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ALCOHOL AND MEDICATION USE IN COMMUNITY-DWELLING OLDER ADULTS: UNDERSTANDING THE EFFECT OF ALCOHOL AND CENTRAL NERVOUS SYSTEM-ACTING MEDICATIONS ON THE RISK FOR FALLS

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A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

by

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Abbreviations

ACh	Acetylcholine
AChR	Acetylcholine-Receptor
AI	Alcohol-Interactive
ADI	Alcohol-Drug Interaction
ADR	Adverse Drug Reaction
ADH	Alcohol Dehydrogenase
ALDH	Aldehyde Dehydrogenase
ARPS	Alcohol Related Problem Survey
AUDIT	Alcohol Use Disorders Identification Test
ADL	Activities of Daily Living
BAL	Blood Alcohol Level
BAC	Blood Alcohol Concentration
CAPI	Computer Assisted Personal Interview
CARET	Comorbidity and Alcohol Risk Assessment Tool
CDC	Center for Disease Prevention and Control
CHAMP	Concord Health and Ageing in Men Project
CHS	Cardiovascular Health Study
CI	Confidence Interval
CNS	Central Nervous System
CYP	Cytochrome P450 enzyme
DAWN	Drug Abuse Warning Network
ED	Emergency Department
IADL	Instrumental Activities of Daily Living
GABA	Gamma-Aminobutyric Acid
g/dl	Grams per deciliter
5-HT3	5-Hydroxy-Tryptamine 3
HAART	Highly Active Anti-Retroviral Therapy
MeSH	Medical Subject Headings
MEPS	Medical Expenditure Panel Survey

MEC	Medical Examination Center
MCBS	Medicare Current
NHANES	National Health And Nutrition Examination Survey
NSDUH	National Survey on Drug Use and Health
NMDA	N-methyl-D-aspartate
NIAAA	National Institute of Alcohol Abuse and Alcoholism
NCPIE	National Council Patient Information and Education
OTC	Over-the-Counter
WHO	World Health Organization
PHQ-9	Patient Health Questionnaire
PA-PACE	Pennsylvania-Program of All-inclusive Care for the Elderly
SHARE	Senior Health and Alcohol Risk Education
SMAST-G	Short Michigan Alcoholism Screening Instrument – Geriatric
SSRI	Selective Serotonin Re-uptake Inhibitors
SP	Sample Persons
TD	Tardive Dyskinesia
U.S.	United States of America

Abstract

ALCOHOL AND MEDICATION USE IN COMMUNITY-DWELLING OLDER ADULTS: UNDERSTANDING THE EFFECT OF ALCOHOL AND CENTRAL NERVOUS SYSTEM-ACTING MEDICATIONS ON THE RISK FOR FALLS

By Maitreyee Mohanty, Ph.D.

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

Advisor: Dr. Patricia Slattum, Professor and Director of Geriatric Pharmacotherapy Program

Department of Pharmacotherapy and Outcomes Science

Virginia Commonwealth University, 2013.

Introduction: Aging, comorbid conditions, and use of medications render older adults more susceptible to alcohol-disease or alcohol-drug interactions that may lead to harmful outcomes. In this dissertation project the risk profile of alcohol and medications use among older adults was investigated. Considering the rise in CNS-acting medication use and the adverse effect profile linked to CNS-acting medications, it was also of interest to find if older adults were at risk of falling due to interactions between alcohol and CNS-acting medication.

Objectives: The objectives were as follows: 1) to determine the prevalence, pattern and factors associated with at-risk drinking, 2) to determine the prevalence and pattern of potential concurrent use of CNS-acting medication and alcohol, and to identify factors associated with alcohol use among CNS-acting medication users, 3) to assess the effects of potential concurrent use of CNS-acting medications and alcohol on the risk for falls in older adults.

Methods: The study population comprised a nationally representative sample of community-dwelling older adults aged 65 years or older. The 2009 Medicare Current Beneficiary Survey (MCBS) data (n=7163) were employed to determine at-risk drinking based on the Comorbidity

Alcohol Risk Evaluation Tool (CARET) and to assess the effects of potential concurrent use of CNS-acting medication and alcohol on the risk for falls. The National Health and Nutrition Examination Survey (NHANES) 2005-2010 data (n=3220) were employed to determine potential concurrent use of alcohol and CNS-acting medications. The effect of combined use of alcohol and CNS-acting medications on risk of falls was assessed using logistic regression modeling and adjusting for confounders. Alcohol consumption was measured by the quantity-frequency method.

Results: In the MCBS study**,** 5.6% of the older adults were identified as at-risk drinkers. Adults aged between 65-74 years, being male, non-married, former or current smoker, and having no comorbid conditions were factors associated with at-risk drinking. In the NHANES study, 8.9% reported potential concurrent use of alcohol and CNS-acting medication. Use of at least one CNS-acting medication and drinking excessive alcohol, or binge drinking, was significantly associated with odds of falling.

Conclusion: Hazardous alcohol use is common among older adults. A substantial proportion of older adults may concomitantly consume alcohol and CNS-acting medications. Odds of falling are greater in the presence of high alcohol intake and CNS-acting medication use. It is important for health care professionals to warn patients against excessive alcohol consumption. Increasing awareness of this issue among older adults and caregivers may help prevent falls. Contributions from healthcare professionals in the form of screening for potentially harmful alcohol use, prescription monitoring, and initiating counseling may help to reduce older adults' risk for falls or other adverse effects.

Chapter 1

Section 1.1 Introduction

Alcohol use is prevalent among community-dwelling older adults and is projected to increase in the coming years with the aging of the baby-boomer generation. Few observational studies have attempted to understand the extent of alcohol use taking comorbid conditions and medication use into consideration. As older adults are the leading consumers of medications in the U.S., it is essential to understand what proportion of older adults could be at risk of experiencing an alcohol-medication interaction due to concurrent use of alcohol and alcohol-interactive medications. Additionally, it is also important to investigate the impact of the potential concurrent use of alcohol and alcohol-interactive medications in older adults on health outcomes. Based on the high rates of use and risk profile of central nervous system (CNS)-acting medications observed in older adults, this class of medication was selected to be studied. In addition, CNS-acting medications share similarity with alcohol, originating from comparable pharmacological effect. The interaction between alcohol and CNS-acting medications potentiates sedation and impairment of psychomotor functions which may lead to falls, and this hypothesis outlines the rationale for the study.

To provide an overview of this document, this section describes the specific aims, hypotheses and significance of this research endeavor. The Chapter 2 provides background information and elucidates the conceptual framework supporting the study. The chapter 3 reviews of literature focusing on alcohol-medication use in older adults. Chapters 4, 6, and 5, details the results and discussion for each of the study objectives. Finally, the chapter 7 summarizes the conclusions and includes suggestions for future research.

Section 1.2 Specific Aims

Specific Aim 1

I. To determine the prevalence and pattern of at-risk drinking among non-institutionalized older adults

II. To identify factors associated with at-risk drinking among non-institutionalized older adults

Specific Aim 2

I. To determine the prevalence and pattern of potential concurrent use of alcohol and central nervous system (CNS)-acting medications among non-institutionalized older adults

II. To identify factors associated with daily alcohol use among older adults taking at least one CNS-acting medication.

Specific Aim 3

I. To determine if alcohol use is associated with the risk of falling among older adults.

II. To determine if alcohol use is associated with risk for injurious falls in older adults.

III. To determine if alcohol use is associated with risk for recurrent falls in older adults.

IV. To determine if varying levels of alcohol use along with CNS-acting medication use is associated with risk for falls among older adults.

Section 1.3 Hypotheses

These hypotheses apply to Specific Aim III. Considering the likelihood that older adults exhibit concurrent use of alcohol and CNS-acting medication, it is of interest to understand the combined effect of alcohol and CNS-acting medication on the risk of falling in older adults. As documented by previous studies, high alcohol consumption and CNS-acting medication use have been separately associated with risk of falling.[1] Pharmacologically, both alcohol and CNS-acting medication (included in this study) have CNS depressant effects and may cause sedation, dizziness, and impairment of psychomotor functions which may lead to accidental falls[2]. Thus, based on evidence available in the literature and pharmacological plausibility, we hypothesize the following.

A. High alcohol consumption is significantly associated with higher odds of falling

B. High alcohol consumption is significantly associated with increased odds of injurious fall

C. High alcohol consumption is significantly associated with increased odds of recurrent falls

D. Older drinkers taking CNS-acting medication and consuming alcohol are at greater odds of falling than older adults either taking CNS-acting medication only or consuming alcohol only

Section 1.4 Significance

The older population constitutes the fastest growing segment of the U.S. population. They formed 12.9% of the U.S. population in the year 2000 and by 2030 this group is projected to grow to be 19% of the population.[3] The coming years will also witness the aging of the baby-boomer generation (individuals born during 1946-1964) ushering in a sustained demand for healthcare services catering to the needs of older adults. This generation reportedly uses more illicit drugs than the preceding generation.[4,5] Assuming that the cohort with greater lifetime rates of drug use will exhibit current drug use, (notwithstanding the trend of decrease in use of drugs of abuse with age) an increase in the number of older adults with substance abuse problems is expected.[5] The large size of this cohort coupled with the higher rate of substance abuse is predicted to result in an unprecedented number of older adults requiring substance abuse treatment in the future.

According to the projections, the nonmedical use of psychotherapeutic drugs will rise from 1.2% (911,000) in 2001 to 2.4% (approximately 2.7 million) in 2020.[5] The increase in prescription drug abuse may result in a rise in emergency department visits and greater healthcare costs. Another study predicted that older adults requiring treatment for substance abuse problem will increase from approximately 1.7 million in 2000-2001 to approximately 4.4 million in 2020.[4]

The use of CNS-acting medications including opioid analgesics, antidepressants, and sedatives-hypnotics by older adults is reportedly rising. A longitudinal study of community-dwelling older adults found that 13.9% (n=2737) of participants used at least one CNS-active medication and the prevalence increased to 17.1% (n=1907) over 5 years.[6] In 2011, emergency

department visits involving drugs and alcohol consumed together by older adults was reported to be 9,190 visits out of total of 606,653 visits.[7] The projected increase in the use of psychoactive substances may translate into greater need for specialized treatment as well as preventive measures catering to substance abuse patients. Historically, preventive measures have focused on young adults. There is a dearth of research on how to address and manage drug abuse problems in the older generation. In addition, since most of the predictions are based on the assumption that lifetime users will continue to use illicit drugs, alcohol, and psychotropic drugs it is important to verify these assumptions. Observational studies conducted among a nationally representation sample of older adults assessing alcohol use, factors and adverse outcomes associated with alcohol use, are needed.

Understanding the impact of the concurrent use of alcohol and CNS-acting medications on the risk of falling in older adults will be helpful in planning preventive measures to lower the incidence of falls in high risk older adults. In situations where CNS-acting medications cannot be discontinued patient at risk for falls due to their concurrent alcohol and CNS-acting medication use can be counselled to monitor, reduce or stop drinking. Falls significantly impact on the health and quality-of-life of older adults.[8,9] Falls are widespread among older adults and are a common cause of hospital admissions. The total direct medical cost of fall-related injuries in older adults in 2010 was estimated to be $30 billion, adjusting for inflation.[10] It is projected that by 2020, the annual direct and indirect cost of fall injuries will reach $54.9 billion (in 2007 dollars).[11] Therefore, generating evidence to identify risk factors for falls in order to inform the development and implementation of appropriate preventive measures to lower the risk for falls in older adults is crucial.

Chapter 2

Section 2.1 Background

2.1.1 Alcohol

Alcohol is one of the oldest psychoactive agents and is widely used in our society for many reasons including stress relief, sleep induction, recreational purposes or for its apparent medicinal value.[12] Currently, 59.6% of American adult women and 71.8% of American adult men reported having at least one drink in the past year.[13]

Beer, wine, and spirits are three major types of alcoholic beverages consumed across the world.[14] In the U.S., a standard drink is defined as any drink that contains about 14 grams of pure alcohol and is equivalent to 12 ounces (oz.) of beer, 8-9 oz. of malt liquor, 5 oz. of table wine and 1.5 oz. of distilled spirits.[15] The pattern of alcohol consumption is a factor which has substantial impact on the health outcomes associated with alcohol use. The pattern of alcohol consumption is often characterized in the following scheme: lifetime abstainers, former drinkers, light drinkers, moderate drinkers, heavy drinkers, and binge or heavy episodic drinkers.[14]

Alcohol consumption can impart a broad range of consequences on the physical and mental health of a drinker, depending on a variety of factors such as age and gender of drinkers, type of alcohol, and pattern of consumption.[14] It may also have adverse social, legal, occupational consequences. Alcohol consumption is the world's third largest risk factor for disease and disability; in middle-income countries, it is the greatest risk factor.[14] Alcohol is a causal factor in 60 types of diseases and injuries and a component cause in 200 others.[14] In the United States, alcohol contributes to 79,000 deaths and $223.5 billion in societal costs

annually.[16] Almost 9% of U.S. adults (approximately 13% of those who drink) meet the criteria for an alcohol-use disorder.[17]

A growing body of literature has shown the beneficial effects of moderate alcohol consumption. Epidemiological studies have found that moderate alcohol consumption (not more than 2 drinks per day) lowers risks for cardiovascular events, mortality, cognitive decline, and fractures.[18] Current findings suggest a U or J-shaped relationship between alcohol consumption and coronary artery disease.[18] Moderate alcohol consumption has an impact on the psychosocial functioning in older adults; by facilitating social interaction, improving mood and stimulating appetite.[18]

2.1.2 Pharmacology of Alcohol

Alcohol has a complex pharmacology and is known to affect a wide variety of neurotransmitter systems. Alcohol exerts its primary action via a number of central nervous system neurotransmitter or neuromodulator systems, including the N-methyl-D-aspartate (NMDA), Gamma-aminobutyric acid ($GABA_A$), glycine, 5-hydroxytryptamine 3 (5-HT3) and nicotinic acetylcholine receptors (nAChRs) as well as L-type Ca2+ channels and G protein-coupled inwardly-rectifying potassium channels (GIRKs).[19] Basically, it acts by disrupting distinct receptor or effector proteins via direct or indirect interactions, whereas at very high concentrations it might even change the composition of lipids in the surrounding membrane.[19] The NMDA function was inhibited by alcohol in a concentration-dependent fashion.[19] Alcohol enhances the function of $GABA_A$ and glycine receptors. In addition, alcohol potentiates serotonin ($5\text{-}HT_3$) and nAChR functions. By acting on the aforementioned receptors, alcohol

increases endogenous serotonin, dopamine and opioid release.[19] Ion channels also constitute a primary target of alcohol. Alcohol inhibits dihydropyridine-sensitive L-type Ca2+ channels.[19]

Alcohol, a CNS depressant, can stimulate pulse, motor activity, and mood in small doses whereas higher dose of alcohol can impair cognitive and motor function, cause respiratory depression and in severe cases cause coma and death. Behavioral, psychomotor, and cognitive changes begin to occur at a blood alcohol concentration (BAC) of 0.02-0.03 (grams of alcohol per 100 grams of individual's blood).[19]

Alcohol ingested by mouth reaches the stomach, where a small portion is metabolized by the enzyme alcohol dehydrogenase (ADH). The remaining alcohol enters the intestine, where most of it is absorbed into the blood and enters the portal system that leads to liver. [20,21] A part of that alcohol is metabolized in the liver by ADH and cytochrome P450 enzymes. The remaining alcohol enters the systemic circulation and from there gets distributed throughout the body water.[20,21] The liver is the primary site of alcohol metabolism. ADH converts alcohol to acetaldehyde in an oxidative reaction. Acetaldehyde is further metabolized by aldehyde dehydrogenase (ALDH) to acetate and acetyl CoA.[20,21]

2.1.3 Alcohol Consumption in Older Adults

Alcohol consumption declines with age with older adults consuming less alcohol than their younger counterparts.[22] Though a plethora of studies have been conducted to understand different facets of alcohol use, comparatively fewer studies have been performed to understand the effect of alcohol consumption on health-related outcomes in older adults.

Alcohol has greater physiological impact on older adults than on younger adults for a variety of reasons. First and foremost, age-related changes in physiology significantly affect the

response of older adults to alcohol. As lean body mass decreases with age, the total body water also decreases while fat increases as a proportion of body weight. Since alcohol distributes in total body water, this alteration in the volume of total body water means that for a given dose of alcohol, the concentration of alcohol in the blood is greater in an older adult than in a younger adult. As a result, the same amount of alcohol that previously had little effect may now cause intoxication.[22,23] Furthermore, it is postulated that this relative change in alcohol concentration in blood accompanied with slower reaction time observed among older adults could be responsible for the accidents or injuries that are observed in this age group.[23] The reduced secretion of gastric alcohol dehydrogenase enzyme causes alcohol to be metabolized more slowly so the blood alcohol level remains raised for a longer time.[2] The widespread use of alcohol and medication by older adults, especially in the presence of chronic comorbid conditions, renders them vulnerable to the adverse effects of alcohol-medication interactions as well. Older adults consume more medication than any other age group. According to the National Council on Patient Information and Education (NCPIE) 34% of all prescription medication and 30% of all over-the-counter medication is used by older adults.[24] In addition, one-third of Medicare beneficiaries have four or more chronic conditions and these may be treated with medications.[24]

Detection of alcohol problems in older adults is often difficult. The social stigma attached to alcohol consumption may prevent older adults from disclosing their actual amount of consumption.[22,25] Driven by biases and stereotypes, healthcare practitioners may not enquire about older patients' alcohol use. Healthcare professionals and older adults may avoid discussing alcohol consumption.[22,25] Symptoms associated with heavy drinking, alcohol dependence or abuse may coincide with symptoms of other diseases such as depression, dementia, and

psychiatric disorders.[22,25] Due to the aforementioned reasons alcohol use in older adults is described as a "hidden epidemic".[22]

The prevalence of alcohol use reported by various studies may differ in proportion but the pattern of consumption remains similar. According to the 2011 National Survey on Drug Use and Health (NSDUH) findings, the prevalence of current alcohol use (at least one drink in the past 30 days) is 40.3% among participants aged 65 years or older. 8.3% of older adults reported binge drinking (five or more drinks on the same occasion on at least 1 day in the past 30 days) while the rate of heavy drinking was 1.7% (five or more drinks on the same occasion on each of 5 or more days in the past 30 days) in this group.[26] Cross-sectional analysis of multisite screening data obtained from older patients in primary care older reported 70.0% had no consumption of alcohol in the past year, 21.5% were moderate drinkers (1-7 drinks/week), 4.1% were at-risk drinkers (8-14 drinks/week), and 4.5% were heavy drinkers (>14 drinks/week).[27] On the other hand, analysis of the Medicare Current Beneficiary Survey (MCBS) data showed that 65.5% of the sample reported drinking no alcohol, 25.4% reported drinking within guidelines (not more than 30 drinks per month), 3.8% exceeded the monthly limit only (more than 30 drinks per month), and 5.4% reported heavy episodic drinking (4 or more drinks in a single occasion), during a typical month in the past year.[28] Thus, comparing the prevalence rates of alcohol use becomes difficult owing to the design and setting of the study, definitions and measures of alcohol consumption used in the study, and characteristics of the study sample. However, the prevalence rates of the aforementioned studies indicate that substantial proportion of older adults consumes alcohol. It is noteworthy that these proportions are likely to be an underestimation of the true proportion. Under-reporting of alcohol consumption, whether unintentional (due to recall

bias or type of survey questions), or intentional (due to social stigma attached to drinking) is common.[22]

Alcohol use imparts various benefits and detriments to the health of older adults. Moderate alcohol consumption has been claimed to be beneficial in reducing the risk of the cardiovascular diseases and dementia.[18] In addition, it is documented to improve cognition, psychological functioning, bone metabolism, and mortality.[18] However, immoderate amount of alcohol intake has been found to have hazardous effects on physical and mental health.[18] Chronic heavy drinking is associated with numerous health issues including but not limited to, hepatic disease, cardiovascular disease, various forms of cancer, diabetes mellitus, alcohol dependence or abuse, injuries, and accidents.[18]

2.1.4 Alcohol and Medication Interactions

A large number of medications have the potential to interact with alcohol. There are two types of alcohol-medication interactions: pharmacokinetic and pharmacodynamics interactions.[2,21,29] Quantity and frequency of alcohol consumption also influences the outcome of alcohol-medication interactions.

In a pharmacokinetic interaction, alcohol interferes with the absorption, distribution, metabolism and elimination of the medication or vice versa. Drinks with a high alcohol concentration will delay gastric emptying and this may affect the absorption of some drugs (for example propranolol, metoclopramide, and cisapride).[20] Some drugs may block the first pass metabolism of the alcohol in the liver resulting in elevated blood alcohol levels. Examples of such medications are H_2 receptor antagonists: cimetidine, ranitidine, and nizatidine. Cytochrome P450 enzymes (primarily CPY2E1) play an important role in the metabolism of alcohol. Hence

certain medications (such as benzodiazepines, barbiturates, warfarin, phenytoin, propranolol, tolbutamide, isoniazid, and highly active antiretroviral therapy (HAART) drugs) require the same enzyme for metabolism as alcohol and therefore compete with alcohol for metabolism.[21] It must be noted that the effect of CYP enzyme related interaction is influenced by the pattern of alcohol consumption. In chronic heavy drinkers, CYP2E1 activity is induced up to tenfold. When such drinkers are sober with no alcohol in the body to compete with medications for metabolism, those medications undergo more rapid metabolic clearance. As a result, medications will require higher doses to achieve a therapeutic effect. However, acute heavy drinking inhibits the hepatic drug metabolism. Thus, the drug competes with alcohol for metabolism and these drugs will be metabolized more slowly.[2,21,29,30]

Several medications can inhibit the ALDH enzyme and thereby increases the aldehyde level in blood causing flushing (dilation of blood vessels, low blood pressure, rapid heartbeat). Some examples of such medications are longer acting hypoglycemic agents, namely chlorpropamide, and tolbutamide, and beta-lactum cephalosporin such as cefamandole.[2] Foods and beverages with tyramine, including red wine and beer, can increase the risk if hypertensive crisis when consumed with nonselective monoamine oxidase inhibitors.[2]

In pharmacodynamic interactions, alcohol alters the effect/response of the medication. They do not involve enzyme inhibition or activation but rather refer to the additive effects of alcohol and certain medications on the body. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) when combined with alcohol may increase the risk of gastrointestinal bleeding by injuring gastric mucosa and increasing bleeding time.[2,21,29] Antiplatelet agents including aspirin, clopidogrel, and ticlopidine also increase the risk of bleeding.[28] Alcohol, when consumed concomitantly with antihypertensive agents potentiates orthostatic hypotension.[2]

Antihypertensive agents such as vasodilators, hydralazine, nitrates, central-acting hydralazine, central-acting antihypertensives, and alpha-blockers, may cause a severe drop in blood pressure leading to dizziness and fall-related injuries when taken with alcohol.[2] Another important class of medication that exhibits additive pharmacodynamic interaction with alcohol is CNS-acting medications.[2,21,29] Alcohol can also have an adverse impact on disease conditions such as hypertension, diabetes mellitus, gout, hepatic diseases, depression, insomnia, and various forms of cancer.[2,21,29]

2.1.5 Interaction between Alcohol and CNS-Acting Medications

Both alcohol and CNS-acting medications are widely used. Both of the agents are psychoactive substances with similar mechanisms of action.[2,21,29] There is more than one ways in which alcohol can interact with CNS-acting medications.[31] The most prevalent type of interaction is the additive pharmacodynamics interaction between CNS depressants and alcohol. Concomitant use of CNS depressants and alcohol synergistically enhances the side effects (including sedation, impairment of judgment and motor functions) of these drugs. Alcohol and some CNS depressants act on the same neurotransmitter system (GABA receptors, release of dopamine, serotonin).[2,21,29] Pharmacokinetic interactions between certain CNS depressants and alcohol also exist. Alcohol and certain CNS depressants such as phenytoin, benzodiazepines, and barbiturates, may compete to be metabolized by the same metabolic enzyme.[21,29] Apart from interacting with CNS-acting medications, alcohol is also associated with behavioral health problems. The literature has documented a complex, bidirectional relationship between alcohol and depression. Problematic alcohol consumption accompanied by depression[32] significantly increases the potential for poor mental and physical health outcomes. The overlapping signs and

symptoms of substance abuse and depression may lead to misdiagnosis, or missed diagnosis by clinicians. Heavy drinking also interferes with the quality of sleep.[2]

2.1.6 CNS-Acting Medication Use in Older Adults

Use of CNS-acting medication, including antidepressants, anxiolytics, sedatives-hypnotics, anticonvulsants, antipsychotics, and opioid analgesics, is widespread among older adults living in all types of settings, including assisted-living facilities, nursing homes, or congregate retirement communities.[33,34] A study using Medical Expenditure Panel Survey (MEPS) data from year 2004-2009 found that there was an increase in the use of following classes of medications; psychotropic medication (from 57.4% to 63.8%, p-value <0.01), benzodiazepines (from 22.7% to 30.5%, p-value <0.01), atypical antipsychotics (from 2.3 to 3.9%, p<0.01) in the span of 5 years.[34] These drugs are prescribed for various purposes including treating psychiatric conditions, sleep disorders, mood disorder, and alleviating pain, stress, and anxiety.[32]

Unfortunately these medications are associated with several adverse effects including falls, fractures, accidents, cognitive impairment, and hospitalizations.[32] Use of some of these drugs, by itself or at a certain dose, is deemed as inappropriate for older adults. Psychotropic drugs listed in the Beer's criteria include, but not limited to, amitriptyline, clomipramine, imipramine, doxepine, atypical antipsychotics, long-acting and short-acting benzodiazepines, chronic use of zolpidem, and zaleplon,.[35]

The growing use of CNS-acting medications and alcohol warrants an investigation on the effect of the potential concomitant use of alcohol and CNS-acting medication. A variety of factors influence the use and potential misuse of CNS-acting medications. The aging process,

coexisting disease conditions, increasing dependency, life-changing events such as retirement, bereavement and other psychosocial stressors may drive older adults to use psychotropic medications.[36]

2.1.7 Falls in Older Adults

The World Health Organization (WHO) defines a fall as "inadvertently coming to rest on the ground floor or other lower level, excluding intentional change in position to rest in furniture, wall or other objects".[37] Falls are the leading cause of injury-related deaths and are a common cause of non-fatal injuries inn older adults. In 2010, 2.3 million nonfatal fall injuries among older adults in the U.S. were treated in emergency departments and more than 662,000 of these patients were hospitalized.[38] Accidental falls may result in fractures, concussions, bruises, dislocation, sprains, and open wounds. Fractures (41.0%) are the most common reason for injurious fall-related emergency department visits, followed by superficial/contusion injuries (22.6%) and open wounds (21.45%).[39]

CNS-acting medications have been implicated as a risk factor for falls in older adults.[40] Acute and or heavy alcohol consumption has also been associated with the risk of falls in older adults.[1] The pharmacodynamic interaction between the alcohol and CNS-acting medications is the basis of the biological plausibility that concomitant use of CNS-acting medication and alcohol may increase the risk of falling.[2]

Section 2.2 Conceptual Framework

2.2.1 Conceptual Framework for At-Risk Drinking

This dissertation study is based on the concept that alcohol can interact with selected diseases, certain classes of medications, and health-related behaviors (such as falls, memory problem, or sleeping problem) and this interaction may lead to adverse health outcomes. Older adults are more susceptible to alcohol-medication or alcohol-disease interactions due to several age-related changes. These age-related physiologic changes[23] include, i) decline in total body water in which alcohol distributes as a result of which older adults achieve higher blood alcohol concentration (BAC) than younger adults after consuming same volume of alcohol, ii) functional changes (including changes in the neurotransmitters, receptors, hormonal changes) in the aging brain increases the brain's sensitivity to the psychoactive effect of alcohol, and iii) decrease in the secretion of gastric enzymes slowing down the metabolism (this may play a minor role).[2] Thus, due to the above mentioned age-related changes older adults may experience exaggerated response to alcohol. Besides, aging may also affect the body's ability to develop tolerance.[23] Moreover, as older adults tend to suffer from comorbid conditions and take numerous medications, the probability of encountering alcohol-disease or alcohol-medication interaction increases.[2]

The first objective of the study is to understand the extent of alcohol use in context with disease conditions, medication use, and health-related behaviors. The purpose is to measure the extent of risk a community-dwelling older adult may exhibit owing to their disease profile, medication use and other health related behaviors.

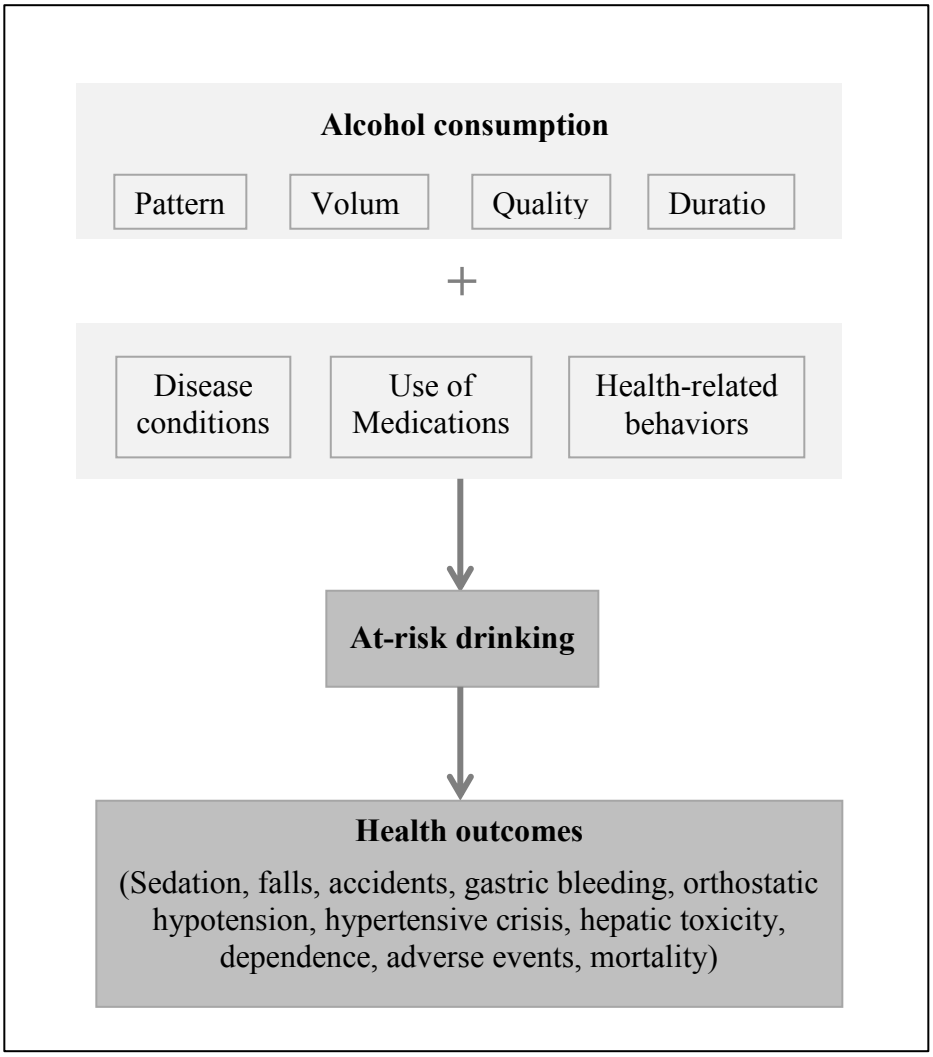

Figure 2.1 Conceptual Framework of At-Risk Drinking

Depending upon the pattern, volume, duration of consumption, and type of alcoholic beverages consumed, alcohol may interact with certain medications or disease conditions causing adverse events.[41] Alcohol may interact with diseases or medication in several ways. This study utilized a risk assessment tool (CARET) to study at-risk drinking which is defined as "alcohol

use that is excessive or potentially harmful in combination with select comorbidities or medications".[41]

This risk assessment tool incorporates a list of disease conditions that may be affected by alcohol intake. Table 2.1 describes the alcohol-disease interaction, the mechanisms of action and its repercussions on the health of older adults.[2] There are other disease conditions that may interfere with alcohol use but this study focused on disease states listed in Table 2.1.

Table 2.1 Alcohol-Disease Interactions[2,21]

Disease	Mechanism of action	Effect
Hypertension	Alcohol can cause a dose-dependent increase in blood pressure	Increases the risk of hypertension
Diabetes	Alcohol suppresses hepatic gluconeogenesis. Drinking without eating may increase the risk of hypoglycemia. Consuming sweet alcohol beverage may induce hyperglycemia.	Affects blood glucose levels
Hepatic disorders	Alcohol worsens hepatic disease through inflammation and accelerates disease progression.	Increases the risk of cirrhosis and hepatocellular cancer.
Gout	Alcohol induces a hyperuricemic effect	Increases the risk of gout
Depression	Alcohol affects mood and depressive symptoms. A strong bidirectional relationship exists between alcohol and depression	Exacerbation of depressive symptoms

The CARET questionnaire also includes selected medications that have the potential to interact with alcohol. There are other medications that may interact with alcohol to cause adverse effects but this study included medications listed in Table 2.2 which describes the mechanism of action as well as effects of each alcohol-medication interaction.[2]

Table 2.2 Alcohol-Medication Interactions[2,21]

Medications	Mechanism	Effect
CNS-acting medications including benzodiazepines, barbiturates, sedatives-hypnotics, anticonvulsants, antidepressants, sedating-antihistamines, opioid analgesics	Alcohol enhances the side effects of these medications such as sedation, drowsiness, impairment of psychomotor functions, postural sway, affects gait and balance.	Drowsiness, sedation, fall, accidents, injuries.
Warfarin	During acute intake, alcohol may compete with liver enzymes decreasing warfarin metabolism resulting in increased anticoagulation. Chronic intake of alcohol induces enzymes resulting in increasing warfarin metabolism thereby decreasing anticoagulation	Interferes with the effectiveness of the drug (may cause bleeding)
Antiplatelet agents (aspirin, clopidogrel, ticlopidine)	Affects gastric mucosa and increases gastric emptying	Gastrointestinal bleeding
Antihypertensives including nitrates, vasodilators, alpha-blockers, diuretics, hydralazine, centrally-acting antihypertensives	Impairs vasoconstriction leading to severe drop in blood pressure	Hypotension
NSAIDs	Due to increase in production of metabolites toxic to the liver, damaging gastric mucosa	Hepatic toxicity
Anti-ulcer medications including proton pump inhibitors and H_2 antagonists	Interferes with alcohol metabolism by reducing ADH activity in gastric mucosa and increasing gastric emptying	Increases blood alcohol levels

Understanding the factors associated with at-risk drinking is important in order to identify "high-risk" individuals and direct preventive measures to maximize the reduction of alcohol-related adverse outcomes. Previous studies have documented relationships between at-risk drinking and other factors including demographic factors (such as age, gender, race, and marital status), socio-economic status (education, income, employment), and health and functional status.[42,43] Few studies have explored the relationship between at-risk drinking, comorbidities, and medication use.[42]

This study aims to identify the factors, including socio-demographic factors, perceived health status, functional status, comorbidities and medications that could be related to at-risk drinking in older adults.

Figure 2.2 graphically depicts the complex inter-relationship between at-risk drinking and diverse factors. More research is needed to understand the directionality and magnitude of these associations and other mediating factors.

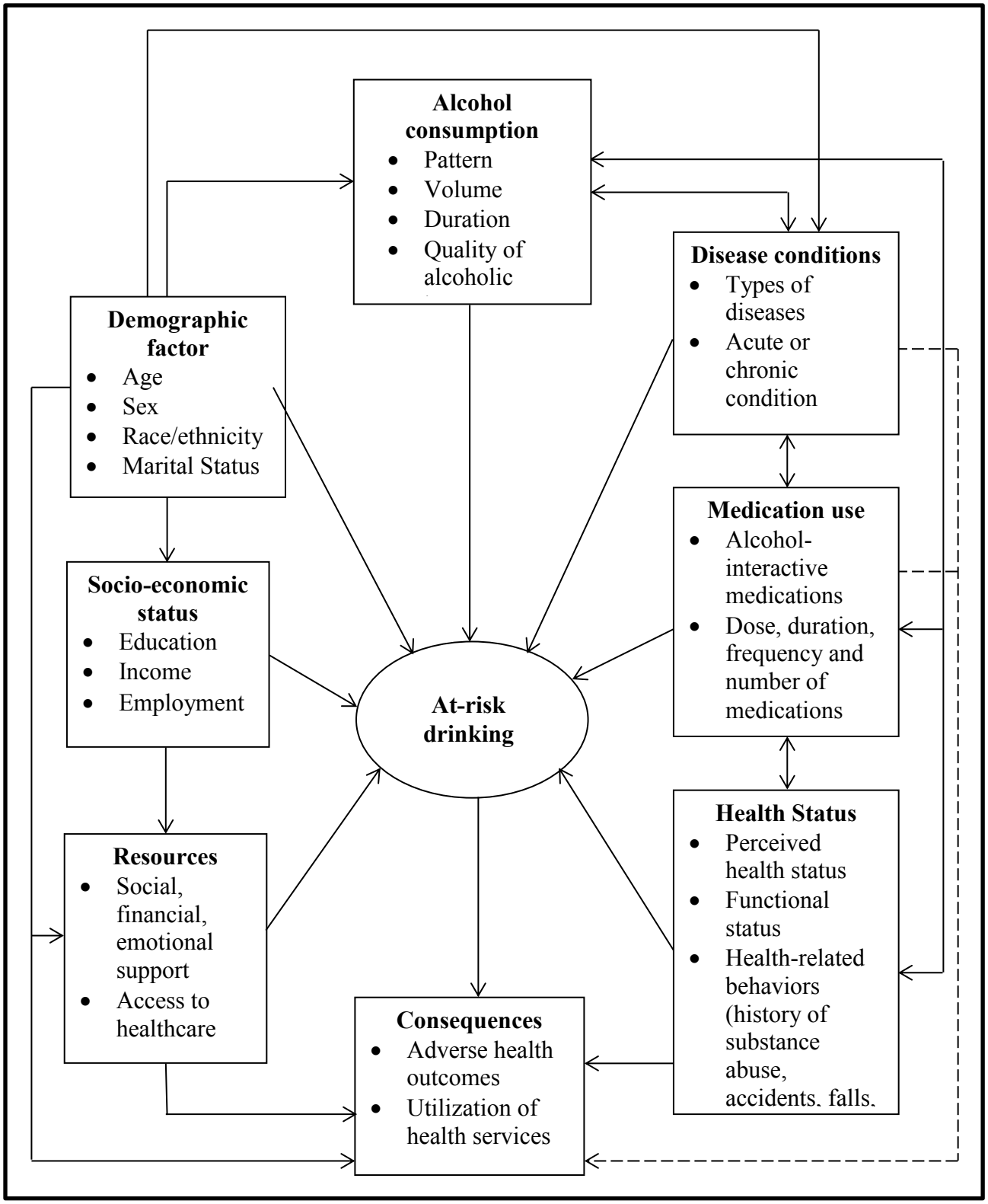

Figure 2.2 Inter-relationships Between Various Factors Associated with At-Risk Drinking

2.2.1 Conceptual Framework for Alcohol and CNS-Acting Medication Interaction

As described in Table 2.2 pharmacodynamic interactions can occurs between alcohol and CNS-acting medications that may lead to sedation, drowsiness, and impairment psychomotor functions. The mechanism behind pharmacodynamic interaction can be explained by two ways: i) additive interaction where the two individual agents act separately to cause an effect that is the sum of the two effects, ii) synergistic interaction in which the observed response is greater than the sum of the individual effect of each drug.[31] Some interaction can be attributed to the common receptor type that is associated with some of the CNS-acting medications and alcohol. This is the $GABA_A$ receptor which is the receptor for GABA, the primary inhibitory neurotransmitter in the CNS. Benzodiazepines, barbiturates, and other sedatives-hypnotics bind at separate sites in the receptor to potentiate the inhibitory action of GABA. Ethanol modifies the receptor by altering the membrane environment so that it has increased affinity for GABA.[44] Opioid analgesics depress the CNS, resulting in analgesia, sedation, drowsiness, mood changes, euphoria, lethargy, and depressed respiration.[31] Alcohol enhances the sedating property of opioids. For antipsychotic drugs extrapyramidal symptoms, tardive dyskinesia (TD), elevated prolactin levels, and sedation contribute to falls and fractures.[45]

Alcohol also interacts with certain types of CNS-acting agents in a pharmacokinetic manner. During acute heavy alcohol consumption, alcohol may compete with certain medication such as benzodiazepines, barbiturates, phenytoin, for cytochrome P450 enzymes (CYP2E1) causing decreased metabolism of the medication which results in higher effectiveness of the drug.[21] This potentiates the effect of alcohol and those CNS-acting medications. For example, alcohol intake followed by tricyclic antidepressant ingestion can cause an over 200% increase in plasma amitriptyline concentrations in humans.[31] In the scenario of acute alcohol ingestion by an

infrequent drinker, the metabolism of the drug is inhibited.[21] On the other hand, regular ingestion of alcohol can induce the normal secretion of the CYP2E1 enzyme thereby increasing the metabolism of those drugs. Chlorpromazine (antipsychotic agent) inhibits alcohol dehydrogenase preventing alcohol metabolism.[21]

Development of cross-tolerance is also a phenomenon altering the effect of the drug in the presence of alcohol.[31] Tolerance is a phenomenon in which a repeated use of a psychoactive agent alters the response of the target tissue to the drug itself or other chemically-related agents.[31] Cross-tolerance is seen when physiologic changes induced by prolonged exposure of the original chemical agent (such as alcohol) is carried over to another drug (such as a barbiturate) wherein the response to the second drug is diminished.[31] An animal study, performed to assess the sedation achieved by co-administration if alcohol and antidepressants, reported the following strength of potentiating effect of alcohol sedation: amitriptyline ≥ imipramine > maprotiline = mianserine > desipramine ≥ chlorimpramine > iprindole ≥ alaproclate ≥ norzimelidine ≥ zimelidine.[46]

Figure 2.3 illustrates the pharmacodynamic interactions between alcohol and CNS-acting medications. Another important aspect of this interaction is the age related changes occurring in older adults that causes an exaggerated response to alcohol and CNS-acting medication. This can be explained by the functional changes in the aging brain which includes alterations in neurotransmitters, number of receptors, hormonal changes, and impaired glucose metabolism.[47] For example, age-dependent changes in $GABA_A$ benzodiazepine receptor complex leads to increased sensitivity to benzodiazepines which may result in negative effects on cognition, gait, and balance.[47]

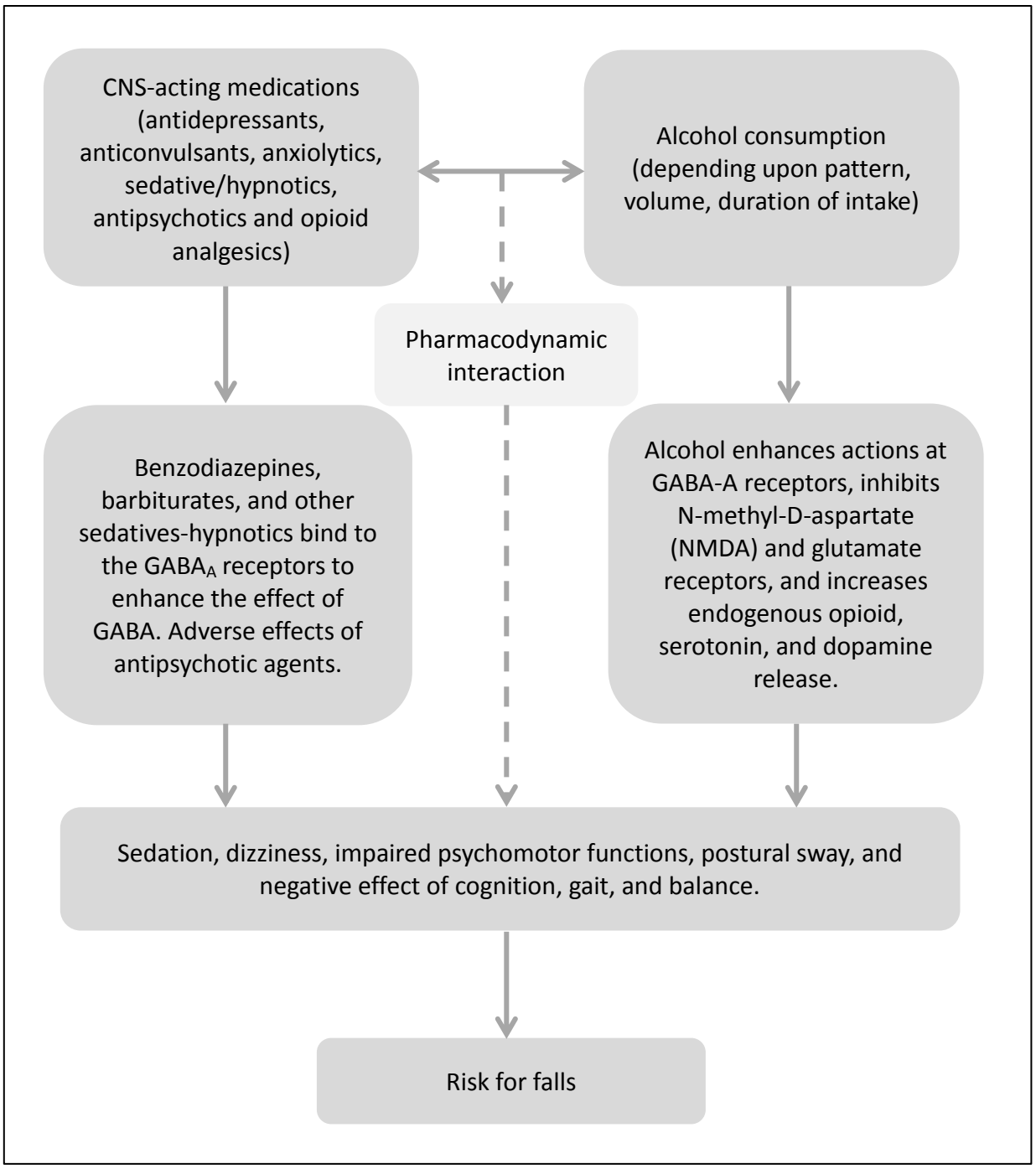

Figure 2.3 Conceptual Description of the Interaction Between Alcohol and CNS-Acting Medications

Based on the concept of pharmacodynamic interactions, concurrent use of alcohol and CNS-acting medications may enhance sedation, loss of balance and gait, postural sway, and impairment of psychomotor function, all of which increases the risk of falls, accidents, and injuries. Hence the idea was to investigate if increased risk of falls was associated concurrent use of alcohol and CNS-acting medications.

Before investigating the effect of the combined use of these agents, it was important to determine the prevalence of potential concurrent use if alcohol and CNS-acting medications as there were no recent data available indicating the extent of potential concurrent use of these agents.

Review of literature showed a dearth of studies looking at the prevalence and extent of at-risk drinking. There is lack of evidence on the effect of the combined use of alcohol and CNS-acting medications on risk for falls in older adults. Based on the conceptual framework and gaps in the literature, the study objectives of this dissertation were formed.

Chapter 3

Section 3 Review of Literature

3.1. Introduction

Consumption of large amounts of alcohol, in an acute or chronic manner, may increase the risk of experiencing alcohol-attributable heath disorders. The volume, pattern and quality of alcohol and duration of exposure impact the health outcomes encountered by drinkers.[48] In addition, consumption of alcohol in the presence of certain disease conditions may have harmful effects.[2] Alcohol may interact with selected medications to cause adverse effects.[2] Even moderate drinking may place older adults at risk of experiencing adverse events owing to their disease profile or medication use.[49] A survey of 17,000 Medicare beneficiaries found that 2 out of 5 patients reported taking five or more prescription medications.[50] More than 90 percent of non-institutionalized older adults in the United States take at least one prescription medication, and those who are seen in physicians' office take six to eight medications on average.[51] Considering the high use of medication in the older population, it is imperative to understand the magnitude of potential concurrent alcohol and medication use.

A literature review was conducted to identify, select, and evaluate the available research studies and synthesize evidence providing insight into the nature of alcohol and medication use among older adults. This review will provide a comprehensive look at the issue of alcohol and medications use in older adults thereby providing evidence to support decision-making by different stakeholders including healthcare professionals, policymakers, and researchers. The objective is to conduct a systematic review to identify and evaluate epidemiological studies describing the use of alcohol and medication in older adults.

3.2 Methods

Peer-reviewed literature published from January 1990 to 19th September 2013 was searched in Pubmed/Medline. Additionally, the reference lists of relevant reviews and research articles were also assessed. Studies were included if: i) they were conducted in older adults (aged 60 years or older), ii) the objective of the research article was to understand alcohol and medication use, and iii) the abstract or full text was available in the English language. Systematic reviews, case reports, and case series were not included in this study. The age limit for older adults was considered to be 60 years since that is the cutoff accepted in many countries.

The search terms included a combination of Medical Subject Headings (MeSH) terms and non-MeSH terms along with Boolean operators. The search terms accompanied with filters (including publication date from 1990/01/01 to 2013/09/19, humans, English language, age: 45-64 years, 65+ years, and 80+ years) were employed to retrieve relevant articles. The search terms included *"alcohol drinking AND aged AND medication AND epidemiology", "alcohol AND aged AND medication", and "at-risk drinking AND (older adults OR aged) AND alcohol"*.

Screening was performed by reviewing the title and abstract for potential eligibility, followed by further examining the full-text for potential eligibility. References of retrieved articles and review papers were screened to find possible articles. A research study with multiple publications is discussed as a single study in this review. Frequency or percentage of combined use of alcohol and medication is discussed in this review.

Table 3.1 Summary of Studies

Study	Country	Setting and sample size	Assessment	Inference
Immonen et al, 2013 [59]	Finland	A stratified random sample of 1,395 home-dwelling adults aged ≥65 years	Alcohol interactive drugs examined using Swedish, Finnish, Interaction X-referencing interaction database	Among 1,142 drug users, 62.6% consumed alcohol. The use of alcohol-interactive drugs was found to be 42.2%, 34.9%, and 52.7% among at-risk users, moderate users and minimal/non-users
Barnes et al, 2010 [42]	U.S.A	3,308 drinkers aged 60 years or older, recruited from non-profit, outpatient clinic	Comorbidity Alcohol Risk Evaluation Tool (CARET) was used	Of the 1,147 at-risk drinkers, 21.2% and 21.5% were at-risk owing to their alcohol use with medication and co-morbidity, respectively.
Moore et al, 2006 [61]	U.S.A	NHANES I, 1971-1974 and NHANES Epidemiologic Follow-up Survey, 1992	Some of the items from Comorbidity Alcohol Risk Evaluation Tool (CARET) were used	Prevalence of at-risk drinking was 10%. 69% of at-risk drinkers were identified as such because of their alcohol use in the presence of comorbidities. Pain medication and medication for anxiety disorders were most commonly used by drinkers.
Aira et al, 2005[63]	Finland	523 home-dwellers (≥ 75 years of age)	Community-based random survey	86.9% of alcohol drinkers use medication on regular basis.
Pringle et al, 2005 [57]	U.S.A	83,321 PA-PACE cardholders	Mailed survey to collect alcohol use data. Prescription drug claims were used. Alcohol interactive medications identified using First DataBank.	19% of AI drug users reported concomitant alcohol use ($p<0.001$). Most common combination of alcohol and alcohol interactive medication occurred with NSAIDs (20.2%)
Moore et al, 2002 [62]	U.S.A	166 drinkers aged 60 years or older recruited from internal medicine clinic	ARPS and shorter version of ARPS	Out of 166 drinkers, 64 were identified at-risk because of their medication and alcohol use.

Study	Country	Setting and sample size	Assessment	Inference
Fink et al, 2002 [43]	U.S.A	549 current drinkers aged 65 years or older recruited from academic and community primary care clinics	Alcohol-related Problem Survey (ARPS)	11% were harmful drinkers and 35% hazardous drinkers. Most hazardous drinkers were identified by their alcohol and medication use. Anti-arthritic, pain medications, and aspirin were commonly used by drinkers.
Johnson et al, 1997 [69]	U.S.A	Volunteer sample of 155 urban women over the age of 85 years was interviewed	Data on health, sleep patterns, use of alcohol and OTC medication	"Seventy-seven (85%) of the women who used alcohol before bedtime also used OTC medication. Of these, 33 (43%) used alcohol and OTC medication in combination each night."
Adams et al,[65] 1995,	U.S.A	311 independently living residents	Alcohol use questions adapted from the Khavari questionnaire and the CAGE questionnaire. Prescription and non-prescription medication use was considered	38% used both alcohol and high-risk medication. High-risk drugs commonly used were antihypertensives, aspirin, NSAIDs and medications for congestive heart failure.
Forster et al,[58] 1993	U.S.A	667 community dwellers in rural setting	Prescription and OTC medications were included. Physician Desk Reference used for ascertaining ADI	25% of the respondents were at risk for at least one alcohol-related ADR and 19% reported using OTC pain medications and alcohol.
Alcohol and Psychotropic drugs				
Ilomaki et al, 2013 [64]	Australia	1,705 Australian men aged 70 years or older. Data collected from 2005-2007.	Alcohol and psychotropic drugs were studied	Of the 135 antidepressant users 27.1% were daily drinkers, as were 42.7% of the 97 sedative-anxiolytic drug users.
Du et al, 2008 [66]	Germany	1,605 older adults aged between 60-79 years. Data from German National Health Interview and Examination Survey 1997-1999.	Alcohol and psychotropic drugs were studied	Last week prevalence of combined psychotropic and alcohol use was 7.6%.

3.3. Results

3.3.1 Summary of Studies

The search yielded a total of 10,180 articles. After removing duplicates or irrelevant articles and applying the inclusion and exclusion criteria, a total of 12 original research studies were selected. All studies were cross-sectional in design and most of them included community-dwelling older adults. Most of the studies were conducted in the U.S. Some of the studies were excluded as they did not match the age criteria[52,53] or they did not study potential combined use of alcohol and alcohol-interactive medications.[54-56] Table 3.1 summarizes the studies included in this review.

3.3.2 Review of Design of the Studies

Interview or mailed survey methods were employed to collect the "usual" alcohol consumption in the past 12 months in the study population in these studies. Information on medication use was collected mostly from survey and/or interview where either participant reported medications they had been using in the past or the interviewer inspected the containers of all the medication products used by the subject and recorded the information. Pringle et al. collected the medication use information of their study sample from administrative claims data.[57]

Potential interactions between alcohol and medications were determined by various methods in these studies. Some studies used a clinical information system such as Physician Desk Reference, First DataBank[57,58], or a country-specific interaction database[59] to ascertain interactions between alcohol and medications.

On the other hand some studies [42,43,50,61] introduced a novel paradigm to understand the combined use of alcohol and medication, referring to it as "at-risk drinking". They defined the use of specific amounts of alcohol in the presence of certain medications, comorbid conditions and health-related behaviors as "at-risk drinking".[41] These studies have used validated questionnaires [Comorbidity Alcohol Risk Evaluation Tool (CARET), Alcohol Related Problem Survey (ARPS), and shorter version of ARPS (ShARPS)] to understand the potentially harmful use of alcohol and alcohol-interactive (AI) medications.[62] These instruments have a series of questions enquiring about the quantity and frequency of alcohol use, heavy episodic alcohol intake, use of different classes of medications, the presence of certain comorbid conditions, and health-related behaviors. ARPS and ShARPS classify drinkers as harmful, hazardous or non-hazardous drinkers while CARET categorizes them as at-risk-drinkers and non-at-risk drinkers.[42,61]

The prevalence of alcohol and medication use was also estimated and reported in more than one manner. Some studies reported alcohol use among medication users.[57,59,63,64] While some studies reported rate and magnitude of medication use among alcohol drinkers.[59,63] Some studies estimated the potential concurrent use of alcohol and medication in the entire study sample.[58,61,65,66] A few studies estimated at-risk drinking among the current drinkers.[42,43,61] Choice of the denominator is relevant in this case as extent of medication use widely differs from alcohol use in older adults. Hence the prevalence reported in these studies should be interpreted accordingly and comparison of these rates to each other should be made with caution.

3.3.3 Review of Prevalence Reported in the Studies

Alcohol use is influenced by many factors including, but not limited to, gender, nationality, cultural or religious beliefs, educational background, life-changing events, health condition, environment, social life and history of substance abuse.[67,68] Prevalence of alcohol use varies widely across the studies summarized in this review. Current alcohol use estimated by these studies ranged from 39% to 62% and heavy or risky alcohol consumption was estimated to be in the range of 7%-20%. Moderate drinkers constituted the largest group among the older drinkers.

At-risk drinking was prevalent among older adults. Fink et al. found that among 549 current drinkers, 11% were harmful drinkers, 35% were hazardous drinkers, and the remaining were non-hazardous drinkers.[43] Hypertension was the top indicator for harmful drinking and anti-arthritic and pain medications followed by aspirin, H_2–antagonists (ranitidine, cimetidine), antihypertensives, and antidepressants were some of the most common indicators of hazardous drinking.[43] Moore et al. studied the validity and reliability of ARPS and ShARPS and found that these instruments were "more sensitive than AUDIT and SMAST-G in identifying older drinkers at risk of experiencing harm as a result of alcohol and comorbidities".[62]

In the SHARE study, 34.7% of the 3,308 current drinkers were identified as at-risk drinkers. Among those, 61.0%, 61.9% and 64.3% were identified as at-risk drinkers owing to their alcohol-medication use, alcohol-comorbidity, and alcohol intake, respectively. Among the at-risk drinkers 56.1% fell into at least two risk categories and 31.0% fell into all three risk categories.[42] Analysis of the 1971-1974 National Health and Nutrition Examination Survey I (NHANES I) revealed that among 4,691 older adults included in this study, 39% were current

drinkers and 10% were at-risk drinkers. 69% of the at-risk drinkers were identified as such because of their alcohol use in context of comorbidities. Gout, gastrointestinal ulcer, and anxiety disorder were the top three disease conditions associated with at-risk drinking. Medications for pain, indigestion, and insomnia were the most common medications responsible for a classification of at-risk drinking.[61]

A recent Finnish study found widespread use of alcohol-interactive (AI) medications among community-dwelling older drinkers.[59] It was reported that among at-risk alcohol users (n=90), 42.2% were on AI medication whereas among moderate users (n=625) and non/minimal users (427), 34.9% and 52.7% were on AI medication respectively. One in 10 at-risk users used warfarin, metformin or sedative-hypnotics. Another study conducted in Finland included 523 community-dwelling older adults aged 75 or older. This study found that most alcohol drinkers (n=231) also used medications on a regular basis (86.9%) or as needed (87.8%). Alcohol use was common among hypertensive, diabetic and depressive patients.[63]

Pringle et al examined the prevalence and pattern of concomitant alcohol and AI drug use in a total of 83,321 older adults enrolled in the Pennsylvania Pharmaceutical Assistance Contract for the Elderly (PA-PACE) program. A total of 20.3% (n=16,886) reported consuming alcohol. The study stated "of current drinkers with at least one concomitant AI medication claim, 44.9% used one AI drug, 28.6% used two, 14.1% used three, 6.9% used four, and 5.5% used five or more AI drug". NSAIDs and prescription antihistaminics, and miscellaneous antihypertensives were the three most frequently used AI drugs in combination with alcohol.[57] Forster et al. found that out of 667 older adults, 25% were at risk of one alcohol-related adverse drug reaction (ADR) while 15% were at risk for multiple ADRs due to their drug use and alcohol intake. Use of over-the-counter (OTC) pain medication, antihypertensives, prescription diuretics, OTC cold

preparations, and prescription arthritis medications was observed in combination with alcohol.[58] A cross-sectional analysis of residents of three retirement communities estimated that 38% of the study sample was using both alcohol and high-risk medications.[65] High-risk drugs commonly used by drinkers were antihypertensives (50%), aspirin (27%), non-steroidal anti-inflammatory drugs (20%), medication for congestive heart failure (18%), antacids or H2 blockers (16%), sedatives (11%), narcotics (5%), and warfarin (5%).[65]

3.3.4 Factors Associated with Concurrent Alcohol and Medication Use

Many studies consistently demonstrate that older men compared to older women were more likely to concurrently use alcohol and AI medications.[42,57,58,61] Advanced age (75-84 years, or 85 years or older) was associated with low alcohol consumption, thus, these groups are less likely to be at-risk drinkers.[42,57] High educational level was positively associated with combined alcohol and medication use.[57,58,61] Moore et al. found that smokers and married individuals were more likely to be at-risk drinkers.[61] Caucasians are at higher odds of being exposed to alcohol-medication interactions.[42,57,61] A study by Pringle et al. showed that older adults taking multiple AI medications were less likely to consume alcohol.[57]

3.3.5 Alcohol and Psychotropic Medication Use

Two studies assessed the potential combined use of alcohol and psychotropic medications in older adults based on the premise that the pharmacodynamic interactions between of alcohol and CNS-acting medications may cause enhanced sedation and impairment of psychomotor functions. A study conducted using the 1998 German National Health Interview and Examination Survey determined that out of 1605 participants, 7.6% reported combined use of alcohol and psychotropic medication.[66] Higher prevalence of combined use of alcohol and

psychotropic medication was seen among participants who were aged between 70 and 79 years, lived alone, used more than one medication, had a history of cardiovascular disease or had poor health status. Psychotropic medications most likely to be concurrently consumed with alcohol were antidepressants, hypnotics/sedatives, and benzodiazepines.[66] A cross-sectional population-based study using the Concord Health and Aging in Men Project (CHAMP) was conducted including 1705 men aged 70 year or older. Overall, 27% of the antidepressant users were daily drinkers and 42.7% of sedative/anxiolytic users were daily drinkers. Users of sedative-hypnotic medication were more likely to engage in daily drinking than non-users of those medications.[64] A study including a convenient sample of 155 older women interviewed about their sleep pattern, alcohol use and over-the-counter medication use. Of the 155 older women, 130 consumed alcohol before bedtime and among those, 77 older women reported consuming medication before going to sleep.[69]

3.4 Discussion

This review was performed to understand and summarize the current literature in the area of alcohol and medication use among older adults. The search yielded twelve studies out of which two were focused on alcohol and psychotropic medication use, and the rest dealt with alcohol and alcohol-interactive medication use. A few studies (n=2) were not included because they did not meet the inclusion criteria, even though these studies focused on alcohol consumption in older adults having comorbid conditions, or taking psychotropic medications.[52,55] The alcohol interactive medications included, but were not limited to, antihypertensives, psychotropic agents, NSAIDs, antihistaminics, opioid analgesics, antihistaminics, H_2-antagonists, warfarin, antiplatelet agents, and non-prescription medications. Older adults may use alcohol for medicinal purposes for certain conditions such as cardiovascular disease, sleep disturbance,

common cold, relaxation, and pain relief.[12,63] On the other hand, some medications used in alleviation of the aforementioned conditions may interact with alcohol to produce undesirable effects.

All the studies included in this review were cross-sectional in design and collected information on alcohol consumption using surveys or through interviews. Most of the studies focused on understanding alcohol and medication use during a reference period/recall time. However, none of the studies could definitively ascertain the concurrent use of alcohol and medications. Methodologically, some of the ways to determine use of alcohol and AI medications concurrently are: i) to determine the emergency department (ED) visits occurring due to alcohol and medication interaction, ii) to use the Drug Abuse Warning Network (DAWN) database that collects ED visits associated with substance abuse, iii) to combine administrative claims data with survey data (for example MCBS, NHANES) to obtain both medication use and alcohol use information, iv) to use administrative claims data coupled with interview, survey or diary methods for data collection to ascertain both medication and alcohol use. With technical advances and upsurge of linked databases, creative ways to collect data to perform such studies may be discovered.

Due to significant variations in the study design and settings, comparing the results of studies of alcohol and medication use may be difficult. However, the proportion of older adults at risk of potential concurrent use of alcohol and medication ranges from 7-50%. Underreporting of alcohol intake is a potential threat in these studies. Questions about “average number of drinks”, “overall frequency” or “typical” amount of alcohol consumption over a period of time can lead to underestimation of alcohol use.[70,71] Besides, questions regarding “standard drinks” of alcohol may not be understood uniformly or accurately among older adults adding to the

variability in estimation.[71,72] Both recent recall and long term drinking patterns should be investigated to obtain more clear and precise data on alcohol use. Social stigma may also discourage older adults from revealing the actual amount of alcohol use.

3.5 Conclusion

The review of recent literature suggests that alcohol consumption is prevalent among older adults with chronic conditions or taking alcohol interactive medications. However, there is wide variation among the prevalence rates reported by these studies. Older adults taking AI medications and consuming alcohol could potentially be at risk of encountering adverse events attributable to the interaction between alcohol and medication, or alcohol and disease. There is a dearth of studies investigating alcohol consumption in the context of disease profile and medication use among American older adults. Moreover, understanding the impact of alcohol and medication use on the health and quality-of-life in older adults is important. There is lack of studies investigating the impact of concurrent use of alcohol and AI medications on health outcomes such as falls, accidents, and cognitive impairment.

Chapter 4

Section 4 At-risk Drinking Among Community-Dwelling Older Adults

4.1 Introduction

Traditionally, alcohol use is studied in the context of quantity and frequency of alcohol intake or through questionnaires addressing behavioral features related to alcohol consumption.[41] These methods may not capture the alcohol-related problems experienced by older adults as older adults, apart from being more sensitive to alcohol, are also likely to suffer from co-morbid conditions and take multiple medications that may interact with alcohol.[29,41] Considering these issues, a new paradigm was introduced that defines at-risk drinking as alcohol use that is excessive or potentially harmful in combination with select comorbidities or medications.[41] At-risk drinking may inflict adverse effects on the health of older adults. For instance, combined use of non-steroidal anti-inflammatory agents and alcohol are associated with increased risk of gastric bleeding.[73] Combined use of alcohol and CNS-acting medications have the potential to cause adverse events such as traffic accidents, injuries, falls, and fractures.[2] Patients with hepatic problems/liver disease are advised against consuming alcohol. Screening tools such as the Alcohol Related Problem Survey (ARPS), shorter version of ARPS and CARET, have been developed to detect at-risk drinking.[62]

It is noteworthy that there is a lack of consensus over the definition of at-risk drinking. Often it is defined only in terms of quantity and frequency of alcohol consumption. The American Geriatric Society's clinical guidelines describe at-risk drinking as consuming two or more drinks per day on average[74] while the National Institute on Alcohol Abuse and Alcoholism (NIAAA) guideline defines it as consuming 4 or more drinks on a given day or 8 or more drinks

in a week.[76] The British Medical Association (BMA) describes at-risk drinking for older adults as the consumption of >20g of alcohol for women and >30g of alcohol for men.[74-76]

A study by Barnes et al., reported that of 3,308 current drinkers, 34.7% were at-risk drinkers, of which 64.3% were at-risk drinkers due to their alcohol behaviors, 61.9% and 61.0% of the at-risk drinkers were categorized as such due their alcohol use in presence of particular co-morbidities and certain classes of medication use, respectively.[42] Examination of NHANES 1971-1975 and NHANES Epidemiologic Follow-up Survey 1992 (NHEFS) showed that 10% (n=425) of the study population consisted of at-risk drinkers. Of the 425 at-risk drinkers, 31% were identified as at-risk drinkers solely because of their alcohol intake, and 69% were regarded as at-risk drinkers for their alcohol use in the presence of selected comorbid conditions.[61] Analysis of the 2005-2006 National Survey on Drug Use and Health (NSDUH) data found that 13% of older men and 8% of older women reported at-risk alcohol use (defined as two or more drinks on a usual drinking day within the past 30 days).[74] A Finnish study defined at-risk drinkers as those who consume: i) more than 7 drinks per week, ii) 3 or more drinks several times in a week, or iii) 5 or more drinks on a typical drinking day.[67] This study found that 8.2% of the study sample (n=1395) were at-risk drinkers. A German study conducted among 3,224 non-demented subjects aged 75 years and over and attending general practitioners in an urban area of Germany, found that 6.5% (95% CI: 5.6-7.4) reported at-risk drinking (defined as consuming more than 20 g of alcohol for women and more than 30 g for men).[75] Analysis of alcohol consumption among older adults in primary care showed 4.1% of the 24,863 older adults were at-risk drinkers (8-14 drinks/week).[27]

There is a dearth of studies examining at-risk drinking among American older adults, especially in the context of their comorbidities and medication use. It is also important to identify the factors associated with at-risk drinking in older adults so that preventive measures can be channeled judiciously. This study aims to determine the prevalence and the pattern of at-risk drinking in a nationally representative sample of older Americans and factors associated with at-risk drinking in this population.

4.2 Objective

The objectives of this study were to determine the prevalence and pattern of at-risk drinking and to identify the factors associated with at-risk drinking among non-institutionalized older adults.

4.3 Methods

4.3.1 Description of the Data Source

The 2009 Medicare Current Beneficiary Survey (MCBS) data was utilized to conduct this study.[77] The MCBS is conducted by the Centers for Medicare and Medicaid Services (CMS) Office of Research, Development, and Information (ORDI) through its contractor, Westat, Inc, a survey research firm located in Maryland. It is described as *"a continuous, multi-purpose survey of a representative sample of the Medicare beneficiary population, including both aged and disabled enrollees"*. The MCBS is unique in combining both survey information and Medicare claims data obtained from the CMS administrative files. It also collects data from community-dwelling as well as institutionalized beneficiaries. The objectives of the MCBS are to estimate the amount and sources of overall expenditures of all types of healthcare services used by Medicare beneficiaries including copayment, deductibles, non-covered services, and Medicare

covered services; and collect data on the overall health status of the beneficiary over a specified period of time.

The MCBS employs a stratified multistage area probability sampling design with three stages of selection. In the first stage of sampling, 107 geographic primary sampling units (PSUs), consisting of groups of counties chosen to represent the nation, are selected. In the second stage, ZIP code clusters are selected from within the PSUs. In the third stage, the beneficiaries residing in these ZIP code areas are selected by systematic random sampling within age strata. The sampling probability varied in the following age groups (0-44, 45-64, 65-69, 70-74, 75-79, 80-85, and 85 or over) in order to over represent the disabled and oldest old by a factor of approximately 1.5.

The MCBS is a longitudinal rotating panel survey wherein "*each sample person or an appropriate proxy respondent, are interviewed three times a year over four years and the average interview recall period is about 4 months"*. A rotating panel is followed for up to 12 interviews. At any given time, there are four panels active and each panel has approximately 3,000 to 5,000 active sample persons depending on when the panel was originally selected. Each year in the fall round new panels are introduced that replace the oldest panel that subsequently retires in the following summer. The 2009 MCBS file consists of selected interview data from the ongoing Medicare Current Beneficiary Survey (MCBS), which were collected during Round 55 (September through December of 2009) or earlier rounds for some variables for individuals in the continuing sample.

MCBS public use files are released as two modules: the "Access to Care" file and the "Cost and Use" file. The Access to Care file is designed to provide early release of MCBS data

related to Medicare beneficiaries' access to care. The focus of this file is to provide information on access to care, satisfaction with care, and usual source of care. The Cost and Use file integrates the survey reported events, expenditure, and other health-related information, collected from Medicare beneficiaries, to Medicare claims data, thus, providing a comprehensive picture of healthcare utilization. The Access to Care module is comprised of those beneficiaries that are part of four separate MCBS panels: round 46, round 49, round 52, and round 55. The Cost and Use module comprises of those beneficiaries that are part of five separate MCBS panels: round 46, round 49, round 52, round 55, and round 58. Both the Access to Care and Cost and Use modules were utilized in this study. Participants included in both of the modules were included in the study, resulting in exclusion of round 58 participants. The unique identifier (BASEID) variable was used to link beneficiary information across various files.

4.3.2 Eligibility of Study Participants

Medicare beneficiaries aged 65 years or older, non-institutionalized, surviving through 2009, and continuously enrolled in Medicare were included in this study. Beneficiaries present in both Access to Care and Cost and Use modules were included in the study. Older adults with complete or partial paralysis, absence or loss of one arm or leg would were excluded from the study as the risk of falls will differ in these individuals. Hence, the study sample represents continuously enrolled community-dwelling Medicare beneficiaries aged 65 years or older.

4.3.3 Selection of the Study Sample from 2009 MCBS Data

Figure 4.1 illustrates the process of sample selection. The data files Key Record (RIC K) and Administrative Identification record (RIC A) consist of both community-dwelling and institutionalized subjects. Survey Health Status and Functioning Record – Community (RIC 2

and 2P) contains community-dwelling older adults participating in the survey. In the Access to Care module, the administrative file contained 14,695 Medicare beneficiaries of which 13,751 were non-institutionalized. Similarly in the Cost and Use module, the administrative file contained 10,859 Medicare beneficiaries of which 10,700 were non-institutionalized. The institutionalized beneficiaries in both the modules and the enrollees of round 58 were excluded. After merging the non-institutionalized beneficiaries from both the modules, 8,978 in beneficiaries (mutual to both modules) remained. After excluding beneficiaries younger than 65 years, those who did not survive through 2009, and those who have complete/partial paralysis or absence of arm or leg, a total of 7,163 community-dwelling, continuously enrolled Medicare beneficiaries aged 65 years or older were eligible to be included in this study.

4.3.4 Selection of Covariates

Socio-demographic Variables: Demographic factors including age, gender, marital status, income, educational level, race, perceived health status, limitations to social activity, activities of daily living, instrumental activities of daily living, number of medications used and number of selected co-morbid conditions were studied. All of the covariates were collected from the MCBS survey. Older adults were categorized into three age groups (in years): 65-74, 75-84, and 85 and above. Race was categorized as white or non-white (includes all other races except white). Marital status was characterized as: married or non-married (includes never married, divorced, separated, and widowed). Annual income was grouped into subjects earning $25,000 or less, or more than $25,000. Employment status records whether the beneficiary is currently working at a job or business (yes/no). Educational status was classified as beneficiaries with no education, less than high school education, high school education, more than high school education.

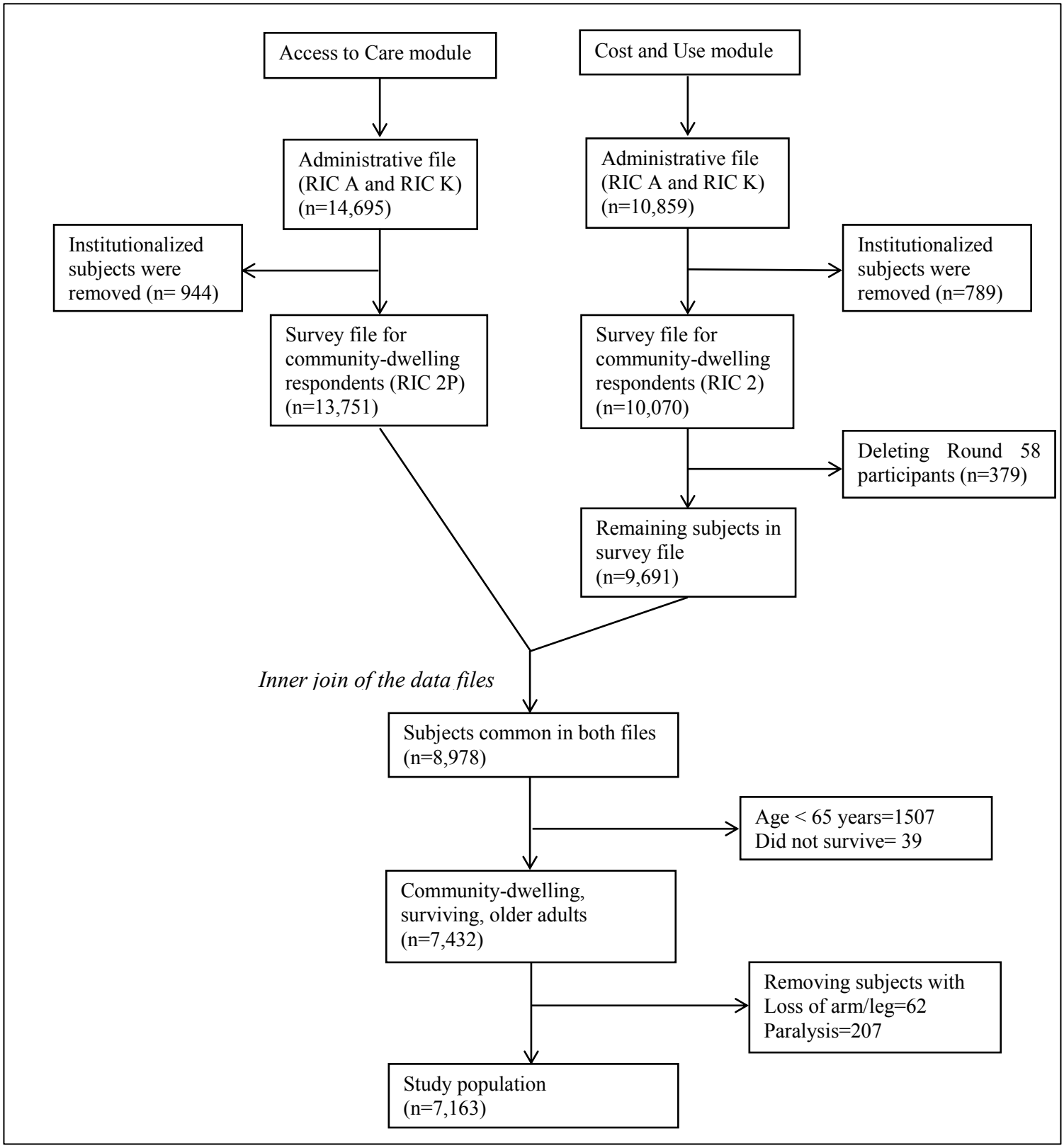

Figure 4.1 Flowchart Depicting the Selection of the Study Sample

Health and Functional Status: The "limitations to social activity" variable inquired if the beneficiary experienced limitations in their social activities due to health conditions in the past month (categorized as no limitations /some of the time/and most of the time). The health status variable was obtained from the survey question asking beneficiaries to rate their current general health condition compared to health condition in the previous year (categorized as better/same/worse). Functional status was measured using the Activities of Daily Living (ADL) scale (including questions addressing difficulty in bathing, dressing, eating, transferring, toileting, and walking) and Instrumental Activities of Daily Living (IADL) scale [including questions addressing difficulty in using the telephone, doing light housework (like washing dishes, straightening up, or light cleaning), heavy housework (like scrubbing floors or washing windows), preparing meals, shopping for personal items (such as toilet items or medicines), and managing money (like keeping track of expenses or paying bills)].[78,79] Variables capturing difficulties in performing ADLs and IADLs were categorized into whether or not the subject had difficulty in performing at least one activity (dichotomous).

To determine chronic comorbidities among the beneficiaries survey data (inquiring about the presence selected disease conditions in the past year) was used. The number of selected comorbid conditions included arthritis, rheumatoid arthritis, diabetes, depression, emphysema, hypertension, osteoporosis, congestive heart disease, myocardial infraction, arrhythmia, cardiac failure, other heart problem, stroke, urinary incontinence, Alzheimer's disease, and Parkinson's disease. The number of medications, both prescription and non-prescription, consumed by beneficiaries in the past year were also included in the analysis.

Regrouping of the covariates: While assessing the factors associated with at-risk drinking the categories of some variables were collapsed and regrouped**.** This was done to achieve adequate size in each cell. Initially, educational status was classified as beneficiaries with: no or less than high school education, high school education, or more than high school education. Since the number of older adults with no education was very small, they were merged with older adults with less than high school education. The variable, limitations in social activities, was categorized as whether or not beneficiaries experienced limitations in social activities due to health conditions (yes/no). Older adults whose social activity was limited, either some of the time or most of the time, were grouped together as "yes".

4.3.5 Missing Data

Data for most of the variables were collected from the MCBS survey. Some of the survey questions contained response items such as "don't know", "refused to answer", and "cannot be ascertained". As these responses could not be utilized in the study, they were deemed as "not available" and were not included in the analysis. Since the frequencies of these "not available" responses were less than 5%, any kind of imputation or sensitivity analyses were not performed. The footnote below Table 4.3 shows the frequency of "not available" response for each of the variables.

4.3.6 Determination of Alcohol Consumption

Data on alcohol use was collected from the MCBS survey. Every alternate year participants of the MCBS are asked three questions addressing their "usual" alcohol use over the past year. The first question is "Please think about a typical month in the past year. On how many days did [you/(sample person (SP))] drink any type of alcoholic beverage?". The second

question enquires about the quantity of alcoholic drinks consumed, “On those days that [you/(SP)] drank alcohol, how many drinks did (you/he/she) have?”. The third questions pertain to heavy episodic drinking “On how many days did [you/(SP)] have 4 or more drinks in a single day?”

The typical monthly alcohol consumption in the past year was measured using the Quantity-Frequency (QF) method.[80] The first two questions inquiring about i) overall frequency of alcohol consumption in the past year and ii) the usual number of drinks consumed on days when the respondent drank were multiplied to estimate monthly alcohol consumption. If the monthly alcohol consumption was estimated to be 31 drinks per month or less then it was considered as within-limit drinking assuming respondents considered 31 days in a month. The monthly alcohol consumption was further categorized into three following groups: i) non-drinkers (respondents who did not consume a single alcoholic beverage in the past year), ii) within-limit drinkers (respondents who consumed 31 drinks or less per month), and iii) exceeding-limit drinkers (respondents who consumed more than 31 drinks per month). Binge drinking or heavy episodic drinking was determined utilizing the third survey question (number of days respondent consumed 4 or more drinks in a single day). Any respondent consuming 4 or more drinks, in a single day, at least once in a month was regarded as a binge-drinker.

4.3.7 Estimation of At-Risk drinking

At-risk drinking was determined by two methods: using the CARET questionnaire and NIAAA definition of at-risk drinking in older adults. According to the NIAAA definition, older adults consuming 4 or more drinks on a given day, or 8 or more drinks in a week, are considered at-risk drinkers.[76] Primarily, at-risk drinking was identified using the CARET, a 7-item validated

questionnaire which classifies subjects into two categories: at-risk or non-at-risk drinkers, based on their alcohol intake, co-morbid conditions as well as medication use.[41,60] It includes 1) comorbid conditions such as high blood pressure, diabetes, depression, gout, hepatitis and other liver conditions, 2) symptoms of feeling sad, memory problems, falling, problem sleeping, heart burn/stomach pain/vomiting/nausea, and tripping/bumping into things, and 3) alcohol-interactive medications including warfarin, antiplatelet medications, nitrates, ulcer medications, antihypertensive agents, opioid analgesics, anticonvulsants, sedatives-hypnotics, sedating antihistaminics, arthritis and pain medications, and psychotherapeutic agents (antidepressants, and anxiolytic). Any older adult satisfying at least one of the conditions (items in the CARET questionnaire) was deemed to be a at-risk drinker. The total number of items that any subject satisfies was also calculated.

The presence of hypertension, diabetes, depression, and history of falls, in the past 12 months, was determined from the MCBS survey questions. *ICD-9-CM* codes[81] from the inpatient and outpatient records were utilized to determine the presence of acute or chronic hepatitis, cirrhosis or any other liver condition, heart burn/stomach pain/nausea/vomiting, and acute and chronic gout. Additionally, use of uricosuric medications (allopurinol, probenecid, colchicine, febuxostat) was indicative of the presence of gout. A problem with memory was determined 1) from the survey question enquiring about the presence of Alzheimer's disease or dementia, and 2) use of any of the following medications: memantine, donezepil, rivastigmine, galantamine.

Table 4.1 Diagnostic Codes for Selected Disease Conditions

Disease Conditions	***ICD-9-CM codes***
Hepatitis, cirrhosis or any other liver condition	570, 571.0-571.9, 572.0-572.8, and 573.0-573.9
Heartburn/stomach pain/nausea/vomiting	530, 531, 532, 533, 534, 525, 577.0-577.1
Acute or chronic gout	274.0-274.9

The information on medication was derived from the medication file that contains both survey and administrative claims data. Selection of alcohol-interactive medications was achieved in two steps. First, the classes of medication enlisted in the CARET questionnaire were selected from the data file. The brand name of the medication was used to do so as that was the medication identifying variable available in the data file. Second, the nature of potential interaction between alcohol and that medication was appraised based on available published literature.[21,29,41] The categories of medications were mutually exclusive. Only those drugs that have been documented to interact with alcohol were included. Medications such as methylphenidate, modafinil-provigil, glargine, prolix, ridilin, memantine, levodopa-carbidopa, fenofibric acid were not included.

A few of the items in the CARET questionnaire including "driving after drinking alcohol" and "bumping or tripping into things" were not collected by the MCBS survey. These variables were not considered while assessing at-risk drinking in the current study. Although the survey did not include question on "problem sleeping", information on assessment of at-risk drinking using CARET was performed based on pre-specified decision rules that have been validated Table 5.3. Respondents who met one or more criteria for at-risk drinking were classified as at-risk drinkers.

Table 4.2 Description of the CARET Questionnaire

Items	Quantity and frequency of alcohol
Comorbid conditions	
High blood pressure Diabetes	≥3 drinks at least 4 times per week, ≥4 drinks at least 2 times per month, ≥5 drinks at any frequency
Acute or chronic gout Depression	≥2 drinks at least 4 times per week, ≥3 drinks at least 2 times per month, ≥4 drinks at any frequency
Acute or chronic hepatitis, cirrhosis or other liver conditions	Any number of drinks at any frequency
Health-related behaviors	
Memory problems occurring often Heart burn/stomach ache/ nausea/vomiting occurring often Falling once or twice	≥3 drinks at least 2 times per week, ≥4 drinks at least 2 times per month, ≥5 drinks at any frequency
Memory problems occurring sometimes Heart burn/stomach ache/ nausea/vomiting occurring sometimes Falling more than twice	≥2 drinks at least 2 times per week, ≥5 drinks at any frequency
Medications (at least 3-4 times a week)	
Antihypertensive medications	≥3 drinks at least 4 times per week, ≥4 drinks at least 2 times per month, ≥5 drinks at any frequency
Blood agents: clopidogrel, aspirin, ticlopidine, dipyridamole, warfarin Gastric medication: proton pump inhibitors, H2 antagonist Nitrates: ISM, ISD, nitroglycerine Pain medications used in arthritis (NSAIDS) Opioid analgesics, Sedatives-hypnotics Anticonvulsants, Psychotherapeutics (antidepressants, anxiolytics, antipsychotics, except CNS stimulants) Non-prescription medication for allergies (anti-histaminics, cough and cold preparations)	≥2 drinks at least 4 times per week, ≥5 drinks at any frequency
Excessive alcohol use	≥3 drinks at least 4 times per week, ≥4 drinks at least 4 times per month, ≥5 drinks at any frequency
Binge drinking	≥4 drinks on one occasion at least once a week or more

*****adapted from the CARET questionnaire**.**

4.3.8 Statistical Analyses

Analysis of the complex survey: The complex sampling design was taken into account during the analysis. Cross-sectional full sample weights have been developed to compensate for non-response, under-coverage, and overlapping coverage of constituent panels. Cross-sectional weights provided for each beneficiary in the dataset reflect the overall selection probability of each sample person. A total of 100 replicate cross-sectional weights developed using Fay's balanced repeated replication (BRR) method, with the Fay coefficient being 0.30, for variance estimation to account for the complex features of the sampling design. The principle behind the replication is "to select subsamples (replicates) from full sample, calculate the statistics of interest for each replicate, and then use these replicate statistics to estimate the variance of full sample statistic".[77,82,83] Thus, both the full-sample weight and the replicate weights are used to compute weighted estimates and their variance.[77,82,83]

Analysis plan for this study: Frequencies and weighted estimates were calculated to describe the study population representing continuously enrolled non-institutionalized Medicare beneficiaries aged 65 years or older surviving through 2009. Chi-square tests were performed to study the bivariate association between at-risk drinking and other covariates. Multi-nominal logistic regression analysis (using SAS procedure PROC SURVEYLOGISITC) was performed to identify the factors associated with at-risk drinking.[84] The multinomial logistic regression model was used to predict probabilities of being either an at-risk drinker or a non-at-risk drinker, compared to non-drinker, given a set of regressor variables (predictors).

Sensitivity analyses were performed to understand the impact of the methodological decisions or assumptions made during the execution of this study. Different definitions of alcohol use were adopted and analyzed to determine the prevalence of at-risk drinking. Weighted analyses were performed to account for the complex sampling design of the study. All analyses were conducted in the SAS version 9.2 and 9.3, at the significance level of $\alpha = 0.05$.

4.4 Results

4.4.1 Characteristics of the Study Sample

Of the 7,163 older adults, 47.5% were aged between 65 and 74 years, 37.0% were between 75 and 84 years of age, and the remaining 15.5% were 85 years or older. The study sample was predominantly white (87.2%), not currently employed (87.5%) and educated (with 77% having high school or advanced level of education). Approximately 57% were female, 53.8% were married, and 53.9% earned more than $25,000 per year. The majority of the older adults (71.8%) did not experience any restriction in their social activity due to health, 18.3% faced it some of the time, and the remaining 9.9% faced it most of the time. A total of 65.5% perceived their general health condition to be same as in the preceding year, however, 20.1% said it worsened and 14.4% said it improved. Although approximately 26% reported having difficulty in performing at least one of the activities of daily living, 74% reported having no difficulty in performing any of the ADLs. A total of 33.5% reported having difficulty in performing at least one of the IADLs but the remaining 66.5% reported having no difficulty in performing any of the IADLs. Most of the study sample have either no smoking history (41.5%) or were former-smokers (49.7%) but only 8.8% reported smoking currently. Approximately 6.7% of the older adults reported not having any disease and 5.1% did not take any medication.

Assessment of comorbidities showed that 34.7% of older adults had 1-2 diseases, 35.4% had 3-4 diseases, and 23.2% had 5 or more diseases. Distribution of medication use reflected polypharmacy with 35.9% older adults taking 1-5 medications, 35.3% taking 6-10 medications, and 23.7% taking more than ten medications. Table 4.3 summarizes the demographic characteristics of the study sample.

Table 4.3 Demographic Characteristics of the Study Population

Variables	Sample persons interviewed	Weighted percent (95% CI)
Age (years)		
65-74	2919	47.51 (46.56-48.47)
75-84	2890	36.95 (35.95-37.94)
85 and older	1354	15.54 (14.73-16.34)
Gender		
Male	3094	43.03 (42.06-44.01)
Female	4069	56.97 (55.99-57.94)
Race		
White	6241	87.23 (86.41-88.06)
Black	586	8.12 (7.54-8.69)
Others	336	4.65 (3.99-5.31)
Marital status		
Married	3723	53.80 (52.47-55.12)
Others	3436	46.20 (44.88-47.53)
Education		
No education	77	0.92 (0.70-1.15)
Less than high school	1707	22.16 (21.08-23.25)
High school	2189	30.75 (29.67-31.82)
More than high school	3164	46.17 (44.75-47.59)
Income		
Less than $25,000	3478	46.06 (44.44-47.68)
More than $25,000	3685	53.94 (52.32-55.56)
Employment		
No	6381	87.52 (86.67-88.37)
Yes	778	12.48 (11.63-13.33)

Limitations in social activity		
No	4965	71.78 (70.55-73.02)
Some of the time	1378	18.32 (17.30-19.35)
Most of the time	768	9.89 (9.15-10.64)
Perceived health status		
Better	1015	14.38 (13.31-15.45)
Same	4594	65.50 (64.40-66.59)
Worse	1506	20.12 (19.36-20.89)
Difficulties in ADL		
No	5166	74.06 (72.83-75.30)
Yes	1997	25.94 (24.70-27.17)
Difficulties in IADL		
No	4603	66.53 (65.37-67.69)
Yes	2560	33.47 (32.31-34.63)
Smoking status		
Never-smoker	3003	41.53 (40.39-42.67)
Former-smoker	3543	49.66 (48.58-50.75)
Current-smoker	595	8.81 (8.09-9.53)
Chronic comorbidities		
No disease	434	6.75 (6.17-7.33)
1-2	2380	34.67 (33.35-35.99)
3-4	2584	35.42 (34.41-36.42)
5 or more	1765	23.16 (22.04-24.29)
Number of medications		
No medication	346	5.13 (4.52-5.74)
1-5	2482	35.89 (34.58-37.20)
6-10	2557	35.29 (34.18-36.41)
11 or more	1778	23.69 (22.49-24.89)
The following indicates covariates and its corresponding frequencies for responses deemed as "not applicable (NA)"		
Income=4	Marital status=4	Education=26
Social activity=52	Smoking status=22	Perceived health=48

4.4.2 Prevalence and Pattern of At-Risk Drinking

The prevalence of current drinkers who reported drinking at least one drink in the past 12 months was estimated to be 34.9% (95% CI: 33.2-36.7 %, n=2316, missing=73). Binge drinking, defined as consuming 4 or more drinks in a single day, was reported to be 4.6% (95% CI: 3.9-5.3 %, n=295). Table 4.4 compares rates of at-risk drinking measured by

more than one method. According to NIAAA guidelines, 11.5% (95% CI: 10.3-12.6 %) of the study population were determined to be at-risk drinkers and 23.2% (95% CI: 22.0-24.4 %) were non-at-risk drinkers. Older adults are advised to consume not more than one drink per day or seven drinks in a week by NIAAA guidelines.[76] As per this recommendation, 28.4% (95% CI: 27.0-29.8 %) of the older adults consume alcohol within the NIAAA recommended limits and 6.3% (95% CI: 5.8-7.2 %) drink alcohol more than the NIAAA recommended limits. Ninety-six older adults provided responses, for at least one of the first two survey questions enquiring alcohol use, which could not be utilized in the analysis. Of the 7163 community-dwelling older adults included in this study, 5.6% (95% CI: 4.8-6.4 %) were assessed to be at-risk drinkers and 29.1% (95% CI: 27.6-30.5 %) were non-at-risk drinkers based on the CARET questionnaire. Non-drinkers comprised 65.3% (95% CI: 63.6-67.1 %) of the study population.

Table 4.4 Prevalence of At-Risk Drinking

Variables	Total		Men		Women	
	N	Weighted Percent (95% CI)	N	Weighted Percent (95% CI)	N	Weighted Percent (95% CI)
Pattern of alcohol use (NIAAA guidelines)						
Non-drinker	4774	65.32 (63.56-67.07)	1800	57.21 (54.79-59.63)	2974	71.43 (69.54-73.32)
Within-limit drinker	1890	28.39 (27.01-29.78)	957	32.54 (30.57-34.51)	933	25.27 (23.59-26.95)
Exceeding-limit drinker	403	6.29 (5.39-7.19)	290	10.25 (8.53-11.97)	113	3.30 (2.64-3.97)
At-risk drinking (NIAAA guidelines)						
Non-drinker	4774	65.32 (63.56-67.07)	1800	57.21 (54.79-59.63)	2974	71.43 (69.54-73.32)
Non-at-risk drinker	1544	23.23 (22.02-24.44)	760	25.92 (24.18-27.65)	784	21.21 (19.64-22.78)
At-risk drinker	749	11.45 (10.29-12.61)	487	16.87 (14.87-18.88)	262	7.36 (6.36-8.37)
At-risk drinking (based on CARET)						
Non-drinker	4774	65.32 (63.56-67.07)	1800	57.21 (54.79-59. 63)	2974	71.43 (69.54-73.32)
Non-at-risk drinker	1927	29.07 (27.63-30.52)	977	33.27 (31.27-35.28)	950	25.91 (24.15-27.66)
At-risk drinker	366	5.61 (4.82-6.40)	270	9.52 (8.05-10.98)	96	2.67 (2.04-3.29)

***** N= No. of sample persons interviewed
Total sample persons =7067, weighted frequency of total sample persons= 19760750, No. of missing = 96
Bivariate analysis (chi-square test) between gender and at-risk drinking was significant p-value <0.05

Table 4.5 Pattern of At-Risk Drinking (Based on CARET Items)

Reasons for identifying at-risk drinker	At-risk drinkers		Non-at-risk drinker	
	Sample persons	Weighted percent 95% CI	Sample persons	Weighted percent 95% CI
Regular alcohol use	155	6.86 (5.66-8.07)	2139	93.14 (91.94-94.34)
Heavy episodic drinking	131	5.98 (4.77-7.19)	2163	94.02 (92.82-95.23)
Medical conditions				
High blood pressure	68	3.13 (2.21-4.04)	2224	96.87 (95.96-97.79)
Gout	26	1.24 (0.80-1.68)	2267	98.76 (98.32-99.20)
Diabetes	21	1.13 (0.62-1.65)	2270	98.87 (98.35-99.38)
Depression	31	1.32 (0.85-1.78)	2261	98.68 (98.22-99.15)
Liver diseases	-		2293	100.00
Health-related behavior				
Memory problems	17	0.68 (0.37-0.99)	2275	99.32 (99.01-99.63)
Heartburn/stomach pain/ nausea/vomiting	18	0.73 (0.34-1.12)	2276	99.26 (98.88-99.65)
History of a fall	51	2.32 (1.64-3.00)	2232	97.68 (96.99-98.36)
Medication use				
Antiplatelets	29	1.36 (0.79-1.93)	2264	98.64 (98.07-99.21)
Arthritis and pain medicines	44	2.02 (1.39-2.65)	2249	97.98 (97.35-98.61)
Ulcer/stomach medicines	88	3.89 (2.95-4.83)	2205	96.11 (95.17-97.05)
Antihypertensive medicines	91	4.14 (3.13-5.15)	2203	95.86 (94.85-96.87)
Nitrates	17	0.79 (0.39-1.19)	2276	99.21 (98.81-99.61)
Warfarin	34	1.32 (0.82-1.82)	2259	98.68 (98.18-99.19)
Non-prescription medicines	32	1.40 (0.88-1.92)	2261	98.60 (98.09-99.12)
Psychotherapeutics	68	3.00 (2.30-3.70)	2225	97.00 (96.29-97.70)
Anticonvulsants	24	1.01 (0.65-1.37)	2269	98.99 (98.63-99.35)
Sedatives/hypnotics	25	1.13 (0.74-1.52)	2268	98.87 (98.48-99.26)
Opioid analgesics	82	3.45 (2.61-4.29)	2211	96.55 (95.71-97.39)

*Denominator: 2293 older adults (includes drinkers only). The rows add up to 100 and are statistically different with p-value less than 0.0001 (Rao-Scott Chi-square analyses).

Of the 2,293 drinkers, 7.6% (95% CI:6.3-8.9 %, n=167) were regarded as "at-risk drinker" owing to their alcohol consumption in the presence of selected disease states. Similarly, 12.2% (95% CI: 10.5-13.8 %, n=276) of the drinkers were considered "at-risk" due to alcohol and medication use, and 8.9% (95% CI: 7.5-10.3 %, n=198) for their higher than recommended alcohol intake.

Of the 2,293 drinkers, 7.4% (95% CI: 6.2-8.6 %) satisfied three or more items in the CARET questionnaire, 3.7% (95%CI: 2.9-4.5 %) fulfilled two items, and 5.1% (95%CI: 4.0-6.2%) fulfilled one item in the CARET questionnaire. Use of antihypertensive medications, anti-ulcer medications, and opioid analgesics, presence of hypertension and history of falls (in the presence of alcohol use of a specified amount) were some of the common factors rendering older adults at-risk drinkers (Table 4.5).

4.4.3 Predictors of at-risk drinking

Bivariate analyses were conducted to study the association between each covariate and at-risk drinking (Table 4.6). The Rao-Scott Chi-square analyses found that age, gender, race, marital status, education, employment, income, perceived health status, difficulties in ADL, difficulties in IADL, chronic comorbidities, polypharmacy, and limitations in social activity were significantly associated with at-risk drinking with p-value <0.0001.

Table 4.6 Distribution of Socio-demographic Characteristics in the Drinking Groups

Variables	Non-drinker		Non-at-risk drinker		At-risk drinker	
	N	Weighted Percent (95% CI)	N	Weighted Percent (95% CI)	N	Weighted Percent (95% CI)
Age (years)						
65-74	1775	59.99 (57.75-62.23)	889	32.73 (30.78-34.69)	203	7.28 (6.07-8.48)
75-84	1980	67.65 (65.47-69.82)	757	27.70 (25.84-29.57)	125	4.65 (3.76-5.55)
85 and older	1019	75.94 (73.55-78.34)	281	21.22 (19.06-23.38)	38	2.84 (1.90-3.78)
Gender						
Male	1800	57.21 (54.79-59.63)	977	33.27 (31.27-35.28)	270	9.52 (8.05-10.98)
Female	2974	71.43 (69.54-73.32)	950	25.91 (24.15-27.66)	96	2.67 (2.04-3.29)
Race						
White	4039	63.19 (61.27-65.11)	1783	30.72 (29.14-32.31)	345	6.09 (5.20-6.97)
Others	735	80.10 (77.10-83.10)	144	17.59 (14.68-20.50)	21	2.31 (1.16-3.45)

Marital Status						
Married	2298	60.20 (57.91-62.48)	1161	33.17 (31.22-35.12)	222	6.63 (5.64-7.63)
Others	2475	71.30 (69.49-73.11)	765	24.28 (22.74-25.83)	144	4.42 (3.52-5.32)
Education						
No or less than high	1475	82.37 (79.87-84.88)	230	14.15 (12.03-16.27)	56	3.48 (2.26-4.71)
school	1553	70.25 (67.71-72.80)	525	24.80 (22.87-26.73)	92	4.95 (3.53-6.37)
High school	1724	53.24 (50.84-55.63)	1170	39.60 (37.46-41.74)	218	7.16 (6.05-8.28)
More than high school						
Income						
$25,000 or less	2729	78.46 (76.50-80.42)	600	18.46 (16.79-20.12)	98	3.08 (2.32-3.85)
More than $25,000	2045	54.09 (52.05-56.14)	1327	38.14 (36.31-39.97)	268	7.77 (6.71-8.83)
Employment						
No	4353	67.10 (65.31-68.99)	1635	27.61 (26.10-29.14)	314	5.29 (4.50-6.08)
Yes	420	52.82 (48.72-56.92)	291	39.35 (35.25-43.46)	51	7.83 (5.45-10.20)
Limitations of social						
activity	3074	60.32 (58.36-62.28)	1566	33.43 (31.75-35.10)	286	6.25 (5.36-7.15)
No	1692	77.94 (76.11-79.76)	360	18.06 (16.39-19.72)	80	4.00 (3.13-4.89)
Yes						
Perceived health status						
Better	693	66.99 (62.70-71.27)	265	27.35 (23.70-31.01)	54	5.66 (3.96-7.37)
Same	2948	62.37 (60.46-64.28)	1356	31.63 (29.92-33.33)	253	6.00 (5.08-6.93)
Worse	1128	73.61 (71.17-76.06)	306	22.07 (19.70-24.45)	59	4.32 (3.18-5.45)
Difficulties in ADL						
No	3247	61.55(59.46-63.65)	1547	32.30 (30.49-43.10)	292	6.15 (5.28-7.02)
Yes	1527	75.96 (73.95-77.97)	380	19.95 (18.05-21.86)	74	4.09 (2.99-5.18)
Difficulties in IADL						
No	2810	59.79 (57.74-61.85)	1443	33.76 (31.98-35.54)	270	6.45 (5.44-7.46)
Yes	1964	76.18 (74.26-78.10)	484	19.85 (18.21-21.50)	96	3.97 (3.16-4.77)
Smoking status						
Never-smoker	2241	72.96 (71.02-74.90)	660	24.48 (22.65-26.31)	65	2.56 (1.93-3.18)
Former-smoker	2151	59.14 (56.75-61.52)	1126	33.59 (31.62-35.56)	239	7.27 (6.12-8.43)
Current-smoker	381	64.25 (60.31-68.20)	141	25.12 (21.44-28.79)	62	10.63 (7.69-13.57)
Chronic comorbidities						
No disease	240	52.97 (47.52-58.42)	157	39.83 (34.47-45.20)	30	7.20 (4.63-9.76)
1-2	1394	57.69 (55.29-60.09)	792	35.60 (33.31-37.89)	145	6.71 (5.44-7.98)
3-4	1773	67.61 (65.19-70.03)	662	27.05 (25.04-29.07)	125	5.34 (4.38-6.29)
5 or more	1367	76.68 (74.42-78.95)	316	19.38 (17.35-21.40)	66	3.94 (2.78-5.10)
Number of medications						
No medication	203	58.73 (52.30-65.15)	116	34.79 (28.31-41.27)	23	6.48 (3.86-9.11)
1-5	1524	60.10 (57.97-62.23)	786	34.17 (32.15-36.19)	128	5.73 (4.48-6.98)
6-10	1728	66.09 (63.50-68.68)	667	28.22 (26.11-30.34)	132	5.69 (4.56-6.81)
11 or more	1319	73.44 (71.19-75.70)	358	21.43 (19.36-23.49)	83	5.13 (4.08-6.18)

Table 4.6 shows the distribution of at-risk drinking for each covariate. Compared to other age groups, 65-74 years age group had higher proportions of at-risk drinkers. Similarly, greater number of males and whites were at-risk drinkers compared to females and older adults of other races, respectively. Relatively higher proportions of at-risk drinkers had attained more than high school education, earned more than $ 25,000 per year, and were employed. Proportions of at-risk drinkers with no difficulties in performing ADLs or IADLs; with either no disease or having1-2 disease; with health status not limiting to their social activity; and with perceived health status being same as previous year, were higher than other corresponding covariate category, suggesting that at-risk drinkers seemed to have better functional status.

Table 4.7 Factors Associated with At-Risk Drinking

Variables	Non-at-risk drinker	p-value	At-risk drinker	p-value
Age				
85 and older	1 (ref)		(ref)	
75-84	1.18 (1.01-1.37)	0.0356	1.47 (0.99-2.18)	0.0568
65-74	1.24 (1.04-1.48)	0.0151	2.22 (1.50-3.30)	<.0001
Gender				
Female	(ref)		(ref)	
Male	1.15 (1.01-1.30)	0.0356	3.16 (2.31-4.34)	<.0001
Race				
White	(ref)		(ref)	
Others	0.65 (0.52-0.82)	0.0002	0.39 (0.22-0.67)	0.0007
Marital status				
Married	(ref)		(ref)	
Others	1.04 (0.91-1.18)	0.6095	1.42 (1.09-1.87)	0.0107
Education				
More than high school	(ref)		(ref)	
High school	0.57 (0.49-0.66)	<.0001	0.69 (0.50-0.97)	0.0327
No or less than high school	0.36 (0.29-0.44)	<.0001	0.50 (0.33-0.77)	0.0018
Income				
More than 25,000	(ref)		(ref)	
Less than 25,000	0.53 (0.45-0.63)	<.0001	0.41 (0.31-0.53)	<.0001

Employment				
No	(ref)		(ref)	
Yes	1.14 (0.92-1.40)	0.2294	1.01 (0.69-1.49)	0.9309
Limitations in social activity				
No	(ref)		(ref)	
Yes	0.65 (0.54-0.77)	<.0001	0.75 (0.56-1.00)	0.0476
Perceived health status				
Worse	(ref)		(ref)	
Same	1.07 (0.89-1.28)	0.4770	1.20 (0.84-1.71)	0.3144
Better	0.93 (0.72-1.20)	0.5933	1.08 (0.70-1.67)	0.7172
Difficulties in ADL				
No	(ref)		(ref)	
Yes	0.95 (0.79-1.14)	0.5552	0.98 (0.68-1.43)	0.9305
Difficulties in IADL				
No	(ref)		(ref)	
Yes	0.88 (0.75-1.03)	0.1071	1.00 (0.71-1.40)	0.9827
Smoking status				
Never-smoker	(ref)		(ref)	
Former-smoker	1.64 (1.44-1.87)	<.0001	2.55 (1.89-3.43)	<.0001
Current-smoker	1.29 (1.02-1.63)	0.0308	3.89 (2.56-5.90)	<.0001
Chronic comorbidities				
5 or more	(ref)		(ref)	
3-4	1.20 (1.02-1.42)	0.0287	1.26 (0.87-1.81)	1.5018
1-2	1.53 (1.29-1.81)	<.0001	1.72 (1.18-2.53)	0.0053
No disease	1.71 (1.27-2.32)	0.0005	1.85 (1.06-3.25)	0.0313
Number of medications				
11 or more	(ref)		(ref)	
6-10	1.15 (0.97-1.37)	0.1195	0.94 (0.70-1.27)	0.6808
1-5	1.19 (1.00-1.42)	0.0536	0.77 (0.55-1.07)	0.1155
No medication	1.17 (0.81-1.69)	0.4169	0.74 (0.41-1.35)	0.3267

A multi-nominal logistic regression model was built to identify factors associated with at-risk drinking and non-at-risk drinking (results in Table 4.7). Older adults belonging to the 65-74 year age group were at higher odds (odds ratio: 2.22, 95%CI: 1.50-3.30) of being at-risk drinkers than older adult aged 85 years or older. Similarly, older adults aged between 65 to 74 years were at 24% higher odds (odds ratio: 1.24, 95%CI: 1.04-1.48) of being non-at-risk drinkers than older

adult aged 85 years or older. Older men were at higher odds of being at-risk drinkers (odds ratio: 3.16, 95%CI: 2.31-4.34) and non-at-risk drinkers (odds ratio: 1.15, 95%CI: 1.01-1.30) compared to women. Older adults of non-white race were less likely to be at-risk drinkers (odds ratio: 1.42, 95%CI: 1.09-1.87). Compared to married older adults, non-married older adults were at higher odds (odds ratio: 1.42, 95%CI: 1.09-1.87) of indulging in at-risk drinking. Older adults with a high school or less than a high school education were at lower odds of being at-risk drinkers and non-at-risk drinkers than older adults with more than a high school education (includes college educated or graduate degree). Older adults with annual income less than $25,000 were less likely to be at-risk drinkers (odds ratio: 0.41, 95%CI: 0.31-0.77). A similar association was observed between non-at-risk drinking and lower income. Employment status was not significantly associated with at-risk drinking in this population where many of the participants were no longer in the workforce.

Perceived health status and functional status as measured by ADLs, and IADLs were not significantly associated with at-risk drinking. Older adults experiencing limitations in social activity owing to their health were less likely to be a non-at-risk drinker (OR: 0.65, 95%CI: 0.54-0.77). The number of chronic comorbidities was found to be significantly associated with at-risk drinking. Compared to older adults suffering from five or more chronic conditions, older adults with no or with less than five disease conditions were more likely to indulge in at-risk drinking as well as non-at-risk drinking. A linear relationship was observed wherein as the number of comorbidities decreases the magnitude of odds of at-risk drinking increases. Number of medication taken by older adults was not significantly associated with at-risk drinking. Former smokers (OR: 2.55, 95% CI: 1.89-3.43) and current smokers (OR: 3.89, 95% CI: 2.56-5.90)

showed greater odds of being at-risk drinkers compared to those who have never smoked before (never-smoker).

4.4.4 Sensitivity Analyses

Sensitivity analyses were performed to understand how the results are affected by changing the methodological decisions or assumptions made during the process of data analysis. Quantity and frequency of alcohol use is the principal component of at-risk drinking. In addition, measuring alcohol consumption is subject to high variability. Hence, it is essential to determine how the prevalence of at-risk drinking changes by altering the alcohol use limits.

A. *Sensitivity Analysis on Prevalence of At-risk Drinking*: Different definitions of at-risk drinking were applied and the following are the conditions and the results of those scenarios:

1) At-risk drinkers were defined as those who experience the diseases and health-related behaviors and/or take medications mentioned in CARET, and consume alcohol (including those who drink within-limit and exceeding limit recommended by NIAAA). In this analysis, older adults consuming 4 or more drinks in a single day were also regarded as at-risk drinkers. 30.98% (95% CI: 29.38-32.58, n=2061) were found to be at-risk drinkers, 3.70% (95% CI: 3.19-4.21, n=232) were non-at-risk drinkers. The Rao-Scott Chi-square test showed proportions were significantly different (p-value <0.0001).
2) At-risk drinkers were defined as those who experience the diseases and health-related behaviors and/or take medications mentioned in CARET, and consume alcohol at an exceeding limit (by NIAAA definition). 5.36% (95% CI: 4.52-6.20, n=343) were considered as at-risk drinkers and 29.33% (95% CI: 27.92-30.73, n=1950) were non-at-

risk drinkers. Heavy episodic drinkers were not included in this analysis. The Rao-Scott Chi-square test showed proportions were significantly different (p-value <0.0001).

3) At-risk drinkers were defined as those who experience the diseases and health-related behaviors and/or take medications mentioned in CARET and exhibit heavy episodic drinking only. 3.78% (95%CI: 3.20-4.37, n=242) were at-risk drinkers and 30.95% (95% CI: 29.38-32.51, n=2053) were non-at-risk drinkers. The Rao-Scott Chi-square test showed proportions were significantly different (p-value <0.0001).
4) At-risk drinkers were defined as those who show the presence of diseases, medications, and/or health-related behaviors mentioned in CARET and exhibit heavy episodic drinking as well as drinking that exceed limit. 6.77% (95% CI: 5.85-7.69, n=436) were at-risk drinkers and 27.96% (95% CI: 26.6-29.3 %, n=1,859) were non-at-risk drinkers. The Rao-Scott Chi-square test showed the proportions were significantly different (p-value <0.0001).
5) At-risk drinkers were defined as those who show the presence of diseases, medications, and/or health-related behaviors mentioned in CARET and consume alcohol ≥4 drinks/day or ≥8 drinks/week (NIAAA guideline for at-risk drinking). 9.82% (95% CI: 8.74-10.89 %, n=645) were at-risk drinkers and 24.87 (95% CI: 23.56-26.17 %, n=1648) were non-at-risk drinkers. The Rao-Scott Chi-square test showed the proportions were significantly different (p-value <0.05).

B. Alcohol use among excluded subjects

Alcohol use among those excluded for having partial/complete paralysis and/or amputation leading to loss of arm or leg was studied. A total of 371 subjects were excluded from the final sample. After removing two subjects from analysis due to missing data on alcohol consumption, 70.2% (95% CI: 64.8-75.6 %) were non-drinkers, 26.3% (95% CI: 21.3-31.3 %) were within limit drinkers, 3.5% (95% CI: 1.5-5.6 %) were exceeding limit drinkers, and 7.7% (95% CI: 4.7-10.7 %) were at-risk drinkers (NIAAA definition).

C. Alcohol use among all the subjects in Access to Care module

Alcohol use among all community-dwelling older adults, aged 65 years or older and surviving through 2009, present in the Access to Care module was studied. A total of 11,393 community-dwelling older adults surviving through 2009, were present in Access to Care module. After removing 119 subjects from the analysis due to missing data on alcohol consumption, 63.7% (95% CI: 62.1-65.2 %) were non-drinkers, 29.8% (95% CI: 28.5-31.0 %) were within limit drinkers, 6.5% (95% CI: 5.9-7.2 %) were exceeding limit drinkers, and 11.9% (95% CI: 11.1-12.8 %) were at-risk drinkers.

D. Proxy Respondents

Proxies were designated when participants were too ill or could not complete the community interview for other reasons. Among the 7,163 study subjects, 7.4% were proxy respondents (n=531). The relationship between the participants and their proxy was collected and assessed. Of the 531 proxy respondents 46.7% were the spouse, 30.1% were a daughter, and 8.5% were a son of the participants.

4.4 Discussion

This population-based cross-sectional study was conducted to understand the prevalence and pattern of at-risk drinking and factors associated with at-risk drinking among community-dwelling Medicare beneficiaries, aged 65 years or older, surviving through 2009. The prevalence of at-risk drinking, based on the CARET questionnaire, was estimated to be 5.6% (95% CI: 4.8-6.4). Age, gender, race, marital status, educational level, income, smoking status, comorbidity, and limitations to social activity were the factors associated with at-risk drinking in this population.

In this study, at-risk drinking was assessed by more than one method. Apart from using the CARET questionnaire, the NIAAA definition of at-risk drinking for older adults was also utilized to determine at risk drinking.[76,41,60] Based on the NIAAA definition, the prevalence of at-risk drinking was estimated to be 11.5% (95% CI: 10.3-12.6). The substantial difference between the two rates could be attributed to the criteria for the NIAAA guidelines and the CARET decisions. The NIAAA guideline defines at-risk drinking in terms of quantity and frequency of alcohol use i.e. consuming 4 or more drinks on a given day, or 8 or more drinks in a week. The CARET describes at-risk drinking not only in terms of quantity and frequency of alcohol use, but also addresses use of alcohol in the presence of alcohol interactive disease and medication use. Hence, sensitivity analyses were performed to understand how the prevalence of at-risk drinking varies under different conditions of alcohol consumption. In the sensitivity analyses, prevalence of at-risk drinking was determined by using different definitions of "risky" alcohol use while keeping the CARET specified disease conditions, health-related behaviors, and medications constant. Sensitivity analyses showed that depending upon the different definitions of alcohol use, at-risk drinking may range from 4% to 31%.

Two studies have investigated at-risk drinking in U.S. older samples employing the CARET tool. Analysis of 1971-1974 NHANES I data estimated 10% at-risk drinking (n=425) among 4,691 U.S. civilian non-institutionalized older adults aged 60-74 years.[60] Barnes et al found 34.7% of the 3,308 currently drinking older adults aged 60 years or more, in Santa Barbara, California area were at-risk drinkers.[42] It must be noted that the above two studies included adults aged between 60 to 64 years that has not been included in the current study. In addition, a Finnish study examining at-risk drinking, using the NIAAA guideline definition of at-risk drinking among a randomly selected sample of older adults aged 65 year or older found that 8.2% of the 2,100 older adults were at-risk drinkers.[67]

In this study, 75.1% (95% CI: 70.0-80.2 %) of the at-risk drinkers were categorized as such due to their alcohol interactive medication use, 46.8% (95% CI 40.6-53.0 %) due to their disease profile and health-related behaviors, and 55.2% (95% CI: 50.1-60.4 %) due to their pattern of alcohol use. Patterns of at-risk drinking in the NHANES I study showed that 69% of at-risk drinkers were classified as such because of their alcohol consumption combined with comorbidities.[60] The SHARE study found that 64.3% were at-risk drinkers due to alcohol behavior, 61.9% were deemed at-risk drinkers owing to alcohol use in the presence of select comorbidities, and 61.0% were classified as at-risk drinkers due to medication use combined with alcohol consumption.[42] Our study found antihypertensive medications, ulcer/stomach medications and, opioid analgesics, presence of hypertension, and history of falls, to be some commonly identified items responsible for classification as an at-risk drinker. The NHANES I study reported presence of gout, ulcer, and anxiety disorder as the three most common comorbidities associated with at-risk drinking, medication for pain and indigestion, and insomnia as the three most frequently consumed medications associated with at-risk drinking. [60] The study

by Ryan et al. assessed the drinking pattern of older adults with chronic medical conditions. Seven percent of the Medicare beneficiaries with one or more of the seven chronic conditions (Alzheimer's disease and other senile dementia, chronic obstructive pulmonary disease, depression, diabetes, heart failure, hypertension, and stroke) reported at-risk drinking (defined as those who exceeded monthly limits but not the single-day limit and heavy episodic drinkers who exceeded the single day limit, with or without exceeding the monthly limit).[55] 6.9% of the older adults with hypertension reported drinking in excess of current guidelines. At-risk drinking prevalence was reported as 3.4% in persons with Alzheimer's disease, 7.4% in persons with COPD, and 4.5% in persons with diabetes.[55]

Many studies have defined unhealthy drinking based on the NIAAA recommendation of "not more than one drink per day or seven per week" for older adults. Examination of 2003 MCBS data showed that 3.8% of 10,523 older adults (community-dwelling, fee-for-service Medicare beneficiaries aged 65 years or older) reported consuming more than 30 drinks per month, and 5.4% reported heavy episodic drinking.[28,55,56] This pattern of heavy alcohol consumption is very similar to that found in our study. Secondary analysis of the 2005 and 2006 National Survey on Drug Use and Health data performed among 4,236 older adults aged ≥65 years established that 13% of men and 8% of women were at-risk drinkers (defined as two or more drinks on a usual drinking day within the past 30 days).[74] A study in the non-institutionalized Belgian elderly population (n=4,825) found 50.4% were non-or-occasional drinkers (mean of zero glasses/week), 29.1% were moderate drinkers (1-7 glasses/week), 10.4% were at-risk drinkers (8-14 glasses/week), 4.6% were heavy drinkers (15-21 glasses/week), and 5.5% problematic drinker (>21 glasses/week).[85] A German study conducted on 3,224 non-demented subjects aged 75 years or older and attending general practitioners, identified 6.5%

(95% CI: 5.6-7.4), of the sample as at-risk drinkers (defined as intake of >30g/day of alcohol for men and >20g/day of alcohol for women).[75]

In this study we identified that older adults aged between 65-74 years were more likely to be at-risk drinkers than those aged 85 years or older. Most studies have reported comparatively higher intake of alcohol by younger elderly than the older ones, thus, as age increases, alcohol consumption decreases. [42,66,85] As reflected by most of the studies, older men tend to drink more than older women.[42,66,75,85,106] Similar to the Barnes et al findings, we found that whites consume more alcohol than individuals of other races.[42] Education and income were recognized as determinants associated with at-risk drinking. Older adults with higher education and higher income may be inclined to consume alcohol at a level considered harmful. Such association of at-risk drinking with education and income was also evident in other studies. [42,61,66,106] Contrary to the findings of other studies[42,61,66] , older adults who lived alone (were separated, widowed, divorced, unmarried) were more likely to be at-risk drinkers when compared to those who were married or were living with partner. A similar observation was made by Merrick et al (2008) reporting higher prevalence of unhealthy drinking by divorced or single older adults. Interestingly, the aforementioned study was conducted using MCBS data.[28] In light of the inconsistent association between marital status and at-risk drinking, a detailed analysis is warranted.

Having one or more comorbid conditions is inversely associated with at-risk drinking and even with non-at-risk drinking. This might suggest that healthier older adults tend to consume more alcohol. ADL, IADL, and perceived health status did not show any significant relationship with at-risk drinking. Not many studies have investigated ADL, IADL and alcohol consumption. A few studies that investigated the relationship between at-risk drinking and self-reported health

status also failed to establish any significant association.[61,67,85] Several studies have established positive association between alcohol intake and at-risk drinking with smoking status. [42,61,67] This seems to strengthen the supposition that subjects, who are currently using a substance of abuse or with the history of the same, may be more prone to at-risk drinking, or problematic alcohol use. Besides, there may be a possibility that the data or this analysis has failed to capture other important aspect of at-risk drinking.

Comparison of our findings with other epidemiological studies is difficult because the setting of the study, the study population, definitions of at-risk drinking, and assessment tools vary from study to study. However, the pattern of alcohol consumption estimated by our study is comparable with the findings of other studies. This study assessed the relationship of at-risk drinking with various socio-demographic factors as well as health-related factors (ADL, IADL, health status, comorbidity, and medication use) providing an understanding of elements connected with at-risk drinking among older adults. The weighted estimates from the study represent the national population of older adults in U.S. in the year 2009. The MCBS consists of survey as well as administrative claims data, thus, enabling the analyses to include large number of variables in the analysis.

Like all studies, our study also has some limitations. There may be underestimation of the prevalence of at-risk drinking determined by this study due to various reasons enlisted below:

1. It could be due to inability to obtain data for all the items mentioned in the CARET. Items including “how many days did you drive a vehicle within 2 hours of drinking 3 or more drinks”, and “how much of the time you have the following problems: i) feeling sad and blue, and ii) tripping, bumping into things” were not included in this study due to lack of this

information in the dataset. The proportion of older adults who drink alcoholic beverage and drive exhibiting risky behavior were not captured in this study due to absence of that information in the dataset. A study found that among older drivers involved in fatal crashes, 5% had blood alcohol concentration (BAC) of 0.08 grams per deciliter (g/dL) or higher.[86]

2. Besides translating and matching the MCBS data with the CARET questionnaire and decisions may have led to loss of information or misclassification. This could be due to the difference in the categorization of items in the CARET and the MCBS survey questions regarding alcohol use. For example, in the CARET questionnaire, subjects were asked to report frequency of their alcohol consumption by choosing one of the following items: never, once a month or less, 2-4 times a month, once a week, 2-3 times a week, 4-5 times a week, 6-7 times a week. While in MCBS subjects are asked to provide the frequency (numerical) of alcohol use in a typical month. No items are provided in the frequency question (to categorize their frequency of consumption). So while matching the frequency of alcohol consumption of a subject to the items in CARET loss of information or misclassification may have resulted.
3. Health utilization data for HMO-covered incidents were not available in the dataset; hence, the inpatient and outpatient hospitalization records of a proportion of individuals were not available. This may misclassify some older adults who could be at-risk drinkers due to their liver conditions or presence of gout, but due to lack of data were classified as non-at-risk drinker in this study. Moreover, mostly severe cases of gout or liver conditions require hospitalization hence the cases that did not result in hospitalization were not considered in this study.

4. Some studies assess at-risk drinking among the current-drinkers, and thus the denominator comprises of current drinkers. But in our study, the denominator comprised of the entire study population (except subjects with missing information n=96).
5. Some studies have included adults aged 60 years or older. This study defined older adults as aged 65 years or older. Hence, older adults aged 60-65 years were not included in the analysis.
6. On comparing the prevalence of alcohol use reported using the NHANES data and the MCBS data, it can be seen that the number of older adults identifying themselves as non-drinkers was 47.85% (95% CI: 44.07-51.63) in the NHANES study while it was 65.32% (95% CI: 63.56-67.07) in the MCBS study. This may suggest that some proportion of under-reporting could be attributed to the source collecting the information. It should be noted that CMS collects MCBS data so some older adults may be hesitant revealing their alcohol intake to the federal health insurance agency.
7. Proxy responses and inability to accurately recall may lead to underreporting of alcohol use.
8. There is likelihood that alcohol dependent or abuse patients may be under-represented in the survey itself.
9. There is a possibility that some non-drinkers may include former drinkers who stopped drinking due to health conditions, side effects of alcohol, or other factors.

Another important limitation is the possibility of intentional under-reporting of alcohol consumption by older adults driven by social desirability response bias.[87,88] Studies have shown that individuals are reluctant to admit indulging in unpopular behaviors such as alcohol intake, to avoid creating a negative impression.[87,88] A study involving undergraduate students found that students who were impression managers reported 20 to 33% less alcohol consumption, and were

about 50% less likely to report risky drinking.[87,88] Social desirability response bias results in underestimating the rate of heavy drinking, however, this bias does not compromise the study of predictors of heavy drinking.[87,88] And self-reporting of alcohol consumption is regarded as a reliable and valid approach of estimating alcohol consumption.[87]

Another factor correlated to possible under-reporting was the quantity-frequency (QF) approach of measuring alcohol consumption. Questions about "typical" frequency of alcohol consumption or "on average" number of alcoholic beverage consumed, may lead to underestimates alcohol consumption.[71,89] When subjects are questioned about their average intake over the past period they tend to report median rather than mean, apparently because they fail to consider the occasional high drinking episodes.[71,89] Studies have shown that the diary method of data collection yields higher mean quantity of alcohol consumed than QF measure.[71,89]

Questions about alcohol consumption pertained to "standard drinks" of alcohol that may be misinterpreted by older adults providing biased information.[55,90] The assumption that older adults can consider the definition of size of standard drink while reporting their alcohol consumption may not hold leading to misclassification bias. Information on types of alcoholic beverages consumed (i.e. wine, beer, spirits) was not collected. Different types of alcoholic beverage have different impact on health. For example two glasses of hard liquor or wine will have different health implications.[90]

There was no way to ascertain if the alcohol consumption was concurrent with medication use in older adults. The CARET question inquires about the medication used by older adults "at least 3-4 times a week". Since the dose and frequency of medication use could not be determined from the MCBS data, it was assumed that all of the medications were consumed at

least 3-4 times a week. This may lead to an over-estimation of medication use. Nonetheless, most of the CARET enlisted medications are used for chronic conditions and taken regularly by older adults, such as antihypertensives, nitrates, antidepressants, anticonvulsants, arthritis and pain medications, warfarin, aspirin, and anxiolytics/sedatives. There is a possibility of individuals with dementia or memory problem not being able to provide accurate information. Moreover, a reference period of 12 months could be too long resulting in recall bias or misclassification bias. Proxy responses may not provide accurate insights on health related behaviors.[91] Association between at-risk drinking and past use of illicit drugs has been documented in the literature.[92] Apart from information on smoking, the MCBS does not capture data on current or past use of other substances of abuse such as heroin, cocaine, and marijuana. Combined use of alcohol and illicit drugs is also considered "risky" behavior but it could not be captured in this study.

This study is generalizable to community-dwelling older adults and does not include institutionalized older adults. The MCBS data only includes older Medicare beneficiaries (older adults who are eligible for Social Security payments), thus, older adults not enrolled in Medicare were not included. As the MCBS is a survey including Medicare beneficiaries voluntarily participating in the survey, the results of this study are not applicable to non-responders. However, it should be noted that the weighting process takes into account the non-responder's bias, attrition rate and post-stratification bias.

This study shows that at-risk drinking is prevalent among older adults and identifies factors associated with at-risk drinking. Considering the proportion of at-risk drinkers, it is imperative to understand the effect of at-risk drinking on health-related outcomes, quality of life, or mortality of older adults. Several studies have assessed the effect of at-risk drinking on health-related outcomes such as fall, gastrointestinal bleeding, injuries/accidents, mortality, and

economic cost of alcohol-related disorders. Previous research had shown that at-risk drinking is associated with greater mortality rates in older men.[60] At-risk drinkers are also more prone to falling or injuring themselves and missing taking their medications.[66] High alcohol consumption is also associated with falling.[1,73,93] Concurrent use of alcohol and NSAIDs or aspirin heightens the risk of gastric bleeding in older adults.[73] Further research needs to be conducted to confirm the impact of at-risk drinking on health outcomes, quality of life, or mortality in American older adults.

Harmful effects of at-risk drinking can be averted by implementing preventive measures. Creating awareness among older adults by providing educational interventions, behavioral or motivational counseling, educational workshops or programs with healthcare professional, may help in reducing at-risk drinking. Previous research has shown that such interventions have been helpful in creating awareness about potential risks associated with alcohol use among older adults and have played a significant role in altering their alcohol consumption.[94,95] A secondary analysis of data obtained from a randomized controlled trial in older at-risk drinkers established "older adults reduce their drinking when they recognize that their drinking habits may be causing them harm". Older adults have cited environment and circumstances as major factors influencing their drinking habits.[111]

Table 4.9 summarizes the studies investigating at-risk drinking measured in different ways. Some of these studies have determined at-risk drinkers from among the current drinkers. The SHARE study conducted the study in a population that may report higher alcohol consumption compared to a nationally representative sample.[42].

Table 4.8 Summary of Studies

Studies	Setting	Sample size	Subjects	Assessment tool	Prevalence of at-risk drinking	Other findings	Factors associated with at-risk drinking
Wilson,[50] 2013 U.S.A	NHANES 2005-2008	1,083	Older adults aged 65 years or older who consume alcohol.	ARPS. 47 of the 63 items applied in this study	Harmful drinkers = 37.4 % of older drinkers (95 % CI: 34.9 %, 40.0 %). Hazardous or harmful drinkers = 53.3 % (95 % CI: 50.1 %, 56.6 %).	14.5 % of older drinkers (95 % CI: 12.1 %, 16.8 %) consumed alcohol above the NIAAA's recommended limits.	Male drinkers had higher odds of being hazardous or harmful drinkers.
Barnes,[42] 2010 U.S.A	Analysis of survey data collected from subjects visiting primary care clinics in Santa Barbara, CA	3,308	Current drinkers aged ≥60 years visiting	CARET 7-item questionnaire	34.7% of the total sample were at-risk-drinkers	61.9% deemed at-risk due to alcohol and comorbid conditions and 61.0% due to medication and alcohol use and 64.3% only due to alcohol use.	At-risk drinking decreased for female gender; adults aged over 80 years; Asians; and individuals with higher education.
Moore,[61] 2006 U.S.A	NHANES I (1971-1974) and NHANES Epidemiologic Follow-up study, 1992	4,691	Older adults aged 60-74 years at baseline and who provided alcohol use data	CARET (few selected items of CARET were employed)	39% (n=1,658) of the sample were drinkers. And 10% (n=425) were at-risk drinkers.	69% of the drinkers were deemed as such due to their alcohol use and comorbidities, and 31% solely based on their alcohol use.	Pain medication use, gout, ulcer diseases, anxiety disorder were most commonly implicated Items.
Fink,[43] 2002 U.S.A	Survey conducted in primary care clinics	549	Older adults aged 65 years or older, English proficiency, and reported drinking at least 1 drink in the past year	ARPS 60 item questionnaire	Harmful drinkers=11% Hazardous drinkers=35%	Anti-arthritic and pain medications were most common followed by antiulcer medications. Hypertension was common comorbidity.	Harmful drinkers were more common in older men, and older adults aged <75 years.

Blazer,[74] 2009, U.S.A	Data from National Survey on Drug Use and Health (2005 and 2006)	4,236	Non-institutionalized older adults aged 65 years or older	At-risk drinking defined as use having two or more drinks on a usual drinking day within the past 30 days	13% of men and 8% of women reported at-risk use	More than 14% of men and 3% of women reported binge drinking	
Immonen,[67] 2011, Finland	Data gathered using postal questionnaire sent to a random sample	2,100	Older adults aged 65 years or older living in the medium sized city of Espoo in Finland	Structured questionnaire. At-risk drinking defined as i) more than 7 drinks per week, ii) five or more drinks on a typical day, or iii) using 3 or more drinks several times a week.	Of the 1395 responders, 8.2% (n=114) were at-risk drinkers	At-risk drinkers were prone to falling and forgetting to take medications.	At-risk drinking was associated with male gender, older adults aged between 65-70 years, married or living with partner, good income, high level of education, current smoking, and better functional status.
Weyerer,[75] 2009 Germany	A part of multi-center longitudinal study	3,224	Non-demented subjects aged 75 years or older, attending general practitioners in an urban area.	Structured clinical interview. At-risk drinking defined as >20 g of alcohol for women and >30 g for men.	At-risk drinking was 6.5% (95% CI: 5.6- 7.4 %).	At-risk drinking was significantly higher among men, current smokers.	At-risk drinking rate decreased with age, was lower in women, higher among current smokers, and was associated with better mobility and fewer depressive symptoms.

4.5 Conclusion

This study determines at-risk drinking, based on the CARET questionnaire, in a nationally representative sample of older adults. It further identifies the socio-demographic or health-related risk factors associated with at-risk drinking in this population. This study not only helps fill gaps in literature, but also builds evidence that can be used to develop and target preventive programs to mitigate alcohol-related problems. Furthermore it underscores the need for additional research to understand the impact of at-risk drinking in this population. Adverse events associated with at-risk drinking are largely preventable. Thus, identifying older adults who are likely to be at-risk drinkers and providing then with an educational intervention may help prevent alcohol-related adverse events, and avert expenditure of healthcare resources. Screening older adults for problematic alcohol use based on the socio-demographic or health-related risk factors determined in this study may streamline the screening process saving time and resources.

Chapter 5

Section 5. Potential Concurrent Use of Alcohol and Central Nervous System-Acting Medications

5.1 Introduction

Combined use of CNS-acting medications and alcohol, even in moderate quantities, may enhance sedation and impairment of psychomotor functions resulting in traffic accidents, injuries, falls, and fractures. Retrospective review of all zolpidem related cases reported, in the span of two-years, to the Illinois Poison Center showed that co-ingestion of alcohol and zolpidem was associated with intensive care unit admissions.[96] A German study found the weighted prevalence of combined use of psychotropic medication and alcohol to be 7.6% among non-institutionalized older adults.[66] Analysis of community-dwelling Australian men aged 70 years or older showed that among 135 men taking antidepressants, 27% were daily drinkers. Among sedative or anxiolytic users (n=97), approximately 43% were daily drinkers. This study also found that use of sedative or anxiolytics was associated with daily drinking.[64]

5.2 Objective

A descriptive, cross-sectional analysis was undertaken to determine the prevalence and pattern of potential alcohol and CNS-acting medication use among non-institutionalized older adults, and to understand the predictors of alcohol use among older adults taking CNS-acting medication.

5.3 Methods

5.3.1 Data Source

The National Health and Nutrition Examination Survey (NHANES) is a continuing, cross-sectional, nationally representative survey of the U.S. non-institutionalized civilian population that employs a complex, stratified, multistage, probability sampling design. The results of this study were obtained by combining the three data cycles (2005-2006, 2007-2008, and 2009-2010). The NHANES data consist of in-person household interviews and standardized health examinations administered in a mobile examination center (MEC).The details on the methods used for data collection and coding can be obtained from the NHANES website.[97] The demographic details, information on medication use, and other covariates were obtained during household interview. The overall response rates for the unweighted interview sample in NHANES 2005-2006, 2007-2008, 2009-2010 were 80.45%, 78.4%, and 79.4%, respectively. Information on alcohol use and depression were obtained during the medical examination. The overall unweighted examination response rates of the sample in NHANES 2005-2006, 2007-2008, 2009-2010 were 77.36%, 75.4%, and 77.3%, respectively.

5.3.2 Study Population

The study population consisted of non-institutionalized adults, aged 65 years or older at the time of interview, taking at least one prescription medication and with complete information on alcohol and medication use. After merging relevant data files and applying eligibility criteria, the final study sample consisted of 3320 individuals (Figure 4.1).

5.3.3 CNS-Acting Medication Use

Prescription medication use information was collected during household interviews. Participants were asked, ‘‘have you taken or used any prescription medicines in the past month?’’ and if the response was affirmative, they were asked to present the medication container. To classify medications, NHANES uses Lexicon Plus®, a proprietary, comprehensive database of Cerner Multum, Inc. that consists of all prescription and some non-prescription drug products available in the U.S. drug market.[98,99] For the purpose of this study, CNS-acting medication was defined as "*those medications which, when consumed concomitantly with alcohol, could intensify the effects of alcohol resulting in increased sedation, drowsiness, and impairment of psychomotor function*".[2] CNS medications were classified into ten mutually exclusive categories; opioid analgesics, anticonvulsants, anxiolytics, antidepressants, antipsychotics, anti-emetics, barbiturates, benzodiazepines, muscle relaxants, and respiratory agents. NHANES does not capture any information on the disease condition for which the medication was prescribed for. Some medications are used for more than one indication, for example, benzodiazepines and barbiturates can be used as either an anticonvulsant agent or an anxiolytic/sedative agent. Hence, the aforementioned categorization was adopted in this study to form mutually exclusive medication groups. A total of 157 CNS-acting medications were included in this study. Combination medications were counted as single medications for the purpose of calculating total number of medications. For example, acetaminophen with codeine was counted as one medication. Information on the dosage and frequency of use were not collected by NHANES. Interviewers could record up to 20 prescription medications.

Lexi-Interact, Lexicomp®, Wolters Kluwer Health (Philadelphia) and Micromedex®, Thomson Reuters Healthcare Inc. were used to ascertain the level of interaction between alcohol and CNS-acting medication.[98,99] Based on Micromedex® any CNS-acting medication suspected of moderate, major or contraindicated types of interactions with alcohol were included in this study.[99] Similarly, based on Lexi-Interact®, C (the use of drugs require monitoring), D (the use of drugs require change in therapy) and X (combined use those drugs should be avoided) types of interactions between any CNS-acting medications and alcohol were included in the study.[98]

5.3.4 Alcohol Use

Alcohol use was recorded by administering an alcohol use questionnaire, using the Computer Assisted Personal Interview (CAPI) system, to participants during mobile examination center interview. The alcohol use questionnaire enquired about lifetime and current alcohol consumption of the participants. Questions were not specific to type of alcohol and one drink was defined as 12 oz. of beer, 5 oz. of wine, or one and half ounces of liquor.

By using the Quantity*Frequency method, the average daily alcohol consumption was calculated.[70,80] To calculate frequency, the number of days respondent's had alcohol (whether recorded as weekly, monthly or yearly) was converted into drinking days per week. Average number of drinks consumed (quantity) was multiplied with "drinking days per week" to obtain average weekly consumption which was further divided by 7 to obtain average daily alcohol consumption.[80] Based on the average daily alcohol consumption, subjects were classified into different drinking categories. The drinking categories were determined depending upon the level of alcohol consumption and drinking guidelines.

According to the NIAAA recommendations, older adults should consume no more than one standard drink per day or seven drinks on average per week.[76] Considering the questions in the alcohol questionnaire and the drinking guidelines for older adults, drinking pattern was described in the following categories:

- Non-drinkers: This category included respondents who, (1) never had at least 12 drinks of any type of alcoholic beverage in their entire life (never drinker), or (2) reported consuming zero drinks in the past 12 months (former drinkers).
- Light-infrequent drinkers: subjects who consumed alcohol but not on a daily basis i.e. the average daily alcohol consumption might be zero but they have reported using alcohol in past 12 months.
- Moderate drinkers: subjects who consumed one drink per day or seven drinks per week
- Heavy drinkers: subjects who consumed more than one drink per day or 7 drinks per week

5.3.5 Concurrent Users

Concurrent users were defined as subjects who consumed alcohol on a daily basis (including moderate and heavy drinkers) and reported using at least one CNS-acting medication from in the past month. Individuals were categorized into concurrent users or non-concurrent user.

5.3.6 Covariates

Demographic factors including age, sex, marital status, educational level, and race/ethnicity were studied. As NHANES truncates the age at 80 years, older adults were categorized into four age groups: 65-69, 70-74, 75-79, and 80 and above. Older adults who were either married or were living with a partner were grouped under one category while those who were divorced, widowed, separated or unmarried were grouped together. Educational level was categorized into three groups: less than high school, high school graduate and more than high school which included college graduates or any higher degree. Non-hispanic white, non-hispanic black and others were the three categories for race/ethnicity. Other factors included smoking status (never smoker, former smoker, or current smoker), perceived health status (excellent/good/fair/poor), health insurance (yes/no), and insurance with prescription medication coverage (yes/no/ don't know or refused). NHANES employs the Patient Health Questionnaire (PHQ-9), a nine-item validated screening instrument that enquires about the frequency of symptoms of depression over the past 2 weeks, to screen for depression.[100] A total score can range from 0 to 27 and a score of 10 or higher is used to identify individuals with depression (yes/no).[100]

5.3.7 Statistical Analyses

Weighted prevalence estimates of alcohol use, CNS-acting medication use and the concurrent use of both, for the combined study period (2005-2010), were reported. The pattern of use of alcohol and CNS-acting medication, in terms of number of sample respondents, weighted percent and 95% confidence interval (CI) were also reported. The Cochran-Armitage trend test of unweighted sample and logistic regression of the weighted sample were done to assess the

change in daily alcohol use, CNS-medication use and concurrent use across the three data cycles. Chi-square analysis was carried out to assess the association between daily alcohol use and the covariates. Logistic regression was performed to identify the factors associated with the use of alcohol among CNS-acting medication users. The weight variables were recalculated since the three NHANES data cycles 2005-2006, 2007-2008, and 2009-2010 were combined. NHANES recommends use of the weight of the smallest sample subpopulation, so for all estimations involving alcohol variable, MEC6YR= 1/3*WTMEC2YR (2-year sample weights during examination at MEC) was used as weight variable while for medication related estimations INT6YR = 1/3 * (2-year sample weights during interview) was used as weight variable.[97] SAS version 9.2 (SAS Institute, Cary, NC) was used to conduct the statistical analyses.[101]

Ethical consideration: This study was reviewed and determined to quality as exempt from federal regulations by Virginia Commonwealth University Institutional Review Board.

5.4 Results

5.4.1 Sample Description

A total of 31,034 persons were interviewed during 2005-2010, out of which 4,268 were older adults. Since the goal of the study was to understand the magnitude of potential alcohol-drug interactions, non-medication users were not included in this study. A total of 3,753 (89.52%, 95%CI: 88.45-90.59) older adults took at least one prescription medication in the past month, of which 3,577 attended the NHANES medical examination. After removing the subjects with missing information on alcohol use, 3,220 subjects were included as the final study population (Figure 5.1). The socio-demographic characteristics of the study population are

described in Table 5.1. Among the 338 sample persons having no information on alcohol use, 6.87% (95%CI: 3.11-10.64, n=20) reported taking CNS-acting medications.

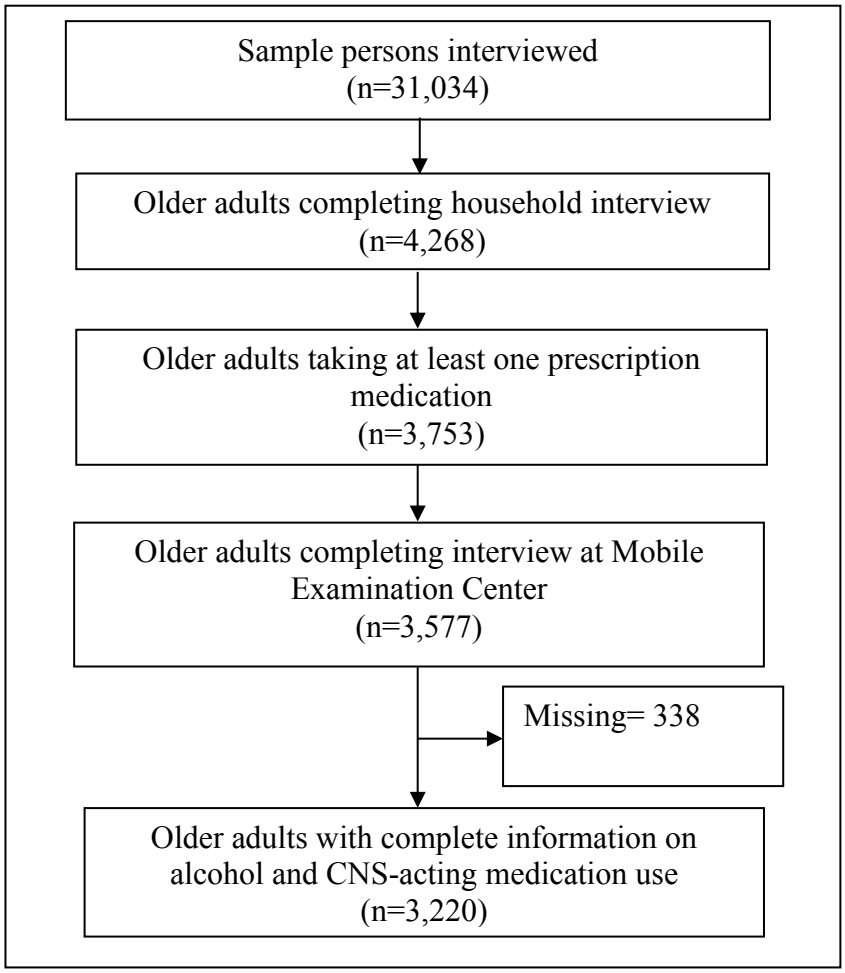

Figure 5.1 Flowchart Depicting Selection of the Final Study Population

Table 5.1 Socio-demographic Characteristics of the Study Population

Characteristics	Number of persons interviewed	Weighted Percent (95% CI)[α]
Age		
65-69	836	30.91 (28.67 – 33.16)
70-74	844	25.44 (23.63 – 27.26)
75-79	642	19.65 (17.87 – 21.43)
80 and above	898	24.00 (21.92 – 26.07)
Sex		
Male	1606	44.39 (42.76 – 46.02)
Female	1614	55.61 (53.98 – 57.24)
Race/ethnicity		
White	2101	84.27 (81.22 – 87.33)
Black	536	7.88 (6.09 – 9.67)
Others	583	7.85 (5.64 – 10.06)
Marital status		
Married/living with partner	1822	61.01 (58.43 – 63.59)
Divorced/separated/widowed/unmarried	1398	38.99 (36.41 – 41.57)
Educational level[&]		
Less than High school	1127	25.70 (22.74 – 28.78)
High school	1261	45.97 (41.90 – 50.03)
More than High School	826	28.33 (25.90 – 30.76)
Smoking status[@]		`
Never smoker	1501	47.30 (45.09 – 49.51)
Former smoker	1437	44.98 (42.70 – 47.27)
Current smoker	280	7.72 (6.81 – 8.63)
Number of medications		
1-5	2097	65.55 (63.60 – 67.52)
6-10	926	28.04 (26.13 – 29.94)
Greater than 10	197	6.41 (5.27 – 7.54)
Perceived health status*		
Excellent	212	7.60 (6.41 – 8.80)
Very good/good	2046	69.03 (67.07 – 70.98)
Fair	782	19.15 (17.73 – 20.58)
Poor	179	4.22 (3.43 – 5.00)
Depression[#]		
No	2989	95.44 (94.50 – 96.38)
Yes	164	4.56 (3.63 – 5.51)
Alcohol Use		
Non-drinker	1702	47.85 (44.07 – 51.63)
Light-infrequent drinker	611	20.36 (18.13 – 22.59)
Moderate drinker	739	26.23 (23.65 – 28.81)
Heavy drinker	168	5.56 (4.20 – 6.92)
Health insurance^		
Yes	3157	99.02 (98.65 – 99.40)
No	62	0.98 (0.60 – 1.36)
Prescription medication coverage®		
Yes	2708	86.47 (83.96 – 88.97)
No	447	13.53 (11.03 – 16.04)

α Total sample person= 3220 and weighted frequency= 30236526

& Don't know=6

@ Don't know=1, refused=1

* Don't know=1

Missing=67

^ Refused=1

® Missing=42,refused=4, don't know=19

5.4.2 Alcohol Use

Using the Quantity-Frequency method, it was found that 20.36% (95% CI: 18.13-22.59) were light-infrequent drinkers, 26.23% (95% CI: 23.65-23.81) were moderate drinkers, 5.56% (95% CI: 4.20-6.92) were heavy drinkers and the remaining 47.85% (95% CI: 44.07-51.63) were non-drinkers. On the days they drink, 33.55% (95% CI: 30.55–36.55, n=937) reported drinking one drink, 12.44% (95% CI: 11.02–13.85, n=363) reported drinking two drinks while 6.16% (95% CI: 5.11-7.21, n=218) reported drinking three or more drinks. 23.37% (95% CI: 19.92–26.81, n=349) of the drinkers reported drinking more than 4 days per week. 5.76% (95% CI: 4.83-6.70, n=192) of older adults reported binge-drinking (5 or more drinks on a single occasion at least once in the past 12 months). No significant difference in trend was observed in the pattern of daily alcohol use between the three data cycles (Figure 5.2).

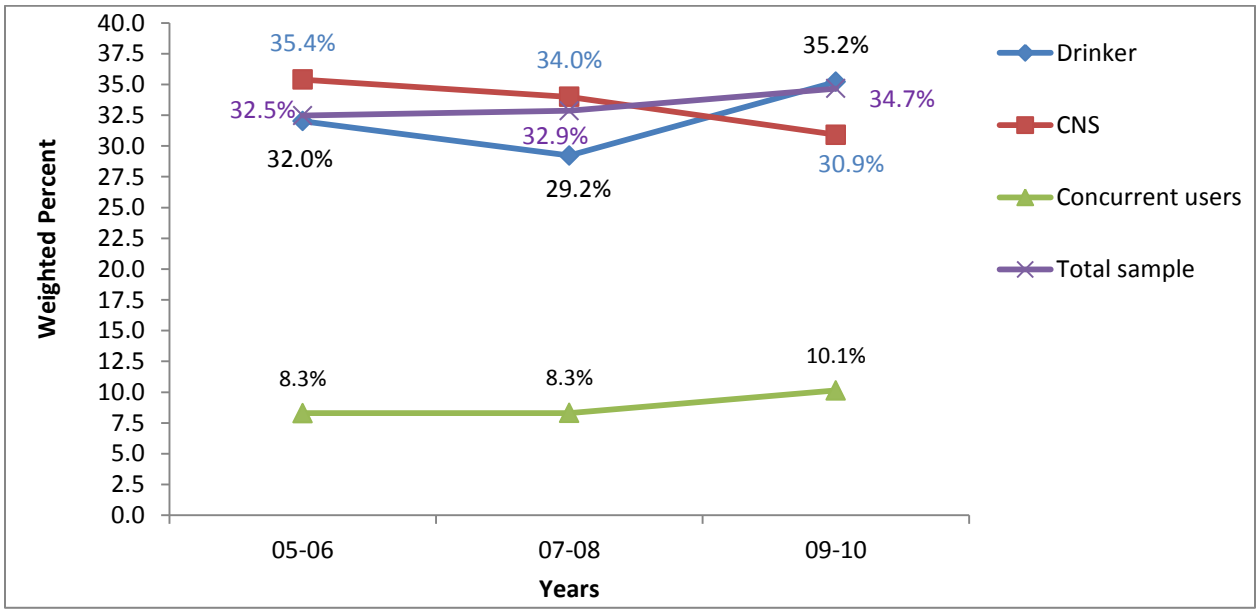

Figure 5.2 Prevalence of Alcohol, CNS-Acting Medication Use, and Concurrent Use Across the Three Data Cycles

5.4.3 CNS-Acting Medication Use

Approximately 33.5% (95% CI: 31.34-35.71, n=1,035) of older adults reported using at least one CNS-acting medication with a total of 1,534 CNS-acting medications being prescribed in the past month. Antidepressants were the most commonly used class of medication followed by opioid analgesics, benzodiazepines, and anticonvulsants (Table 5.2). Among CNS-acting medication users, 67.34% took one CNS-acting medication, 21.35% took two CNS-acting medications while the rest used more than two CNS-acting medications, in the past month. Gabapentin, combination of acetaminophen and hydrocodone, sertraline, alprazolam, fexofenadine, tramadol, zolpidem, citalopram, escitalopram, and fluoxetine were the ten most frequently used CNS-acting medications by the study population. CNS-acting medication use did not differ significantly over the three data cycles (Figure 5.2).

Table 5.2 Use of CNS-Acting Medications by Therapeutic Class

CNS-medication class	Prescription frequency*	Sample persons^	Weighted percentage#	95% CI
Antidepressants	422 (27.51%)	399	40.37	37.50 – 43.25
Opioid analgesics	327 (21.32%)	297	26.87	24.04 – 29.70
Benzodiazepines	201 (13.10%)	198	18.16	15.65 – 20.68
Anticonvulsant	173 (11.28%)	168	14.77	12.71 – 16.84
Respiratory agents	137 (8.93%)	136	12.99	10.69 – 15.29
Anxiolytics	79 (5.15%)	77	7.06	5.25 – 8.86
Anti-emetic	73 (4.76%)	73	6.63	5.12 – 8.13
Muscle relaxants	69 (4.50%)	68	6.93	5.05 – 8.81
Antipsychotics	39 (2.54%)	38	3.62	2.23 – 5.01

*The total number of CNS-medications used by older adults=1534.
^Out of 3220, the total number of participants taking CNS-medication=1035
Weighted frequency of users of the drug class/Weighted frequency of the 1035 CNS-medication users i.e. 9665992.48*100

5.4.4 Potential Concurrent Use of Alcohol and CNS-Acting Medication

The prevalence of older adults taking at least one CNS-acting medication and drinking daily was found to be 8.85% (95%CI: 7.22-10.49, n=244). Approximately 81% of these 244 older adults were moderate drinkers, and the 19% rest were heavy drinkers. The proportion of potential concurrent use of alcohol and CNS-acting medication did not differ significantly over the three data cycles. 19.74% (95% CI: 15.87–23.70, n=183) took one CNS-acting medication, 4.26% (95% CI: 2.58 – 5.94, n=39) took two CNS-acting medications, and 2.41% (95%CI: 0.89 – 3.93, n=22) took three CNS-acting medications while reporting daily alcohol consumption. Antidepressants, opioid analgesics and benzodiazepines have a greater possibility of being concomitantly consumed with alcohol as they were most commonly used by daily drinkers. Some of the CNS-acting medications most commonly used by drinkers were fexofenadine, combination of acetaminophen and hydrocodone, escitalopram, sertraline, gabapentin, alprazolam, and zolpidem. CNS-acting medication users were less likely to drink alcohol on a regular basis than non-users (OR=0.68, 95% CI: 0.54 – 0.86).

The relationship between daily alcohol use and other covariates among CNS-acting medication users is described in Tables 5.3 and 5.4. Due to the small cell size, “non-Hispanic blacks” were combined with “other” race, and health status was grouped as “poor/fair” versus “excellent/good/very good”. A chi-square test of association demonstrated that sex, race/ethnicity, marital status, educational level, smoking status, and perceived health status were significantly associated with daily alcohol use (Table 5.3), while age and prescription medication insurance coverage were not. The association between health insurance and depression and daily alcohol use could not be computed due to low cell sample size.

Table 5.3 Demographic Factors among CNS-Acting Medication Users by Daily Alcohol Use

Characteristics	Daily alcohol users		Non-daily alcohol users	
	Sample persons	Weighted percent (95%CI)	Sample persons	Weighted percent (95%CI)
Age				
65-69	65	27.92 (21.35-34.50)	222	72.08 (65.50-78.65)
70-74	73	31.35 (24.30-38.40)	183	68.65 (61.60-75.70)
75-79	45	24.82 (16.97-32.67)	154	75.18 (67.33-83.03)
80 and above	61	20.97 (16.33-25.62)	232	79.03 (74.38-83.67)
Sex				
Male	138	34.75 (28.40-41.09)	311	65.25 (58.91-71.60)
Female	106	21.69 (16.63-26.75)	480	78.31 (73.26-83.37)
Race/ethnicity				
White	196	28.35 (23.00-33.70)	506	71.65 (66.30-76.99)
Others	48	14.74 (10.12-19.36)	285	85.26 (80.64-89.88)
Marital status				
Married/living with partner	152	30.35 (25.11-35.60)	397	69.65 (64.40-74.89)
Divorced/separated/widowed/unmarried	92	21.37 (15.55-27.19)	394	78.63 (72.81-84.45)
Educational level[&]				
Less than High school	51	12.32 (7.99-16.66)	348	87.68 (83.34-92.01)
High school	64	26.44 (20.35-32.53)	195	73.56 (67.47-79.65)
More than High School	129	36.29 (29.47-43.11)	248	63.71 (56.89-70.53)
Smoking status*				
Never smoker	79	20.33 (15.01-25.65)	387	79.67 (74.35-84.99)
Former smoker	141	33.85 (27.84-39.87)	313	66.15 (60.13-72.16)
Current smoker	24	21.26 (12.73-29.78)	90	78.74 (70.22-87.27)
Number of medications				
1-5	95	25.53 (19.35-31.71)	314	74.47 (68.29-80.65)
6-10	113	27.74 (22.90-32.59)	357	72.26 (67.41-77.10)
Greater than 10	36	24.68 (15.28-34.08)	120	75.32 (65.92-84.72)
Comorbid conditions				
No comorbid conditions	45	39.09 (27.41-50.77)	99	60.91 (49.23-72.58)
1-2	142	25.86 (21.32-30.39)	484	74.14 (69.61-78.68)
3 or more	57	20.76 (15.59-25.93)	208	79.24 (74.07-84.40)
Perceived health status				
Good/very good/excellent	183	31.93 (25.81-38.05)	441	68.07 (61.96-74.19)
Poor/fair	61	15.15 (11.07-19.23)	350	84.85 (80.77-88.93)
Depression[#]				
No	226	27.85 (23.09-32.61)	684	72.15 (67.39-76.91)
Yes	14	13.84 (8.75-18.94)	77	86.16 (81.06-91.25)
Health insurance				
Yes	224	26.61 (21.98-31.23)	776	73.39 (68.77 -78.02)
No	0		15	
Prescription medication coverage®				
Yes	215	27.27 (22.23-32.32)	674	72.73 (67.68-77.77)
No	27	19.88 (12.01-27.75)	100	80.12 (72.25-87.99)

[#]Depression: missing=34, ®Prescription medication coverage: missing 19, *Smoking: missing=1

The logistic regression model was built to identify factors associated with daily alcohol consumption. Males had 49% (OR= 1.49, 95% CI: 1.02–2.60) higher odds of consuming alcohol daily when compared to females. Former smokers were more likely (OR=1.79, 95% CI: 1.21–2.63) to consume alcohol daily compared to never smokers. Older adults who did not complete high school are less likely to drink daily (OR=0.33, 95%CI: 0.21-0.54) compared to college graduates. Older adults with comorbidities were less likely to be daily drinkers compared those with no chronic condition. Good health status and being white were predictors of daily alcohol use.

5.5 Discussion

This cross-sectional study found the prevalence of potential concurrent use of alcohol and CNS-acting medications among non-institutionalized older adults to be 8.8%. Though the majority of concurrent users were moderate drinkers, alcohol consumption juxtaposed with prescription medication use may render them susceptible to adverse effects of interactions between alcohol and CNS-acting medication. The comparison of alcohol use between studies is difficult owing to the differences in measures of alcohol consumption, definition of drinking categories, and settings of the studies. Nonetheless, the pattern of alcohol use reported in this study is consistent with other published studies adhering to the NIAAA alcohol consumption guidelines for older adults.[27,56,57]

Table 5.4 Factors Associated with Daily Alcohol Use

Factors	Unadjusted odds Ratio	Adjusted odds Ratio
Age		
80 and above	Reference	Reference
75-79	1.24 (0.76-2.05)	1.08 (0.68-1.73)
70-74	1.72 (1.20-2.47)*	1.43 (0.93-2.19)
65-69	1.46 (1.01-2.11)*	0.98 (0.57-1.69)
Sex		
Female	Reference	Reference
Male	1.92 (1.39-2.67)*	1.49 (1.02-2.6)*
Race		
White	Reference	Reference
Others	0.44 (0.27-0.70)*	0.68 (0.39-1.16)
Marital		
Married or living with partner	Reference	Reference
Divorced/separated/widowed/unmarried	0.62 (0.43-0.90)*	0.76 (0.51-1.14)
Perceived health status		
Good/very good/excellent	Reference	Reference
Poor/fair	0.38 (0.25-0.57)*	0.51 (0.31-0.83)*
Education		
More than high school/college	Reference	Reference
High school	0.63 (0.41-0.96)*	0.67 (0.44-1.03)
Less than high school	0.25 (0.16-0.38)*	0.33 (0.21-0.54)*
Smoking Status		
Never smoker	Reference	Reference
Former smoker	2.01 (1.42-2.83)*	1.79 (1.21-2.63)*
Current smoker	1.06 (0.63-1.76)	1.19 (0.68-2.09)
No. of medications		
1-5	Reference	Reference
6-10	1.12 (0.81-1.55)	0.99 (0.72-1.40)
Greater than 10	0.96 (0.61-1.50)	0.80 (0.51-1.24)
Chronic comorbid conditions		
No chronic conditions	Reference	Reference
1-2	0.54 (0.34-0.88)	0.54 (0.31-0.95)*
3 or more	0.41 (0.24-0.69)	0.44 (0.24-0.78)*

#Number of observations used in the multivariable logistic regression model is 1034

* p-value <0.05

Our findings suggest that antidepressants, opioid analgesics, and benzodiazepines are not only widely used but are also consumed by daily drinkers. The pattern of use of CNS-acting medications observed in this study is similar to other published studies.[66,102,103] Consistent with the findings of previous studies, selective serotonin reuptake inhibitors (SSRIs), namely sertraline, escitalopram, citalopram, and fluoxetine, were the most frequently prescribed class of antidepressant in our study.[66,102-104] Detection of high use of acetaminophen and hydrocodone combination medication was similar to previous findings.[66] Importantly, both of these medication components interact with alcohol, albeit through separate mechanisms of action, increasing the risk of liver toxicity and injuries.[29] As sedatives/hypnotics/anxiolytics grouped as one category did not include benzodiazepines in this study, the proportion of users was lower compared to other studies.[66,102,103] It should be noted that certain CNS-acting medications included in this study such as naltrexone, topiramate, and SSRIs, are also used in the treatment of alcohol dependence. Such medication use would be considered intentional and, possibly, more controlled; however, due to the absence of information on diagnosis, the proportion of older adults undergoing alcohol dependence treatment could not be ascertained.[105]

Trend analysis revealed no significant change in the use of CNS-acting medications, daily alcohol use, and potential concurrent use of alcohol and CNS-acting medications across the data cycles. Using data collected over a greater number of years may be required to understand the trend of use of these variables within the older adult population. Some researchers have reported higher alcohol consumption in the recent cohort of older adults compared to their predecessors.[106] The absence of significant change in the prevalence of concurrent use of alcohol and CNS-acting medications indicates that the magnitude of the problem is consistent and warrants further investigation. Several studies have documented an increase in the use of CNS-

acting medications in the U.S. adult population over a span of 6-10 years.[106,107] A cross-sectional study conducted in Spain showed an increase in the use of prescription anxiolytics and antidepressants among older adults.[108] Considering these findings, longitudinal trend analysis of CNS-acting medication utilization and alcohol consumption in older adults is necessary.

Some factors associated with daily alcohol use in older adults taking CNS-acting medications identified in this study are comparable to those stated in other studies.[57,66,109] Previous studies found that females are more likely to use psychotropic medications while males report drinking more often than females.[110] Even among CNS-acting medication users, males are more likely to drink daily than females (as shown in Table 4.4). As demonstrated in the literature, other races consume less alcohol than whites. Level of education is a factor associated with daily alcohol use. While some studies have shown that older adults with less than a high school education were more likely to be moderate or heavy drinkers[41,109] others have demonstrated the reverse.[56,66] Unlike previous findings, living alone was not found to be a risk factor of daily alcohol use in our study population.[66] Education is an indicator of socio-economic status, as is income and employment status. Our findings suggest that former smokers showed higher risk of consuming alcohol on a daily basis. The association between current smoking and daily alcohol use could be biased due to a small sample size. Current or previous history of health risks such as smoking, major depression, and substance abuse has been associated with alcohol use.[27,66,106,111] In our study, however, the relationship between depression and daily alcohol use could not be assessed due to small sample size. Older adults who perceive their health status as either poor or fair are less likely to drink daily.[66] Conversely, Kirchner el al. found alcohol use to be positively associated with perceived poor health among older adults in the primary care setting[27]. The absence of significant change in potential concurrent use of

alcohol and CNS-acting medications indicates that daily alcohol use is not associated with medication use unlike the inverse associated observed between daily alcohol use and co-morbid conditions. It was observed that as co-morbid conditions increased the likelihood of being daily drinker decreased but this relationship was not observed between daily alcohol use and medication use which raises concern.

This study has several limitations. It could not be definitively ascertained whether alcohol was consumed concomitantly with CNS-acting medications. NHANES data does not permit studying the type and size of alcoholic drink consumed by respondents or the dose and frequency of CNS-acting medication used. This study did not include employment status and income of older adults. These two factors would have provided insight on the relationship between socio-economic status and alcohol use. Previous research has shown that questions regarding typical quantity and frequency of alcohol consumed can lead to underestimation of actual consumption.[71] Deliberate under-reporting of alcohol use and CNS-acting medication use has also been documented in this population.[22] Although questions on alcohol use focused on average frequency and amount of alcohol consumed by respondents certain events such as loss of spouse, retirement, and dependence, may influence the drinking pattern of older adults.[22] It could not be determined if non-drinkers in this study stopped drinking alcohol due to any health-related issues in the past. The possibility of error in reporting or recall bias due to potential cognitive impairment or memory loss experienced by the older adult respondent is also present. In addition, small sample sizes in certain subgroups could have influenced the precision of our estimates.

Several review articles have emphasized the need to understand alcohol and psychotropic medication use among older adults.[92,110] This study makes a unique contribution to the literature by determining the pattern, prevalence and associated factors of alcohol and CNS-acting medication use among community-dwelling older adults. Some strengths of the study are that, 1) it utilizes a recent, nationally representative sample of non-institutionalized older adults, 2) NHANES data collection follows a specified protocol and quality assurance process, 3) potential concurrent use of alcohol and CNS-acting medications is estimated in a conservative manner (by including only moderate and heavy drinkers), and 4) employing an broader definition of "CNS-acting medication" for the purpose of the study.

There are few studies assessing the adverse outcomes resulting from alcohol-medication interactions. Understanding the consequences of the combined use of alcohol and CNS-acting medication and determining its impact on healthcare utilization is essential. Duru et al. reported that the probability of an alcohol-related discussion between older adults and their physician declined with the patient's age, and factors such as having comorbidities and using medications were not associated with alcohol-related discussions.[112] The findings of our study underscore the need to address issues related to alcohol use among older adults. Alcohol and prescription drug misuse among older adults is regarded as a "hidden" epidemic facing the country which needs to be further explored.[92,110]

5.6 Conclusion

In summary, a considerable proportion of older adults are susceptible to consume alcohol and CNS-acting medications, concurrently, and are therefore at risk of experiencing enhanced sedation and impaired psychomotor functions, leading to adverse events such as falls, fractures and accidents. Early identification of older adults at risk for alcohol-CNS-acting medication interactions may prevent adverse events. Initiation of prescription monitoring programs and screening for harmful alcohol use may be useful to overcome some of the alcohol use-related problems in the older population. Discussions or counseling about safe alcohol use are necessary between healthcare professionals and older adults.

Chapter 6

Section 6 Effects of Alcohol and Central Nervous System-Acting Medications on Risk of Falling

6.1 Introduction

One out of three community-dwelling older adults falls each year.[113] Falls may result from multiple risk factors that can be broadly classified into three the following categories; environmental (poor lighting, slippery floor, loose carpet), intrinsic (chronic disease conditions such as arthritis, vision impairment, dementia), and extrinsic (medications, alcohol).[114,115]

Several studies have documented CNS-acting medications to be a risk factor for falls. A meta-analysis of observational studies found a small but consistent association between psychotropic medication use and falls in older adults (weighted odds ratio 1.7 and 95% CI: 1.5 to 2.0).[40] Antidepressants, antipsychotics, sedatives, hypnotics and anxiolytics are some of the drug classes implicated as risk factor for falls.[40] Other classes of CNS-acting medications such as opioid analgesics and anticonvulsants have also been associated with falls.[40] A prospective cohort study found that compared to non-users, older women taking benzodiazepines (multivariate odds ratio: 1.51, 95% CI: 1.14-2.01), and anticonvulsants (multivariate odds ratio: 2.56, 95% CI: 1.49-4.41) were at higher risk for falls. [116]

Age-related pharmacokinetic and pharmacodynamic changes render older adults more sensitive to the pharmacological effects of CNS-acting medications.[47,117,118] Consequently, adverse effects of most of the psychotropic drugs such as dizziness, sedation, cognitive impairment, impaired psychomotor function and postural sway are exacerbated in older adults, contributing to risk of falling.[40,116] In addition, older adults using CNS-acting medications are

likely to have depression, sleeping problems, psychiatric disorders, or poor health status that may augment their risk of falling.[40,116] Initiation of CNS-acting medication therapy, use of multiple CNS-acting medications and any sudden change in the psychotropic drug regimen may increases the risk of fall in older adults.[116,117, 118]

Alcohol is a CNS depressant that acts via various neurochemical systems in the brain and causes sedation, dizziness, and also altered gait and balance.[2] Longitudinal analysis of the Cardiovascular Health Study (CHS) data showed that risk of falls increases by 25% in consumers of 14 or more alcoholic drinks per week.[1] A systematic review concluded that acute alcohol use is an important risk factor for falls among young and middle-aged adults.[119] A review of the literature showed that studies examining the association between alcohol use and falls among older adults have documented an inconsistent relationship between the two.[120] A few studies have shown that high alcohol use is associated with increased risk of falls in older adults [1,108, 120] while other others fail to find a significant relationship.[120] Inconsistent findings could be attributed to under-reporting of alcohol use, deficiencies of study design resulting in selection and information biases or confounding effect, or publication bias. [120]

Both alcohol and CNS-acting medications act on the CNS via various neurochemical systems causing alterations in mood, behavior, cognition and physical movement which may result in falls, fractures, and other injuries, especially in older adults.[2] In 2009, the Drug Abuse Warning Network (DAWN) detected that 519,650 emergency department visits were associated with use of alcohol in combination with other drugs, out of which 44.1% were CNS-acting agents (sedatives, anxiolytics and analgesics) and 8.5% were psychotherapeutic agents (antidepressants and antipsychotic drugs).[7] This indicates that combined use of alcohol and CNS-acting medications may cause adverse events requiring medical care. Thus, the central

hypothesis of the proposed study is to determine if the combined use of alcohol and CNS-acting medications increases the risk of falls in older adults.

6.2 Objective

The objectives of this study were to determine if alcohol use was associated with risk for falls, injurious falls, and recurrent falls. It is also of interest to determine if varying levels of alcohol consumption with CNS-acting medication use is associated with risk for falls among older adults.

6.3 Methods

6.3.1 Study population

The study sample was obtained from the 2009 MCBS study.[77] Community-dwelling Medicare beneficiaries aged 65 years or older, surviving through 2009 were included in this study. Subjects with complete or partial paralysis and/or amputation were excluded from this study. The description of the data source, sample selection, sample characteristics, and weighting process has been described in Chapter 4.

6.3.2 Alcohol consumption

Data on alcohol use was collected from the MCBS survey. Every alternate year participants in the MCBS are asked three questions probing about their "usual" alcohol use over the past year. The first question is "Please think about a typical month in the past year. On how many days did [you/(SP)] drink any type of alcoholic beverage?". The next question enquires about quantity of alcoholic drinks consumed; "On those days that [you/(SP)] drank alcohol, how

many drinks did (you/he/she) have?". The third question pertains to heavy episodic drinking "On how many days did [you/(SP)] have 4 or more drinks in a single day?"

Monthly alcohol consumption was assessed using the quantity-frequency method. Beneficiaries were categorized into three groups based on alcohol consumption; i) non-drinkers (those who did not consume alcohol in past 12 months) ii) within-limit drinkers (those who drank not more than 30 or 31 drinks in a month) iii) exceeding-limit drinkers (those who drank more than 30 or 31 drinks in a month).[56] These categories are based on the NIAAA recommendations for alcohol use among older adults. Binge drinkers were described as those who consumed more than 4 drinks in a single day over the past 12 months.

6.3.3 CNS-Acting Medication Use

The five mutually exclusive categories of CNS-acting medications utilized for this study included opioid analgesics, non-benzodiazepine anticonvulsant agents, non-benzodiazepine sedative-hypnotics, and non-benzodiazepine psychotherapeutics (antidepressant, antipsychotic) and benzodiazepines. The information on CNS-acting medication use was collected using survey as well as claims data. Number of refills was not included since that information was not available on every study subject.

Both CNS-acting medication use (users vs. non-users) and alcohol use (non-drinkers, within-limit drinkers, and exceeding-limit drinkers) were combined to form a variable with six subcategories. Similarly binge drinking (non-drinker, non-binge drinker, and binge-drinker) and CNS-acting medication use (users vs. non-users) were combined to form a variable with six subcategories. These subcategories of exposure variables are described in Table 6.1.

Table 6.1 Subcategories of Exposure Variables

CNS-acting medication use and drinking status	CNS-acting medication use and binge drinking
1. Non-user and non-drinkers	1. Non-user and non-drinkers
2. Non-users and within-limit drinkers	2. Non-users and non-binge drinkers
3. Non-users and exceeding limit drinkers	3. Non-users and binge drinkers
4. Users and non-drinkers	4. Users and non-drinkers
5. Users and within-limit drinkers	5. Users and non-binge drinkers
6. Users and exceeding limit drinkers	6. Users and binge drinkers

6.3.4 Outcome Variables

During the interview, subjects were asked seven questions regarding falls including number and severity of falls, how it affected their lives, and fear of falling. To elaborate, subjects were asked, "Since the last interview have you fallen down?". If subjects answered affirmatively, they were further asked about the number of times they had fallen, if the most recent fall hurt them badly enough to seek medical help, and the kind of injury they suffered. Fear of falling was rated on a 6 point scale ranging from "not at all afraid" to "extremely afraid".

The outcome variable (dichotomous) was described in two ways: i) subjects who either fell or not (fallers and non-fallers), and ii) among fallers, whether subjects had an injurious fall or not. Subjects who required medical help after the most recent fall were considered to have an injurious fall. Non-fallers were considered the reference group for the logistic regression model.

6.3.5 Covariates

Several variables have been documented as risk-factors of fall in older adults. Some of these factors could confound the relationship between use of CNS-acting medication and alcohol, and risks of falls. In this study, a fall risk assessment tool known as "Falls Risk for Older People-Community setting (FROP-Com) was followed to select the variables regarded as risk factors for falls in older adults.[121] Not all variables enlisted in FROP-Com were available in MCBS dataset. Variables such as fear of fall, eye impairment, body mass index, use of antihypertensive medications, functional status, chronic co-morbid conditions, health status, and other socio-demographic characteristics have been found to be associated with risk of falls in the literature (Table 6.2).

Table 6.2 Confounders Included in the Regression Model

Categories	Variables
Socio-demographic factors	Age, gender, race, marital status, education level
Fall risk factors	Eye impairment Use of blood pressure medication Fear of fall Body Mass Index (BMI)
Functional status	Activities of daily living Instrumental activities of daily living Limitations to social activity
Health status	Perceived health status Polypharmacy No. of chronic co-morbid conditions

Most of the variables were categorized as described earlier in chapter 5. Older adults were categorized into two groups based on history of eye impairment (no impairment vs. presence of impairment). The body mass index of the older adults was calculated using their weights (in kilograms) and heights (in meters). The following formula was used to calculated the

BMI weight (kg) / [height (m)]^2. BMI lower than 18.5 was considered as underweight, BMI ranging between 18.5 and 24.9 was considered normal weight, BMI ranging from between 25.0 to 29.9 was regarded as overweight, and BMI of 30.0 or above was regarded as obese.[122] The total number of chronic conditions was calculated as a sum of the number of disease conditions a respondent suffered from in the past year. The disease conditions included arthritis, rheumatoid arthritis, osteoporosis, diabetes, depression, emphysema, hypertension, congestive heart disease, myocardial infraction, arrhythmia, cardiac failure, other heart problem, urinary incontinence, Alzheimer's Disease (AD), and Parkinson's Disease (PD).

6.3.6 Statistical Analyses

Frequency and weighted percent were used to describe the characteristics of the study sample. Bivariate association was studied by performing Chi-square tests. Separate logistic regression was employed to determine the association between outcome variables (falls, injurious falls and recurrent falls) and exposures (use of alcohol and CNS-acting medications), controlling for confounders. Confounders were identified based on available evidence in the literature, bivariate association with exposure variables and outcome variable, and if there is a 10% change in the odds ratio of exposure variable when the potential confounder was added to the regression model. In case the association between the confounder and the outcome variable was not found to be significant in this study but there is sufficient evidence in the literature indicating that the variable is a risk factor for falls, then the variable is added to the model to control for its effect.

Multi-nominal logistic regression was used to study the association between injurious falls or recurrent falls with exposure variables where non-fallers were the reference group. The effect of CNS-acting drug classes included in this study and the number of CNS-acting medications being prescribed on the risk of falls were also investigated. Adjusted odds ratio (with 95% CI) and the p-value described the relationship between the outcome variable and exposure variables. Multicollinearity between explanatory variables was investigated by assessing the correlation between continuous variables, or chi-square test between categorical variables. Test of multicollinearity was also performed in the regression model using variance inflation factor (VIF). If the VIF was greater than 10 then the variables were said be multi-collinear. SAS statistical software versions 9.2 and 9.3 were employed to perform all of the statistical analysis[78], at significance level of α=0.05.

6.4 Results

6.4.1 Description of the Sample Characteristics

A total of 7,163 (weighted frequency=20070176 and standard deviation= 116981) community-dwelling older adults were included in this study. A total of 21.5% (95% CI: 20.5-22.5 %, n=1601) of the individuals in the study sample reported falling in the past month. Fifty-four (0.8%, 95% CI: 0.5-1.2 %) older adults did not provide a usable response to this question in the study. Among those who fell in the past 12 months, 28.2% (95% CI: 25.57-30.88 %, n=462) had an injurious fall requiring medical help. Approximately 53% (95% CI: 95% CI: 50.9-55.8 %, n=818) experienced a single fall and 47% (95% CI: 44.2-49.1 %, n=755) had recurrent falls, in the past year. Among the fallers, 28 older adults did not respond to how many times they fell in the previous year and one older adult did not mention if he or she had needed medical help after

the fall. Thus, these individuals are considered missing in the analyses. The distribution of outcome variables is described in Figure 6.1.

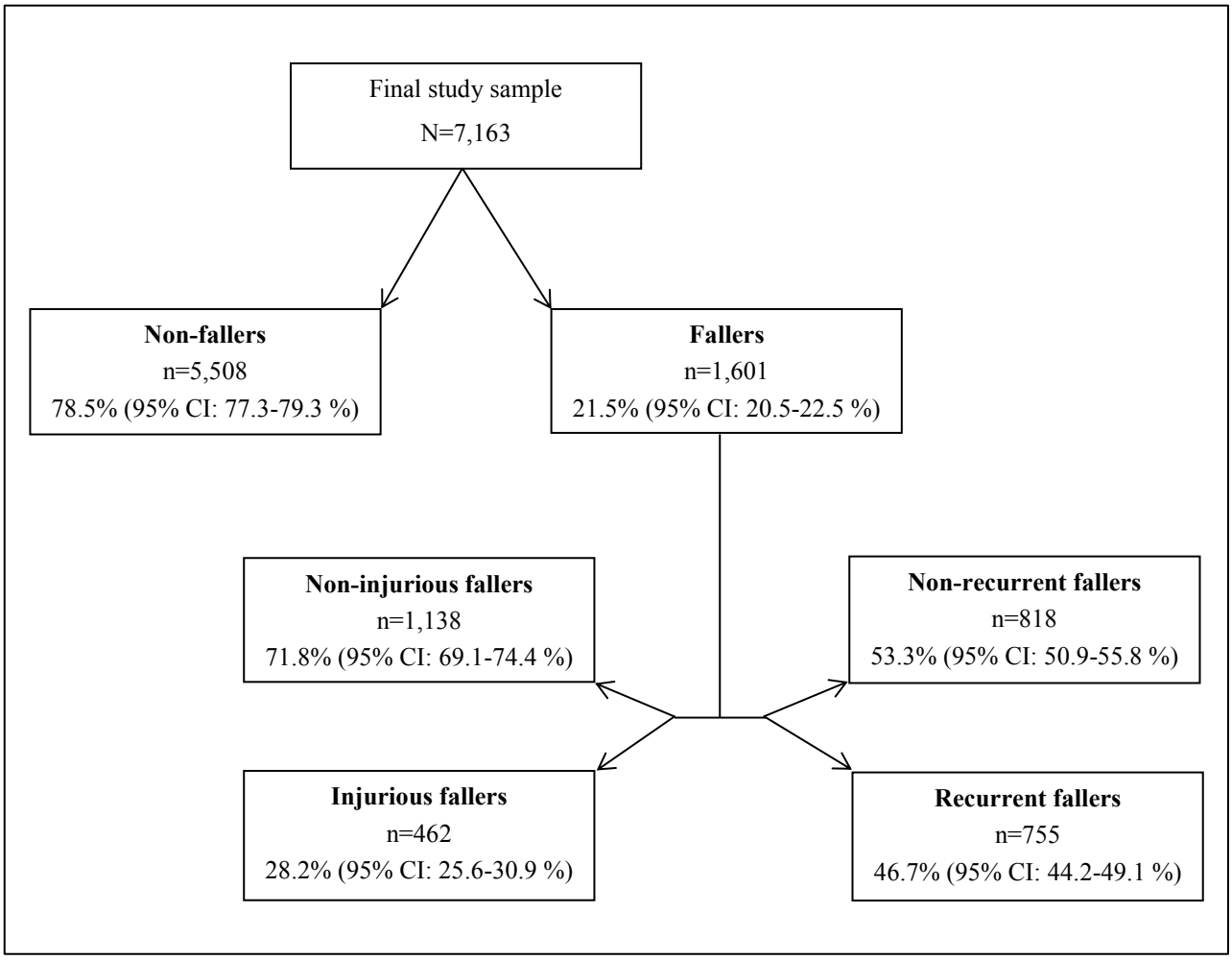

Figure 6.1 Flowchart Depicting Outcome Variables

The socio-demographic characteristics of the fallers and non-fallers are described in Table 6.3. The fallers were likely to be older in age (21% of the fallers were aged 85 years or older while 14% were of the fallers were aged the same). A greater proportion of fallers were identified as Caucasians than non-fallers though smaller proportions of African American were fallers than non-fallers.

Table 6.3 Socio-demographic Characteristics of Fallers and Non-fallers

Variables	Fallers		Non-fallers	
	Frequency	Weighted Percent (95% CI)	Frequency	Weighted Percent (95% CI)
Age				
85 and older	396	21.1 (19.3-22.8)	950	14.0 (13.1-14.9)
75-84	662	37.7 (35.3-40.2)	2210	36.8 (35.5-38.1)
65-74	543	41.2 (38.3-43.9)	2348	49.2 (48.0-50.3)
Gender				
Female	938	58.7 (56.0-61.3)	3099	56.4 (55.5-57.4)
Male	663	41.3 (38.7-44.0)	2409	43.6 (42.6-44.5)
Race				
Caucasian	1415	88.4 (86.5-90.3)	4662	84.8 (83.8-85.8)
African American	87	5.8 (4.4-7.1)	482	8.6 (7.9-9.3)
Others	94	5.8 (4.4-7.2)	350	6.6 (5.8-7.3)
Marital				
Married	766	49.6 (46.7-52.4)	2931	55.0 (53.6-56.5)
Non-married	835	50.4 (47.6-53.3)	2573	45.0 (43.6-46.4)
Education				
More than high school	713	46.2 (43.8-48.7)	2423	46.0 (44.5-47.6)
High school	472	29.1 (26.9-31.2)	1708	31.3 (30.1-32.6)
Less than high school	396	23.8 (21.7-25.9)	1295	21.7 (20.5-22.8)
No Education	18	0.9 (0.5-1.3)	59	1.0 (0.7-1.2)
Income				
More than 25,000	781	48.5 (45.6-51.5)	2878	54.6 (53.0-56.2)
25,000 or less	820	51.5 (48.5-54.4)	2630	45.4 (43.8-46.9)
Employment				
No	1462	89.9 (87.9-91.8)	4876	87.0 (86.0-88.0)
Yes	139	10.1 (8.2-12.0)	628	13.0 (11.9-14.0)
Social activity				
No	916	58.6 (55.7-61.4)	4044	75.5 (74.2-76.7)
Yes	684	41.4 (38.6-44.2)	1456	24.5 (23.3-25.8)
Health status				
Worse	523	31.8 (29.2-34.4)	980	16.9 (16.1-17.7)
Same	855	54.2 (51.6-56.8)	3733	68.6 (67.3-69.9)
Better	220	14.0 (12.2-15.9)	793	14.5 (13.2-15.7)
Difficulties in ADL				
No difficulty	888	57.8 (55.0-60.6)	4228	78.3 (77.0-79.6)
1-2	455	27.2 (24.8-29.6)	980	16.5 (15.5-17.6)
3-6	258	15.0 (13.2-16.8)	300	5.2 (4.4-5.8)

Difficulties in ADL				
No difficulty	766	50.1 (47.2-52.9)	3790	70.8 (69.5-72.1)
1-2	510	31.3 (28.6-34.1)	1234	21.4 (20.3-22.6)
3-6	325	18.6 (16.4-20.7)	484	7.7 (7.0-8.5)
Smoking status				
Never-smoker	694	42.4 (39.6-45.3)	2280	41.0 (39.7-42.3)
Former-smoker	796	50.1 (46.9-53.3)	2743	49.8 (48.5-51.1)
Current-smoker	111	7.5 (5.8-9.1)	483	9.2 (8.4-10.0)
Chronic comorbidity				
5 or more	568	34.2 (31.6-36.7)	1187	20.2 (19.0-21.4)
3-4	606	37.5 (31.6-36.7)	1961	34.9 (33.7-36.1)
1-2	366	24.1 (21.6-26.7)	1991	37.4 (35.9-39.0)
No disease	61	4.2 (2.8-5.4)	369	7.5 (6.7-8.2)
Number of medications				
11 or more	575	35.3 (32.7-37.8)	1185	20.4 (19.2-21.6)
6-10	549	33.8 (31.6-36.0)	1992	35.8 (34.5-37.0)
1-5	423	27.4 (25.1-29.6)	2040	38.2 (36.7-37.0)
No medication	54	3.5 (2.5-4.5)	291	5.6 (4.9-6.3)
Eye impairment				
No impairment	1011	63.4 (61.1-65.7)	4046	74.7 (73.3-76.2)
Impairment/Blind	588	36.6 (34.3-38.9)	1447	25.3 (23.8-26.7)
Use of antihypertensive medication				
No	444	28.5 (26.1-30.9)	1799	34.3 (32.7-36.0)
Yes	1157	71.5 (69.1-73.9)	3709	65.7 (64.0-67.3)
Obesity				
Underweight	11	0.6 (0.2-0.9)	54	1.0 (0.7-1.3)
Normal weight	213	12.7 (10.8-14.7)	753	13.1 (12.2-14.0)
Over-weight	442	27.4 (25.1-29.7)	1504	26.9 (25.8-27.9)
Obese	935	59.3 (56.9-61.7)	3197	59.0 (57.8-60.2)

Column percentages are significantly different
(Rao-Scott-Chi-square test showed p-value <0.05)
Bivariate analysis between the covariate and fall outcome showed significant association (p-value<0.05)

Fallers seem to suffer from higher numbers of chronic comorbid conditions and consume more medications. Approximately 35% of the fallers were taking 11 or more medications whereas 20% of the non-fallers were taking the same. Similarly, while 20% of the non-fallers reported suffering from 5 or more co-morbid conditions, 34% of the fallers reported the same. Functional status of fallers seemed to be worse than non-fallers. Greater proportion of fallers reported encountering limitations in social activity due to health, difficulties in performing usual and instrumental activities of daily living (ADL and IADL), and worsening of health in the past year. Moreover, 36.6% of fallers reported having eye impairment compared to 25% of the non-fallers. Similarly greater proportions of fallers reported taking antihypertensive medications than non-fallers. Bivariate analysis was performed using Chi-square test of association which showed that variables including age, race, marital status, income, employment, perceived health status, limitations in social activity, comorbidities, number of medications used, eye impairment, and use of antihypertensive medications were significantly associated with the falls outcome variable.

The relationship between the exposure variables and any fall in the past 12 months was studied using logistic regression analysis. As risk factors foe falls are multifactorial in nature so the confounding effect of age, sex, race, marital status, educational level, perceived health status, difficulty in social activity due to health conditions, ADLs, IADLs, presence of eye impairment, use of blood pressure medications, number of medications taken and comorbid conditions were controlled.

6.4.2 Effect of CNS-Acting Medication on the Risk of Falling

Of the 7,613 older adults included in this study 41.5% (95% CI: 40.0-43.0 %, n=3,019) took CNS-acting medications in the past year. The distribution of each class of CNS-acting

medication (figure 6.2) in the overall study sample comprised of; 22.5% (95% CI: 21.3-23.7 %, n=1637) taking at least one opioid analgesic; 17.9 % (95% CI: 16.8-19.0 %, n=1288) consuming at least one psychotherapeutic medication; 8.0% (95% CI: 7.3-8.7 %, n=611) taking at least one anticonvulsants; 6.8% (95% CI: 6.3-7.3 %, n=509) taking at least one benzodiazepines; and 5.5% (95% CI: 4.9-6.0 %, n=404) taking at least one sedative-hypnotics in the past 4 months. Figure 6.2 shows the distribution of each class of CNS-acting medication use among CNS-acting medication users (denominator=3,019). Approximately 50% (95% CI: 48.18-51.56%, n=1482) of the CNS-acting medication user took one CNS-acting medication, 24.77% (95% CI: 23.07-26.46 %, n=762) took two CNS-acting medications, while 25.36% (95% CI: 23.58-27.15, n=774) took more than two CNS-acting medications.

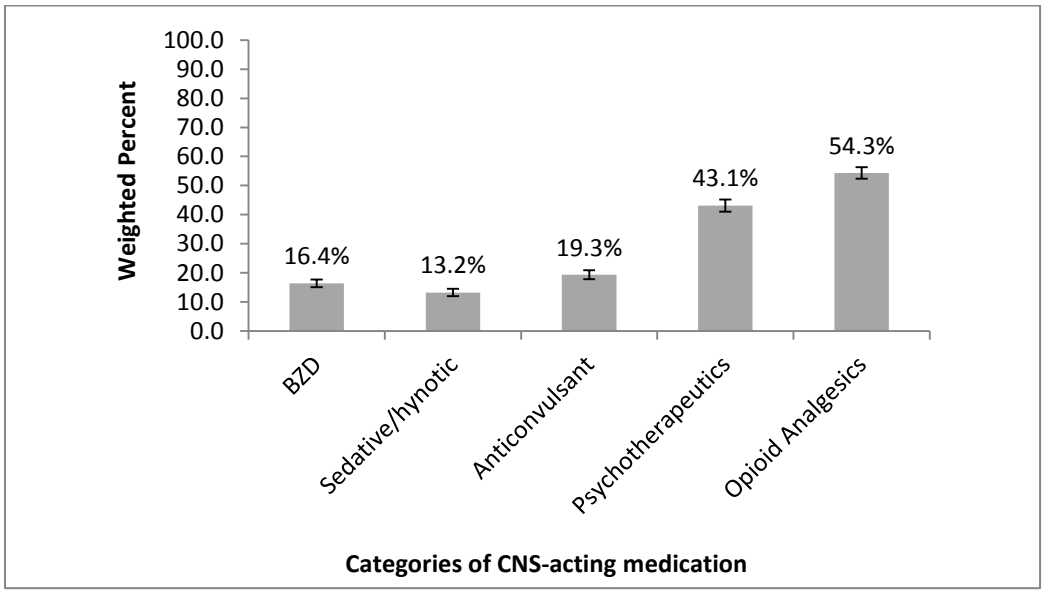

Figure 6.2 Pattern of use of CNS-acting medication

The effect of individual CNS-acting medication class on risk of falling is described in Table 6.4. It was observed that 32.8% of opioid analgesic users were fallers while 19.7% were non-fallers. The adjusted logistic regression analysis showed that use of opioid analgesics (OR:

1.41, 95% CI: 1.21-1.65) was associated with increased the odds of experiencing fall in older adults.

Table 6.4 Relationship Between each Class of CNS-Acting Medication and the Risk of Falling

Variables	Fallers		Non-fallers		Adjusted Odds Ratio (95% CI)
	Sample Persons	Weighted Percent (95% CI)	Sample Persons	Weighted Percent (95% CI)	
Opioid analgesics					
Non-users	1074	67.2 (65.0-69.4)	4409	80.3 (79.1-81.5)	1 (ref)
Users	527	32.8 (30.6-35.0)	1099	19.7 (18.5-20.9)	1.41 (1.21-1.65)**
Psychotherapeutics					
Non-users	1192	74.1 (71.9-76.2)	4640	84.4 (83.2-85.6)	1 (ref)
Users	409	25.9 (23.8-28.1)	868	15.6 (14.4-16.9)	1.26 (1.08-1.47)**
Benzodiazepines					
Non-users	1439	90.6 (89.2- 91.9)	5164	93.9 (93.3-94.5)	1 (ref)
Users	162	9.4 (8.1-10.8)	344	6.1 (5.5-6.7)	1.30 (1.06-1.60)**
Anticonvulsants					
Non-users	1419	89.3 (87.8-90.7)	5087	92.8 (92.0-93.5)	1 (ref)
Users	182	10.7 (9.3-12.2)	421	7.2 (6.5-8.0)	1.03 (0.84-1.25)
Sedative-hypnotics					
Non-users	1476	92.7 (91.3-94.0)	5232	95.0 (94.4-95.6)	1 (ref)
Users	125	7.3 (6.0-8.7)	276	5.0 (4.4-5.6)	1.13 (0.88-1.45)
Total CNS-acting medication					
Zero	745	46.9 (44.5-49.4)	3366	61.7 (60.0-63.3)	1 (ref)
One	338	21.5 (19.3-23.7)	1134	20.5 (19.3-21.7)	1.15 (0.96-1.37)
Two	217	12.7 (11.0-14.4)	545	9.7 (8.8-10.6)	1.21 (0.98-1.51)
Three or more	301	18.8 (16.5-21.2)	463	8.1 (7.4-8.9)	1.73 (1.36-2.20)**

**Wald's Chi-square test significant (p-value < 0.05)
The bivariate Chi-square test of association between fall and each class of CNS-acting medication was found to be significant with p-value <0.0001.
The Chi-square test of association between falls and total number of CNS-acting medication was found to be significant (p-value <0.0001).

The percentage of fallers taking psychotherapeutic agents was 25.9% compared to 15.6% non-fallers taking the same. The users of psychotherapeutic agents including antidepressants, anxiolytics, and antipsychotics, had 26% higher risk of falling than non-users (OR: 1.26, 95% CI: 1.08-1.47). Use of benzodiazepine was also found to be associated with higher risk of falls. The association between use of sedative/hypnotic and anticonvulsants was not found to be statistically significant. Moreover, taking three or more CNS-acting medications increases the odds of having a fall by 73% (OR: 1.73, 95% CI: 1.36-2.20).

6.4.3 Effect of Alcohol and CNS-Acting Medication on the Risk of Falling

Out of the total 7,163 study sample, 96 older adults did not provide useful response to alcohol intake questions in the survey. Hence these 96 older adults were not included in most analyses including the alcohol use variable. Among the 3,019 CNS-acting medication users, 23.6% (95% CI: 21.8-25.4 %, n=656) were within-limit drinkers, 5.5% (95% CI: 4.4-6.6 %, n=148) consumed alcohol at an exceeding level, and 10.1% (95% CI: 8.7-11.5 %, n=277) were NIAAA-defined at-risk drinkers.

Of the 7,067 study sample, the potential concurrent use of alcohol and CNS-acting medication was found to be 12.2% (95% CI: 11.3-13.2 %, n=814). Among the 814 potential concurrent users, 52.9% (95% CI: 49.7-56.1 %, n=425) took opioid analgesics, 36.2% (95% CI: 32.9-39.5 %, n=289) used psychotherapeutic agents, 15.7% (13.0-18.3%, n=129) were anticonvulsant users; 15.0% (95% CI: 12.3-17.7 %, n=122) were benzodiazepine users; and 14.9% (95% CI: 12.3-17.4 %, n=123) used sedative-hypnotic agents (Figure 6.3).

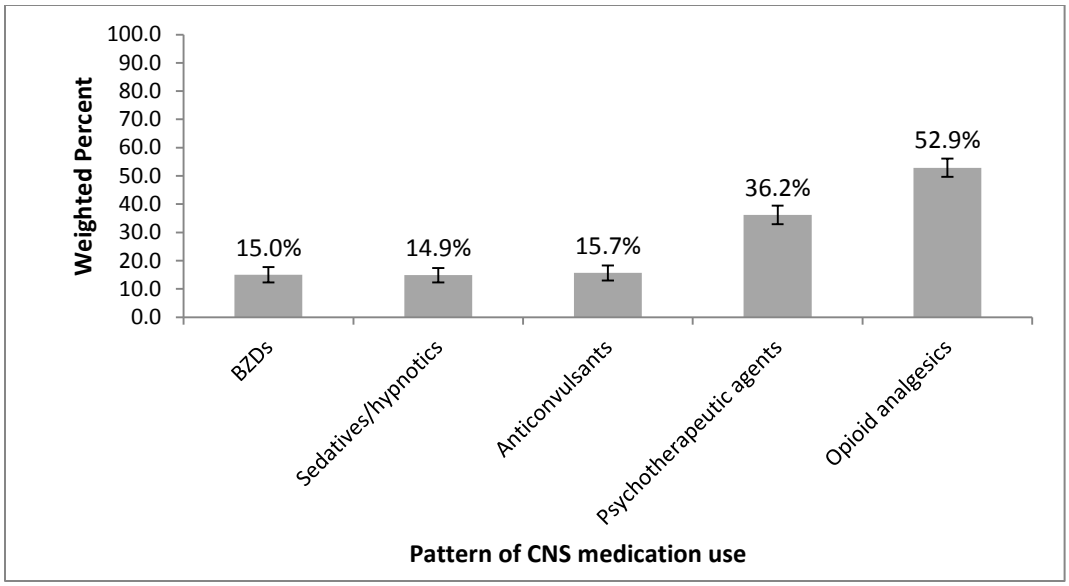

Figure 6.3 Pattern of CNS-Acting Medication use among Concurrent Users

Among the potential concurrent users (Figure 6.4), approximately 81% (95% CI: 77.9-84.3 %, n=656) consumed alcohol within limit; 18.9% (95% CI: 15.7-22.1, n=148) were exceeding-limit drinkers; and 34.5% (95% CI: 30.6-38.5 %, n=277) were at-risk drinkers (defined by NIAAA guidelines).

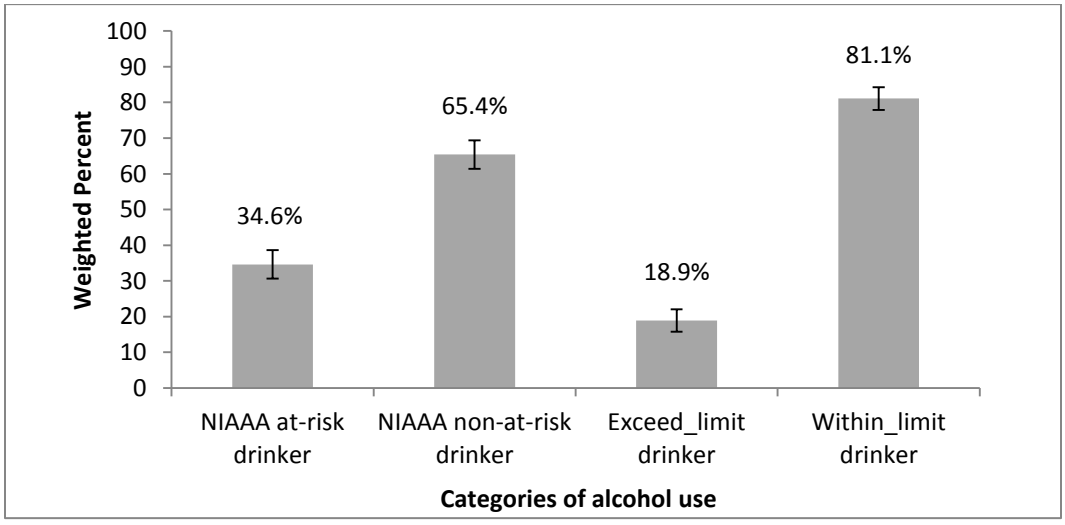

Figure 6.4 Pattern of Alcohol Consumption among Concurrent Users

The majority of exceeding-limit drinkers were older men whereas a greater proportion of non-drinkers were older women. Interestingly, the proportion of older men and women was similar for within-limit drinkers suggesting moderate drinking is not only more prevalent but also common in both genders. A larger proportion of CNS-acting medication users were older women. Among concurrent users, 54.4% were women and 45.6% were men. Figure 6.5 depicts the proportion of older men and women across the exposure groups

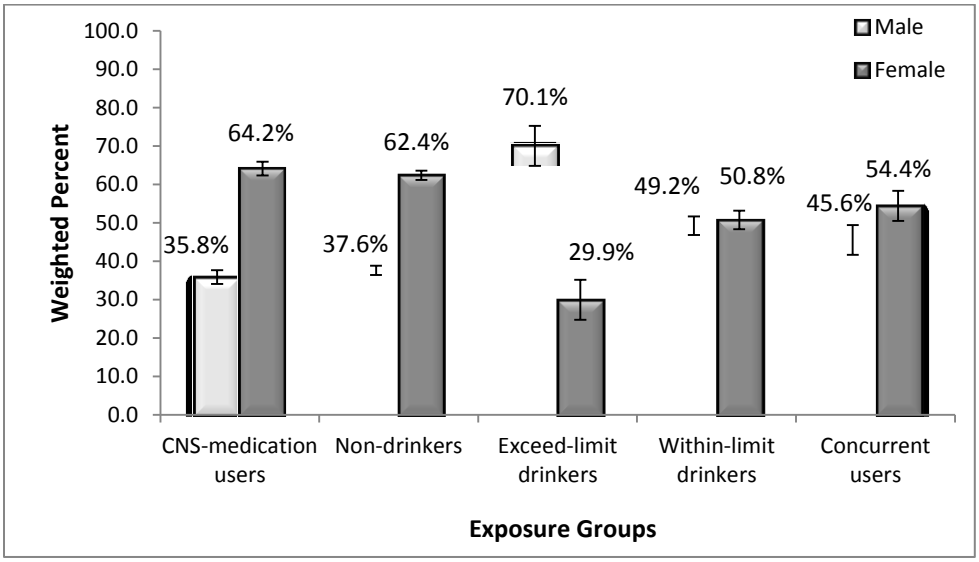

Figure 6.5 Gender Distributions in the Exposure Groups

A logistic regression model was built to understand the effect of use of alcohol and CNS-acting medication on the risks of fall, after adjusting for confounders (Table 6.5). After adjusting for confounders no significant association between alcohol consumption and fall was detected. CNS-acting medication was found to be a risk factor for falls in older adults (OR: 1.26, 95% CI: 1.08-1.46). Older adults taking at least one CNS-acting medication may have 26% higher odds of falling than non-users of CNS-acting medication.

Table 6.5 Effect of Alcohol and CNS-acting Medications on Risk of the Falling

Variables	Fallers		Non-fallers		Adjusted Odds Ratio (95% CI)
	Sample persons	Weighted percent (95% CI)	Sample persons	Weighted percent (95% CI)	
Drinking status					
Non-drinkers	1143	69.8 (67.0-72.7)	3626	64.1 (62.2-65.9)	1 (ref)
Within-limit drinkers	364	24.3 (21.9-26.7)	1523	29.5 (28.0-31.0)	0.91 (0.78-1.05)
Exceeding-limit drinkers	85	5.9 (4.3-7.4)	318	6.4 (5.4-7.4)	1.05 (0.76-1.45)
CNS-acting medication use					
Non-users	856	46.9 (44.5-49.4)	2142	61.7 (60.0-63.3)	1 (ref)
Users	745	53.1 (50.6-55.5)	3366	38.3 (36.7-40.0)	1.26 (1.08-1.46)*
CNS-acting medication user + drinking status					
Non-users + non-drinkers	499	30.4 (28.0-32.8)	2098	37.5 (35.7-39.2)	1 (ref)
Users + exceeding-limit drinkers	48	3.2 (2.1-4.2)	100	2.0 (1.6-2.5)	1.72 (1.13-2.61)*
Users + within-limit drinkers	157	10.2 (8.5-11.8)	499	9.7 (8.8-10.5)	1.05 (0.81-1.37)
Users + non-drinkers	644	39.4 (37.0-41.9)	1528	26.6 (25.1-28.1)	1.27 (1.07-1.51)*
Non-users + exceeding-limit drinkers	37	2.7 (1.8-3.7)	499	4.4 (3.6-5.2)	0.86 (0.56-1.32)
Non-users + within-limit drinkers	207	14.1 (12.3-15.9)	1024	19.8 (18.5-21.2)	0.97 (0.79-1.18)

* Wald's Chi-square test significant with p-value <0.05.
Number of observations included in the model= 6988 and weighted frequency of these observations =19541101
Number of observations deleted due to missing values in response or explanatory variables=175

Comparing to those who neither use CNS-acting medication nor drink, it was observed that the odds of falling was 72% (OR: 1.72 95% CI: 1.13-2.61) higher among CNS-acting medication users who drink at an exceeding level. However, no significant association was observed among CNS-acting medication users who drink within limit and risk of fall. However,

CNS-acting medication use in the presence of drinking within limit did not show significantly greater odds of falling. Alcohol use in the absence of CNS-acting medication use did not demonstrate significant association with risk of falling.

Table 6.6 Use of CNS-acting Medications and Binge Drinking and Risk of Falling

Variables	Fallers		Non-fallers		Adjusted Odds Ratio (95% CI)
	Sample Persons	Weighted Percent (95% CI)	Sample Persons	Weighted Percent (95% CI)	
Binge drinking					
Non-drinkers	1143	69.6 (66.7-72.5)	3626	64.0 (62.2-65.9)	1 (ref)
Non-binge drinkers	395	26.3 (23.8-28.7)	1606	31.2 (29.6-32.9)	0.93 (0.81-1.08)
Binge drinkers	55	4.1 (2.9-5.3)	240	4.7 (4.0-5.5)	1.06 (0.72-1.54)
Binge drinking + CNS-acting medication					
Non-users + non-drinkers	499	30.3 (27.9-32.7)	2098	37.4 (35.6-39.2)	1 (ref)
Non-users + non-binge drinkers	220	2.3 (1.4-3.2)	1085	1.5 (1.2-1.9)	0.97 (0.80-1.18)
Non-users + binge drinkers	24	11.3 (9.6-13.0)	162	10.2 (9.2-11.1)	0.83 (0.49-1.41)
Users + non-drinkers	644	39.3 (36.8-41.8)	1528	26.6 (25.1-28.1)	1.27 (1.07-1.51)*
Users + non binge drinkers	175	1.9 (1.1-2.6)	521	3.2 (2.6-3.8)	1.12 (0.87-1.44)
Users + binge drinkers	31	14.9 (13.2-16.7)	78	21.1 (19.6-22.5)	1.77 (1.07-2.92)*

* Wald's Chi-square test significant with p-value <0.05.
Number of observations included in the model=6994 and weighted frequency of these observations =19568317 Number of observations deleted due to missing values in response or explanatory variables=169

The association between binge drinking and risk of falling was also investigated (Table 6.6). Binge drinking was not found to be associated with risk of falling. The exposure variables, CNS-acting medication use and binge drinking, were combined to form six subcategories. Older adults who do not drink or take CNS-acting medications were the reference group. So compared to non-drinker and non-user, older adults taking CNS-acting medication and binge drinking were 77% times (OR: 1.77, 95% CI: 1.07-2.92) more likely to encounter a fall in the past year. Similar

to the previous observation, CNS-acting medication use among non-drinkers was significantly associated with the risk of falls. However, CNS-acting medication use in the presence of non-binge drinking was not significantly associated with higher odds of falling.

Table 6.7 Use of Alcohol and Opioid Analgesics and Risk of Falling

Variables	Fallers		Non-fallers		Adjusted Odds Ratio (95% CI)
	Sample Persons	Weighted Percent (95% CI)	Sample Persons	Weighted Percent (95% CI)	
Opioid analgesics + Drinking status					
Non-users + non-drinkers	748	45.7 (42.8-48.6)	2835	50.3 (48.4-52.0)	1 (ref)
Users + exceeding-limit drinkers	26	1.7 (0.9-2.4)	51	1.0 (0.7-1.3)	1.87 (1.08-3.24)*
Users + within-limit drinkers	100	6.6 (5.2-8.0)	248	4.8 (4.3-5.4)	1.26 (0.92-1.73)
Users + non-drinkers	395	24.1 (21.8-26.4)	791	13.8 (12.7-14.9)	1.39 (1.16-1.66)*
Non-users + within-limit drinkers	264	17.7 (15.8-19.5)	1275	24.7 (23.3-26.1)	0.90 (0.76-1.07)
Non-users + exceeding-limit drinkers	59	4.2 (3.0-5.4)	267	5.4 (4.5-6.3)	0.98 (0.69-1.41)

* Wald's Chi-square test significant with p-value <0.05.
Number of observations included in the model=6994 and weighted frequency of these observations =19568317 Number of observations deleted due to missing values in response or explanatory variables=169

Assessment of risk of falls associated with alcohol consumption and opioid analgesics (Table 6.7) revealed that exceeding-limit drinkers taking opioid analgesics had 87% (OR: 1.87, 95% CI: 1.08-3.24) higher odds of having a fall though the sample size of this group was small (n=26). Older adults using opioid analgesic and drinking within limit did not demonstrate significantly greater risk of falls. However, older adults taking opioid analgesics but abstaining from alcoholic beverage seemed to have greater odds of falling compared to non-drinkers and non-users. Effect of combined use of alcohol and other classes of CNS medication could not be ascertained due to small sample sizes (n < 20) in these groups.

6.4.4 Effect of alcohol and CNS-acting medication on risk for injurious falls

The fallers were further categorized into two groups (injurious falls and non-injurious falls) based on whether or not they experienced a fall that required medical assistance. Of the entire study sample, 6.1% (95% CI: 5.4-6.8 %, n=462) reported seeking medical assistance after the fall, and 15.6% (95% CI: 14.8-16.4 %, n=1,138) did not require medical assistance after the fall. The proportion of CNS-acting medication use was greater in fallers than non-injurious fallers and non-fallers. It can be observed in Table 6.8 that the proportions of alcohol use were lower as the severity of fall increased. Exceeding-limit drinking was reported by 5.5% of injurious fallers compared to 6.0% of non-injurious fallers and 6.4% of non-fallers. A similar trend was observed for within-limit drinkers as well. However, the proportion of non-drinkers was greater in injurious fallers followed by non-injurious fallers and further by non-fallers. It must be noted that the confidence interval of the percentage of alcohol use in three different groups of fallers overlapped. After joining the two exposure groups (alcohol use and CNS-acting medication use) the distribution of the six subcategories against fallers was studied. It was seen that many of the cell sizes were small (n <20).

Table 6.8 Distribution of Exposure Variables against Injurious Fallers

Variables	Non-fallers		Non-injurious Fallers		Injurious Fallers	
	Sample persons	Weighted percent (95% CI)	Sample persons	Weighted percent (95% CI)	Sample persons	Weighted percent (95% CI)
Drinking status						
Non-drinkers	3626	64.1 (62.2-65.9)	808	68.6 (65.3-71.9)	335	73.1 (68.4-77.8)
Within-limit drinkers	1523	29.5 (27.9-31.0)	264	25.4 (22.6-28.2)	99	21.4 (17.6-25.2)
Exceeding-limit drinkers	318	6.4 (5.4-7.4)	61	6.0 (4.3-7.7)	24	5.5 (2.9-8.1)
CNS-acting medication use						
Non-users	3366	61.7 (60.0-63.3)	563	49.7 (46.7-52.6)	181	39.9 (35.7-44.2)
Users	2142	38.3 (36.7-40.0)	575	50.3 (47.3-53.3)	281	60.1 (55.8-64.3)
CNS-acting medication use + **drinking status**						
Users + exceeding-limit drinkers	100	2.0 (1.6-2.5)	35	3.4 (1.9-4.7)	13	2.7 (1.1-4.3)
Users + within-limit drinkers	499	9.7 (8.8-10.5)	101	9.5 (7.5-11.5)	56	11.9 (8.8-15.0)
Users + non-drinkers	1528	26.6 (25.1-28.1)	435	37.3 (34.5-40.1)	209	45.0 (40.7-49.4)
Non-users + exceeding -limit drinkers	218	4.4 (3.6-5.2)	26	2.7 (1.7-3.7)	11	2.8 (0.6-5.1)
Non-users + within limit drinkers	1024	19.8 (18.5-21.2)	163	15.8 (13.6-18.1)	43	9.5 (6.8-12.1)
Non-users + non-drinkers	2098	37.5 (35.6-39.2)	373	31.3 (28.6-34.0)	126	28.1 (23.6-3.6)

Column percentages are significantly different (Rao-Scott Chi-square test showed p-value <0.05)

Multi-nominal logistic regression (Table 6.9) was conducted to investigate the effect of alcohol and CNS-acting medication use on the risk of falls. Non-fallers were considered the reference group. Compared to non-users of CNS-acting medications, users were 61% (OR: 1.61, 95% CI: 1.30-2.00, p-value <0.0001) more likely to experience an injurious falls. However,

CNS-acting medication use did not seem to affect the risk of non-injurious fall. Alcohol use was not found to be associated with risk of injurious falls as well as non-injurious falls. Due to small cell size the joint effect of alcohol and CNS-acting medication could not be analyzed.

Table 6.9 Association Between Exposure Variables and Injurious Fallers

Variables	Non-injurious fallers		Injurious fallers	
	Adjusted Odds Ratio (95% CI)	p-value	Adjusted Odds Ratio (95% CI)	p-value
Drinking status				
Non-drinkers	1 (reference)		1 (reference)	
Within-limit	0.96 (0.81-1.12)	0.5772	0.80 (0.61-1.04)	0.0912
Exceeding-limit	1.03 (0.74-1.44)	0.8458	1.13 (0.65-1.95)	0.6627
CNS-medications				
Non-users	1 (reference)		1 (reference)	
Users	1.15 (0.95-1.39)	0.1594	1.61 (1.30-2.00)	<0.0001*

Number of observations included in the model= 6987
Weighted frequency of these observations =19539027
Number of observations deleted due to missing values in response or explanatory variables=176

6.4.5 Effect of alcohol and CNS-acting medication on risk for recurrent falls

Older adults falling more than once in the past year were defined as recurrent fallers. Of the overall study sample 10.0% (95% CI: 9.4-10.6 %, n=755) reported falling more than once in the past year and 11.4% (95% CI: 10.6-12.2%, n=818) reported a single fall in the previous year (Table 6.10). The proportion of CNS-acting medication use in the three groups reflected a pattern. Older adults taking CNS-acting medication were 60% among recurrent fallers, 48% among single fallers, and 38% among non-fallers. On the other hand, the proportion of non-users of CNS-acting medications was 61.7% in non-fallers, 52.4% in single fallers, and 41.1% in recurrent fallers. Recurrent fallers were demonstrated to have a higher proportion of exceeding

limit drinkers as well as non-drinkers compared to non-fallers. After joining the subgroups of alcohol use and CNS-acting medication use variables the resulting exposure variable had six subcategories. However, the cell sample size of few cells was less (n < 20).

Table 6.10 Distribution of Exposure Variables against Recurrent Fallers

Variables	Non-fallers		Non-recurrent fallers		Recurrent fallers	
	Sample persons	Weighted percent (95% CI)	Sample persons	Weighted percent (95% CI)	Sample persons	Weighted percent (95% CI)
Drinking status						
Non-drinkers	3626	64.1 (62.2-65.9)	577	68.9 (65.0-72.8)	546	70.9 (67.3-74.6)
Within-limit drinkers	1523	29.5 (27.9-31.0)	200	26.2 (23.0-29.4)	158	21.9 (18.7-25.1)
Exceeding-limit drinkers	318	6.4 (5.4-7.4)	39	4.9 (2.7-7.0)	45	7.2 (5.1-9.2)
CNS-acting medications use						
Non-users	3366	61.7 (60.0-63.3)	424	52.4 (48.8-56.1)	311	41.1 (37.7-44.4)
Users	2142	38.3 (36.7-40.0)	394	47.6 (43.9-51.2)	444	58.9 (55.6-62.3)
CNS medication use + drinking status						
Users + exceeding-limit drinkers	100	2.0 (1.6-2.5)	23	2.9 (1.6-4.1)	25	3.6 (2.1-5.1)
Users + within-limit drinkers	499	9.7 (8.8-10.5)	80	9.9 (7.6-12.2)	75	10.6 (8.0-12.9)
Users + non-drinkers	1528	26.6 (25.1-28.1)	289	34.6 (31.3-37.9)	340	44.6 (41.0-48.2)
Non-users + exceeding limit drinkers	218	4.4 (3.6-5.2)	16	2.0 (0.71-3.3)	20	3.5 (2.0-5.1)
Non-users + within limit drinkers	1024	19.8 (18.5-21.2)	120	16.3 (13.5-19.1)	83	11.4 (8.9-13.8)
Non-users + non-drinkers	2098	37.5 (35.7-39.2)	288	34.3 (30.6-37.9)	206	26.3 (23.2-29.4)

Column percentages are significantly different (Rao-Scott Chi-square test showed p-value <0.05)

Multi-nominal logistic regression was conducted to investigate the effect of alcohol and CNS-acting medications on the risk of recurrent falls (Table 6.11). Non-fallers were considered as reference group. Compared to non-users of CNS-acting medications, users were 35% (OR: 1.35, 95% CI: 1.15-1.59, p-value= 0.0002) more likely to experience a recurrent fall. However, CNS-acting medication use did not seem to affect the risk of non-recurrent falls. Older adults who were exceeding-limit drinkers were found that have 48% (OR: 1.48, 95% CI: 1.06-2.07, p-value=0.0225) greater odds of being recurrent fallers compared to non-drinkers. Within-limit drinking did not demonstrate significant association with to the risk of recurrent falls. Due to a small cell size the joint effect of alcohol and CNS-acting medication could not be analyzed.

Table 6.11 Association Between Exposure Variables and Recurrent Fallers

Variables	**Non-Recurrent Fallers**		**Recurrent Fallers**	
	Adjusted Odds Ratio (95% CI)	**p-value**	**Adjusted Odds Ratio (95% CI)**	**p-value**
Drinking status				
Non-drinkers	1 (reference)		1 (reference)	
Within-limit	0.89 (0.73-1.09)	0.2566	0.92 (0.75-1.13)	0.4130
Exceeding-limit	0.79 (0.48-1.31)	0.3670	1.48 (1.06-2.07)	0.0225*
CNS-acting medication use				
Non-users	1 (reference)		1 (reference)	
Users	1.19 (0.96-1.47)	0.1181	1.35 (1.15-1.59)	0.0002*

Number of observations included in the model=6961
Weighted frequency of these observations =19472994
Number of observations deleted due to missing values in response or explanatory variables=202

6.5 Discussion

This study aims at to understand the effect of the combined use of CNS-acting medications and alcohol, at different consumption levels, on the risk of falls in community dwelling Medicare beneficiaries aged 65 years or older. The complex, non-linear relationship observed between risk of falls and the use of CNS-acting medication and alcohol at varying degrees is the most interesting and novel aspect of this study.

The potential concurrent use of alcohol and CNS-acting medication in the past year was found to be approximately 12% (n=814), with almost 80% of these potential concurrent users being within-limit drinkers and 20% drinking at an exceeding limit. Approximately 40% of the concurrent users took more than one CNS-acting medication in the past year. The proportion of potential concurrent users was substantial. Hence, it was important to understand the effect of the potential concurrent use of alcohol and CNS-acting medications on the risks of falling.

Our findings showed that the use of CNS-acting medication by older drinkers who exceeded the NIAAA recommended drinking guidelines (no more than one drink per day) experienced 77% higher odds of falling. In addition, binge drinking in the presence of CNS-acting medication use also increases the odds of falling by 87% among older adults. Increased fall risk was also observed among exceeding-limit drinkers who consumed opioid analgesics. Interestingly, CNS-acting medication users drinking within NIAAA recommended limit did not seem to significantly have higher odds of falling, though non-drinking CNS-acting medication users demonstrated 27% greater odds of falling. This suggests a complex non-linear effect of combined use of alcohol and CNS-acting medications on the risks of falling, driven by labyrinth of known and unknown factors.

Some of the possible explanations for this finding are summarized below:

1. Our findings seemed to parallel the theory of protective effect of moderate drinking on the risk of falls in older adults.[1,120] The risk estimate observed in our study might be interpreted as the protective effect of moderate alcohol intake negating the harmful effect of CNS-acting medication use. However, it is noteworthy that the relationship between moderate alcohol use and risk of fall has been unclear and documented inconsistently in the literature[120]
2. Older adults who take CNS-acting medication and report consuming higher amount of alcohols may tend to have psychiatric conditions, depressive symptoms, pain, or history of problem drinking, which may increase their risk of falls.[9]
3. Another potential premise is the effect of alcohol on bone mineral density (BMD); alcoholics are reported to have lower BMD, possibly due to accompanying nutritional deficiencies whereas moderate drinking might be associated with greater BMD.[123,124]
4. Moderate drinkers might be healthier than heavy drinkers. Thus, the healthier profile of moderate drinkers could be confounding the association between moderate drinking and risk of falling.[125] Moreover, such healthier older adults may have been following a healthier lifestyle, endorsing healthy eating habits, exercising, refraining from harmful activities such as smoking or heavy drinking. Although, the effect of health and functional status of older adults have been controlled in the logistic regression analysis, other variables such as diet, and exercise could not be taken into account due to lack of this information in the dataset.
5. Studies have shown that people with higher educational level or belonging to upper socio-economic background tend to drink regularly but moderately. There is a possibility

that the link between the benefits of moderate drinking observed in our study could be explained by premorbid intellect, and its correlation with cognitive reserve. To elaborate, individuals with better premorbid cognition (person's intellectual functioning prior to known or suspected onset of brain disease or dysfunction) or with higher education level tend to have more cognitive reserve. Hence such individuals may have elevated threshold for experiencing functional impairment and less sensitive to the effect of alcohol.[126,127] Besides, several studies have advocated the beneficial effect of moderate drinking on cognitive function in older adults.[126,127]

6. Another possible explanation could be development of tolerance (requirement to consume higher amount of the drug to achieve the same response) to alcohol due to regular, moderate drinking. Continuous, constant and moderate exposure to alcohol may result in lesser effect of alcohol due to metabolism driven by induced enzyme secretion or several other mechanisms involved at a cellular or molecular level.[128,129] The CNS-acting medications such as benzodiazepines, barbiturates, anticonvulsant agents, and other sedative-hypnotics potentiate the inhibitory action of GABA by acting on a separate binding site on the receptors and changing the conformation of the receptor Alcohol modified the GABA receptor by "altering the membrane environment such that the receptor has an increases affinity for GABA and other sedative-hypnotics". Thus the pharmacological action of these benzodiazepines, barbiturates, sedatives-hypnotics, and alcohol on the same receptor explains the similar impact of these agents and development of cross-tolerance. [128]
7. The beneficial effect of moderate drinking observed in our study could also be an artefact of residual confounding or the cross-sectional study design.

Some of the above explanations such as the healthy drinker effect, high cognitive reserve, development of tolerance, and potential benefits of moderate drinking could also explain the absence of a significant relationship between alcohol and risk of falling, controlling for CNS-medication use. The relationship between alcohol consumption and risk of falls has been inconsistent and unclear in the literature. Some studies have found that high alcohol consumption is associated with risk of falling[1,93,114,130,131] while other studies have failed to establish the association.[132] A systematic review summarized the relationship between falls or fall injuries and alcohol use in older adults. The review summarized four studies that reported increased risk of falls or fall injuries associated with alcohol use (ranging from daily use to an average weekly consumption of greater than 21 drinks) however, twenty-one studies found no association between alcohol consumption and risk of falls or fall injuries.[119] A study involving older participants of the Cardiovascular Health Study (CHS) reported that the cross-sectional analysis indicated an apparent inverse association between alcohol intake and risk of frequent falls (adjusted OR: 0.41, 95% CI: 0.14-1.17), but the longitudinal analysis found 25% (95% CI: 3-52%) higher risk in drinkers of 14 or more drinks per week. A possible explanation for this observation could be that older adults at risk for falling tend to decrease their alcohol use over time or heavy drinkers at risk of fall tend not to enroll in cohort studies.[1] Stenbacka *et al*. found that high levels of alcohol intake (greater than 500 grams/month) were associated with higher risk of injurious falls (relative risk: 2.27, 95% CI: 1.45-3.57).[93] Few studies have described a protective association between moderate drinking and fall risk in older adults. A case-control study determined a protective effect (adjusted OR: 0.49, 95% CI: 0.25-0.95) of moderate drinking on the risk of hip fracture in mid and older aged adults.[118] A study by Cawthon *et al*. concluded that light alcohol intake may decrease the risk if falling, but a history of problem

drinking increased fall risk.[123] Mostly the CNS depressant effect of alcohol (causing sedation, drowsiness, dizziness, impaired and psychomotor function) has been implicated as an underlying rationale for the increase in fall risk.[2] However, the effect of alcohol on bone mineral density may influence the association between alcohol and risk of falling. Several studies have been conducted to assess the relationship between bone mineral density and alcohol consumption. The evidence generated by this study is unclear and inconsistent; however, several longitudinal studies reported moderate alcohol intake was not predictive of the rate of bone loss.[123]

Consistent with the literature, our findings suggest that CNS-acting medication use is a risk factor for fall in older adults. Furthermore, use of opioid analgesics, benzodiazepines, and psychotherapeutic agents (including antidepressants, anxiolytics, and antipsychotics) were associated with increased risk of falls. However, use of sedative-hypnotic medications or anticonvulsants was not significantly associated with fall risk. The higher risk for falling has been associated with the use of CNS-acting medications or psychotropic medication as detected by various observational studies including studies with prospective cohort and case control designs. A nested case-control study established that using psychotropic medications within three months of falling was associated with a higher risk of falling accidents among older men (OR: 2.14, 95% CI: 1.87-2.44) and older women (OR: 2.21, 95% CI: 2.04-2.39).[133]A cross-sectional analysis of data from a large population of community-dwelling older adults estimated that the risk of falling increases by nearly 47% (OR: 1.47, 95% CI: 1.24-1.74) in users of psychotropic drugs.[134] Previous studies have found the use of sedative-hypnotics or anticonvulsants to be significantly associated with fall risk.[115,132] Contrary to the literature, our study did not detect significant association between the use of sedative-hypnotic or anticonvulsant, and fall risk. Possible explanations for this could be: i) the drug classification employed by the data source, ii)

under-reporting of sedative-hypnotic use, iii) use of newer sedative-hypnotic or anticonvulsants with better safety profiles such as zaleplon, in older adults prone to falling, or iv) an artefact of study design or residual confounding.

Effects of alcohol consumption and CNS-acting medication use on the risk for injurious falls were studied separately employing a multi-nominal logistic regression model. CNS-acting medication use was found to be a risk factor for injurious falls but not a risk factor for non-injurious falls. CNS-acting medication users had 61% greater likelihood of having an injurious fall compared to nonusers. Alcohol use, both within-limit drinking and exceeding-limit drinking, was not found to be associated with the odds of falling. The absence of a relationship between high alcohol use and risk of injurious falls observed in our study could also be due to the low sample size in that subgroup. A Swedish study found that high alcohol consumption (≥ 1,000 g of 100% ethanol per month) was associated with increased risk for one injurious fall in older women aged 60 years and older.[93] The effect of concurrent use of alcohol and CNS-acting medication could not be investigated in this study due to the small sample size in some subgroups.

The effects of alcohol consumption and CNS-acting medication use on the risks for recurrent falls were estimated separately utilizing a multi-nominal logistic regression model. CNS-acting medication use was found to be a risk factor for recurrent falls. Users of CNS-acting medications were 35% more likely to be recurrent fallers than non-users but association between CNS-acting medication use and risk for single fall was not significant. Drinking at an exceeding limit was associated with 48% higher odds of recurrent falls. However, it should be noted that only 24 older adults were recurrent fallers who are exceeding-limit drinkers. An analysis with a larger sample size can help confirm this finding. Other studies have also demonstrated

association between alcohol and risk for recurrent falls in older adults.[131,135] A longitudinal study found that igh alcohol consumption (18 or more drinks per week) was a predictor of recurrent falls.

The prevalence of falls and injurious falls reported in our study is similar to that seen in other studies as well. An analysis of survey reported data from MCBS 2002 Cost and Use file found that 22.1% (2909 out of 12669 respondents) of Medicare beneficiaries aged ≥65 years fell in the previous year and 33% of the participants who reported at least one fall required medical attention for at least one fall.[136] The prevalence and pattern of alcohol consumption reported in this study is comparable to the prevalence estimated in using other national datasets. Analysis of the 2003 MCBS data showed that during a typical month in the past year 65.5% of the sample reported drinking no alcohol, 25.4% reported drinking within guidelines, 3.8% exceeded the monthly limit only, and 5.4% reported heavy episodic drinking.[137] In general, the pattern and prevalence of alcohol or CNS-acting medication use differs depending upon the setting and design of the study or data source, definitions, cut-off limits, types of CNS-acting drug class used, data collection method, or country of study. Hence comparison of the magnitude of use of alcohol or CNS-acting medications between studies is difficult. Psychotropic medications are more prevalent among community-dwelling older adults than other age groups with research findings suggesting that between 35% and 53% of assisted living residents receive one or more psychotropic medications.[33]

There are several limitations to this study. It is a cross-sectional study hence the cause-effect relationship between the exposures and risk of fall cannot be determined. Further research using a case-control or cohort study design is necessary to confirm the findings of this study. It is beyond the scope of this study to definitively ascertain the concurrent use of CNS-acting

medication and alcohol. However the alcohol consumption measured in this study depicts typical or regular consumption in the past year. Usually older adults follow a consistent pattern of alcohol intake, however, certain events such as bereavement, retirement, loneliness, and disease conditions may cause them to increase or decrease their alcohol intake.[22,109,125] Under-reporting of alcohol intake or fall events could bias the risk estimate assessed in this study. The duration, dose, and regimen of CNS-acting medications were not considered in this study. Residual confounding could also be a possibility. Inaccurate reporting or random error in collection or coding of data could have occurred. The findings of this study are only applicable to non-institutionalized older adults.

This study has several strengths. The risk estimates obtained in this study are controlled for the confounding effect of various risk factors including antihypertensive medication use[138], eye impairment, functional status of the participants (using ADL and IADL, perceived health status), comorbidity, polypharmacy, age, gender, education, race,and social activity.[9,139] The medication use has been captured using survey as well as administrative data. This study uses a nationally representative sample of community-dwelling older adults aged 65 years or older.

6.6 Conclusion

The major findings of this study i.e. the risk of falls is higher among older adults taking CNS medication and either binge drinking or consuming alcohol at a level that exceeds the recommended limit, provide evidence of harmful effects of high alcohol intake by CNS-acting medication users. Based on the premise that alcohol consumption is a modifiable behavior and CNS-acting medication use in this group of older adults is justified, high alcohol consumption should be discouraged among CNS-acting medication users. Furthermore, this study confirms

that CNS-acting medication use is a risk factor for falls in older adults. To our knowledge, no other study has investigated the combined effect of alcohol and CNS-acting medication on risk of falls in older adults. Thus, the findings of this study may play an important role in drawing the attention of researchers and healthcare professionals to this area of study as well as adding to the literature

Findings of this study highlight the potential value of screening older adults for high alcohol use, apart from other risk factors of falls. Dissemination of this information among health professionals will create awareness about the potentially deleterious effect of high alcohol consumption, especially among those prescribed CNS-acting medication. Greater attention should be given to patients on multiple CNS-acting medications or taking psychotherapeutic agents and opioid analgesics while screening for fall risk. In the era of evidence-based practice, the findings of our study will play a significant role in clinical practice to identify older adults at risk of fall. To summarize, these findings underscored the harmful effect of potential concurrent use of CNS-acting medications and excessive alcohol consumption

Chapter 7

Section 7.1 Conclusion

This dissertation aimed to provide a comprehensive perspective on alcohol use considering medication use and comorbid conditions. The first goal was to understand the pattern and prevalence of alcohol use that is deemed "risky" owing to the excessive amount of alcohol consumption, and immoderate alcohol intake in the presence of certain disease conditions and medications. In the next step, potential concurrent use of alcohol and CNS-acting medication was studied to determine the proportion of older adults at risk of experiencing alcohol-CNS medication interactions. Additionally, the effect of potential concurrent use of alcohol and CNS-acting medication on the risk of falls was investigated by performing a cross-sectional analysis. The findings of this study are applicable to community-dwelling American older adults aged 65 years or older.

The MCBS 2009 data showed at-risk drinking varied between 5.6%-11% among older adults, depending on the definition of at-risk drinking. Potential concurrent use of CNS-acting medications and alcohol was observed to be 12.1% among non-institutionalized, Medicare beneficiaries aged 65 years or older. On the other hand, analyses of the NHANES data showed 8.9% of non-institutionalized older adults reported drinking daily and taking at least one CNS-acting medication in the past month. The prevalence rate obtained from NHANES data was a conservative estimate. These findings strongly suggest that a substantial proportion of older adults reported potentially harmful alcohol use and could be susceptible to alcohol-related adverse effects. Thus, identifying these vulnerable older adults and providing appropriate intervention is necessary. Interventions such as screening for at-risk drinking, counselling, and

screening for potential alcohol-medication or alcohol-drug interactions could minimize the risk among those older adults. However, to maximize the utilization of healthcare resources, older adults more likely to be at risk of alcohol-related adverse events need to be managed at the outset. The socio-demographic factors identified in this study can provide an insight into those risk factors. Age between 65-74 years, male gender, being white, history of smoking, high education, and, good health condition were some factors associated with hazardous alcohol use, identified using MCBS and NHANES data.

The effect of potential concurrent use of alcohol and CNS-acting medication on the risk of falls was studied employing a cross-sectional study design. Though alcohol consumption was not found to be significantly associated with fall risk, high alcohol consumption (more than 30 drinks/month) accompanied by CNS-acting medication use was associated with an increased odds of falling (OR: 1.72, 95% CI: 1.13-2.61). Older adults taking CNS-acting medication and reportedly binge-drinking encounter a significant increased risk of falls. CNS-acting medication use, in the absence of alcohol intake, was found to increase the odds of falling by 27% (OR: 1.27, 95% CI: 1.07-1.51). CNS-acting medication use was also associated with risks for recurrent falls and injurious falls. High alcohol consumption (more than one 30 drinks/month) was found to be associated with risk for recurrent falls. The effect of combined use of alcohol and CNS-acting medication on the risks for recurrent falls and injurious falls could not be studied due to lack of small size.

The baby-boomer generation is known to use substances of abuse at a higher rate than the previous generations, so with the aging of this generation, the number of older adults requiring treatment for substance abuse is likely to increase. Additionally, older adults constitute the fastest growing segment of U.S. population. Thus, the demand for specialized health care

services will expand in future. In this scenario, understanding the adverse effects of risky drinking and identifying the factors associated with at-risk drinking is of utmost importance.

By measuring the prevalence of at-risk drinking or potential concomitant use of alcohol and alcohol-interactive drugs, the proportion of older adults who could be at risk was determined which provided an insight into the magnitude of the problem. By identifying the factors associated with at-risk drinking or daily drinking, preventive measures or screening processes can be directed to those "high-risk" older adults. On the other hand, understanding the effects of concurrent use of alcohol and alcohol-interactive medications (in the case of our study, CNS-acting medications) on health outcomes may play a significant role in evidence-based practice. In this current age, evidence forms the basis for framing treatment guidelines, planning preventive measure, and creating awareness among older adults. Hence this study not only fills a gap in literature but also creates evidence that can influence healthcare practices to achieve better outcomes. This study can also play a role in increasing awareness among older adults about the potential adverse effects of alcohol use in the presence of comorbid conditions or when concomitantly consumed with medications.

Section 7.2 Future Directions

The findings of this study can play a significant role in encouraging further research in this area, especially understanding the effect of the concomitant use of alcohol and alcohol-interactive medications in older adults. Based on the findings of our study, further research to understand the effect of alcohol and CNS-acting medications on the risks for falling by employing case-control or cohort study designs is very important to confirm the findings this study.

In the current age of "big data", databases obtained from different sources, such as survey-collected data, administrative claims data, and electronic medical record, can be a useful and efficient base for conducting an epidemiological study. By using multiple years of MCBS data, a retrospective cohort study can be designed to evaluate the aforementioned research questions. In addition, Health Retirement Study (HRS) data linked to CMS data, or NHANES linked with CMS data can also be potential data sources for such studies.[97,140] Several longitudinal studies such as The Health, Aging, and Body Composition (Health ABC) study and Cardiovascular Health study (CHS) are also potential sources of data for conducting this research.[141,142] Moreover, assessing emergency department visits resulting from co-administration of alcohol and psychotherapeutic agents can also help us understand the implications of concurrent use of alcohol and CNS-acting medications. DAWN is one of the data sources to conduct such a study.[26]

Understanding the relationship between at-risk drinking and healthcare utilization and cost of this utilization in older adults is an important and interesting question that needs further research. Such a study will help assess the impact of at-risk drinking on healthcare resource utilization.

The MCBS data combines administrative claims records and information on out-of-pocket costs, access to care and other such variables collected from survey. Linking Part D data with other MCBS study data can also help obtain information of medication utilization. In addition, conducting a prospective study in congregate living facilities can be an alternative which can provide rich qualitative information about the drinking habits of older adults which a secondary database may not be able to provide.

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Appendix A

SAS Codes

Logistic Regression

```
proc surveylogistic data=newCNS_fall_medddrnk    varmethod=brr (fay=0.3);
repweight CS1YR001-CS1YR100;
   class   meddrnk (ref="nomed_nodrnk")
      educate  (ref="more highschool")
      marital  (ref= "married")
      race     (ref= "white")
      social   (ref="no")
      age      (ref=">85")
      H_SEX    (ref="2")
     polypharm (ref=">=11")
      IADL_cat (ref= "no")
       ADL_cat (ref= "no")
     old_health(ref="worse")
          bp   (ref= "0")
        eye   (ref= "no_impair")
        comorbid (ref="zero") / param=ref;
   model fall (event='yes')  = meddrnk  age H_SEX educate marital race social
polypharm IADL_cat ADL_cat old_health  bp eye comorbid ;
 weight CS1YRWGT;
run;
```

Multi-nominal Logistic Regression

```
proc surveylogistic data=Newlib.atrisk_wt varmethod=brr (fay=0.3);
class educate  (ref="more highschool")
      marital  (ref= "married")
      race     (ref= "white")
      earn     (ref=">25000")
      social   (ref="no")
      age      (ref=">85")
      smoke    (ref="neversmoker")
      H_SEX    (ref="2")
     polypharm (ref=">=11")
     old_health(ref="worse")
       comorbid (ref=">=5")
      jobstat   (ref="No")
       IADL_cat (ref= "no")
       ADL_cat (ref= "no")  / param=ref;
   model allrisk (ref="non-drinker") = age H_SEX race marital educate social
earn jobstat smoke polypharm comorbid IADL_cat ADL_cat old_health /
link=glogit;
weight CS1YRWGT;
repweight CS1YR001-CS1YR100;
run;
```

Curriculum Vitae

Maitreyee Mohanty

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Summary

An experienced researcher with specialized training in health economics and outcomes research. Interested in integration of my diverse training in pharmaceutical sciences, epidemiology, biostatistics, and clinical research to address the challenges in healthcare system.

Skills

Epidemiological research methods	Regression modeling
Survey research methods analyses	Retrospective database
Systematic review and meta-analysis	Geriatric Pharmacotherapy
Propensity score matching	Decision modeling
Cost-effectiveness analysis	Evidence-based medicine

Education

Ph.D. in Pharmacotherapy and Outcomes Science 2009-present
Virginia Commonwealth University (VCU), Richmond, VA

Master of Pharmacy Practice 2007 - 2009
National Institute of Pharmaceutical Education and Research (NIPER), India

Bachelor of Pharmacy 2003 - 2007
Manipal College of Pharmaceutical Sciences, Manipal, India

Professional Diploma in Clinical Research 2007-2008
Catalyst Clinical Services, New Delhi, India

Research Experiences

Systematic review and meta-analysis 2012-2013

Collaborated with a team to perform systematic review and meta-analysis determining the effect of statins in delaying the progression of diabetic nephropathy, using the Cochrane guidelines.

Retrospective analysis of secondary data 2011-2012

Designed and performed a cross-sectional analysis using the National Health and Nutrition Examination Survey (NHANES) 2005-2010 data to determine the prevalence and pattern of potential concurrent use of alcohol and central nervous system medications in older adults.

Prospective observational study in a tertiary care setting 2008-2009

Conducted a prospective observational study to determine the prevalence and predictors of inappropriate prescribing in geriatric inpatients, using the chart review method for data collection.

Teaching Experiences

Teaching assistant, Department of Pharmacy 2009-2011

Duties included managing course load, grading tests, and training students.

Teaching assistant, Department of Biostatistics 2011-2012

Duties included teaching graduate students biostatistical methods and assisting them to perform statistical analyses using the JMP software.

Dissertation Project 2012-present

Alcohol and medication use among older adults: understanding the effects of alcohol and central nervous system (CNS) medications on the risk of falls. The Medicare Current Beneficiary Survey (MCBS) 2009 data is used to conduct an observational study employing SAS 9.3 statistical software.

Summer Internships

Summer project at the Medicine Information Centre (MIC), NIPER (Mohali), India | 2008
Six-week training focused on understanding the function and operational procedures of the MIC.

Summer training at the National Pharmacovigilance Centre, Cuttack, India | 2007
Two-week clinical training engaging in collection, assessment and interpretation of data for adverse drug reactions (ADR) monitoring.

Summer internship at the Orissa Drugs & Chemicals Limited (ODCL), India | 2006
Four-week industrial training learning about various aspects of manufacturing and analytical techniques employed in developing different formulations.

Publications

- Mohanty M, Harpe SE, Slattum PW. *"Potential Concurrent Use of Alcohol and Central Nervous System-Acting Medications Among Older Adults; Cross-sectional Analysis of NHANES 2005-2010"* (in preparation for Journal of American Geriatric Society).
- Mohanty M, Slattum PW. *"Case study: Alcohol, Medication and Older Adults"* Age in Action Newsletter. Volume 26, Number 3, Summer 2011.

Scientific Presentations

- Mohanty M, Harpe SE, Barnes AJ, Carroll NV, Weaver MF, Slattum PW. *Association Between Risk of Falls and Use of Central Nervous System-Acting Medication and Alcohol Among Community-dwelling Older Adults: An Analysis of the Medicare Current Beneficiary Survey 2009.* Poster presentation at 66th Annual Scientific Meeting of Gerontological Society of America, 21st November, 2013. New Orleans, LA.
- Mohanty M, Thakker D, Gor D, Raval A. *Effect of Statins in Delaying the Progression of Diabetic Kidney Disease: Systematic Review and Meta-Analysis of Randomized Controlled Trials*. Poster presentation at 18th Annual International Meeting of International Society of Pharmacoeconomics and Outcomes Research, 21st May, 2013. New Orleans, LA.

- Mohanty M, Harpe SE, Slattum PW. *Concurrent Use of Alcohol and Central Nervous System-Acting Medications Among Older Adults*. Poster presentation at Annual Meeting of American Society for Clinical Pharmacology and Therapeutics, 17th March 2012, National Harbor, MD.
- Mohanty M, Malhotra S, Tiwari P. *Prevalence and Predictors of Inappropriate Prescribing Among Elderly Inpatients in India.* Poster presentation at 31st Annual Meeting of Southern Gerontological Society, 9th April 2010, Richmond VA.

Scholarly Contributions

Farley Center at Williamsburg Place and Senior Advocate Networking Guide 2012

Assisted in writing article titled "Prescription abuse in older adults". Published on May 16, 2012.

Virginia Health Quality Center 2010-2011

Compiled brochures titled "Alcohol-medication interaction in older adults" and "Drug-induced arrhythmias".

Computer Skills

Data analysis softwares: SAS, SPSS, R, JMP, RevMan, TreeAge, nQuery

MS Office (Word, PowerPoint, Excel, Access), Refworks, Endnote

Award

The Graduate School Dissertation Assistantship Award 2013

Professional Memberships

International Society of Pharmacoeconomics and Outcomes Research (ISPOR) 2012-2013

American Association of Pharmaceutical Scientists (AAPS) 2012-2013

American Association for the Advancement of Science (AAAS) 2011-2013

Leadership Experiences

Representative of School of Pharmacy for VCU-Graduate Student Association

President of the Graduate Student Organization of Dept. of Pharmacotherapy and Outcomes Science