CONCORDANCE WITH A STOPP (SCREENING TOOL OF OLDER PERSONS' POTENTIALLY INAPPROPRIATE PRESCRIPTIONS) CRITERION IN NOVA SCOTIA, CANADA: BENZODIAZEPINE AND ZOPICLONE PRESCRIPTION CLAIMS BY OLDER ADULTS WITH FALL-RELATED HOSPITALIZATIONS

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ABSTRACT

Background

Optimization of prescribing in older adults is needed. The STOPP criteria provide a systematic way of identifying potentially inappropriate prescribing in this population. Previous research indicates poor concordance between benzodiazepine prescribing and STOPP.

Objectives

To determine the extent and predictors of benzodiazepine and zopiclone (BZD-Z) pharmacy dispensations in older adults with a history of a recent fall, in concordance with STOPP.

Methods

Prescription claims data from the Nova Scotia Seniors' Phamacare Program were linked with fall-related injury data from the CIHI Discharge Abstract Database. Adults aged \geq 66 years making a claim for a BZD-Z in the 100 days prior to fall-related hospitalization were identified. Their BZD-Z claims in the 100 days following discharge were also identified. Descriptive statistics, trend tests and logistical regression modelling were performed to examine predictors for continued use of BZD-Z post-fall.

Results

Over 5 years, from a pool of 8,271 older adults discharged following a fall-related hospitalization, 1,789 (21.6%) had made a claim for a BZD-Z in the 100 days prior to admission. Of these, 82% were women. Younger age and female sex were predictors of continuing BZD-Z dispensations post-fall. In the 100 days following discharge, 74.2% (n=1327) made a claim for at least one BZD-Z.

Conclusion

BZD-Z use continued in 74% of patients following discharge from a fall-related hospitalization, representing limited concordance with the STOPP criterion. Such hospitalizations and follow-up care present an opportunity to address an ongoing modifiable risk factor.

Key Words: Benzodiazepines, zopiclone, STOPP criteria, screening tool, inappropriate prescribing, aged

Optimization of drug prescribing in older humanistic, clinical and economic impacts of adverse drug events in this age group. Age-related

changes in physiology lead to changes in drug pharmacokinetics and pharmacodynamics, which predispose older adults to adverse drug events such as falls.^{1,2} Approximately 30% of adults over 65 years old, who live in a community setting, fall each year.^{1,2} One in five falls requires medical attention. Fractures, which occur in 6-10% of falls requiring medical attention often result in hospitalization and may lead to functional decline, loss of independence, social withdrawal, fear, activity avoidance, and death. 1-6 A recent report based on 2011/2012 data from the Canadian Hospital Morbidity Database found that 33% of senior's fall-related hospitalizations involved a hip fracture, which may result in significant health care costs.⁴ Additionally, 26% of communitydwelling patients who fell were transferred to long term nursing home care after a fall-related hospitalization.4 Psychotropic medication (antipsychotics, anxiolytics, hypnotics sedatives) use in this age group has been associated with an increased fall-risk. 1,3,6,7 Inappropriate prescribing, including benzodiazepines, has been shown to increase the relative risk of mortality by 28% in the three years following a hip fracture.8 Falls should, therefore, present an opportunity to re-evaluate medication-related risk. 1,6-8

The STOPP (Screening Tool of Older Persons' Potentially inappropriate Prescriptions) criteria were developed to facilitate systematic screening for potentially inappropriate medication (PIM) use in older adults. The 2008 version of STOPP identifies five medication classes as potentially inappropriate in patients with a history of falls, and as such, this criterion has been used to study medication prescribing in people at risk of falls. Of particular interest to this study is evidence documenting the relationship between benzodiazepine and zopiclone (BZD-Z) use and the complex issue of older adults' falls.

In a six-site European study of PIMs identified by STOPP, 9.1% (range 1.3% in Madrid to 26.7% in Geneva) of long-term care residents determined to be prone to falls were prescribed benzodiazepines. The criterion "Drugs that adversely affect fallers - benzodiazepines" was identified as the most prevalent of the 65 criteria identifying PIMs. ¹⁰ In Australia, a STOPP-based review of hospital pre-admission drug use by

older adults found this criterion as the second most frequently encountered PIM (10.1%).¹¹ A review of drug use by adults aged 70 years and older presenting to an Irish emergency department with a fall found that there was a high prevalence of psychotropic medication prescription claims in the year prior to the fall. Of the total study 29.5% population. were exposed hypnosedatives including benzodiazepines (ATC N05C). Long-term use (>4 weeks duration) of long-acting benzodiazepines decreased from 10.7 to 8.6% in the year prior versus the year post-fall. However, new hypnosedative initiation occurred post-fall in 15.4%. In the study population's year post-fall. hypnosedative prescription increased to a total prevalence of 32.1%.¹²

De Vries and colleagues explored another STOPP criterion. The criterion advised against the use of "long-term long-acting benzodiazepines, and benzodiazepines with long-acting metabolites". The researchers attempted to establish the relationship between the duration of action of benzodiazepines and the fall-risk in community-dwelling older adults. They found that the duration of action of benzodiazepines did not change the fall-risk, and concluded that the use of both short-acting and long-acting benzodiazepines should be avoided in older adults.¹³

Other studies have improved understanding of the role of benzodiazepine and zopiclone drug use in older adults' falls. Finkle et al found that zolpidem, alprazolam, lorazepam, and diazepam increased the rates of fractures requiring hospitalization following an initial treatment (rate ratios 2.55, 1.14, 1.53, and 1.97, respectively).⁶ Davila Barboza and Fernandez reported that the most common fall-risk medication used by older patients admitted with hip fractures to an orthogeriatric unit were benzodiazepines (41.6%).¹⁴ The combination of fall-risk medications (such as BZD-Z) and antithrombotics was found to increase the risk of injury severity. The risk of fall-related intracranial hemorrhage was 4 times higher in adults prescribed the combination of antithrombotics and fall-risk medications versus antithrombotics alone.15 Benzodiazepines have been found to increase the risk of falls (odds ratio of 1.34 - 3.4). Risk factors include sex (female), specific

benzodiazepine used, duration of treatment course, rapid dose increase, and use of multiple benzodiazepines.⁵

Previous research has demonstrated a limited concordance between two STOPP criteria (use of long-term, long-acting benzodiazepines and benzodiazepines with long-acting metabolites and duplicate drug classes) and BZD-Z dispensing in Nova Scotia. A related STOPP criterion requires that benzodiazepines be avoided by older adults who are prone to falls. This research investigates the concordance between this criterion and the dispensing of benzodiazepines. The criterion from the 2008 version of STOPP was adapted to include zopiclone in this study.

The objective of this study was to determine the extent that BZD-Z prescribing in Nova Scotia was in concordance with the STOPP criterion requiring older adults prone to falls to avoid the use of BZD-Z. We examined the rate of, and predictors for, post-discharge BZD-Z exposure in older adults who had made at least one claim for BZD-Z prior to being hospitalized for a fall-related injury.

METHODS

This is a retrospective observational study linking fall-related hospitalization data from the Canadian Institute for Health Information's (CIHI) Discharge Abstract Database (DAD) to BZD-Z outpatient pharmacy dispensation (claims) data from the Nova Scotia Seniors' Pharmacare Program (NSSPP).

Study population and design

Nova Scotia is a province of 940,000, approximately 17.2% of which are aged 65 and older. The NSSPP is the prescription insurer of last resort for 70.5% (2006) to 68.4% (2010) of the population of older adults aged 65 years and older in Nova Scotia. In 2013/14, approximately 7.5% of NSSPP beneficiaries lived in long term care homes (Personal correspondence, Director Health Economics, Government of Nova Scotia). The NSSPP database contains demographic details (age, sex), information on prescriptions dispensed including the generic and brand name of the medication, strength, quantity, and cost

(http://novascotia.ca/dhw/pharmacare/seniors-pharmacare.asp).

During the study period. 14benzodiazepines were on the NSSPP formulary bromazepam, chlordiazepoxide. (alprazolam. clobazam, clonazepam, clorazepate, diazepam, flurazepam, lorazepam, midazolam, nitrazepam, oxazepam, temazepam, and triazolam). Drugs that were excluded during some of the study period were flurazepam, nitrazepam, triazolam and temazepam. Two benzodiazepines were excluded from this study (clobazam, which is used almost exclusively as an anticonvulsant, and midazolam, which was only available for injection). Zopiclone, also a benefit of NSSPP, was added to the 12 remaining benzodiazepines for our analysis. No other benzodiazepine-related drugs (for example zolpidem) were on the NSSPP formulary and were therefore not included. Medications were identified by WHO-ATC codes (http://www.whocc.no/atc ddd index/) for data extraction. BZD-Z claims data from April 1, 2006 to March 31, 2011 were identified in a previous analysis.16

DAD (http://www.cihi.ca/CIHI-ext-portal/internet/en/document/types+of+care/hospital+care/acute+care/dad_metadata) records acute patient discharge information from 33 acute care facilities in Nova Scotia. Fall-related injuries requiring hospitalization were identified using ICD-10-CA W00-W19

(http://www.cihi.ca/cihi-ext-

portal/internet/en/document/standards+and+data+submission/standards/classification+and+coding/codingclass_icd10).

DAD was used to create a pool of Nova Scotian adults aged 66 years and older admitted to hospital with a fall-related injury. The age of 66 years was chosen to allow for a 100 day window prior to the hospitalization to examine for BZD-Z claims from the NSSPP. Patients with multiple hospitalizations were counted as unique patients. The two databases were linked through the unique patient identifier issued by the Nova Scotia Department of Health and Wellness. Records were anonymized following the linkage. All fall-related hospitalizations identified in the DAD pool were examined for BZD-Z claims in the 100 days prior to admission. From this cohort, we then

identified NSSPP beneficiaries making a claim for a BZD-Z in the 100 days following discharge.

Statistical analysis

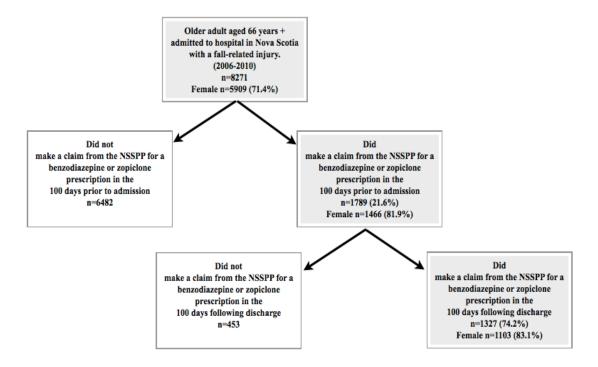
Descriptive statistics were used to summarize NSSPP beneficiaries by age categories and sex, and drug exposure in the 100 days prior to admission and in the 100 days following discharge. Multiple BZD-Z claims were counted only by the longest-acting BZD-Z for which a claim was made. Length-of-stay was calculated. The Cochrane-Armitage trend test was used to test for a linear trend in proportions of patients prescribed BZD-Z over the following variables; fiscal year of discharge, age at admission for fall, and duration of action of BZD-Z prior to fall. Chisquare test was performed to look at the association between patients prescribed BZD-Z within 100 days of discharge and sex. Univariate and multivariate logistic regression analyses were performed to examine predictors for NSSPP beneficiaries aged 66 and over making a claim for BZD-Z in the 100 days following discharge. Variables included sex, age category, BZD-Z duration of action prior to admission for fall and fiscal year of discharge. All analyses were performed using SAS/STAT software, Version 9.2 of the SAS System for Windows (SAS Institute Inc., Cary, NC, USA.).

This research received ethics approval from the Health Sciences Research Ethics Board, Dalhousie University, Halifax, NS (#2012-2657).

RESULTS

From April 1, 2006 to March 31, 2011 there were 8,271 older adults aged \geq 66 years hospitalized in Nova Scotia with a fall-related injury. Of these, 1,789 (21.6%) NSSPP beneficiaries had made a claim for at least one prescription of BZD-Z in the 100 days prior to being hospitalized (Figure 1). The majority (58.5%) of our cohort were 80 years of age and older (mean age 81.6 years). Age category distribution of the study population is shown in Table 1 and Figure 2.

FIG. 1 Study population



NSSPP = Nova Scotia Seniors' Pharmacare Program

FIG. 2 Percent of Nova Scotian Seniors' Pharmacare beneficiaries making a claim for benzodiazepine and/or zopiclone in the 100 days prior to a fall-related hospitalization who also received a benzodiazepine and/or zopiclone following discharge by age category

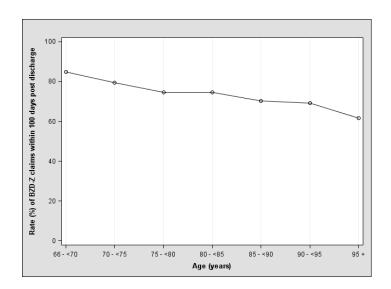


TABLE 1 Nova Scotian Seniors' Pharmacare beneficiaries making a pharmacy claim for a benzodiazepine and/or zopiclone prescription in the 100 days prior to admission to hospital for a fall-related injury, by age category.

Age Category	Number (%)				
66 - < 70	159 (8.9)				
70 - < 75	249 (13.9)				
75 - < 80	334 (18.7)				
80 - < 85	401 (22.4)				
85 - < 90	369 (20.6)				
90 - < 95	217 (12.1)				
95 +	60 (3.4)				
Total	1789 (100)				

Sixty-six (3.7%) persons claimed two or more different BZD-Z drugs in the period prior to injury. Eighty-two percent of our study cohort were women and 83% who also received BZD-Z following discharge were women (Figure 1). The distribution by sex of adults aged 66 and over and experiencing a fall-related hospitalization in the study population is shown in Figure 1. The mean length-of-stay in hospital was 36 days \pm 52, (range 1- 581 days) (Table 2). The mean time between BZD-Z prescription claim hospitalization was 70 days. In the 100 day period prior to admission, 6.6% (n=118) of the study population made a claim for a long-acting BZD (chlordiazepoxide, clorazepate, diazepam, flurazepam), 91.6% (n=1,638) made a claim for intermediate-acting BZD-Z (alprazolam, bromazepam, clonazepam, lorazepam, nitrazepam, oxazepam, temazepam or zopiclone) and 1.8% (n=33) made a claim for a short-acting BZD (triazolam) (Table 3).

In the 100 days following discharge from hospital, 74.2% (n=1327) of our study population made a claim for at least one prescription for BZD-Z. Sixty-eight percent (n=1,217) made a claim for an intermediate-acting BZD-Z. Longacting benzodiazepine exposure decreased slightly from pre-admission (6.60%) to post-discharge (5.03%) - a relative reduction of 23.8% (95% CI 0.5%, 41.6%) or an absolute reduction 1.57% (95% CI 0.03%, 3.10%). Short-acting benzodiazepine exposure also decreased slightly. (Table 3)

From 2006 to 2010, the odds of being prescribed a BZD-Z following discharge was positively associated with sex (female vs male 1.6, 95% CI 1.22, 2.13) and negatively associated with age (per each 10 year decrease in age 1.5, 95% CI 1.28,1.69) (Table 4). The year of discharge or the duration of action of the BZD-Z prior to admission were not associated with an increased odds of making a claim for a BZD-Z following discharge.

TABLE 2 Characteristics of Nova Scotian Seniors' Pharmacare beneficiaries making a claim for a benzodiazepine and/or zopiclone prescription in the 100 days pre- and post- a fall-related hospitalisation

Variable	Mean	Std Dev	Median	Minimum	Maximum	N
Age at admission	81.6	7.9	81.9	66.1	102.9	1789
Age at discharge	81.7	7.9	82.0	66.1	102.9	-
Length of hospital stay, days	36.3	52.2	17	1	581	1789
Time from BZD-Z outpatient prescription claim to admission, days	70.1	25.6	78	1	100	1789
Time from discharge to outpatient prescription claim for BZD-Z, days	25.2	22.0	20	1	100	1327*

BZD-Z = 12 benzodiazepines and/or zopiclone. *Note 462 beneficiaries did not receive a BZD-Z in the 100 days after discharge.

TABLE 3 The type of benzodiazepine and/or zopiclone prescription claimed by Nova Scotian Seniors' Pharmacare Program beneficiaries in the 100 days prior to admission to hospital for a fall-related injury, and in the 100 days after discharge

	Number prior to admission (%)	Number after discharge (%)
Short-acting*	33 (1.8)	20 (1.1)
Intermediate-acting**	1638 (91.6)	1217 (68.0)
Long-acting***	118 (6.6)	90 (5.0)
No BZD-Z	0	462 (25.8)

^{*}triazolam; **alprazolam, bromazepam, clonazepam, lorazepam, nitrazepam, oxazepam, temazepam or zopiclone; ***chlordiazepoxide, clorazepate, diazepam, flurazepam; BZD-Z = benzodiazepine and/or zopiclone; †Rounding error results in total of 99.9%

TABLE 4 Predictors of Nova Scotian Seniors' Pharmacare Program beneficiaries making a claim for a benzodiazepine and/or zopiclone prescription in the 100 days prior to a fall-related hospitalization receiving a benzodiazepine and/or zopiclone prescription in the 100 days after discharge (Wald Confidence Interval for Odds Ratios)

Effect	Unit	Odds ratio	95% Confidence Limits		p-value
Sex female (reference)	1	1.61	1.22	2.13	0.0007
Per each 10 year decrease in age	-10	1.47	1.28	1.69	<.0001
BZD-Z prior to admission: Intermediate- acting** vs Long-acting*** (reference)	1	0.90	0.58	1.41	0.6417
BZD-Z prior to admission: Short acting* vs Long acting*** (reference)	1	0.73	0.31	1.75	0.4830
Year 2007 vs 2006	1	0.79	0.56	1.11	0.1767
Year 2008 vs 2006	1	0.88	0.62	1.25	0.4713
Year 2009 vs 2006	1	0.88	0.62	1.23	0.4307
Year 2010 vs 2006 (reference)	1	0.80	0.57	1.12	0.1975

^{*}triazolam; **alprazolam, bromazepam, clonazepam, lorazepam, nitrazepam, oxazepam temazepam or zopiclone;

^{***}chlordiazepoxide, clorazepate, diazepam, flurazepam; BZD-Z = benzodiazepine and/or zopiclone

DISCUSSION

Of all fall-related hospitalizations by adults over the age of 66 in Nova Scotia, 21.6% had exposure to a BZD-Z in the 100 days prior to admission. Of these, almost three-quarters continued to receive BZD-Z following discharge. Our results appear higher than those reported by McMahon and colleagues for primary care patients in Dublin. They identified an overall combined anxiolytic and hypnosedative prevalence of 41.1% in the year post-fall. However, the age of their cohort was slightly older than our cohort, at 70 years and older, and they examined all patients with falls regardless of prior BZD-Z exposure, and the medications collected in their analysis include a wider range of psychotropics covered by ATC classifications N05B and N05C (benzodiazepines, barbiturates, chloral hydrate, z-drugs, melatonin, and others). They do note that there was "no substantial improvements in prescribing following the [fall] event."12

There was a significantly percentage of women claiming for BZD-Z in the 100 days following discharge from a fall-related hospitalization (P=0.0007). Over our study period, women made up 60 - 62% (data from 2010, 2006 respectively) of the NSSPP population.¹⁷ However, 82% of our study participants were women. In a report of older adult fallers in Newfoundland, the rate of women's fall-related hospitalization was twice that of men, which, the authors suggest, may be partially explained by osteoporosis increasing women's potential for more serious injury.¹⁹ Fall prevention experts agree that multiple factors such as age-related physical changes (impairments to vision and balance, cognition, gait health and muscle strength), co-morbidities, vitamin D levels, fallrisk medications and environmental hazards all contribute to fall rates and risks. 1,2,5 The rate of BZD use by Canadians aged 65 years and older has been reported as 15.4% in women versus 9.0% by men.²⁰ In Nova Scotia over the same time period, BZD-Z exposure in women has been reported as 28% in contrast to 19% by older men.16

The mean length-of-stay for fall-related hospitalization in our study population was 36 days, which contrasts with a recent report by the

Canadian Institute for Health Information (CIHI) based on seniors' fall-related hospitalizations. That report, based on 2011/12 data, found an average length-of-stay for all seniors' fall-related hospitalizations in Canada to be 15 days. The average length-of-stay for seniors' non-fall hospitalizations was 9 days. Also in the CIHI report, Nova Scotia was found to have slightly longer length-of-stay for fall-related hospitalizations (19 days). BZD-Z claims prior to hospitalization may be a proxy for other health problems that are associated with longer fallrelated hospitalizations.

Long-acting benzodiazepine use in older adults is of particular concern and a STOPP criterion identifies their use as potentially inappropriate. Similar to our findings, McMahon and researchers found that the rate of long-acting benzodiazepine usage was reduced from pre- to post-fall. We do not know if this was a result of a conscious recognition of the greater risk with longer-acting agents or due to lorazepam being the benzodiazepine on formulary in most hospitals in Nova Scotia.

As well as sex, the other significant predictor for the continuation of BZD-Z exposure following discharge from a fall-related hospitalization was age. For each 10 year decrease in age the odds of being prescribed BZD-Z in the 100 days following discharge is 1.5 times greater. This may be an encouraging finding as the very old may be frail and especially sensitive to BZD-Z, and prescribing practices may be changing to reflect cautious prescribing in this group.

A recently updated Cochrane review identified that the gradual withdrawal of psychotropic medication reduced the rate of falls in community-living older people in one trial. As well, one trial using medication review to adjust the use of fall-risk medications did reduce falls. However, three other trials based on medication review did not significantly change fall rates. As well as reducing fall-risk, benefits such as improved cognition and reduced long-term mortality may accompany BZD-Z drug cessation. 38,20,21

Health care providers must continue to review patients to determine if fall-risk medications such as benzodiazepines and zopiclone offer sufficient benefits as to justify their use especially in older adults. Issues of patient control and autonomy must be considered in the re-evaluation of BZD-Z use. 22,23 The dependence potential of BZD-Z makes the discontinuation of long-term use challenging. However, strategies have been developed to help physicians, pharmacists and others in the health care system teach older patients about changes in the patterns of sleep and the safety of long-term BZD-Z. 1,2,5,22-25 For example, direct-to-consumer educational interventions in the community have shown success in benzodiazepine discontinuation.²⁵ These strategies will help those patients willing to discontinue BZD-Z use, and in Scotia an educational intervention, Sleepwell (http://sleepwellns.ca) has recently been launched. Hospitalization has been shown to be a "turning point" for both the discontinuation and initiation of hypnosedatives, and presents an opportunity to re-evaluate fall-risk medication use. 26 As our patients had a mean hospital stay of 36 days, there would be opportunities for medication review, discharge planning, and referral to an outpatient falls prevention program for community-living patients.

Skill and knowledge deficit may also occur in health care providers, and there may be systematic issues in the health care system. As one researcher using STOPP criteria in long-term care facilities noted "Excessive use of psychoactive drugs is a problem which may be explained by an underdeveloped mental health primary care network, poor access to nondrug treatments, and by poor general practitioner education in this area."

This research may help inform the development of a local adaptation of this STOPP criterion for electronic decision support tools and continuing professional education. By identifying and quantifying specific local examples of PIM use in older adults, and contributing to ongoing healthcare professional education, it may be possible to reduce the rate of older person's falls.

The strength of our study design is the five year horizon and the large, relatively stable homogeneous population. Several limitations may affect the interpretations of our data. This study is based on prescription claims data, and there may be differences between dispensing and consumption of the medications. It is possible that

the BZD-Z prescription claimed in the 100 days prior to the fall was not being consumed at the time of the fall, or that it was being used only intermittently. Similarly, falls in people using BZD-Z medications prescribed to others will not be included in our cohort. We were unable to determine the dosage of BZD-Z prior to hospitalization, or after discharge - therefore we were unable to know if appropriate tapering of BZD-Z was occurring following hospitalization. The median time from discharge to the claim for a BZD-Z was 20 days. This suggests that the discharged patients may have had medication available for the immediate post-discharge period. By using CIHI DAD to identify fall-related injuries, we only identified serious falls requiring hospitalization. Although there are additional criteria in STOPP which relate to additional fallrisk medications (for example: antihistamines and neuroleptics), this research did not identify them.

We did not have access to patient variables such as diagnostic information that would clarify the appropriateness of the BZD-Z, for example, indications such as alcohol withdrawal where the benefit may outweigh risk. As well, patient variables such as frailty, comorbidities including vision impairment, living arrangements (community dwelling vs long term care), severity of illness, drug effectiveness, offlabel drug use, over-the-counter drug use, and contraindications were not available. We were also unaware of drugs prescribed and dispensed during the hospital stay (including BZD-Z initiations and/or duplicate therapy), in emergency departments, and/or given as samples.

The second version of the STOPP/START criteria was published in October of 2014.²⁸ We note that there are several changes to the criteria, including the inclusion of zopiclone as a medication to avoid in fall-prone older adults.

CONCLUSIONS

While it was encouraging to note that BZD-Z dispensations following a fall-related hospitalization were slightly less frequent with increasing age, BZD-Z use did continue in 74% of NSSPP beneficiaries following discharge. Younger age and female sex were predictors of continuing BZD-Z dispensations post-fall. This

discordance with a STOPP criterion highlights significant potentially inappropriate and modifiable fall-risk prescribing behaviour. The hospitalization of an older adult with a fall-related injury should sound an alarm requiring a reevaluation of medication use.

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Disclaimer

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