Risk of Injury Associated with Opioid Use in Older Adults

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OBJECTIVES: To estimate the dose-related risk of injuries in older adults associated with the use of low-, medium-, and high-potency opioids.

DESIGN: Historical population-based cohort study: 2001 to 2003.

SETTING: Quebec, Canada's, universal healthcare system.

PARTICIPANTS: Four hundred three thousand three hundred thirty-nine adults aged 65 and older.

MEASUREMENTS: Population-based health databases were used to measure preexisting risk factors for injuries in 2001/02 and drug use and injuries during follow-up (2003). Type and dose of opioids were measured as time-dependent variables, as were other drugs that may increase the risk of injury from sedating side-effects or hypotension. The risk of injury per one adult dose increase in opioid dose was estimated using multivariate Cox proportional hazards models.

RESULTS: During the follow-up year, 50.7% of the study population were prescribed drugs with sedating side effects, 15.3% were prescribed an opioid, 20.7% were concurrently using more than one sedating medication, and 3.7% were treated for an injury, fractures (55.1%) being the most common. After adjusting for concurrent drug use and baseline risk factors, low- (hazard ratio (HR) = 1.36, 95% confidence interval (CI) = 1.33–1.39) and intermediate-potency (HR = 1.05, 95% CI = 1.02–1.07) opioids were associated with the risk of injury. Use of codeine combinations was associated with the highest risk of injury, a 127% greater risk (HR = 2.27, 95% CI = 2.21–2.34) per one adult dose increase. (The mean World Health Organization standardized dose in the study population was 1.71 ± 0.85 adult doses.)

CONCLUSION: Opioids increase the risk of injury in older adults, particularly codeine combinations. **J Am Geriatr Soc 58:1664–1670, 2010.**

Key words: opioid; injury; pharmaceuticals

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DOI: 10.1111/j.1532-5415.2010.03015.x

In the last decade, there has been a dramatic increase in the use of opioid analgesics for non-cancer-related pain, particularly in older adults.[1,2] This upward trend in opioid use has been attributed to a variety of factors, including greater attention to the importance of pain management in improving quality of life and the arrival of new lower-potency opioids that were marketed as having fewer adverse effects than their predecessors,[3–5] yet there are early warnings of undesirable adverse effects. Coroner-adjudicated deaths from unintended drug poisoning rose at the staggering rate of 18.1% per year between 1990 to 2002, in comparison with an annual increase of 5.3% between 1979 and 1990.[6] Moreover, the majority of the increase in mortality is attributable to an increase in the clinical use of prescription opioids and unintended adverse effects.[6]

Part of the increase in opioid-related mortality may be due to fall-related injuries, particularly in older adults. In this age group, injuries are the sixth leading cause of death, and a substantial proportion are attributable to fall-related fractures.[7–9] Medications, particularly those having central nervous system (CNS) side effects of sedation and compromised coordination, are known to increase the risk of fractures and other fall-related injuries.[10–12] Use of older opioids, such as propoxyphene, with long half-lives and the potential for cumulative effects has been shown to increase the risk of fractures in most studies, and these medications are now considered inappropriate for use in older persons,[12–17] but there is little information about the safety of newly marketed lower-potency opioids such as oxycodone, which are believed to have a better safety profile for pain management. A recent population-based Danish study reported the surprising finding that use of oxycodone had almost double the risk of fractures as its predecessor propoxyphene, even at equivalent doses.[18] These interesting results may have arisen from the concurrent use of other medication, such as benzodiazepines and antidepressants, drugs that are commonly prescribed to older adults and are known to increase the risk of injury.[12]

The purpose of this study was to provide an estimate of the relative risk of injuries in older adults related to the use of low-, medium-, and high-potency opioids within a

0002-8614/10/$15.00

population-based cohort. Dose-related effects were estimated for each drug class, adjusting for the concurrent use of other medications, as well as comorbidities that increase the risk of injury.

METHODS

Context and Data Sources

The study was conducted in Quebec, the second largest province in Canada, which accounts for 25% of the population. All hospital and medical services are covered through a universal public health insurance program managed by the Régie de l'assurance maladie du Québec (RAMQ). Prescription drug insurance is mandatory, and the public insurance program covers all older Quebec residents. The RAMQ prescription claims database records the drug, date, quantity, and duration of each prescription dispensed from the 1,800 community-based pharmacies in the province. The medical services claims database records the date, diagnosis, procedure, and location (e.g., emergency department, intensive care unit) of each medical service provided to Quebec residents. The hospitalization database records the date, admission, and discharge diagnosis and procedure for each hospital admission. Data are linked through a unique lifetime health insurance number. The provincial privacy commission, RAMQ, and the McGill University institutional review board provided approval for data extraction and linkage.

Study Design

A historical cohort study of community-dwelling older adults was conducted. A 2-year baseline interval (2001–2002) was used to assemble the cohort and assess nonpharmaceutical risk factors for fall-related injury: the presence of medical conditions associated with the risk of fall-related injury, including gait and balance disturbances; cognitive impairment; lower extremity weakness; and previous injuries.[9,19,20] A 1-year follow-up (2003) was then conducted to measure prescription drug use and fall-related injuries. In the follow-up year, time-dependent measures of prescription drug use and dose were constructed. Survival analysis was used to estimate the risk of fall-related injury associated with the use of opioids and other classes of drugs over the 1-year follow-up period.

Study Population

The study population was a sample from a larger cohort of approximately 60% of the population of the province of Quebec that was constructed to examine medical practice of newly licensed physicians.[14] This cohort was restricted to persons aged 65 and older in 2002 who were alive at the start of follow-up (January 1, 2003). Data on medical and prescription claims for the interval January 1, 2001, to December 31, 2003, were obtained for all cohort members from the Quebec health insurance agency (RAMQ).

Prescription Drug Use

CNS side effects of sedation and compromised coordination are the primary mechanisms by which opioids and other psychoactive medication affect accident-related injuries.[12] Because these effects are relatively acute, time-varying measures of drug exposure were used to provide the most-precise measure of current use. Opioids were grouped into three categories: low (codeine, oxycodone, pentazocine, butorphanol), intermediate (hydromorphone, morphine, meperidine, methadone), and high (fentanyl) potency. Other drugs with CNS side effects were grouped into 13 categories based on mechanism of action and half-life: antidepressants (selective serotonin reuptake inhibitors (SSRIs), selective serotonin norepinephrine reuptake inhibitors (SSNRIs), tricyclics, other antidepressants), anxiolytics and hypnotics (long-acting, intermediate, and short-acting benzodiazepines, other anxiolytics), muscle relaxants, anticonvulsants, antihistamines, and antimigraine and antipsychotic medications. All prescriptions dispensed during the follow-up period in each drug group were retrieved, and a time-dependent measure of current use was created for each patient based on the start and end dates of the prescription. During the period of use, daily dose was measured by first determining the prescribed number of tablets to be taken each day (quantity of medication dispensed divided by the duration of the prescription). The daily number of tablets was then multiplied by the strength of each tablet to determine daily dose. To compare the dose-related risk of injury between drugs, a standardized dose was created for each medication by dividing the prescribed dose by the World Health Organization (WHO) recommended daily dose for adults for each medication.[21,22] When multiple drugs within a therapy class were dispensed, the standardized dose for each drug was summed to create an overall daily dose within a drug class.

Injuries

A previously validated set of procedure codes from medical services claims files was used to measure occurrence of injury in the study population, date of first treatment, and type of injury.[23] The majority of injuries in older adults are fractures and soft-tissue injuries related to falls.[7,8] Although motor vehicle crash–related injuries are less common, they have also been identified as another source of injury related to use of drugs with sedating side effects.[24–26] Injuries included all fractures of the upper and lower extremity, hip, pelvis, skull, and thorax, as well as lacerations and subluxations.[23] Vertebral fractures were excluded.

Other Risk Factors for Injury

Medical conditions that are known to increase the risk of injuries—cognitive impairment, lower extremity weakness, and gait and balance disorders—were measured using diagnostic codes recorded in the claims for medical services submitted for each patient to the RAMQ in the baseline period (2001–2002) using codes previously validated by other researchers.[27,28] Using the same set of procedures codes employed for the outcome, the number of injuries in the 2 baseline years was measured because it is one of the most important predictors of future injury.[10,17,19,29] Use of antihypertensive medication was also measured as a time-varying exposure because there is evidence suggesting that these drugs may increase the risk of injury through hypotensive side effects.[11] Information in the beneficiary file from the RAMQ was used to determine age and sex.

Statistical Analysis

A Cox proportional hazards model was used to estimate the risk of injury. Each therapy class was first modeled separately as a time-varying exposure in a model that included demographic characteristics and medical conditions as fixed covariates and time-varying measures of antihypertensive drug use.[22,30] The main outcome was time until first injury in the follow-up year. The estimated hazard ratio (HR) for each drug class represented the change in risk per one adult dose increase in therapy. Patient follow-up was censored at first injury or death. A combined model was then estimated to adjust for the use of multiple classes of drugs with CNS side effects. The combined model included therapy classes that had a statistically significant association with the risk of injury and with all patient characteristics. To assess the sensitivity of the results to potentially incomplete control for confounding by other CNS medications, the analysis was repeated after excluding individuals taking CNS medications other than opioids. The large size of the cohort and the inclusion of time-varying covariates made it computationally intractable to estimate the model in a standard manner. To overcome this, the analysis was stratified according to day using all patients with an injury on a given day and a random sample of 1,000 patients without an injury on that day, with each patient without an injury weighted to reflect the total number of patients in the cohort with the same profile.

RESULTS

Overall, 403,339 older adults were followed over a 1-year period to estimate the risk of injury associated with opioid use. The average age of the study population was 74.9, 58.6% were women, 7.1% had treatment for at least one injury in the prior year, and 5.8% to 19.4% had other comorbidities that would increase the risk of injury (Table 1). The most prevalent medical condition associated with risk of injury was gait or balance impairment (19.4%), of which dizziness, fatigue, and syncope were the three most common problems.

There were 14,846 people who sustained injuries requiring medical treatment in the follow-up year, for an annual prevalence of 3.7% (Table 2). Of these 14,846, 7.6% had more than one injury treated in the first episode, for a total of 16,095 injuries. The majority of injuries were fractures (55.1%), mainly of the extremities or hip (Table 2). Lacerations were also common, accounting for 41.9% of all injuries.

During the follow-up year, 204,618 (50.7%) older adults were dispensed at least one drug with CNS-depressant side effects, and 61,569 (15.3%) were prescribed an opioid. Low-potency opioids were the most prevalent, including codeine products (10.8%) and oxycodone (1.4%) (Table 3, Column 2). Other drugs that were commonly used were intermediate-acting benzodiazepines (33.2%), SSNRIs and SSRIs (10.1%), antipsychotics (6.7%), and anticonvulsants (4.5%), mainly gabapentin (3.6%). Overall, 83,584 (20.7%) of the study population were dispensed two or more classes of therapy concurrently, of which intermediate-acting benzodiazepines and SSNRIs and SSRIs (5.2%) was the most common combination,

Table 1. Characteristics of the Study Population and Risk Factors for Injury in the Baseline Year

Patient Characteristics and Risk Factors	Value
Age, mean ± SD	74.9 ± 7.0
Female, n (%)	236,322 (58.6)
Household income, $, mean ± SD*	47,785.40 ± 22,698.81
Geographic location, n (%)	
Urban	326,225 (80.9)
Rural or remote	74,887 (18.7)
Missing	2,227 (0.6)
Number of previous injuries, n (%)	
0	374,528 (92.9)
1	25,204 (6.2)
≥2	3,607 (0.9)
Lower extremity weakness, n (%)	30,566 (7.6)
Gait and balance problem, n (%)	78,356 (19.4)
Cognitive impairment, n (%)	23,573 (5.8)

*Household income was estimated using the mean household income for persons living in the same postal code (approximately 366 households) as the individual in the study population based on Statistics Canada census data.
SD = standard deviation.

Table 2. Types and Frequency of 16,095 Injuries in 14,846 Persons Injured in the Follow-Up Year

Injury	n (%)
Fracture	8,875 (55.1)
Unspecified	3,040 (18.9)
Upper extremity	1,895 (11.8)
Ulna or radius	773 (4.8)
Carpal or hand	834 (5.2)
Humerus	288 (1.8)
Hip	1,948 (12.1)
Lower extremity	1,801 (11.1)
Foot	1,071 (6.7)
Femoral shaft	356 (2.2)
Ankle	192 (1.2)
Tibia or fibula	149 (0.9)
Patella	33 (0.2)
Scapula or clavicle	59 (0.3)
Skull and face	48 (0.3)
Spine	40 (0.2)
Pelvis	36 (0.2)
Thorax	8 (0.05)
Soft-tissue injury	7,220 (44.9)
Laceration	6,736 (41.9)
Subluxation	484 (3.0)
Upper extremity	386 (2.3)
Hip	54 (0.3)
Lower extremity	40 (0.2)
Other	4 (0.02)

Injury was the unit of analysis. Although patients may have had multiple injuries during the follow-up year, only the first injury episode was assessed. Site was not specified in fractures that were treated using casting only.

Table 3. Risk of Injury Associated with Use of Opioids and Other Medications that Produce Central Nervous System Side Effects in 403,339 Older Adults

Medication	Patients, n (%)	Daily Proportion of Standardized Adult Dose, Mean ± Standard Deviation	Risk of Injury per 1 Adult Increase in Drug Dose	
			Hazard Ratio (95% Confidence Interval)	*P*-Value
Opioids				
High potency	4,546 (1.1)	0.39 ± 0.41	1.43 (1.05–1.95)	.02
Intermediate potency	20,564 (5.1)	0.67 ± 1.38	1.06 (1.03–1.08)	<.001
Low potency*	47,441 (11.8)	1.61 ± 0.94	1.37 (1.34–1.40)	<.001
Codeine combinations	37,478 (9.3)	1.71 ± 0.85	2.30 (2.23–2.36)	<.001
Codeine	8,074 (2.0)	1.38 ± 0.83	1.15 (1.10–1.21)	<.001
Oxycodone	5,684 (1.4)	0.49 ± 0.81	1.22 (1.13–1.33)	<.001
Anxiolytics, sedatives, and hypnotics				
Benzodiazepines				
Intermediate acting	134,049 (33.2)	0.66 ± 0.57	1.13 (1.09–1.17)	<.001
Short acting	1,026 (0.3)	1.27 ± 0.63	0.97 (0.70–1.35)	.84
Long acting	13,371 (3.3)	0.93 ± 0.54	1.22 (1.10–1.35)	<.001
Other anxiolytics	10,794 (2.7)	0.75 ± 0.58	1.30 (1.05–1.54)	.01
Antidepressants				
Selective serotonin reuptake inhibitors and selective serotonin norepinephrine reuptake inhibitors	40,693 (10.1)	1.13 ± 0.62	1.33 (1.28–1.38)	<.001
Tricyclics	19,419 (4.8)	0.44 ± 0.39	1.27 (1.11–1.46)	<.001
Other antidepressants	11,492 (2.9)	0.57 ± 0.97	1.08 (1.00–1.17)	.04
Other sedating drugs				
Muscle relaxants	12,195 (3.0)	0.77 ± 0.80	1.20 (1.04–1.38)	.01
Anesthetics and analgesics	645 (0.2)	0.29 ± 0.23	1.48 (0.47–4.69)	.51
Anticonvulsants	18,097 (4.5)	0.66 ± 0.47	1.50 (1.37–1.65)	<.001
Antihistamines	549 (0.1)	4.04 ± 25.24	1.15 (1.04–1.26)	.005
Antimigraine medications	693 (0.2)	1.73 ± 1.17	1.15 (0.84–1.59)	.39
Antipsychotics	26,911 (6.7)	0.56 ± 0.78	1.29 (1.22–1.37)	<.001

Each drug group was modeled separately as a time-dependent covariate, adjusting for age, sex, previous fall count, cognitive impairment, gait and balance, and cardiovascular drug use.

* Low-potency opioids were first modeled as a group, and then the low-potency classification was replaced by the three drugs within this class: codeine, codeine combinations, and oxycodone.

followed by an intermediate-acting benzodiazepine combined with a low-potency opioid (3.0%).

During periods of medication use, the mean dose exceeded the recommended WHO daily dose for healthy adults for low-potency opioids, short-acting benzodiazepines, antihistamines, SSRIs and SNRIs, and antimigraine treatments. For low-potency opioids, the mean dose was 1.57, more than 50% higher than the maximum adult dose, with a range from one-tenth of the recommended adult dose to more than 14 times the adult dose (Table 3, Column 3).

After adjustment for patient characteristics, there was a statistically significantly greater risk of injury with opioid use: 43% greater per one adult dose with the high-potency opioid fentanyl (HR = 1.43, 95% confidence interval (CI) = 1.05–1.95), 37% for low-potency opioids (HR = 1.37, 95% CI = 1.34–1.40), and 6% for intermediate-potency opioids such as hydromorphone (Table 3, Columns 4–7). Other drugs with CNS side effects that were associated with a statistically significantly greater risk of injury were all antidepressants, intermediate- and long-acting benzodiazepines, and other anxiolytics, anticonvulsants, muscle relaxants, antipsychotics, and antimigraine medications.

To adjust for confounding related to combined exposures to different drug classes, all classes of drugs with CNS side effects that were significantly associated with injury were included in one model. The model also adjusted for patient demographics, comorbidity, injury history, and cardiovascular drug use (Table 4). As expected, older persons; women; and people with gait and balance problems, prior injury, and cognitive impairment were more likely to have significant injury requiring medical treatment. Cardiovascular drug use was not associated with injury risk, except for cardiac medications, which showed a modestly greater risk (HR = 1.08, 95% CI = 1.01–1.15). After adjusting opioid use for concurrent use of drugs with CNS side effects, only low- and intermediate-potency opioids were associated with risk of injury. With low-potency opioid use, injury risk was 36% greater per one-unit increase in adult dose (HR = 1.36, 95% CI = 1.33–1.39). Within low-potency opioids, codeine combinations were associated with the greatest risk, a 127% increase in risk of injury per

Table 4. Risk of Injury Associated with Patient, Opioids, and Other Drug with Central Nervous System (CNS) Side Effects (Adjusting for Concurrent Use of Medications with CNS Side Effects)

	HR (95% CI)	*P*-Value
Patient demographics		
Age (risk per 5-year increase in age)	1.21 (1.19–1.22)	<.001
Female	1.05 (1.01–1.08)	.01
Comorbidity and injury history		
Previous injury count (risk per each additional prior injury)	1.57 (1.53–1.62)	<.001
Gait and balance problems	1.13 (1.08–1.17)	<.001
Cognitive impairment	1.27 (1.20–1.35)	<.001
Lower extremity weakness	1.01 (0.95–1.07)	.73
Use of CNS depressants		
Opioids		
Low-potency opioids*	1.36 (1.33–1.39)	<.001
Codeine combinations	2.27 (2.21–2.34)	<.001
Codeine	1.10 (1.03–1.17)	<.001
Oxycodone	1.19 (1.09–1.30)	<.001
Intermediate-potency opioids	1.05 (1.02–1.07)	<.001
High-potency opioids	1.06 (0.77–1.46)	.73
Anxiolytics, sedatives, and hypnotics		
Long-acting benzodiazepines	1.15 (1.03–1.27)	.01
Intermediate-acting benzodiazepines	1.07 (1.03–1.11)	<.001
Other anxiolytics and hypnotics	1.12 (0.92–1.36)	.27
Antidepressants		
Selective serotonin reuptake inhibitors and selective serotonin norepinephrine reuptake inhibitors	1.28 (1.24–1.33)	<.001
Tricyclics	1.12 (0.97–1.30)	.12
Other antidepressants	1.03 (0.91–1.16)	.66
Other sedating drugs		
Muscles relaxants	1.13 (0.98–1.31)	.10
Anticonvulsants	1.31 (1.19–1.44)	<.001
Antipsychotics	1.24 (1.17–1.32)	<.001
Antihistamines	1.13 (1.01–1.26)	.04

Statistically significant drug groups were modeled together as time-dependent covariates, adjusting for age, sex, previous fall count, cognitive impairment, gait and balance, and cardiovascular drug use.

Only cardiac drugs were associated with a modestly greater risk of injury (hazard ratio (HR) = 1.10, 95% confidence interval (CI) = 1.03, 1.17). Calcium channel blockers (HR = 0.94, 95% CI = 0.91–0.96), alpha adrenergics (HR = 0.84, 95% CI = 0.73–0.98), and beta adrenergics (HR = 0.88, 95% CI = 0.84–0.93) were associated with a modest but statistically significantly lower risk of injury.

*Low-potency opioids were first modeled as a group, and then the low-potency classification was replaced by the three drugs within this class: codeine, codeine combinations, and oxycodone.

one adult dose increase (HR = 2.27, 95% CI = 2.21–2.34). Other drugs with CNS side effects that were significantly associated with the risk of injury were SSRIs and SSNRIs, intermediate- and long-acting benzodiazepines, anticonvulsants, antihistamines, and antipsychotics (Table 4). When the analysis was restricted to patients who did not use psychoactive drugs other than opioids, similar results were found but with a greater effect. The risk of injury in this population was 195% greater with low-potency opioids (HR = 2.95, 95% CI = 2.94–2.96).

DISCUSSION

Consistent with prior studies, older adults who were prescribed opioids had a greater risk of injury.[11,12,15,31] It was also found that many older adults were prescribed opioids often above the WHO-recommended dose for healthy adults. Low-potency opioids were also frequently prescribed in conjunction with other drugs with sedating side effects. Even after adjustment for concurrent use of benzodiazepines, antidepressants, antipsychotics, muscle relaxants, and antihistamines, greater doses of intermediate- and low-potency opioids were associated with significantly greater risk of injury. Moreover, low-potency opioids, particularly codeine combinations, were associated with the greatest risk, possibly because they were the only subgroup of opioids of which patients were receiving relatively high daily doses of therapy.

Opioids have established dose-related side effects of sedation and compromised coordination.[32,33] Even at recommended doses, significant sedation occurs in 29% of the population.[33–35] Thus, it is not unexpected that substantially higher doses in older persons would be associated with greater dose-related side effects that would increase the risk of injury. Recent reports from population-based studies in Norway have established that a subset of the population is exposed to high cumulative doses of opioids, as well as concurrent use of other sedating medication.[36] This study confirms that the concurrent use of multiple sedating medications is prevalent in older adults. It also extends prior research to show important variation in the daily dose prescribed, even in a vulnerable population: older adults. High opioid doses were evident, even in the most-vulnerable patients, who were older and had other comorbidities that would already lead to a greater risk of injury. Norwegian[26] and Danish[18] studies have also showed a greater risk for fractures[18] and automobile accidents[26] with more-continuous use and at higher doses.

It was found that codeine combinations were associated with a substantially greater risk than oxycodone. Higher doses of codeine, particularly in combination with benzodiazepines, have also been recently reported to increase the risk of motor vehicle accidents and driving impairment. The unexpected finding of a significant but substantially lower risk of injury with oxycodone use than the Danish studies[18] may be because of the introduction of long-acting oxycodone products that are hypothesized to reduce adverse effects while improving pain control.[37,38] In this study, 57.3% of oxycodone use was for long-acting formulations.

Most past research on the predictors of accident-related injuries have identified that falls, fractures, and motor vehicle accidents are associated with older age, sex, cognitive impairment, past injuries, lower extremity weakness, and gait and balance problems.[19,20,24–26] The only inconsistency in the results from the current study was related to lower extremity weakness that was not associated with injuries, probably because *International Classification of Diseases, Ninth Revision*, diagnostic codes are not sensitive enough to measure this disability.

With the exception of short-acting benzodiazepines and antimigraine medication, it was found that most drugs with CNS side effects were associated with greater risk of injury, a finding that has been reported previously,[10,12,15] although it may be that some of the effects reported in prior research were overestimated, particularly for the benzodiazepines, antidepressants, and antipsychotics, because the current study found that these drugs are commonly used in combination with opioids. Past investigations that adjusted for concurrent use of opioids have shown attenuated effects for the risk of injury with benzodiazepines and antidepressants, but none have adjusted for contemporaneous dose-related effects.[10,12,15,18] The magnitude of the risk of injury associated with benzodiazepines and antidepressants was attenuated when all doses for all classes were included in the same model.

This study had a number of strengths. It provided a population-based assessment of opioid use and injury occurrence in older adults because universal health insurance coverage allowed opioid use and all medically treated injuries to be assessed for each citizen. Restriction of the population to those treated by newly licensed physicians permitted the effects of current therapy approaches to be studied, rather than potentially inappropriate, "older style" practices that are more common in older physicians. Unlike previous studies,[12,18,26] problems in the misclassification of drug exposure were minimized by using time-dependent covariates to assess use and current dose of opioids and other confounding medications, such as antidepressants and benzodiazepines, that are frequently coprescribed with opioids.[36] By using a prospective cohort design and survival analytical methods, the ability to establish cause-and-effect relationships between antecedent prescription drug use and injury occurrence was strengthened.

Nevertheless, readers should consider several limitations in the interpretation of the results. Actual drug use was not measured, only the supply of medication. Although prior studies have shown that prescription refills are good markers of drug use,[39–41] this may be less so for drugs that are prescribed on an as-needed basis, such as pain killers. This source of measurement error in this study would lead to an underestimation of the adverse effects of opioid use, so the risk of injury in older adults is probably underestimated. Clinical indications for opioid treatment could not be assessed, and therefore confounding by treatment indication may bias comparisons. Most high- and intermediate-potency opioids are used for terminal cancer pain, whereas almost all low-potency opioids are used for acute and chronic pain. Persons who experience chronic pain, particularly for musculoskeletal conditions such as rheumatoid arthritis and osteoarthritis may be at greater risk of injury.[19] Failure to adjust adequately for the severity of these conditions, which may also be associated with higher doses of opioids, may lead to an overestimation of the adverse effects of opioids. Other comorbidities that increase the risk of injury may also have been underestimated using medical service billing diagnostic codes, which have been shown to have high specificity but lower sensitivity.[42,43]

In summary, older adults commonly use opioids, often in conjunction with other medications with sedating side effects. Higher doses of low-potency opioids, particularly codeine combinations, are prevalent and result in twice the risk of injury. Early detection and intervention in increasing use of opioids for pain management may be beneficial in reducing the risk of injury.

ACKNOWLEDGMENTS

The authors wish to thank the Quebec provincial privacy commission (CAI) and the Quebec public health insurance program (RAMQ) for providing data for the study and the McGill University institutional review board, which provided approval for data extraction and linkage.

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

This project was supported by a grant from the Canadian Institutes of Health Research.

Author Contributions: David Buckeridge and Robyn Tamblyn: study concept, design, and preparation of manuscript. Allen Huang and Aman Verma: acquisition of subjects and data. Armel Kelome, James Hanley, Aman Verma, Nancy Winslade, and Kristen Reidel: analysis and interpretation of data.

Sponsor's Role: The Canadian Patient Safety Institute played no role in the design methods, subject recruitment, data collection, analysis, or preparation of the manuscript.

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