Medications and fall-related fractures in the elderly

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Abstract

Objectives

This article examines associations between the use of selected medications and fall-related fractures in the household population aged 65 or older.

Data source

The analysis was based on cross-sectional data from the household component of the 1996/97 cycle of the National Population Health Survey. Data were from a sample of 13,363 respondents aged 65 or older.

Analytical techniques

Descriptive statistics and multivariate analyses were used to study cross-sectional associations between selected medications used in the previous month and fractures occurring in the previous year. Multiple logistic regression analyses controlled for potentially confounding factors.

Main results

Among elderly individuals who sustained any activity-limiting injury in 1996/97, an estimated 65,000 reported the most serious such injury had been a fall-related fracture. The odds of a fall-related fracture were significantly low among people who were taking diuretics/antihypertensives. Arthritis and urinary incontinence were positively associated with fall-related fractures.

Key words

drugs, falls, risk factors, aged, injury

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Falls account for two-thirds of the most serious activity-limiting injuries sustained by seniors, and about half such falls involve bone fractures.[1] The consequences of fractures are substantial, not only because of individual distress and debility, but also because of the ensuing need for health care and personal assistance.

As people age, anatomical and physiological changes such as decreasing bone density and muscle mass contribute to frailty and increase susceptibility to fractures. As well as aging-related influences, extrinsic factors affect the risk of falls and fractures. Medications comprise an important category of such factors, partly because of their extensive use at older ages and also because of the increased sensitivity to the chemical effects of drugs that occurs with age.[2,3]

Research findings about the relationship between medications and fracture risk in the elderly are somewhat inconsistent. For example, numerous studies suggest that drugs prescribed for depression or anxiety increase the risk of fracture or fall.[4-8] Other research has revealed no such association.[9] Studies of diuretics, used to reduce fluid retention and high blood pressure, report that some

preparations of these drugs lower the risk of falling or fracture.[10-14] Other studies have failed to find such associations, or have even reported increases in fall-related injury or fracture risk attributable to

Methods

Data source

The data are from the 1996/97 cross-sectional Health file of Statistics Canada's National Population Health Survey (NPHS). The NPHS, which began in 1994/95, has both a longitudinal and a cross-sectional component and collects information related to the health of the Canadian population every two years, for up to 20 years. The NPHS surveys household and institutional residents in all provinces and territories, except persons living on Indian reserves, Canadian Forces bases, and in some remote areas. The data file used for this analysis pertains to the household population in the provinces.

The 1996/97 cross-sectional sample is made up of longitudinal respondents and respondents who were selected as part of supplemental samples, or buy-ins, in three provinces. The additional respondents for the buy-ins were chosen with the random digit dialing (RDD) technique and were included for cross-sectional purposes only.

Individual data are organized into two files: General and Health. Socio-demographic and some health information was obtained for each member of participating households. These data are found in the General file. Additional in-depth health information was collected for one randomly selected household member. The in-depth health information, as well as the information on the General file pertaining to that individual, is found in the Health file.

In households belonging to the cross-sectional buy-in component, one knowledgeable person provided the socio-demographic and health information about all household members for the General file. As well, one household member, not necessarily the same person, was randomly selected to provide in-depth health information about himself or herself for the Health file.

Among individuals in the longitudinal component, the person providing in-depth health information about himself or herself for the Health file was the randomly selected person for that household in cycle 1 (1994/95) and was usually the person who provided information on all household members for the General file in cycle 2.

In 1996/97, there were 81,804 respondents to the questions on the Health file. The 1996/97 cross-sectional response rates for the Health file were 93.1% for the longitudinal component and 75.8% for the RDD component, yielding an overall response rate of 79.0%.

This analysis is based on data from the sample of 13,363 people aged 65 or older (weighted to represent 3.4 million people) who completed the Health file interview in 1996/97. Of this number, 564 reported that an accidental fall had caused the most serious activity-limiting injury they had had during the previous 12 months, and 281 of these people had sustained a fracture (Appendix Tables A and B). Although it would have been preferable to use longitudinal data to study relationships between medications and fractures, the sample size of the longitudinal file was not large enough.

A more detailed description of the NPHS design, sample, and interview procedures can be found in published reports.[15,16]

Analytical techniques

All analyses were based on data weighted to represent the household population aged 65 or older in the 10 provinces. Cross-sectional data from the Health file were used to calculate descriptive statistics. This article focuses on people who reported in 1996/97 that they had sustained at least one injury serious enough to interfere with their usual activities in the 12 months before their NPHS interview, and that the most serious such injury was a fracture due to a fall.

Multiple logistic regression was used to model cross-sectional associations of the reported use of certain medications with a fall-related fracture.

The following medications were examined in relation to injurious falls: antidepressants, diuretics, antihypertensives (medicine for blood pressure), heart medication, sleep medication and tranquilizers. It is recommended that antihypertensives be prescribed in conjunction with other drugs, particularly diuretics.[17] Therefore, because people who report using antihypertensives might also inadvertently include diuretics as a medication used for blood pressure, a variable combining diuretics and antihypertensives was defined. For this variable, a report of using either blood pressure medication or diuretics was considered as use.

Other factors relevant to the risk of accidental falls or fractures that were included in the logistic model were: age, sex, household income, alcohol use, smoking, chronic conditions (arthritis/rheumatism, diabetes, the effects of a stroke, urinary incontinence, impaired vision), and body mass index. Standard errors and coefficients of variation were estimated with the bootstrap technique to account for survey design effects.[18,19]

diuretic use.[4,9,20,21] Similarly contradictory results have been reported for drugs used to treat cardiovascular disorders.[5]

Although most studies of fracture risk in the elderly are based on data from clinical patients or residents of specific communities, some research on fracture risk has been carried out on larger, population-representative samples in the United States and elsewhere.[22,23] In Canada, the largest population-based study of drug-related fracture was in Saskatchewan, where researchers using administrative data found a negative association between diuretic use and hip fracture risk.[13]

Data representative of the population of all provinces of Canada have only recently become available. The National Population Health Survey (NPHS) provides the opportunity to study fall-related fractures in relation to medications and to personal, social, demographic and health characteristics (see *Methods, Limitations* and *Definitions).*

The purpose of this article is to provide a better understanding of the association of selected

Limitations

The cross-sectional nature of the National Population Health Survey (NPHS) data used for this analysis precludes any inference of causality. Cross-sectional data do not reveal the temporal sequence of events occurring in the same reference period. Therefore, it was not possible to determine whether variables that have been reported to be risk factors for fractures were antecedents or consequences of fracture. For example, the use of medications to control pain, low level of physical activity, or impaired mobility could precede a fracture, in which case it would be appropriate to consider their contributions as risk factors. However, cross-sectional associations between fracture and any of these factors might also occur because they *resulted* from a fracture. Consequently, these factors were not included in the regression model.

Some differences in the reference periods of the independent and dependent variables limit the interpretation of the findings. For example, data on drug use pertained only to medications that respondents reported taking in the month before being interviewed, while the reference period for a fracture was the entire year before the interview. Although most of the medications selected for study are prescribed for long-term conditions and thus would be more likely to have been in use throughout the year and prior to the fall, it is nonetheless probable that some respondents were misclassified (regarding medication use) in the analysis. This would weaken the observed associations, relative to their true strength.

The NPHS data on medications used in the month before the interview contained no details about the active ingredients. The lack of such information limits the interpretation of the analysis, especially if previous research has associated particular substances with the risk of falling. Similarly, NPHS questionnaire items grouping medications with different active ingredients (for example, "antidepressants," "medicine for the heart" and "medicine for blood pressure") hinder the interpretation of associations of specific medications with fall-related fractures.

The sample size of the NPHS restricts the scope of the analysis. Some variables previously reported to influence the risk of fracture in the elderly could not be examined because of the small number of cases. These variables included hormone replacement therapy. Small numbers may also partially account for the failure of the analysis to reveal associations between some of the independent variables, such as limited vision and fall-related fracture. Although it would have been preferable to analyze each sex separately, the small sample size necessitated pooling the data.

The use of the body mass index for people over age 65 is not universally recommended because the loss of height at older ages may affect the validity of self-report for that measure.[24] Nonetheless, the measure is used frequently in research focused on body weight of older people, as well as in reports dealing with falls and fall-related injury in relation to body weight.[7,23,25-32] However, many studies reporting BMI are based on actual measures of height and weight, whereas NPHS data are self-reported.

The analysis was restricted to the NPHS household sample. Therefore, the results are not generalizable to the total senior population, 5% of whom reside in long-term care facilities.[33] In addition, the unavailability of information on people who experienced falls that resulted in death or institutionalization before data were collected weakens the strength of the observed associations.

Finally, because NPHS data were self-reported, their degree of validity is not known.

Table 1
Fall-related fractures arising from most serious activity-limiting injury, by fracture site, household population aged 65 or older, Canada excluding territories, 1996/97

Fracture site	Number	Percentage
Total	**64,822†**	**100**
Arms/Hands	21,731†	34†
Legs/Feet	16,657†	26†
Hip	12,011‡	19‡
Trunk	5,736†	9†
All others	8,687†	13†

***Data source**: 1996/97 National Population Health Survey, cross-sectional sample, Health file*
***Notes:** See Appendix Table A for sample counts. Because of rounding, detail may not add to total.*
† Coefficient of variation between 16.6% and 25.0%
‡ Coefficient of variation between 25.1% and 33.3%

Table 2
Medication use in past month and selected characteristics, by sex, household population aged 65 or older, Canada excluding territories, 1996/97

	Total	Men	Women
		%	
Medication use			
Antidepressants	4	4†	5
Diuretics/Antihypertensives	36	32	40*
Heart medication	19	21	17*
Sleep medication	8	7	9*
Tranquilizers	5	3	6
Age			
65-74	61	63	60
75+	39	37	40
Household income			
Higher	61	68	56*
Lower	19	14	23*
Missing	20	18	21*
Alcohol use			
Less than daily	90	85	93*
Daily	9	14	6*
Missing	1	1	1†
Smoking			
Never	44	26	58*
Ever smoked	56	74	42*
Chronic conditions			
Arthritis/Rheumatism	42	34	49*
Diabetes	11	12	9
Effects of stroke	4	5	3
Urinary incontinence	6	4	7*
Impaired vision	5	4	7*
Body Mass Index (BMI)			
Not underweight (BMI ≥ 20)	88	93	85*
Underweight (BMI < 20)	8	5	11*
Missing	4	2	5*

***Data source**: 1996/97 National Population Health Survey, cross-sectional sample, Health file*
***Notes:** See Appendix Table B for sample counts. Because of rounding, detail may not add to total.*
‡ Coefficient of variation between 16.6% and 25.0%
** Significantly different from estimate for other sex*

medications with fall-related fractures in the household population aged 65 or older, while controlling for numerous factors that may also affect the risk.

Many fractures

As a result of the most serious activity-limiting injury they experienced in 1996/97, an estimated 65,000 people aged 65 or older (22,000 men and 43,000 women) sustained a fall-related fracture. About one-

Table 3
Adjusted odds ratios of fall-related fracture for selected covariates, household population aged 65 or older, Canada excluding territories, 1996/97

Risk factor	Adjusted odds ratio	95% confidence interval
Medication use†		
Antidepressants	0.7	0.3, 1.7
Diuretics/Antihypertensives	0.5*	0.3, 0.9
Heart medication	1.6	0.9, 2.9
Sleep medication	0.7	0.3, 1.8
Tranquilizers	1.3	0.5, 3.6
Age		
65-74‡	1.0	...
75+	1.7*	1.0, 2.7
Female§	1.2	0.6, 2.2
Household income		
Higher‡	1.0	...
Lower	1.5	0.8, 3.1
Alcohol use		
Less than daily‡	1.0	...
Daily	0.8	0.4, 1.5
Smoking		
Never‡	1.0	...
Ever	0.9	0.5, 1.5
Chronic conditions††		
Arthritis/Rheumatism	1.9*	1.2, 3.0
Diabetes	0.8	0.3, 2.2
Effects of stroke	2.3	0.4, 13.4
Urinary incontinence	2.9*	1.1, 7.2
Impaired vision	2.0	0.7, 6.2
Body mass index (BMI)		
Not underweight‡ (BMI ≥ 20)	1.0	...
Underweight (BMI < 20)	2.1*	1.0, 4.3

***Data source**: 1996/97 National Population Health Survey, cross-sectional sample, Health file*
***Notes:** Because of rounding, some confidence intervals with 1.0 as the lower limit were significant. Analysis is based on 13,156 people. An "unknown" category for household income, alcohol use, and body mass index was included in the model, but the respective odds ratios are not shown.*
† Reference category is not using medication.
‡ Reference category for which odds ratio is 1.0.
§ Reference category is male.
†† Reference category is absence of the condition.
** $p < 0.05$*
··· Not applicable

third of these fractures were of the arms/hands; another quarter, of the legs/feet. Nearly one-fifth of fractures (12,000) were of the hip (Table 1).

Medication use common

More than one-third of seniors reported that they used antihypertensives, diuretics or both, and 19% reported the use of heart medication (Table 2). Sleep medication was reported by 8%, aged 65 or older, and tranquilizer and antidepressant use, by 5% and 4%, respectively. The use of diuretics/antihypertensives and sleep medication was more common among women, while heart medications were in greater use among men.

The causal pathway

Previous reports indicate that numerous factors alter the risk of falls and fall-related injuries. A number of chronic conditions, as well as some medications, have been associated with falls. But it is sometimes difficult to disentangle the effects of variables that are themselves related. For example, an association between falls and a medication might actually be due to another factor that has not been considered, such as the illness for which the medication is being taken. It is thus important to control for the effects of variables that could confound an apparent association.[4,5]

Where possible, multiple logistic regression models of fall-related fractures were constructed to include not only independent variables for medications, but also variables to control for any effects of underlying disease. For example, a variable for high blood pressure was entered in a model with diuretics/antihypertensives (data not shown). High blood pressure was not associated with any altered risk of fracture, suggesting that it is the medication, not the condition for which it is indicated, that is associated with the lower odds of fracture. Similarly, heart disease was included in a model with heart medications and diuretics/antihypertensives (data not shown). The odds ratio for heart disease was not significant.

Because previous research has shown arthritis to be related to falls, it was included in the model as a control variable. To verify that the elevated odds ratio observed for arthritis was associated with the condition rather than with medications taken for it, a variable for pain medication was also included in the model: its odds ratio was not significant (data not shown). These findings suggest that arthritis has an effect independent of analgesics taken by people with the condition.

The only one of these categories of drugs associated with fractures was diuretics/antihypertensives. The odds ratio of fracture among individuals using diuretics or antihypertensives was half that of people not using these drugs (Table 3). This is consistent with numerous reports in the literature. Although the cross-sectional nature of the NPHS data limits the interpretation of observed associations, several large prospective studies carried out in the United States show a protective effect of thiazide diuretics against fracture.[11,12,34] The lowered risk of fracture is thought to relate to the effects of thiazide diuretics in reducing calcium excretion in urine, which results in a positive effect on bone density[11-14,34-36] (see *The causal pathway*).

In contrast to other research,[4,7,37] the NPHS data revealed no association between the use of antidepressants or tranquilizers and fall-related fractures. This may have resulted from the relatively small numbers reporting the use of these medications rather than a true lack of association.

Body mass, chronic conditions

The odds of a fracture were elevated among individuals with a low body mass index. However, because the NPHS data are self-reported and people tend to overstate their height—especially as they get older—the NPHS may overestimate the prevalence of underweight.[38] But despite the probable misclassification of some seniors who were actually the appropriate weight for their height, an association between underweight and fracture persisted. This relationship, which has previously been observed in prospective studies as well as others, relates to lower bone mineral density in people of lower body weight.[17,28,29,39-41]

The association of low body mass with fracture probably also reflects less muscle mass, poor nutrition and greater frailty, factors also related to risk of fracture. The percentage of underweight people who reported their general health as poor or fair was 28%, compared with 22% of those who were not underweight (data not shown).

The odds of fracture among seniors with arthritis/rheumatism or urinary incontinence were significantly elevated, indicating independent

associations with fracture even after controlling for age and other factors. These findings corroborate previously published studies.[9,26,42,43] The physiological relationship between arthritis/rheumatism and fall-related fracture arises from the mobility problems imposed by this disease. For urinary incontinence, the association is probably less direct. Earlier research linking urinary incontinence with hip fracture reported a higher prevalence of neurological disorders in incontinent women than in others.[26] Disorders such as Parkinson's disease and dementia give rise to a cluster of symptoms, including incontinence and gait and balance disturbances. The latter problems are more likely to account for the increase in fall-related injury than urinary incontinence per se. The cross-sectional nature of the NPHS data precluded any interpretation of an association between mobility problems and fall-related fracture. It is possible that urinary incontinence is a proxy for mobility problems arising from neurological disorders.

Concluding remarks

This analysis is the first use of population-based, nationally representative data to examine medication use in relation to fall-related fractures among the elderly. The findings are fairly consistent with other studies, except for the lack of association between tranquilizer use and fall-related injury. Although the cross-sectional nature of the data limits the

Definitions

National Population Health Survey (NPHS) respondents were asked if, in the year before the survey, they had experienced any injury serious enough to limit their normal activities. Those who reported at least one such injury were asked about the type (for example, broken bone or burn) of their most serious injury, the body part injured, and what caused the injury (for example, fall, motor vehicle accident, physical assault). Because the NPHS collected data on only the single most serious activity-limiting injury sustained over the previous 12 months, it was not possible to measure the number and frequency of fall-related fractures.

Data on *medication use* were based on responses to the question, "In the past month, did you take any of the following medications?" Those included for this analysis were "antidepressants," "diuretics or water pills," "medicine for blood pressure," "medicine for the heart," "sleeping pills," and "tranquilizers such as Valium."

A variable for *age* was included in the regression analysis. Age was categorized into two groups: 65 to 74 and 75 and older.

Household income levels were defined as "lower" and "higher," based on total household income and the number of people in the household:

	Income level	
People in household	**Lower**	**Higher**
1 or 2	Less than $15,000	$15,000 or more
3 or 4	Less than $20,000	$20,000 or more
5 or more	Less than $30,000	$30,000 or more

Data on income were unavailable for 20% of respondents aged 65 or older. So that other information about these people could be included in the regression analysis, a variable for unknown income was included in the model.

On the basis of previous research, four *chronic conditions* (arthritis/rheumatism, diabetes, effects of stroke and urinary incontinence) and limited vision were examined in relation to fracture risk.[9,25,26,37,44] The NPHS asked, "Does . . . have any of the following long-term conditions (conditions that have lasted or are expected to last six months or more) that have been diagnosed by a health professional?" *Impaired vision* was defined as any problem seeing that was not correctable by lenses.

Variables for alcohol use, smoking and body mass, all of which have been reported to relate to fracture risk in the elderly, were included in the analysis.[23,28,45-48] Frequency of *alcohol use* was categorized as less than daily (including never) or daily. *Smoking* was dichotomized as either never having smoked or ever having smoked. *Body mass index* (BMI), which is calculated by dividing weight in kilograms by height in metres squared, was grouped into two categories: not underweight (a BMI of 20 or more) and underweight (a BMI of less than 20). For example, underweight would be equivalent to less than 50 kg (110 pounds) for a person 160 cm (63 inches) tall, or less than 60 kg (132 pounds) for a person 173 cm (68 inches) tall.

interpretation of the findings, the inclusion of several relevant variables available from the National Population Health Survey in the multivariate analysis diminishes the potential for observing associations that are actually due to confounding factors.

This analysis supports the evidence that people using medications to treat high blood pressure are at reduced risk for fracture. Noting that thiazide diuretics have a low risk of serious side effects, at least one observer has mentioned (but not advocated) the possibility of their general use in elderly people to prevent bone loss.[40] However, this practice is not currently widespread.

The NPHS data also echo reports of the added risk of fracture conferred by low body weight. Except in cases when low weight results from debilitating chronic illness, helping underweight seniors achieve or maintain an appropriate body weight could lower their risk of fracture. However, because low body mass affects only a small percentage of the elderly population, the number of preventable fractures among such individuals is much lower than among people with other more common risk factors such as arthritis.

Even after age and other related characteristics were controlled, arthritis and urinary incontinence were each associated with increased odds of fracture. Research on community-dwelling seniors identified as being at high risk of fracture suggests that exercise and education programs could be effective in preventing falls and reducing fall-related injury. Interventions tailored to the needs of the individual, including balance or strengthening exercises, gait training and teaching in the use of assistive devices, were associated with a reduction in falls and fall-related injuries.[49] Because of the extent of falls and fall-related injuries in the senior population, it has been recommended that an assessment of risk factors of falling, followed by intervention programs as appropriate, should be a routine part of the health care of patients older than 75.[50] The benefits of such an approach could be considerable, especially if undertaken with people who have a condition such as arthritis that puts them at risk of fall-related fractures. ●

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Appendix

Table A

Counts of fall-related fractures arising from most serious activity-limiting injury, by fracture site, household sample aged 65 or older, Canada excluding territories, 1996/97

Fracture site	Number
Total sample	**281**
Arms/Hands	79
Legs/Feet	63
Hip	62
Trunk	36
All others	41

Data source: *1996/97 National Population Health Survey, cross-sectional sample, Health file*

Table B

Counts of medication use in past month, selected characteristics, by sex, household sample aged 65 or older, Canada excluding territories, 1996/97

	Total	Men	Women
Total sample	**13,363**	**5,357**	**8,006**
Medication use			
Antidepressants	522	155	367
Diuretics/Antihypertensives	5,060	1,737	3,323
Heart medication	2,577	1,166	1,411
Sleep medication	1,004	302	702
Tranquilizers	567	148	419
Age			
65-74	7,780	3,390	4,390
75+	5,583	1,967	3,616
Household income			
Lower	2,780	762	2,018
Higher	7,119	3,301	3,818
Missing	3,464	1,294	2,170
Alcohol use			
Less than daily	11,925	4,475	7,450
Daily	1,207	793	414
Missing	231	89	142
Smoking			
Never	6,221	1,519	4,702
Ever	7,034	3,801	3,233
Missing	108	37	71
Chronic conditions			
Arthritis/Rheumatism	6,256	1,975	4,281
Diabetes	1,314	593	721
Effects of stroke	555	269	286
Urinary incontinence	904	306	598
Impaired vision	721	220	501
Body mass index (BMI)			
Not underweight (BMI ≥ 20)	11,870	5,048	6,822
Underweight (BMI < 20)	953	194	759
Missing	540	115	425

Data source: *1996/97 National Population Health Survey, cross-sectional sample, Health file*