:42–9.
20. Li F, Hamer P, Fischer KJ, McAuley E. Tai chi: improving functional balance and predicting subsequent falls in older persons. Med Sci Sports Exerc. 2004;36(12):2016–52.
21. Ray WA, Thapa PB, Gideon P. Benzodiazepines and the risk of falls. Rev Clin Gerontol. 2004;14(5):163–84.
22. Darowski A, Dwight J, Reynolds J. Medicines and Falls in Hospital: Guidance Sheet. 2011. Available at: https://www.shropshireccg.nhs.uk/media/2475/guidance-sheet-medicines-and-falls-in-hospital.pdf Accessed Sep 2017.
23. Shubert TE. Evidence-based exercise prescription for balance and falls prevention: a current review of the literature. J Geriatr Phys Ther. 2001;34(3): 100–8.
24. Morse JM. Preventing patient falls. Establishing a fall intervention program. 2nd ed. New York: Springer Publishing Company; 2009.
25. World Health Organization Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index 2019. Available at: https://www.whocc.no/atc_ddd_index/ Accessed Jan 2018.
26. World Health Organization. Medication Safety in Polypharmacy: Technical Report. 2019. Available at: https://apps.who.int/iris/handle/10665/295454. Accessed Sep 2020.
27. Rubenstein LZ. Falls in older people: epidemiology, risk factors and strategy for prevention. Age Ageing. 2006;35(2):37–41.
28. World Health Organization, WHO Global Report on Falls Prevention in Older Age. 2008. Available at: https://www.who.int/summaries/publications/2008/WHO_report_on_falls_prevention_in старшеЅе_r0_u=1 Accessed Sep 2017.
29. Perel KL, Nelson A, Goldman RL, et al. Fall risk assessment measures: an analytic review. J Gerontol A Biol Sci Med Sci. 2001;56(12):761–6.
30. European Commission. A Guideline on Summary of Product Characteristics. 2009. Available at: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-2/cmpc_guideline_rev2_en.pdf Accessed Sep 2017.
31. Ericsson KL, Wooding FG, Tuiskula KA. Medication-related falls in the elderly: mechanism and prevention strategies. Consult Pharm. 2014; 29(6):413–7.