Potentially Inappropriate Medications (PIMs) and Falls Risk in Older American Indians and Alaska Native Adults: A Pilot Study

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Introduction

Each year in the United States, one in three older adults experiences a fall. Falls are the leading cause of nonfatal injuries, hospitalizations, and injury-related deaths for individuals aged 65 and older.^{1,2}

The association between medications and increased risk of falls applies to both the number of medications used currently (polypharmacy); and to specific medications and medication classes. In a previous article, we called attention to the frequency of "polypharmacy" (concurrent use of multiple medications) among older American Indians and Alaska Natives (AI/AN) represented in the IHS National Data Warehouse (NDW) data.³ Polypharmacy increases the risk of falls by increasing the risk of medication compliance errors, adverse events, and drug-drug interactions.⁴

Specific medications and medication classes are independent risk factors for falls in the elderly.^{4,5} For example, neuroleptics, benzodiazepines, and antidepressants are noted by the American Geriatric Society to increase the risk of falls, especially in high-risk patients (e.g., those with previous falls or dementia).^{6,7} In a 2005 study, the relative risk for falls among users of olanzapine and other psychotropics was 3.25 (95% CI 1.96 - 5.40).⁸ A 2009 study found the relative risk of falling for users of long-acting benzodiazepines was 1.46 (95% CI 1.23 - 1.74).⁹

There are numerous mechanisms by which specific medications can contribute to an increased risk of falls. They include impairment of balance, lowered reaction times, sedation, dizziness, hypoglycemia, orthostatic hypotension, cardiac arrhythmias, and gait disturbances. Medications with anticholinergic properties can predispose the elderly to falls through multiple mechanisms, such as blurred vision, arrhythmias, impaired cognition, and unsteady gait.¹⁰ Anticholinergic medications are additive in their adverse effects.¹¹

In this pilot study, we explored the value and limitations of National Data Warehouse data to identify prescribing practices for older AI/AN that are potentially inappropriate due to falls risk.

Methods

To create our list of potentially inappropriate medications (PIMS) related to falls risk, we first conducted a literature review of medications associated with an increased risk of falls. Based on this review, we chose two categories with a strong evidence base for falls risk: medications with anticholinergic properties and medications associated with cognitive impairment (dizziness, confusion, sedation). Medications in these classes typically have safer alternatives to substitute.

We then referred to two sources of information that are commonly used to avoid prescribing potentially inappropriate medications for the elderly: the "2003 Beers list"¹² and the Health Plan Employer Data and Information Set (HEDIS).¹³ The Beers list was developed using Delphi methods to obtain consensus among content experts. "The criteria covered two types of statements: 1) medications or medication classes that *should generally be avoided* in persons 65 years or older because they are either ineffective or they pose unnecessarily high risk for older persons and a safer alternative is available; and 2) medications that should not be used in older persons known to have *specific medical conditions*."¹⁴

HEDIS measures are widely used to assess the quality of managed care plans and federal health care programs, such as Medicare and the Veterans Administration.¹⁵ We included medications on the most recent HEDIS lists, as well as proposed changes for HEDIS 2012.¹⁶ The HEDIS lists are from two categories, "Use of High Risk Medications in the Elderly"; and "Potentially Harmful Drug-Disease Interactions in the Elderly" (anticholinergic agents, antipsychotics and sleep agents, tricyclic antidepressants).

To create our PIMS list, we identified ten medications/

(1) Name of drug or class	(2) VA Classification Code(s)	(3) Examples*	(4) Common reasons for prescribing	(5) Falls risk	(6) Comments	(7) % of population receiving a prescription
Propoxyphene	Searched by name	Darvon™	Pain relief	Cognitive impairment, Confusion, Sedation	Ordered removed from the market in November 2010	2.3%
Antihistamines	AH100, AH102, AH104,AH105, AH107, AH200	diphenhydramine (BenadrylTM), chlorpheniramine (Chlor-Trimeton TM)), hydroxyzine (AtaraxTM)), promethazine (PhenerganTM)	Allergies, insomnia, nausea, urticaria.	Anti-cholinergic	Excluded "non-sedating" histamines such as loratadine (AH109) and fexofenadine (AH106).	11.2%
Parasympatholy tics/Gl antispasmodics	AU350	dicyclomine (BentylTM), hyoscyamine, propantheline Treat irritable	bowel syndrome.	Anti-cholinergic	Excluded benztropine (indicated for treatment of certain neurologic disorders) and glycopyrrolate (indicated for ulcer treatment).	0.8%
Tricyclic antidepressants	CN601	amitriptyline (ElavilTM)), imipramine, doxepin	Depression, fibromyalgia, neuropathic pain, insomnia	Anti-cholinergic, sedative	Excluded nortriptyline and desipramine. Desipramine was specifically excluded in Beers 2003. Nortriptyline has far less anticholinergic properties than amitriptyline, and is proposed for exclusion in HEDIS 2012.	2%
Phenothiazine/ related anti- psychotics	CN701	thioridazine (MellarilTM))	Anti-psychotic.	Cognitive impairment, confusion, Sedation,	FDA Black Box Warning (FDA's highest level of warning) for treating dementia in the elderly	< 0.1%
Other anti- psychotics	CN709	clozapine (ClozarilTM), aripiprazole, haloperidol	Anti-psychotic	Cognitive impairment, Confusion, Sedation	FDA Black Box Warning for treating dementia in the elderly.	0.4%
Barbiturates	CN301	phenobarbital, secobarbital, pentobarbital	Sedative/ hypnotics, pain relief, phenobarbital for seizures	Cognitive impairment, Confusion, Sedation	Beers 2003 excludes phenobarbital for use in seizures, HEDIS includes phenobarbital.	0.1%
Benzodiazepine derivatives and clonazepam	CN302 + clonazepam (searched by name)	diazepam (ValiumTM), chlordiazepoxide (Librium)	Sedative/ hypnotic, anxiolytic, anti- epileptic.	Cognitive impairment, Confusion, sedation	Beers 2003 includes all benzodiazepines when an individual is at risk for falls.	2.8%
Antispasmodics, urinary	GU201	oxybutynin (DitropanTM)	Urinary incontinence	Anti-cholinergic	Beers 2003 specifically excluded oxybutynin extended release.	1.3%
Skeletal muscle relaxants	MS200	cyclobenzaprine (FlexerilTM), methocarbamol (RobaxinTM), metaxalone (SkelaxinTM), orphenadirine (NorflexTM)	Muscle Spasm	Anti-cholinergic	Excluded baclofen tizanidine and dantrolene – not on Beers 2003.	3.5%

medication classes that are associated with the two categories of falls risk and that are potentially inappropriate for elders in general or who have a history of falls according to Beers 2003 criteria and/or HEDIS lists. These are shown in Table 1, along with the Veterans Administration (VA) classification for each medication class.

We then submitted our PIMs list to the NDECI Data Mart to determine how many patients 65 years and older were

prescribed one of the focus medications or medication classes in FY 2008. We described the NDECI data mart in our previous publication.3 Briefly, IHS Environmental Health Division's Notifiable Disease and External Cause of Injury (NDECI) data mart contains data and analytical information derived from the National Data Warehouse (NDW). The latter is a national repository of health care information, over 90% of which comes from local IHS and tribal sites that use RPMS (Resource and Patient Management System) as their information technology system. NDW data includes demographic data, third-party eligibility information, and clinical data. Prescription information in the NDW includes the medication name, National Drug Code (NDC) code, and VA drug class code. We chose the VA drug class codes for our search because they are broader than the NDC codes. The latter are especially cumbersome because for the same medication, there are separate codes for each manufacturer, strength, dosage form, and package size.

We searched the NDW data for all patients age 65 years and older receiving one or more of the targeted medications in fiscal year 2008. All the counts were based on distinct integrity identity numbers, which refer to distinct patients. Two medications, propoxyphene and clonazepam, were searched by name rather than by drug class. The age and gender of each patient was recorded; no patient identifiers were collected. Permission to publish this manuscript was obtained from the National IHS Publication and Review Committee.

Results

Overall, nearly one in five older adults (19%) in the NDW database received a potentially inappropriate medication associated with increased falls risk due to central nervous system effects or anticholinergic properties (Table 2). There was a clear male/female disparity: 15.3% of males were prescribed a PIM compared to 22% of females. For both males and females, the percentage of individuals receiving a PIM declined with increasing age. About a fourth (24%) of women 65 - 74 years of age, and 16% of men, received one or more PIMs, compared to 16% of women and 12% of men 85 years and older.

As shown in Table 1, the most frequently-prescribed PIM was a sedating antihistamine: 11% of patients 65 years and older received a prescription for a sedating antihistamine during FY 2008. Other medications prescribed to 2% or more of the target population were skeletal muscle relaxants (4%), benzodiazepines (3%), propoxyphene (2%) and tricyclic

	User Pop	# Receiving One or More Meds	% Receiving One or More Meds
MALES			
Males 65–74	17,154	2,706	15.8%
Males 75–84	7,460	1,115	14.9%
Males 85+	1,875	233	12.4%
Subtotal	26,489	4,054	15.3%
FEMALES			
Females 65–74	24,107	5,791	24.0%
Females 75–84	11,647	2,396	20.6%
Females 85+	3,763	595	15.8%
Subtotal	39,517	8,782	22.2%
TOTAL			
All 65–74	41,261	8,497	20.6%
All 75-84	19,107	3,511	18.4%
All 85+	6,638	828	14.7%
Subtotal	66,006	12,836	19.4%

Table 2. National Data Warehouse: Patients 65 years and older receiving one or more selected potentially inappropriate
medications for falls risk FY 2008

antidepressants (2%). Medications prescribed to 1% or less of the target population were urinary antispasmodics (excluding extended release forms of oxybutynin), parasympatholytics/GI antispasmodics, phenothiazines, other anti-psychotics, and barbiturates.

Discussion

Medication therapy in the elderly is always a balancing act, requiring assessment of the benefit for a specific medication against potential risks.^{14,17} This pilot study focused on medications for which there is strong evidence for potential percentage (11%) of patients received first generation antihistamines such as diphenhydramine, chlorpheniramine, or hydroxyzine. These may cause somnolence, central nervous (CNS) system dysfunction, and other anticholinergic side effects. Except to treat severe allergic reactions, a first generation antihistamine should rarely be used, given that safer alternatives are available for all other indications (e.g., loratadine for allergies and ondansetron for nausea).²⁰

Two percent of the elderly were being prescribed propoxyphene during FY 2008. This was in spite of the substantial evidence that propoxyphene was no better than

increased risk of falls and published expert recommendations for avoidance of use in older adults (2003 Beers list and HEDIS tables).

The percent of individuals who received prescriptions for PIMs decreased from 20.6% in the 65 - 74 age group, to 18.4% in the 75 - 84 age group, to 14.7% in the 85+ age group. This may represent an awareness by prescribers of both the increased likelihood of falls and the increased risk of these medications in the elderly; or may represent a general pattern of declining medication use in the older cohorts.

Antipsychotics are among the most consistently-cited class of medications that are potentially inappropriate for the elderly, especially those with pre-existing risks for falls.^{4,7,18,19} We found that antipsychotics (both typical and atypical) are rarely prescribed to the NDW older population. with less than 0.5% of this population receiving prescriptions 2008. in Prescriptions for barbiturates were also very infrequent (0.1%).

A relatively large

Table 3. PIM prescription rates: Guidlines for local RPMS services

Item	Comments		
Determine the goal	Determine the goal of this search. For example: publication, support for		
of the search	policy & procedure change, education of clinical staff, falls program		
	development, measurement of programmatic success, etc.		
Determine what	Depending on what the goal of the search, you may need chart numbers for		
data will be	chart review, ages for stratification, medications of concern for		
collected	quantification/comparison by medication or class, dates for discovering		
	trends over time, other prescribed medications for polypharmacy		
	identification, prescribing physician for targeted education, etc.		
IHS & Local Data	Determine what type of permission from what authority (IHS – National		
Collection Rules	and/or local, tribal, or other) must be obtained. Typically, the wider the		
	distribution more permission needed.		
Drug(s)/medication	Determine what medications are to be searched by using Beer's List, HEDIS,		
list(s) used to guide	other lists, and/or a selection of these lists based on local formulary as a		
search	guide and combine facility specific information such as falls report trends,		
	incident reports, adverse reactions reported or other mechanisms that may		
	be in place.		
Searching by drug	Searching by NDC may be appropriate for a local search with a small		
	number of medications for the search over a short period of time. Searching		
	by drug name or VA drug class is more efficient than obtaining individual		
	NDC numbers for reasons discussed in the text. Most RPMS systems are		
	automatically downloaded with this information; however, drug file patches		
	may require some VA classes to be entered manually.		
RPMS Search	Multiple search methods are available in RPMS to extract the necessary		
Methods	data. VGEN and QMAN are two such searches. If unfamiliar with VGEN		
	and QMAN, the RPMS Site Manager may be able to run the report if		
	provided the proper information. Some other positions within most facilities		
	that use VGEN and QMAN frequently are the HIM Director, PQS Director,		
	Infection Control Officer, and Utilization Review Officer. Parameters for the		
	search that will provide the most complete and accurate data will be		
	dictated by the topics mentioned above.		
	Tips: These searches will include all patients unless otherwise stated.		
	Reduce the number of results by searching living patients only. When		
	building searches it will be helpful to answer yes when asked to include all		
	drugs in similar classes. Results for these searches can be exported into		
	Excel® where they can be further manipulated.		
Review Results	Data may be missing, or unnecessary data may be included in the results		
	due to improper search parameters, wrong or outdated VA class codes in		
	drug file, missing VA class codes in drug file, or drugs with multiple possible		
	VA class codes. Therefore, verification of search results is recommended to		
	assure all appropriate drugs are included in the RPMS search and to		
	eliminate unnecessary data captured in error.		

acetaminophen for pain relief, caused sedation, and was associated with an increased risk of fractures in the elderly. The FDA requested that manufacturers voluntarily remove all propoxyphene-containing products from the market in November 2010.²¹

Comparing the rate of use of PIMs in different studies is problematic because there are numerous, differing lists of what constitutes a PIM,²²⁻²⁶ specific medications are sometimes not identified, and study populations differ by age, presence of comorbidities, and other variables. Nevertheless, two studies involving Veterans Administration (VA) populations are relevant to our study. A 2006 study of inappropriate prescribing in a VA population of older adults utilized the 2006 HEDIS list. In that study, 20% of patients were prescribed a PIM, very similar to the 19% that we identified.15 Another VA study examined gender differences in rates of PIM prescribing.27 Utilizing the Beers criteria in FY 2000, the study documented that "analgesic, psychotropic, and anticholinergic medications that should be avoided contributed to higher rates of inappropriate drug use among older women than among older men." The disparity remained even after controlling sociodemographic characteristics, number of medications, and care characteristics. These findings are consistent with our results of a higher percentage of women than men receiving PIMs (22%) vs. 15%).

Strategies to improve pharmaceutical care quality in ambulatory older adults using multiple medications include pharmacist-centered interventions (such as face-to-face consultations with patients), multidisciplinary teams, and computer feedback.^{17,28} Several studies have explored the role of pharmacists in helping to reduce PIMs in the elderly.²⁹⁻³² In fact, The Patient Protection and Affordable Care Act states that Medicare Part D beneficiaries should, at a minimum, have "an annual comprehensive medication review furnished person-toperson or using telehealth technologies . . . by a licensed pharmacist or other qualified provider."33 The CDC includes education programs for older adults and their caregivers and medication review and management as two of the five building blocks of effective community-based fall prevention programs.² The American Geriatrics Society Clinical Practice Guideline for Prevention of Falls in Older Persons suggests withdrawal or minimization of psychoactive medications and other medications as part of a comprehensive, evidence-based strategy.6 A recent Cochrane meta-analysis showed that prescribing modification programs can decrease the risk of falling in the community dwelling elderly (RR = 0.61).³⁴

Conclusions

The National Data Warehouse is a rich source of prescribing information for IHS and tribal health facilities. Our methods for extracting and analyzing data can be generalized and used locally to assess prescribing practices for both individual medications and entire medication classes; and to serve as a baseline for interventions to reduce inappropriate prescriptions and subsequent adverse outcomes, such as falls (Table 3). The literature supports specific clinical-, community-, and pharmacy-based interventions to reduce prescribing of potentially inappropriate medications.

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