

**Alcohol and Select Medications as Fall Risk Factors in Community  
Dwelling Older Adults in Canada**

by

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### **Author's Declaration**

This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in the tehsis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

## Statement of Contributions

With the exception of the content noted below, the work of this thesis consists of content I authored.

### *Survey*

The survey was developed in partnership with Drs. Alexander Crizzle, Philip Bigelow, Anita Myers, and Emmanuel Lagarde.

### *Chapter 2*

I conducted the literature review with guidance from Jackie Stapleton. I wrote the content with assistance of Dr. Alexander Crizzle.

### *Chapters 3 and 4*

I collected the data for these chapters. I performed the data analysis with the assistance of Drs. Alexander Crizzle and Philip Bigelow.

## Abstract

**Introduction:** Falls are the leading cause of accidental injury in community dwelling older adults, often resulting in emergency room visits, hospitalization and early admission to long-term care. Studies have identified many risk factors for falls including increasing age, diagnosis of a chronic disease, poor vision, fear of falling, hazards in the home, alcohol and prescription medications. While studies have examined many risk factors associated with falls, there is limited information on whether prescription medications and alcohol are risk factors in community dwelling older adults.

**Purposes:** The primary thesis objectives were to: i) conduct a literature review to synthesize the literature on whether alcohol and psychotropic, anti-depressant and anti-hypertensive medications are risk factors for falls in community dwelling older adults; ii) examine what health and social factors are associated with high-risk alcohol use in community-dwelling older adults in Canada,; and iii) examine whether alcohol and select medications are predictive of falls in community dwelling older adults.

**Methods:** The first aspect of this thesis was to conduct a literature review on select medications (psychotropics, benzodiazepines or anti-psychotics, anti-depressants, and anti-hypertensives) and alcohol, both singly and in combination, on fall risk in community dwelling older adults using the following search terms: drug or medication, aged or elderly or older adult or senior, accidental falls or falls or falling, and alcohol or alcohol drinking. These search terms were entered into four databases (PubMed, EMBASE, CINAHL and SCOPUS). A total of 1,146 articles were retrieved and screened for inclusion. Studies were included if 1) was a primary study; 2) included community dwelling persons aged 60 years and older; 3) included alcohol use as an independent variable; 4) included medications of interest; 5) falls were the primary

outcome variable; and 6) published in English. We excluded studies if they were: 1) review articles, conference proceedings, books, editorial, case studies or commentary; 2) if articles relied on qualitative data (interviews, focus groups); 3) if they were not in English; and 4) included institutionalized persons (e.g. living in LTC or hospital).

Chapters 3 and 4 used data from the Canadian Injury Prevention Survey. The survey was distributed online to local, provincial and national organizations across Canada that cater to older adults (2016-2017) and collected information on demographics, perception of physical and mental health, fall history, alcohol use, use of psychotropic, anti-depressant and anti-hypertensive medication use, smoking status, diagnosis of a chronic disease, physical activity, usual sleep quantity, likelihood of daytime sleepiness, and executive duties. While data was collected on community dwelling individuals 45 years and older, only data of those 65 years and older was examined in the present thesis (n=2,281).

Chapter 3 examined alcohol use in community dwelling older adults (n=2,279). Participants reported the number of drinks they consumed per week and the number of days per week they consumed alcohol. The purpose of this chapter was to: 1) examine alcohol use in community dwelling older adults in Canada using current alcohol consumption guidelines; 2) develop and test new alcohol consumption guidelines to determine if they better differentiate drinking habits on health outcomes; and 3) determine risk factors of high-risk drinking. Low risk drinking was defined as 1-2 drinks per week for both males and females. Moderate drinking was defined as 3-9 drinks per week for males and 3-6 drinks for females. High risk drinking limits were defined as  $\geq 10$  drinks per week for males and  $\geq 7$  drinks per week for females. Using logistic regression, we examined demographic and health factors to predict low and high-risk

drinking. Multinomial regression was used to examine predictors of low, moderate and high-risk drinking.

Chapter 4 examined the use of alcohol and select medications as risk factors for falls, both as independent predictors of falls, and together with alcohol (n=2,281). Participants reported prescription medication, alcohol use on a weekly basis and fall history. Medications examined included psychotropic (anxiolytics, anti-psychotics, hypnotics/sedatives), anti-depressants (selective serotonin reuptake inhibitors (SSRI), serotonin antagonist reuptake inhibitors (SARI), serotonin-norepinephrine reuptake inhibitors (SNRI), tricyclic anti-depressants, or other) and cardiovascular agents (diuretics, beta-blockers, angiotensin converting enzyme inhibitors, angiotensin II receptor antagonist, calcium channel blockers) on fall risk. Correlations were performed to determine health factors correlated with falls. Logistic regression determined medications predictive of falls.

**Results:** The literature review (Chapter 2) found 29 observational studies that met the inclusion criteria after screening. Sample sizes ranged from 307 to 321,422. Twenty-six studies examined the effects of benzodiazepines, hypnotics/sedatives or anti-psychotic use on falls, and twenty found benzodiazepines, hypnotics/sedatives or anti-psychotics were predictive of falls. Thirteen studies examined anti-depressant use and falls; 10 studies found that anti-depressants are predictive of falls. Twelve studies examined anti-hypertensives as a risk factor for falls and four found anti-hypertensives were predictive of falls. Fifteen studies examined alcohol use and five found alcohol was a predictor of falls.

Findings from Chapter 3 show that 70% of participants reported drinking at least once per week. Using the current Canadian alcohol consumption guidelines, 6.2% of older males and 10.1% of older females were classified as high-risk drinkers. Moderate drinking was reported by

32.8% of males and 23.3% of females. When comparing current alcohol consumption guidelines to the new additional category (moderate drinking), there were no significant difference on health outcomes.

Findings from Chapter 4 show that 33.4% of older adults had a fall in the previous two years. In fallers, 5.3% reported psychotropic use, 10.4% reported anti-depressant use, and 51.6% reported anti-hypertensive use. Anti-hypertensive medication and alcohol use was not associated with falls. As a group, psychotropic drug use was predictive of falls after controlling for potential confounding factors ( $p < 0.05$ ). Anti-depressant sub-classes SSRIs, SARIs and SNRIs were predictive of falls on their own and when controlling for sex ( $p < 0.05$ ).

## **Conclusions**

The literature review found benzodiazepines, hypnotics/sedatives, anti-psychotic and anti-depressants are predictive of falls in community dwelling older adults. Anti-hypertensive medication and alcohol use were not predictive of falls. Compared to females, males were more likely to be moderate drinkers, however, overall adding a moderate drinking category did not help differentiate health and social factors associated with alcohol consumption. Psychotropic drug use overall, as well as individual anti-depressant drug classes (i.e. SSRI, SNRI and SARI) were all predictive of falls after controlling for sex. Anti-hypertensives and alcohol were not predictors of falls in community dwelling older adults based on the survey data. Findings of the literature review and survey data confirm psychotropic and anti-depressant use increase fall risk in community dwelling older adults. Clinicians should exercise caution when prescribing psychotropic and anti-depressant medications to older adults.

## Acknowledgements

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# **Chapter 1: Introduction**

## **1.1 Thesis Overview**

Chapter 1 outlines the thesis objectives and a brief overview of the original University of Bordeaux project. Chapter 2 presents a literature review on the effects of select medications and alcohol on fall risk in older adults followed by Chapters 3 and 4 that are original research papers using data from the Canadian Injury Prevention Survey. Chapter 3 describes health and social factors associated with alcohol use and predictors of alcohol use in community dwelling older adults in Canada and Chapter 4 examines whether psychotropic, anti-depressants and anti-hypertensives, both singly and in combination with alcohol, are associated and/or predictive of fall risk in community dwelling older adults. Lastly, Chapter 5 is a general discussion and summary of the main findings, implications for research and practice, followed by limitations, future directions and conclusions.

## **1.2 Thesis Objectives**

The purpose of this thesis is to examine the role of alcohol and its interaction with various medications (i.e., psychotropic, anti-depressants, and anti-hypertensives) on fall risk in Canadian older adults (aged 65+). While studies have identified a plethora of risk factors for falls (e.g. age, chronic illness, previous falls, poor vision), a few studies have also suggested that select medications and alcohol may be risk factors (Milos et al. 2014; Sorock et al. 2006). However, there is a paucity of research in this area.

Evidence suggests that older adults make up the highest percentage of prescription medication users in Canada (CIHI, 2012; PHAC, 2015). Prescription medication use including anti-psychotics, benzodiazepines such as sedatives/hypnotics and anti-depressants are identified as risk factors for falls in older adults (PHAC, 2014). Furthermore, some research also suggests

that anti-hypertensive medications also increase fall risk (Tinetti et al. 2014). The first aspect of this thesis aims to synthesize articles on anti-psychotic and benzodiazepines, anti-depressant and anti-hypertensive medications, as well as alcohol, that have examined fall risk in community dwelling older adults aged >60 years. The second aspect of this thesis is to examine alcohol use in older adults, develop new categories to determine if there was better differentiation between low, moderate and high-risk alcohol use in older adults on various health and social outcomes, and to compare current guidelines and new drinking categories for applicability to older adults. The third aspect of this thesis will examine the effects of medications, both individually and in combination with alcohol, on fall risk.

### **1.3 Project Background**

This project was done in collaboration with Dr. Emmanuel Lagarde and the University of Bordeaux (France). Dr. Lagarde and his research team developed a survey on occupational health and transportation that was disseminated in a cohort of blue-collared workers in France over 25 years ago (called the GAZEL cohort study). Participants are followed every year, completing the same survey, which allowed for longitudinal assessment of how changes in health and occupation were related to changes in mobility patterns.

Building from the GAZEL cohort study, their survey was adapted to a Canadian context prompting the addition and deletion of several items and questions. Questions concerning daytime sleepiness, physical activity, medication use (type, dosage per day), and day dreaming were added. In consultation with Dr. Lagarde, some questions that were not considered relevant or useful in the Gazel survey were removed (i.e. date of birth, marital status, number of children living in the home, assistance performing activities of daily living, assisting family members, weight and height, owners of pets, perceptions of balance, income, major life events, pain or

infections in past year, and hospitalization in past 12 months). After these revisions, the Canadian Survey consisted of 89 questions which aimed to examine how health and associated functional impairments, as well as behaviours (e.g. smoking, alcohol consumption, medication intake and sleep) are related to mobility (e.g. falls) in adults aged 45 years or older.

## **Chapter 2: A Literature Review of Psychotropic Medications and Alcohol as Risk Factors for Falls in Community Dwelling Older adults**

### **Overview**

**Background:** Studies suggest that psychotropic medications, specifically anti-psychotics, benzodiazepines, anti-depressants, and anti-hypertensives are potential risk factors for falls, as is alcohol. However, these studies have consisted of older adults living in institutionalized care which include higher rates of medications and falls. There has been no appraisal of the literature on whether medications and alcohol are associated with falls in community dwelling older adults. The objective of this study is to review and synthesize peer-reviewed studies that examined select medications, both singularly and in combination with alcohol, on fall risk in community dwelling older adults.

**Methods:** Four databases (PubMed, EMBASE, CINAHL and SCOPUS) and the grey literature (i.e. World Health Organization, Public Health Agency of Canada, Canadian Institute of Health Information) were searched using the following terms: benzodiazepines or anti-psychotics, anti-depressants, anti-hypertensives: drug or medication, aged or elderly or older adult or senior, accidental falls or falls or falling, and alcohol. Studies were included if 1) was a primary study; 2) included community dwelling persons aged 60 years and older; 3) included alcohol use as an independent variable; 4) included medications of interest; 5) falls were the primary outcome variable; and 6) published in English. Articles published until December 2017 were included. The search yielded 29 peer reviewed articles relevant to select medication and falls.

**Results:** Twenty-nine studies were included in the review. Twenty-six studies examined the effects of benzodiazepine, hypnotic/sedative or anti-psychotic use on falls; twenty studies showed benzodiazepines, hypnotic/sedative or anti-psychotic use was predictive of falls in community dwelling older adults. Thirteen studies examined anti-depressant use and falls; ten

predicted falls. Twelve studies examined anti-hypertensive and falls; four were predictive of falls. Fifteen studies examined alcohol use and five found a significant association with falls. Only one study examined the concurrent use of alcohol with central nervous system (CNS) medications and falls but no association was found.

**Conclusion:** The use of psychotropic and anti-depressant medications appears to be associated with falls in community dwelling older adults. Consequently, physicians and health care professionals should be cognizant of prescribing these medications to older adults who are already a high risk for falls.

## 2.1 Introduction

Select medications are suggested as risk factors for falls in older adults (WHO, 2007; PHAC, 2014). Four prior meta-analyses concluded that psychotropic medications including benzodiazepines/anti-psychotics and anti-depressants (Bloch et al. 2011; Leipzig et al. 1999; Woolcott et al. 2009), as well as anti-hypertensive medication increases fall risk in older adults (Leipzig et al. 1999; Woolcott et al. 2009). Two other systematic reviews found similar findings (Hartikainen et al. 2007; Park et al. 2015). However, these meta-analyses and reviews included studies with older adults living in institutional settings where medication use and the number of falls is substantially higher compared to the general population. For example, anti-depressants use, specifically selective serotonin reuptake inhibitors (SSRIs) are used by 36.1% of long-term care older adults compared to 9.5% of community dwelling older adults (CIHI, 2012). Additionally, approximately one in three community dwelling older adults fall at least once per year (Chang et al. 2015; Gill et al. 2005; O’Loughlin et al. 1993; Tinetti et al. 1988) compared to 46% of long-term care residents (Rojas-Fernandez, 2015).

In community dwelling older adults (defined as individuals aged 60 years and older living independently), prescription use is common with 83 to 90% using at least one medication (Rotermann et al. 2015; National Center for Health Statistics, 2016; Scholes et al. 2013). Psychotropic medications including anti-psychotics, anti-depressants, as well as anti-hypertensive medications are some of the most commonly prescribed medications to community dwelling older adults (Rotermann et al. 2015; Merel et al. 2017; National Center for Health Statistics, 2016; Scholes et al. 2013).

Anti-psychotics are categorized as typical (first-generation) or atypical (second-generation). First generation anti-psychotics were developed in the 1950s (Ramachandriah et al.

2009) and are prescribed to treat schizophrenia. Second generation anti-psychotics, developed in the 1990s and are more commonly prescribed to treat insomnia and symptoms of dementia (e.g. hallucinations, delusions) (Ramachandraiah et al. 2009). Compared to second generation medications, first generation medications have more severe side effects including drowsiness, agitation, muscle stiffness or spasms, and blurred vision (CAMH, 2012). However, the side effects of second generation anti-psychotics can also elevate fall risk from increased sedation and hypotension (CIHI, 2014).

Anti-depressants are primarily used to treat depression. The most common anti-depressants prescribed to older adults are selective serotonin reuptake inhibitors (SSRI), tricyclic anti-depressants (TCA) and selective norepinephrine reuptake inhibitors (SNRIs). Side effects of anti-depressants include orthostatic hypotension, sleep disturbance, daytime drowsiness and sedation, and can contribute to falls (Darowski et al. 2009). Previous reviews have found that anti-depressants are associated with falls, however, the included studies had samples with both community dwelling and institutionalized older adults, which were never examined separately (Haritkainen et al. 2007; Leipzig et al. 1999; Woolcott et al. 2009).

Hypertension or high blood pressure is treated with anti-hypertensive medications. Side effects related to anti-hypertensive medication use include dizziness, poor balance and gait, and postural hypotension which can cause falls (Gandhi et al. 2003; Gurwitz et al. 2003; Gray et al. 1999; Field et al. 2004; Gray et al. 1998; Tinetti et al. 2014). However, findings concerning whether anti-hypertensive medications are associated with fall risk are limited and mixed. For example, a review found anti-hypertensive medication use was associated with falls in both community dwelling and institutionalized older adults (Woolcott et al. 2009), however, a second

review of community and LTC older adults concluded use of anti-hypertensive medications and falls was mixed (Park et al. 2015)

The World Health Organization recognizes alcohol as a risk factor for falls (WHO, 2007); however, few studies have examined alcohol use as a risk for falls in community dwelling older adults. Alcohol use in older adults is common ranging from 63% to 81% (Cousins et al. 2014; Du et al. 2016; Bye & Rossow, 2017). Physiological changes related to aging may increase sensitivity to alcohol use in older adults. Additionally, the combined use of alcohol with either psychotropic, anti-depressants and anti-hypertensive use can result in increased sedation, psychomotor impairment, drowsiness, hypotension and disorientation, resulting in increased risk of falls (Moore et al. 2007; Weathermon and Crabb, 1999).

To date, there has been no literature reviews that have synthesized the literature pertaining to whether anti-psychotics, anti-depressants and anti-hypertensives are associated with an increased fall risk in community dwelling older adults. While medications such as benzodiazepines, anti-psychotics, anti-depressants, and anti-hypertensives have been associated with falls in prior reviews, the samples included older adults living in long-term care and few studies have examined alcohol use when taking medication as a predictor of falls. Thus, the objective of this study is to synthesize peer-reviewed studies that examined psychotropic (including benzodiazepines, hypnotics/sedatives, anti-psychotics, anti-depressants, and anti-hypertensive medications), both singularly and in combination with alcohol, on fall risk in community dwelling older adults.

## **2.2 Methods**

### **2.2.1 Search Strategy**

We searched for peer-reviewed primary studies that examined anti-psychotic/benzodiazepines, anti-depressant, anti-hypertensive medications, as well as alcohol, both singly and in combination, on fall risk in community dwelling older adults. In consultation with the university librarian, four electronic databases were searched (e.g., PUBMED, EMBASE, CINAHL and SCOPUS). An initial search was conducted in November 2016 with a follow-up search in December 2017 for any new articles that might have been published. We also searched for grey literature using the World Health Organization IRIS search engine, Public Health Agency of Canada search engine, Canadian Institute of Health Information, and the Canadian Agency for Medications and Technologies in Health, but no studies in the grey literature were included as they did not meet the inclusion criteria. Articles/reports were included if they were: 1) a primary study; 2) included community-dwelling persons aged 60 years or older 3) included alcohol consumption as an independent variable; 4) included medications of interests (i.e. psychotropics, benzodiazepines, hypnotics/sedatives, anti-psychotics or anti-depressants, and anti-hypertensives); 5) falls as an outcome variable; and 6) were published in English. Studies with samples having a large age range (e.g. 18-97 years) were included if authors performed specific analyses in older adults aged 60 years and older. Articles were excluded if they were: 1) review articles, conference proceedings, books, editorial, case studies or commentary; 2) if articles relied on qualitative data (interviews, focus groups); 3) if they were not in English; and 4) included institutionalized persons (e.g. living in LTC or hospital). Studies defining alcohol consumption as alcohol misuse were excluded because it is unknown if participants were current consumers of alcohol.

A general search was performed using each medication class of interest (e.g. psychotropic medication or benzodiazepine or anti-psychotic, anti-depressant medication, anti-hypertensive medication) using the following terms: drug or medication, aged or elderly or older adult or senior, accidental falls or falls or falling, and alcohol or alcohol drinking. Each medication class was also used to search medical subject headings (MeSH) such as: accidental falls, alcohol drinking/ adverse effects, alcohol drinking/ drug effects and aged.

### **2.2.2 Study Selection**

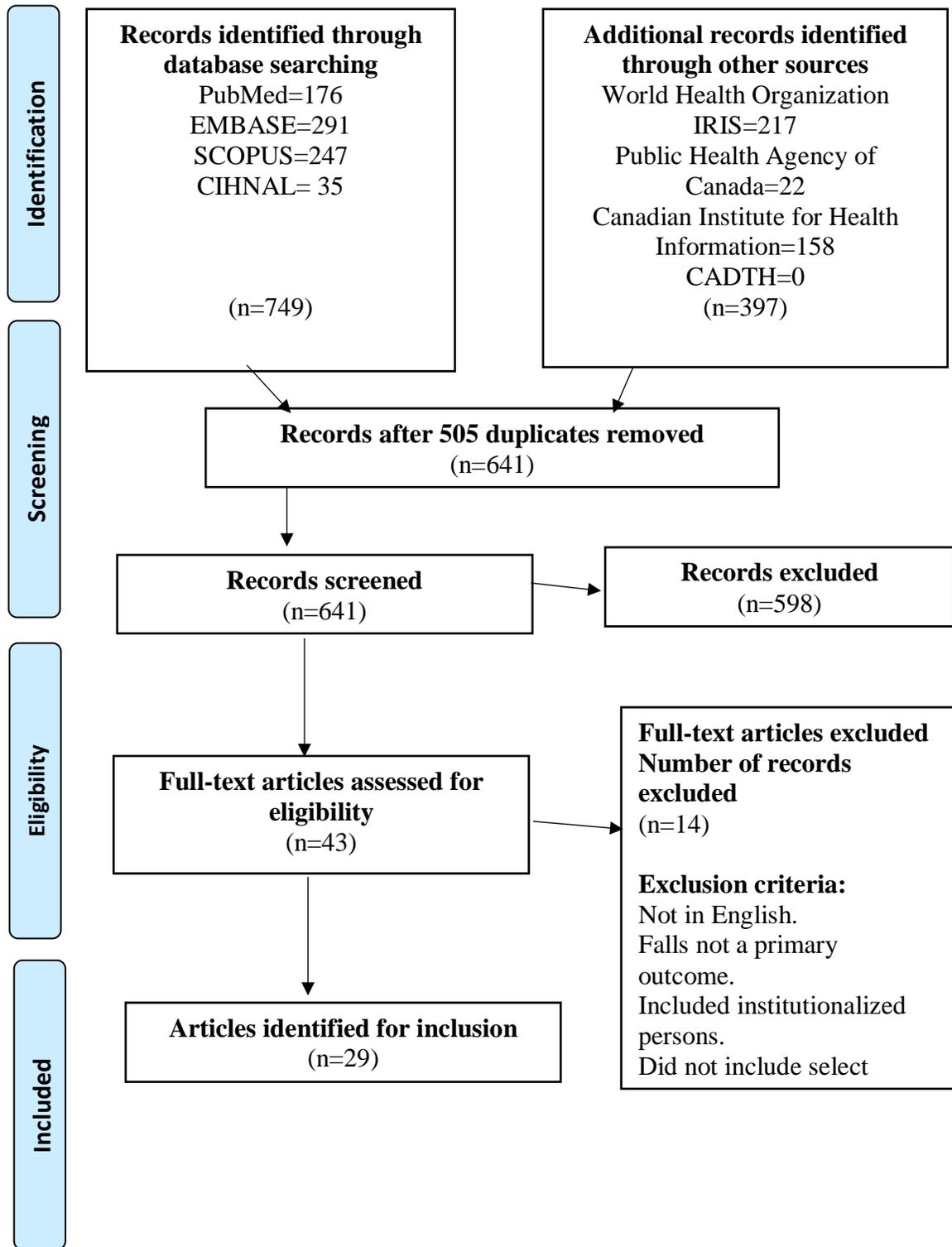
As shown in **Figure 1**, the search yielded 1,146 sources of literature. Using a database management system (RefWorks), 505 duplicates were removed. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) framework was used to track the number of articles identified in each stage of the review (identification, screening, eligibility and included articles) (Moher et al. 2009). After duplicate articles were removed, article titles and abstracts were screened for potential full-text review using the inclusion and exclusion criteria. Five hundred and ninety-eight records were removed because the articles: 1) were not in English (n=1); 2) were review articles, reports, books, editorial, case studies or commentary (n=383); 3) falls was not an outcome variable (n=208); 4) included persons living in institutionalized care (n=4); and 5) did not perform any analysis in older adults (n=2). After full text review, twenty-nine articles were included. The reference list of the selected articles and previous literature reviews were searched for additional studies that might be relevant.

### **2.2.3 Data Extraction**

Included articles had relevant information extracted and entered into a table. **Table 1** summarizes the following information for each article: study title, first author, year published,

country, study objective, design and methods, inclusion and exclusion criteria, sample characteristics (e.g. sample size, age), independent and dependent variables, and key findings.

**Figure 1: PRISMA Flow Diagram of Phases of Literature Review**



**Table 1. Studies on alcohol and psychotropic, anti-depressant, and anti-hypertensive medication use on fall risk in community dwelling older adults**

<b>Authors (year), Title, Country</b>	<b>Study Design &amp; Methods</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Sample Size &amp; Characteristics (N, age, sex)</b>	<b>Independent Variables</b>	<b>Outcome Variables</b>	<b>Key Findings</b>
Number and dosage of central nervous system (CNS) medications on recurrent falls in community elders: the health, aging and body composition study  Hanlon et al. 2009  United States	Prospective cohort survey; 5-year follow-up.	Inclusion: 1) no difficulty walking for ¼ mile 2) no difficulty climbing 10 steps 3) no difficulty performing basic ADLs 4) between the ages of 70 to 79 years	N=3,055  Mean Age=74±2.9  Males=49% Females=51%	Age, sex, race, education, living alone, smoking status, alcohol use (current, past, never), health condition, health status, BMI, diuretic use, digoxin use, Type IA anti-arrhythmic use, polypharmacy, use of CNS medications at years 1,2,3 and 5, number of CNS medications and dosage, pain, severe depression, cognitive impairment	≥2 falls within the past year (comparison group 1 fall or less)	Recurrent falls predicted by high-doses (>3 doses) (OR= 2.89; 95% CI 1.96-4.25; p<.0001), and use of 2+ CNS medications (OR=1.95; 95% CI 1.35-2.81; p<.001)  Both long and short CNS medications were associated with recurrent falls (p<0.05).  Interaction between alcohol and CNS medication was not significant.
An epidemiological	Retrospective cohort survey	Inclusion:	N=704	Age, marital status, circumstance of fall,	Single or recurrent falls	A significant dose-response relationship

<p>study of falls in older community-dwelling females: the Randwick falls and fractures study</p> <p>Lord et al. 1993</p> <p>Australia</p>		<p>1) Age &gt;65 years 2) Community dwelling</p>	<p>Mean age=74.6 SD not reported</p> <p>Females=100%</p>	<p>cognitive status, self-perceived health, health conditions, psychoactive medication use (sedatives, antianxiety, antipsychotics, antidepressants, medications with a hypotensive effect (antihypertensive, diuretics, anticholinergic), disability, physical activity, smoking history, alcohol consumption.</p>		<p>was found between users of psychoactive and non-users.</p> <p>Females taking two psychoactive medications were 2.17x more likely to fall, and those taking one psychoactive medication were 1.25x more likely to fall compared to non-users (<math>\chi^2 = 4.60</math>, <math>p &lt; 0.05</math>).</p> <p>Use of hypertensive medications were not associated with falls.</p> <p>Alcohol consumption was not significantly associated with falls.</p>
<p>Psychoactive medication use, sensori-motor</p>	<p>Prospective cohort study, 1-year follow-up</p>	<p>Inclusion: 1) Community dwelling</p>	<p>N=414 females</p> <p>Mean age = 73.7 ±6.3</p>	<p>Age, use of psychoactive medications (antipsychotics, tricyclic</p>	<p>Single fall</p>	<p>Users of one psychoactive medication were 2.08x more likely to</p>

<p>function and falls in older females.</p> <p>Lord et al. 1995</p> <p>Australia</p>		<p>2) females &gt;65 years</p> <p>3) English speaking</p>	<p>Females=100%</p>	<p>anti-depressants), anti-hypertensives, physical activity, number of alcoholic drinks per week, cognitive status, medical conditions</p>	<p>fall, while those taking &gt;2 psychoactive medications were 8.99x more likely to fall compared to those not taking medications</p> <p>Users of long-acting BZN were 7.03x likely to report recurrent falls (95% CI 2.12-23.28). Short acting BZN did not increase fall risk.</p> <p>Users of anti-depressants were 2.84x likely to report recurrent falls (95% CI 1.00-8.02). Psychoactive medication use was an independent risk factor for falls (p&lt;0.001) after</p>
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						adjusting for frequency of alcohol consumption. Use of anti-hypertensive medications was not associated with falls.
Alcohol and benzodiazepines in falls: An epidemiological view  Kurzthaler et al. 2005  Austria	Cross sectional; examined sub-sample of older adults from total sample  Hospital records.	Inclusion: 1) aged 18 years and older 2) injured by a fall 3) visited the ER and admitted to the hospital	N=615  Mean age=64.8±20.8  Males=44.1% Females=55.9%  >70 years, N=299	Age, sex, severity of injury, blood alcohol concentration, benzodiazepine blood sample	Injurious fall	Falls due to alcohol was more common in males compared to females (p<0.001).  BZN use and falls were not significantly associated with falls among males and females.  No males or females tested positive for both alcohol and BZNs at the time of the fall.
Risk factors for injurious falls leading to hospitalization or	Longitudinal; retrospective cohort; 8-11 years follow-up; examined sub-sample of	Inclusion: 1) Age >20 years	N=19  Age range: 20 to 92	Age, sex, education, marital status, smoking, weekly alcohol consumption	Injurious fall	Males who consumed >1000g of alcohol per month had an 8.45x greater risk of an

<p>death in a cohort of 19,500 adults</p> <p>Malmivaara et al. 1993</p> <p>Finland</p>	<p>older adults from total sample</p>	<p>2) hospitalized or death due to injurious fall</p>	<p>Mean age: 45; SD not reported</p> <p>N (&gt;60) =3909</p> <p>Men (&gt;60) =1769</p> <p>Females (&gt;60) =2140</p>	<p>during previous month, physical activity, weight, medications, medical conditions, and prior injuries</p>	<p>injurious fall (95% CI 2.47-28.89) compared to those who consumed 500-999g (RR=1.32; 95% CI 0.37-4.69).</p> <p>Females who consumed 500-999g of alcohol per month had 14.42x the risk of an injurious fall (95% CI 1.19-110.16) compared to those who consumed less (<math>\geq</math>99g) (RR=0.83; 95% CI 0.46-1.53).</p> <p>Males using psychotropic medications had 2.9x the risk of injurious falls (95% CI 1.15-7.09) compared to non-users.</p> <p>Females using psychotropic</p>
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						medications had 1.7x the risk of injurious falls (95% CI 1.09-2.68) compared to non-users.
<p>Association between use of sedatives or hypnotics, alcohol consumption, or other risk factors and a single injurious fall or multiple injurious falls: a longitudinal general population study</p> <p>Stenbacka et al. 2002</p> <p>Sweden</p>	<p>Longitudinal; retrospective cohort; 12-year follow-up; examined sub-sample of older adults from total sample</p> <p>Survey; Stockholm Health of the Population Study.</p>	<p>Inclusion:</p> <p>1) Age 20 to 89 years</p> <p>2) hospitalized or death due to injurious fall</p>	<p>N= 4,023</p> <p>Mean age±SD not reported</p> <p>Males (&gt;60) =471</p> <p>Females (&gt;60) =637</p>	<p>Age, sex, health, living conditions, alcohol consumption per month, use of hypnotics or sedatives</p>	<p>Single or recurrent injurious falls</p>	<p>High levels of alcohol consumption (500+g/month) was not associated with falls in men &gt;60 years of age.</p> <p>Among males ≥60, use of hypnotics or sedatives was not associated with falls (RR=0.87; 95% CI 0.48-1.74).</p> <p>Females ≥60 years of age who consumed high levels of alcohol and used sedatives had 2.13x and 1.50x the risk of having an injurious fall, respectively (95% CI</p>

						1.05-4.32) and (95% CI 1.03-2.19).
Falls, depression and anti-depressants in later life: a large primary care appraisal  Kerse et al. 2008  Australia	Cross-sectional survey	Inclusion: 1) >60 years of age 2) community-dwelling	N=21,900  Mean age: 71.8±7.7  Females=12,074 (58.4%)	Age, sex, living arrangements, marital status, physical activity, education, social support, BMI, medications (antipsychotics, hypnotics, anxiolytics), individual types of type of anti-depressants (cyclic, SSRIs, MAOI, MAOI-A), medical conditions smoking, weekly alcohol use, self-rated health, balance confidence, depression, anxiety, suicidal thought/attempt.	Single or recurrent falls	Users of SSRIs were 1.55x more likely to report a single fall (95% CI 1.26-1.90), 1.66x more likely to report recurrent falls (95% CI 1.36-2.02) and 1.52x as likely to report an injurious fall (95% CI 1.25-1.84).  Females >80 years with depressive symptoms and taking anti-depressants were 1.85x as likely to report recurrent falls (95% CI 1.17-2.93), and 2.59x as likely to report injurious falls (95% CI 1.65-4.37) compared to those without depressive symptoms.

						Females >80 years with depression and users of SSRIs were 3.96x more likely to report injurious falls (95% CI 2.13-7.36) compared to those without depression and using SSRI's.
Association of psychotropic medication use with falls among older adults in Germany  Du et al. 2013  Germany	Cross-sectional survey  Data obtained from National Health Interview and Examination Survey for Adults 2008-2011.	Inclusion: 1) 65-79 years	N=1,833  Mean age±SD not reported  Males=46% Females=54%	Age, sex, living arrangements, socioeconomic status, BMI, disability, medication use (all psychotropics, anti-depressants, narcotics, anti-diabetes, anti-epileptics, antiparkinson, anti-hypertensives) polypharmacy, yearly alcohol consumption, vision impairment, frailty.	Single fall and recurrent falls (>2)	Use of psychotropic medications overall was associated with higher risk of falls (OR=1.64; 95% CI 1.14-2.37).  Use of synthetic anti-depressants and specifically SSRIs increased fall risk by 2.66x and 6.22x, respectively (95% CI 1.50-4.73) and (95% CI 2.28-17.0).  Daily alcohol

						consumption was not associated with fall risk.
<p>Serotonin-norepinephrine reuptake inhibitor antidepressants and the risk of falls in older adults</p> <p>Gribbin et al. 2011</p> <p>United Kingdom</p>	<p>Case-control and case series</p> <p>Data obtained from the Health Improvement Network (primary care database).</p>	<p>Inclusion:</p> <p>1) &gt;60 years with first fall between 2003-2006</p> <p>Case-series analysis:</p> <p>1) first fall between 2001-2008</p> <p>2) cases defined as 'first fall within study period'</p> <p>3) controls had no record of falls and contributed data</p>	<p>Cases=9,862 Controls= 52, 100</p> <p>Mean age cases= 77.5 SD not reported</p> <p>Mean age controls= 76.4 SD not reported</p> <p>Males=32% Females=68%</p>	<p>Age, sex, coronary heart disease, diabetes or cardiovascular disease, current prescription of antipsychotic, hypnotic/anxiolytic, diuretic, digoxin, type 1a anti-arrhythmic, exposure of SNRI, SSRI, TCA (never, previously, recently, currently).</p>	<p>Single fall</p>	<p>Increased risk of falls within 28 days of first prescription of SNRI (OR=1.79; 95% CI 1.42-2.25); SSRI (OR=2.04; 95% CI 1.86-2.24); TCA (OR=1.61; 95% CI 1.46-1.76).</p> <p>Falls were 2.5x higher in those y prescribed a SNRI; 2.04x higher in those prescribed an SSRI; and 1.61x higher in those prescribed a TCA compared to non-users. Risk of falls increased with age in TCA users (p=0.003).</p>

<p>Medications and multiple falls in elderly people: the St Louis OASIS study</p> <p>Cumming et al. 1991</p> <p>United States</p>	<p>Retrospective cohort survey</p>	<p>Inclusion: 1)aged 65 years and older 2) community dwelling</p>	<p>N=1, 358</p> <p>Mean age± SD not reported</p>	<p>Age, sex, socio-demographic characteristics, self-rated health status, illness (arthritis, cancer, congestive heart failure, diabetes, emphysema, heart trouble, respiratory infection, stroke), cognitive impairment, stressful life events, vision, hearing, alcohol use, exercise, medication use (over the counter and prescribed).</p>	<p>2 or more falls</p>	<p>Diazepam use resulted in 3.7x greater risk of recurrent falls; use of anti-hypertensives diltiazem and diuretic use resulted in 1.8x greater risk of recurrent falls, respectively.</p> <p>Increased dose of diazepam (&gt;2.5mg per day) was associated with a 10.8x greater risk of having recurrent falls.</p> <p>Increased dose of diltiazem (&gt;180mg per day) was associated with a 10x greater risk of having recurrent falls.</p>
<p>New evidence on benzodiazepine</p>	<p>Prospective cohort survey</p>	<p>Inclusion:</p>	<p>N= 321,322</p> <p>Mean age± SD not reported</p>	<p>Age, sex, use of concomitant medications (other</p>	<p>Fall-related hospitalization following</p>	<p>Fall risk in older adults within first four weeks of using</p>

<p>use and falls: the time factor</p> <p>Neutel et al. 1996</p> <p>Canada</p>	<p>Saskatchewan Health Databases.</p>	<p>1) aged 20 years and older</p> <p>Controls: not received a BZN prescription in previous 6 months</p>	<p>Cases (&gt;60) BZN sedatives= 35,308</p> <p>Cases (&gt;60) BZN tranquillizers= 45,724</p> <p>Controls (&gt;60) = 51,841</p>	<p>tranquilizers, sedatives, narcotics, analgesics, antipsychotics, antidepressants, anticonvulsants), history of treatment for alcohol/medication abuse preceding 12 months, presence or absence of social assistance</p>	<p>prescription use</p>	<p>BZN (OR=4.0; 95% CI 2.4-6.6) in males and (OR=2.3; 95% CI 1.7-3.2) in females; BZN tranquillizers in older adults increased fall risk in males (OR=2.5; 95% CI 1.4-4.3) and females (OR=1.6; 95% CI 1.2-2.3)</p> <p>Risk of hospitalization for falls BZN prescription in persons &gt;60 years: Triazolam (OR=2.7; 95% CI 2.0-3.6); Flurazepam (OR=3.4; 95% CI 2.5-4.7); Diazepam (OR=1.8; 95% CI 1.3-2.5); Lorazepam (OR=2.0; 95% CI 1.3-3.1); Oxazepam (OR=2.2; 95% CI 1.4-3.4).</p>
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						Persons $\geq 80$ years and using BZN sedatives had hospitalization fall rates from BZN sedatives and tranquilizer use (94.5 per 10,000 and 52.8 per 10,000) compared to unexposed controls.
Psychological well-being is an independent predictor of falling in an 8-year follow-up of older adults  Anstey et al. 2008  Australia	Prospective cohort survey  Australian Longitudinal Study of Ageing	Inclusion: 1) aged 70 years and older  Exclusion: 1) diagnosed with dementia	N= 787 Mean age $\pm$ SD not reported  Males=42.3% Females=57.7%	Age, sex, education, mini-mental state exam score, visual acuity, grip strength, balance, heart condition, hypertension, stroke or transient ischemic attack, diabetes, psychotropic medication use, smoking, frequency of alcohol use, psychological well-being	Single fall and $\geq 2$ falls	Psychotropic use was not associated with falls. Association between alcohol consumption and falls was dependent on level of consumption: 2-3 drinks per week increased recurrent fall risk by 1.24x (95% CI 1.06-1.46) and $\geq 4$ drinks per week reduced fall rate (OR=0.81; 95% CI 0.71-0.92).

<p>Falls risk among a very old home-dwelling population</p> <p>Inattiniemi et al. 2009</p> <p>Finland</p>	<p>Prospective cohort survey</p>	<p>Inclusion: 1) aged 85 years and older</p>	<p>N=555</p> <p>Fallers mean age= 88±3</p> <p>Non-fallers mean age= 88±2</p> <p>SD not reported</p>	<p>Age, sex, home-nursing care, education, living alone, recurrent falls in previous years, sedentary physical activity in previous year, self-rated physical and mental health, symptoms of anxiety/nervousness or fear of falling, sleeping problems, breathlessness, poor vision when moving, short geriatric depression score <math>\geq 7</math>, mini mental state exam score, lower extremity performance score, use of psychotropic medications (anti-psychotics, anxiolytics, hypnotics, antidepressants, anti-</p>	<p>Single or recurrent falls</p>	<p>Users of antipsychotics were 2.15x more likely to fall (95% CI 1.36-3.40); users of hypnotics were 1.40x more likely to fall (95% CI 1.10-1.79); and users of antidepressants were 1.82x more likely to fall (95% CI 1.32-2.50) compared to non-users. Use of anti-hypertensive medications were not associated with falls.</p>
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				hypertensives) number of medications.		
<p>Risk of falls in 85-year-olds is associated with functional and cognitive status: the Octabaix study</p> <p>Ferrer et al. 2012</p> <p>Spain</p>	<p>Cross-sectional survey</p> <p>Octabaix Study Group</p>	<p>Inclusion: 1) were 85 years old</p>	<p>N=328</p> <p>Mean age=85</p> <p>Females fallers=72%</p> <p>Females non-fallers=57.4%</p>	<p>Sex, marital status, education, living alone, visual and hearing impaired, over al comorbidity, hypertension, dyslipidemia, diabetes, ischemic cardiopathy, heart failure, atrial fibrillation, previous stroke, dementia, Parkinson's disease, Gijon test, activities of daily living and instrumental activities of daily living, cognitive status, quality of life, gait, nutrition, psychotropic medication use, total number of medications</p>	<p>Single fall</p>	<p>Psychotropic medication use was not associated with falls.</p>

<p>Do older adults with cancer fall more often? A comparative analysis of falls in those with and without cancer</p> <p>Spoelstra et al. 2013</p> <p>United States</p>	<p>Longitudinal, cohort survey</p>	<p>Inclusion: 1) aged 65 years and older 2) enrolled in home and community-based service program 3) diagnosed with cancer no earlier than the year 2000 4) met Medicaid-defines nursing facility level-of-care criteria</p>	<p>N=9,481</p> <p>Males=29.2% Females=67.5% Missing data (sex)=3.3%</p> <p>Cancer patients N= 862 Cancer patients: 77±7.5</p> <p>Non-cancer patients N=8,617 Non-cancer patients: 77±6.5</p>	<p>Age, sex, race and ethnicity, marital status, lives with someone time alone during the day, medication use (hypnotics, anti-depressants, antipsychotics, anti-anxiety), cognition, vision, weight loss, pain, comorbidities, activities of daily living</p>	<p>Single or recurrent falls</p>	<p>Use of anti-depressants increased fall risk (OR=1.29; 95% CI 1.19-1.40) compared to non-users (diagnosis of cancer was not controlled for).</p> <p>Anti-anxiety, anti-psychotics and hypnotics were not associated with falls.</p>
<p>Central nervous system medications and falls risk in men</p>	<p>Cross-sectional survey</p>	<p>Inclusion: 1) Males aged 60-75 years</p>	<p>N=4,696</p> <p>Median age (IQR)=66.3</p>	<p>Use of CNS medications in last year including anti-depressants,</p>	<p>Single and recurrent falls</p>	<p>Users of SSRIs (OR=3.1; 95% CI 2.0-5.0); TCAs</p>

<p>aged 60-75 years: the study on male osteoporosis and aging (SOMA)</p> <p>Masud et al. 2013</p> <p>Denmark</p>			<p>(63.1-70)</p>	<p>antipsychotics, BZN, anti-epileptics, opiates, other analgesics</p>		<p>(OR=2.2; 95% CI 1.0-4.7); and BZN (OR=1.5; 95% CI 0.9-2.6) resulted in increased fall risk compared to non-users.</p> <p>Persons with recurrent falls were more likely to be taking anti-depressants (OR=2.9; 95% CI 1.8-4.8), specifically SSRIs (OR=3.1; 95% CI 1.8-5.6); and BZN (OR=2.3; 95% CI 1.2-4.3).</p> <p>Alcohol use did not significantly affect results.</p>
<p>Angiotensin system-blocking medications are associated with</p>	<p>Prospective cohort survey</p>	<p>Inclusion: 1) aged 70 years and older</p>	<p>N=520</p> <p>Mean age±SD= 79.7±4.4</p>	<p>Age, sex, BMI, hypertension, previous heart attack, previous</p>	<p>Single fall</p>	<p>Non-fallers were more likely to be users of anti-hypertensive</p>

fewer falls over 12 months in community dwelling older people.  Wong et al. 2013  Australia			Males=49.2% Females=50.8%	stroke, diabetes, blood pressure, orthostatic hypotension, physical strength, anti-hypertensive medications (alpha-blocker, angiotensin receptor blocker, ACEi, ASBMs, BB, any diuretic, thiazide only, statin), psychotropic medication, total number of medications		medications (e.g. ASBM) (OR=0.68; 95% CI 0.48-0.97) compared to fallers. Fallers were more likely to use psychotropic medications (OR=1.68; 95% CI 1.11-2.53) compared to non-fallers.
Risk factors for serious fall related injury in elderly females living at home  Bergland et al. 2004  Norway	Prospective cohort survey	Inclusions: 1) aged 75 years and older 2) females	N=307  Mean age= 80.8 (range 75-93)	Activities of daily living and disability in instrumental activities of daily living, medications (anti-hypertensives), total number of medications, rheumatic disorder, osteoporosis, cognitive	Single injurious fall	Use of anti-hypertensive medications increased risk of injurious falls by 2.4x (95% CI 1.1-6.5).

				impairment, impaired vision, comorbidities, lower limb amputated, inability to climb more than 30cm step, arthrosis of the hip, inability to get up from floor, maximum walking speed, needs care from health professional or caregiver		
Medication use and falls in community dwelling older persons  Kelly et al. 2003  Canada	Case-control  Regional health database.	Inclusion: 1) aged 66 years and older 2) visit to ER	N=11,390  Females Cases=69% Controls= 57%  Fallers= 2,278 Mean age± S.D= 78.5±7.7  Non-fallers= 9,112 Mean age±S.D= 74.5±6.7	Medication use 30 days prior to the fall (anti-histamines, narcotic pain killers, anti-inflammatories, anti-convulsants, anti-depressants, anti-psychotics, sedatives, anti-parkinsonian, visual impairment agents, anti-ulcer agents, corticosteroids, sex	Single injurious fall	Use of anti-depressants increased injurious fall risk by 1.46x (95% CI 1.21-1.78).  Anti-psychotics and sedatives were not associated with injurious falls.  Anti-hypertensive medication use was

				hormones, diabetes agents, thyroid agents, anti-coagulants and anti-hypertensives), age, sex, median income, hospitalization within previous year, comorbidities		not associated with injurious falls.
Fall-risk screening test: a prospective study on predictors for falls in community dwelling elderly  Tromp et al. 2001  Netherlands	Prospective cohort survey  Longitudinal Aging Study Amsterdam	Inclusion: 1) aged 65 years or older 2) participation in previous data collection cycle	N=1,285  Mean age± S.D= 75.2±6.5	Age, sex, living situation, education, urbanization, BMI, height and weight, diagnosis of chronic disease (COPD, CVD, stroke, urinary incontinence, diabetes, joint disorders, malignant neoplasms), medication use, Mini Mental State Exam score, physical function, blood pressure, distant vision and hearing, level of activity,	Any falls (≥1) and recurrent (≥2) falls	Use of benzodiazepines was a significant predictor for any falls (OR=1.6; 95% CI 1.1-2.2), but not recurrent falls (OR=1.4; 95% CI 0.9-2.2).  Alcohol was not associated with falls.

				ability to walk, alcohol, smoking, fear of falling.		
Predictors of falls and fracture in the longitudinal aging study Amsterdam  Tromp et al. 1998  Netherlands	Prospective longitudinal cohort study  Survey	Inclusion: 1) aged 65 years or older 2) born before 1930	N=1, 469  Mean age± S.D= 72.6±6.6  Males=48% Females=52%	Age, sex, education level, living situation, chronic disease (stroke, urinary incontinence), CVD, joint disorders, comorbidities, past fractures, use of medications (anti-arrhythmic, anti-hypertensives, anti-epileptic, analgesics, sedatives), use of multiple medications, depression, cognitive impairment, physical function, level of activity, body weight and height	Any fall (≥1), recurrent (≥2) falls, and injurious falls	Anti-hypertensive medication use was associated with any fall (OR=1.4; 95% CI 1.0-1.9) and recurrent fall risk (OR=1.6; 95% CI 1.1-2.3).  Users of sedatives were 1.8x more likely to experience an injurious fall compared to non-users (95% CI 1.0-3.3).  Alcohol was not associated with falls.
Psychotropic medications and risk for falls	Cross sectional survey	Inclusion: 1) participant	N=2,854	Age, sex, marital status, living alone, activities of daily	Single fall within 90 days of assessment	Use of psychotropics was associated with a 47% increased risk of

<p>among community dwelling frail older people: an observation study</p> <p>Landi et al. 2005</p> <p>Italy</p>		<p>in Network Home Care project</p>	<p>Mean age± SD= 77.2±12.1</p> <p>Males= 42%</p> <p>Females=58%</p>	<p>living, cognitive performance score, number of diseases, number of medications, foot problems, gait problems, fear of falling, visual impairment, wandering, depression, medication use (anti-psychotics, BZN, anti-depressants, sedatives/hypnotics)</p>	<p>falls (adjusted OR: 1.47; 95% CI 1.24-1.74) compared to non-users.</p> <p>Compared to non-users, fall risk was associated with the following medications:</p> <p>Typical anti-psychotics (OR=1.49; 95% CI 1.10-2.51);</p> <p>Atypical anti-psychotics (OR=1.45; 95% CI 1.00-2.11);</p> <p>BZN (long-acting) (OR=1.45; 95 % CI 1.00-2.19)</p> <p>BZN (short-acting) (OR=1.32; 95% CI 1.02-1.72)</p> <p>Anti-depressants were not associated with increased fall risk.</p>
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<p>Central nervous system-active medications and risk for falls in older females</p> <p>Ensrud et al. 2002</p> <p>United States</p>	<p>Prospective cohort survey</p> <p>Study of Osteoporotic Fractures</p>	<p>Inclusion: 1) females aged 65 years and older</p>	<p>N= 8,127</p> <p>Non-users Mean age± SD=76.9±5.0</p> <p>BZN users Mean age± SD =77±4.7</p> <p>Anti-depressant users Mean age± SD =77.1±4.8</p>	<p>Age, self-reported health, physical activity, smoking, dizziness, history of falls, history of stroke, diabetes, Parkinson's, dementia, chronic obstructive lung disease, osteoarthritis, non-skin cancer, activities of daily living, Mini-Mental State Exam score, depressive symptoms, body weight, and medication history (BZN, anti-depressants, anti-convulsants and narcotics)</p>	<p>Single or recurrent falls</p>	<p>Compared to non-users, users of BZN and anti-depressants were 1.51x and 1.54x more likely to have recurrent falls (95% CI 1.14-2.01), (95% CI 1.14-2.07), respectively. Use of anti-depressants increased fall risk by 54%.</p> <p>Females using short or long acting BZN had an increased risk of recurrent falls compared to non-users (OR=1.42; 95% CI 0.98-2.04) and (OR=1.56; 95% CI 1.00-2.43).</p> <p>Compared to non-users, users of SSRIs were more likely to have recurrent falls</p>
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						by 3.45x (95% CI 1.89-6.30).  TCAs were not associated with falls.
Falls in African American and white community dwelling elderly residents  Hanlon et al. 2002  United States	Prospective cohort survey  Established Populations for Epidemiologic Studies of the Elderly	Inclusion: 1) aged 65 years or older	N=2, 996  Mean age±SD= 72.3±5.8	Age, race, sex, income, educational in years, urban/rural residence, smoking, alcohol use, BMI, number of disabilities, self-rated health, sleep difficulty, chronic disease (arthritis, stroke, history of broken bones, diabetes), severe depression, cognitive impairment, visual function, medication use (BZN, anti-hypertensives (i.e. diuretics), prednisone, other cardiac medications, nonsteroidal anti-	Single or recurrent falls	Compared to non-users, BZN use was as associated with single and recurrent falls (crude OR=1.50; 95% CI 1.14-1.96).  Anti-hypertensives (e.g. diuretics) and other cardiac medications were not associated with falls.  Alcohol was not associated with falls.

				inflammatory medications) and number of prescription and non-prescription medications being taken		
<p>Is a fall just a fall: correlates of falling in health older persons. The health, aging and body composition study</p> <p>de Rekeneire et al. 2003</p> <p>United States</p>	<p>Cross sectional survey</p> <p>Health, Aging and Body Composition Study</p> <p>Survey</p>	<p>Inclusion: 1) aged 70-79 years</p>	<p>N=3,050</p> <p>Mean age±SD not reported</p> <p>Fallers: Males=18.3% Females=24.1%</p>	<p>Sex, race, functional status, health status, diagnosis of osteoporosis, cerebrovascular disease, depression, poor eyesight, urinary incontinence symptoms, joint pain, cognitive function, medication use (BZN), number of medications, physical performance, BMI</p>	<p>Single and recurrent falls</p>	<p>BZN use was associated with a history of falls (OR= 1.6; 95% CI 1.0-2.6) in females, but not males.</p>
<p>Falls in 84- to 85-year old people living at home</p>	<p>Cross sectional survey</p>	<p>Inclusion: 1) aged 84 or 85 years</p>	<p>N=732</p> <p>Mean age=85</p> <p>Fallers:</p>	<p>Sex, marital status, living situation, activities, smoking, need of community service, dizziness,</p>	<p>Single fall</p>	<p>Anti-depressant use was an independent risk factor for falls (p&lt;0.01).</p>

<p>Svensson et al. 1992</p> <p>Sweden</p>			<p>Males=32% Females=68%</p>	<p>quality of night sleep, well-being and tiredness, hearing function, heart rate and blood pressure, balance tests, activities of daily living, mobility, medication use (sedative/hypnotics, anti-hypertensives (i.e. diuretics)) Mini Mental State Exam.</p>		<p>Sedatives/hypnotics, and anti-hypertensive medications were not associated with falls.</p>
<p>Falls by elderly people at home: prevalence and associated factors</p> <p>Blake et al. 1988</p> <p>United Kingdom</p>	<p>Cross sectional study</p>	<p>Inclusion: 1) aged 65 years and older</p>	<p>N=1,042</p> <p>Fallers: Males=24.3% Females=41.6%</p>	<p>Age, sex, reason for fall, poor vision or blind, hard of hearing, arthritis, CVD, stomach issues, giddiness, headaches, foot trouble, urinary incontinence, long-term disabilities, handgrip strength, joint flexibility, total number of medications</p>	<p>Single or recurrent falls</p>	<p>Use of anti-depressants and hypnotics were significantly associated with falls (<math>\chi^2=7.16</math>, <math>p&lt;0.01</math>; and <math>\chi^2=4.39</math>, <math>p&lt;0.05</math>). Falls was not associated with diuretics, anti-hypertensives or tranquilizers.</p>

				prescribed, medication use (anti-hypertensives, diuretics, hypnotics, tranquilizers, anti-depressants)		
Risk factors for falls among elderly persons living in the community Tinetti et al. 1988  United States	Prospective cohort  Yale Health and Aging Project	Inclusion: 1) aged 75 years and older 2) English speaking 3) not ambulatory	N=336  Mean age±SD= 78.3±5.1  Males=45% Females=55%	Age, sex, race, living situation, activities of daily living, balance and gait assessment, BMI, history of falls, environmental hazards, cognitive impairment, depression, mobility, hospitalized in past year, urinary incontinence, use of cane or walker, physical activity, alcohol use, use of medications (sedatives, anti-hypertensives and diuretics), physical	Single fall	Use of sedatives increased fall risk by 2.5x after controlling for cognitive impairment (95% CI 1.6-3.9) and by 2.0x after controlling for depression (95% CI 1.3-3.0).  Individually, use of sedatives increased fall risk by 28.3x (95% CI 3.4-239.4). Alcohol use was not associated with falls.

				symptoms or impairments		
<p>Antihypertensive medications and serious fall injuries in a nationally representative sample of older adults</p> <p>Tinetti et al. 2014</p> <p>United States</p>	Prospective cohort survey study	<p>Inclusion:</p> <p>1) aged 70 years or older</p> <p>2) traditional Medicare beneficiary</p>	<p>N=4,961</p> <p>Mean age±SD= 80.2±6.8</p> <p>Males=38.5%</p> <p>Females=61.5%</p>	<p>Age, sex, race, education level, self-rated health, smoking, BMI, weight loss, prescription medication insurance, blood pressure measured &lt;6 months, dependent in basic or instrumental activities of daily living, mobility difficulty, diagnosis chronic illness, psychosis, medication other than anti-hypertensives, type of anti-hypertensive medications (diuretics, ACEi, ARB, BB, CCB, centrally acting</p>	Injurious fall	<p>Use of moderate dosage anti-hypertensives was associated with serious falls (adjusted hazard ratios=1.40; 95% CI 1.03-1.90).</p> <p>Use of high dosage anti-hypertensives was not associated with serious falls (adjusted hazard ratios=1.28; 95% CI 0.91-1.80).</p> <p>Those with a history of fall and taking a high dosage anti-hypertensive medication were more likely to have a serious fall (adjusted hazard ratio= 2.31; 95% CI 1.01-5.29)</p>

				antiadrenergic agents), number of anti-hypertensive medications		compared to moderate-intensity users (adjusted hazard ratio= 2.17; 95% CI 0.98-4.80).
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**Footnotes:** CVD: cardiovascular disease; COPD: chronic obstructive pulmonary disease; BZN: benzodiazepine; CNS; Central Nervous System; MAOI: monoamine oxidase inhibitors; MAOI-A: monoamine oxidase inhibitors; SSRIs: selective serotonin reuptake inhibitors; ACEi: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blockers; ASBMs: angiotensin system-blocking medication; BB: beta-blocker; CCBs: calcium channel blockers; BMI: Body Mass Index; OR: Odds ratio; RR: Relative risk; IRR: Incidence rate ratio

## 2.3 Results

### 2.3.1 Description of Primary Studies

As shown in **Table 1**, studies were published between 1988 and 2017. Sample sizes ranged from 307 to 321,422. Sixteen studies had follow-up periods, ranging from 11 months to 12 years (Anstey et al. 2008; Bergland et al. 2004; Ensrud et al. 2002; Gribbin et al. 2011; Hanlon et al. 2002; Hanlon et al. 2009; Iinattiniemi et al. 2009; Lord et al. 1995; Malmivaara et al. 1993; Stenbacka et al. 2002; Svensson et al. 1992; Tinetti et al. 1988; Tinetti et al. 2014; Tromp et al. 1998; Tromp et al. 2001; Wong et al. 2013). Four studies included samples with females only (Bergland et al. 2004; Ensrud et al. 2002; Lord et al. 1993; Lord et al. 1995), one study included males only (Masud et al. 2013); the other 22 studies had samples with mixed sex composition. Five studies were conducted in Australia (Anstey et al. 2008; Kerse et al. 2008; Lord et al. 1993; Lord et al. 1995; Wong et al. 2013), fourteen in Europe (Bergland et al. 2004; Blake et al. 1988; Du et al. 2017; Ferrer et al. 2012; Gribbin et al. 2011; Iinattiniemi et al. 2009; Kurzthaler et al. 2005; Landi et al. 2005; Malmivaara et al. 1993; Masud et al. 2013; Stenbacka et al. 2002; Svensson et al. 1992; Tromp et al. 1998; Tromp et al. 2001), eight in the United States (Cumming et al. 1991; de Rekeneire et al. 2003; Ensrud et al. 2002; Hanlon et al. 2002; Hanlon et al. 2009; Spoelstra et al. 2013; Tinetti et al. 1988; Tinetti et al. 2014); and two in Canada (Kelly et al. 2003; Neutel et al. 1996).

Eleven studies conducted surveys (Anstey et al. 2008; Blake et al. 1988; Cumming et al. 1991; Kerse et al. 2008; Lord et al. 1993; Masud et al. 2013; Stenbacka et al. 2002; Svensson et al. 1992; Tinetti et al. 2014; Tromp et al. 1998; Tromp et al. 2001); fourteen studies conducted both a survey and a clinical assessment (e.g. height, weight, blood pressure, Mini Mental State Examination) (Bergland et al. 2004; de Rekeneire et al. 2003; Du et al. 2017; Ensrud et al. 2002;

Ferrer et al. 2012; Hanlon et al 2002; Hanlon et al. 2009; Iinattiniemi et al. 2009; Landi et al. 2005; Lord et al. 1995; Malmivaara et al. 1993; Spoelstra et al. 2013; Tinetti et al. 1988; Wong et al. 2013), two studies relied on hospital records for data (Gribbin et al. 2011; Neutel et al. 1996), one study relied on a regional database (Kelly et al. 2003), and one study relied on blood samples (Kurzthaler et al. 2005).

Studies examined single falls, recurrent falls or both. Four studies examined single falls (Ferrer et al. 2012; Gribbin et al. 2011; Landi et al. 2005; Svensson et al. 1992), twelve examined recurrent falls (Blake et al. 1988; Cumming et al. 1991; de Rekeneire et al. 2003; Du et al. 2017; Ensrud et al. 2002; Hanlon et al. 2009; Iinattiniemi et al. 2009; Lord et al. 1993; Spoelstra et al. 2013; Tromp et al. 1998; Tromp et al. 2001; Wong et al. 2013), and six examined both single and recurrent falls (Anstey et al. 2008; Hanlon et al. 2002; Kerse et al. 2008; Lord et al. 1995; Masud et al. 2013; Tinetti et al. 1988). Seven studies had a primary outcome of fall related injury, hospitalization or death (Bergland et al. 2004; Kelly et al. 2003; Kurzthaler et al. 2005; Malmivaara et al. 1993; Neutel et al. 1996; Stenbacka et al. 2002; Tinetti et al. 2014).

### **2.3.2 Anti-Psychotics/Benzodiazepines**

Twenty-six studies examined whether psychotropic medications increased fall risk: sixteen cohort (Anstey et al. 2008; Cumming et al. 1991; Ensrud et al. 2002; Hanlon et al. 2002; Hanlon et al. 2009; Iinattiniemi et al. 2009; Lord et al. 1993; Lord et al. 1995; Malmivaara et al. 1993; Neutel et al. 199; Spoelstra et al. 2013; Stenbacka et al. 2002; Tinetti et al. 1999; Tromp et al. 1998; Tromp et al. 2001; Wong et al. 2013); nine cross-sectional studies (Blake et al. 1988; de Rekeneire et al. 2003; Du et al. 2017; Ferrer et al. 2012; Kerse et al. 2008; Kurzthaler et al. 2005; Landi et al. 2005; Masud et al. 2013; Svensson et al. 1992) and one case-control (Kelly et al. 2003). Sample sizes ranged from 328 to 321,422. Fourteen studies defined falls as “falling to the

ground unintentionally” (Bergland et al. 2004; Cumming et al. 1991; Du et al. 2017; Ensrud et al. 2002; Ferrer et al. 2012; Hanlon et al. 2009; Kerse et al. 2008; Landi et al. 2005; Lord et al. 1993; Lord et al. 1995; Tinetti et al. 1988; Tromp et al. 1998; Tromp et al. 2001; Wong et al. 2013), twelve did not provide a definition of falls.

Nineteen studies found that psychotropic medication use significantly increased fall risk after controlling for age (Blake et al. 1988; Cumming et al. 1991; de Rekeniere et al. 2003; Du et al. 2017; Ensrud et al. 2002; Hanlon et al. 2002; Hanlon et al. 2009; Iinattiniemi et al. 2009; Landi et al. 2005; Lord et al. 1993; Lord et al. 1995; Malmivaara et al. 1993; Masud et al. 2013; Neutel et al. 1996; Stenbacka et al. 2002; Tinetti et al. 1988; Tromp et al. 1998; Tromp et al. 2001; Wong et al. 2013); one study did not control for age but a significant association was found between psychotropic medication use and falls (Spoelstra et al. 2013); six studies found no association (Anstey et al. 2008; Ferrer et al. 2012; Kelly et al. 2003; Kerse et al. 2008; Kurzthaler et al. 2005; Svensson et al. 1992).

#### *2.3.2.1 Anti-Psychotics/Benzodiazepines and Single Falls*

Between 9% and 58.7% of single fallers were taking some form of psychotropic medication. Anti-psychotics, hypnotics and anxiolytics were not associated with single falls; however, other CNS medications (not defined) significantly increased fall risk by 1.22x (Kerse et al. 2008). In contrast, anti-psychotics, both first generation and second generation were used by up to 9.4% of single fallers and were found to be associated with falls (Landi et al. 2005). One study found sedative use increased fall risk by 2.5x after controlling for cognitive impairment and 2.0x after controlling for depression (Tinetti et al. 1988). Fall risk in users of psychotropic medications was not stated in one study (Ferrer et al. 2012).

### *2.3.2.2 Anti-Psychotics/Benzodiazepines and Recurrent Falls*

Users of psychotropic medications were 64% more likely to have recurrent falls compared to non-users, and 1.84x more likely to experience recurrent falls compared to non-users (Du et al. 2017). Two studies found females using benzodiazepines were more likely to experience recurrent falls compared to non-users (de Rekeneire et al. 2003; Ensrud et al. 2002). Fall history was also associated with prospective falls. For example, in a study of females, users of benzodiazepines were 1.51x more likely to experience recurrent prospective falls compared to non-users (Ensrud et al. 2002). Similarly, males using benzodiazepines were 2.3x more likely to have recurrent prospective falls compared to non-users (Masud et al. 2013).

Overall use of central nervous system medications increased the risk of recurrent falls by 1.55x (Hanlon et al. 2009). Furthermore, while benzodiazepines predicted single falls (OR=1.6; 95% CI 1.1-2.2), they were not predictive of recurrent falls ( $\geq 2$ ) in a prospective cohort study (Tromp et al. 2001). Specific types of anti-psychotics or benzodiazepines may increase recurrent fall risk. For example, diazepam resulted in a 3.7x greater risk of recurrent falls compared to non-users (Cumming et al. 1991) and anti-psychotics increased recurrent fall risk by 1.66x. One study found that hypnotics and anxiolytics were not associated with falls in the multivariate analysis (Iinattiniemi et al. 2009).

### *2.3.2.3 Anti-Psychotics/Benzodiazepines and Injurious Falls*

Injurious falls were defined as a fall resulting in a fracture, emergency room visit, or hospital admission. One study found that sedative use increased fall-related fractures by 1.8x compared to non-injurious and recurrent falls (Tromp et al. 1998). Four studies compared sex, psychotropic medication use and hospitalization rates. (Kurzthaler et al. 2005; Malmivaara et al. 1993; Neutel et al. 1996; Stenbacka et al. 2002). A longitudinal study found males using

benzodiazepines medications (individual medications not reported) were 2.9x more likely to have an injurious fall compared to non-users; and females were 1.7x more likely to have an injurious fall compared to non-users (Malmivaara et al. 1993). Similarly, males using a benzodiazepine sedative or tranquilizer were 4.0x more likely to be hospitalized due to falls compared to non-users; and females were 2.5x more likely to be hospitalized due to falls compared to non-users, respectively (Neutel et al. 1996). One study reported females >60 years using hypnotics/sedatives were 1.5x more likely to have an injurious fall resulting in hospitalization compared to males (Stenbacka et al. 2002). One study found no differences between sex and the use of benzodiazepines on injurious fall risk (Kurzthaler et al. 2005). Use of anti-psychotics was not associated with fall-related emergency room visits in one study (Kelly et al. 2003). Additionally, a cohort study found no association between injurious falls and anxiolytic, anti-psychotic, hypnotic or other central nervous system medication use (Kerse et al. 2008).

#### *2.3.2.4 Short vs Long-Acting Anti-Psychotics*

Five studies examined the effects of short and long-term anti-psychotics or benzodiazepines on fall risk (Cumming et al. 1991; Ensrud et al. 2002; Landi et al. 2005; Lord et al. 1995; Neutel et al. 1996). Short acting benzodiazepines (e.g. alprazolam, temazepam, oxazepam) were not associated with increased risk of single or recurrent falls in two studies (Cumming et al. 1991; Lord et al. 1995). However, one study found oxazepam, a short acting anti-psychotic increased the risk of fall-related hospitalizations by 2.2x and one study found short-acting benzodiazepines increased fall risk by 1.3x (Landi et al. 2005; Neutel et al. 1996). Females  $\geq 65$  years and using short benzodiazepines had a 1.42x greater risk of recurrent falls compared to non-users (Ensrud et al. 2002). Use of short-term CNS medications (duration not

stated) was also significantly associated with recurrent falls ( $p < 0.05$ ), however, authors did not state which benzodiazepines were examined (Hanlon et al. 2009).

Older adults using long acting benzodiazepines had a 2.18x greater risk of recurrent falls, and in particular, users of diazepam had 3.7x greater risk compared to single or non-fallers (Cumming et al. 1991). Users of long-acting benzodiazepines were 1.45x more likely to fall compared to non-users (Landi et al. 2005). Females  $\geq 65$  years taking long-acting benzodiazepines (e.g. diazepam) were 7.03x more likely to fall compared to females taking short-acting benzodiazepines (Lord et al. 1995). Similarly, females  $\geq 65$  years and using long-acting benzodiazepines had a 1.56x greater risk of recurrent falls compared to non-users (Ensrud et al. 2002). Furthermore, long-term usage (for two continuous years) of CNS medications was found to be significantly associated with recurrent falls ( $p < 0.05$ ), however, authors did not state which benzodiazepines were examined (Hanlon et al. 2009).

#### *2.3.2.5 Multiple Medication Use*

Multiple psychotropic medication use was associated with falls in three studies (Hanlon et al. 2009; Lord et al. 1993; Lord et al. 1995). In females, users of one and two or more psychoactive medications were 1.25x and 2.17x more likely to fall compared to non-users (Lord et al. 1993). Similarly, Lord et al. (1995) also found that females taking two or more psychoactive medications were 8.99x more likely to fall compared to non-users, and those taking one psychoactive medication were 2.88x more likely to fall compared to non-users. Older adults using two or more CNS medications were 1.95x more likely to experience recurrent falls compared to those who only took one CNS medication (OR=1.55) (Hanlon et al. 2009).

### *2.3.2.6 Anti-psychotic Dosages*

Two studies examined the effect of dosages on fall risk. Users of CNS medications taking 3 or more standard doses/day had a 2.89x higher risk of having recurrent falls compared to those who took less than 2 standard doses per day (Hanlon et al. 2009). Another study found those taking < 2.5mg of diazepam per day were more likely to have recurrent falls than non-users (odds ratio not stated) and those taking >2.5mg of diazepam were 10.8x more likely to have recurrent compared to non-users (Cumming et al. 1991).

### *2.3.3.1 Anti-depressants*

Thirteen studies examined anti-depressant medication use as a risk factor for falls (Blake et al. 1988; Cumming et al. 1991; Du et al. 2017; Ensrud et al. 2002; Gribbin et al. 2011; Iinattiniemi et al. 2009; Kelly et al. 2003; Kerse et al. 2008; Landi et al. 2005; Lord et al. 1995; Masud et al. 2013; Spoelstra et al. 2013; Svensson et al. 1992). Sample sizes ranged from 414 (Lord et al. 1995) to 21,900 (Kerse et al. 2008). Five studies were cohort (Cumming et al. 1991; Ensrud et al. 2002; Iinattiniemi et al. 2009; Lord et al. 1995; Spoelstra et al. 2013), six were cross-sectional (Blake et al. 1988; Du et al. 2017; Kerse et al. 2008; Landi et al. 2005; Masud et al. 2013; Svensson et al. 1992), and two were a case-control and/or case series analysis (Gribbin et al. 2011; Kelly et al. 2003). Six studies defined falls as “falling to the ground unintentionally” (Cumming et al. 1991; Du et al. 2017; Ensrud et al. 2002; Kerse et al. 2008; Landi et al. 2005; Lord et al. 1995). One study defined falls as a ‘fall-accident’ (Gribbin et al. 2011). Ten studies found anti-depressant use significantly increased fall risk in older adults (Blake et al. 1988; Du et al. 2017; Ensrud et al. 2002; Gribbin et al. 2011; Kelly et al. 2003; Kerse et al. 2008; Lord et al. 1995; Masud et al. 2013; Spoelstra et al. 2013; Svensson et al. 1992). Two studies found anti-

depressants were associated of falls, however, the odds ratios were not stated (Blake et al. 1988; Svensson et al. 1992).

#### *2.3.3.2 Anti-Depressants and Single Falls*

The prevalence of anti-depressant use in single fallers ranged from 2.2%-18.9%. Previous prescription of anti-depressants such as SNRIs, SSRIs and TCAs were associated with single falls (Gribbin et al. 2011). Other studies found fallers were 2.88x, 2.80x and 1.29x more likely to be taking anti-depressants than non-fallers (Du et al. 2017; Masud et al. 2013; Spoelstra et al. 2013), respectively. Three studies did not find that anti-depressants were predictive of falls (Cumming et al. 1991; Iinattiniemi et al. 2009; Landi et al. 2005).

#### *2.3.3.3 Anti-Depressants and Recurrent Falls*

In one study of 21,596 Australian community-dwelling older adults (aged >60 years), 18.9% of those who had  $\geq 1$  falls in the past year were taking an anti-depressant (Kerse et al. 2008). The use of anti-depressants was associated with recurrent falls in four studies. Two studies showed that taking anti-depressants resulted in a fall risk of 3.15x and 2.9x, respectively (Du et al. 2017; Masud et al. 2013). Females aged  $\geq 65$  years taking anti-depressants were 2.84x (Lord et al. 1995) and 1.54x (Ensrud et al. 2002) more likely to have recurrent falls compared to non-users, respectively.

#### *2.3.3.4 Anti-Depressants and Injurious Falls*

Anti-depressants were significantly associated with injurious falls (OR=1.46; 95% CI 1.21-1.78) (Kelly et al. 2003). In females aged  $\geq 80$  years, those taking SSRI's had a 3.96 greater risk of suffering an injurious fall compared to females taking other anti-depressants (e.g. tricyclics, MAIOs) (Kerse et al. 2008). Kerse and colleagues (2008) also examined TCAs,

MAIOs and ‘other’ anti-depressants on falls, but no significant differences between these medications and fall risk emerged.

#### *2.3.3.5 SSRI Anti-Depressant Use*

The use of SSRIs was examined in five studies (Du et al. 2017; Ensrud et al. 2002; Gribbin et al. 2011; Kerse et al. 2008; Masud et al. 2013). One study found that users of SSRIs had the highest risk of falls (OR= 6.22; 95% CI 2.28-17.9) compared to users of other anti-depressants medications (i.e. synthetic anti-depressants (OR=2.66; 95%CI 1.50-4.73) and non-selective mono-amino reuptake inhibitor anti-depressants (OR=1.84; 95%CI 0.83-4.10) (Du et al. 2017). Similarly, another study reported that users of SSRIs were 1.55x more likely to have a single fall, 1.66x more likely to have recurrent falls, and 1.52x more likely to have injurious falls compared to those using other types of anti-depressants (Kerse et al. 2008). Females aged  $\geq 65$  years and using SSRIs were 3.54x more likely to experience recurrent falls, however, TCAs were not significantly associated with recurrent falls (Ensrud et al. 2002). In a study of males, users of SSRIs were associated with single and recurrent falls (OR=3.1; 95% CI 2.0-5.0) and (OR=3.1; 95% CI 1.8-5.6), respectively, as were TCA’s and falls (OR=2.2; 95% CI 1.0-4.7) (Masud et al. 2013)

The onset of medication use is also a risk factor of prospective falls. Within the first 28 days of usage, SSRI’s resulted in a 2.04x, TCA usage a 1.61x and SNRI’s a 1.79x greater risk for prospective falls (Gribbin et al. 2011). There were two studies that included anti-depressants in their definition of CNS or sedative medications, however, no findings were reported specific to anti-depressant use and falls in their studies (Hanlon et al. 2009; Tinetti et al. 1988).

### **2.3.4 Studies using Anti-Hypertensive Medications**

Twelve studies examined anti-hypertensive medication use and fall risk in older adults (Bergland et al. 2004; Blake et al. 1988; Cumming et al. 1991; Hanlon et al. 2002; Iinattiniemi et al. 2009; Kelly et al. 2003; Lord et al. 1993; Lord et al. 1995; Svensson et al. 1992; Tinetti et al. 2014; Tromp et al. 1998; Wong et al. 2013). Sample sizes ranged from 307 (Bergland et al. 2004) to 2,996 (Hanlon et al. 2002). The term falls was defined as “falling to the ground unintentionally” in six studies (Bergland et al. 2004; Cumming et al. 1991; Lord et al. 1993; Lord et al. 1995; Tromp et al. 1998; Wong et al. 2013) but not defined in the other six studies. In fallers, 13% to 85.9% were taking some form of anti-hypertensive medication.

#### *2.3.4.1 Anti-Hypertensives and Single and Recurrent Falls*

Seven studies found that anti-hypertensive medications were not associated with single or recurrent falls in males and females (Blake et al. 1988; Hanlon et al. 2002; Iinattiniemi et al. 2009; Kelly et al. 2013; Lord et al. 1993; Lord et al. 1995; Svensson et al. 1992), four studies found a significant association (Bergland et al. 2001; Cumming et al. 1991; Tinetti et al. 2014; Tromp et al. 1998), and one found mixed results (Wong et al. 2013). Compared to non-users, users of anti-hypertensive medications had a 1.4x greater risk of falls and 1.6x greater risk of prospective falls (Tromp et al. 1998). Use of angiotensin-system blocking medication including ACEi and angiotensin receptor blockers was associated with fewer falls (Wong et al. 2013). In females, anti-hypertensives medication use increased injurious fall risk by 2.4x (Bergland et al. 2004).

#### *2.3.4.2 Anti-Hypertensive Dosages*

One study found that diuretics and diltiazem were associated with recurrent falls in community dwelling older adults (Cumming et al. 1991). Higher doses of diltiazem (>180mg per

day) were also associated with a 10x greater risk of recurrent falls (Cumming et al. 1991). Moderate dosages, defined as (0.2-2.5 defined daily dose), increased injurious fall risk by 1.4x and 1.28x in high dosage users (defined as >2.5 defined daily dose) (Tinetti et al. 2014).

### **2.3.5 Alcohol and fall risk**

#### *2.3.5.1 Alcohol use and Older Adults*

Fourteen studies measured alcohol use via surveys (Anstey et al. 2008; Cumming et al. 1991; Du et al. 2017; Hanlon et al. 2002; Hanlon et al. 2009; Kerse et al. 2008; Lord et al. 1993; Lord et al. 1995; Malmivaara et al. 1993; Masud et al. 2013; Stenbacka et al. 2002; Tinetti et al. 1988; Tromp et al. 1998; Tromp et al. 2001) and one study measured alcohol concentration through blood samples (Kurzthaler et al. 2005). Alcohol use was defined as daily (Du et al. 2017; Hanlon et al. 2002; Lord et al. 1993; Lord et al. 1995), number of drinks per week (Anstey et al. 2008; Kerse et al. 2008; Masud et al. 2013), alcohol intake per month (Anstey et al. 2008; Cumming et al. 1991), alcohol consumption as grams/per month (Malmivaara et al. 1993; Stenbacka et al. 2002), and as current, past or never drinker (Hanlon et al. 2009). Alcohol consumption was controlled for in three of the fourteen studies, however, quantity of alcohol was not described (Tinetti et al. 1988; Tromp et al. 1998; Tromp et al. 2001). Only one study defined high risk drinking;  $\geq 7$  drinks per week for females and  $\geq 14$  drinks per week for males (Kerse et al. 2008). Only three studies provided alcohol consumption rates which ranged from 18% to 70% (Anstey et al. 2008; Du et al. 2017; Hanlon et al. 2009; Kerse et al. 2008).

#### *2.3.5.2 Alcohol use and Falls*

Seven studies reported fall risk based on the number of drinks per day, week or month (Anstey et al. 2008; Cumming et al. 1991; Du et al. 2017; Kerse et al. 2008; Lord et al. 1993; Lord et al. 1995; Masud et al. 2013), one study reported alcohol use and falls based on ounces

per day (Hanlon et al. 2002), two studies reported alcohol use and falls based on grams consumed per month (Malmivaara et al. 1993; Stenbacka et al. 2002), and one study reported alcohol use and falls based on blood alcohol concentration levels (Kurzthaler et al. 2005).

Alcohol consumption was significantly associated with falls in five studies (Anstey et al. 2008; Kerse et al. 2008; Kurzthaler et al. 2005; Malmivaara et al. 1993; Stenbacka et al. 2002), but not in ten other studies (Cumming et al. 1991; Du et al. 2017; Hanlon et al. 2002; Hanlon et al. 2009; Lord et al. 1993; Lord et al. 1995; Masud et al. 2013; Tinetti et al. 1988; Tromp et al. 1998; Tromp et al. 2001). Older adults who consumed less alcohol per month (<4 drinks) were more likely to fall compared to those who consumed more often (e.g. 2-3 times per week and  $\geq 4$  times per week) (56.2% vs. 17.4% vs. 26.4%) (Anstey et al. 2008).

Of the ten studies that found no association with falls, eight were cohort (Cumming et al. 1991; Hanlon et al. 2002; Hanlon et al. 2009; Lord et al. 1993; Lord et al. 1995; Tinetti et al. 1988; Tromp et al. 1988; Tromp et al. 2001) and two were cross-sectional (Du et al. 2017; Masud et al. 2013). Sample sizes ranged from 336 (Tinetti et al. 1988) to 4,696 (Masud et al. 2013). Three studies measured alcohol based on the ounces consumed per day, number of drinks consumed on a drinking day and/or number of drinking days per week (Hanlon et al. 2002; Lord et al. 1993; Masud et al. 2013); however, seven studies did not report on the number of drinks consumed per day, week or month (Cumming et al. 1991; Du et al. 2017; Hanlon et al. 2009; Lord et al. 1995; Tinetti et al. 1988; Tromp et al. 1988; Tromp et al. 2001). Seven studies had a mixed sex composition (Cumming et al. 1991; Du et al. 2017; Hanlon et al. 2002; Hanlon et al. 2009; Tinetti et al. 1988; Tromp et al. 1988; Tromp et al. 2001) while one study examined males only (Masud et al. 2013) and two examined females only (Lord et al. 1993; Lord et al. 1995).

### *2.3.5.3 Alcohol use and Injurious Falls*

Compared to younger adults, persons aged 51-70 years were more likely to be injured by a sudden fall after consuming alcohol ( $p < 0.001$ ) (Kurzthaler et al. 2005). Furthermore, 18% of males aged  $>70$  years had consumed significantly more alcohol at the time of the fall compared to females (0.9%) (Kurzthaler et al. 2005). Males and females  $>64$  years who heavily drank ( $\geq 1000$  g/month for males,  $\geq 500$  g/month for females) were 8.45x and 14.63x more likely to have an injurious fall leading to hospitalization or death, respectively (Malmivaara et al. 1993). Similarly, females  $>60$  years who consumed high levels of alcohol ( $\geq 500$  g/month) were more likely to have an injurious fall compared to males (Stenbacka et al. 2002).

### **2.3.6 Medications and Alcohol Together on Fall Risk**

One study examined the effects of CNS medications as a group (e.g. benzodiazepines, opioid receptor agents, anti-psychotics and anti-depressants) together with alcohol on fall risk (Hanlon et al. 2009). A two-way interaction between alcohol and CNS medications on recurrent fall risk was performed, however, the interaction was not significant (Hanlon et al. 2009).

## **2.4 Discussion**

The findings from our review show that between 9% and 50.5% of community dwelling older adults reported a fall with 20% to 45.4% constituted as an injurious fall. Comparatively, more than 60% of older adults living in long-term care facilities fall each year (Rojas-Fernandez et al. 2015; Prudham et al. 1981; Tinetti et al. 1988; Campbell et al. 1989; Clark et al., 1993) with between 16.2% and 35% sustain an injurious fall once a year (Ek et al. 2017; Thapa et al. 1996; Wang et al. 2001). Given that residents of long-term care are frailer than those living in community settings, it is not surprising fall rates are higher. However, it is surprising that injurious rates are comparable to that of community settings. Injurious falls in the community

may be more common due to external factors such as uneven sidewalks, uneven steps, icy roads, inappropriate use of equipment (e.g. climbing ladders, use of heavy machinery), other pedestrians, cyclists or motor vehicles (Chippendale et al. 2015; Li et al. 2006).

The majority of studies found that psychotropic medications including benzodiazepines, sedatives/hypnotics, anti-psychotics and anti-depressants were associated with falls in community dwelling older adults. Between 6.2% and 53.8% of benzodiazepine, sedative/hypnotic or anti-psychotic users reported a fall. The sedating side effects of benzodiazepines may impair psychomotor function, cognitive function and increase daytime sleepiness, which can lead to falls (de Groot et al. 2013). Long-acting benzodiazepines have oxidative pathways that are more likely accumulate and stay in the body and are related to side effects such as prolonged sedation and cognitive impairment (Madhusoodanan and Bogunovic, 2004). This may partly explain why long-acting (>24 hours) compared to short-acting benzodiazepines (<24 hours) had higher fall rates. Diazepam is a long acting benzodiazepine and found to be predictive of falls in four studies (Cumming et al. 1991; Ensrud et al. 2002; Landi et al. 2005; Lord et al. 1995). Prior studies have hypothesized that diazepam may increase fall risk due its postural sway side effects (de Groot et al. 2013; Madhusoodanan et al. 2004).

Most studies found that anti-depressants had a significant association with falls in community dwelling older adults. This finding is consistent with prior reviews with mixed samples of older adults living in the community dwelling and long-term care (Leipzig et al. 1999; Hartikainen et al. 2007; Park et al 2015; Woolcott et al. 2009). One particular anti-depressant, SSRIs, had the greatest risk for falls compared to all other anti-depressant medications. SSRIs may result in a higher fall risk compared to other anti-depressant medications due to increased daytime sleepiness that often results from disrupted sleep cycles,

however, these side effects are not unique to SSRIs (Darowski et al. 2009; Diem et al. 2007). When examining other anti-depressant medications, TCA medications were also consistently associated with fall risk in two studies (Gribbin et al. 2011; Masud et al. 2013), which may be attributed to side effects such as sedation, daytime sleepiness and orthostatic hypotension (Darowski et al. 2009).

Although the included studies found that between 13% and 85.9% were using anti-hypertensive medication (Bergland et al. 2004; Blake et al. 1988; Cumming et al. 1991; Hanlon et al. 2002; Iinattiniemi et al. 2009; Kelly et al. 2003; Lord et al. 1993; Lord et al. 1995; Svensson et al. 1992; Tinetti et al. 2014; Tromp et al. 1998; Wong et al. 2013), most studies in this review found no association between anti-hypertensive medication and falls. Three studies did not report the number of older adults using anti-hypertensive medications (Hanlon et al. 2002; Iianttiniemi et al. 2009; Lord et al. 1995). Additionally, eleven studies examined anti-hypertensive medications as a broad category, and six studies examined individual anti-hypertensive medications (Blake et al. 1998; Cumming et al. 1991; Hanlon et al. 2002; Iianttiniemi et al. 2009; Svensson et al. 1992; Wong et al. 2013). Only one study found an association between specific anti-hypertensive medication and falls. Diltiazem and diuretics were associated with recurrent falls (Cumming et al. 1991) whereas other studies did not find any association between falls and diuretics, as well as calcium channel blockers and beta-blockers. One study found that specific anti-hypertensive medications, angiotensin-receptor blockers (ACEi) and angiotensin system-blocking medications, were protective of fall risk in a small sample of community dwelling older adults compared to statins and psychotropic medications, however, the authors could not provide any reasons for this finding (Wong et al. 2013; Park et al. 2015). Taken together, even though anti-hypertensive medications are commonly used in

community older adults, the evidence on fall risk is mixed and requires further investigation, particularly when examining individual anti-hypertensive medications.

Fifteen studies examined alcohol consumption on fall risk with five studies finding an association. No studies produced rates of alcohol use. Differences in how alcohol consumption was measured made comparing studies challenging. For example, four studies measured daily alcohol consumption, three measured alcohol consumptions by week, and two measured alcohol by month. Furthermore, fourteen studies measured alcohol consumption was measured via surveys which is subject to recall and social desirability bias. Specific types of alcohol (i.e. spirits, wine, beer) were not specified in any study. While alcohol use typically declines with age (Britton et al. 2015; Wong et al. 2016), some studies suggest alcohol consumption increases with age (Han et al. 2017; Sorock et al. 2006). Future studies should consider measuring alcohol via blood samples to improve accuracy.

No studies found an association between alcohol and medications of interest together on fall risk. Concomitant alcohol and medication use at the time of the fall is nearly impossible to measure due to reporting bias, stigma and potential impaired memory. However, in western countries, concomitant alcohol and medication use ranges between 6% to 28% in older adults (Bye et al. 2017; Ilomaki et al. 2012; Ilomaki et al. 2013), suggesting it may be more common than previously assumed. Older adults represent the highest percentage of medication users. Polypharmacy is also associated with advanced age and falls (Chang et al. 2015; CIHI, 2012). Some research suggests as the population ages, alcohol use will become more common (Han et al. 2017; Wong et al. 2016; Babatunde et al. 2014; Blow & Barry, 2012). Medications such as psychotropics and anti-depressants, as well as alcohol are identified as risk factors for falls (PHAC, 2014; WHO, 2007). Given that only one study examined medication use together with

alcohol, there is clearly a gap in research. Future studies should ask participants to report their frequency of alcohol consumption in combination with psychotropic, anti-depressant and anti-hypertensive medication use.

This review found there was substantial variation in study design, sample size, assessment of alcohol use, assessment of medication use, and falls. Differences in sampling techniques, sample size (<2000 vs. >300 000), sex, highest level of education achieved, income, diagnosed chronic illnesses, and cognitive function could explain why studies varied in results. While some studies were longitudinal studies, no two studies were identical in study design, sample size, independent variables, and statistical analysis, including controlling for confounding variables. The inconsistent terminology/definitions regarding medication classes made comparing studies challenging. For example, Haritkainen et al. (2007) defined psychotropics as hypnotics/sedatives, anxiolytics, anti-psychotics and anti-depressants; however, Bloch et al. (2011) defined psychotropics as benzodiazepines, anti-depressants, hypnotics, narcotics, neuroleptic tranquilizers, and psychotropics as a whole. In this review, Hanlon et al. (2009) categorized CNS medications as one whole group, but others separated medications by class and sub-class (Cumming et al. 1991; Gribbin et al. 2011; Du et al. 2017; Kerse et al. 2008; Lord et al. 1995; Neutel et al. 1996). No study performed a randomized controlled trial. Future studies examining medications and fall risk should describe medications in detail (e.g. medication sub-classes, the prescribed dosage and medication adherence) to warrant high quality analysis and replication. Future studies should classify medications according to the universal Anatomical Therapeutic Chemical Classification System to promote consistency of medication classification.

## **2.5 Conclusion**

Anti-psychotic, benzodiazepines and anti-depressants, particularly SSRIs, were associated with increased fall risk in community dwelling older adults. Findings on anti-hypertensive medications and alcohol consumption as a risk factor for falls are weak. Healthcare professionals should educate older adults on the potential risk for falls when taking these medications.

## Chapter 3: Alcohol Use in Community Dwelling Older adults in Canada

### Overview

**Background and Objectives:** Current Canadian alcohol consumption guidelines are developed for adults, however, their applicability to older adults is unknown. We seek to examine alcohol use in Canadian community dwelling older adults, determine risk factors associated with high-risk drinking based on current guidelines, and determine whether the current low-risk drinking guidelines are applicable to older adults.

**Methods:** Using data from the Canadian Injury Prevention Survey, we examined personal and health characteristics in community dwelling older adults (aged 65 and older) living in Canada as potential risk factors for high-risk alcohol drinking (N=2,279). Current Canadian alcohol consumption guidelines define high risk drinking as >10 drinks for females and >15 drinks for men, however, there is no moderate alcohol consumption category. We developed and examined new categories to determine if there was better differentiation between low, moderate and high-risk alcohol use in older adults on various health and social outcomes. Descriptive statistics (mean, standard deviation and range) and comparative analysis (i.e. Chi-Square tests, independent t-tests and analysis of variance) were used compare alcohol consumption categories. Using logistic regression, we compared demographic and health factors to predict low and high-risk drinkers using the current guidelines. Multinomial regression used demographic and health factors to predict low, moderate and high-risk drinking on health outcomes.

**Results:** Participants age ranged between 65-96 years (Mean  $72.8 \pm 5.9$ ); 58% were females. 70.1% of the sample reported having at least one drink on a weekly basis; 29.9% reported not consuming alcohol, 6.2% of men and 10.1% of women reported high-risk drinking. The regression models (Men: N=950, -2Log Likelihood Ratio=1452.0; Nagelkerke  $R^2 = 0.09$ ;

Women: N=1332, -2Log Likelihood Ratio=1818.1; Nagelkerke  $R^2 = 0.08$ ) showed having diabetes and being less likely to have daytime sleepiness were protective of high risk drinking in both males and females. The inclusion of the moderate alcohol consumption category showed no substantial differences in health and social outcomes in comparison to the current alcohol consumption guidelines.

**Conclusions:** Canada's current alcohol consumption guidelines appear to be suitable for older adults, however, more research on the risks and benefits of drinking alcohol in older adults is needed.

### 3.1 Introduction

The Canadian Tobacco, Alcohol and Drug Survey (CTADS) (2015) showed 66.2% of older adults consumed alcohol within the previous year (Health Canada, 2015; Health Canada, 2017). The Canadian Community Health Survey (CCHS) (2016) also found that 10.5% of males and 4.3% of females  $\geq 65$  years reported drinking heavily (Statistics Canada, 2017). Drinking problems in older adults have the potential to become a large public health concern as hospital admission rates due to alcohol misuse are increasing (Sacco et al. 2015; Adams et al. 1993). For example, in older adults aged  $>65$  years, alcohol related admissions have increased over seven years ( $b=0.88$ ;  $t=8.84$ ;  $p<.001$ ) (Sacco et al. 2015).

A study in the United States found that alcohol use increased by 40% between 2005-2014, and females reported the largest increase by 84.6% (Han et al. 2017). The increasing use of alcohol may result in higher alcohol-related health problems (e.g. liver diseases, cardiovascular disease, poor oral health, decreased bone strength, increased risk of mortality) (Heuberger et al. 2009) as the population lives longer. For example, deaths related to alcoholic liver disease in Canada increased by 15.9% from 2010 to 2014 (Statistics Canada, 2014). However, some research shows that alcohol may have a protective effect on certain health conditions. For instance, one study found that community dwelling females aged  $\geq 70$  years who consumed 1-2 drinks per day over the week had better self-reported health (e.g. improved quality of life) and a greater survival rate compared to non-drinkers (Byles et al. 2006).

Alcohol consumption guidelines for older adults may be necessary as they retain alcohol longer in the gastrointestinal track (e.g. stomach, liver, upper and small intestine) (Heuberger et al. 2009), are more likely to have mild cognitive impairment leading to poor decision making and judgement, suffer multiple comorbidities, practice polypharmacy, have a higher risk of

alcohol-drug interaction (Weathermon and Crabb, 1999), and are related to greater risk of motor vehicle accidents (Orces et al. 2013; Sorock et al. 2006), injuries and falls (Heuberger et al. 2009; Kurzthaler et al. 2005; Stenbacka et al. 2006; WHO, 2009). Additionally, while drinking alcohol is often a social activity, excessive drinking can lead to financial strain, social isolation, and can worsen chronic health conditions (CDC, 2018; Heuberger, 2009; Statistics Canada, 2016).

The Canadian Centre for Substance Abuse (CCSA) provides alcohol consumption guidelines for the general population between the ages of 18 and 64 years to reduce the long-term health effects of alcohol (e.g. some cancers such as liver, colorectal, laryngeal and oral, cirrhosis of the liver) and promote a culture of moderation and a healthy lifestyle (Health Canada, 2015). The current guidelines state females should not drink more than two drinks per day or ten drinks per week and that males should not drink more than three drinks per day or 15 drinks per week. High risk drinking is defined as having >5 drinks for males and >4 drinks for females on one occasion at least once a month in the past year based on the World Health Organization and Health Canada guidelines for high risk drinking (Statistics Canada, 2016). High-risk drinking standards are used as an indicator for long-term health consequences (e.g. increased risk of cardiovascular disease) and risky behaviours (e.g. impaired driving, illicit drug use) (Statistics Canada, 2016). However, no alcohol consumption guidelines were created for older adults because of increased sensitivity to the effects of alcohol and medication use (Butt et al. 2011). Additionally, the current guidelines do not have a category for non-drinkers. In the current guidelines, non-drinkers are included in the low-risk category.

In countries such as the United States, there are specific alcohol consumption guidelines for older adults. For example, the American Geriatrics Society and National Institute on Alcohol

Abuse and Alcoholism defines high risk drinking for older adults as having more than seven drinks per week or having three or more drinks on a given day based on clinical guidelines (National Institute on Alcohol Abuse and Alcoholism, n.d.). Italy is the only country to provide drinking guidelines to older adults in Europe, recommending that older adults do not consume more than one drink, or 12g of alcohol per day (Hallgren et al. 2010). In Singapore, it is recommended that males should not consume more than two drinks and females should not consume one drink per day, respectively (Ministry of Health Singapore, 2015).

In the United States, alcohol consumption guidelines for older adults were developed by the National Institute on Alcohol Abuse and Alcoholism (NIAAA), a national organization of scientists and experts in alcohol use (NIH, n.d). Alcohol consumption guidelines in Italy were developed based on collaboration with the Italian Ministry of Health, Italy's National Health Institute, the Italian Society of Alcoholology and indicators from the World Health Organization (Hallgren et al. 2009). Singapore's guidelines are based on scientific evidence, although the source of the scientific evidence is not clear. Canada's guidelines were developed by the National Alcohol Strategy Advisory Committee, consisting of independent Canadian and international experts (Butt et al. 2011; Canadian Centre on Substance Use and Addiction, 2011).

Globally, there have been a limited number of studies examining alcohol consumption in older adults and few conducted in Canada. There has been no study to determine if the current alcohol guidelines are suitable for community dwelling older adults as they were not developed with older adults in mind. The primary objectives of this study are: 1) to examine alcohol consumption in Canadian community dwelling older adults using the present guidelines; 2) to develop and test a moderate alcohol consumption category on health and social outcomes; 3) to determine factors associated with high-risk drinking.

## **3.2 Methods**

### **3.2.1 Study population**

This population-based study recruited persons over the age of 45 from local, provincial and national organizations (e.g. Canadian Association of Retired Persons, Royal Canadian Legion) between July 2016 and June 2017. A list of all persons and organizations contacted can be found in **Appendix B**. Emails were sent to each organization consisting of a brief overview of the study, a letter of information, web-links to the surveys in both English and French and contact information for the Principal Investigator (**Appendix C**). The survey consisted of 89 questions (**Appendix D**) and was completed using SurveyMonkey, an online survey management program. Prior to completing the survey, participants read a letter of information and provided informed consent.

Any person aged 45 and older could complete the survey. In total, 4,614 participants completed the survey, however, the present study was restricted to persons 65 years of age, who were living in the community and completed the alcohol consumption module of the questionnaire. The final sample was 2,279. Persons were excluded from completing the survey if they were living in a long-term care facility or were using memory care services in a retirement home. This study was approved by the Office Research Ethics Board at the University of Waterloo.

### **3.2.2 Measures**

#### *Alcohol*

Alcohol consumption was quantified as number of alcoholic drinks per week and number of drinking days per week. A dichotomous variable was created for alcohol use (yes or no) based on how participants answered the question “how many drinks do you have per week”. Canada’s alcohol consumption guidelines for persons aged 18-64 years define high risk drinking as 10 or

more drinks per week for females, and 15 or more drinks for men (Butt et al. 2011). Based on the distribution of the number of drinks participants reported to have consumed per week, we created drinking categories as follows for females: non-drinker (0), low (1-2), moderate (3-6), high ( $\geq 7$ ); and non-drinker (0), low (1-2), moderate (3-9), high ( $\geq 10$ ) for males. Categories were designed based on previous studies related to alcohol consumption in older adults (Immonen et al. 2011; Mukamal et al. 2004).

### *Demographics*

Demographic variables included age, sex, living situation (alone, with a spouse or partner, with family members, with roommates unrelated), years retired, illness or disability before retirement, diagnosis of chronic illness, and self-perception of physical and mental health. Categorical variables were dichotomous (yes or no) or polytomous with more than two categories. Self-perceived physical and mental health scores were rated on a 10-point scale.

Participants indicated whether they had a diagnosis of one or more of the following chronic health conditions. Health conditions included the following chronic conditions: arthritis, rheumatism, or osteoporosis; multiple sclerosis; Parkinson's disease; stroke; dementia; high blood pressure, cholesterol, or heart problems; asthma or other breathing issues; diabetes; back problems; foot problems; hearing problems; cataracts, glaucoma, or macular degeneration; sleeping disorders; and depression.

### *Behavioural Risk Factors*

Behavioural variables included smoking status, sleep quantity in 24 hours, and falls in previous two years. Smoking status was defined as current smoker or non-smoker.

### *Physical Activity*

Participants completed the short version of the International Physical Activity Questionnaire (IPAQ). The IPAQ is a valid tool for assessing physical activity in older adults (Chun, 2012; Tomioka et al. 2011). Scores were calculated using energy estimates (multiples of the resting metabolic rate or MET) assigned to each activity category (3.3 for walking, 4.0 for moderate, 8.0 for vigorous) x minutes of activity x days per week and produced a score for weighted MET minutes per week ([www.ipaq.ki.se](http://www.ipaq.ki.se); Tomioka et al. 2011). Total MET scores are calculated by combining MET scores of walking, moderate physical activity, and vigorous activity (e.g. Total MET-min/week= (3.3 x minutes x days per week) + (4.0 x minutes x days per week) + (8.0 x minutes x days per week). Participants were scored as low, moderate and high physical activity levels ([www.ipaq.ki.se](http://www.ipaq.ki.se), 2005).

### *Sleep*

The potential for daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS). The ESS has eight questions that assesses daytime sleepiness in older adults who do not have serious cognitive impairment (Johns, 1991). Participants rated, on a 4-point scale (0-3), their likelihood of dozing off or falling asleep during an activity. Scores on the ESS range from 0-24. Likelihood of daytime sleepiness is divided into categories based on score, normal (0-10), borderline (11-15), and abnormal (16-24) chance of falling asleep during the day. The ESS has shown good test-retest reliability, with high levels of internal consistency measured by Cronbach's alpha (0.88) (Johns, 1991). We also asked participants to indicate the number of hours they usually sleep in 24 hours.

### *Cognitive function*

The Dysexecutive Questionnaire (DEX-S) is a reliable and valid measure for assessing executive function in older adults (Emmanouel et al., 2014; Shinagawa et al., 2007; Burgees et al., 1998). The DEX-S examines changes and difficulties in adults in the areas of emotion or personality, behaviour and cognition (Shaw et al. 2015; Gerstof et al. 2013). The 20-item questionnaire is scored on a 5-point scale from (0-4) with scores ranging from 0-80. During pilot testing of the survey, participants indicated that some questions on the DEX-S overlapped with other questions, prompting us to remove one of the items. Consequently, the current DEX-S includes 19 items; scores range from 0-76. Higher scores indicate more severe executive dysfunction (Shaw et al. 2015).

### **3.2.3 Statistical analysis**

Data was coded and cleaned in Microsoft Excel before being transferred to SPSS (Version 24) for analysis. The following statistical analyses were performed for each objective:

*1) To examine alcohol consumption in Canadian community dwelling older adults using the present guidelines*

Descriptive information was presented using mean and standard deviation (Mean±SD) and range while categorical variables were presented using frequencies and percent. The Chi-square test compared the association between categorical variables. If cell sizes were too small ( $n < 5$ ), a Fisher's exact test was used. Independent t-tests compared the means of continuous health and social variables between low and high alcohol consumption categories. Statistical significance was set at  $p < 0.05$ .

2) *To develop and test a moderate alcohol consumption category on health and social outcomes*

Analysis of variance (ANOVA) compared personal and health characteristics between low, moderate and high alcohol classifications.

3) *To determine predictors of high-risk alcohol drinking and compare current alcohol drinking consumption guidelines and a moderate alcohol consumption category*

Logistic regression identified risk factors for high-risk drinking using the current alcohol consumption guidelines. Multinomial regression identified risk factors for high-risk alcohol consumption.

### **3.3 Results**

**Table 3.1** illustrates the demographic and health related characteristics of our sample, separated by sex, using the current alcohol consumption guidelines.

#### *Males*

In males, the mean age was  $72.7 \pm 5.9$ , and almost 80% lived with a spouse or partner. Sixty percent of males were retired for  $\geq 10$  years; self-perceived physical and mental health scores were  $8.2 \pm 1.7$  and  $8.9 \pm 1.4$ , respectively. Only 3.6% of males were currently smoking. The most common medical conditions in males included high blood pressure, cholesterol or heart problems (60.3%), followed by arthritis, osteoporosis or rheumatism (38.5%). Overall, males reported usually sleeping  $5.9 \pm 2.0$  hours within 24 hours (day and night), and 90.6% reported a normal likelihood ( $4.6 \pm 3.0$ ) of dozing off or falling asleep during the day. The mean score of the DEX-S questionnaire was  $14.0 \pm 7.7$ , meaning the sample had a low likelihood of severe cognitive impairment. Less than 1% of males were diagnosed with dementia.

### *Females*

In females, the mean age was  $72.8 \pm 5.9$ , and 51% lived with a spouse or partner. Nearly 60% have been retired for  $\geq 10$  years; self-perceived physical and mental health scores were  $8.2 \pm 1.7$  and  $8.9 \pm 1.4$ , respectively. Only 3.1% of reported currently smoking. A diagnosis of arthritis, osteoporosis or rheumatism was reported by 59.7% of females, followed by high blood pressure, cholesterol or heart problems (49.4%). Similar to males, females also reported typically sleeping  $5.9 \pm 2.0$  hours within 24 hours (day and night), and 93.4% reported a normal likelihood ( $4.6 \pm 3.0$ ) of daytime sleepiness. The mean score of the DEX-S questionnaire for females was  $14.0 \pm 7.7$ . Less than 1% of females were diagnosed with dementia.

### *Alcohol use*

As shown in **Table 3.1**, alcohol was consumed by 70% of participants, consuming an average of  $5.8 \pm 5.0$  drinks per week, and drinking  $3.7 \pm 2.2$  days per week. Using the current alcohol consumption guidelines, 6.2% of males ( $>15$  drinks per week) and 10.1% of females reported high-risk drinking ( $>10$  drinks per week). Males classified as high-risk drinkers ( $>15$  drinks) consumed  $21.6 \pm 3.5$  drinks per week, and females classified as high-risk drinkers ( $>10$  drinks) consumed  $15.1 \pm 3.8$  drinks per week. Both males and females categorized as high-risk drinkers reported drinking  $6.7 \pm 0.6$  days per week. Males classified as high-risk drinkers were more likely to smoke compared to females who were high-risk drinkers. Females high-risk drinkers were significantly more likely to have, high blood pressure, cholesterol or heart problems, less likely to have diabetes, and sleep more hours in 24 hours compared to males (Table 3.1).

### *Alcohol Use in Males*

Males who smoked were more likely to be high-risk vs. low-risk drinkers (9.3% vs. 3.3), but differences were not significant. Compared to low-risk drinkers, high-risk drinkers were more likely to have higher self-perceived physical health and mental scores ( $8.4 \pm 1.5$  and  $9.2 \pm 0.9$ ), live with a spouse or partner (86%), and have high blood pressure, cholesterol or heart problems (69.2%) compared to low-risk drinkers, however, differences were not significant.

### *Alcohol Use in Females*

Females who smoked were more likely to be high-risk vs. low-risk drinkers (5.5% vs. 2.9%), but differences were not significant. There were no significant differences between low and high-risk drinking and living situation. For example, 43.7% of females living alone were low-risk drinkers compared to 42.9% of females who were high-risk drinkers and lived alone. Similar to males, self-perceived physical and mental health scores were higher in high-risk drinkers. Females with asthma or other breathing problems were significantly more likely to be high-risk drinkers compared to low-risk (24.1% vs. 13.8%;  $p < 0.05$ ), as were females with high blood pressure, cholesterol or heart problems (60.8 vs. 48.6%;  $p < 0.05$ ).

**Table 3.1. Descriptive statistics for males and females aged 65 and over for current Canadian Low-Risk Drinking Guidelines**

<b>Variable</b>	<b>Males</b>				<b>Females</b>			
	<b>Total (N=950)</b>	<b>Low risk (N=891)</b>	<b>High risk (N=59)</b>	<b>Significance (p&lt;0.05)</b>	<b>Total (N=1329)</b>	<b>Low risk (N=1194)</b>	<b>High risk (N=135)</b>	<b>Significance (p&lt;.05)</b>
		<15 drinks per week	>15 drinks per week			<10 drinks per week	>10 drinks per week	
<b>Age</b>	72.7±5.9 (60-90)	73.6±6.1 (65-90)	72.6±4.6 (65-81)	$t=1.00, p=0.31$	72.8±5.9 (65-96)	72.3±5.8 (65-96)	71.5±5.0 (65-86)	$t=1.25, p=0.20$
<b>Living situation</b>								
Alone	145 (15.3)	141 (15.6)	4 (9.3)	$\chi^2=1.66, p=0.64$	578 (43.7)	539 (43.7)	39 (42.9)	$\chi^2=0.11, p=0.99$
With a spouse/partner	755 (79.9)	718 (79.6)	37 (86)		675 (51)	628 (50.9)	47 (51.6)	
With family	38 (4)	36 (4)	2 (4.7)		60 (4.5)	56 (4.5)	4 (4.4)	
With roommates (not related)	7 (0.7)	7 (0.8)	0 (0)		11 (0.8)	10 (0.8)	1 (1.1)	
<b>Illness or disability before retirement</b>								
Yes	198 (21.6)	193 (22.1)	5 (11.9)	$\chi^2=2.44, p=0.11$	295 (23)	279 (23.4)	16 (18.2)	$\chi^2=1.26, p=0.26$
No	719 (78.4)	682 (77.9)	37 (88.1)		985 (77)	913 (76.6)	72 (81.8)	
<b>Years Retired</b>								
Range	13.1±8.6 (1-58)	13.6±8.7 (1-58)	12.7±9.5 (3-52)	$t=0.50, p=0.61$ $\chi^2=0.87, p=0.83$	13.1±8.6 (1-52)	12.8±8.6 (1-52)	13.3±7.8 (2-33)	$t=-0.39, p=0.69$ $\chi^2=4.74, p=0.19$
1-3	58 (9.4)	56 (9.6)	2 (6.5)		102 (11.5)	98 (11.9)	4 (6.7)	
4-6	92 (15)	87 (14.9)	5 (16.1)		152 (17.2)	142 (17.2)	10 (16.7)	
7-9	90 (14.7)	84 (14.4)	6 (19.4)		107 (12.1)	95 (11.5)	12 (20)	
10+	374 (60.9)	356 (61.1)	18 (58.1)		525 (59.3)	491 (59.4)	34 (56.7)	

<b>Self-rated physical health</b> Range	8.2±1.7 (1-10)	8.2±1.6 (1-10)	8.4±1.5 (3-10)	$t=-0.93, p=0.35$	8.2±1.7 (1-10)	8.2±1.7 (1-10)	8.3±1.5 (5-10)	$t=-1.07, p=0.28$
<b>Self-rated mental health</b> Range	8.9±1.4 (1-10)	8.9±1.5 (1-10)	9.2±0.9 (7-10)	$t=-1.07, p=0.28$	8.9±1.4 (1-10)	8.8±1.4 (1-10)	8.9±1.2 (4-10)	$t=-0.90, p=0.36$
<b>Smoking Status</b> Yes No	34 (3.6) 911 (96.4)	30 (3.3) 872 (96.7)	4 (9.3) 39 (90.7)	$\chi^2=4.18, p=0.06$	41 (3.1) 1275 (96.9)	36 (2.9) 1189 (97.1)	5 (5.5) 86 (94.5)	$\chi^2=1.83, p=0.17$
<b>Arthritis, rheumatism, osteoporosis</b> Yes No	326 (38.5) 520 (61.5)	307 (38) 500 (62)	19 (48.7) 20 (51.3)	$\chi^2=1.79, p=0.18$	728 (59.7) 492 (40.3)	676 (59.2) 465 (40.8)	52 (65.8) 27 (34.2)	$\chi^2=1.32, p=0.24$
<b>Stroke</b> Yes No	17 (2) 829 (98)	17 (2.1) 790 (97.9)	0 (0) 39 (100)	$\chi^2=0.83, p=0.36$	21 (1.7) 1199 (98.3)	21 (1.8) 1120 (98.2)	0 (0) 79 (100)	$\chi^2=1.47, p=0.39$
<b>High blood pressure, cholesterol or heart problems</b> Yes No	510 (60.3) 336 (39.7)	483 (59.9) 324 (40.1)	27 (69.2) 12 (30.8)	$\chi^2=1.36, p=0.24$	603 (49.4) 617 (50.6)	555 (48.6) 586 (51.4)	48 (60.8) 31 (39.2)	$\chi^2=4.34, p<0.05$
<b>Asthma or other breathing problems</b> Yes No	85 (10) 761 (90)	77 (9.5) 730 (90.5)	8 (20.5) 31 (79.5)	$\chi^2=4.95, p<0.05$	177 (14.5) 1043 (85.5)	158 (13.8) 983 (86.2)	19 (24.1) 60 (75.9)	$\chi^2=6.20, p<0.05$

<b>Diabetes</b>								
Yes	157 (18.6)	152 (18.8)	5 (12.8)	$\chi^2=0.89,$ $p=0.34$	159 (13)	156 (13.7)	3 (3.8)	$\chi^2=6.35, p<0.05$
No	689 (81.4)	655 (81.2)	34 (87.2)		1061 (87)	984 (86.3)	76 (96.2)	
<b>Depression</b>								
Yes	11 (1.3)	10 (1.2)	1 (2.6)	$\chi^2=0.50,$ $p=0.40$	39 (3.2)	36 (3.2)	3 (3.8)	$\chi^2=0.09, p=0.75$
No	835 (98.7)	797 (98.8)	38 (97.4)		1181 (96.8)	1105 (96.8)	76 (96.2)	
<b>Sleeping disorder</b>								
Yes	127 (15)	121 (15)	6 (15.4)	$\chi^2=0.00,$ $p=0.94$	210 (17.2)	200 (17.5)	10 (12.7)	$\chi^2=1.23, p=0.26$
No	719 (85)	686 (85)	33 (84.6)		1010 (82.8)	941 (82.5)	69 (87.3)	
<b>Usual sleep quantity in 24 hours</b>	5.9±2.0 (1-11)	6.1±1.9 (1-11)	6.0±1.9 (1-10)	$t=0.28, p=0.78$	5.9±2.0 (1-11)	5.8±2.0 (1-11)	6.3±1.9 (3-11)	$t=-2.19, p<0.05$
<b>ESS Scores</b>	4.6±3.0 (0-20)	5.1±3.0 (0-20)	4.7±2.7 (1-10)	$t=0.85, p=0.39$ $\chi^2=1.10,$ $p=0.57$	4.6±3.0 (0-20)	4.4±3.0 (0-20)	3.9±2.7 (0-11)	$t=1.27, p=0.20$ $\chi^2=0.46, p=0.79$
Normal (0-10)	836 (90.6)	796 (90.5)	40 (93)		1217 (93.4)	1131 (93.3)	86 (94.5)	
Borderline (11-15)	65 (7)	62 (7)	3 (7)		59 (4.5)	55 (4.5)	4 (4.5)	
Abnormal (16-24)	22 (2.4)	22 (2.5)	0 (0)		27 (2.1)	26 (2.1)	1 (1.1)	
<b>Fall in previous 2 years</b>								
Yes	256 (27.2)	244 (27.2)	12 (27.9)	$\chi^2=0.01,$ $p=0.91$	495 (37.7)	458 (37.4)	37 (41.6)	$\chi^2=0.60, p=0.43$
No	685 (72.8)	654 (72.8)	31 (72.1)		817 (62.3)	765 (62.6)	52 (58.4)	
<b>Number of falls</b>	0.5±0.9 (0-12)	0.4±0.8 (0-12)	0.4±0.7 (0-2)	$t=0.07, p=0.94$	0.5±0.9 (0-11)	0.6±1.0 (0-11)	0.7±1.1 (0-5)	$t=-0.86, p=0.38$
<b>Physical Activity</b>								
Low	32 (30.2)	31 (30.4)	1 (25)	$\chi^2=3.22,$ $p=0.19$	42 (25.8)	37 (25.5)	5 (27.8)	$\chi^2=0.04, p=0.97$

Moderate High	38 (35.8) 36 (34)	35 (34.3) 36 (35.3)	3 (75) 0 (0)		74 (45.4) 47 (28.8)	66 (45.5) 42 (29)	8 (44.4) 5 (27.8)	
<b>Receive home delivery services</b>				$\chi^2=0.05,$ $p=1.00$				$\chi^2=1.01, p=0.37$
Yes	28 (3)	27 (3)	1 (2.4)		48 (3.7)	43 (3.5)	5 (5.6)	
No	908 (97)	863 (97)	41 (97.6)		1256 (96.3)	1172 (96.5)	84 (94.4)	
<b>Dysexecutive Syndrome</b>	14.0±7.7 (0-43)	14.2±7.9 (0-43)	15.6±7.7 (2-31)	$t=-1.04, p=0.29$	14.0±7.7 (0-37)	13.9±7.6 (0-37)	12.9±6.3 (2-35)	$t=-2.19, p=0.24$

Continuous variables are shown as means (SD); range and categorical variables as frequencies (%). Differences between groups were tested through Chi-Square or independent t-tests.

The numbers reported in each cell represent the exact percentage of drinkers and non-drinkers for each of the exposures. Due to missing values, the denominator was not always 891 for low risk drinkers and 59 for high risk drinkers in males, and 1194 for low risk drinkers and 135 for high risk drinkers in females.

**Table 3.2** illustrates descriptive statistics and comparative analyses for males which includes a new moderate category (3-9 drinks per week), and reduced limits for high-risk drinking (>10 drinks per week). Most males (32.8%) were categorized as moderate drinkers compared to none (25.3%), low (20.7%) and high-risk drinkers (21%). High-risk drinkers were more likely to live with a spouse or partner (85.4%), have higher rated self-rated physical health  $8.4 \pm 1.5$ , and be diagnosed with high blood pressure, cholesterol, or heart problems (59.1%). High-risk drinkers were significantly more likely to have higher self-rated mental health ( $9.2 \pm 1.1$ ), normal likelihood of daytime sleepiness ( $4.7 \pm 2.9$ ); and less likely to have an illness or disability prior to retirement and diabetes. The number of drinks was significantly positively correlated with physical ( $r=0.06$ ;  $p<.01$ ) and mental health ( $r=0.04$ ;  $p>.05$ ), however, age was not.

**Table 3.2. Characteristics of males aged 65 and over with new alcohol consumption guidelines**

<b>Variables</b>	<b>Total (N=950)</b>	<b>None (N=241) 25.3%</b>	<b>Low (N=197) 20.7%</b>	<b>Moderate (N=312) 32.8%</b>	<b>High (N=200) 21%</b>	<b>Significance (p&lt;.05)</b>
		<b>0 drink/ per week</b>	<b>1-2 drink/ per week</b>	<b>3-9 drinks/ per week</b>	<b>&gt;10 drinks per/week</b>	
<b>Age</b>	73.5±6.1 (65-95)	73.2±5.9 (65-91)	73.8±6.5 (65-95)	74.1±5.9 (65-91)	72.9±5.9 (65-90)	F=2.03, p=0.10
<b>Living situation</b>						$\chi^2=14.53, p=0.10$
Alone	145 (15.3)	41 (17)	37 (18.9)	47 (15.2)	20 (10.1)	
With a spouse/partner	756 (79.9)	184 (76.3)	148 (75.5)	254 (81.9)	170 (85.4)	
With family	38 (4)	12 (5)	9 (4.6)	9 (2.9)	8 (4)	
With roommates (not related)	7 (0.7)	4 (1.7)	2 (1)	0 (0)	1 (0.5)	
<b>Illness or disability before retirement</b>						$\chi^2=14.59, p<0.01$
Yes	198 (21.6)	67 (29)	37 (19.3)	67 (22.1)	27 (14.1)	
No	720 (78.4)	164 (71.7)	155 (80.7)	236 (77.9)	165 (85.9)	
<b>Years Retired</b>						F=1.90, p=0.12 $\chi^2=10.83, p=0.28$
Range	13.5±8.7 (1-58)	13.3±8.8 (1-48)	13.2±8.3 (1-35)	14.7±9.2 (1-58)	12.5±8.2 (1-52)	
1-3	58 (9.4)	14 (8.9)	19 (14.3)	14 (7.2)	11 (8.5)	
4-6	92 (15)	28 (17.7)	16 (12)	23 (11.9)	25 (19.4)	
7-9	90 (14.7)	22 (13.9)	18 (13.5)	29 (14.9)	21 (16.3)	
10+	374 (60.9)	94 (59.5)	80 (60.2)	128 (66)	72 (55.8)	
<b>Smoking Status</b>						$\chi^2=1.25, p=0.73$
Yes	34 (3.6)	6 (2.5)	8 (4.1)	13 (4.2)	7 (3.5)	
No	912 (96.4)	233 (97.5)	188 (95.9)	298 (95.8)	193 (96.5)	
<b>Self-rated physical health</b>	8.2±1.6 (1-10)	8.1±1.8 (1-10)	8.1±1.7 (1-10)	8.2±1.6 (1-10)	8.4±1.5 (2-10)	F=2.51, p=0.057

<b>Self-rated mental health</b>	8.9±1.4 (1-10)	8.9±1.5 (1-10)	8.7±1.7 (1-10)	9.0±1.4 (2-10)	9.2±1.1 (1-10)	<b>F=2.93, p&lt;0.05</b>
<b>Arthritis, rheumatism, osteoporosis</b>						$\chi^2=2.52, p=0.47$
Yes	521 (61.5)	74 (35.1)	77 (42.8)	107 (38.9)	68 (37.6)	
No	326 (38.5)	137 (64.9)	103 (57.2)	168 (61.1)	113 (62.4)	
<b>Stroke</b>						$\chi^2=7.00, p=0.07$
Yes	17 (2)	4 (1.9)	7 (3.9)	6 (2.2)	0 (0)	
No	839 (98)	207 (98.1)	173 (96.1)	269 (97.8)	181 (100)	
<b>High blood pressure, cholesterol</b>						$\chi^2=0.42, p=0.93$
Yes	511 (60.3)	127 (60.2)	107 (59.4)	170 (61.8)	107 (59.1)	
No	336 (39.7)	84 (39.8)	73 (40.6)	105 (38.2)	74 (40.9)	
<b>Asthma or other breathing problems</b>						$\chi^2=1.47, p=0.68$
Yes	85 (10)	19 (9)	19 (10.6)	25 (9.1)	22 (12.2)	
No	762 (90)	192 (91)	161 (89.4)	250 (90.9)	159 (87.8)	
<b>Diabetes</b>						$\chi^2=44.28, p<0.01$
Yes	157 (18.5)	67 (31.8)	35 (19.4)	44 (16)	11 (6.1)	
No	690 (81.5)	144 (68.2)	145 (80.6)	231 (84)	170 (93.9)	
<b>Depression</b>						$\chi^2=2.69, p=0.44$
Yes	11 (2.5)	5 (2.4)	2 (1.1)	2 (0.7)	2 (1.1)	
No	836 (97.5)	206 (97.6)	178 (98.9)	273 (99.3)	179 (98.9)	
<b>Sleeping disorder</b>						$\chi^2=5.21, p=0.15$
Yes	127 (15)	25 (11.8)	25 (13.9)	41 (14.9)	36 (19.9)	
No	720 (85)	186 (88.2)	155 (86.1)	234 (85.1)	145 (80.1)	

<b>Usual sleep quantity in 24 hours</b>	6.1±1.9 (1-11)	6.2±2.1 (1-11)	6.1±1.9 (1-11)	5.9±1.9 (1-11)	6.2±1.8 (1-11)	F=0.96, p=0.40
<b>ESS Score</b>	5.1±3.0 (0-20)	5.3±3.3 (0-20)	5.5±3.3 (0-20)	4.8±2.7 (0-13)	4.7±2.9 (0-15)	F=3.23, <b>p&lt;0.05</b> $\chi^2=13.16$ , <b>p&lt;0.05</b>
Normal (0-10)	836 (90.5)	210 (89)	164 (85.4)	280 (93.3)	182 (92.9)	
Borderline (11-15)	66 (7.1)	17 (7.2)	23 (12)	15 (5)	11 (5.6)	
Abnormal (16-24)	22 (2.4)	9 (3.8)	5 (2.6)	5 (1.7)	3 (1.5)	
<b>Fall in previous 2 years</b>						$\chi^2=1.84$ , p=0.60
Yes	256 (27.2)	62 (26.1)	59 (30.3)	78 (25.2)	57 (28.5)	
No	686 (72.8)	176 (73.9)	136 (69.7)	231 (74.8)	143 (71.5)	
<b>Number of falls</b>	0.4±0.8 (0-12)	0.4±1.0 (0-12)	0.4±0.8 (0-6)	0.3±0.6 (0-4)	0.4±0.8 (0-6)	F=0.87, p=0.45
<b>Physical Activity</b>						$\chi^2=6.62$ , p=0.35
Low	32 (30.2)	7 (26.9)	8 (38.1)	41 (36.8)	3 (14.3)	
Moderate	38 (35.8)	10 (38.5)	4 (19)	14 (36.8)	10 (47.6)	
High	36 (34)	9 (34.6)	9 (42.9)	10 (26.3)	8 (38.1)	
<b>Receive home delivery services</b>						$\chi^2=2.24$ , p=0.52
Yes	28 (3)	9 (3.8)	7 (3.6)	9 (2.9)	3 (1.5)	
No	909 (97)	230 (96.2)	187 (96.4)	297 (97.1)	195 (98.5)	
<b>Dysexecutive Syndrome</b>	14.3±7.9 (0-46)	14.1±8.7 (0-46)	14.2±8.2 (0-33)	13.8±7.3 (0-37)	15.2±7.7 (1-40)	F=1.07, p=0.35

Continuous variables are shown as means (SD), range; and categorical variables as frequencies (%). Differences between groups were tested through Chi-Square or ANOVA.

The numbers reported in each cell represent the exact percentage of low, moderate and high-risk drinkers for each of the exposures.

Due to missing values, the denominator was not always representative of low, moderate and high-risk drinkers.

**Table 3.2.1** demonstrates descriptive statistics and comparative analyses for females, with a moderate drinking category (3-6 drinks per week), and reduced limits for high-risk drinking (>7 drinks per week). In females, more reported non-drinking (33.1%) compared to 22.1% who reported low-risk drinking, 23.3% who reported moderate drinking and 21% who reported high-risk alcohol drinking. High-risk drinkers were significantly more likely to live with a spouse or partner (59.9%), have high self-rated physical health  $8.3 \pm 1.7$ , arthritis, osteoporosis or rheumatism (61.2%), sleep longer in a 24hr period ( $6.1 \pm 2.0$ ) and have a normal likelihood of daytime sleepiness ( $3.9 \pm 2.7$ ) compared to none, low and moderate drinkers. Similar to males, females high-risk drinkers were also less likely to have an illness or disability before retirement, and less likely to have diabetes, and there were no differences between smoking status and level of drinking.

**Table 3.2.1. Characteristics of females aged 65 and over with new alcohol consumption guidelines**

<b>Variables</b>	<b>Total (N=1332)</b>	<b>None (N=442) 33.1%</b>	<b>Low (N=296) 22.2%</b>	<b>Moderate (N=311) 23.3%</b>	<b>High (N=283) 21%</b>	<b>Significance (p&lt;.05)</b>
		<b>0 drink/ per week</b>	<b>1-2 drink/ per week</b>	<b>3-6 drinks/ per week</b>	<b>&gt;7 drinks per/week</b>	
<b>Age Range</b>	72.2±5.7 (65-96)	72.7±6.3 (65-96)	72.1±5.3 (65-91)	71.7±5.5 (65-92)	72±5.4 (65-87)	F=2.34, p=0.07
<b>Living situation</b>						$\chi^2=29.48, p<0.01$
Alone	579 (43.6)	220 (50.2)	140 (47.3)	120 (38.6)	99 (35.1)	
With a spouse/partner	677 (51)	192 (43.8)	138 (46.6)	178 (57.2)	169 (59.9)	
With family	60 (4.5)	20 (4.6)	17 (5.7)	10 (3.2)	13 (4.6)	
With roommates (not related)	11 (0.8)	6 (1.4)	1 (0.3)	3 (1)	1 (0.4)	
<b>Illness or disability before retirement</b>						$\chi^2=14.19, p<0.01$
Yes	295 (23)	119 (27.9)	63 (22.2)	48 (16.1)	65 (23.7)	
No	988 (77)	307 (72.1)	221 (77.8)	251 (83.9)	209 (76.3)	
<b>Years Retired</b>	12.8±8.6 (1-55)	13.6±8.9 (1-55)	11.8±7.5 (1-35)	13.2±9.4 (1-52)	12.4±8.0 (1-37)	F=1.86, =0.13 $\chi^2=5.92, p=0.74$
1-3	102 (11.5)	35 (12)	24 (11.9)	21 (10)	22 (12)	
4-6	152 (17.1)	40 (13.7)	37 (18.3)	42 (20)	33 (17.9)	
7-9	107 (12.1)	37 (12.7)	27 (13.4)	20 (9.5)	23 (12.5)	
10+	526 (59.3)	179 (61.5)	114 (56.4)	127 (60.5)	106 (57.6)	
<b>Smoking Status</b>						$\chi^2=2.95, p=0.39$
Yes	41 (3.1)	17 (3.9)	5 (1.7)	9 (2.9)	10 (3.5)	
No	1278 (96.9)	421 (96.1)	286 (98.3)	299 (97.1)	272 (96.5)	
<b>Self-rated physical health</b>	8.2±1.7 (1-10)	7.9±1.9 (1-10)	8.3±1.6 (1-10)	8.5±1.5 (2-10)	8.3±1.7 (2-10)	F=9.88, p<0.001
<b>Self-rated mental health</b>	8.8±1.5 (1-10)	8.8±1.6 (2-10)	8.9±1.3 (1-10)	8.9±1.4 (1-10)	8.8±1.5 (1-10)	F=1.29, p=0.27

<b>Arthritis, rheumatism, osteoporosis</b>						$\chi^2=8.14, p<0.05$
Yes	731 (59.8)	262 (63.3)	142 (52.6)	171 (60.2)	156 (61.2)	
No	492 (40.2)	152 (36.7)	128 (47.4)	113 (39.8)	99 (38.8)	
<b>Stroke</b>						$\chi^2=7.60, p=0.055$
Yes	21 (1.7)	13 (3.1)	3 (1.1)	3 (1.1)	2 (0.8)	
No	1202 (98.3)	401 (96.9)	267 (98.9)	281 (98.9)	253 (99.2)	
<b>High blood pressure, cholesterol</b>						$\chi^2=3.13, p=0.37$
Yes	603 (49.3)	215 (51.9)	127 (47)	131 (46.1)	130 (51)	
No	620 (50.7)	199 (48.1)	143 (53)	153 (53.9)	125 (49)	
<b>Asthma or other breathing problems</b>						$\chi^2=6.31, p=0.09$
Yes	177 (14.5)	71 (17.1)	31 (11.5)	34 (12)	41 (16.1)	
No	1046 (85.5)	343 (82.9)	239 (88.5)	250 (88)	214 (83.9)	
<b>Diabetes</b>						$\chi^2=45.48, p<0.001$
Yes	159 (13)	81 (19.6)	47 (17.4)	17 (6)	14 (5.5)	
No	1064 (87)	333 (80.4)	223 (82.6)	267 (94)	241 (94.5)	
<b>Depression</b>						$\chi^2=3.75, p=0.94$
Yes	40 (3.3)	14 (3.4)	10 (3.7)	8 (2.8)	8 (3.1)	
No	1183 (96.7)	400 (96.6)	260 (96.3)	276 (97.2)	247 (96.9)	
<b>Sleeping disorder</b>						$\chi^2=2.22, p=0.52$
Yes	210 (17.1)	79 (19.1)	43 (15.9)	43 (15.1)	45 (17.6)	
No	1013 (82.8)	335 (80.9)	227 (84.1)	241 (84.9)	210 (82.4)	
<b>Usual sleep quantity in 24 hours</b>	5.9±2.0	6.0±2.1	5.9±1.9	5.6±1.8	6.1±2.0	$F=2.87, p<0.05$
Range	(1-11)	(1-11)	(1-11)	(1-11)	(1-11)	
<b>ESS Scores</b>	3.9±2.7	4.6±3.2	4.5±3.2	4.1±2.9	3.9±2.7	$F=3.94, p<0.01$

Normal (0-10)	(0-20) 1220 (93.4)	(0-20) 402 (92.6)	(0-15) 264 (92)	(0-15) 287 (93.8)	(0-15) 267 (95.7)	$\chi^2=6.26, p=0.39$
Borderline (11-15)	59 (4.5)	19 (4.4)	16 (5.6)	14 (4.6)	10 (3.6)	
Abnormal (16-24)	27 (2.1)	13 (1)	7 (2.4)	5 (1.6)	2 (0.7)	
<b>Fall in previous 2 years</b>						$\chi^2=3.52, p=0.31$
Yes	497 (37.8)	178 (41.2)	103 (35)	115 (37.3)	101 (35.9)	
No	818 (62.2)	254 (58.8)	191 (65)	93 (62.7)	180 (64.1)	
<b>Number of falls</b>	0.6±1.0 (0-11)	0.7±1.2 (0-11)	0.5±0.8 (0-4)	0.6±0.9 (0-7)	0.6±1.2 (0-11)	F=1.84, p=0.13
<b>Physical Activity</b>						$\chi^2=6.40, p=0.38$
Low	42 (25.6)	15 (33.3)	6 (15.8)	9 (23.7)	12 (27.9)	
Moderate	75 (45.7)	18 (40)	23 (60.5)	15 (39.5)	19 (44.2)	
High	47 (28.7)	12 (26.7)	9 (23.7)	14 (36.8)	12 (27.9)	
<b>Receive home delivery services</b>						$\chi^2=4.17, p=0.24$
Yes	48 (3.7)	22 (5.1)	10 (3.4)	7 (2.3)	9 (3.2)	
No	1259 (96.3)	413 (94.9)	280 (96.6)	298 (97.7)	268 (96.8)	
<b>Dysexecutive Syndrome</b>	13.9±7.5 (0-54)	14.1±7.8 (0-37)	14.0±7.6 (0-36)	13.9±7.2 (0-36)	13.3±7.0 (0-54)	F=0.63, p=0.59

Continuous variables are shown as means (SD); range and categorical variables as frequencies (%). Differences between groups were tested through Chi-Square or ANOVA.

The numbers reported in each cell represent the exact percentage of low, moderate and high-risk drinkers for each of the exposures. Due to missing values, the denominator was not always representative.

Continuous variables are shown as means (SD); range and categorical variables as frequencies (%). Differences between groups were tested through Chi-Square or ANOVA.

The numbers reported in each cell represent the exact percentage of low, moderate and high-risk drinkers for each of the exposures. Due to missing values, the denominator was not always representative of low, moderate and high-risk drinkers.

**Tables 3.3** shows a comparison of the current alcohol consumption guidelines and the new alcohol consumption guidelines in males using logistic and multinomial regression. Having an illness or disability before retirement or diabetes, high self-rated physical and mental scores, and likelihood of daytime sleepiness were not predictive of the current low (<15 drinks per week) or high-risk (>15 drinks per week) drinking guidelines. There was a negative, but significant association with having an illness or disability before retirement, diagnosis of diabetes and likelihood of daytime sleepiness and high-risk drinking.

**Table 3.4** is a comparison of the current alcohol consumption guidelines and the new alcohol consumption guidelines for females using logistic and multinomial regression. After adjusting for confounding variables, the current guidelines show that females whom have asthma or other breathing problems were 2.15x more likely to be high-risk drinkers (consuming >10 drinks per week). There was a negative, but significant association between diabetes and moderate and high-risk drinking ( $p<0.01$ ).

In comparison, after controlling for the same variables, the new alcohol consumption guidelines show that having asthma or other breathing problems was not predictive of high-risk drinking (>7 drinks per week). Arthritis, osteoporosis or rheumatism was protective of low-risk drinking (1-2 drinks per week) ( $p<0.01$ ), however, it was not protective of moderate (3-6 drinks per week) or high-risk drinking ( $p=0.96$  and  $p=0.69$ ), respectively. There was a negative, but significant association with moderate and high-risk drinking ( $p<0.001$ ), as well as, a normal likelihood of daytime sleepiness. Self-rated physical health increased moderate drinking by 1.21x ( $p<0.01$ ), but was not associated with low or high-risk drinking. In turn, persons with higher self-rated physical health scores were more likely to be moderate drinkers.

**Table 3.3 Comparison of current drinking guidelines and new alcohol consumption guidelines for males**

Current guidelines				New Drinking Guidelines				
Variables	Low (N=891)	High (N=59)	Significance (p<.05)	None (N=241)	Low (N=197)	Moderate (N=312)	High (N=200)	Significance (p<.05)
	<15 drinks per week	>15 drinks per week		0 drinks/ per week	1-2 drink/ per week	3-9 drinks/ per week	>10 drinks per/week	
	OR 95%CI	OR 95%CI		OR 95%CI	OR 95%CI	OR 95%CI	OR 95%CI	
Illness or disability before retirement	1.79 (0.67-4.77)	0.55 (0.21-1.48)	0.24	Reference	0.60 (0.36-1.00)	0.81 (0.52-1.26)	0.51 (0.29-0.89)	<b>0.01</b>
Self-rated physical health	0.97 (0.76-1.24)	1.02 (0.80-1.31)	0.83	Reference	0.98 (0.85-1.13)	0.95 (0.83-1.08)	1.06 (0.90-1.24)	0.44
Self-rated mental health	0.84 (0.61-1.17)	1.17 (0.85-1.62)	0.31	Reference	0.93 (0.80-1.08)	1.02 (0.88-1.18)	1.05 (0.87-1.25)	0.58
Diabetes	1.41 (0.53-3.73)	0.70 (0.26-1.87)	0.48	Reference	0.55 (0.33-0.89)	0.39 (0.24-0.62)	0.16 (0.08-0.31)	<b>&lt;0.02</b>
Likelihood of daytime sleepiness	1.02 (0.91-1.14)	0.97 (0.87-1.09)	0.69	Reference	0.97 (0.91-1.04)	0.92 (0.87-0.98)	0.92 (0.86-0.99)	<b>&lt;0.02</b>

**Table 3.4 Comparison of current drinking guidelines and new alcohol consumption guidelines for females**

Current guidelines				New Alcohol Consumption Guidelines				
Variables	Low (N=1194)	High (N=135)	Significance (p<.05)	None (N=441)	Low (N2=95)	Moderate (N=312)	High (N=200)	Significance (p<.05)
	<10 drinks per week	>10 drinks per/week		0 drinks/ per week	1-2 drink/ per week	3-6 drinks/ per week	>7 drinks per/week	
	OR 95%CI	OR 95%CI		OR 95%CI	OR 95%CI	OR 95%CI	OR 95%CI	
Illness or disability before retirement	1.43 (0.78-2.65)	0.69 (0.37-1.28)	0.24	Reference	0.98 (0.67-1.44)	0.69 (0.46-1.04)	1.03 (0.70-1.52)	0.85
Self-rated physical health	0.96 (0.83-1.11)	1.03 (0.89-1.20)	0.62	Reference	1.09 (0.99-1.20)	1.21 (1.09-1.35)	1.08 (0.98-1.19)	0.09
Arthritis, osteoporosis, rheumatism	0.67 (0.40-1.13)	1.48 (0.88-2.49)	0.13	Reference	0.63 (0.45-0.88)	1.00 (0.71-1.41)	0.93 (0.65-1.32)	0.69
Asthma or other breathing problems	0.46 (0.26-0.82)	2.15 (1.21-3.81)	<b>0.009</b>	Reference	0.70 (0.43-1.14)	0.75 (0.47-1.22)	1.01 (0.64-1.58)	0.94
Diabetes	3.33 (1.02-10.83)	0.30 (0.09-0.97)	<b>0.04</b>	Reference	0.77 (0.50-1.18)	0.28 (0.15-0.49)	0.23 (0.12-0.43)	<b>0.00</b>
Likelihood of daytime sleepiness	1.03 (0.94-1.12)	0.97 (0.89-1.05)	0.48	Reference	1.00 (0.95- 1.05)	0.98 (0.93-1.04)	0.93 (0.87-0.98)	<b>0.01</b>

### 3.4 Discussion

The present study found that 70% of community dwelling older adults reported drinking alcohol weekly; 74.6% of males and 66.8% of females. In our sample, 6.2% of males (defined as >15 drinks per week) and 10.1% of females were high-risk drinkers (defined as >10 drinks per week). Our prevalence rates are similar to findings of the Canadian Tobacco, Alcohol and Drug Survey (CTADS) that found 66.2% of community dwelling older adults consumed alcohol within the previous year (Health Canada, 2015; Health Canada, 2017). Population studies in other countries show that prevalence rates of alcohol use in community dwelling older adults are similar and range from 63% to 81% in Ireland (Cousins et al. 2014), Germany (Du et al. 2016) and Norway (Bye & Rossow, 2017).

Other studies have also found that high risk drinking is more prevalent in males compared to females (Blazer and Wu, 2009; French et al. 2014; Immonen et al. 2011), however, definitions of high risk drinking were not consistent. With the inclusion of the moderate alcohol drinking category, we found 21% of males (>10 drinks per week) and 15% of females (>7 drinks per week) would be classified as high-risk drinkers. In males, asthma and other breathing problems was the only variable to predict high-risk drinking using the current alcohol consumption guidelines. No variables predicted high-risk drinking in men using the new alcohol consumption guidelines. In females, a diagnosis of asthma or other breathing problems was associated with high-risk drinking with the current alcohol consumption guidelines, and high self-rated physical health scores were predictive of moderate drinking. The majority of participants are within the current alcohol consumption drinking guidelines, suggesting the current guidelines may be adequate for community dwelling older adults. However, high-risk drinking is defined as consuming >15 drinks per week for males and >10 drinks per week for

females, which is a generous amount of alcohol for an older adult to consume per week. Active community dwelling older adults, such as the ones presented in this study may be aware that this amount of alcohol in a week is not healthy and choose to drink less.

Physical activity and smoking were both not associated with high-risk drinking. There is a paucity of studies that have examined physical activity and alcohol consumption in older adults, however, one study found older adults who are more physically active consume more alcohol (Westerterp et al. 2004). Prior studies have found an association between low physical activity levels (low MET scores) with advanced age (Valim-Rogatto, 2011) and with females (Tomioka et al. 2011). Physical activity has also been linked to improved cognition (Bherer et al. 2013; Olanrewaju et al. 2016; Weuve et al. 2004), sleep quality (Benloucif et al. 2004), and decreases fall risk (Suzuki et al. 2004) in community dwelling older adults. Overall, only 3.4% reported smoking which could explain why smoking was not a predictor of high-risk drinking. This finding was unexpected given that other large population studies in older adults have found that smoking is related to high-risk drinking in both males and females (Immonen et al. 2011; Merrick et al. 2008; Kirchner et al. 2007).

In general, high-risk drinking can lead to a number of adverse events for older adults such as hypertension (Sesso et al. 2008), drug-alcohol interaction (Weathermon and Crabb, 1999) and injurious falls (Immonen et al. 2011; Stenbacka et al. 2002). High blood pressure, cholesterol and heart problems were associated with high-risk drinking in females but were not independently predictive in the logistic regression model. In this sample, almost half of females (49.4%) reported a diagnosis of high blood pressure, cholesterol or heart problems, with rates being significantly higher (53.3%) in older females (>80 and >85 years). However, in males, high blood pressure, cholesterol and other heart problems was not associated with high-risk alcohol

drinking. Our findings are similar to previous studies indicating that hypertension in females over the age of 60 is common (48.8%) and increases with advanced age ( $\geq 85$  years) (63.3%) (Lionakis et al. 2012). Elevated blood pressure after menopause and increased body mass index may also contribute to why high blood pressure is more common in older females compared to men (Cifkova et al. 2008).

### **3.5 Limitations**

Our study relied on self-reported data which is subject to recall and social desirability bias. Consistent with prior studies, it is likely that alcohol use may have been under-reported despite 70% of the sample stating they drink weekly (Livingston & Callinan, 2015; Stockwell et al. 2016). Additionally, our survey did not ask questions on marital status (divorced or single), income or education which are associated with drinking in older adults in prior studies (French et al. 2014; Merrick et al. 2008). Moreover, given the age of our sample, some individuals may suffer from memory loss although the majority of the sample performed adequately on the executive function test. Nevertheless, our results cannot be generalized to the broader population as our sample was generally healthy, belonged to community and advocacy organizations, and were familiar with computers. Additionally, given the large number of participants recruited from advocacy organizations, it is likely our sample was well educated with adequate financial means. Future studies should aim to include a more diverse population, and examine changes in alcohol use in community dwelling older adults over time.

### **3.6 Conclusions**

The majority of Canadian community dwelling older adults are within the recommended low-risk drinking guidelines. Our findings show that males consume more alcohol than females. The current alcohol consumption drinking guidelines in Canada appear to be adequate.

## Chapter 4: Alcohol and Select Medications as Risk Factors for Falls in Community Dwelling Older Adults

### Overview

**Background and Objectives:** Older adults are frequently prescribed psychotropic medications and are consumers of alcohol, all of which are risk factors for falls. The objective of this study is to examine the associations between psychotropic medications (i.e. anti-psychotics, benzodiazepines), anti-depressants, and anti-hypertensives, both individually and concomitantly with alcohol on fall risk in community dwelling older adults.

**Methods:** A sample of 2,281 community dwelling older adults aged  $\geq 65$  were analyzed from the Canadian Injury Prevention Survey. Data was collected on demographics, medication (e.g. psychotropics, anti-depressants, anti-hypertensives), alcohol use, and fall status. A univariate analysis was conducted to select variables for the regression models. Logistic regression models were fitted to determine predictors of falls.

**Results:** The sample ranged in age from 65 to 96 years (Mean  $73.1 \pm 6.2$ ); 58% were woman. More than half of the sample were using anti-hypertensive medication (52%), 13.6% were using anti-depressants medication and 6.2 % psychotropic medication. Approximately 70% consumed alcohol on a weekly basis. One third of the sample reported falling in the previous two years (33.4%). Falls was significantly correlated with self-rated physical and mental health, comorbidity score, total psychotropic and anti-depressant medication use, and total number of medication use. Anti-hypertensive medication and alcohol use was not predictive of falls. Psychotropics as a group were predictive of falls, as were selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors and serotonin antagonist reuptake inhibitors anti-depressants.

**Conclusions:** Caution is needed when prescribing psychotropic and anti-depressant medications to older adults who may be at a high risk for falls.

## 4.1 Introduction

Approximately 20-30% of all Canadian older adults fall each year (Public Health Agency of Canada, 2014) resulting in extended hospital stays, fractures (hip, wrist, and upper arm), immobilization, depression, loss of autonomy, morbidity, early admission to long-term care, and premature death (de Jong et al. 2013; PHAC, 2014; Todd et al. 2004; WHO, 2007). Fall risk is influenced by many factors including increased age, female sex, living alone, poor self-perceived health, development of chronic disease (e.g. arthritis, rheumatism or osteoporosis, cardiovascular disease, depression, sleep disorders), and polypharmacy (Brassington et al. 2000; Deandrea et al. 2010; Kerse et al. 2008; Ocampo-Chaparro et al. 2013; PHAC, 2014). Medications such as psychotropic, anti-depressants and anti-hypertensives have been suggested as fall risk factors for community dwelling older adults (Deandrea et al. 2010), as has alcohol (PHAC, 2014; WHO, 2007), however, there is paucity of empirical evidence in community dwelling older adults.

Between 81 to 88% of community dwelling older adults use at least one prescription medication (Rotermann et al. 2015; Qato et al. 2008; Scholes et al. 2013). Psychotropic medications such as anxiolytics, anti-psychotics, hypnotics/sedatives or anti-depressants and anti-hypertensives are among the most widely prescribed medications to older adults (Merel et al. 2017), used to treat anxiety, depression, insomnia and psychological distress (Lindsey, 2009). In 2012, approximately 15% of community dwelling older adults were prescribed a benzodiazepine, 4.4% an anti-psychotic, 19% an anti-depressant, and between 15 and 28% were prescribed a sub-class of anti-hypertensive medications (e.g. angiotensin converting enzyme inhibitor, beta-blocker, calcium channel blocker, angiotensin II antagonists or thiazide), meaning the overall rate of use is likely close to half the population of persons over 65 years (CIHI, 2012).

Psychotropic medications are known to cause falls in older adults due to side effects such as psychomotor and cognitive deficits (e.g. confusion, muscle weakness, dizziness, loss of coordination) (de Groot et al. 2013; Madhusoodanan and Bugunovic, 2004). A recent study found that in community dwelling older adults, users of psychotropic medications were 1.57x times more likely to fall compared to non-fallers (Du et al. 2017). Furthermore, females using sedatives/ hypnotics were 1.5x more likely to have an injurious fall compared to males (Stenbacka et al. 2002). Psychotropic medications encompass a large group of sub-classes (e.g. hypnotics, sedatives, anti-psychotics, anxiolytics), however, little information exists on the effects of individual sub-classes on fall risk in community dwelling older adults.

Anti-depressant medications, meanwhile, are used to treat depression. Sub-classes of anti-depressants include selective serotonin reuptake inhibitors (SSRIs), tricyclic anti-depressants (TCAs), monoamine oxidase inhibitors (MAOIs), serotonin antagonist reuptake inhibitors (SARI), and serotonin-norepinephrine reuptake inhibitors (SNRI). Anti-depressant medications can cause side effects such as sedation, disrupted sleep, orthostatic hypotension impaired balance and coordination, all of which can increase the risk of falls (Darowski et al. 2009; Milos et al. 2014). Several studies in community dwelling older adults have found an association between anti-depressant use and falls (Gribbin et al. 2011; Du et al. 2017; Kerse et al. 2008; Marcum et al. 2016). Of all anti-depressant medications, SSRIs are the mostly widely prescribed and appear to have the greatest effect on falls, increasing fall risk by 1.55x for a single fall (Kerse et al. 2008) and 7.02x for recurrent falls compared to non-users (Du et al. 2017).

Anti-hypertensives are used to treat high blood pressure. Sub-classes including diuretics, angiotensin converting enzyme inhibitor (ACEi), calcium channel blockers (CCB), beta-blockers, and angiotensin II receptor antagonist (ARB). Findings on anti-hypertensive

medication use and falls are mixed (Cumming et al. 1991; Gribbin et al. 2010; Tinetti et al. 2014; Wong et al. 2013), which may be in part be to differences in terminology, study design and sample sizes (Wong et al. 2013). For example, Wong et al. (2013) found angiotensin-system blocking medications reduced fall risk in community dwelling older adults, however, the definition of angiotensin-system blocking medications included ACEi, CCB and ARB, that each come with its own set of side effects that can also elevate fall risk.

Furthermore, the combined use of alcohol with either psychotropic, anti-depressants and anti-hypertensive use can result in increased sedation, psychomotor impairment, drowsiness, hypotension, disorientation, and falls (Moore et al. 2007; Weathermon and Crabb, 1999). While alcohol is a known risk factor for falls, few studies have examined alcohol and select medication use as a risk for falls in community dwelling older adults. Given the paucity of literature on the impact of psychotropic, anti-depressant and anti-hypertensive medications on fall risk, the primary aim of this study is to examine the association of psychotropic, anti-depressant, and anti-hypertensive medications, both individually and together with alcohol on fall risk in community dwelling older adults.

## **4.2 Methods**

### **4.2.1 Study population**

The survey consisted of 89 questions (**Appendix B**) and was completed using SurveyMonkey, an online survey management platform. This population-based study recruited participants aged 45 years and older from local, provincial and national organizations (e.g. Canadian Association of Retired Persons, Royal Canadian Legion) between July 2016 to June 2017. Emails were sent to each organization consisting of a brief overview of the study, a letter of information, web-links to the surveys in both English and French, and contact information for the Principal Investigator (**Appendix C**). A list of all organizations contacted can be found in **Appendix D**. Prior to completing the survey, participants read a letter of information and provided informed consent.

The survey was completed by 4,614 participants, however, the present study only examined fall risk in older adults. Participants were included if they were 65 years and older, community dwelling (e.g. living independently in a house, apartment, retirement home), and completed all questions on survey pertaining to alcohol and medication use, as well as falls. Participants were excluded if they were living in a long-term care facility, or a resident of a memory ward in a retirement home. The final sample size for the present study was 2,281. This study was approved by the Ontario Research Ethics Board at the University of Waterloo.

### **4.2.2 Measures**

#### *Demographics*

Demographic variables included age, sex, living arrangements, employment status, illness or disability before retirement, years retired, and self-rated physical and mental health. Participants were asked to indicate if they had a diagnosis of one or more of the following health

conditions: arthritis, rheumatism, or osteoporosis; multiple sclerosis; Parkinson's disease; stroke; dementia; high blood pressure, cholesterol, or heart problems; asthma or other breathing issues; diabetes; back problems; foot problems; hearing problems; cataracts, glaucoma, or macular degeneration; sleeping disorders; and depression. If participants had a health condition not listed on the survey, they were asked to indicate their diagnosis in the "other" category. Common 'other' conditions included joint problems (shoulder, hip, knee), and leg cramps.

### *Behavioural Risk Factors*

Behavioural variables included smoking status, alcohol use, prescribed medication use, physical activity, usual sleep quantity in 24 hours, and daytime sleepiness.

### *Medication Use*

All participants self-reported their current prescribed medication. Subsequently, we classified participant medications according to the Anatomical Therapeutic Chemical (ATC) Classification System (WHO, 2007). Only medications listed as psychotropics (e.g. anti-psychotics, anxiolytics, hypnotics/sedatives), anti-depressants including selective serotonin reuptake inhibitors (SSRI), serotonin antagonist reuptake inhibitors (SARI), serotonin-norepinephrine reuptake inhibitors (SNRI), tricyclic anti-depressants (TCA), or other anti-depressants; and anti-hypertensive medications including diuretics, beta-blockers, angiotensin converting enzyme inhibitors (ACEi), angiotensin II receptor antagonist (ARB), and calcium channel blockers (CCB) were examined. Medication use was classified as a binary variable (yes/no). A list of participants prescribed medications are shown in **Appendix E**.

### *Alcohol*

Alcohol consumption was quantified as number of alcoholic drinks per week and number of days per week a person had a drink. Participants were asked "How many alcoholic drinks do

you consume per week”, “How many days per week do you drink”, and how many do you have per day”. A variable was created for alcohol use (yes or no) based on how participants answered, “how many drinks do you have per week”.

### *Physical Activity*

Participants completed the short version of the International Physical Activity Questionnaire (IPAQ). The IPAQ is a valid tool for assessing physical activity in older adults (Chun, 2012; Tomioka et al. 2011). Scores are calculated using energy estimates (multiples of the resting metabolic rate or MET) assigned to each activity category (3.3 for walking, 4.0 for moderate, 8.0 for vigorous) x minutes of activity x days per week, producing a score for weighted MET minutes per week ([www.ipaq.ki.se](http://www.ipaq.ki.se); Craig et al. 2003). Total MET scores are calculated by combining MET scores of walking, moderate physical activity, and vigorous activity (e.g. Total MET-min/week= (3.3 x minutes x days per week) + (4.0 x minutes x days per week) + (8.0 x minutes x days per week). Participants were classified as having a low, moderate or high physical activity level (IPAQ, 2005). Prior studies have associated low MET scores with advanced age, (Valim-Rogatto, 2011), female sex (Tomioka et al. 2011) and worse cognition (Bherer et al. 2013; Olanrewaju et al. 2016; Weuve et al. 2004) and poorer sleep quality (Benloucif et al. 2004) in community dwelling older adults.

### *Sleep*

Sleep quantity was assessed using the Epworth Sleepiness Scale (ESS). The ESS has 8 questions that assess daytime sleepiness in older adults (Johns, 1991). Participants are asked to rate on a 4-point scale (0-3) their likelihood of dozing off or falling asleep during an activity. Scores on the ESS range from 0-24. Likelihood of daytime sleepiness is divided into categories based on score, normal (0-10), borderline (11-15), and abnormal (16-24) chance of falling asleep

during the day. The ESS has shown good test-retest reliability, with high levels of internal consistency measured by Cronbach's alpha (0.88) (Johns, 1992). ESS scores >10 have shown to be independently associated with falling in the previous year among older females, but not males (Hayley et al. 2015). We also asked participants to indicate the number of hours they usually sleep in 24 hours.

### *Cognitive function*

The Dysexecutive Questionnaire (DEX-S) is a reliable and valid measure for assessing executive function in older adults (Emmanouel et al., 2014; Shinagawa et al, 2007; Burgees et al., 1998). The DEX-S examines changes and difficulties in adults in the areas of emotion or personality, behaviour and cognition (Shaw et al. 2015; Gerstof et al. 2013). The 20-item questionnaire is scored on a 5-point scale from (0-4) with scores ranging from 0-80. Higher scores indicate poor executive functioning (Emmanouel et al. 2014; Shaw et al. 2015; Wilson et al. 1996). During pilot testing of the survey, participants indicated that some questions on the DEX-S overlapped with other questions, prompting us to remove one of the items. Consequently, the current DEX-S includes 19 items; scores range from 0-76.

### *Falls*

Falls are the primary outcome variable and were assessed by asking participants "Have you fallen in the previous two years?". Participants were classified as fallers and non-fallers. Fallers were defined as having one or more falls in the previous two years. If the participant had fallen, they were asked to report how many times and if they required hospitalization due to the fall.

### 4.2.3 Statistical analysis

Data was cleaned and coded in Microsoft Excel before being transferred to SPSS (Version 24) for analysis. Descriptive information was presented using mean and standard deviation and range while categorical variables were presented using frequencies and percent. Chi-Square tests for categorical variables and independent t-tests for continuous variables were performed to compare independent risk factors between fallers and non-fallers. Fischer's exact test was used when expected frequencies had a sub-sample of less than 5 participants. Pearson's correlation was used to determine associations between continuous variables. Variables were selected for regression models based on univariate statistical significance. A logistic regression analysis was performed with each individual medication class adjusting for possible confounders (e.g. sex). Statistical significance was set as  $p < 0.05$ .

### 4.3 Results

#### *Characteristics of the study participants*

**Table 4.1** represents the demographic and health related factors between fallers and non-fallers. The mean age of the sample was  $73.1 \pm 6.2$  (range of 65 to 96 years); over half (58.2%) of the sample were females. More than 60% of the sample currently live with a spouse or partner (62.9%) and have been retired for  $\geq 10$  years (60.1%). Almost 30% reported using at least one prescription medication (29.3%) while 23.4% reported taking 5 or more medications. Alcohol use was reported by 70% of the sample drinking on average  $4.1 \pm 4.9$  drinks per week.

**Table 4.1. Demographic characteristics of fallers and non-fallers**

<b>Variables</b>	<b>Total N=2281</b>	<b>Fallers n=762 (33.4%)</b>	<b>Non-Fallers n=1519 (66.6%)</b>	<b>Significance (<math>p &lt; .05</math>)</b>
<b>Age (years)</b>	73.1 $\pm$ 6.2 (65-96)	73.3 $\pm$ 6.1 (65-94)	72.6 $\pm$ 5.8 (65-96)	$t = -2.44, p < .05$
<b>Sex</b>				
Males	954 (41.8)	259 (33.9)	695 (45.8)	$\chi^2 = 29.25, p < .001$

Females	1327 (58.2)	504 (66.1)	823 (54.2)	
<b>Living situation</b>				
Alone	727 (32)	276 (36.3)	451 (29.8)	$\chi^2=15.30, p<.001$
With a spouse or partner	1430 (62.9)	450 (59.1)	981 (64.7)	
With family members	99 (4.4)	25 (3.3)	74 (4.9)	
With roommates (not related)	19 (0.8)	10 (1.3)	9 (0.6)	
<b>Employment Status</b>				
Full-time	82 (3.6)	23 (3)	59 (3.9)	$\chi^2=2.43, p=.29$
Part-time	266 (11.8)	98 (12.9)	168 (11.2)	
Neither	1915 (84.6)	639 (84.1)	1276 (84.9)	
<b>Work is physically tiring</b>				
Yes	184 (16.7)	83 (24.9)	101 (13.2)	$\chi^2=22.72, p<.001$
No	916 (83.3)	251 (75.1)	665 (86.8)	
<b>Work is mentally tiring</b>				
Yes	206 (19.2)	80 (24.5)	126 (16.8)	$\chi^2=8.53, p<.05$
No	869 (80.8)	247 (75.5)	622 (83.2)	
<b>Illness or disability before retirement</b>				
Yes	495 (22.5)	210 (28.3)	285 (19.5)	$\chi^2=21.45, p<.001$
No	1706 (77.5)	533 (71.1)	1173 (80.5)	
<b>Years retired</b>	13.5±8.7	14.2±8.9	12.7±8.5	
1-3	160 (10.6)	43 (8.3)	117 (11.9)	$t=-3.29, p<.01$
4-6	242 (16.1)	75 (14.5)	167 (17)	
7-9	197 (13.1)	67 (12.9)	130 (13.2)	$\chi^2=7.84, p<.05$
≥10	904 (60.1)	334 (64.4)	570 (57.9)	
<b>Self-rated physical health</b>				
Range (1-10)	8.2±1.7	7.8±1.8	8.4±1.5	$t=7.27, p<.001$
<b>Self-rated mental health</b>				
Range (1-10)	8.9±1.5	8.7±1.5	8.9±1.4	$t=3.72, p<.001$
<b>Last eye exam</b>				
Less than 2 years ago	2119 (93.5)	712 (93.9)	1407 (93.3)	$\chi^2=.32, p=.56$
More than 2 years ago	147 (6.5)	46 (6.1)	101 (6.7)	
<b>Smoking</b>				
Current	73 (3.2)	26 (3.4)	47 (3.1)	$\chi^2=.17, p=.69$
None	2189 (96.8)	731 (96.6)	1458 (96.9)	
<b>Alcohol use</b>				
Yes	1586 (70.3)	513 (68.1)	1073 (71.4)	$\chi^2=2.55, p=.11$
No	670 (29.7)	240 (31.9)	430 (28.6)	

<b>Alcoholic drinks per week</b>	4.1±4.9	4.0±5.0	4.2±4.9	
None (0)	670 (29.7)	240 (31.9)	430 (28.6)	$t=.78, p=.43$
Low (1-2)	489 (21.7)	160 (21.5)	327 (21.7)	
Moderate (3-9)	765 (33.9)	241 (32)	524 (34.8)	$\chi^2=3.03, p=.38$
High (>10)	333 (14.8)	110 (14.6)	223(14.8)	
<b>Arthritis, rheumatism, osteoporosis</b>				$\chi^2=6.92, p<.01$
Yes	1057 (51.1)	392 (55.1)	665 (49)	
No	1010 (48.9)	319 (44.9)	691 (51)	
<b>Stroke</b>				$\chi^2=19.85, p<.001$
Yes	38 (1.8)	26 (3.7)	12 (0.9)	
No	2029 (98.2)	685 (96.3)	1344 (99.1)	
<b>Dementia</b>				$\chi^2=5.57, p<.05$
Yes	12 (0.6)	8 (1.1)	4 (0.3)	
No	2055 (99.4)	703 (98.9)	1352 (99.7)	
<b>High blood pressure, cholesterol, heart problems</b>				$\chi^2=.61, p=.43$
Yes	1115 (53.9)	392 (55.1)	723 (53.3)	
No	952 (46.1)	319 (44.9)	633 (46.7)	
<b>Asthma or other breathing problems</b>				$\chi^2=5.93, p<.05$
Yes	263 (12.7)	108 (15.2)	155 (11.4)	
No	1804 (87.3)	603 (84.8)	1201 (88.6)	
<b>Back problems</b>				$\chi^2=18.18, p<.001$
Yes	480 (23.2)	204 (28.7)	276 (20.4)	
No	1587 (76.8)	507 (71.3)	1080 (79.6)	
<b>Foot problems</b>				$\chi^2=33.05, p<.001$
Yes	232 (11.2)	119 (16.7)	113 (8.3)	
No	1835 (88.8)	592 (83.3)	1243 (91.7)	
<b>Hearing problems</b>				$\chi^2=6.78, p<.01$
Yes	450 (21.8)	178 (25)	272 (20.1)	
No	1617 (78.2)	533 (75)	1084 (79.9)	
<b>Cataracts, glaucoma, macular degeneration</b>				$\chi^2=10.07, p<.001$
Yes	382 (18.5)	158 (22.2)	224 (16.5)	
No	1685 (81.5)	553 (77.8)	1133 (83.5)	
<b>Sleeping disorder</b>				$\chi^2=9.97, p<.001$
Yes	334 (16.2)	140 (19.7)	194 (14.3)	
No	1733 (83.8)	571 (80.3)	1162 (85.7)	

<b>Leg cramps, muscle spasms</b>				
Yes	15 (0.7)	9 (1.3)	6 (0.4)	$\chi^2=4.38, p<.05$
No	2052 (99.3)	700 (98.7)	1350 (99.6)	
<b>Joint issues</b>				
Yes	41 (2)	23 (3.2)	18 (1.3)	$\chi^2=8.72, p<.01$
No	2026 (98)	688 (96.8)	1338 (98.7)	
<b>Depression</b>				
Yes	51 (2.5)	24 (3.4)	27 (2)	$\chi^2=3.71, p=.054$
No	2016 (97.5)	687 (96.6)	1329 (98)	
<b>Number of comorbidities</b>	2.5±1.6	2.9±1.8	2.3±1.4	
1	575 (28.3)	146 (20.8)	429 (32.2)	$t=-8.59, p<.001$
2	591 (29.1)	189 (27)	402 (30.2)	
3	410 (20.2)	146 (20.8)	264 (19.8)	$\chi^2=72.13, p<.001$
4	224 (11)	90 (12.8)	134 (10.1)	
≥5	234 (11.5)	130 (18.5)	104 (7.8)	
<b>Usual sleep quantity in 24 hours</b>	5.9±2.0	5.9±2.1	5.9±1.9	$t=0.11, p=0.91$
<b>ESS Scores</b>				
Normal (0-10)	4.6±3.0	4.8±3.2	4.5±2.9	$t=-2.33, p<.05$
Borderline (11-15)	2051 (92.2)	670 (90.7)	1381 (92.9)	
Abnormal (16-24)	125 (5.6)	49 (6.6)	76 (5.1)	$\chi^2=3.57, p=0.16$
	49 (2.2)	20 (2.7)	29 (2)	
<b>IPAQ Score</b>				
Low	75 (27.5)	36 (30.3)	39 (25.3)	$\chi^2=2.75, p=0.25$
Moderate	115 (42.1)	53 (44.5)	62 (40.3)	
High	83 (30.4)	30 (25.2)	53 (34.3)	
<b>DEX-S Score</b>	14.0±7.6	15.2±8.0	13.4±7.4	$t=-4.94, p<.001$

Continuous variables are shown as Mean±SD and range; categorical variables as frequencies (%). Categorical variables between groups were examined using Chi-Square or Fisher's exact test. The numbers reported in each cell represent the exact numbers of fallers and non-fallers for each of the exposures. Due to missing values, the denominator was not always 762 for fallers and 1,519 for non-fallers.

IPAQ: International Physical Activity Questionnaire

#### *Fallers vs. Non-Fallers*

Approximately 33.4% of the sample reported falling in the past 2 years; 9% were hospitalized; and 11.2% experienced recurrent falls (≥2). The average age of those that fell were 73.2±6.1 (range of 65 to 94 years). Compared to non-fallers, fallers were significantly more

likely to be older, a woman, to live with a partner or spouse, to have an illness or disability before retirement, to be physically and mentally tired, and poorer self-perceived physical and mental health scores. Fallers were also significantly more likely to have arthritis, rheumatism or osteoporosis, and have a diagnosis of two chronic health conditions. Fallers were also significantly more likely to use multiple medications compared to non-fallers ( $3.5 \pm 2.8$  versus  $2.9 \pm 2.2$ ). More females reported hospitalizations than males after a fall (55.9% vs. 44.1%), however, sex differences were not significant ( $p=0.44$ ). Those who were hospitalized were slightly older than those who were not hospitalized (Mean  $74 \pm 7.0$  vs. Mean  $72.9 \pm 5.9$ ); age difference was not significant. Higher self-rated physical and mental health were protective of falls.

#### *Medication use*

**Table 4.2** shows the associations of psychotropic, anti-depressant and anti-hypertensive medication use and respective sub-classes between fallers and non-fallers. Almost 30% reported using at least one prescription medication while 23.4% reported taking 5 or more medications. There were no significant sex differences in the number of medications being used. Psychotropic medications were used by 6.2% of the sample, anti-depressant medications were used by 13.5%; and 52% reported using an anti-hypertensive medication.

**Table 4.2. Associations of select medication use between fallers and non-fallers**

<b>Medication use</b>	<b>Total N=2281</b>	<b>Fallers n=762 (33.4%)</b>	<b>Non-Fallers n=1519 (66.6%)</b>	<b>Significance (<math>p &lt; .05</math>)</b>
<b>Psychotropics</b>				
All psychotropics				
Yes	92 (6.2)	42 (7.8)	50 (5.3)	$\chi^2 = 3.79, p=0.053$
No	1392 (93.8)	496 (92.2)	896 (94.7)	
Anti-psychotics				
Yes	11 (0.7)	4 (0.7)	7 (0.7)	$\chi^2 = 0.00, p=.99$
No	1473 (99.3)	534 (99.3)	939 (99.3)	
Anxiolytics				$\chi^2 = 0.39, p=.53$

Yes	39 (2.6)	16 (3)	23 (2.4)	
No	1445 (97.4)	522 (97)	923 (97.6)	
Hypnotics/Sedatives				
Yes	47 (3.2)	23 (4.3)	24 (2.5)	$\chi^2=3.37, p=.06$
No	1437 (96.8)	515 (95.7)	922 (97.5)	
<b>Anti-Depressants</b>				
All anti-depressants				
Yes	201 (13.5)	103 (19.1)	98 (10.4)	$\chi^2= 22.60, p<.001$
No	1283 (86.5)	435 (80.9)	848 (89.6)	
SSRI				
Yes	83 (5.6)	44 (8.2)	39 (4.1)	$\chi^2=10.68, p<.01$
No	1401 (94.4)	494 (91.8)	907 (95.9)	
SARI				
Yes	24 (1.6)	17 (3.2)	7 (0.7)	$\chi^2=12.62, p<.001$
No	1460 (98.4)	521 (96.8)	939 (99.3)	
SNRI				
Yes	55 (3.7)	28 (5.2)	27 (2.9)	$\chi^2=5.30, p<.05$
No	1429 (96.3)	510 (94.8)	919 (97.1)	
TCA				
Yes	41 (2.8)	19 (3.5)	22 (2.3)	$\chi^2=1.87, p=.17$
No	1443 (97.2)	519 (96.5)	924 (97.7)	
Other				
Yes	21 (1.4)	10 (1.9)	11 (1.2)	$\chi^2=1.19, p=.27$
No	1463 (98.6)	528 (98.1)	935 (98.8)	
<b>Anti-Hypertensives</b>				
All anti-hypertensives				
Yes	771 (52)	283 (52.6)	488 (51.6)	$\chi^2=.14, p=.70$
No	713 (48)	255 (47.4)	458 (48.4)	
Diuretics				
Yes	206 (13.9)	75 (13.9)	131 (13.8)	$\chi^2=.002, p=.96$
No	1278 (86.1)	463 (86.1)	815 (86.2)	
Beta-blockers				
Yes	193 (13)	71 (13.2)	122 (12.9)	$\chi^2=.027, p=.86$
No	1290 (87)	467 (86.8)	824 (87.1)	
ACEi				
Yes	293 (19.7)	109 (20.3)	184 (19.5)	$\chi^2=.14, p=.70$
No	1191 (80.3)	429 (79.7)	762 (80.5)	
ARBs				
Yes	265 (17.9)	95 (17.7)	170 (18)	$\chi^2=0.02, p=.88$
No	1219 (82.1)	443 (82.3)	776 (82)	
CCBs				
Yes	217 (14.6)	87 (16.2)	130 (13.7)	$\chi^2=1.62, p=.20$
No	1267 (85.4)	451 (83.8)	816 (86.3)	

<b>Total medication use</b>	3.1±2.4	3.5±2.8	2.9±2.2	
1	433 (29.3)	138 (25.7)	295 (31.3)	$t=-4.29, p<.001$
2	302 (20.4)	99 (18.5)	203 (21.5)	$\chi^2=12.51, p<.05$
3	241 (16.3)	91 (17)	150 (15.9)	
4	156 (10.6)	59 (11)	97 (10.3)	
≥5	346 (23.4)	149 (27.8)	197 (20.9)	

Continuous variables are shown as Mean±SD and range; categorical variables as frequencies (%). Categorical variables between groups were examined using Chi-Square or Fisher's exact test. The numbers reported in each cell represent the exact numbers of fallers and non-fallers for each of the exposures. Due to missing values, the denominator was not always 762 for fallers and 1,519 for non-fallers.

**Table 4.3** displays correlations among continuous variables. Age was not associated with number of falls but was with number of comorbidities and anti-hypertensive medication use, and negatively associated with self-perceived physical health and anti-depressant use. The number of falls were significantly and positively associated with comorbidity score, psychotropic and anti-depressant medication use, while being significantly and negatively associated with self-rated physical and mental health score. Alcohol use was associated with anti-depressant use, specifically TCA medications, living with a spouse or partner and self-perceived physical health. Alcohol use was not associated with psychotropic and anti-hypertensive medication use and number of falls.

**Table 4.3. Correlations of continuous variables and falls**

	Age	# Alcoholic drinks per week	# of Falls	Self-Rated Physical Health	Self-Rated Mental Health	Comorbidity Score	Psychotropic medication use	Ant-depressant medication use	Anti-hypertensive medication use	# of prescription medications
Age		-0.03	0.02	<b>-0.06**</b>	0.02	<b>0.07**</b>	-0.4	<b>-0.12**</b>	<b>0.10**</b>	0.04
# of alcoholic drinks per week	-0.03		-0.009	<b>0.06**</b>	<b>0.04*</b>	-0.02	0.03	-0.02	0.01	-0.02
# of falls	0.02	-0.009		<b>-0.19**</b>	<b>-0.09**</b>	<b>0.22**</b>	<b>0.06*</b>	<b>0.15**</b>	0.02	<b>0.15**</b>
Self-perceived physical health	<b>-0.06**</b>	<b>0.06**</b>	<b>-0.19**</b>		<b>0.50**</b>	<b>-0.38**</b>	<b>-0.8**</b>	<b>0.14**</b>	<b>-0.10**</b>	<b>-0.27**</b>
Self-perceived mental health	0.02	<b>0.04*</b>	<b>-0.09**</b>	<b>0.50**</b>		<b>-0.18**</b>	<b>-0.10**</b>	<b>-0.18**</b>	0.01	<b>-0.11**</b>
Comorbidity score	<b>0.07**</b>	-0.02	<b>0.23**</b>	<b>-0.38**</b>	<b>-0.18**</b>		<b>0.15**</b>	<b>0.20**</b>	<b>0.21**</b>	<b>0.44**</b>
Psychotropic medication use	-0.04	0.03	<b>0.06*</b>	<b>-0.08**</b>	<b>-0.10**</b>	<b>0.15**</b>		<b>0.13**</b>	<b>-0.06*</b>	<b>0.18**</b>
Anti-depressant medication use	<b>-0.12**</b>	-0.02	<b>0.15**</b>	<b>-0.14**</b>	<b>-0.18**</b>	<b>0.20**</b>	<b>0.13**</b>		0.004	<b>0.28**</b>
Anti-hypertensive medication use	<b>0.10**</b>	0.01	0.02	<b>-0.10**</b>	<b>-0.10**</b>	<b>0.21**</b>	<b>-0.06*</b>	0.004		<b>0.53**</b>
Total # of prescription medications	0.04	-0.05*	<b>0.15**</b>	<b>-0.27**</b>	<b>-0.11**</b>	<b>0.44**</b>	<b>0.18**</b>	<b>0.28**</b>	<b>0.53**</b>	

Values are Pearson r; \*p<.05 \*\*p<.01

Logistic regression models were performed with each medication class and sub-classes with falls (**Table 4.4**). Overall anti-depressants and specific individual classes (SSRIs, SARIs and SNRIs) were predictive of falls. When sex was entered into the model, all significant variables for Model 1 remained significant.

**Table 4.4 Logistic regression model showing individual medications as predictors of falls in older adults**

	<b>Model 1</b>	<b>Model 2</b>
Use of any psychotropic	1.51 (0.99-2.32)	1.43 (0.93-2.19)
Anxiolytics	1.23 (0.64-2.34)	1.21 (0.63-2.32)
Anti-psychotics	1.00 (0.29-3.44)	0.98 (0.28-3.42)
Hypnotics/Sedatives	1.71 (0.95-3.07)	1.54 (0.86-2.78)
Use of any anti-depressants	<b>2.04 (1.51-2.76)</b>	<b>1.88 (1.38-2.55)</b>
Use of SSRI	<b>2.07 (1.32-3.23)</b>	<b>1.89 (1.20-2.96)</b>
Use of SARI	<b>4.27 (1.80-10.62)</b>	<b>4.23 (1.73-10.32)</b>
Use of SNRI	<b>1.86 (1.08-3.20)</b>	<b>1.74 (1.01-2.99)</b>
Use of any anti-hypertensive	1.04 (0.84-1.28)	1.09 (0.88-1.35)
Use of diuretics	1.00 (0.74-1.36)	0.99 (0.73-1.35)
Use of beta-blockers	1.02 (0.75-1.40)	1.06 (0.77-1.46)
Use of ACEi	1.05 (0.80-1.37)	1.13 (0.86-1.48)
Use of ARBs	0.97 (0.74-1.29)	0.98 (0.74-1.30)
Use of calcium channel blockers	1.21 (0.90-1.62)	1.27 (0.94-1.72)

Model 1: Medications individually predictive of fall risk

Model 2: Adjusted for sex (female)

SSRIs: Selective serotonin reuptake inhibitors

SARIs: Selective antagonist and reuptake inhibitors

SNRIs: Serotonin-norepinephrine reuptake inhibitor

Figures in bold denote statistical significance (p<0.05)

#### 4.4 Discussion

Thirty-three percent of the sample reported falls in the previous two years. Females reported falls more frequently than males (54.2% vs. 45.8%). Female sex and advanced age was associated with falls, consistent with other studies (Gale et al. 2016; Kerse et al. 2008; Stevens & Sogolow, 2005). Unsurprisingly, a diagnosis of arthritis, rheumatism or osteoporosis, and vision

problem (e.g. cataracts, glaucoma and macular degeneration) was associated with falls.

Furthermore, a diagnosis of two or more chronic health conditions (Gale et al. 2016), and use of multiple medications was also associated with falls, consistent with other studies (Hanlon et al. 2009; Lord et al. 1993; Lord et al. 1995). Compared to males, females were significantly more likely to fall and have asthma or other breathing problems, and sleep disorders.

Psychotropic medication use was not predictive of falls, which is surprising given that previous studies have found significant associations between psychotropic medications and falls in community dwelling older adults (de Rekeneire et al. 2003; Du et al. 2017; Lord et al. 1993; Lord et al. 1995; Wong et al. 2013). Over 6% of participants in this cohort used at least one psychotropic medication (e.g. anti-psychotic, anxiolytics, hypnotics/sedatives), and in fallers, 7.8% used psychotropic medications. Hypnotics/sedatives were used by 4.3% of fallers, which is identical to prevalence rates in a cross-sectional survey of community dwelling older adults by Du and colleagues (2017). Sub-classes of psychotropic medications such as hypnotics, anxiolytics and anti-psychotics were not associated with falls in this study. In contrast, studies have found the aforementioned sub-classes are associated with falls in community dwelling older adults (Blake et al. 1988; Cumming et al. 1991; Ensrud et al. 2002; Hanlon et al. 2002; Iinattiniemi et al. 2009; Landi et al. 2005; Malmivaara et al. 1993; Masud et al. 2013; Neutel et al. 1996; Stenbacka et al. 2002; Tinetti et al. 1988; Tromp et al. 1998; Tromp et al. 2001). Dissimilarities in findings could be attributed to differences in sampling techniques, data collection (e.g. online vs. mail), medication terminology, sample size and characteristics of users vs. non-users.

Use of anti-depressants, SSRI, SNRI and SARI medications were predictive of falls after controlling for sex. Anti-depressant medications were used by 13.5% of participants, and 10.4%

of fallers. All anti-depressants are known to disrupt sleep, cause insomnia, nocturia, and daytime sleepiness, potentially resulting in an elevated fall risk (Darowski et al. 2009). As a group, anti-depressants were predictive of falls which has been found in other studies of community dwelling older adults (Blake et al. 1988; Du et al. 2017; Ensrud et al. 2002; Gribbin et al. 2011; Kelly et al. 2003; Kerse et al. 2008; Lord et al. 1995; Masud et al. 2013; Spoelstra et al. 2013; Svensson et al. 1992). When examining specific anti-depressants, SSRIs, SNRIs and SARIs were predictive of falls. SSRI medications were the most commonly prescribed sub-class of anti-depressants in the sample (5.6%) and used more often in fallers (8.2%) compared to other sub-classes. These rates are similar to prior studies of community dwelling older adults that show between 4.3% and 10.3% of SSRI users experienced a fall in the previous year (Du et al. 2017; Gribbin et al. 2011; Kerse et al. 2008). SNRI medications are newer anti-depressants, however, research on their association with fall risk is scarce. In the literature review (Chapter 2) only one study examined SNRI use and fall risk and found SNRI use predicted fall risk (Gribbin et al. 2011). Seventy percent of SARI users in this cohort reported falls. This is consistent with studies in LTC that show depressed users of SARI medications were 20% more likely to fall compared to non-users (Thapa et al. 1998). However, only a few studies suggest SARI medications elevate fall risk in older adults living in both community dwelling and LTC older adults. Regardless of our findings, a review on anti-depressant medications found no individual anti-depressant medications is associated of falls in community and LTC older adults (Darowski et al. 2009).

More than 50% of the sample used anti-hypertensive medications, however, use of anti-hypertensive medications as a group and sub-classes were not associated with falls in this cohort. The literature review (Chapter 2) found twelve studies that examined anti-hypertensive

medication use and fall risk in community dwelling older adults, four of which found an association with falls (Bergland et al. 2001; Cumming et al. 1991; Tinetti et al. 2014; Tromp et al. 1998). Angiotensin system-blocking medications which include diuretics, ACEis, ARBs and calcium channel blockers were associated with fewer falls in a sample of community dwelling older adults, however, the protective mechanisms are unclear.

Although more than 70% of the sample reported drinking, there was no significant association with falls, consistent with previous studies (Du et al. 2017; Hanlon et al. 2009; Lord et al. 1993; Stuart et al. 2015; Tromp et al. 1998; Tromp et al. 2001; Williams et al. 2015). Females who consumed alcohol were more likely to report a fall compared to males (36% vs 27.6%) but these differences were not significant. While it is impossible to know whether the fall was related to alcohol use, studies have shown alcohol use or abuse is a predictor of falls (Anstey et al. 2008; Kerse et al. 2008; Kurzthaler et al. 2005; Chang et al. 2015; Malmivaara et al. 1993; Stenbacka et al. 2002). However, due to the cross-sectional nature of this study we cannot determine causality inference between alcohol use and falls.

#### **4.5 Limitations**

There are several study limitations. The present study relied on survey data which is subject to recall and social desirability bias. However, our sample rated their physical and mental health as being above average, and few had cognitive limitations based on the DEX-S, suggesting that the sample was relatively healthy with little memory impairments. This is not surprising given our sample consisted of community dwelling older adults who were part of community-based senior organizations. Participants who are part of these organizations are generally more active, engaged, educated and more likely to be familiar with online surveys (computer technology). Moreover, we asked participations whether they had fallen in the past

two years. Unfortunately, we cannot determine directionality, whether medications resulted in falls or whether falls resulted in the use of medications. Furthermore, it is impossible to know if the participants were drinking and taking anti-depressants on the same day as the fall. However, we are following our participants longitudinally and will be able to determine causality in the future.

#### **4.6 Conclusion**

The use of anti-depressant medications as a group, as well as individual anti-depressant medications (i.e. SSRI, SARI and SNRI) were predictive of falls in community dwelling older adults. Falls are common in older adults, as are use of prescription medications. Consequences of falls are significantly more severe in older adults and healthcare providers should exercise caution when prescribing anti-depressant medications to older patients.

## **Chapter 5: General Discussion and Summary**

### **5.1 Introduction**

Falls are common in community dwelling older adults. The objectives of this thesis were to: i) synthesize peer-reviewed studies that have examined anti-psychotic, hypnotic/sedatives and benzodiazepines, anti-depressant and anti-hypertensive medications, both singly and in combination with alcohol as a risk for falls in community dwelling older adults; ii) examine alcohol use in community dwelling older adults in Canada using current drinking guidelines, develop and test new alcohol consumption guidelines to better differentiate drinking habits on health outcomes, determine risk factors of high-risk drinking, and compare current drinking guidelines to moderate drinking; and iii) examine the effects of select medications, both individually and in combination with alcohol, on fall risk in Canadian community dwelling older adults.

This chapter begins by discussing the findings of the literature review on select medications and alcohol on fall risk. Chapter 3 and 4 are original research articles and the first studies to use data from the Canadian Injury Prevention Survey. Conclusions and limitations are discussed, followed by a final section presenting implications for future research and practice.

### **5.2 General Discussion**

Chapter 2 provides a foundation for the thesis by reviewing primary studies on anti-psychotic, hypnotics/sedatives and benzodiazepines, anti-depressant and anti-hypertensive medications, as well as alcohol as a risk for falls in community dwelling older adults. A literature search using four electronic health databases, and a grey literature search yielded 1,146 articles for screening. Twenty-nine articles met the inclusion criteria. Overall females were more likely to be users of anti-psychotic, hypnotics/sedative, benzodiazepines and anti-depressant

medications compared to males. Females were also more likely to fall, which has been found in other studies (Chang et al. 2015).

Up to 58.7% of anti-psychotic, hypnotics/sedative and benzodiazepines users reported a fall. Users of anti-depressant medications, specifically SSRI medications had the highest risk of falls compared to other sub-classes of anti-depressants (Du et al. 2017; Ensrud et al. 2002; Kerse et al. 2008; Masud et al. 2013). Overall, anti-hypertensive medication use was not associated with increased fall risk in community dwelling older adults. Compared to younger and middle-aged adults, older adults consumed alcohol less frequently; however, they were also more likely to have an injurious fall after consuming alcohol (Kurzthaler et al. 2005; Malmivaara et al. 1993; Stenbacka et al. 2002). Alcohol and select medication use was not associated with falls in community dwelling older adults.

Chapter 3 explored alcohol use in community dwelling older adults in Canada. We sought to determine risk factors associated with high-risk drinking based on the current alcohol consumption guidelines; and determine whether the current guidelines are applicable to older adults. Seventy percent of Canadian older adults reported drinking. Findings suggest the current alcohol drinking guidelines for adults aged 18-64 may be adequate for community dwelling older adults.

Chapter 4 examined the role of alcohol and its interaction with various medications (i.e., psychotropic, anti-depressants, and anti-hypertensives) on fall risk in Canadian older adults. Females reported falls more frequently compared to males. Diagnosis of arthritis, osteoporosis, or rheumatism, cataracts, glaucoma or macular degeneration, asthma or other breathing problems and foot problems were directly significantly associated with falls. Strong self-rated physical and mental health were protective of falls. Alcohol use was not associated with falls. Logistic

regressions indicated that the use of anti-depressants as a group, SSRI, SNRI and SARI anti-depressants were predictive of falls.

Overall, participants were healthy. This is the first set of results from the Canadian Injury Prevention Survey, and to our knowledge, the first study to examine alcohol and select medication use as a risk for falls in older adults in Canada. Polypharmacy is a growing public health concern. Within our sample, 23.4% reported taking 5 or more medications on a daily basis. Alcohol drinking is common in older adults and evidence suggests that high-risk episodic drinking is not uncommon among older males (St John et al. 2010). Furthermore, there is concern that as the baby boomers begin to age, the prevalence of high-risk drinking will increase (Han et al. 2017; Wong et al. 2016; Babatunde et al. 2014; Blow & Barry, 2012). While fall risk is multifactorial, alcohol and medication use are recognized as fall risk factors by the WHO (WHO, 2007). Falls are preventable and healthcare professionals should educate older patients and caregivers of the negative consequences.

## **5.3 Implications**

### **5.3.1 Research**

To date, few studies have examined concomitant alcohol and psychotropic and anti-depressant medication in community dwelling older adults (Bye et al. 2017; Ilomaki et al. 2012; Ilomaki et al. 2013). No studies have examined concomitant alcohol and select medication use as a risk for falls in community dwelling older adults. Future studies are needed in this area to confirm if concomitant alcohol and medication use is a risk factor for falls in older adults. Findings of this thesis indicate research on the use of anti-hypertensive medications as a risk for falls is scarce. Future research is required to explore the associations between anti-hypertensive

medication use, both overall as a class and individual medications and falls in community dwelling older adults.

### **5.3.2 Practice**

Clinicians should be transparent with their patients and identify the risks of using psychotropic, anti-depressant and anti-hypertensive medications. Each medication class is known to be accompanied by side effects such as poor balance, sedation and sleep disturbance (de Groot et al. 2013; Madhusoodanan and Bugunovic, 2004; Milos et al. 2014). Physicians should discuss alcohol use and the potential adverse reactions with medications, including falls and injurious falls (Immonen et al. 2013; Stenbacka et al. 2002) with older patients. Furthermore, alcohol should be consumed in moderation to prevent worsening of chronic illnesses.

## **5.4 Limitations**

This thesis is not without limitations including. The limitations and future directions are discussed below.

### **5.4.1 Study Design**

The primary limitation of this thesis is the cross-sectional study design. Cross-sectional studies are inadequate at measuring causation and determining risk. The survey consists of 89 questions in length, taking approximately 45 minutes to complete and many responses were incomplete at the end. The Canadian Association for Retired Persons (CARP) e-mail blasted over 300,000 members at once and as a result we encountered many technical difficulties including server failure. Although these issues were resolved with the assistance of SurveyMonkey technicians, we received many complaints from respondents. We also learned that SurveyMonkey is not very compatible with iPads or smart phones, decreasing our response rate. The survey was available in print and online in English and French, however, no persons

used a print version, and the French response rate was very low ( $n < 40$ ). All data was collected online, potentially eliminating older adults ( $\geq 85$ ) who do not have e-mail, or a computer. Lastly, this was the first wave of participants to complete this survey and we found a few questions were subject to misinterpretation even after pilot work.

#### **5.4.2 Sample**

Our sample consisted of community dwelling older adults living in Canada and the primary source of recruitment was from CARP, Probus Clubs, and the Canadian Association of Retired Teachers. Members of these organizations are typically more engaged and active in the community. Furthermore, to be a member there is usually an annual fee, therefore, our sample likely consists of persons in high income brackets whom have achieved high levels of education. However, we cannot be sure of the socioeconomic status or education level of our participants because in consultation with researchers from Bordeaux, questions about income and education were eliminated as they did not serve importance in previous Gazel cohort studies.

#### **5.5 Conclusions**

In summary, the literature review findings confirmed that psychotropic and anti-depressant use are predictive of falls in community dwelling older adults. However, based on the survey with community dwelling older adults, only anti-depressant drug use was found to be significantly associated with fall risk. Anti-hypertensive medications were not associated with falls, nor was alcohol. Physicians should exercise a high degree of caution when prescribing psychotropic and anti-depressant medications to older adults whom may be at a high fall risk.

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## **Appendices**

There is a separate document titled Laberge\_Sarah\_Appendies.pdf for the Appendices' section.