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Drugs and Falls in Community-Dwelling Older People: A National Veterans Study

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ABSTRACT

Objective: The aim of this study was to identify which specific medications within recognized major problematic drug categories that increase risk of falling were prescribed to veterans before their outpatient treatment for a fall.

Methods: This was a retrospective, cross-sectional national secondary outpatient data analysis with an age- and sex-matched comparison group. The setting was the national Veterans Health Administration (VHA) ambulatory health care system in fiscal year (FY) 2004. The study population was VHA patients aged ≥65 years who had fall-related outpatient clinical health care encounters in FY 2004 (as indicated by diagnostic codes) and who received ≥1 outpatient medication during the study period. The age- and sex-matched comparison group consisted of an equal number of patients with nonspecific chest pain. The percentage of patients in each group receiving medications (at the time of the outpatient encounter) that affect the cardiovascular system (CVS), central nervous system (CNS), or musculoskeletal system (MSS) was compared with Bonferroni-adjusted *P* values.

Results: The study sample consisted of 20,551 patients; the comparison group included the same number of patients. More patients with fall-coded encounters used CNS drugs than those with nonspecific chest pain (42.05% vs 29.29%). Also, within the CNS category, more patients with fall-coded encounters used antiparkinsonian medications (3.67% vs 1.32%), Alzheimer's disease medications (ie, cholinesterase inhibitors [5.40% vs 2.35%]), anticonvulsants/barbiturates (8.95% vs 5.18%), antidepressants (22.50% vs 14.16%), antipsychotics (4.68% vs 2.01%), opioid analgesics and narcotics (11.21% vs 9.09%), and benzodiazepines (7.60% vs 5.96%) (all, $P < 0.002$). More patients with nonspecific chest pain received CVS drugs compared with the fall-coded group (69.13% vs 63.07%; $P < 0.002$). Within the CVS category, more patients in the nonspecific chest pain group received angiotensin-II receptor antagonists, angiotensin-converting enzyme inhibitors, β-blockers, calcium channel blockers, vasodilators, diuretics, and antiarrhythmics (all, $P < 0.002$). No differences were noted between groups in the MSS category, except for NSAIDs, which more patients in the nonspecific chest pain group used than in the fall-coded group (6.44% vs 5.63%; $P < 0.002$).

Conclusion: In this study, subjects with a health care encounter for a fall (as indicated by diagnostic code) were prescribed significantly more CNS-category medications than subjects in the age- and sex-matched comparison group. (*Clin Ther.* 2006;28:619–630)

Key words: accidental falls, chest pain, pharmacoepidemiology, patient safety, veterans.

INTRODUCTION

Unintentional injury due to falls is a serious health problem among older people (ie, those aged ≥65 years) in the United States, with fall-related injuries incurring an estimated US $27.3 billion (year-2005 value) in health care expenses alone.[1] Approximately one third of community-dwelling persons aged ≥65 years fall each year,[2] with ~10% of falls resulting in serious

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nonfatal injury.[3–6] Older men and women appear to be equally likely to fall, although men are less likely to suffer fall-related injuries.[7] Even so, the provision of health services for fall-related injuries among older men is substantial.[8]

Previous studies have found associations between certain medications and the risk of falling. Medications such as antidepressants, antihypertensives, some analgesics, sedative hypnotics, and anxiolytics have been identified as risk factors for falls.[9–14] Meta-analysis of 40 studies of psychotropic medications (eg, neuroleptics, analgesics, hypnotics, antidepressants, and benzodiazepines [BZDs]) also found a relationship between drug use and falls.[15] Another meta-analysis of 29 studies that investigated cardiac and analgesic drugs found increased risk of falling.[16] Taking ≥4 medications or any psychoactive medication is also associated with an increased risk of a fall.[17–20]

Although some studies have associated medications with the risk of a fall-related injury, there is no single comprehensive, evidence-based, published list of specific problematic medications that clinicians can use to evaluate potential risk contribution of medications in a fall risk assessment. Perhaps the most widely known published compilation of potentially inappropriate drugs in the elderly is the Beers criteria.[21–23] However, the Beers criteria are neither a comprehensive list nor a sufficient tool for fall risk assessment. Although the Beers criteria list of potentially inappropriate medications in the elderly is useful, the majority of these drugs do not seem to directly affect fall risk. The drugs in the Beers criteria list that do influence fall risk primarily affect the central nervous system (CNS), musculoskeletal system (MSS), or cardiovascular system (CVS).[21–23] In fiscal year (FY) 2004, nearly 52% of all outpatient prescriptions filled within the US Veterans Health Administration (VHA) were in these 3 drug categories, suggesting the potential impact of these medications on fall risk in this aging population. There were ~23 million prescriptions for CNS medications, 31.6 million prescriptions for CVS medications, and 4.8 million prescriptions for MSS medications (VHA report, *Pharmacy Workload and Cost by Major Drug Class: Pharmacy Cost Summary by Major Drug Class Nation Summary—FY 04*).

In contrast to the Beers criteria, the Canadian Safety Council's Fall Risk Assessment Tool is a list of drugs that specifically affect fall risk in older individuals, and is divided into classes with generic and trade names for the drugs.[24] The Canadian fall risk assessment tool was originally developed at the University of Toronto's Baycrest Centre for Geriatric Care and was revised by pharmacists for use by the Niagara Health Systems Fall Prevention Program. This list is consistent with drug classes and categories that have been identified by other studies of medications linked to increased fall risk.[9–20] The Canadian fall risk assessment tool may also be responsive to the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) patient safety goals for 2006.[25]

One of the year-2006 JCAHO patient safety goals focuses on reducing the risk of patient harm resulting from falls in health care settings.[25] This JCAHO goal requires health care providers to implement and evaluate fall risk reduction programs, which include medication reviews.[25] Multifactorial fall reduction programs, including a comprehensive review of medications, have been shown to be effective in outpatients and nursing home patients.[3] This JCAHO patient safety goal underscores the importance of fall risk assessments that link particular medications with falls.

The VHA is a national, vertically and horizontally integrated managed-care system, and is subject to JCAHO accreditation requirements. The VHA has incentives to foster injury prevention and patient safety initiatives to reduce fall injuries in veterans that occur within its institutions or in the community. Identifying medications that could be linked in some way to injurious falls might permit more efficient and effective targeting of fall risk reduction programs.

The VHA has unique data sets that allow the linkage of outpatient prescriptions to fall-related health care encounters. The primary goal of the present study, the first national analysis of fall-related outpatient encounters in the VHA (as identified by diagnostic codes) linked to medications, was to identify specific medications within recognized major problematic drug categories that increase the risk of a fall and were prescribed before the fall-related encounter. In contrast to our previous studies that employed multivariate models to estimate the risk of a fall-related injury or adverse event associated with a single drug class,[26–28] the current study was intended to provide a descriptive analysis of the use of several drug classes within 3 major drug categories (ie, CVS, CNS, and MSS).[29] To provide a context for our analysis, we included a comparison group of patients with outpatient health care encounters for nonspecific chest pain.

MATERIALS AND METHODS

Sources of Data

Data were obtained from the national VHA ambulatory event database. This database captures ambulatory encounters occurring in hospital outpatient departments as well as smaller satellite facilities and community clinics. The database contains information on diagnosis, procedure, type of clinic visited, and demographic characteristics of patients, as well as a unique encrypted patient identifier. In FY 2004, the database included data from all of the 21 Veterans Integrated Service Networks for ~5.1 million unique patients with ~72 million outpatient encounters.[30] The study population was all VHA patients aged ≥65 years who had a fall-related outpatient health care encounter (as indicated by diagnostic code for external cause of injury [E code]) during FY 2004 and who received ≥1 outpatient medication during the study period.

Using the unique encrypted patient identifiers, the encounter data were merged with outpatient pharmacy data from the VHA decision support system (DSS) for FY 2004. The DSS pharmacy data provided information on the drug, fill date, and quantity supplied for each patient. The DSS data set does not include medications filled outside the VHA system, nor does it include information on nonprescription drugs or drug samples acquired independently by the patient. However, many veterans have an incentive to use the VHA for their medications because of the low VHA copayment. The working data set included detailed information on all patients with fall E-coded outpatient encounters coupled to detailed information on the patients' drug utilization.

Identifying Outpatient Fall E-Coded Encounters and Comparison Group

The *International Classification of Diseases, 9th Revision, Clinical Modification* (*ICD-9-CM*)[31] uses E codes (E880–E888) to signify fall-related injuries due to slips, trips, or falls unrelated to transportation. Records were included in the analysis if a fall E code appeared in any of the 10 diagnosis fields (1 primary diagnosis and 9 secondary diagnosis fields). E codes are historically underreported in hospital discharge, emergency department, and outpatient encounter data sets.[32] We recognize that E codes are also underutilized in the VHA outpatient setting. However, previous research on VHA outpatient fall E-coded encounters found that when E codes were assigned, there was a fall noted in the medical record, supporting the validity of their use.[33] The type of comorbidities, injuries, and clinic sites of service have been described in our recently published work.[33]

We identified patients with fall-coded encounters and an exact age- and sex-matched comparison group from a pool of >180,000 outpatient nonspecific chest pain patients identified in FY 2004. We selected this comparison group to identify and analyze differences in the particular medications between this patient group and those who fell. Patients with chest pain were identified by their primary diagnosis *ICD-9-CM* codes, using clinical classification software (CCS 102) from the Agency for Healthcare Research and Quality (AHRQ [Rockville, Maryland]) to identify *ICD-9-CM* codes for nonspecific chest pain.

We chose patients with nonspecific chest pain for the comparison group because nonspecific chest pain ranks as one of the most common reasons for outpatient visits and is an important symptom in cardiovascular disease.[34] There are 3 *ICD-9-CM* codes in the AHRQ's classification for CCS 102 that identify patients with nonspecific chest pain (ie, 786.50 for chest pain not otherwise specific, 786.51 for precordial pain, and 786.59 for chest pain not elsewhere classified). The use of CCS 102 underscores the clinical importance of ruling out a cardiac cause of chest pain (eg, myocardial infarction, angina, pericarditis) versus a noncardiac cause (eg, gastroesophageal acid reflux, panic attack, pleurisy, cholecystitis). Additionally, recent data about the VHA population for outpatient fall visits found that nonspecific chest pain ranked among the most frequent reasons for an ambulatory care visit.[33]

The first outpatient health care encounter with the requisite coding for each unique patient was included in the analysis. Then we temporally linked both groups' encounters to their respective outpatient medications in the 3 major drug categories of interest. The medication usage of the 2 groups of patients could thus be compared.

Reconciliation of Drug Lists

The data from the DSS outpatient prescription file only contain information about drugs that are on the VHA formulary. To analyze outpatient medications, we first had to reconcile differences between the drug lists. Reconciliation was accomplished by first reclas-

sifying drugs from the Canadian fall risk assessment tool and the Beers criteria list using the US national drug code (NDC). We used the pharmacy benefit management (PBM) VHA drug class NDC crosswalk to determine whether the drugs from the Canadian and Beers criteria drug lists were on the VHA formulary.[35–37] Most medications on the Canadian list are in the corresponding PBM drug categories for medications affecting the CNS, MSS, and CVS. There were additional drugs within these 3 PBM drug categories that were not on the list included in the Canadian fall risk assessment tool but were on the Beers list; these drugs were included in the present analysis because they are related to falls or were new at the time of the study. The drugs included in the analysis and that were found to be linked to outpatient health care encounters through the temporal alignment process, described in the next subsection, are listed in **Table I.**

Temporal Linkage of Outpatient Medications with Outpatient Encounters

We specified time constraints to account for the temporal relationships between use of prescribed medications and outpatient health care encounters. For the purposes of this study, a medication associated with a fall-coded or chest pain encounter was of in-

Table I. Medications used before outpatient health care encounters for falls or nonspecific chest pain (as indicated by diagnostic codes) during fiscal year 2004 among 20,551 patients aged ≥65 years in the Veterans Health Administration system.

Category	Drug(s)
Cardiovascular system	
α-Blockers	Clonidine,* doxazosin,* methyldopa,* prazosin
β-Blockers	Betaxolol, bisoprolol fumarate, carvedilol,† labetalol,† metoprolol,† nadolol, penbutolol, pindolol, propranolol,† sotalol,† timolol†
Angiotensin-II receptor antagonists	Candesartan cilexetil,† irbesartan,† losartan,† telmisartan,† valsartan†
Angiotensin-converting enzyme inhibitors	Amlodipine besylate/benazepril, benazepril,† captopril,† enalapril,† fosinopril,† lisinopril,† moexipril, perindopril,† quinapril,† ramipril†
Antiarrhythmics	Amiodarone,* atenolol, bepridil, digoxin,* dofetilide, eplerenone, esmolol, flecainide acetate, mexiletine, moricizine, nesiritide, procainamide, propafenone, quinidine, verapamil
Blood modifiers	Pentoxifylline
Calcium channel blockers	Amlodipine,† diltiazem,† felodipine,† isradipine, nicardipine, nifedipine,*† nimodipine
Diuretics	Amiloride,† bumetanide, chlorthalidone, furosemide,† hydrochlorothiazide,† indapamide, metolazone, spironolactone, torsemide, triamterene†
Platelet aggregation inhibitors	Cilostazol
Vasodilators	Hydralazine,† isosorbide,† milrinone, nitroglycerin,† papaverine, terazosin†
Central nervous system	
Alzheimer's disease drugs (ie, cholinesterase inhibitors)	Donepezil,† galantamine,† rivastigmine†
Anticonvulsants/barbiturates	Butabarbital,* butalbital,* carbamazepine,*† divalproex,*† ethosuximide,* felbamate,* fosphenytoin,* gabapentin,*† lamotrigine,*† levetiracetam,* mephobarbital, oxcarbazepine,* phenobarbital,† phenytoin,*† primidone,* tiagabine,* topiramate,*† valproic acid,*† zonisamide*

(continued)

terest if it was actively prescribed up to the time of the initial encounter. By using the drug refill date, days' supply, and date of encounter, we programmed 2 simple inequalities:

If drug refill date ≥ encounter date, then delete. (1)

If drug refill date + days supplied ≥ encounter date, then output. (2)

The first inequality eliminated all outpatient medications prescribed after the time of the outpatient encounter. This was important because a patient might have been prescribed a narcotic or opioid after the initial outpatient encounter, but not before the encounter, and therefore the drug could not be a potentially contributing factor. On the other hand, the second inequality retained the potentially problematic medications for which there was a sufficient supply prescribed up to the time of a health care encounter. Finally, after implementing our constraints, we analyzed the data with bivariate statistics. Because our analysis incorporated a large number of χ^2 tests, we used a Bonferroni adjustment to control for experiment-wise type I error.[38] All analyses were conducted with SAS version 9.1 (SAS Institute Inc., Cary, North Carolina).

Table I. (Continued)

Category	Drug(s)
Antidepressants	Amitriptyline,*† amoxapine, bupropion,† buspirone, citalopram,† clomipramine,† desipramine,† doxepin,*† fluoxetine,*† fluvoxamine,† imipramine,† maprotiline, mirtazapine,† nefazodone, nortriptyline,† paroxetine,† phenelzine, protriptyline, sertraline,† tranylcypromine, trazodone,† venlafaxine†
Antihistamines and antinauseants	Acetazolamide, meclizine,*† methazolamide*
Antiparkinsonian agents	Carbidopa/levodopa,† entacapone,† pergolide,† pramipexole,† ropinirole, selegiline,† tolcapone
Antipsychotics	Aripiprazole, chlorpromazine,† clozapine,† fluphenazine, haloperidol,† lithium,† loxapine,† mesoridazine besylate, molindone, olanzapine,† perphenazine,† pimozide, quetiapine,† riluzole, risperidone,† thioridazine,*† thiothixene, trifluoperazine,† ziprasidone
Benzodiazepines	Alprazolam,*† chlordiazepoxide,*† clonazepam,*† clorazepate,*† diazepam,*† flurazepam,*† lorazepam,*† midazolam,*† oxazepam,*† temazepam,*† triazolam*†
Hypnotics	Chloral hydrate, meprobamate,* zaleplon, zolpidem tartrate
Narcotics, opioid analgesics	Bupivacaine, buprenorphine/naloxone, butorphanol, codeine,† fentanyl,† hydrocodone, hydromorphone,† levorphanol, lidocaine, meperidine,* methadone, morphine,† nalbuphine, naloxone, opium, oxycodone,† pentazocine,*† propoxyphene,† tramadol
Musculoskeletal system	
Muscle relaxants	Baclofen, carisoprodol, chlorzoxazone,* cyclobenzaprine,* dantrolene, metaxalone,* methocarbamol,* mivacurium, orphenadrine,* tizanidine
NSAIDs‡	Celecoxib, diclofenac, diflunisal, etodolac, flurbiprofen, indomethacin,* ketoprofen, ketorolac,* nabumetone, naproxen,* oxaprozin,* piroxicam,* rofecoxib, sulindac, tolmetin,† valdecoxib

*Beers criteria drugs.
†Canadian fall risk assessment tool drugs.
‡Excludes acetaminophen, aspirin, and ibuprofen because they do not require a prescription.

This study was reviewed by all relevant institutional review boards and complied with human protection standards. The cutoff for statistical significance was $P < 0.002$, based on the Bonferroni adjustment.

RESULTS

We identified 20,551 patients with fall-coded encounters and 20,551 exact age- and sex-matched comparison patients from a pool of >180,000 patients with outpatient nonspecific chest pain encounters in FY 2004 (**Figure 1**). Of the patients selected for our study, 95.25% (19,574/20,551) were male, and the mean (SD) age was 78 (6.48) years (range, 65–105 years). **Figure 2** shows the distribution of fall-coded encounters by age. The age and sex distributions were the same for both study groups because they were matched. **Table I** lists the specific medications, aggregated into drug classes and the 3 major drug categories, that were used before the outpatient health care encounter. **Table II** shows how many patients in each group used drugs in these categories and classes. The percentages represent the proportion of total patients that were prescribed the medication in each patient group. For example, of the patients with fall-coded encounters, 63.07% (12,962/20,551) were prescribed a drug in the CVS category.

There was no significant difference in the number of patients who used fall-related medications in the nonspecific chest pain and fall-coded groups (15,567 [75.75%] vs 15,366 [74.77%]; P = NS). However, more patients with nonspecific chest pain received CVS medications (14,207 [69.13%] vs 12,962 [63.07%]; $P < 0.002$) and more patients with fall-coded encounters received CNS medications (8642 [42.05%] vs 6019 [29.29%]; $P < 0.002$). There were no statistically significant differences in the overall MSS category between the 2 groups. However, within the MSS category, more patients in the nonspecific chest pain group than in the fall-coded group used NSAIDs (6.44% vs 5.63%; $P < 0.002$).

Within the CVS category, significantly more patients with nonspecific chest pain than fall-coded encounters received antiarrhythmics and drugs from the antihypertensive drug classes of angiotensin-II receptor antagonists, angiotensin-converting enzyme inhibitors, β-blockers, calcium channel blockers, vasodilators, and diuretics (all, $P < 0.002$). However, there was no difference in the proportion of patients who used α-blockers. Within the CNS category, significantly more fall-coded patients used opioid analgesics and narcotics, hypnotics, antiparkinsonian agents, and the psychotropic drug classes of cholinesterase inhibitors, anticonvulsants and barbiturates, antidepressants (including the selective serotonin reuptake inhibitors, tricyclic antidepressants, and others), antipsychotics (including both atypical antipsychotics and typical

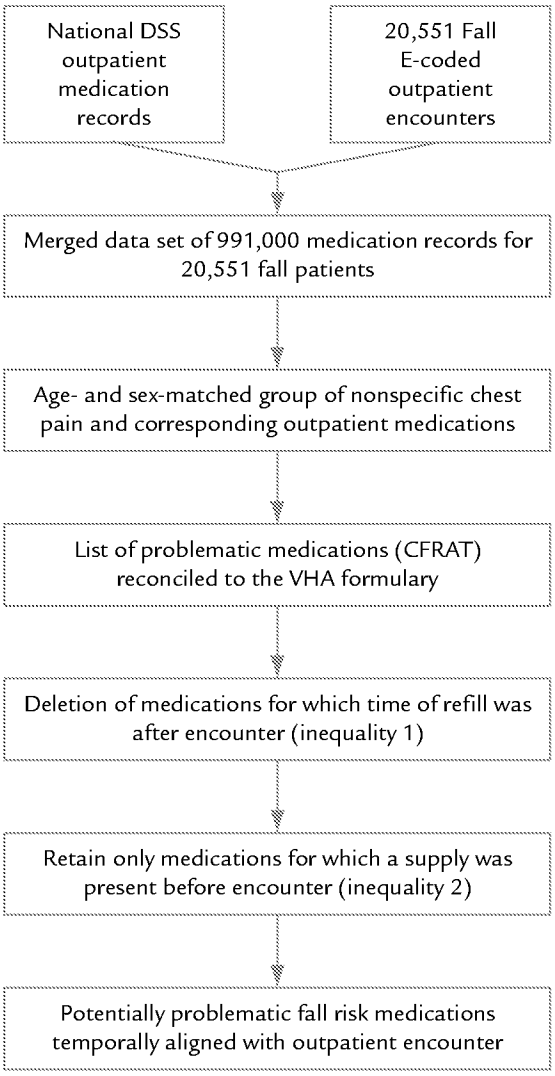

Figure 1. Data set linkages for outpatient health care encounters for falls or nonspecific chest pain (as indicated by diagnostic codes) during fiscal year 2004 among patients aged ≥65 years in the Veterans Health Administration (VHA) system. DSS = decision support system; CFRAT = Canadian fall risk assessment tool.

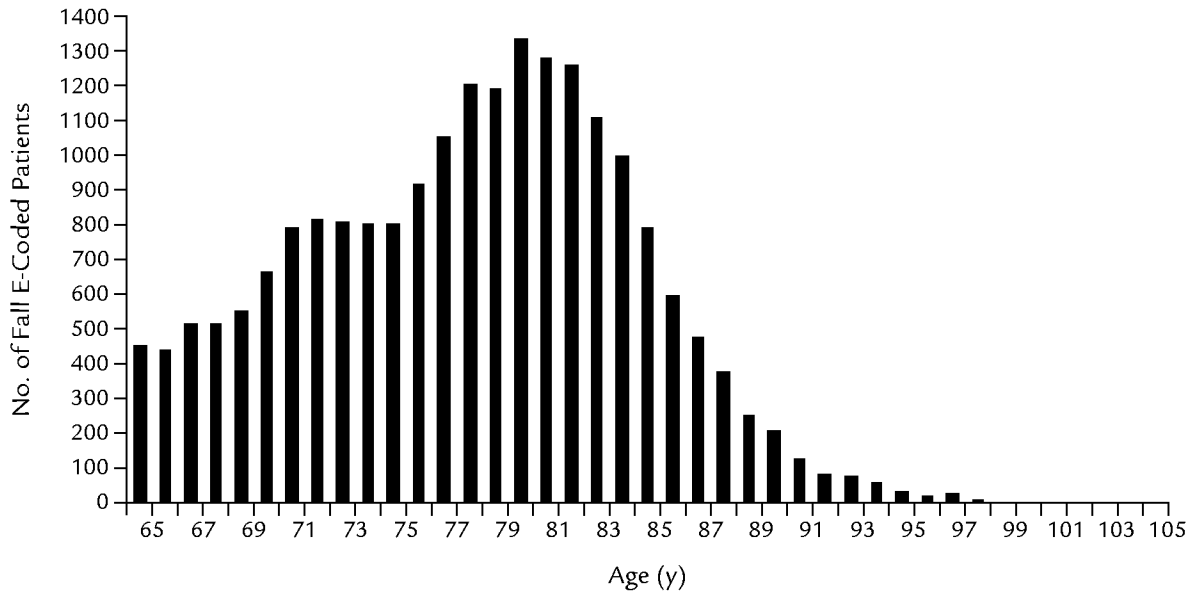

Figure 2. Distribution of patients seen at outpatient health care encounters, by age, for falls (as indicated by diagnostic codes) during fiscal year 2004 among patients aged ≥65 years in the Veterans Health Administration system.

neuroleptics), and BZDs (all, $P < 0.002$). However, there was no difference between groups in the use of antihistamines and antinauseants.

Finally, using structured query language, we calculated the mean number of fall-related medications and total medications per patient. Those in the fall-coded group used a mean (SD) of 3.34 (2.24) (n = 15,366) fall-related medications, compared with 3.20 (2.14) (n = 15,567) in the nonspecific chest pain group (P = NS). The mean (SD) total number of medications used was 6.56 (4.95) (n = 17,451) in the fall-coded group and 6.20 (4.71) (n = 17,540) in the nonspecific chest pain group (P = NS).

DISCUSSION

This is the first national study of veterans that examined their outpatient use of particular drugs temporally linked with a fall-coded health care encounter. A comparison group of veterans with nonspecific chest pain was used to provide context for the impact of these medications. This comparison group was particularly useful in the analysis because the overall assessment of the number of individuals in both groups receiving prescriptions for these selected medications, and the mean number of prescriptions in each patient group, might have suggested there were no differences between the groups. However, a more focused analysis of differences between the major drug categories revealed an important difference between the 2 patient groups: significantly more of those with fall-coded health care encounters were prescribed CNS medications ($P < 0.002$).

We examined 3 categories of potentially high-risk medications that have been implicated in increasing the risk of falling. Within these broad drug categories, certain drug classes were more commonly associated temporally with falls. Our results suggest that some drugs, mainly in the CNS drug category, deserve particular attention, especially for elderly male veterans. Anticonvulsants and barbiturates, antidepressants, antipsychotics, opioid analgesics, antiparkinsonian drugs, agents used to treat Alzheimer's disease (ie, cholinesterase inhibitors), and muscle relaxants may, in fact, have some influence on the risk for falls in community-dwelling older veterans. Against the backdrop of the large number of outpatient prescriptions filled in the VHA for these 3 major drug categories, our study suggests that it might be more appropriate to narrow the focus of future studies to the high-risk category of CNS medications.

In our previous research examining concomitant use of BZDs and other high-risk medications in conjunction with the risk of injury,[26,27] we found that

Table II. Medications used by patients seen at outpatient health care encounters for falls or nonspecific chest pain (as indicated by diagnostic codes) during fiscal year 2004 among patients aged ≥65 years in the Veterans Health Administration system.*

Variable	Fall-Coded Encounters (n = 20,551)	Nonspecific Chest Pain Encounters (n = 20,551)
Cardiovascular system, no. (%)†	12,962 (63.07)	14,207 (69.13)‡
Antihypertensives		
Angiotensin-II receptor antagonists	806 (3.92)	957 (4.66)‡
Angiotensin-converting enzyme inhibitors	5713 (27.80)	6,254 (30.43)‡
α-Blockers	647 (3.15)	688 (3.35)
β-Blockers	3356 (16.33)	3921 (19.08)‡
Calcium channel blockers	2520 (12.26)	2909 (14.16)‡
Vasodilators	4271 (20.78)	5952 (28.96)‡
Diuretics	5711 (27.79)	5986 (29.13)‡
Antiarrhythmics	3815 (18.56)	4272 (20.79)‡
Blood modifiers	128 (0.62)	108 (0.53)
Platelet aggregation inhibitors	51 (0.25)	52 (0.25)
Central nervous system, no. (%)†	8642 (42.05)‡	6019 (29.29)
Psychotropics		
Alzheimer's disease agents§	1110 (5.40)‡	483 (2.35)
Anticonvulsants/barbiturates	1839 (8.95)‡	1065 (5.18)
Antidepressants	4624 (22.50)‡	2909 (14.16)
Selective serotonin reuptake inhibitors	3332 (16.21)‡	1846 (8.98)
Tricyclic antidepressants	707 (3.44)‡	492 (2.39)
Other	1230 (5.99)‡	893 (4.35)
Antipsychotics	962 (4.68)‡	413 (2.01)
Atypical antipsychotics	847 (4.12)‡	338 (1.64)
Typical neuroleptics	145 (0.71)‡	87 (0.42)
Benzodiazepines	1562 (7.60)‡	1224 (5.96)
Antihistamines/antinauseants	259 (1.26)	250 (1.22)
Narcotics and opioid analgesics	2303 (11.21)‡	1869 (9.09)
Hypnotics	118 (0.57)‡	72 (0.35)
Antiparkinsonian agents	754 (3.67)‡	271 (1.32)
Musculoskeletal system, no. (%)†	1520 (7.40)	1636 (7.96)
Muscle relaxants	435 (2.12)	383 (1.86)
NSAIDs	1157 (5.63)	1323 (6.44)‡
Fall-related drugs		
Patients, no. (%)	15,366 (74.77)	15,567 (75.75)
Drugs used before encounter, mean (SD), no.	3.34 (2.24)	3.20 (2.14)
Any medication before encounter, mean (SD), no.	6.56 (4.95)	6.20 (4.71)

*Groups were matched for age and sex.
†Some patients had prescriptions for ≥1 drug.
‡$P < 0.002$, based on Bonferroni adjustment and 30 independent χ^2 tests.
§Cholinesterase inhibitors.

~72% (790/1110) of the injuries were associated with major drug–drug interactions at the time of injury. These 2 studies consisted of a subset of BZD patients (13,745/17,558) at James A. Haley Hospital from 1999 through 2001 for whom we had complete vital data measures recorded (eg, height, weight, body mass index, blood pressure). A multivariate model was specified that examined injuries in these patients while controlling for age, major drug–drug interactions, vital measures, dose and duration of BZDs, and selected Elixhauser comorbidities[39,40] with a look-back period for historical comorbidities (ie, 1998). Examples of this relationship between drug use and injury risk included concomitant use of BZDs with azole antifungals, barbiturates, and other medications. In the multivariate analyses for one of these studies,[27] interaction between a BZD and another drug was associated with a more than 2-fold increase in injury risk, while controlling for comorbidities and other characteristics. In the current study, patients may have had similar types of drug interactions, particularly those taking drugs in the CNS category. Further research is warranted to appreciate the impacts of combinations of these high-risk medications.

The present study was possible because of the unique national data sets available in the VHA. A PubMed search was conducted with the key terms *national*, *outpatient medication*, *injury*, and *United States* for all years and languages to identify national studies in the United States of outpatient medications as a risk factor associated with outpatient health care encounters for unintentional injuries. We excluded studies that only examined adverse drug events because we were interested in the medications as a risk factor for injuries. Based on a review of the literature, no US medication safety studies have been based on national outpatient medication data linking detailed information about outpatient prescriptions, including dosing and timing, to health care utilization associated with injuries. The data available through the VHA system allows one to study the association between a particular drug and an injury or adverse event by identifying a population at risk and then linking outpatient medications with health care utilization in that population. In our opinion, there is no other comparable national drug safety research capability that includes a national electronic medical record and data on health care utilization across as many care settings in the United States.

Comprehensive national outpatient medication usage data at the patient level are currently not available for researchers from the Medicare program. The new Medicare Part D outpatient medication benefit was implemented nationally in January 2006. Because of the large number of private Medicare prescription drug plans with nonstandardized formularies, it is not clear how, when, or if any of the outpatient medication data in the Part D benefit will be available to researchers. In our opinion, countries with national health care systems (eg, Canada, Australia, Finland, Sweden, the United Kingdom) and large managed health care systems in the United States currently have the ability to link data in such a way.

This study had several limitations. Our population was predominantly older and male, and all patients were military veterans; the results may not be generalizable to the overall population of the United States. The analyses relied on E codes to identify fall-related outpatient health care encounters, which are typically underreported; furthermore, we do not know the exact magnitude of the underreporting in the VHA outpatient setting.[33] Additionally, some veterans can receive care under the Medicare program from non-VHA providers and facilities[41]; these data were not captured in our analyses. Future research at the Patient Safety Center in Tampa, Florida, will link available Medicare data from the US Department of Veterans Affairs Medicare data sets so that this health care utilization is captured.[42]

We temporally linked potentially problematic medications with fall-coded encounters without adjustments for dose and duration. We recognize that our analysis does not imply causation. However, the medications we examined have been linked by other researchers to increased fall risk. Particular diseases and disabilities are known to be associated with high risk for falls and injuries (eg, Parkinson's disease, dementia, seizure disorders, amputation).[43] It was not possible, with this study design, to determine the relative contribution of the disease, the medications, or other confounding factors to the risk of an injury due to a fall, nor was it possible to determine the exact indication for which the medication was prescribed. Future research based on national data will use multivariate models similar to previously published single-site studies of medications linked to injuries.[26,27] Investigators using multivariate models should include information on medication dose and duration, along with comorbidities (eg, alcohol abuse, drug abuse, hyper-

tension) linked to specific types of fall-related injuries treated in the outpatient setting.

This study was part of a patient safety research agenda at the Patient Safety Center that includes developing a medication safety surveillance system that uses national data to link medications with falls, fall-related injuries, and other adverse events in older individuals. Previous studies have reported that a considerable proportion of older individuals are being prescribed potentially inappropriate medications.[22,23,44–46] Few studies have examined the temporal linkages between particular medications and actual injuries and other adverse events.[8,26–29] Establishing such connections is critical to developing evidence-based fall risk assessment tools and effective interventions for fall-prevention programs.[3,6,24,43,47] The results of the present study are consistent with our previous findings that CNS medications may be related to increased risk for injuries and other adverse events.[8,26–29] Additionally, this study reinforces the importance of a medication review as part of the JCAHO 2006 patient safety goal to implement and evaluate fall risk reduction programs.

CONCLUSIONS

In this study, subjects with a health care encounter for a fall (as indicated by diagnostic code) were prescribed significantly more CNS-category medications than subjects in the age- and sex-matched comparison group. Medication reviews are an important component of a comprehensive fall risk assessment in older patients. Multifactorial fall reduction programs, which include a comprehensive review of medications, have been shown to be effective in outpatient and nursing home patients.

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