ALCOHOL USE AND WEIGHT IN US ADULTS AND BARIATRIC SURGERY PATIENTS

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ABSTRACT

Over the last several decades, alcohol use, alcohol use disorder (AUD), and obesity, which are leading contributors to preventable death, have increased in prevalence. Research has shown that the three are related but much is still unclear. We examined associations between alcohol use, AUD, and weight status.

Using National Health and Nutritional Examination Survey data, we examined associations between alcohol use and weight status, and between weight loss attempt and alcohol use. Among current drinkers, lower frequency of alcohol use and higher number of drinks beyond one drink per drinking day were independently associated with higher odds of class 1-3 obesity versus healthy weight in males and females; associations were stronger with higher classes of obesity. Females reporting weight loss attempt were more likely to endorse current drinking and more frequent heavy drinking.

We examined whether associations between alcohol use and AUD differed by weight status using National Epidemiological Survey on Alcohol and Related Conditions-III data. Among males, interactions (*P* for all <.01) indicated that at the same average quantity of drinks per drinking day and frequency of heavy drinking, those with class 3 obesity had higher odds of AUD versus lower classes or no obesity. Among females, at the same frequency of any alcohol

use, those with healthy weight had the highest odds of AUD, while females with class 3 obesity had the lowest odds of AUD ($P<.001$).

We used Longitudinal Assessment of Bariatric Surgery-2 data to determine the sensitivity and specificity of potential thresholds of alcohol use for identifying alcohol-related problems in women post-Roux-en-Y-gastric bypass (RYGB). The sensitivity and specificity of an elevated Alcohol Use Disorder Identification Test-Consumption score, per standard scoring directions, were 76.4% (95%CI: 73.2-79.7) and 81.6% (95%CI: 80.2-83.0), respectively.

Considering associations between alcohol use, AUD, and weight status is critical to public health efforts to develop more effective prevention and treatment strategies for both diseases. We provide evidence that females trying to lose weight do not follow clinical weight loss guidelines and that AUD screening may be improved if modified for populations with different gender, weight status, and bariatric surgery history.

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ACKNOWLEDGEMENTS

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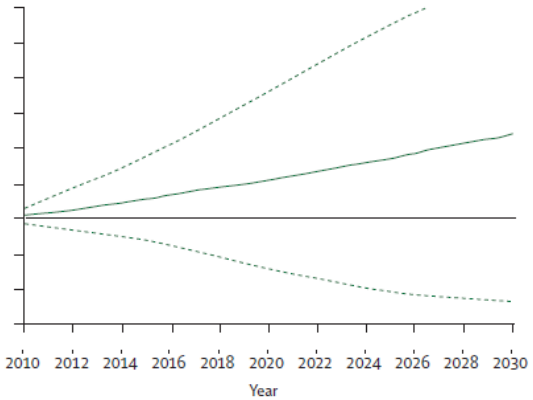
1.0 INTRODUCTION

There are nearly 80 million adults in the United States with obesity (body mass index, BMI ≥ 30 kg/m^2) and nearly 35 million with class 2 or 3 obesity (BMI ≥ 35 kg/m^2).[1] Obesity is associated with high morbidity (type 2 diabetes, cardiovascular disease, dyslipidemia, hypertension, stroke, osteoarthritis, and musculoskeletal disorders), and cost.[2-4] Alcohol, an addictive and highly energy dense macronutrient, reduces fat oxidation and increases fat storage,[5] which may lead to weight gain and obesity.[6,7] However, findings from literature examining the relationship between alcohol use and obesity are unclear and some studies demonstrating that light to moderate alcohol use is associated with lower risk of obesity[8-12] and others showing that heavy alcohol use is associated with higher risk of obesity[12].

2.0 BACKGROUND

2.1 OBESITY

Obesity, or excess adiposity, is a complex disease resulting from a combination of environmental and genetic factors.[13-15] Obesity is currently the second leading cause of preventable death in the United States, surpassed only by tobacco use.[16] Moreover, obesity is associated with high morbidity, mortality, and cost.[2-4,17] Inpatient and ambulatory health care costs are 27-46% higher for those with obesity than those with healthy weight and medication costs are 77-80% higher than those with healthy weight.[2,18] Additionally, due to the increasing prevalence of obesity and obesity-related comorbidities such as type 2 diabetes and cardiovascular disease, the costs associated with obesity are projected to continue to rise through 2030 (Figure 2.1).[19]



Projected trend based on data from 2000-2008; Dashed lines=95% confidence intervals.

Figure 2.1. **Projected healthcare costs from obesity-related comorbidities in the United States, 2010-2030**

2.1.1 Measurement

Adiposity is measured using various methods including BMI, waist circumference, and waist-to-hip ratio. BMI is defined as weight in kilograms divided by height in meters squared. Weight is either ascertained directly or self-reported and the two assessment methods are highly correlated ($r>0.90$).[20] Although differences are small, measured and self-reported weight are generally closer among those with lower weight than among those with higher weight.[20] However, measured and self-reported weight are closely correlated among adults following bariatric surgery and do not systematically differ based on BMI.[21] Obesity is commonly defined as a BMI of $\geq$ 30 kg/m^2 and is further broken down into class 1, class 2, and class 3 obesity (Table 2.1) to categorize severity.[4] Severe obesity is defined as class 3 obesity (BMI $\geq$ 40 kg/m^2) or at least class 2 obesity (BMI $\geq$ 35 kg/m^2) with an obesity-related comorbidity.[22]

Table 2.1. Classification of weight status based on body mass index

Weight classification	Body mass index
Underweight	< 18.5
Healthy	18.5-<25
Overweight	25-<30
Obese	≥ 30
Class 1	30-<35
Class 2	35-<40
Class 3	≥ 40

Body mass index, weight(kg)/height(m)^2 [4]

Two thresholds, based on whether there is an increased or substantially increased cardiometabolic risk, are commonly used for waist circumference (Table 2.2).[4,23] Variability in the measurement of waist circumference is introduced through subject posture, measuring tape tightness, and location of the measuring tape (i.e. at the naval, umbilicus, or iliac crest).[23]

Because abdominal fat mass is related to cardiometabolic risk and can vary largely within a narrow range of BMI, waist-to-hip ratio, waist circumference divided by hip circumference, is a third commonly used measure of obesity.[23] There is one recommended threshold for waist-to-hip ratio indicating substantially increased cardiometabolic risk (Table 2.2).[23]

Table 2.2. World Health Organization anthropometric thresholds for increased cardiometabolic risk

	Males	Females
Waist circumference		
Increased cardiometabolic risk	>94 cm	>80 cm
Substantially increased cardiometabolic risk	>102 cm	>88 cm
Waist-to-hip ratio		
Substantially increased cardiometabolic risk	≥0.90	≥0.85

2.1.2 Epidemiology

2.1.2.1 Common Datasets with Weight Status in the United States

The National Health and Nutrition Examination Survey (NHANES) is a cross-sectional, stratified, multistage probability sample of the civilian non-institutionalized US population conducted by the National Center for Health Statistics at the Centers for Disease Control and Prevention (CDC). It is designed to assess the health, nutritional status, and health behaviors of the US population through both interviews and physical examinations.[24,25] Body measurement data, including height and weight, are measured by trained personnel using standardized procedures and calibrated equipment.[26] Prior to 1999, NHANES was conducted in three waves; NHANES 1 (1971-1974), NHANES II (1976-1980), and NHANES III (1988-1994). Beginning in 1999, NHANES has been conducted continuously in 2 year increments. Because participants are selected using stratified random sampling methods, results from NHANES represent the US population.

2.1.2.2 Prevalence

According to data from NHANES, the prevalence of obesity in the United States has increased over the last five decades.[27] In recent years, from 1999-2000 to 2007-2008, the prevalence of obesity significantly increased from 27.5% to 32.2% among males aged 20 and older but remained stable among females (33.4% versus 35.5%) of the same age.[28] In contrast, examining trends in the prevalence of obesity and class 3 obesity from 2005-2006 to 2013-2014, Flegal and colleagues found that the prevalence of obesity and class 3 obesity did not significantly increase over time among males but did among females.[29] In 2013-2014, the estimated prevalence of obesity in US adults was 37.7% and the prevalence of class 3 obesity was 7.7%.[29] Models forecasting the future prevalence of obesity estimate that by 2030, the prevalence of obesity and class 3 obesity in the United States will increase to 42% and 11%, respectively.[30]

2.1.2.3 Factors Associated with Obesity

The prevalence of obesity in the United States differs by demographic characteristics. The likelihood of having obesity is higher among the middle aged,[30] non-Hispanic blacks,[28] Hispanics,[30] those with only a high school education,[29] those who have ever been married,[30] and those with lower income.[30] The prevalence of obesity also differs by gender. Findings from 2013-2014 indicate that the prevalence of obesity (class 1, 2 and 3 combined) and class 3 obesity are lower among males (35.0%; 5.5%, respectively) than among females (40.4%; 9.9%, respectively) in the United States.[29] While class-specific obesity prevalence rates are not yet available for 2013-2014, the 2007-2008 prevalence of class 1 obesity in adults aged ≥20 years was higher among males than among females (21.5% versus 17.8%), while the prevalence of class 2 and class 3 obesity was lower among males than among females (6.5% versus 10.5% and 4.2% versus 7.2%, respectively).[31]

2.1.3 Treatment for Obesity

Clinical guidelines for the management of obesity recommend weight loss treatment for individuals with obesity as well as individuals who are overweight and have at least one indicator of increased cardiovascular disease risk or obesity-related comorbidity.[4] Even small reductions in weight have large impacts on health.[32-35] The first step in weight loss management is lifestyle intervention of behavioral weight control which consists of diet, exercise, and behavioral therapy.[36] If individuals are unable to lose weight or maintain sufficient weight loss with comprehensive lifestyle intervention programs alone, it is recommended that interventions be supplemented by weight loss medications that suppress appetite or decrease fat absorption and may help individuals adhere to low calorie diets.[4]

2.1.3.1 Bariatric Surgery

According to multiple medical societies, adults who have severe obesity and who want to lose weight but have not responded to behavioral treatment for weight loss, should be referred to a bariatric surgeon for consultation and evaluation.[4] Bariatric weight loss surgery is a commonly performed surgical intervention performed on approximately 216,000 people per year in the United States[37] with the aim to reduce weight and maintain weight loss over time.[38,39] Bariatric surgery is currently the most effective long-term weight-loss treatment for severe obesity and results in improved quality of life, remission of obesity-related comorbidities such as type 2 diabetes and hypertension, and reduction in long-term mortality following surgery.[38,40-42]

The four most common types of bariatric surgery performed in the United States are vertical sleeve gastrectomy (SG), Roux-en-Y gastric bypass (RYGB), laparoscopic adjustable gastric banding (LAGB), and doudenal switch[43] (Figure 2.2)[44]. Vertical sleeve gastrectomy

divides the stomach vertically and reduces the stomach size to about 25% of the original size. By leaving the pyloric valve at the bottom of the stomach, stomach function is largely unaltered. Weight loss is promoted through increased satiety due to reduced stomach size and lower food intake due to decrease in ghrelin production, a gastrointestinal hormone that stimulates hunger.[43,45,46] The RYGB procedure involves partitioning the upper part of the stomach to create a small pouch that contains a small outlet to the intestine. In RYGB, satiety is increased by limiting the amount of food that can be consumed in the small stomach pouch and altered secretion of gastrointestinal hormones related to hunger.[43,47] Additionally, altered flow of nutrients through the proximal intestine leads to malabsorption of some macronutrients and calories.[47] LAGB is one of the least invasive procedures and regulates food intake through placement of an adjustable constricting ring on the top end of the stomach that allows for variation in the size of the outlet to the intestine. Smaller stomach pouch size leads to increase in satiety and decrease in food intake, resulting in weight loss.[43] Doudenel switch begins with sleeve gastrectomy but also involves bypassing the proximal small intestine, which is then reconnected to the last portion of the small intestine so the bile and pancreatic enzymes necessary for digestion are able to mix with food.

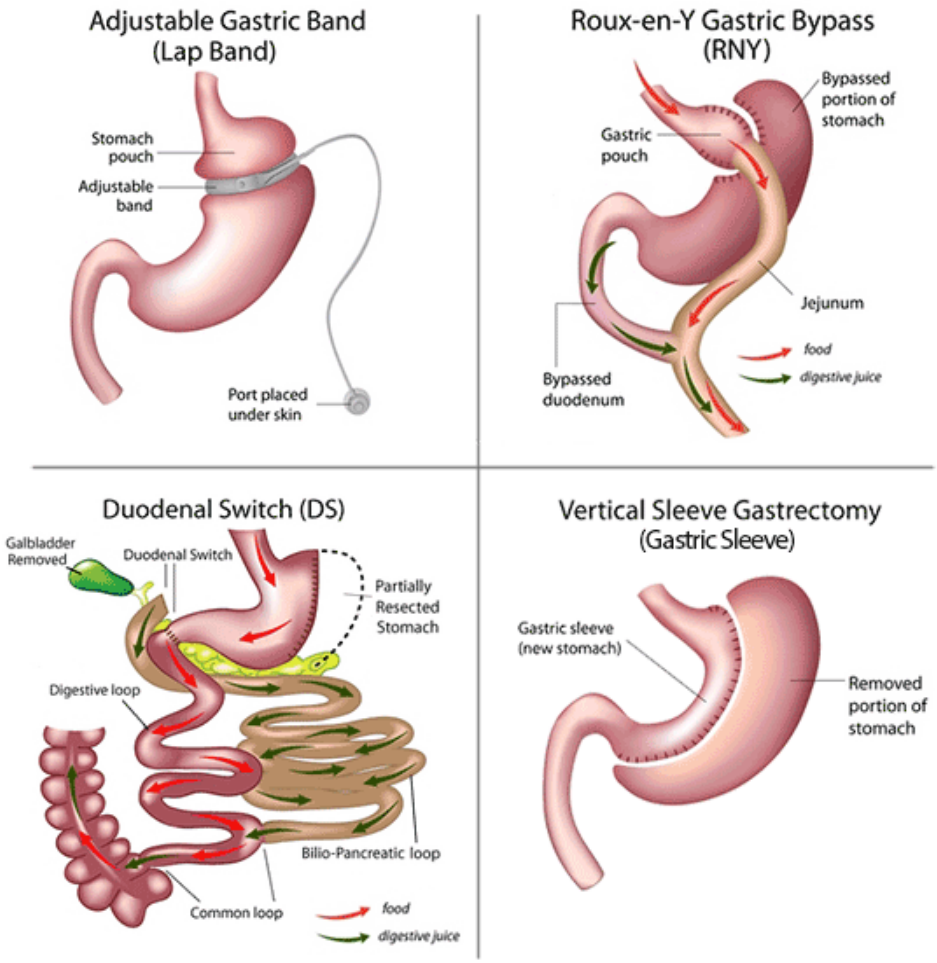


Figure 2.2. Common bariatric surgery procedures in the United States

The popularity of surgical procedures performed has changed over time. A prospective study of primary inpatient and outpatient bariatric surgerical procedures in Michigan found that vertical sleeve gastrectomy increased in popularity from 6.0% of all bariatric surgical procedures performed in 2008 to 67.3% of all procedures performed in 2013 (Figure 2.3)[48]. At the same time, RYGB decreased from 58.0% to 27.4% and LAGB decreased from 35.5% to 4.6% of all procedures performed.[48] Research from other university health systems have found similar trends in the types of bariatric surgery performed.[49,50]

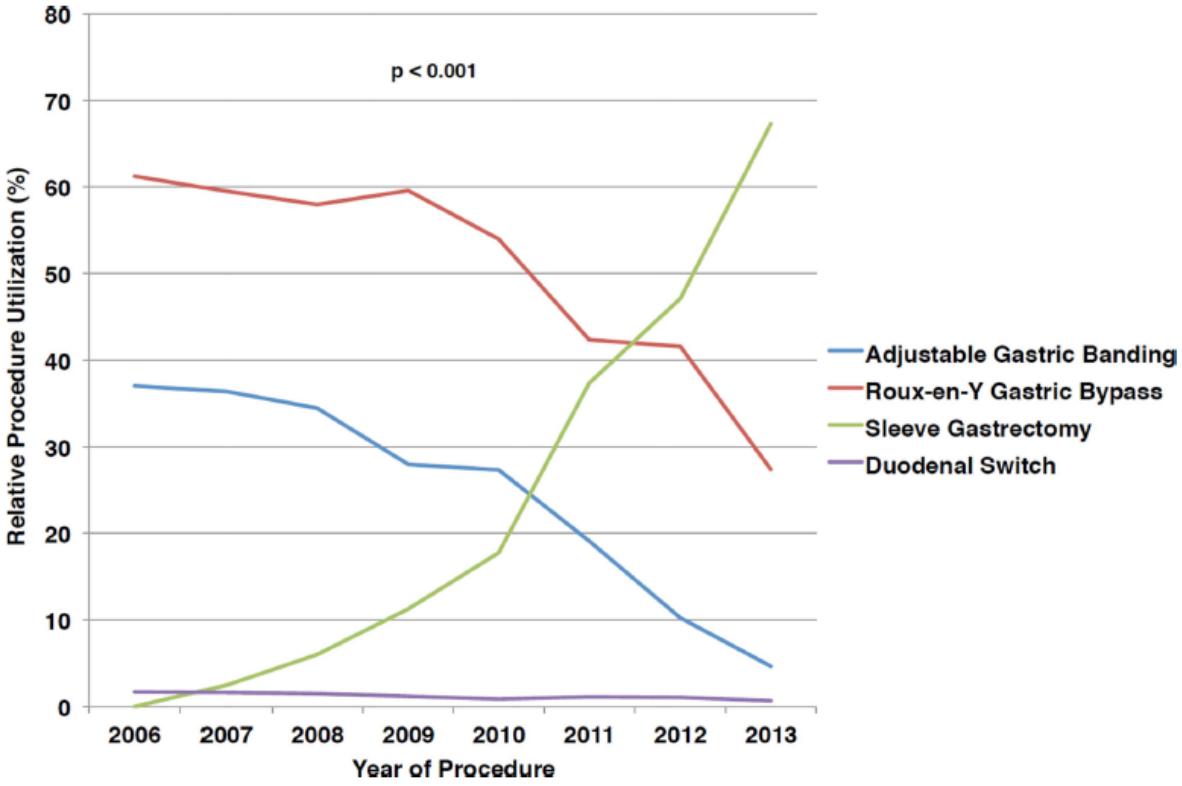


Figure 2.3. Relative utilization of common bariatric procedures in Michigan, June 2006 to December 2013

Individuals who undergo bariatric surgery are not representative of the US population with severe obesity. Males are under-represented in the bariatric surgery population (i.e., approximately 80% of individuals who undergo bariatric surgery are female,[51-53] compared to 60% of adults with severe obesity[31]). Although the proportion of patients who are male has increased over time,[51] compared to females, males who undergo bariatric surgery are typically older and have higher rates of severe comorbidities.[51] Additionally, several studies have shown that sociodemographic and clinical factors differ by surgical procedure. People who have had vertical sleeve gastrectomy are younger,[48] have higher BMI,[54] and are less likely to have gastroesophageal reflux disease[48] and diabetes[48,54] when compared to those who underwent other bariatric procedures. Individuals who have undergone RYGB versus LAGB are younger, have

higher BMI, and are more likely to be female, to be non-White, and to have diabetes, dyslipidemia, and hypertension.[54]

2.2 ALCOHOL USE

The World Health Organization (WHO) estimates that alcohol use is a component cause of more than 200 different diseases and injuries in the International Statistical Classification of Diseases and Health Problems.[55] In particular, frequency and quantity of alcohol consumed is associated with cancer,[55] cardiovascular disease,[55] Type 2 diabetes,[56,57] metabolic syndrome,[58] obesity,[58] and mortality[59]. In 2010, the overall cost of binge drinking was $191.1 billion in the United States.[60]

2.2.1 Measurement

2.2.1.1 Alcoholic Drink-Equivalents

Because alcoholic beverages vary in alcohol content, it is important to determine how many alcoholic drink-equivalents are in a beverage. According to the US Department of Health and Human Services (HHS) and the US Department of Agriculture (USDA) 2015-2020 Dietary Guidelines for Americans, one drink equivalent is defined as 14 grams of pure alcohol.[61] The Dietary Guidelines for Americans recommend that calories consumed from alcohol be accounted for when totaling overall calorie consumption.[61] The amount of alcohol in one drink equivalent contains approximately 98 calories[61] but the total calories in alcoholic beverages vary greatly depending on the portion size, brand, alcohol content, and other ingredients. Definitions for

standard alcoholic drinks containing one drink equivalent and average caloric content for alcohol beverages in the United States are shown below (Table 2.3).[61-63]

Table 2.3. Standard drink definitions for one drink equivalent (14 grams of alcohol) in the United States

Beverage	Amount (fl. oz.)	Colloquial amount	Alcohol (% by vol.)	Calories
80-proof liquor	1.5	one shot	40	97
Wine	5.0	one glass	12	120
Malt liquor	8.0	one bottle	7	--*
Beer	12.0	one can	5	150

*Not available

2.2.1.2 Patterns of Alcohol Use

Patterns of alcohol use are generally quantified by the number of drinks per drinking day and drinking days per week to be consistent with definitions of patterns of alcohol use put forth by the National Institute of Alcohol Abuse and Alcoholism (NIAAA) or the USDA (Table 2.4).[61,64] Females have lower alcohol use thresholds for moderate, heavy, heavy episodic, binge and excessive drinking than males because females usually have lower body weight, smaller livers, and a larger fat to muscle ratio than males.[65] However, the NIAAA recognizes that the amount of alcohol consumed to reach a blood alcohol concentration of 0.08 gram percent varies between people and involves many factors in addition to sex.[66]

Table 2.4. Definitions for patterns of alcohol use in the United States

Drinking level	Source	Male	Female
Low-risk for developing AUD	NIAAA[66]	≤ 4 drinks in single day and ≤ 14 drinks per week	≤ 3 drinks in single day and ≤ 7 drinks per week
Moderate	USDA[61]	< 2 drinks/day	< 1 drink/day
Heavy	USDA[61]	≥ 5 drinks in single day *or* ≥ 15 drinks/week	≥ 4 drinks in single day *or* ≥ 8 drinks/week
	SAMHSA[67]	≥ 5 drinks within a couple of hours on each of ≥ 5 days in the past 30 days	
Heavy episodic	WHO[55]	Consumed ≥ 60 grams (4.3 drinks) of alcohol in one episode at least once in past 30 days	
Binge	USDA[61]	≥ 5 drinks in 2 hours	≥ 4 drinks in 2 hours
	NIAAA[66]	Amount of alcohol per occasion needed to bring blood alcohol concentration to ≥ 0.08 gram percent which is usually	
		≥ 5 drinks in 2 hours	≥ 4 drinks in 2 hours
	SAMHSA[67]	≥ 5 drinks within a couple of hours at least once in past 30 days	
Excessive	Tuithof et. al[68]	> 21 drinks/week and at least 3 drinking days with ≥ 5 drinks	> 14 drinks/week and at least 3 drinking days with ≥ 5 drinks

AUD, alcohol use disorder; NIAAA, National Institute on Alcohol Abuse and Alcoholism; SAMHSA, Substance Abuse and Mental Health Services Administration; USDA, United States Department of Agriculture; WHO, World Health Organization

2.2.2 Epidemiology

2.2.2.1 Common Datasets with Patterns of Alcohol Use in the United States

The National Epidemiological Survey on Alcohol and Related Conditions (NESARC) is a survey of a nationally representative sample of non-institutionalized US adults aged 18 and older. The survey was designed and conducted by NIAAA to gather information on alcohol and drug use and disorders as well as related risk factors and associated disabilities using the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS). As part of NESARC, self-reported height and weight were collected, allowing for calculation of BMI and

determination of weight status. Wave 1 of NESARC was conducted in 2001-2002 with participants followed up in 2004-2005 in Wave 2 of NESARC. NESARC-III is a cross-sectional study collected during 2012-2013.[69]

The WHO collects information on alcohol use through the 44-item Global Survey on Alcohol and Health, which is sent to and completed by WHO Member States every 3-5 years.[55] The Behavioral Risk Factor Surveillance System (BRFSS) is an annual nationally representative cross-sectional telephone survey that collects state-level health and health behavior data from US adults. BRFSS collects information on frequency and quantity of alcohol use as well as binge drinking in the past 30 days.[70] The National Survey on Drug Use and Health (NSDUH) is a nationally representative cross-sectional survey conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA) that collects information on alcohol, tobacco, and illegal drug use and abuse in the US population aged 12 years and older through face-to-face interviews.[71] The survey has been conducted annually since 1971 with the most recent available data from 2014. Information on alcohol use is also available in NHANES as described in Section 2.1.2.1.

2.2.2.2 Mean Alcohol Use

Using Wave 1 NESARC data, Gearhardt and Corbin found that, US adults consumed, on average, alcohol 1.0 day per week and consumed 1.6 drinks per drinking day.[72] Using Wave 2 NESARC data, French and colleagues found that US males consumed, on average, 2.1 drinks per drinking day and US females 1.2 drinks per drinking day.[7]

2.2.2.3 Prevalence

The proportion of males and females in the United States with different patterns of alcohol use, as defined in Table 2.4, is shown in Table 2.5. Despite higher thresholds for patterns of alcohol use definitions, males consume alcohol at higher rates than females for all alcohol use patterns.

Table 2.5. Prevalence of patterns of alcohol use in the United States

Drinking level	Data source	Year	Male	Female
Lifetime	NSDUH [67]	2014	90.7%	84.6%
	Global Survey on Alcohol and Health[55]	2010	93.8%	82.6%
Past year	NSDUH [67]	2014	74.4%	67.9%
Past month	NSDUH [67]	2014	62.4%	51.9%
	Global Survey on Alcohol and Health[55]	2010	75.2%	63.0%
Heavy	NSDUH [67]	2014	10.2%	3.4%
Heavy episodic	Global Survey on Alcohol and Health[55]	2010	23.2%	10.9%
Binge	BRFSS[61]	2010	23.2%	11.4%
	NSDUH[67]	2014	32.6%	17.4%

BRFSS, Behavioral Risk Factor Surveillance System; NSDUH, National Survey on Drug Use and Health

2.2.2.4 Factors Associated with Binge Drinking

In addition to male sex,[61,67,71,73] those who are younger aged,[73] those with race/ethnicity other than non-Hispanic black[71,73] those with higher education,[73] those with higher income[73] have a higher prevalence of binge drinking in the United States.

2.3 ALCOHOL USE DISORDER

Alcohol use disorder (AUD) is a serious condition that leads to problems in both short- and long-term health such as memory loss, cancer, liver cirrhosis, cardiovascular disease, and death.[74-76] Additionally, AUD is associated with other mental health disorders including other substance use

disorders, major depressive disorder, personality disorders, bipolar I disorder, panic disorder, attention deficit hyperactivity disorder, and generalized anxiety disorder.[77,78]

2.3.1 Measurement

AUD consists of a problematic pattern of alcohol use leading to clinically significant distress or impairment within a 12-month period.[79] Prior to 2013, the American Psychiatric Association described two distinct alcohol-related disorders, alcohol abuse and alcohol dependence, in the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV).[80] Alcohol abuse is a maladaptive pattern of drinking leading to clinically significant impairment or distress with at least one pre-specified symptom of abuse in a 12-month period. Alcohol dependence is a chronic disease characterized by a strong craving for alcohol, continued use despite problems, and the inability to limit drinking. Alcohol dependence includes at least 3 pre-specified symptoms of dependence in a 12-month period to be diagnosed as such.[80] The current revision of the Diagnostic and Statistical Manual of Mental Disorders, DSM-5, defines only one alcohol-related disorder, still termed AUD, but with mild, moderate, and severe subcategories.[79] As seen in Figure 2.4,[81] there is great overlap between DSM-IV criteria for alcohol abuse and dependence and DSM-5 criteria for AUD. Concordance between 12-month and lifetime DSM-IV and DSM-5 AUD is high (Kappa = 0.76 and Kappa = 0.61, respectively).[82] However, someone could meet the criteria for DSM-5 AUD but not DSM-IV alcohol abuse or dependence, and vice versa.

The US Preventive Services Task Force (USPSTF) recommends that primary care clinicians screen adults 18 years and older for alcohol misuse.[83] The grade of this recommendation is B, meaning that there is high certainty that there is at least a moderate net benefit or moderate certainty that there is a moderate to substantial net benefit to screening.[83]

Screening instruments for the diagnosis of AUD have varying sensitivity and specificity. The USPSTF recommends three screening instruments for use in primary care because of their performance characteristics: The Alcohol Use Disorders Identification Test (AUDIT), the AUDIT-Consumption (AUDIT-C), and a single-question screening.[83,84] The AUDIT is a 10-item questionnaire which assesses past-year frequency of alcohol use, average quantity of drinks per drinking day, frequency of consuming ≥6 drinks, and alcohol-related problems (i.e., symptoms of alcohol dependence and/or alcohol-related harm); it takes 2-5 minutes to complete. The AUDIT-C is an abbreviated version of the AUDIT which contains 3 questions (past-year frequency of alcohol use, average quantity of drinks per drinking day, and frequency of consuming ≥6 drinks) and takes 1-2 minutes to complete. The single question screening recommended by the NIAAA is, "How many times in the past year have you had 5 (for men ≤65 years) or 4 (for women and all adults older than 65 years) or more drinks in a day?". Sensitivities and specificities of these screening instruments in primary care, as described in a meta-analysis, are reported in Table 2.6.[83,84] Other screening tools for identifying alcohol-related problems and their corresponding sensitivity and specificity are described elsewhere.[84,85] Thresholds may differ in settings with varying populations since the sensitivity and specificity varies by subpopulation (i.e., race and gender). For example, the suggested thresholds for the AUDIT and AUDIT-C are 1 point lower for women than for men, respectively.[84]

Table 2.6. Alcohol Use Disorder screening tools

Screening instrument	Threshold	Sensitivity	Specificity
AUDIT[83,84]	≥4	0.84-0.85	0.77-0.84
	≥5	0.70-0.92	0.73-0.94
	≥8	0.44-0.51	0.96-0.97
AUDIT-C[83]	≥3	0.74-0.88	0.64-0.83
	≥4	0.74-0.76	0.80-0.83
Single-question[83,84]	Yes	0.82-0.87	0.61-0.79

AUDIT, Alcohol Use Disorder Identification Test; AUDIT-C, AUDIT-Consumption

2.3.2 Epidemiology

2.3.2.1 Common Datasets with Alcohol Use Disorder in the United States

Nationally representative data on the prevalence of AUD are available in NESARC. Waves 1 and 2 of NESARC assessed DSM-IV disorders while NESARC-III assessed DSM-IV and DSM-5 disorders. See Figure 2.4 for DSM-IV and DSM-5 AUD definitions.

2.3.2.2 Prevalence

In 2001-2002, using Wave 1 NESARC data, an estimated 8.5% of non-institutionalized US adults had DSM-IV alcohol abuse or dependence in the past 12 months and 30.3% had DSM-IV alcohol abuse or dependence during their lifetime.[86] The prevalence of 12-month (12.7%) and lifetime (43.6%) DSM-IV AUD in 2012-2013, using NESARC-III data, show that the rates of AUD have increased substantially in the United States since 2001-2002.[77]

In 2012-2013, using NESARC-III data, the 12-month and lifetime prevalence of AUD, using the DSM-5 definition, was 13.9% (7.3% mild, 3.2% moderate, 3.4% severe) and 29.1% (8.6% mild, 6.6% moderate, and 13.9% severe), respectively; only 7.7% with 12-month AUD and 19.8% of US adults with lifetime AUD ever sought treatment or help for AUD.[77] The proportion with lifetime AUD who have sought treatment has not substantially changed over time and is similar to the 2001-2002 estimate of 19% of US adults with lifetime alcohol abuse or dependence sought treatment or perceived a need for care.[87]

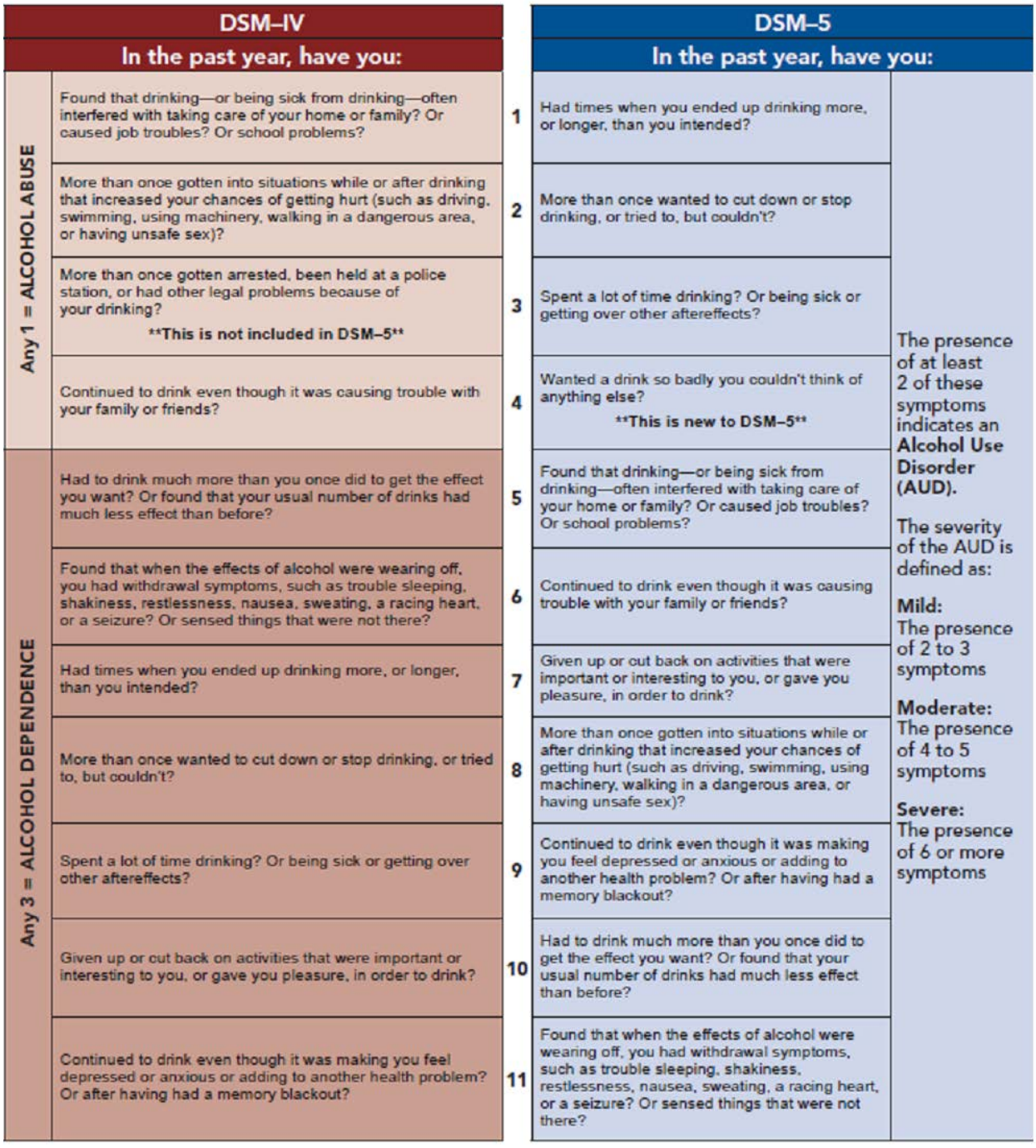


Figure 2.4. Comparison of DSM-IV and DSM-5 criteria for Alcohol Use Disorder

2.3.2.3 Factors Associated with Alcohol Use Disorder

The 12-month and lifetime prevalence of AUD in the United States differ by demographic characteristics. The likelihood of having AUD is higher among males, younger aged (18-29 years), non-Hispanic whites, Native Americans, those who were previously or never married, those with lower income, and those with any other substance use disorder.[77] Additionally, increasing levels of alcohol use and increasing frequency of binge drinking are associated with developing AUD.[88] Among people who consumed alcohol in the past year, individuals without DSM-IV alcohol abuse or dependence consumed, on average, significantly fewer drinks per drinking day at 3.1 alcoholic drinks per drinking day compared to 5.2 drinks per drinking day among individuals with alcohol abuse only and 7.0 drinks per drinking day among individuals with alcohol dependence.[89]

The prevalence of DSM-IV alcohol dependence increases linearly with increasing frequency of days with binge drinking while the prevalence of alcohol dependence without alcohol abuse and alcohol abuse without dependence were greatest among those with binge drinking twice a week or more.[88] While higher alcohol use is associated with AUD,[89-91] a minority (17.7%) of individuals with DSM-IV AUD concurrently engage in excessive alcohol use (see definition in Table 2.4).[68] It is important to note that the risk factors for binge drinking and AUD largely overlap (male sex, younger age, non-Hispanic white and Native American race/ethnicity) but that some risk factors are in the opposite direction.[71,73,77] Particularly, high income is a risk factor for binge drinking while low income is a risk factor for AUD.[73,77]

2.4 ALCOHOL USE AND WEIGHT STATUS

People who consume alcohol at moderate levels may add alcohol to their usual daily energy intake rather than substituting alcohol for food, consequently increasing their energy consumption.[92] Additionally, when alcohol is consumed to intoxicating levels, it can influence individuals to eat more and exercise less.[93,94] In converse, heavy drinkers may lose interest in food.[7] Consequently, the relationship between alcohol use and weight status, as measured by BMI, waist circumference, and waist-to-hip ratio is complex and often conflicting.[10,12] In a systematic review of 31 studies published between 1984 and 2010 that examined the association between alcohol use and weight status, conclusions were unclear.[12] Most cross-sectional studies found that heavy alcohol use was positively associated with weight status or waist-to-hip ratio.[12] However, moderate alcohol use was negatively or not associated with weight status.[12]

Prospective cohort studies have shown that alcohol use is associated with weight gain, but findings from these studies are also inconsistent, particularly when males and females are examined separately.[12] One explanation for the lack of consistency is that studies have been performed in different populations and used different measurements of alcohol use and obesity. The following review will be limited to studies conducted in the United States because of wide variation in patterns of alcohol use and obesity throughout the world.[55,95,96]

2.4.1 Alcohol Use and Weight Status

2.4.1.1 Frequency

Research findings from NHANES indicate the odds of obesity differ among drinkers and non-drinkers in the United States.[8,11] Arif and colleagues found, using 1988-1994 NHANES, after

controlling for confounders, that among lifetime non-smokers, current drinkers had lower odds of obesity when compared to non-drinkers (i.e., never or former drinkers).[8] Chakrabotry found, using 1999-2002 NHANES data that current or former drinkers had lower odds of having obesity when compared to never drinkers, after controlling for confounders.[11] Arif and colleagues also found that odds of obesity were significantly lower among those with frequency of days with alcohol use in the 2nd-4th quartile when compared with those who did not drink in the past year.[8] Likewise, using Wave 1 NESARC data, Gearhardt and Corbin found, after controlling for age and socioeconomic status, an inverse association between frequency of drinking days and BMI where those with class 3 obesity had the lowest mean number of drinking days (0.47) and those with healthy weight had the highest (1.09).[72]

Using cross-sectional data from a convenience sample of three community medicine clinics serving low-income populations, Roher and colleagues found that people who consumed alcohol, on average, three or more days per month had lower odds of obesity (OR=0.49) compared to non-drinkers.[97] However, this study did not adjust for some factors known to be associated with alcohol use and obesity such as sex and race/ethnicity because they were not significantly associated with obesity in their sample.

2.4.1.2 Quantity

Research has also pointed to associations between quantity of alcohol consumed and obesity. Using 1988-1994 NHANES data, Freiberg and colleagues found that the amount of alcohol consumed was inversely related to waist circumference after adjusting for age, sex, race/ethnicity, education, income, tobacco use, physical activity, and diet. Specifically, they found that those who consumed 1-19 alcoholic drinks per month (OR=0.74, 95%CI=0.62-0.89) and those who consumed ≥ 20 alcoholic drinks per month (OR=0.41, 95%CI=0.32-0.52) had

significantly decreased odds of larger waist circumference, defined as > 102 cm in males and > 88 cm in females, when compared to drinkers who consumed less than 1 drink per month.[58]

Also using 1988-1994 NHANES data, Arif and colleagues found that light and moderate drinkers, defined as consuming 1 or 2 drinks per drinking day, respectively, versus non-drinkers had decreased odds of obesity ($OR_{light\ drinking}$=0.46 [95%CI=0.34-0.62], $OR_{moderate\ drinking}$=0.59 [95%CI=0.41-0.86]) after adjusting for the potential confounding effects of age, sex, race/ethnicity, poverty income ratio, education, marital status, rural/urban, self-rated health, and leisure time physical activity. However, they also found that the odds of obesity (OR=1.46 [95%CI=0.98-2.17]) was higher among those who were heavy drinkers, defined as consuming 4 or more drinks per drinking day on average, versus non-drinkers after adjusting for the same covariates.[8]

Chakraborty, using the 1999-2002 NHANES, reported that among ever drinkers, higher levels of alcohol use (defined as consuming alcohol for more than 45 days in the past 12 months, having more than 5 drinks per drinking day for more than 90 days in the past 12 months, and consuming more than 5 drinks per drinking day nearly every day in the past 12 months) versus no current alcohol use were associated with higher odds of having obesity in both males and females. Likewise, moderate drinking (defined as 3 drinks per drinking day in females and 4 drinks per drinking day in males) versus no moderate drinking, was associated with significantly higher odds of having obesity in females. However, moderate drinking was associated with lower odds of having obesity in males.[11] It is important to note that moderate drinking in males in the study by Chakrabotry et al. is defined the same way as heavy drinking in the study by Arif et al (i.e., 4 drinks per drinking day).

2.4.1.3 Frequency and Quantity

Few studies have evaluated both frequency and quantity together in one measure. In cross-sectional analyses of two cohort studies, alcohol use was inversely associated with weight status.[98,99] In the Pound of Prevention study, a 3-year randomized trial of 1,044 community volunteers evaluating the efficacy of a weight gain prevention program, percent energy consumption from alcohol was significantly inversely associated with body weight among females but not among males.[98] In cross-sectional analyses of the Nurses' Health Study II, a prospective cohort study of 116,671 female nurses aged 27-44 years old without a history of cardiovascular disease, cancer or diabetes, those who consumed alcohol at light to moderate levels (consumed 0-<1 alcoholic drink per day) had lower mean BMI than non-drinkers.[99]

2.4.1.4 Sex as an Effect Modifier

Using Wave 1 NESARC data, Gearhardt and Corbin examined whether the association between weight status and alcohol use was modified by gender.[72] In this study, they evaluated class 1 and 2 obesity combined, and class 3 obesity. They found that males with healthy weight, overweight, and class 1or 2 obesity had significantly higher frequency of alcohol use than females of the same weight status. However, there was no difference by gender in the effect of weight status on frequency of drinking among those with underweight and class 3 obesity.

2.4.1.5 Summary

The sum of these studies indicate that the relationship between alcohol use and weight status is complex and may be modified by sex.[11,72,98] Generally those who drink versus do not drink and those with higher frequency in the number of days with alcohol use have lower odds of obesity. The association between quantity of alcohol consumed is more complex, where compared to

non-drinkers (both former and never), those who drink low to moderate quantities of alcohol have decreased odds of obesity and those who drink heavy quantities of alcohol have higher odds of obesity.[8,11,98,99]

2.4.1.6 Gaps in the Literature

A systematic review of studies examining the association between alcohol use and weight status concluded that the association is unclear and that future research should examine alcohol use patterns rather than frequency or quantity of alcohol use alone.[12] In addition, the current literature is limited in that most studies have not differentiated between class 1, 2, and 3 obesity despite the differences in degree of excess adiposity and health status that exist between these groups. Evidence suggests that individuals with class 2 and 3 obesity metabolize alcohol differently and may need to consume larger quantities of alcohol to reach intoxicating levels, which may affect food intake and exercise habits, than individuals with class 1 obesity.[65,100] Furthermore, alcohol use may be contraindicated among individuals with higher classes of obesity who have higher prevalence of comorbidities and associated medication use, such as hypertension, diabetes, cardiovascular disease, and dyslipidemia.[101,102] Future research should therefore examine the association between measures of alcohol use, which take both frequency and quantity into account, and weight status, differentiating between class 1, 2 and 3 obesity. In addition, because non-drinkers are different than current drinkers in ways that may not be controlled for, comparing frequency and quantity of alcohol use by weight status to non-drinkers, as in previous research, is inappropriate.

2.4.2 Alcohol Use and Weight Change

2.4.2.1 Alcohol Use and Weight Over Time

Longitudinal assessments examining alcohol use and weight over time have found that, on average, both alcohol use and weight increase over time. In a longitudinal assessment of US adults using Waves 1 and 2 of NESARC, French and colleagues found that BMI and average number of days with alcohol use in the past year increased over time (1.8% increase in BMI for males and 2.6% increase in BMI for females; 73.0 drinking days to 74.0 drinking days, respectively).[7] In a prospective 3-year study of adults from the Pound of Prevention study, Sherwood and colleagues found that over time, participants gained 1.36-1.81 kg (3-4 pounds), decreased total energy intake, and increased percentage energy intake from alcohol.[98] In a prospective cohort of over 300 pre-menopausal females followed for 4 years, Sammel and colleagues found that over a quarter of the cohort gained over ten pounds during the study period.[103]

2.4.2.2 Alcohol Use as a Predictor of Weight Change

Two large prospective cohort studies of healthy females found inverse associations between amount of alcohol consumed at baseline and weight gain over follow-up.[99,104] In the Nurses' Health Study II, described above, compared to non-drinkers (i.e., former and never), females who consumed, on average, less than 2.5 alcoholic drinks per week (OR=0.94, 95%CI=0.89-0.99), those who consumed 2.5-<7 alcoholic drinks per week (OR=0.92, 95%CI=0.85-0.99), and those who consumed 7-<14 alcoholic drinks per week (OR=0.86, 95%CI=0.76-0.78) at baseline had decreased odds of weight gain ≥ 5 kg (11 pounds) over 8 years while those who consumed more than 14 alcoholic drinks per week at baseline (OR=1.07, 95%CI=0.89-1.28) had similar

odds of weight gain ≥ 5 kg.[99] In the large, prospective Women's Health Study, which included females aged 38 years and older who were free of chronic diseases and had a healthy baseline BMI, compared to non-drinkers (i.e., former and never), the odds of developing obesity over the 13-year follow-up period was lower among those who, at baseline, consumed on average less than 2.5 alcoholic drinks per week (OR=0.75, 95%CI=0.63-0.89), 2.5-<7 alcoholic drinks per week (OR=0.43, 95%CI=0.34-0.56), 7-<14 alcoholic drinks per week (OR=0.39, 95%CI=0.25-0.60), and 14 or more alcoholic drinks per week (OR=0.29, 95%CI=0.15-0.54).[104] The findings for females who consumed 14 or more alcoholic drinks per week versus non-drinkers appear to be conflicting. However, the Nurses' Health Study evaluated weight gain of at least 5 kg over 8 years among females of different weight status, while the Females's Health Study evaluated development of obesity over 13 years among females of healthy weight. While both studies provide important information on the association between alcohol use and weight change, data for both studies were collected primarily during the 1990s and patterns in alcohol use and obesity in the United States have changed drastically since then. Furthermore, more research should be done to clarify conflicting associations and to include males.

2.4.2.3 Changes in Alcohol Use and Weight Change

French and colleagues found, using data on participants from Waves 1 and 2 of NESARC, that increase in past-year frequency of drinking days and average number of drinks consumed per episode were significantly associated with small increases in BMI among US males but not among US females.[7]

A series of prospective cohort studies found no statistically significant associations between change in alcohol use and weight change.[98,99,103,105] Over the three year period of the Pound of Prevention study, increase in energy intake from alcohol was not significantly

associated with increased weight in either males or females.[98] Sammel and colleagues found that increase in frequency of alcohol use was not associated with weight gain ≥ 10 pounds.[103] In a large prospective cohort of over 16,000 males aged 40-75 years, changes in alcohol use, defined as the sum of the amount of alcohol consumed, multiplied by the average number of servings of alcohol per day, was not statistically significantly associated with gain in waist circumference over the 9-year study time period.[105] Conversely, in the Nurses' Health Study II, those who consumed low to moderate levels of alcohol (≤ 2 drinks per day) throughout follow-up (OR=0.88, 95%CI=0.83-0.93; OR=0.81, 95%CI=0.75-0.87, respectively), and those who increased alcohol intake up to 2 drinks per day (OR=0.82, 95%CI=0.78-0.87) had decreased odds of weight gain ≥ 5 kg when compared to non-drinkers.[99]

2.4.2.4 Alcohol and Clinical Guidelines for Weight Loss

Clinical guidelines on treatment for overweight and obesity recommend that patients be educated about the benefits of limiting alcohol use for weight loss.[106] Because alcohol contains calories with minimal nutritional value and will impede weight loss, alcohol use is also not recommended after bariatric surgery.[107-109]

2.4.2.5 Summary

Although clinical guidelines recommend that limiting alcohol use has a beneficial impact on weight loss, research on alcohol use and change in weight is unclear. Among females, contrary to expectation, there appears to be an inverse association between the amount of alcohol consumed and future weight gain or development of obesity.[99,104] There are no similar studies in males. One study found that increase in alcohol use was associated with increase in BMI over time in males[7] and one study found that increase in alcohol use was associated with decreased odds of weight

gain in females[99]. However, one study found no such association in males or females[98] and another found no such association in females[105].

Because alcohol contains excess calories and may negatively influence weight loss, individuals may try to decrease the amount of calories consumed by restricting alcohol use.[110] Future research should examine whether individuals who report trying to lose weight have different patterns of alcohol use than those who do not. NHANES recently introduced new survey questions that allow alcohol use to be examined among individuals who have tried to lose weight in the past year. Furthermore, future research should acknowledge the interaction between gender, weight status, and alcohol use and involve stratified analyses. For example, males who drink alcohol may not compensate for calorie consumption by consuming fewer calories from other food sources but females who drink may substitute calories from alcohol for calories from other sources.[104,111] Investigating the association of frequency and quantity of alcohol use with weight loss is also important because it could help lead to intervention studies that test the effect of weight-related alcohol recommendations.

2.4.2.6 Gaps in the Literature

It is unclear whether individuals who are trying to lose weight have different patterns of alcohol use than those who are not trying to lose weight. Moreover, it is unclear how alcohol use is related to weight loss, particularly in the population of individuals who have actively tried to lose weight.

2.4.3 Alcohol Use Disorders and Weight Status/Weight Gain

Studies examining associations between AUD and obesity are extremely limited. To date, no studies examining the effect of AUD on weight status have been conducted. One prospective study by Pickering and colleagues examined associations between Wave 1 AUD and mean change in BMI between Wave 1 and Wave 2, but found no statistically significant associations.[112]

2.4.4 Bariatric Surgery and Alcohol Use

Alcohol use below the threshold for AUD diagnosis following bariatric surgery may negatively impact liver function and weight loss, and induce vitamin deficiencies.[113] Additionally, higher rates of accidents and suicide in bariatric surgery patients may be partially explained by postoperative alcohol use.[114] Despite nutritional recommendations to refrain from alcohol post-surgery,[108,109] studies suggest that the majority of post-operative patients consume alcohol within the first year following surgery[115,116] and may be at increased risk for developing AUD compared to before surgery.[115,117-119] Results from a retrospective study indicate that 28% of those undergoing bariatric surgery report difficulties in controlling alcohol intake after surgery compared to 5% before surgery.[120]

2.4.4.1 Theories for Increased Risk of Alcohol Use Disorder Post-Bariatric Surgery

Proposed mechanisms for the increase in AUD symptoms after bariatric surgery include the addiction transfer model, where pre-operative addiction to food (over-eating) transforms into

post-operative addiction to alcohol,[121] altered alcohol metabolism,[113] and changes in brain reward mechanisms[122-124] from the surgery.

Addiction Transfer Hypothesis

Research on the addiction transfer model suggests that individuals undergoing bariatric surgery may substitute addiction to food with addiction to alcohol post-surgery.[117,120] Additionally, some individuals undergoing bariatric surgery have addictive personality traits that lead to needing increasing amounts of food to feel satisfied and are similar to addictive personality traits in individuals addicted to substances.[125] Moreover, the same neurobiological pathways that are implicated in drug abuse are implicated in food consumption.[126,127] However, this hypothesis has not been validated in the literature.[119]

Pharmacokinetics

The etiology of physiologic changes after bariatric surgery may change patients' vulnerability to problematic alcohol use.[117] Pharmacokinetic studies suggest anatomical changes from surgery may increase risk for AUD. First, the large reduction in body weight post-surgery results in greater concentration of ethanol per drink consumed than prior to surgery.[128] Second, physiological changes associated with RYGB cause rapid emptying of liquids from the gastric pouch, which may hasten the absorption of alcohol in the jejunum and the stomach, i.e., the main source of alcohol dehydrogenase.[129-131] Gastric bypass patients absorb alcohol faster (reach peak blood levels quicker) and have higher peak alcohol concentrations.[113,128,132,133] Sleeve gastrectomy, a procedure that is gaining popularity, is similar to RYGB in that it creates a smaller stomach pouch. Emerging evidence suggests that compared to pre-surgery, adults who have undergone sleeve gastrectomy also experience higher peak alcohol concentrations,[133,134]

which are reached more quickly[134] and take longer to decrease[133], as well as increased feelings of drunkenness[134].

Because individuals undergoing RYGB metabolize alcohol differently than others, the effect of 5 drinks, the cutoff generally used by NIAAA, is substantially different for those undergoing RYGB than for others.[132] More research is needed in developing guidelines for defining moderate and high-risk drinking in the bariatric surgery population. Particularly, determining the amount of alcohol consumed that is associated with AUD in this population is warranted.

Brain Reward Mechanisms

Other hypothesized pathways for the increased prevalence of AUD following RYGB include surgery-induced changes to the ghrelin system[124] and altered genetic expression in brain regions associated with reward[122,123]. However, the literature is sparse and contradictory.[119]

2.4.4.2 Alcohol Use and Bariatric Surgery

The literature examining frequency and quantity of alcohol intake before and after bariatric surgery is sparse, and is limited by small sample size, poor retention, short follow-up (≤ 2 years), no stratification by surgical procedure, and mixed findings.[115,116,131,135-138] In addition, only the Longitudinal Assessment of Bariatric Surgery (LABS)-2 study has examined how pre-surgery alcohol intake relates to risk of post-surgery AUD.[115] A 2016 review article by Li and Wu that examined the change in prevalence of substance use following surgery concluded that patterns of alcohol use over time after bariatric surgery were inconsistent across studies.[139] A review article by Spadola and colleagues concluded that more prospective, longitudinal studies on alcohol use and bariatric surgery that follow patients for more than 2 years are needed.[118]

Pre- to Post- Surgery

In a sample of 186 LAGB and 90 RYGB patients, de Araujo Burgos et al. reported a decrease in prevalence of any alcohol use from pre-surgery through the first 2 years post-surgery (24.2% to 9.4%; p<.001),[136] although only 42% of participants were followed through 2 years. Conversely, Conason et al. found that the mean frequency of alcohol use increased from baseline to 2 years post-surgery. However, by year 2, only 25% of the original 155 participants remained in the study.[116] In the first LABS-2 analysis of alcohol data (N=1945), King et al. found that among RYGB patients, there was a significant decrease in the number of alcoholic drinks on a typical drinking day in the first year after surgery, compared to the year before surgery, but that in the second year post-surgery, alcohol quantity returned to pre-surgery levels, the frequency of alcohol intake was higher than pre-surgery levels.[115] Similarly, following LAGB, frequency of alcohol use increased in the second year post-surgery, but there was not a significant change in the number of alcoholic drinks on a typical drinking day between baseline and years 1 or 2.[115]

Svensson et al. reported on medium risk alcohol use (i.e., 3 or more drinks/day for males and 1.5 or more drinks/day for females) as defined by WHO. Among people without medium risk alcohol use at baseline, prevalence of medium risk alcohol use increased over the 10 years of post-surgery follow-up.[137]

Between Surgical Procedures

De Araujo Burgos and colleagues reported no difference in frequency of alcohol use through 2 years post-surgery between procedure groups.[136] Results from the case-control study by Cuellar-Barboza et al. indicate that individuals who had undergone RYGB have significantly fewer drinks per day and drinking days per week than individuals who did not undergo RYGB.[140] This

may reflect that those who undergo RYGB metabolize alcohol faster and feel the effects of alcohol after less alcohol.[132]

Svensson et al. reported that medium risk alcohol use was higher among RYGB patients 1-10 years post-surgery compared to a non-surgical control group. Additionally, 10% of the 260 people who had undergone RYGB and did not have medium risk alcohol use pre-surgery had incident medium risk alcohol use by 10 years post-surgery versus 5% of the 370 LAGB patients.[137] Although high-risk alcohol use is generally quantified by number of drinks per day and drinking days per week to be consistent with definitions put forth by NIAAA,[64] pharmacokinetic studies[119] suggest that alcohol is metabolized differently following RYGB and possibly some other bariatric surgery procedures, which calls into question the appropriateness of the WHO definition for medium risk alcohol use in the bariatric surgery population.

2.4.4.3 Alcohol Use Disorder and Bariatric Surgery

Current AUD is rare among preoperative patients, likely reflecting the fact that AUD is a contraindication for bariatric surgery. However, despite lower prevalence of any alcohol use among adults with obesity,[8] lifetime history of AUD is higher in those with bariatric surgery than in the general population, indicating vulnerability in this population.[109,141] Moreover, some of the most common bariatric surgical procedures may increase the risk for developing AUD following surgery.[115,117,137,142]

Pre- to Post-Surgery

Research from a limited number of prospective studies suggests that individuals who undergo RYGB, but not LAGB have higher prevalence of AUD after surgery when compared to before surgery.[115,137]

Between Surgical Procedures

The prevalence of AUD is higher among those who have undergone RYGB than it is among individuals with obesity who do not undergo bariatric surgery,[137] and those who have undergone LAGB.[115,137,143,144] Whether there is increased risk of AUD following gastric sleeve, one of the most common procedures performed today, is unclear.[131,133]

Risk Factors

Studies examining factors related to AUD found that the following baseline factors increased risk for post-surgery AUD: male sex,[115,137] younger age,[115,135] smoking,[115,137] any alcohol use,[137] regular alcohol use (≥ 2 drinks per week),[115] AUD,[115,143] recreational drug use,[115] attention deficit hyperactivity disorder,[145] and higher BMI.[135] Research has shown that alcohol use patterns are a risk factor for AUD.[88,91-94] However, it is unclear whether the association between alcohol use patterns and AUD differs according to weight status or by bariatric surgical procedure, which could modify the associations because alcohol metabolism is dependent on weight and percent body fat.[65]

2.4.4.4 Gaps in the Literature

It is unclear whether the association between alcohol use patterns and alcohol-related harm and dependence differ according to surgical procedure, despite the fact that alcohol metabolism is dependent on weight and percent body fat.

3.0 SPECIFIC AIMS

1) Examine associations between alcohol use and weight status, between weight loss attempt and alcohol use and, among adults who attempted to lose weight over the past year, associations between past-year alcohol use and weight change, by sex.

2) Determine whether associations between alcohol use and AUD differ by weight status and sex.

3) Examine change in alcohol use over seven years following RYGB and SG, respectively and determine alcohol use thresholds for identifying alcohol-related problems among women pre- and post-RYGB.

4.0 MANUSCRIPT 1 – ALCOHOL USE AMONG US ADULTS, BY WEIGHT STATUS AND WEIGHT LOSS ATTEMPT, NHANES, 2011-2014

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4.1 ABSTRACT

Objectives: To examine associations between alcohol use and weight status, differentiating between class 1, 2 and 3 obesity, as well as between weight loss attempt and alcohol use.

Methods: This report includes 9,346 of 10,840 eligible 2011-2014 National Health and Nutrition Examination Survey participants. Logistic and linear regression were used to test associations between 1) past-year alcohol use and current weight status, and 2) past-year weight loss attempt and alcohol use, controlling for potential confounders. Analysis was stratified by gender.

Results: Male current drinkers had lower odds of class 3 obesity versus healthy weight (AOR=0.51 [95%CI: 0.31-0.81]) and female current drinkers had lower odds of overweight (AOR=0.73 [95%CI: 0.58-0.91]), class 1 (AOR=0.64 [95%CI: 0.46-0.88]), class 2 (AOR=0.53 [95%CI: 0.38-0.75]), and class 3 (AOR=0.64 [95%CI: 0.45-0.91]) obesity versus healthy weight. Among current drinkers, lower frequency of any alcohol use and higher continued volume (i.e., number of drinks beyond one drink per drinking day) were independently associated with higher

odds of class 1-3 obesity versus healthy weight in males and females; associations that were stronger with higher classes of obesity. Females reporting weight loss attempt had higher odds of being current drinkers (AOR=1.30; 95%CI:1.02-1.65) and more frequent heavy drinking.

Conclusions: Lower frequency of alcohol use and higher continued volume are independently associated with higher odds of obesity. Females trying to lose weight do not drink less, despite clinical guidelines suggesting they should.

4.2 INTRODUCTION

Nearly 80 million adults in the United States have obesity (body mass index, BMI $\geq$ 30 kg/m^2) and nearly 35 million of these have class 2 (BMI 35-<40 kg/m^2) or 3 (BMI $\geq$ 40 kg/m^2) obesity.[1] Obesity, particularly class 2 or 3 obesity, is associated with high morbidity (e.g., type 2 diabetes, cardiovascular disease, dyslipidemia, hypertension, stroke, osteoarthritis, musculoskeletal disorders, and psychiatric disorders), and medical spending.[2,4]

Alcohol, an addictive and highly energy dense macronutrient, reduces fat oxidation and increases fat storage,[5] which may lead to weight gain and obesity.[6,7] Alcohol also influences behaviors that may impact weight status. When alcohol is consumed to intoxicating levels, it may prompt individuals to eat more and exercise less.[93,94] Conversely, those who frequently consume high levels of alcohol may lose interest in food[7] or experience decreased absorption and metabolism of nutrients leading to lower weight.[146] Consequently, the relationship between alcohol use and weight status is complex.[10,12]

Two systematic reviews of studies examining the association between alcohol use and weight change concluded that the association is unclear,[12,147] in part because most studies

evaluated frequency or quantity of alcohol use alone. Thus, they noted that future research should examine alcohol use patterns that take both frequency and quantity into account.[12] The literature on alcohol use and weight status includes at least two other limitations. First, the majority of previous studies have made non-drinkers the reference group when evaluating associations with alcohol use. This is problematic as non-drinkers differ from current drinkers in more than alcohol use[148-150] (e.g., non-drinkers may have underlying health conditions that make them "sicker" than current drinkers). Thus, the potential for residual confounding is large. Second, most studies evaluating alcohol use and weight status have not differentiated between class 1, 2, and 3 obesity, despite the differences in degree of excess adiposity and health status that exist between individuals in the three groups. Evidence suggests that individuals with class 2 and 3 obesity metabolize alcohol differently and may need to consume larger quantities of alcohol to reach intoxicating levels than individuals with class 1 obesity.[65,100] On the other hand, alcohol use may more often be contraindicated among individuals with higher classes of obesity who have higher prevalence of comorbidities and associated medication use, such as hypertension, diabetes, cardiovascular disease, and dyslipidemia. This may lead those with higher classes of obesity to drink less frequently and/or consume smaller quantities than those with lower classes of obesity.[101,102]

Clinical guidelines on the treatment of overweight and obesity recommend that patients be educated on the benefits of limiting alcohol use on weight loss,[3] with the goal of decreasing the number of calories consumed by restricting alcohol use.[110] However, it is unclear whether individuals are following these guidelines. In particular, it is unknown whether individuals who are trying to lose weight have different patterns of alcohol use than those who are not trying to lose weight, and whether alcohol intake is related to weight loss.

To address these limitations in the literature, we examined associations between alcohol use, taking both frequency and quantity into account simultaneously, and weight status, differentiating between class 1, 2 and 3 obesity, using 2011-2014 National Health and Nutrition Examination Survey (NHANES) data. We also examined relationships between weight loss attempt and alcohol use and, among adults who attempted to lose weight over the past year, associations between past-year alcohol use and weight change. Because non-drinkers are different than current drinkers, we examined frequency, quantity and continued volume of alcohol use among current drinkers only.

4.3 METHODS

Data Source

NHANES is a cross-sectional, stratified, multistage probability sample of the civilian non-institutionalized US population designed to assess the health, nutritional status, and health behaviors of the population through both interviews and physical examinations.[24,25] All participants gave informed consent and ethics approval was obtained from the National Center for Health Statistics Research Ethics Review Board. We used 2011-2014 NHANES data for non-pregnant adults aged 20 years and older who had non-missing BMI of at least 18.5 kg/ m^2 (i.e., healthy weight or higher) and had completed at least one item on the Alcohol Use Questionnaire, which assessed lifetime and past 12-month alcohol use (Figure 4.1).

Definitions

Alcohol Use

Lifetime drinkers were defined as individuals who consumed 12 or more alcoholic drinks in their lifetime, while never drinkers consumed fewer than 12 drinks in their lifetime.[8,11] Among lifetime drinkers, current drinkers consumed at least one alcoholic drink in the past 12 months while former drinkers did not.[8,11] Frequency of days with any drinking in the past 12 months was reported as number of days per week or per month and converted to total number of days in the past 12 months. Average quantity of drinks consumed per drinking day was reported as a whole number. Continued drinking volume, which represents the total number of drinks in the past year beyond one drink per drinking day (i.e., heavier drinking), was defined as volume (frequency of days with any drinking*average quantity of drinks consumed per drinking day) - frequency of days with any drinking.[151-153] Heavy drinking was defined as consuming at least 5 drinks in a day among males or at least 4 drinks in a day among females.[11] Due to the rarity of heavy drinking, frequency of heavy drinking days in the past 12 months was categorized into the following groups: none, once -< monthly, 2-4 days per month, and at least 2 days per week.

Weight Status and Weight Loss

Anthropometric data, including current height and weight, were measured by trained personnel using standardized procedures and calibrated equipment.[26] BMI was defined as weight in kg divided by height in m^2 and was categorized into healthy weight (18.5-<25 kg/m^2), overweight (BMI 25-<30 kg/m^2), and class 1 (BMI 30-<35 kg/m^2), class 2 (BMI 35-<40 kg/m^2), and class 3 (BMI $\geq$40.0 kg/m^2) obesity.[4]

Individuals who reported that they intentionally lost at least 10 pounds in the past 12 months and those who reported trying to lose weight in the past 12 months were defined as having a weight loss attempt. Participants self-reported their weight one year prior to the assessment. Among individuals who attempted to lose weight, past-year percent weight change was defined as ((current weight - weight one year prior) divided by weight one year prior)*100.

Other Measures

Demographic variables were self-reported via questionnaire. Birth date was reported by the participant and actual or imputed birth date was used to calculate age in years. Ages 80 years and older were reported as 80 years.[154] Race/ethnicity was categorized into Hispanic (Mexican American and other Hispanic), non-Hispanic white, non-Hispanic black, and other race – including multi-racial. Education level was defined as less than high school (less than 9th grade and 9-11th grade – includes 12th grade with no diploma), high school graduate/General Equivalency Diploma (GED) or equivalent, some college or associate's degree, college graduate or higher. Annual household income was categorized as under $35,000, $35,000-$64,999, $65,000-$99,999, and $100,000 and over. People who reported working at a job or business in the past week or with a job or business but not at work in the past week were considered to be employed.[155] Marital status was categorized as married or living with a partner; never married; or widowed, divorced, or separated. Smoking status was self-reported as current smoker (now smoking every day or some days), former smoker (smoked at least 100 cigarettes in lifetime but no current use), and never smoker (smoked fewer than 100 cigarettes in lifetime).[156] Depression symptoms were measured using the standardized and validated Patient Health Questionnaire (PHQ-9), which examines the severity of depressive symptoms during past two weeks. Using

previously defined methods,[157] the following scores for each of the 9 items were assigned: not at all=0, several days=1, more than half the days=2, nearly every day=3. Individuals with a summed score ≥10 (range 0-27) were defined as having current depression. Physical activity was measured using a self-reported questionnaire based on the Global Physical Activity Questionnaire (GPAQ), which was used to calculate metabolic equivalent of task (MET)-minutes per week from all activities of moderate or vigorous intensity.[158]

Statistical Analysis

We used SAS® software version 9.4 (SAS Institute Inc., Cary, NC) survey procedures to account for non-response differences in the sample and the unequal probability of sample selection. Respondents not included in the study population (i.e., had BMI <18.5 kg/m^2 or missing data on weight status or alcohol use) were included in the standard error computations to fully account for the complex sample design. All analyses were stratified by gender.

Descriptive statistics were used to report the distribution of participants across weight status categories by alcohol use and the distribution of participants across alcohol use variables by weight loss attempt groups.

Multinomial logistic regression was used to examine associations between current drinking (yes/no) and weight status among all adults (model 1), as well as associations between alcohol use patterns (i.e., frequency of days with any drinking and continued volume (model 2), and frequency of heavy drinking days (model 3)) and weight status among current drinkers. Models were adjusted for potential confounders: age, race/ethnicity, education, employment status, income, marital status, smoking status, depression symptoms, physical activity, and weight loss attempt.[7,8,11,147,159] Because the parallel assumption was not met in ordinal logistic

regression models, multinomial logistic regression models were used to test the odds of higher weight categories versus healthy weight by level of alcohol use. The overall *P* value from each model is reported, as well as the adjusted odds and 95% CI of each weight category (overweight, class 1, 2, and 3 obesity, respectively) versus healthy weight for higher versus the lowest levels of alcohol use. The null hypothesis for each model indicates that alcohol use is not associated with weight status. Comparisons of each weight category versus healthy weight were made by examining 95% CI for the adjusted odds ratios.

Logistic regression was used to examine associations between past-year weight loss attempt and current drinking among all adults (model 4). Linear regression was used to examine associations between past-year weight loss attempt and frequency of days with any drinking (model 5) and quantity of drinks consumed per drinking day (model 6) among current drinkers. Multinomial logistic regression was used to examine associations between past-year weight loss attempt and frequency of heavy drinking days (model 7) among current drinkers; the adjusted odds and 95% CI of each frequency category (once -< monthly, 2-4 days per month, and at least 2 days per week) versus none is reported. Models were adjusted for potential confounders previously described, in addition to categorical weight status one year ago. Those who were underweight one year ago were excluded from these analyses.

Among adults who attempted weight loss in the past year, linear regression was used to determine associations between current drinking and percent weight change over the past year (model 8). Among current drinkers who had attempted weight loss in the past year, linear regression was used to determine associations between alcohol use patterns (i.e., frequency of days with any drinking and continued volume (model 9), and frequency of heavy drinking days (model 10) and percent weight change over the past year. Models were adjusted for the same

covariates previously described, including weight status one year ago. Those who were underweight one year ago were excluded from these analyses.

As a sensitivity analysis, we repeated all modeling with adjustment for self-reported caloric intake; results did not change in a meaningful way.

4.4 RESULTS

This report includes 9,346 of 10,840 eligible 2011-2014 NHANES participants aged 20 and older (Figure 4.1), representing an estimated 199 million US adults. An estimated 49.9% were male. Among males, the median age was 47.3 years; an estimated 38.7% (95%CI: 36.7-40.7) were overweight, 22.5% (95%CI: 20.8-24.2) had class 1 obesity, 7.8% (95%CI: 6.9-8.6) had class 2 obesity, and 5.0% (95%CI: 3.7-6.2) had class 3 obesity; 26.4% (95%CI: 24.7-28.2) attempted to lose weight in the past year (Table 4.1). Among females, the median age was 45.8 years; an estimated 29.0% (95%CI: 26.8-31.2) were overweight, 19.6% (95%CI: 18.1-21.1) had class 1 obesity, 10.6% (95%CI: 9.6-11.6) had class 2 obesity, and 9.3% (95%CI: 8.1-10.6) had class 3 obesity; 41.6% (95%CI: 38.8-44.4) attempted to lose weight in the past year (Table 4.1). An estimated 78.2% (95%CI: 75.2-81.1) of males and 70.3% (95%CI: 66.7%-74.0) of females were current drinkers (Table 4.1).

Alcohol Use and Weight Status

The proportions of participants in each weight status category by alcohol use variables are reported in Table 4.2. With adjustment for potential confounders, compared to males who were not current drinkers, current drinkers had lower odds of class 3 obesity versus healthy weight

(AOR=0.51 [95%CI: 0.31-0.81]). There were no statistically significant associations between current drinking and odds of overweight-class 2 obesity versus normal weight (Table 4.3 model 1). Table 4.3 also provides the adjusted odds of each weight category (overweight-class 3 obesity) versus healthy weight among current drinkers for higher frequencies or continued volume versus the lowest frequency or continued volume, respectively.

Among male current drinkers, with adjustment for confounders, lower frequency of days with any drinking and higher continued volume were independently associated with higher weight status versus healthy weight (Table 4.3, model 2). For example, every 30 more days of drinking in the past year was associated with an adjusted odds ratio of 0.91 (95%CI: 0.87-0.96) for class 1 obesity, 0.90 (95%CI: 0.84-0.97) for class 2 obesity, and 0.87 (95%CI: 0.79-0.96) for class 3 obesity versus healthy weight. Every 30 drinks per year beyond one drink per drinking day was associated with an adjusted odds ratio of 1.02 (95%CI: 1.01-1.03) for class 2 obesity and 1.02 (95%CI: 1.003-1.03) for class 3 obesity versus healthy weight, indicating that heavier drinking was associated with higher weight classes. There was not a significant association between frequency of heavy drinking days and weight status (Table 4.3, model 3).

With adjustment for potential confounders, female current drinkers had lower odds of overweight (AOR=0.73 [95%CI: 0.58-0.91]), class 1 (AOR=0.64 [95%CI: 0.46-0.88]), class 2 (AOR=0.53 [95%CI: 0.38-0.75]), and class 3 (AOR=0.64 [95%CI: 0.45-0.91]) obesity versus healthy weight (Table 4.3, model 1).

Among female current drinkers, with adjustment for potential confounders, lower frequency of days with any drinking and higher continued volume (model 2), as well as lower frequency of heavy drinking days (model 3) were significantly associated with higher weight status versus normal weight; for both frequency measures the associations were more

pronounced with greater obesity severity (Table 4.3). For example, every 30 more days in the past year when one drink was consumed was associated with an adjusted odds ratio of 0.89 (95%CI: 0.84-0.95) for class 1 obesity, 0.71 (95%CI: 0.63-0.81) for class 2 obesity, and 0.68 (95%CI: 0.60-0.77) for class 3 obesity versus healthy weight. A continued volume of 30 drinks per year beyond one drink per drinking day was associated with an adjusted odds ratio of 1.03 (95%CI: 1.01-1.05) for class 1 obesity, 1.04 (95%CI: 1.01-1.06) for class 2 obesity, and 1.04 (95%CI: 1.01-1.07) for class 3 obesity versus healthy weight. In general, any heavy drinking vs none was associated with lower odds of class 2 or class 3 obesity versus healthy weight (Table 4.3, model 3). For example, odds of class 3 obesity versus healthy weight associated with heavy drinking was 0.42 (95%CI: 0.18-0.97) for once -< monthly, 0.33 (95%CI: 0.17-0.65) for 2-4 days per month and 0.74 (95%CI: 0.50-1.10) for at least 2 days per week.

Weight Loss Attempt and Alcohol Use

The distribution of participants across alcohol use variables by weight loss attempt are reported in Table 4.4. There were no significant associations between attempting to lose weight and any alcohol use variable among males (Table 4.5, models 4, 6 and 7). In contrast, among females, weight loss attempt was significantly associated with current drinking and frequency of heavy drinking days. Compared to females with no weight loss attempt in the past year, females who attempted to lose weight had greater odds of current drinking (AOR=1.46 [95%CI: 1.12-1.90]). Additionally, females who were current drinkers and attempted to lose weight were more likely to have reported heavy drinking in the past year (AOR=1.50 [95%CI: 1.18-1.91] for once -< monthly, AOR=2.02 [95% CI: 1.39-2.98] for 2-4 days per month) versus female current drinkers who did not attempt to lose weight. However, there were no significant associations between

attempting to lose weight and frequency of any drinking or average quantity of drinks per drinking day (Table 4.5, models 5 and 6).

Alcohol Use and Weight Change

Among adults who reported trying to lose weight at some point in the past year (n=4,156), the estimated median weight change in the past year was 0.36% (IQR:-2.36-6.41) of weight one year ago for males and 0.26% (IQR:-4.18-6.23) for females. All associations between alcohol use variables and weight change were non-significant (Table 4.6).

4.5 DISCUSSION

Results of this nationally representative study are the first to demonstrate that the magnitude of the inverse association between frequency of alcohol use and odds of overweight-obesity is larger with each level of higher weight status (through class 3 obesity). These findings are important because health status, on average, is substantially worse with each higher grade of obesity and prevalence of higher classes of obesity is increasing in the United States[29,30]. The fact that higher frequency of any alcohol use was associated with lower weight status may reflect that, because we examined frequency of days with any drinking and continued volume simultaneously, frequency of days with any drinking represents the number of days consuming one drink while continued volume represents heavier drinking. Moreover, despite controlling for potential confounders, higher frequency of days with any drinking may be a proxy for better health since drinking is often contraindicated among individuals with poorer health. In addition, individuals who drink more frequently may consume less food and in turn fewer calories than

those who drink less frequently.[160] This study also determined that greater continued volume, or how much alcohol is consumed beyond one drink per drinking day, is associated with higher odds of obesity. This association may reflect that continued volume is a marker of heavier drinking, which is strongly correlated with higher calorie consumption from alcohol.

Because we examined alcohol use among current drinkers, rather than among all adults, our findings address a prior weakness in the published literature which used non-drinkers as their reference group.[8,11] We also built upon the previous literature by examining the associations between patterns of alcohol use (i.e., continued volume and frequency of heavy drinking days) and weight status, as suggested by a review article on the topic, rather than frequency or quantity of alcohol use alone.[12]

Although clinical guidelines recommend limiting alcohol use for weight control, we found few associations between trying to lose weight and alcohol use. Females who were trying to lose weight had higher odds of being current drinkers and higher odds of heavy drinking at any frequency than females not trying to lose weight. We did not find any statistically significant associations among males. This may be because females who are trying to lose weight change other behaviors, such as diet quality or quantity or physical activity level, so they can drink alcohol while still achieving a caloric deficit.[104,111,161] However, it is important to note that we did not measure weight and alcohol use at the start and stop of the weight loss attempt period itself, but rather weight was measured at the start and stop of a one-year period in which any weight loss was attempted, no matter how short in duration. Furthermore, alcohol use was measured over the same one-year period and not exclusively during the time of weight loss attempt. Inaccuracy in either measure would bias the results towards the null hypothesis.

The impact of alcohol use on weight loss is unclear in the current body of literature. Past research shows that, among females, contrary to expectation, there appears to be an inverse association between the amount of alcohol consumed and future weight gain or development of obesity.[99,104] To our knowledge, there are no published studies in males evaluating the predictive nature of alcohol use on weight. Studies evaluating concurrent change in alcohol use and weight change have mixed findings. One study found that increase in alcohol use was associated with concurrent increase in BMI over time in males[7] while a study in females found that increase in alcohol use was associated with decreased odds of concurrent weight gain[99]. However, one study found no such association in males[98] and two found no such association in females[98,105]. While we did not find any statistically significant associations between alcohol use and weight loss, this study is unique in that we examined the association between alcohol use and weight loss among a group of individuals trying to lose weight rather than the whole population. It is possible that potential confounders, such as patterns of eating and genetic determinants of alcohol metabolism, which we did not have information on, would further explain the lack of association between alcohol use and weight loss. More research, particularly prospective studies that take into account change in alcohol use and weight over a one year period, should be done on this topic.

Because of the cross-sectional design of this study, causality cannot be determined; it is possible that drinking patterns change after adults become obese or contract comorbities. In addition, some drinking patterns were rare, especially among females and among adults with class 3 obesity, such that we had to collapse frequency of heavy drinking categories that might have slightly different effects. Likewise, we were unable to evaluate whether associations between weight loss attempt or weight loss and alcohol use differed by weight status. Finally, because weight one year ago was self-reported while current weight was objectively measured,

percent weight loss may be underestimated. However, the strengths of this study are that it uses a large, nationally representative sample that allows for the examination of associations between alcohol use and weight status, differentiating class 1-3 obesity, as well as weight loss attempt and weight loss with alcohol use.

4.6 CONCLUSIONS

These findings suggest that among current drinkers, higher frequency of days with alcohol use is associated with lower odds of obesity, while higher continued volume is associated with higher odds of obesity; associations are stronger with higher classes of obesity. We found no associations between alcohol use and weight loss in males or females. Additional research is needed to determine the appropriateness of clinical guidelines that suggest individuals limit alcohol use for weight control.

4.7 TABLES AND FIGURES

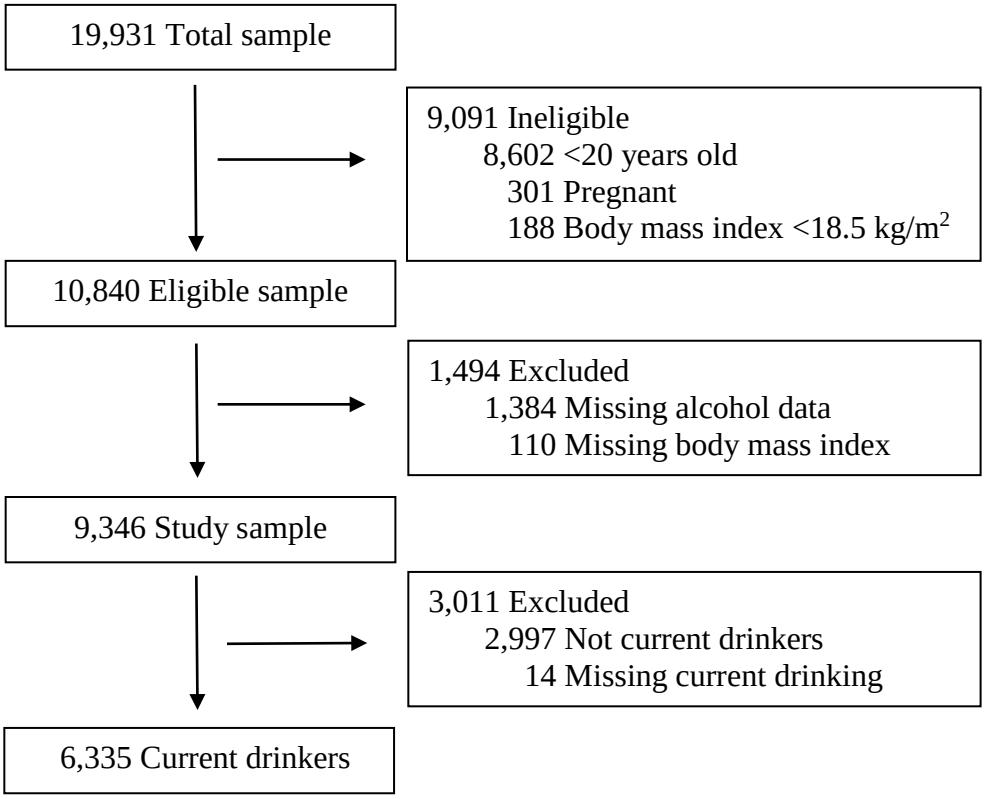

Figure 4.1. Study participant flow diagram, 2011-2014 National Health and Nutrition Examination Survey

Table 4.1. Characteristics of non-pregnant US adults aged 20 and older with body mass index ≥18.5 kg/m^2, by gender, 2011-2014 National Health and Nutrition Examination Survey (N=9,346)

	Total		Male		Female	
Characteristics	Weighted N[a]	% (95% CI)[b]	Weighted N[a]	% (95% CI)[b]	Weighted N[a]	% (95% CI)[b]
Age, years (median, IQR)	47.3	(33.0-60.4)	48.7	(34.6-61.9)	45.8	(31.8-59.0)
Race/Ethnicity						
Hispanic	27881	14.0(10.5-17.5)	14450	14.5(11.0-18.1)	13431	13.5(10.0-17.0)
Non-Hispanic white	135182	67.9(62.8-72.9)	67497	67.9(62.9-72.9)	67685	67.8(62.6-73.1)
Non-Hispanic black	21613	10.8(8.2-13.5)	10022	10.1(7.6-12.6)	11591	11.6(8.7-14.5)
Other race	14543	7.3(6.1-8.5)	7457	7.5(6.2-8.8)	7086	7.1(5.8-8.4)
Education						
Less than high school	30329	15.2(12.8-17.6)	15820	15.9(13.5-18.4)	14509	14.5(12.0-17.1)
High school	41796	21.0(19.0-23.0)	22075	22.2(19.9-24.5)	19720	19.8(17.4-22.1)
Some college	65321	32.8(30.9-34.7)	30151	30.3(28.5-32.2)	35170	35.3(32.9-37.7)
College graduate or higher	61718	31.0(27.7-34.3)	31363	31.5(28.1-35.0)	30355	30.4(26.9-33.9)
Employed	123782	62.2(59.9-64.4)	68730	69.1(66.5-71.8)	55052	55.2(52.5-57.8)
Annual household income						
Under $35,000	59558	31.9(28.0-35.7)	27084	29.1(25.2-33.0)	32474	34.6(30.5-38.7)
$35,000-64,999	46332	24.8(22.7-26.8)	22684	24.4(22.2-26.5)	23647	25.2(22.9-27.5)
$65,000-99,999	32116	17.2(15.3-19.0)	17043	18.3(16.4-20.2)	15073	16.1(13.9-17.2)
$100,000 and over	48942	26.2(22.0-30.4)	26277	28.2(23.8-32.7)	22665	24.1(20.0-28.3)
Marital status						
Married or living with partner	123611	62.1(59.5-64.6)	64989	65.4(62.5-68.2)	58622	58.8(56.2-61.3)
Never married	37927	19.0(16.3-21.7)	21762	21.9(18.8-25.0)	16165	16.2(13.6-18.8)
Widowed, divorced, separated	37648	18.9(17.8-20.0)	12669	12.7(11.4-14.1)	24979	25.0(23.6-26.4)
Smoking status						
Current	38533	19.3(17.7-21.0)	21792	21.9(20.0-23.9)	16741	16.8(14.6-18.9)
Former	49293	24.7(22.8-26.6)	28182	28.4(26.1-30.6)	21110	21.2(18.6-23.7)
Never	111339	55.9(53.7-58.1)	49411	49.7(47.0-52.5)	61928	62.1(59.6-64.6)
Depression symptoms in past 2 weeks	16302	8.2(7.2-9.2)	5739	5.8(4.8-6.8)	10562	10.6(9.2-12.0)
Physical activity, MET-minutes per week (median, IQR)	1304.3	(167.6-3827.6)	1909.1	(357.2-5724.2)	816.8	(0.0-2592.4)

Table 4-1 continued next page.

Table 4-1 (continued).

Characteristics	Total		Male		Female	
	Weighted N[a]	% (95% CI)[b]	Weighted N[a]	% (95% CI)[b]	Weighted N[a]	% (95% CI)[b]
BMI, kg/m^2 (median, IQR)	27.8	(34.3-32.4)	27.8	(24.7-31.7)	27.9	(23.9-33.4)
Weight status						
Healthy weight (18.5-<25 kg/m^2)	57340	28.8(26.9-30.6)	25961	26.1(24.2-28.0)	31379	31.4(29.2-33.7)
Overweight (25-<30 kg/m^2)	67419	33.8(32.1-35.6)	38483	38.7(36.7-40.7)	28936	29.0(26.8-31.2)
Class 1 Obesity (30-<35 kg/m^2)	41900	21.0(19.9-22.2)	22346	22.5(20.8-24.2)	19554	19.6(18.1-21.1)
Class 2 Obesity (35-<40 kg/m^2)	18314	9.2(8.5-9.9)	7710	7.8(6.9-8.6)	10604	10.6(9.6-11.6)
Class 3 Obesity (≥ 40 kg/m^2)	14247	7.2(6.2-8.1)	4925	5.0(3.7-6.2)	9322	9.3(8.1-10.6)
Weight loss attempt in past year						
No	101087	51.5(49.9-53.1)	58663	59.5(57.3-61.7)	42425	43.4(41.5-45.4)
Yes	95228	48.5(46.9-50.1)	39947	40.5(38.3-42.7)	55281	56.6(54.6-58.5)
Lifetime drinker						
No	22521	11.3(9.2-13.5)	6861	6.9(5.0-8.8)	15660	15.7(13.1-18.3)
Yes	176646	88.7(86.5-90.8)	92564	93.1(91.2-95.0)	84082	84.3(81.7-86.9)
Current drinker[c]						
No	51251	25.7(22.6-28.9)	21700	21.8(18.9-24.8)	29550	29.7(26.0-33.3)
Yes	147789	74.3(71.1-77.4)	77696	78.2(75.2-81.1)	70093	70.3(66.7-74.0)
Frequency of days with any drinking[c,d] (median, IQR)	48.1	(10.3-103.9)	50.2	(11.5-149.5)	22.8	(5.3-101.6)
Average quantity of drinks per drinking day[c,d] (median, IQR)	1.5	(1.0-2.8)	1.9	(1.0-3.6)	1.1	(1.0-1.9)
Continued volume[c,d,e] (median, IQR)	22.8	(0.0-166.1)	57.0	(0.1-301.2)	2.6	(0.0-71.4)
Frequency of heavy drinking days[c,f]						
Non-drinker	51251	25.7(22.6-28.9)	21700	21.8(18.9-24.8)	29550	29.7(26.0-33.3)
0 days	81092	40.8(38.6-42.9)	36575	36.8(34.9-38.7)	44517	44.7(41.7-47.7)
Once-<monthly	39116	19.7(18.2-21.1)	21361	21.5(20.0-23.0)	17756	17.8(15.8-19.8)
2-4 days per month	15325	7.7(6.7-8.7)	10698	10.8(9.4-12.1)	4627	4.6(3.5-5.8)
At least 2 days per week	12198	6.1(5.3-6.9)	8960	9.0(7.9-10.2)	3238	3.2(2.5-4.0)

BMI, body mass index; IQR, interquartile range; MET, metabolic equivalent

[a]In thousands. [b]Unless otherwise specified. [c]In past year. [d]Among current drinkers. [e]Total number of drinks beyond one drink per drinking occasion, (frequency of days with any drinking*average quantity of drinks consumed per drinking day) - frequency of days with any drinking. [f]Consumed 5 or more drinks in a single day in males and 4 or more drinks in a single day in females.

Table 4.2. Alcohol use among non-pregnant US adults aged 20 and older with body mass index ≥18.5 kg/m^2, by weight status, 2011-2014 National Health and Nutrition Examination Survey (N=9,346)

	Weight status[a]									
	Healthy weight		Overweight		Class 1 Obesity		Class 2 Obesity		Class 3 Obesity	
	Weighted N[b]	% (95% CI)[c]	Weighted N[b]	% (95% CI)[c]	Weighted N[b]	% (95% CI)[c]	Weighted N[b]	% (95% CI)[c]	Weighted N[b]	% (95% CI)[c]
Males										
Lifetime drinker										
No	1923	28.0(22.5-33.5)	2437	35.5(28.4-42.6)	1769	25.8(20.4-31.2)	332	4.8(2.4-7.3)	401	5.8(2.2-9.5)
Yes	24038	26.0(24.0-28.0)	36046	38.9(37.0-40.9)	20578	22.2(20.5-24.0)	7378	8.0(7.1-8.9)	4524	4.9(3.6-6.1)
Current drinker[d]										
No	5070	23.4(19.7-27.1)	7893	36.4(32.3-40.4)	5513	25.4(22.5-28.3)	1546	7.1(5.4-8.9)	1678	7.7(5.0-10.5)
Yes	20879	26.9(24.6-29.2)	30572	39.3(37.2-41.5)	16834	21.7(19.6-23.7)	6164	7.9(6.9-8.9)	3247	4.2(3.1-5.3)
Frequency of days with any drinking[d,e] (median, IQR)	51.69	(16.44-152.04)	51.02	(11.99-152.51)	48.89	(11.35-119.13)	31.11	(10.15-110.23)	22.33	(9.43-100.64)
Average quantity of drinks per drinking day[d,e] (median, IQR)	2.00	(1.00-4.08)	1.83	(1.00-3.20)	1.97	(1.00-3.70)	1.95	(1.00-3.98)	2.06	(1.21-4.61)
Continued volume[d,e,f] (median, IQR)	91.84	(0.00-299.42)	64.83	(0.15-301.99)	51.48	(0.06-256.27)	46.82	(0.00-289.86)	39.18	(5.54-275.92)
Frequency of heavy drinking days[d,g]										
Non-drinker	5070	23.4(19.7-27.1)	7893	36.4(32.3-40.4)	5513	25.4(22.5-28.3)	1546	7.1(5.4-8.9)	1678	7.7(5.0-10.5)
0 days	9492	26.0(23.2-28.7)	14578	39.9(36.2-43.5)	8174	22.3(19.6-25.1)	2891	7.9(6.0-9.8)	1439	3.9(2.9-5.0)
Once-<monthly	5457	25.5(21.4-29.7)	8643	40.5(36.8-44.1)	4535	21.2(17.5-25.0)	1664	7.8(5.4-10.2)	1062	5.0(2.6-7.3)
2-4 days per month	2979	27.8(21.3-34.4)	4251	39.7(34.8-44.7)	2120	19.8(13.9-25.7)	839	7.8(4.2-11.5)	509	4.8(2.4-7.1)
At least 2 days per week	2881	32.2(25.7-38.7)	3099	34.6(26.1-43.1)	1995	22.3(16.2-28.4)	748	8.3(4.8-11.9)	237	2.6(0.6-4.7)

Table 4.2 continued next page

Table 4.2 (continued).

	Weight status[a]									
	Healthy weight		Overweight		Class 1 Obesity		Class 2 Obesity		Class 3 Obesity	
	Weighted N[b]	% (95% CI)[c]	Weighted N[b]	% (95% CI)[c]	Weighted N[b]	% (95% CI)[c]	Weighted N[b]	% (95% CI)[c]	Weighted N[b]	% (95% CI)[c]
Females										
Lifetime drinker										
No	3657	23.4(19.8-27.0)	5255	33.6(30.7-36.4)	3701	23.6(20.2-27.1)	1744	11.1(9.0-13.3)	1302	8.3(6.3-10.3)
Yes	27714	33.0(30.5-35.4)	23643	28.1(25.7-30.5)	15852	18.9(17.2-20.5)	8854	10.5(9.4-11.7)	8019	9.5(8.1-11)
Current drinker[d]										
No	7045	23.8(20.8-26.9)	8946	30.3(27.8-32.8)	6594	22.3(19.3-25.3)	3881	13.1(11.3-15.0)	3085	10.4(8.1-12.8)
Yes	24319	34.7(32.0-37.3)	19953	28.5(25.8-31.1)	12912	18.4(16.7-20.2)	6682	9.5(8.3-10.8)	6228	8.9(7.4-10.4)
Frequency of days with any drinking[d,e] (median, IQR)	48.70	(10.62-144.06)	23.29	(6.35-101.82)	21.24	(4.30-70.17)	10.68	(3.30-45.21)	10.55	(3.08-32.66)
Average quantity of drinks per drinking day[d,e] (median, IQR)	1.18	(1.00-1.93)	1.00	(1.00-1.84)	1.24	(1.00-2.05)	1.19	(1.00-2.24)	1.16	(1.00-1.98)
Continued volume[d,e,f] (median, IQR)	5.62	(0.00-100.15)	0.00	(0.00-53.20)	5.14	(0.00-68.74)	1.83	(0.00-42.37)	1.88	(0.00-22.59)
Frequency of heavy drinking days[d,g]										
Non-drinker	7045	23.8(20.8-26.9)	8946	30.3(27.8-32.8)	6594	22.3(19.3-25.3)	3881	13.1(11.3-15.0)	3085	10.4(8.1-12.8)
0 days	14102	31.7(28.9-34.4)	13206	29.7(26.7-32.6)	8135	18.3(15.7-20.8)	4793	10.8(8.9-12.7)	4281	9.6(7.8-11.4)
Once-<monthly	7031	39.6(34.3-44.9)	4409	24.8(20.1-29.6)	3473	19.6(15.1-24.0)	1318	7.4(5.5-9.4)	1525	8.6(6.1-11.1)
2-4 days per month	2060	44.5(34.5-54.5)	1228	26.5(17.8-35.3)	674	14.6(8.9-20.3)	389	8.4(3.6-13.2)	276	6.0(1.7-10.2)
At least 2 days per week	1132	35.0(23.9-46.0)	1109	34.2(20.7-47.8)	667	20.6(10.6-30.6)	191	5.9(0.2-11.6)	139	4.3(1.9-6.6)

IQR, interquartile range.

[a]Healthy weight (18.5-<25 kg/m^2), overweight (BMI 25-<30 kg/m^2), and class 1 (BMI 30-<35 kg/m^2), class 2 (BMI 35-<40 kg/m^2), and class 3 (BMI ≥40.0 kg/m^2) obesity. [b]In thousands. [c]Unless otherwise specified. [d]In past year. [e]Among current drinkers. [f]Total number of drinks beyond one drink per drinking occasion, (frequency of days with any drinking*average quantity of drinks consumed per drinking day) - frequency of days with any drinking. [g]Consumed 5 or more drinks in a single day in males and 4 or more drinks in a single day in females.

Table 4.3. Adjusted odds of overweight and obesity by past-year alcohol use, among non-pregnant US adults aged 20 and older with body mass index ≥18.5 kg/m^2, 2011-2014 National Health and Nutrition Examination Survey (N=9,346)

	Adjusted odds (AOR) of overweight and obesity vs healthy weight[a]								
	Overweight[a]		Class 1 Obesity[a]		Class 2 Obesity[a]		Class 3 Obesity[a]		
Alcohol use in past year	AOR[b]	(95% CI)	AOR	(95% CI)	AOR	(95% CI)	AOR	(95% CI)	*P*
Among all males									
Model 1									
Current drinker (ref=no)	1.01	(0.79-1.30)	0.81	(0.60-1.09)	1.17	(0.78-1.75)	0.51	(0.31-0.82)	0.02
Among male current drinkers									
Model 2									
Frequency of days with any drinking (per 30 more days/year)	0.98	(0.94-1.02)	0.91	(0.87-0.96)	0.90	(0.84-0.97)	0.87	(0.79-0.96)	<.001
Continued volume (per 30 more drinks/year)	1.00	(0.99-1.01)	1.01	(0.99-1.02)	1.02	(1.01-1.03)	1.02	(1.00-1.03)	0.002
Model 3									
Frequency of heavy drinking days[c] (ref=0 days)									0.85
Once-<monthly	1.35	(0.87-2.09)	1.20	(0.70-2.05)	1.19	(0.60-2.38)	1.31	(0.58-2.96)	
2-4 days per month	1.01	(0.62-1.64)	0.98	(0.63-1.53)	1.25	(0.69-2.28)	0.78	(0.35-1.74)	
At least 2 days per week	1.19	(0.81-1.73)	1.15	(0.81-1.63)	1.10	(0.63-1.91)	1.28	(0.78-2.09)	
Among all females									
Model 1									
Current drinker (ref=no)	0.73	(0.58-0.91)	0.64	(0.46-0.88)	0.53	(0.38-0.75)	0.64	(0.45-0.91)	0.004
Among female current drinkers									
Model 2									
Frequency of days with any drinking (per 30 more days/year)	0.97	(0.93-1.02)	0.89	(0.84-0.95)	0.71	(0.63-0.81)	0.68	(0.60-0.77)	<.001
Continued volume (per 30 more drinks/year)	1.01	(0.98-1.03)	1.03	(1.01-1.05)	1.04	(1.01-1.06)	1.04	(1.01-1.07)	0.03
Model 3									
Frequency of heavy drinking days[c](ref=0 days)									<.001
Once-<monthly	0.79	(0.48-1.29)	0.75	(0.42-1.33)	0.61	(0.26-1.41)	0.42	(0.18-0.97)	
2-4 days per month	1.17	(0.65-2.11)	1.14	(0.51-2.56)	0.36	(0.10-1.31)	0.33	(0.17-0.65)	
At least 2 days per week	0.77	(0.56-1.06)	1.09	(0.67-1.75)	0.61	(0.38-0.98)	0.74	(0.50-1.10)	

BMI, body mass index.

[a]Healthy weight (18.5-<25 kg/m^2), overweight (BMI 25-<30 kg/m^2), and class 1 (BMI 30-<35 kg/m^2), class 2 (BMI 35-<40 kg/m^2), and class 3 (BMI ≥40.0 kg/m^2) obesity. [b] All models adjusted for age, race/ethnicity, education, employment status, annual household income, marital status, smoking status, depression symptoms, physical activity, and weight loss attempt. [c]Consumed 5 or more drinks in a single day among males or 4 or more drinks in a single day among females.

Table 4.4. Alcohol use among non-pregnant US adults aged 20 and older with body mass index ≥18.5 kg/m^2, by weight loss attempt in past year, 2011-2014 National Health and Nutrition Examination Survey (N=9,346)

	Male				Female			
	No weight loss attempt		Weight loss attempt		No weight loss attempt		Weight loss attempt	
Alcohol use in past year	Weighted N[a]	% (95% CI)[b]	Weighted N[a]	% (95% CI)[b]	Weighted N[a]	% (95% CI)[b]	Weighted N[a]	% (95% CI)[b]
Current drinker								
No	12855	22.2(18.9-25.5)	8196	20.6(17.3-23.9)	13917	33.9(29.8-37.9)	13586	25.1(20.9-29.2)
Yes	44984	77.8(74.5-81.1)	31616	79.4(76.1-82.7)	27184	66.1(62.1-70.2)	40649	74.9(70.8-79.1)
Frequency of days with any drinking[c] (median, IQR)	50.9	(11.9-152.6)	49.0	(11.1-146.3)	22.5	(5.1-102.1)	23.1	(5.5-101.5)
Average quantity of drinks per drinking day[c] (median, IQR)	2.0	(1.0-3.8)	1.8	(1.0-3.4)	1.0	(1.0-1.9)	1.2	(1.0-2.0)
Continued volume[c,d] (median, IQR)	71.3	(0.0-304.6)	51.4	(0.6-256.7)	0.0	(0.0-70.3)	4.6	(0.0-90.8)
Frequency of heavy drinking days[e]								
Non-drinker	12855	22.3(19.0-25.5)	8196	20.6(17.3-23.9)	13917	33.8(29.7-37.9)	13586	25.1(20.9-29.2)
0 days	21288	36.8(33.8-39.9)	14714	37.0(34.0-40.0)	18583	45.1(41.1-49.2)	24386	45.0(41.5-48.5)
Once-<monthly	11586	20.1(18.1-22.0)	9514	23.9(21.2-26.6)	5911	14.4(11.7-17)	11278	20.8(18.4-23.2)
2-4 days per month	6329	11.0(9.1-12.8)	4194	10.5(8.6-12.4)	1499	3.6(2.3-4.9)	3031	5.6(4.1-7.1)
At least 2 days per week	5717	9.9(8.1-11.7)	3176	8.0(5.8-10.1)	1269	3.1(1.7-4.5)	1921	3.5(2.7-4.4)

IQR, interquartile range.

[a]In thousands. [b]Unless otherwise specified. [c]Among current drinkers. [c]Total number of drinks beyond one drink per drinking occasion, (frequency of days with any drinking*average quantity of drinks consumed per drinking day) - frequency of days with any drinking. [d]Consumed 5 or more drinks in a single day in males and 4 or more drinks in a single day in females.

Table 4.5. Associations of past-year weight loss attempt with alcohol use, among non-pregnant US adults aged 20 and older with body mass index ≥18.5 kg/m^2, 2011-2014 National Health and Nutrition Examination Survey (N=9,346)

	Weight loss attempt (Ref=no attempt)			
Alcohol use in past year	Male		Female	
Among all adults				
Model 4	AOR[a] (95% CI)	*P*	AOR[a] (95% CI)	*P*
Current drinker (ref=no)	1.01 (0.85-1.21)	0.90	1.46 (1.12-1.90)	0.005
Among current drinkers				
Model 5	Beta[b] (95% CI)	*P*	Beta[b] (95% CI)	*P*
Frequency of days with any drinking	-11.77 (-24.87-1.34)	0.08	5.28 (-5.02-15.58)	0.30
Model 6	Beta[b] (95% CI)	*P*	Beta[b] (95% CI)	*P*
Average quantity of drinks per drinking day	-0.14 (-0.41-0.13)	0.31	0.15 (-0.03-0.34)	0.11
Model 7	AOR[a] (95% CI)	*P*	AOR[a] (95% CI)	*P*
Frequency of heavy drinking days[d] (ref=0 days)		0.99		<.001
Once-<monthly	0.99 (0.79-1.23)		1.50 (1.18-1.91)	
2-4 days per month	1.02 (0.74-1.40)		2.02 (1.39-2.93)	
At least 2 days per week	1.06 (0.68-1.64)		1.48 (0.96-2.26)	

[a]Adjusted odds ratio (AOR) of alcohol use as described in the table, for those who attempted weight loss in the past year versus those who did not. All models adjusted for age, race/ethnicity, education, employment status, annual household income, marital status, smoking status, depression symptoms, physical activity, and weight status one year ago. [b]Per 1 more day with any drinking. [c]Per 1 more drink per drinking day. [d]Consumed 5 or more drinks in a single day among males and 4 or more drinks in a single day among females.

Table 4.6. Associations between past year alcohol use and percent weight change, among non-pregnant US adults aged 20 and older with BMI ≥18.5 kg/m^2 who tried to lose weight in past year, 2011-2014 National Health and Nutrition Examination Survey (N=4,156)

	Percent weight change in past year			
	Male		Female	
Alcohol use in past year	Beta[a] (95% CI)	*P*	Beta[a] (95% CI)	*P*
Among all adults				
Model 8				
Current drinker (ref=no)	0.05(-1.33-1.43)	0.94	-0.05(-1.77-1.68)	0.95
Among current drinkers				
Model 9				
Frequency of days with any drinking (per 30 more days/year)	-0.14(-0.33-0.06)	0.17	-0.04(-0.23-0.15)	0.67
Continued volume (per 30 more drinks/year)	0.002(-0.05-0.05)	0.95	-0.04(-0.13-0.05)	0.42
Model 10				
Frequency of heavy drinking days[b] (ref=0 days)		0.47		0.61
Once-<monthly	0.38(-1.04-1.81)		0.23(-1.45-1.92)	
2-4 days per month	-0.23(-2.08-1.62)		-0.64(-3.05-1.77)	
At least 2 days per week	-0.85(-3.07-1.36)		-1.24(-3.81-1.33)	

[a]Per 1 percent weight change, adjusted for age, race/ethnicity, education, employment status, annual household income, marital status, smoking status, depression symptoms, physical activity, and weight status one year ago. [b]Consumed 5 or more drinks in a single day among males and 4 or more drinks in a single day among females.

5.0 MANUSCRIPT 2 – DO ASSOCIATIONS BETWEEN ALCOHOL USE AND ALCOHOL USE DISORDER VARY BY WEIGHT STATUS? RESULTS FROM THE NATIONAL EPIDEMIOLOGICAL SURVEY ON ALCOHOL AND RELATED CONDITIONS-III

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5.1 ABSTRACT

Objectives: To determine if associations between alcohol use and alcohol use disorder (AUD) differ by weight status.

Methods: 24,869 National Epidemiological Survey on Alcohol and Related Conditions-III participants with a body mass index ≥18.5 kg/m^2 who reported past-year alcohol use were

included. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 was administered to identify past-year AUD. Logistic regression was used to test associations between levels and patterns of alcohol use and AUD; interactions between weight status and alcohol use variables in relation to AUD were examined. Analyses were stratified by gender.

Results: For males and females, the odds of AUD were higher with greater frequency of any alcohol use and heavy drinking, higher average quantity of drinks per drinking day, and past-year high-risk drinking. Among males, interactions (p for all <.01) indicated that at the same average quantity of drinks per drinking day, frequency of heavy drinking, or presence of high-risk drinking, those with class 3 obesity had higher odds of AUD versus lower classes or no obesity. Among females, at the same frequency of any alcohol use, those with healthy weight had the highest odds of AUD, while females with class 3 obesity had the lowest odds of AUD (p<.001).

Conclusions: Associations between some measures of alcohol use and AUD differed by weight status for both males and females. Further AUD screening may be needed at lower levels of alcohol use among males with class 3 obesity and females of healthy weight.

5.2 INTRODUCTION

Both alcohol use disorder (AUD) and obesity (body mass index, BMI $\geq$ 30 kg/m^2)[4] have increased in prevalence since the early 2000s[29,162] and are leading contributors to comorbidities and excess cost in the United States.[2,17,60,163] Obesity is currently the second leading cause of preventable death in the United States[16] and is associated with a number of health risk behaviors, including higher alcohol use.[164,165] In 2012-2013, nearly two-thirds (72.7%) of US adults aged 18 and older consumed alcohol in the past year; an increase of 7.3% from 2001-2002.[166]

Greater alcohol use, often quantified by the average number of days with alcohol consumption per week, the average number of drinks consumed per day, and/or the highest number of drinks consumed in a single day[61,64] is positively associated with risk for developing AUD.[64,77,88,89,91] Guidelines put forth by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and the United States Department of Agriculture for the general US population recommend that adults not drink heavily (defined as at least 5 drinks in a single day among males or at least 4 drinks in a single day among females)[11] or at high-risk levels (defined as at least 15 drinks per week, on average, among males, and at least 8 drinks per week, on average, among females, or any heavy drinking occasions).[64] While the risk of AUD associated with exceeding these drinking limits has been demonstrated in the general population,[88,90,163,167] it has not been evaluated by weight status.

The relationship between alcohol use and weight is complex. Individuals with lower weight status generally experience the intoxicating effects of alcohol more rapidly than people with higher weight status.[168] However, because alcohol is absorbed more slowly into fat than muscle, people of the same weight with higher versus lower percent body fat experience a higher blood alcohol concentration (BAC) from the same amount of alcohol.[168] Moreover, compared to individuals of healthy weight, those with higher weight status have higher prevalence of comorbidities and medication use, which may lead them to drink less.[101,102] Given this, weight status may modify the associations between level and pattern of alcohol use and AUD.

Understanding whether the associations between alcohol use and AUD differ by weight status may be useful in screening for AUD in populations where obesity is common. Therefore, using National Epidemiological Data on Alcohol and Related Conditions (NESARC)-III data, we examined the prevalence of AUD according to varying levels and patterns of alcohol use by

weight status, and determined if associations between alcohol use and AUD differed by weight status. Given the evidence that associations between alcohol use and AUD differ by gender,[88] all analyses were stratified by gender.

5.3 METHODS

Data Source

The NESARC-III is a cross-sectional survey of a nationally representative sample of 36,309 non-institutionalized US adults aged 18 and older collected during 2012-2013. The survey was designed and conducted by NIAAA to gather information on alcohol and drug use and disorders, as well as related risk factors and associated disabilities.[69] Informed consent was given and informed consent procedures were approved by the institutional review boards of the National Institutes of Health and Westat. We used data for non-pregnant US adults aged 18 and older who had non-missing BMI of at least 18.5 kg/m^2 (i.e., healthy weight or higher) and had consumed at least one alcoholic drink in the past 12 months (n=24,869) (Figure 5.1).

Definitions

Past-Year Levels and Patterns of Alcohol Use and AUD

Current drinkers were those who reported consuming at least one alcoholic drink in the past year.[169,170] Frequency of past-year alcohol use was defined as drinking alcohol 1-2 times, 3-6 times, 7-11 times, once a month, 2-3 times a month, once a week, 2 times a week, 3-4 times a week, nearly every day, and every day. Daily and near daily frequencies were collapsed due to low frequencies. Average quantity of drinks consumed per drinking day was reported as a whole

number and capped at 7 drinks because quantities higher than this were rare. Heavy drinking was defined as consuming at least 5 drinks in a single day among males <65 years old or at least 4 drinks in a single day among males ≥65 years old and among females of any age. Frequency of heavy drinking was assessed with the same frequency categories as any alcohol use, and collapsed into 1 to 6 times in the past year, 7 to 12 times a year, 2 to 4 times a month, 2 to 4 times a week, and daily or near daily due to low frequencies. High-risk drinking was defined as at least 15 drinks per week, on average, among males, and at least 8 drinks per week, on average, among females or heavy drinking at least once in the past year.[88,171] The NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5), which has good reliability and validity for AUD,[172,173] was administered to identify Diagnostic and Statistical Manual of Mental Disorders-5 (DSM-5) past-year AUD.[79]

Weight Status

Anthropometric data, including height and weight, were self-reported. BMI was defined as weight in kg divided by height in m^2 and was categorized into healthy weight (18.5-<25 kg/m^2), overweight (BMI 25-<30 kg/m^2), and class 1 (BMI 30-<35 kg/m^2), class 2 (BMI 35-<40 kg/m^2), and class 3 (BMI ≥40 kg/m^2) obesity.[4]

Other Measures

Race/ethnicity was categorized as Hispanic, any race; non-Hispanic white; non-Hispanic black; and other (non-Hispanic American Indian/Alaska Native or non-Hispanic Asian/Native Hawaiian/other Pacific Islander). When an individual selected more than one race category, a single race was assigned in the following order of preference: black or African American,

American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, Asian, white.[174] Education was grouped into the following categories based on highest grade of school completed: less than a high school education (no formal schooling, completed grade K-11), high school (completed high school, general equivalency diploma [GED]), some college (no degree), and college graduate or higher (completed associate or other technical 2-year degree, Bachelor's degree, some graduate or professional studies, completed Master's degree or equivalent or higher graduate degree). People who reported currently working full time; working part time; or employed but not at work because of temporary illness or injury, paid vacation, or on unpaid leave were defined as being employed.[175] Income was defined as total combined family income in the past 12 months as under $35,000, $35,000-$69,999, and $70,000 and over. Marital status was defined as being currently married or living with someone as if married; never married; or widowed, divorced, or separated.[86] Participants were asked to report how often and for how long they participated in vigorous or moderate-intensity activities in the past 12 months. Those who reported, on average, at least 150 minutes of moderate-intensity or 75 minutes of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate and vigorous physical activity per week were classified as meeting physical activity guidelines.[176]

Smoking status was self-reported as current smoker (tobacco or nicotine use in the past 12 months), former smoker (no tobacco or nicotine use in the past 12 months), and never smoker.[169] Past-year major depression was determined per the DSM-5 and identified using AUDADIS-5.[79,177] Family history of alcohol problems was described to the respondent as a person having "physical or emotional problems because of drinking; problems with a spouse, family, or friends because of drinking; problems at work or school because of drinking; problems because of driving after drinking; or a person who seems to spend a lot of time drinking or being

hung over." Participants were then asked whether each first- and second-degree relative had alcohol problems. In this study, family history was categorized as unknown family history, no family history, only second-degree relatives (biological grandparents, aunts, and uncles) with problem drinking, only first-degree relatives (biological parents, children, full siblings) with problem drinking, and first- and second-degree relatives with problem drinking.[170]

Statistical Analysis

We used SAS® software version 9.4 (SAS Institute Inc., Cary, NC) survey procedures to account for non-response differences in the sample and unequal probability of sample selection, and to produce results representative of the US population. All analyses were stratified by gender. Descriptive statistics were used to report sociodemographics and level and pattern of alcohol use.

Descriptive statistics were used to report the prevalence of AUD as a function of level and pattern of alcohol use in the past 12 months by weight status. Logistic regression was used to test associations of level and pattern of alcohol use variables (i.e., frequency of days with any alcohol use and average quantity of drinks per drinking day (model 1), frequency of heavy drinking days (model 2), and presence of high-risk drinking (model 3)) with AUD. Interactions between alcohol use variables and weight status in relation to AUD were examined. Based on prior literature, all logistic regression models were adjusted for the following potential confounders: age, race/ethnicity, education, employment status, income, marital status, physical activity, smoking status, past-year major depressive disorder, and family history of alcohol problems.[77,169,178-180]

5.4 RESULTS

Among male current drinkers, an estimated 41.0% (95% CI: 39.9-42.0) were overweight, 19.4% (95% CI: 18.4-20.3) had class 1 obesity, 6.6% (95% CI: 6.1-7.1) had class 2 obesity, and 3.3% (95% CI: 2.8-3.7) had class 3 obesity. Among female current drinkers, an estimated 28.5% (95% CI: 27.4-29.5) were overweight, 17.0% (95% CI: 16.2-17.8) had class 1 obesity, 7.9% (95% CI: 7.2-8.6) had class 2 obesity, and 5.2% (95% CI: 4.7-5.8) had class 3 obesity. An estimated 23.0% (95% CI: 21.9-24.0) of male current drinkers and 15.1% (95% CI: 14.1-16.1) of female current drinkers had past-year AUD (Table 5.1).

The prevalence of AUD by level and pattern of alcohol use and weight status is reported in Table 5.2. Among males, the estimated prevalence of AUD in current drinkers was 27.5% (95% CI: 25.4-29.5) with healthy weight, 21.5% (95% CI: 20.1-23.0) with overweight, 21.1% (95% CI: 19.1-23.0) with class 1 obesity, 17.6% (95% CI: 14.4-20.8) with class 2 obesity, and 21.7% (95% CI: 17.6-25.8) with class 3 obesity. Corresponding prevalence estimates for females were 17.6% (95% CI: 16.2-19.0), 14.4% (95% CI: 13.0-15.8), 12.0% (95% CI: 10.3-13.7), 11.9% (95% CI: 9.7-14.1) and 13.4% (95% CI: 10.7-16.2) for healthy weight through class 3 obesity categories, respectively.

For males and females, the adjusted odds of AUD were higher with greater frequency of any alcohol use, higher average quantity of drinks per drinking day, greater frequency of heavy drinking, and presence of high-risk drinking (Table 5.3 and Table 5.4). Among males, with adjustment for potential confounders, there were significant interactions between weight status and average quantity of drinks per drinking day ($p<.001$), frequency of heavy drinking ($p<.001$), and presence of high-risk drinking ($p=0.002$), but not frequency of any alcohol use ($p=0.36$). At the same quantity of drinks per drinking day or frequency of heavy drinking, males with class 3

obesity generally had higher odds of AUD than males with healthy weight to class 2 obesity; likewise, high-risk drinking was associated with greater odds of AUD among males with class 3 obesity versus lower weight status groups (Table 5.3).

Conversely, among females, with adjustment for potential confounders, there was not a significant interaction between weight status and average quantity of drinks per drinking day ($p=0.22$), frequency of heavy drinking ($p=0.12$), or presence of high-risk drinking ($p=0.08$). However, there was a significant interaction between weight status and frequency of any alcohol use ($p<.001$), such that at the same frequency, females with higher weight status generally had lower odds of AUD than females with lower weight status (Table 5.4).

5.5 DISCUSSION

Results of this nationally representative study of US adults indicate that the relationship between alcohol use and AUD differs by weight status. Furthermore, the interplay between weight status and alcohol use in relation to AUD differed by sex. Among males, at the same quantity of drinks per drinking day, same frequency of heavy drinking, and with high-risk drinking, those with class 3 obesity had higher odds of AUD than those with healthy weight to class 2 obesity. Among females, at the same frequency of any alcohol use, those with class 3 obesity had lower odds of AUD versus lower weight status groups. When screening for AUD, clinicians should be aware that the relationships between levels and patterns of alcohol use and AUD differ by weight status. In particular, these results indicate that further AUD screening may be warranted at lower levels of alcohol use among males with class 3 obesity. In contrast, among females, frequent use of any alcohol may be more concerning among lower weight status groups.

This paper builds upon past research[88] by presenting the prevalence of DSM-5 AUD by level and pattern of alcohol use among adults by weight status in a manner that can be easily communicated by clinicians and educators. This is important given the increasing prevalence of obesity and severe obesity in the United States. Furthermore, we found that nearly one quarter of male current drinkers and 15% of female current drinkers met criteria for AUD and that the prevalence of AUD increased with higher frequency of any alcohol use, quantity of drinks consumed per drinking day, and frequency of heavy drinking in the past year in both males and females of all weight status categories.

Consistent with our findings, past research has found that males consume alcohol at higher frequencies and quantities than females.[7,181] Gender differences also play a role in neurobiological processes associated with AUD such as the ability of alcohol to influence the mesolimbic pathway, how males and females perceive the rewarding effects of alcohol, and the pharmacokinetics of alcohol metabolism.[7,182-186] Moreover, the prevalence of obesity and its relationship to alcohol use differ by gender.[7,187] Thus, it is not surprising that we found differences between males and females regarding interactions between weight status and level and pattern of alcohol use with AUD. Still, it is noteworthy that the associations between level and pattern of alcohol use and AUD, by weight status, were very different between males and females.

The stronger associations between level and pattern of alcohol use and AUD among males with class 3 obesity versus males of other weight status categories are unexpected given the relationship between alcohol metabolism and weight status,[65,100] but may reflect that poorer health[101,102] precludes males with class 3 obesity from consuming alcohol at the same levels as males of other weight status categories. Because this analysis excluded non-drinkers, who are

less healthy than current drinkers, it is possible that we eliminated non-drinkers disproportionately from higher weight status categories. Given our findings, future work should examine if and how the association between level of alcohol use and intoxication differs in men with class 3 obesity versus lower weight status categories.

The higher odds of AUD at the same frequency of any alcohol use among females with lower weight status categories indicates that obesity, particularly class 3 obesity, may be protective against AUD when compared to other weight status categories. However, given that a similar interaction was not seen with quantity of drinks per drinking day, frequency of heavy drinking, or presence of high-risk drinking, it is unlikely that this is the case. Previous research has hypothesized that because food competes with other addictive substances for brain reward sites, obesity may serve to protect against substance use disorders, including AUD.[188-190] Moreover, alcohol metabolism is slower among individuals with higher percentage of body fat.[61,65,182] It is also possible that residual confounding explains these associations as there are factors, such as sleep, that we did not control for. Due to the cross-sectional nature of the current study, we were unable to determine mechanisms through which weight status modified the associations between alcohol use and AUD.

For many reasons, we examined associations between four different alcohol measures and AUD. First, frequency and quantity of alcohol use are two of the most commonly used measures of alcohol use.[191] Second, most discussions about alcohol use in the primary care setting are short (last less than one minute).[192] It is unlikely that many primary care physicians would take the time to calculate more detailed measures of alcohol use such as continued volume of alcohol, therefore a shorter screening approach may be more useful.[192] Third, we expect that the associations between continued volume of alcohol use and AUD would mirror those we saw

for the associations between quantity of alcohol use and AUD. Finally, the NIAAA recommends that when AUD screening is done through a single-question, the question should assess frequency of heavy drinking.[83]

The strengths of this study are its use of a large, nationally representative sample that allows for the examination of associations between level and pattern of alcohol use and AUD, by weight status, including higher levels of obesity. This study used a validated measure of AUD but BMI was self-reported. While self-reported and measured weight are highly correlated ($r>0.90$), they are generally closer among those with lower weight than among those with higher weight.[20] In addition, despite the large sample size, some drinking patterns were rare, especially among adults with class 3 obesity, such that some estimates had large confidence intervals. Moreover, we did not have the power to examine associations between alcohol use and AUD among those in the highest risk groups for each alcohol measure. Finally, due to the cross-sectional nature of this study, the directionality of the relationships between alcohol use, AUD, and weight status cannot be determined. For example, it is unclear whether males with class 3 obesity are more likely to develop AUD at lower levels of alcohol use, or if males with class 3 obesity and AUD consume alcohol at lower levels than those with other weight status categories. Regardless, the associations are relevant when using patient-reported alcohol use to determine whether further screening for AUD is warranted.

5.6 CONCLUSIONS

These findings suggest that, at the same average quantity of drinks per drinking day, frequency of heavy drinking and high-risk drinking, males with class 3 obesity have higher odds of AUD

than males of healthy weight to class 2 obesity. In contrast, at the same past-year frequency of alcohol use, females with lower weight status have higher odds of AUD than females of higher weight status, in particular, class 3 obesity. AUD screening and advice delivered in the primary care setting results in substantial improvements in individual health, as well as decreases in the population burden of disease.[193,194] These results can aid health care providers in screening patients with different weight status for AUD and hopefully lead to improved individual health.

5.7 TABLES AND FIGURES

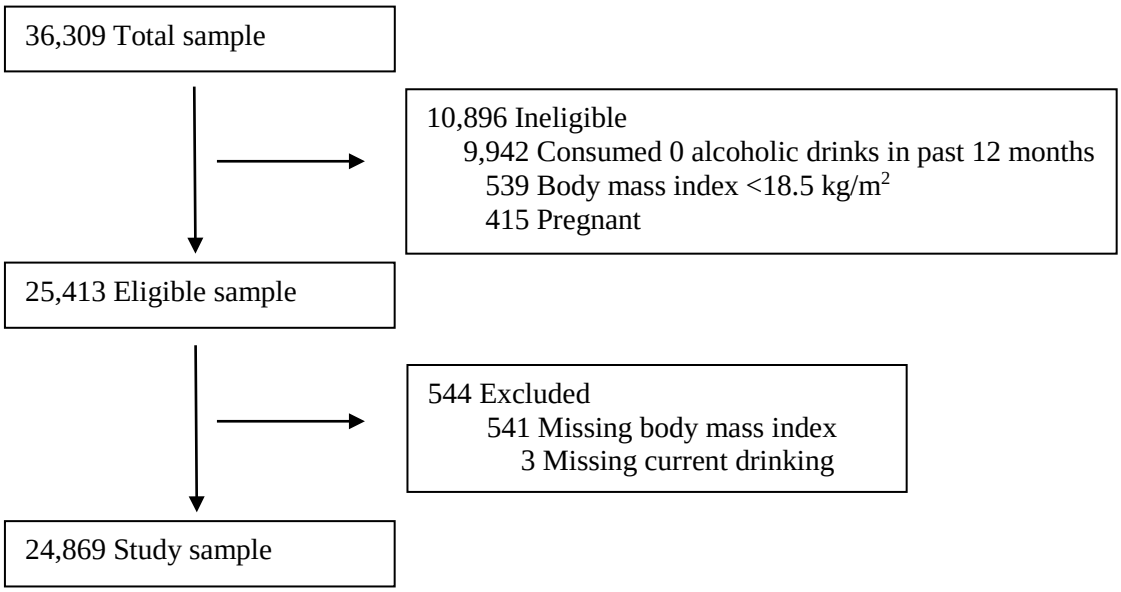

Figure 5.1. Study participant flow diagram, US adults ≥ 18 years, National Epidemiological Survey on Alcohol and Related Conditions-III

Table 5.1. Characteristics of non-pregnant US current drinkers ≥ 18 years with body mass index ≥ 18.5 kg/m^2, by sex, National Epidemiological Survey on Alcohol and Related Conditions-III

Characteristics	Total		Male		Female	
	Weighted N[a]	% (95% CI)	Weighted N[a]	% (95% CI)	Weighted N[a]	% (95% CI)
Age, years (median, IQR)	43.3	(29.8, 56.5)	42.8	(29.6, 56.2)	43.7	(30.1, 56.8)
Race/Ethnicity						
Hispanic	23577	14.3(13.0-15.5)	12943	15.1(13.7-16.5)	10634	13.4(12.1-14.6)
Non-Hispanic white	113433	68.6(67.1-70.0)	58313	67.9(66.3-69.5)	55120	69.2(67.6-70.8)
Non-Hispanic black	17725	10.7(9.6-11.9)	8872	10.3(9.2-11.5)	8853	11.1(9.9-12.4)
Other race	10710	6.5(5.6-7.3)	5711	6.7(5.6-7.7)	4999	6.3(5.5-7.1)
Education						
Less than high school	16448	9.9(9.2-10.7)	9689	11.3(10.4-12.2)	6759	8.5(7.8-9.2)
High school	39877	24.1(23.1-25.1)	22139	25.8(24.6-27.0)	17738	22.3(21.1-23.5)
Some college	37465	22.6(21.9-23.4)	18512	21.6(20.6-22.5)	18953	23.8(22.8-24.8)
College graduate or higher	71654	43.3(41.7-44.9)	35498	41.4(39.6-43.1)	36156	45.4(43.7-47.1)
Employed	106844	64.6(63.5-65.7)	58948	68.7(67.3-70.0)	47896	60.2(58.9-61.4)
Annual household income						
Under $35,000	57856	35.0(33.6-36.4)	27959	32.6(31.0-34.1)	29897	37.6(36.0-39.1)
$35,000-69,999	46776	28.3(27.5-29.0)	24650	28.7(27.7-29.7)	22126	27.8(26.8-28.8)
$70,000 and over	60813	36.8(35.3-38.2)	33230	38.7(37.1-40.4)	27583	34.6(33.1-36.2)
Marital status						
Married or living with partner	96344	58.2(57.1-59.4)	51681	60.2(58.8-61.6)	44663	56.1(54.8-57.4)
Never married	39078	23.6(22.6-24.7)	21956	25.6(24.4-26.8)	17121	21.5(20.2-22.8)
Widowed, divorced, separated	30023	18.1(17.4-18.9)	12201	14.2(13.4-15.0)	17821	22.4(21.3-23.4)
Smoking status						
Current	51237	31.0(29.9-32.0)	31429	36.6(35.4-37.9)	19808	24.9(23.6-26.2)
Former	30440	18.4(17.6-19.2)	16590	19.3(18.3-20.3)	13850	17.4(16.5-18.3)
Never	83768	50.6(49.4-51.8)	37820	44.1(42.5-45.6)	45947	57.7(56.4-59.1)
Meets physical activity guidelines	113916	68.9(67.9-69.8)	63567	74.1(72.8-75.3)	50348	63.2(62.0-64.5)
BMI, kg/m^2 (median, IQR)	26.6	(23.6, 31.0)	27.2	(24.4, 30.8)	26.3	(22.8, 31.1)
Weight status						
Healthy weight (18.5-<25 kg/m^2)	58529	35.4(34.4-36.4)	25579	29.8(28.6-31.0)	32951	41.4(40.1-42.7)
Overweight (25-<30 kg/m^2)	57817	34.9(34.2-35.7)	35154	41.0(39.9-42.0)	22663	28.5(27.4-29.5)
Class 1 Obesity (30-<35 kg/m^2)	30172	18.2(17.6-18.9)	16630	19.4(18.4-20.3)	13543	17.0(16.2-17.8)
Class 2 Obesity (35-<40 kg/m^2)	11957	7.2(6.8-7.7)	5671	6.6(6.1-7.1)	6286	7.9(7.2-8.6)
Class 3 Obesity (≥ 40 kg/m^2)	6969	4.2(3.8-4.6)	2805	3.3(2.8-3.7)	4164	5.2(4.7-5.8)
Frequency of any alcohol use						
1-2 times/ year	18406	11.1(10.5-11.8)	6993	8.2(7.4-8.9)	11413	14.3(13.5-15.2)
3-6 times/year	17853	10.8(10.2-11.3)	7069	8.2(7.5-9.0)	10784	13.6(12.8-14.3)
7-11 times/year	9590	5.8(5.5-6.1)	4163	4.9(4.4-5.3)	5427	6.8(6.3-7.4)
Once/month	17001	10.3(9.8-10.7)	7875	9.2(8.6-9.8)	9126	11.5(10.8-12.2)
2-3 times/month	21599	13.1(12.5-13.7)	10940	12.8(11.8-13.7)	10660	13.4(12.7-14.1)
Once/week	19564	11.8(11.3-12.4)	10698	12.5(11.7-13.3)	8866	11.1(10.5-11.8)
2 times/week	21620	13.1(12.5-13.6)	12753	14.9(14.0-15.7)	8867	11.1(10.4-11.9)
3-4 times/week	19779	12.0(11.4-12.6)	12033	14.0(13.2-14.8)	7746	9.7(9.1-10.4)
Daily/nearly daily	19946	12.1(11.5-12.6)	13266	15.5(14.6-16.3)	6680	8.4(7.8-9.0)

Table 5.1 continued next page

Table 5.1 (continued).

Characteristics	Total		Male		Female	
	Weighted N[a]	% (95% CI)	Weighted N[a]	% (95% CI)	Weighted N[a]	% (95% CI)
Average quantity of drinks per drinking day						
1	57523	34.9(33.7-36.0)	23220	27.2(25.8-28.5)	34303	43.2(41.9-44.5)
2	47925	29.1(28.3-29.8)	23714	27.7(26.7-28.7)	24211	30.5(29.5-31.5)
3	24123	14.6(14.0-15.3)	14025	16.4(15.6-17.3)	10098	12.7(11.9-13.5)
4	12451	7.6(7.1-8.0)	7628	8.9(8.2-9.6)	4823	6.1(5.6-6.6)
5	6243	3.8(3.5-4.1)	4157	4.9(4.4-5.4)	2086	2.6(2.3-3.0)
6	8032	4.9(4.5-5.3)	5905	6.9(6.3-7.5)	2127	2.7(2.3-3.0)
7 or more	8591	5.2(4.8-5.6)	6845	8.0(7.3-8.7)	1746	2.2(1.8-2.6)
Frequency of heavy drinking[b]						
Never	90219	54.7(53.6-55.8)	41677	48.7(47.3-50.1)	48543	61.2(60.0-62.5)
1-6 times/year	25774	15.6(15.0-16.3)	13491	15.8(14.8-16.7)	12282	15.5(14.7-16.3)
7-12 times/year	15807	9.6(9.2-10.0)	8985	10.5(9.9-11.1)	6822	8.6(8.1-9.1)
2-4 times/month	15713	9.5(9.0-10.0)	9695	11.3(10.6-12.1)	6017	7.6(7.0-8.2)
2-4 times/week	12357	7.5(7.0-8.0)	8101	9.5(8.8-10.1)	4256	5.4(4.8-6.0)
Daily/nearly daily	4994	3.0(2.7-3.3)	3644	4.3(3.8-4.7)	1350	1.7(1.4-2.0)
High-risk drinking[c]						
No	78212	47.3(46.2-48.5)	36620	42.7(41.3-44.1)	41592	52.3(51.0-53.6)
Yes	87022	52.7(51.5-53.8)	49095	57.3(55.9-58.7)	37927	47.7(46.4-49.0)
Alcohol Use Disorder						
No	133723	80.8(80.0-81.7)	66135	77.0(76.0-78.1)	67588	84.9(83.9-85.9)
Yes	31722	19.2(18.3-20.0)	19704	23.0(21.9-24.0)	12018	15.1(14.1-16.1)

CI: Confidence interval; IQR: Interquartile range.

[a]In thousands. [c]Consumed at least 5 drinks in a single day among males <65 years old and at least 4 drinks in a single day among males ≥65 years old and females of any age. [e]Consumed at least 15 drinks per week, on average, among males, and at least 8 drinks per week, on average, among females or heavy drinking at least once in the past year.

Table 5.2. Prevalence of alcohol use disorder as a function of levels and patterns of alcohol use in the past 12 months among non-pregnant US current drinkers ≥18 years, National Epidemiological Survey on Alcohol and Related Conditions-III

	Prevalence [%(95% CI)] of Alcohol Use Disorder									
	Weight Status[a]									
	Healthy weight		Overweight		Class 1 Obesity		Class 2 Obesity		Class 3 Obesity	
Males	27.5	(25.4-29.5)	21.5	(20.1-23.0)	21.1	(19.1-23.0)	17.6	(14.4-20.8)	21.7	(17.6-25.8)
Frequency of any alcohol use										
1-2 times/year	0.7	(0.0-1.5)	1.0	(0.0-2.0)	1.2	(0.0-2.5)	1.5	(0.0-4.5)	4.0	(0.0-12.0)
3-6 times/year	5.6	(2.4-8.9)	5.2	(2.3-8.0)	3.0	(0.0-6.9)	3.7	(0.1-7.3)	2.9	(0.0-7.0)
7-11 times/year	7.9	(2.6-13.1)	6.5	(2.6-10.4)	6.7	(2.0-11.4)	5.7	(0.0-12.4)	13.7	(0.0-32.7)
Once/month	16.0	(10.8-21.2)	5.9	(3.6-8.2)	7.2	(3.5-10.9)	10.2	(3.2-17.1)	12.7	(0.0-31.3)
2-3 times/month	19.6	(15.3-23.9)	14.2	(10.7-17.7)	16.1	(11.1-21.0)	9.5	(3.5-15.4)	15.1	(4.6-25.6)
Once/week	24.4	(18.5-30.3)	17.6	(14.0-21.3)	20.6	(14.8-26.5)	21.8	(11.6-31.9)	33.4	(18.9-48.0)
2 times/week	34.4	(30.2-38.7)	24.5	(20.9-28.1)	25.9	(19.6-32.2)	25.8	(16.1-35.5)	38.2	(21.6-54.7)
3-4 times/week	43.7	(37.9-49.6)	36.0	(32.1-40.0)	39.4	(31.2-47.5)	36.2	(23.3-49.1)	44.0	(25.8-62.2)
Daily/nearly daily	46.3	(41.9-50.8)	43.7	(39.5-48.0)	44.1	(37.6-50.6)	46.3	(31.7-60.9)	52.4	(35.8-68.9)
Average quantity of drinks per drinking day										
1	5.6	(3.5-7.6)	2.8	(1.8-3.7)	3.1	(1.3-4.9)	3.5	(1.1-6.0)	1.4	(0.0-3.6)
2	16.4	(13.2-19.6)	12.7	(10.7-14.8)	8.5	(6.1-10.8)	8.0	(3.2-12.8)	5.0	(0.1-9.8)
3	35.1	(29.9-40.2)	22.2	(18.8-25.6)	23.8	(17.9-29.7)	17.3	(9.0-25.6)	43.6	(24.8-62.4)
4	38.3	(31.7-44.9)	38.1	(33.3-42.9)	38.2	(28.8-47.6)	15.4	(5.0-25.7)	41.4	(24.1-58.7)
5	52.0	(44.7-59.3)	50.4	(41.7-59.0)	31.4	(21.2-41.6)	34.1	(18.2-50.0)	29.4	(0.5-58.3)
6	56.4	(50.3-62.4)	45.4	(39.1-51.6)	54.6	(46.2-62.9)	50.3	(36.0-64.6)	47.3	(28.2-66.4)
7 or more	66.5	(60.3-72.6)	66.0	(60.8-71.1)	60.5	(52.4-68.6)	49.9	(35.0-64.9)	62.5	(45.3-79.8)
Frequency of heavy drinking[b]										
Never	4.7	(3.5-6.0)	4.4	(3.5-5.3)	3.8	(2.5-5.0)	4.2	(2.0-6.4)	0.9	(0.0-2.0)
1-6 times/year	25.0	(20.0-29.9)	15.0	(12.3-17.7)	13.4	(8.8-17.9)	12.2	(5.7-18.7)	28.5	(12.7-44.4)
7-12 times/year	40.9	(35.2-46.7)	30.0	(25.4-34.5)	29.5	22.8-36.3)	24.4	(13.3-35.4)	33.6	(15.0-52.2)
2-4 times/month	51.0	(46.0-57.7)	43.6	(38.1-49.1)	42.9	(36.8-48.9)	37.3	(24.7-49.8)	47.7	(33.3-62.0)
2-4 times/week	70.3	(64.9-75.7)	62.5	(56.9-68.2)	65.5	(58.0-72.9)	51.6	(34.7-68.5)	87.3	(76.6-98.0)
Daily/nearly daily	74.7	(67.4-82.0)	79.2	(72.5-85.9)	73.9	(61.7-86)	76.6	(56.6-96.6)	82.3	(65.9-98.6)
High-risk drinking[c]										
No	2.6	(1.6-3.5)	3.0	(2.1-38.1)	2.1	(1.2-3.0)	2.9	(1.0-4.7)	0.3	(0.0-0.7)
Yes	44.8	(42.0-47.6)	36.0	(33.9-38.1)	35.1	(32.0-38.3)	28.5	(23.3-33.7)	41.4	(34.2-48.7)

Table 5.2 continued next page.

Table 5.2 (continued).

	Prevalence [%(95% CI)] of Alcohol Use Disorder									
	Weight status[a]									
	Healthy weight		Overweight		Class 1 Obesity		Class 2 Obesity		Class 3 Obesity	
Females	17.6	(16.2-19.0)	14.4	(13.0-15.8)	12.0	(10.3-13.7)	11.9	(9.7-14.1)	13.5	(10.7-16.2)
Frequency of any alcohol use										
1-2 times/year	0.3	(0.0-0.6)	0.6	(0.0-1.5)	0.3	(0.0-0.8)	1.2	(0.0-2.6)	1.7	(0.2-3.2)
3-6 times/year	2.8	(1.1-4.6)	0.7	(0.0-1.3)	3.7	(1.1-6.3)	3.0	(0.4-5.5)	1.6	(0.0-3.5)
7-11 times/year	10.9	(6.6-15.2)	10.7	(5.1-16.2)	6.1	(2.3-9.9)	10.6	(2.7-18.6)	7.5	(0.5-14.6)
Once/month	5.5	(3.1-7.8)	7.4	(4.1-10.7)	8.0	(4.5-11.6)	4.5	(1.3-7.7)	5.9	(0.3-11.4)
2-3 times/month	14.8	(11.7-17.9)	15.9	(11.5-20.3)	9.6	(5.7-13.5)	18.7	(10.1-27.2)	18.5	(8.8-28.2)
Once/week	19.7	(15.9-23.6)	19.5	(14.8-24.2)	15.7	(10.2-21.3)	16.2	(8.3-24.2)	20.8	(12.0-29.7)
2 times/week	29.0	(24.6-33.4)	22.0	(17.2-26.8)	21.3	(15.2-27.4)	21.5	(12.0-31.0)	29.7	(14.3-45.1)
3-4 times/week	34.5	(30.1-38.8)	30.3	(24.4-36.1)	34.5	(25.7-43.3)	42.4	(28.9-55.9)	38.5	(20.9-56.1)
Daily/nearly daily	35.8	(30.3-41.2)	34.9	(27.6-42.1)	39.9	(29.0-50.8)	40.6	(27.0-54.3)	63.8	(48.5-79.1)
Average quantity of drinks per drinking day										
1	3.6	(2.6-4.6)	1.9	(1.1-2.7)	1.7	(0.8-2.7)	2.3	(0.5-4.0)	1.6	(0.1-3.1)
2	15.7	(13.5-17.9)	10.7	(8.7-12.7)	8.3	(6.0-10.7)	6.7	(3.5-10.0)	9.7	(4.0-15.4)
3	31.6	(27.1-36.0)	26.9	(21.8-32.0)	23.6	(18.2-29.0)	19.3	(11.7-27.0)	19.3	(10.1-28.5)
4	41.4	(34.5-48.2)	40.0	(32.0-48.1)	30.2	(20.5-40.0)	41.3	(26.0-56.7)	34.5	(20.0-49.0)
5	56.1	(45.4-66.7)	48.2	(37.5-59.0)	47.0	(33.7-60.3)	46.8	(28.7-65.0)	31.4	(13.3-49.6)
6	66.9	(57.6-76.3)	56.2	(46.5-66.0)	42.6	(30.6-54.5)	53.7	(32.9-74.5)	43.6	(14.3-72.8)
7 or more	72.4	(63.1-81.6)	75.6	(64.7-86.5)	70.4	(54.5-86.3)	60.7	(36.1-85.3)	75.6	(56.7-94.6)
Frequency of heavy drinking[b]										
Never	3.2	(2.5-4.0)	2.2	(1.6-2.9)	2.5	(1.6-3.4)	1.0	(0.2-1.8)	1.9	(0.6-3.2)
1-6 times/year	20.7	(17.2-24.2)	14.1	(10.2-18.0)	10.9	(7.4-14.4)	19.6	(13.0-26.2)	11.6	(4.2-18.9)
7-12 times/year	34.5	28.6-40.4)	35.9	(29.5-42.4)	25.7	(18.0-33.4)	20.2	(10.5-29.9)	27.3	(14.7-39.9)
2-4 times/month	49.2	(43.4-55.0)	46.3	(39.0-53.8)	43.3	(32.5-53.8)	51.3	(37.7-65.0)	46.6	(31.0-61.9)
2-4 times/week	63.0	(55.4-70.6)	57.6	(49.0-66.2)	55.1	(44.6-65.7)	59.2	(44.7-73.8)	60.7	(41.6-79.7)
Daily/nearly daily	71.9	(61.4-82.5)	80.2	(69.4-91.0)	69.5	(52.8-86.3)	80.0	(56.7-100.0)	84.7	(65.9-100.0)
High-risk drinking[c]										
No	2.3	(1.6-3.0)	1.2	(0.7-1.6)	1.8	(1.0-2.6)	0.6	(0.0-1.2)	1.5	(0.5-2.4)
Yes	32.9	(30.5-35.3)	29.0	(26.4-31.7)	24.6	(21.3-27.8)	27.4	(22.7-32.2)	27.7	(22.1-33.3)

[a]Healthy weight (18.5-<25 kg/m^2), overweight (BMI 25-<30 kg/m^2), and class 1 (BMI 30-<35 kg/m^2), class 2 (BMI 35-<40 kg/m^2), and class 3 (BMI ≥40.0 kg/m^2) obesity. [b]Consumed at least 5 drinks in a single day among males <65 years old and at least 4 drinks in a single day among males ≥65 years old and females of any age. [c]Consumed at least 15 drinks per week, on average, among males, and at least 8 drinks per week, on average, among females or heavy drinking at least once in the past year.

Table 5.3. Associations between levels and patterns of alcohol use and alcohol use disorder in the past 12 months, among US male current drinkers ≥18 years, National Epidemiological Survey on Alcohol and Related Conditions-III

	Odds [AOR[a](95% CI)] of Alcohol Use Disorder										*P* for Interaction[b]
Model 1											
Frequency of any alcohol use (ref.=1-2 times/year)											0.36
3-6 times/year					3.55	(1.69-7.45)					
7-11 times/year					3.65	(1.80-7.41)					
Once/month					5.41	(2.63-11.09)					
2-3 times/month					8.04	(4.20-15.39)					
Once/week					11.74	(6.41-21.51)					
2 times/week					17.41	(9.38-32.34)					
3-4 times/week					34.06	(17.85-65.00)					
Daily/nearly daily					68.46	(35.69-131.34)					
	Weight status[c]										
	Healthy weight		Overweight		Class 1 Obesity		Class 2 Obesity		Class 3 Obesity		
Average quantity of drinks per drinking day (ref.=1)											<.001
2	1.92	(1.23-3.02)	3.10	(2.06-4.67)	1.65	(0.83-3.25)	1.03	(0.38-2.82)	2.70	(0.53-13.75)	
3	4.13	(2.63-6.49)	5.44	(3.35-8.82)	4.36	(2.22-8.57)	2.29	(0.93-5.65)	35.18	(7.03-175.98)	
4	4.26	(2.67-6.77)	10.36	(6.56-16.38)	8.55	(3.93-18.59)	1.47	(0.44-4.93)	25.92	(4.99-134.48)	
5	7.84	(4.68-13.14)	16.86	(9.28-30.64)	6.35	(2.89-13.94)	4.55	(1.55-13.33)	16.31	(2.03-131.25)	
6	7.58	(4.58-12.54)	12.79	(7.98-20.50)	17.23	(8.58-34.61)	10.17	(3.75-27.56)	29.74	(7.13-124.12)	
7 or more	13.42	(7.99-22.53)	25.85	(16.06-41.60)	19.86	(10.13-38.96)	9.85	(3.65-26.54)	110.16	(15.72-771.83)	
Model 2											
Frequency of heavy drinking[d] (ref.=never)											<.001
1-6 times/year	5.03	(3.45-7.35)	3.07	(2.28-4.14)	3.09	(1.86-5.12)	2.58	(1.22-5.43)	39.29	(8.32-185.57)	
7-12 times/year	15.75	(10.80-22.97)	13.02	(9.41-18.02)	15.57	(9.99-24.28)	11.79	(5.21-26.68)	82.75	(19.86-344.74)	
2-4 times/month	34.92	(23.38-52.14)	25.89	(18.42-36.40)	42.40	(26.14-68.79)	21.56	(8.88-52.34)	638.12	(132.01-1000.00)	
2-4 times/week	10.21	(6.77-15.40)	7.03	(5.25-9.42)	8.74	(5.60-13.65)	5.83	(2.67-12.77)	54.68	(12.66-236.19)	
Daily/nearly daily	55.05	(35.93-84.35)	70.61	(44.91-111.03)	64.41	(29.61-140.14)	67.64	(17.58-260.17)	485.17	(79.59-1000.00)	
Model 3											
High-risk drinking[e] (ref.=no)	22.01	(14.84-32.64)	14.22	(10.28-19.66)	20.15	(13.03-31.15)	10.89	(5.43-21.84)	219.67	(52.50-919.13)	0.002

AOR: Adjusted odds ratio; CI: Confidence interval.

[a]Adjusted for age, race/ethnicity, education, employment status, income, marital status, physical activity, smoking status, past-year major depressive disorder, and family history of alcohol problems. [b]Interaction between alcohol use variable and weight status. If interaction p >0.05 AOR are reported for all weight status

groups combined. [c]Healthy weight (18.5-<25 kg/m^2), overweight (BMI 25-<30 kg/m^2), and class 1 (BMI 30-<35 kg/m^2), class 2 (BMI 35-<40 kg/m^2), and class 3 (BMI ≥40.0 kg/m^2) obesity. [d]Consumed at least 5 drinks in a single day among males <65 years old or at least 4 drinks in a single day among males ≥65 years old. [e]Consumed at least 15 drinks per week, on average, among males <65 years old and at least 8 drinks per week, on average, among males ≥65 years old or heavy drinking at least once in the past year.

Table 5.4. Associations between levels and patterns of alcohol use and alcohol use disorder in the past 12 months, among non-pregnant US female current drinkers ≥18 years, National Epidemiological Survey on Alcohol and Related Conditions-III

	Odds [AOR[a](95% CI)] of Alcohol Use Disorder					*P* for Interaction[c]
	Weight status[b]					
	Healthy weight	Overweight	Class 1 Obesity	Class 2 Obesity	Class 3 Obesity	
Model 1						
Frequency of any alcohol use (ref.=1-2 times/year)						<.001
3-6 times/year	7.34 (1.90-28.43)	0.79 (0.11-5.54)	10.23 (1.41-73.99)	2.58 (0.51-12.90)	0.46 (0.09-2.42)	
7-11 times/year	22.78 (6.06-85.61)	7.02 (1.33-37.04)	11.30 (1.38-92.59)	8.25 (1.80-37.68)	2.32 (0.68-7.89)	
Once/month	10.84 (2.99-39.36)	7.04 (1.23-40.18)	17.05 (2.72-106.77)	3.01 (0.71-12.75)	1.16 (0.31-4.30)	
2-3 times/month	28.86 (8.37-99.52)	13.27 (2.50-70.32)	15.52 (2.36-102.33)	11.48 (3.17-41.53)	4.09 (1.36-12.36)	
Once/week	36.49 (10.59-125.72)	20.44 (3.87-107.95)	34.74 (5.19-232.73)	13.88 (3.59-53.75)	4.98 (1.98-12.52)	
2 times/week	73.35 (21.71-247.88)	25.32 (4.70-136.51)	39.49 (6.06-257.37)	8.17 (1.86-35.91)	8.93 (2.73-29.20)	
3-4 times/week	133.40 (41.01-433.95)	48.53 (9.12-258.18)	90.53 (13.42-610.72)	57.08 (15.48-210.39)	13.58 (3.55-51.95)	
Daily/nearly daily	207.34 (63.45-677.57)	96.43 (16.71-556.48)	170.69 (25.40-999.99)	63.12 (14.45-275.75)	35.92 (12.37-104.36)	
	Odds [AOR[a](95% CI)] of Alcohol Use Disorder					
Average quantity of drinks per drinking day (ref.=1)						0.22
2			2.66 (2.12-3.33)			
3			6.43 (4.89-8.46)			
4			8.37 (6.27-11.16)			
5			13.87 (9.59-20.05)			
6			20.12 (13.72-29.50)			
7 or more			33.74 (21.90-51.97)			
Model 2						
Frequency of heavy drinking[d] (ref.=never)						0.12
1-6 times/year			5.84 (4.69-7.26)			
7-12 times/year			24.29 (19.06-30.97)			
2-4 times/month			40.02 (30.73-52.11)			
2-4 times/week			13.38 (10.58-16.92)			
Daily/nearly daily			93.43 (60.95-143.23)			
Model 3						
High-risk drinking[e](ref.=no)			18.42 (14.76-22.98)			0.08

AOR: Adjusted odds ratio; CI: Confidence interval.

[a]Adjusted for age, race/ethnicity, education, employment status, income, marital status, physical activity, smoking status, past-year major depressive disorder, and family history of alcohol problems. [b]Healthy weight (18.5-<25 kg/m^2), overweight (BMI 25-<30 kg/m^2), and class 1 (BMI 30-<35 kg/m^2), class 2 (BMI 35-<40 kg/m^2), and class 3 (BMI ≥40.0 kg/m^2) obesity. [c]Interaction between alcohol use variable and weight status. If interaction p >0.05 AOR are reported for all weight status groups combined. [d]Consumed at least 4 drinks in a single day. [e]Consumed at least 8 drinks per week, on average, or heavy drinking at least once in the past year.

6.0 MANUSCRIPT 3 – ALCOHOL AND ALCOHOL-RELATED PROBLEMS IN THE LONGITUDINAL ASSESSMENT OF BARIATRIC SURGERY COHORT: 7-YEAR FOLLOW-UP

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6.1 ABSTRACT

Background: Despite evidence that Roux-en-Y gastric bypass (RYGB) alters alcohol pharmacokinetics and is associated with increased risk for Alcohol Use Disorder (AUD), the level of alcohol use that should prompt further screening for AUD following RYGB is unclear.

Objective: To determine the sensitivity and specificity of potential thresholds of alcohol use for identifying alcohol-related problems in women post-RYGB.

Setting: Six US clinical settings.

Methods: The Longitudinal Assessment of Bariatric Surgery-2 is a prospective cohort study. Prior to surgery and annually for ≤7 years following surgery, participants completed the 10-item Alcohol Use Disorder Identification Test (AUDIT), which assesses past-year frequency and quantity of alcohol, frequency of consuming ≥6 drinks, and alcohol-related problems (i.e.,

symptoms of alcohol dependence and/or alcohol-related harm). The AUDIT-Consumption (AUDIT-C) score was determined from the first three AUDIT items.

Results: 1,176 women completed the AUDIT pre-RYGB and at ≥1 post-RYGB assessments. Prior to and following surgery, drinking ≥2 times/month had the highest combined sensitivity (69.4% and 85.3%, respectively) and specificity (71.4% and 61.4%, respectively), and drinking ≥3 drinks/drinking day, had the highest combined sensitivity (65.3% and 64.2%, respectively) and specificity (79.0% and 87.2%, respectively) for identifying alcohol-related problems compared with higher frequency and quantity thresholds, respectively. An AUDIT-C score ≥3 had the highest combined sensitivity and specificity prior to (66.7% and 84.4%, respectively) and following (76.4% and 81.6%, respectively) surgery.

Conclusions: Alcohol use thresholds for identifying alcohol-related problems did not differ prior to and following RYGB. All thresholds had relatively low sensitivity prior to and following RYGB.

6.2 INTRODUCTION

Bariatric surgery results in long-term weight loss, remission of obesity-related comorbidities, and reduced all-cause mortality.[195,196] Roux-en-Y gastric bypass (RYGB) is one of the two most common bariatric procedures performed in the United States,[37] likely due to its impressive long-term outcomes.[114,197,198] However, RYGB is also associated with negative health outcomes such as vitamin deficiencies,[113] accidents and self-harm,[114,199] and Alcohol Use Disorder (AUD).[115] The association between RYGB and AUD may be explained by a change in alcohol pharmacokinetics. Post-RYGB, individuals experience higher peak alcohol concentrations and

slower alcohol elimination when compared to pre-surgery[132] and to non-surgical controls[113,128,134]. Emerging evidence suggests that compared to pre-surgery, adults who have undergone sleeve gastrectomy (SG), now the most popular bariatric procedure in the United States,[37] also experience higher peak alcohol concentrations,[133,134] which are reached more quickly[134] and take longer to decrease[133], as well as increased feelings of drunkenness[134].

The US Preventive Services Task Force recommends that primary care clinicians screen all adults for alcohol misuse using one of three screening tools: The Alcohol Use Disorders Identification Test (AUDIT), the AUDIT-Consumption (AUDIT-C), or a single-question screening assessing frequency of heavy drinking (consuming ≥5 drinks in a day for men ≤65 years or ≥4 drinks in a day for women and all adults older than 65 years).[83,84] The sensitivity and specificity of these screening tools for identifying alcohol-related problems have been assessed in many patient populations,[83,84,200] but not among individuals who have undergone bariatric surgery. Current recommendations suggest that clinicians screen for AUD both before and after bariatric surgery but offer no further guidance on what screening tools should be used.[201] Given evidence that RYGB and SG may alter the effect of alcohol, surgery-specific alcohol use thresholds for identifying those at high-risk for AUD may be warranted.

Because of the negative consequences of alcohol use,[110,115,202] understanding changes in alcohol use over time following bariatric surgery is also important. A report from the Longitudinal Assessment of Bariatric Surgery (LABS)-2, a large multi-center prospective cohort study, indicated that prevalence of any alcohol use and regular alcohol use, defined as at least twice a week, and AUD symptoms increase pre-surgery to 7 years post-RYGB.[203] Additionally, regular alcohol use in the year prior to RYGB increases risk of developing AUD post-RYGB. However, other thresholds of alcohol use were not examined. Furthermore, change in quantity of

alcohol (i.e., the average quantity of drinks per drinking day) was only examined in an earlier report with two-year follow-up, and was not evaluated with respect to having AUD symptoms.[115] That report found that quantity of alcohol use decreased in the first year after RYGB but then returned to pre-RYGB levels in the second year after RYGB[115]; it is unknown whether quantity of alcohol use continued at the same pre-RYGB levels or if it continued to increase in the post-surgical period. Finally, these reports did not include patients who underwent SG. To our knowledge, a study examining alcohol use over time among adults who have undergone SG has not been conducted.

This study builds upon prior LABS-2 reports by examining change in alcohol use over 7 years following RYGB and SG. Additionally, among the larger RYGB sample, we examined the sensitivity, specificity, and area under the receiver operating characteristic curve (AUROC), to determine whether alcohol use thresholds (i.e., frequency of alcohol use, average quantity of drinks per drinking day, and AUDIT-C score) were adequate screening tools for identifying alcohol-related problems, defined as symptoms of alcohol dependence or alcohol-related harm, both prior to and following surgery. We hypothesized that alcohol use thresholds for identifying alcohol-related problems would be lower following RYGB versus prior to RYGB.

6.3 METHODS

Data Source

LABS-2 is a prospective cohort study of 2,458 adults who underwent their first bariatric surgery at one of six clinical centers throughout the United States.[204] The study is registered at ClinicalTrials.gov (NCT00465829). Institutional Review boards at each center approved

protocols; all participants provided written informed consent. Participants were informed during the consent process that responses were confidential unless there was concern of serious harm. A safety protocol was triggered when participants reported consuming, on average, at least 5 drinks per drinking day.

LABS-2 participants were recruited between February 2006 and February 2009 and followed annually for 7 years or until January 31, 2015, whichever came first.[204] Participants included in this report completed alcohol questions pre-surgery and at least one follow-up assessment after RYGB or SG (1,523 of 1,797; 85%). The flow of participants from recruitment through the analysis sample is presented in Figure 6.1.

Definitions

Alcohol Use

The AUDIT is a 10-item test designed to assess alcohol use and consequences of alcohol use in the prior 12 months.[205] LABS-2 participants completed the AUDIT as part of a self-assessment packet. Frequency of alcohol use (i.e., having a drink containing alcohol) categories are never, monthly or less, 2-4 times a month, 2-3 times per week, or 4 or more times a week. Average quantity of drinks per drinking day categories are 1 or 2 drinks, 3 or 4 drinks, 5 or 6 drinks, 7 to 9 drinks, or 10 or more drinks containing alcohol on a typical day when drinking. Respondents who reported never having a drink containing alcohol in the past 12 months were categorized as having an average quantity of zero drinks per drinking day.

Established At-Risk Alcohol Use Threshold

The AUDIT-C is a validated, three-question, abbreviated version of the AUDIT used to identify potential hazardous drinking or AUD.[206] The three questions assess the frequency of alcohol use, average quantity of drinks per drinking day, and frequency of occasions consuming 6 or more drinks of alcohol. A score ranging from 0-12, is computed from responses. An elevated AUDIT-C score for the general population is defined as at least 3 among women and at least 4 among men.[206]

Alcohol-Related Problems

The remaining seven AUDIT questions assess the frequency or occurrence of alcohol-related problems. Participants were categorized as having experienced symptoms of alcohol dependence if they reported, at least once in the past 12 months, not being able to stop drinking once started, failing to meet normal expectations because of drinking, or needing a drink in the morning to get going. Participants were categorized as having experienced symptoms of alcohol-related harm if they reported, at least once in the past 12 months, feeling guilt or remorse, being unable to remember, injuring someone, or eliciting concern due to drinking. Endorsement of symptoms of alcohol dependence and/or alcohol-related harm was defined as alcohol-related problems. [115,203]

Other Measures

Participants underwent measurement of weight to the nearest pound and height to the nearest inch, which was used to calculate body mass index (BMI; kg/m^2).[204] Past-year counseling and lifetime history of hospitalizations for psychiatric or emotional problems were assessed with the

LABS-2 Psychiatric and Emotional Test Survey.[203] Smoking was assessed with the LABS-2 Behavioral Form.[203]

Statistical Analysis

Analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA). *P* values <0.05 were statistically significant. Potential selection bias was examined by comparing pre-surgery characteristics of LABS-2 participants in the analysis sample to those excluded due to missing data using the Pearson chi-square test, the Cochran-Armitage test, or the Wilcoxon rank sum test.

Pre-surgery characteristics of the sample by surgical procedure were compared using the Pearson chi-square test for categorical variables, the Cochran-Armitage test for ordinal variables, and the Wilcoxon rank sum test for continuous variables. The remaining analyses were stratified by surgical procedure. All longitudinal analyses used a person-level random intercept and controlled for clinical site, age, and pre-surgery smoking status, which were associated with missing follow-up data,[207] as fixed effects. Assessment-level data were set to missing when women reported being pregnant.

Mixed effects ordinal logistic regression models were used to estimate frequency of alcohol use and average quantity of drinks per drinking day over time. Pairwise comparisons were made between pre-surgery and Year-7. Change following surgery was examined by testing for linear and quadradic trends from Year-1 to Year-7. To control for Type 1 error, *P* values were adjusted for the two comparisons.[208] Due to low frequencies, these models would not converge unless the following responses were collapsed: 2-3 times per week and 4 or more times

a week for frequency of alcohol use; 3 or 4 drinks, 5 or 6 drinks, 7 to 9 drinks, and 10 or more drinks for average quantity of drinks per drinking day.

Because previous research indicates that the association between alcohol use and alcohol-related problems differs by gender,[64] and may differ by surgical procedure,[115,203] the remaining analyses were conducted among women in the RYGB sample (n=1,176), who accounted for the majority of study participants. Due to the relatively small sample size of men in this study, which is consistent with the makeup of bariatric surgery patients,[50] as well as the small sample of participants who underwent SG, analyses were not performed separately in these subgroups.

Assessment-level data were set to missing when no alcohol consumption in the past 12 months was reported. Descriptive statistics were used to report the prevalence of alcohol-related problems at each time point by frequency of alcohol use, average quantity of drinks per drinking day, and AUDIT-C score. Poisson mixed models with robust error variance[209] were used to determine the associations between alcohol use measures (i.e., frequency of alcohol use, average quantity of drinks per drinking day, and AUDIT-C score) and alcohol-related problems, with time in relation to surgery entered as a discrete fixed effect. Interactions between alcohol use and time were assessed.

Among women who had at least some alcohol use, the sensitivity and specificity of potential alcohol use thresholds for identifying alcohol-related problems were calculated at each time point using descriptive statistics. Given the AUDIT response sets, the following thresholds could be considered: ≥2 times/month, ≥2 times/week, and ≥4 times/week (frequency); ≥3 drinks, ≥5 drinks, ≥7 drinks, and ≥10 drinks/drinking day (quantity); ≥1-12 (AUDIT-C score). Weighted averages of sensitivity and specificity at post-surgery time points were computed for overall post-surgery values. A series of Poisson mixed models with robust error variance[209] were used to

determine the AUROC for each potential alcohol use threshold for identifying alcohol-related problems. Separate models were constructed for pre- and post-RYGB, with time since surgery entered as a discrete fixed effect in the post-RYGB models. The AUROC is a summary measure of the overall performance of the threshold where a value of 1.0 represents 100% sensitivity at all levels of specificity and 100% specificity at all levels of sensitivity; an AUROC of 0.5 indicates that the threshold did no better than that expected by chance alone. For this report, the thresholds with the highest combined values of sensitivity and specificity are identified.[210] When multiple thresholds have similar values (differ by <1.0%), the threshold with the highest sensitivity is identified, since it is better at correctly identifying people with alcohol-related problems. These analyses were repeated replacing the outcome, alcohol-related problems, with its subcomponents, symptoms of alcohol dependence and alcohol-related harm, respectively.

6.4 RESULTS

Among LABS-2 participants who underwent RYGB or SG, completed the AUDIT at baseline, and were not dead or pregnant at the indicated follow-up, alcohol data were obtained from 78% (1,272/1,625), 70% (1,124/1,616), 67% (1,077/1,615), 66% (1,057/1,611), 67% (1,074/1,602), and 69% (788/1,134) at Years 1, 2, 3, 4, 5, and 7, respectively. Those included in the full analysis sample (n=1,523) versus excluded due to missing data (n=274) differed by age, race, and pre-surgery smoking status; alcohol use was similar between the two groups (Table 6.1).

Pre-surgery characteristics of the full analysis sample, by surgical procedure (n=1,472 RYGB and n=51 SG), and the female RYGB subsample (n=1,176), are shown in Table 6.2. Compared to individuals who underwent RYGB, those who underwent SG were less likely to

have been married or living as married, had higher BMI, and were more likely to have had past-year psychiatric counseling; alcohol use between the two groups was similar.

Frequency of alcohol use and average quantity of drinks per drinking day by time point among those who underwent RYGB and SG are shown in Figure 6.2 and Figure 6.3, respectively. For those who underwent RYGB, the frequency of alcohol use was significantly higher in Year-7 vs. pre-surgery ($P<.001$) and significantly increased from Years 1-7 post-surgery (P for quadratic trend <.001). Likewise, the average quantity of drinks per drinking day was significantly higher in Year-7 vs pre-surgery ($P=0.04$) and increased from Years 1-7 (P for quadratic trend <.001) (Figure 6.2). For those who underwent SG, there was not a statistically significant difference in the frequency of alcohol use ($P=0.29$) or average quantity of drinks per drinking day ($P=0.74$) by time point (Figure 6.3). However, due to the small sample size this analysis may have been underpowered to detect clinically meaningful differences. Observed and modeled data with 95% CI by surgical procedure and time point are reported in Table 6.3 and Table 6.4.

Table 6.5 shows the prevalence of alcohol-related problems among female current drinkers by frequency of alcohol use, average quantity of drinks per drinking day, and AUDIT-C score, and by time point in relation to RYGB. Nearly all women who underwent RYGB and reported drinking at least 4 times per week, 7 or more drinks per drinking day, or had an AUDIT-C score of at least 5 had alcohol-related problems (Table 6.5). The risk of alcohol-related problems was significantly higher with higher frequencies of alcohol use, average quantities of drinks per drinking day, and higher AUDIT-C scores; these relationships did not differ by time (Table 6.6). In a sensitivity analysis, we stratified by pre-/post-surgery status; estimates were similar (data not shown).

The sensitivity, specificity, and AUROC of potential alcohol use thresholds for identifying alcohol-related problems in women pre- and post-RYGB are reported in Table 6.7 for the three thresholds with the highest combined sensitivity and specificity. The frequency of alcohol use with the highest combined sensitivity and specificity for identifying alcohol-related problems and its subcomponents was ≥2 times per month (vs. ≥2 times per week or ≥4 times per week) among women both pre- and post-RYGB (Table 6.7). The sensitivity and specificity for identifying alcohol-related problems at this level was 69.4% (95%CI: 58.8-80.1) and 71.4% (95%CI: 67.7-75.0), respectively, pre-RYGB and 85.3% (95%CI: 82.6-88.0) and 61.4% (95%CI: 59.6-63.1), respectively, post-RYGB.

The average quantity of drinks per drinking day with the highest combined sensitivity and specificity for identifying alcohol-related problems and its subcomponents was ≥3 drinks per drinking day (vs. ≥5 drinks, ≥7 drinks, or ≥10 drinks) among women both pre- and post-RYGB (Table 6.7). The sensitivity and specificity for identifying alcohol-related problems at this level was 65.3% (95%CI: 54.3-76.3) and 79.0% (95%CI: 75.7-82.3), respectively, pre-surgery and 64.2% (95%CI: 60.5-67.9) and 87.2% (95%CI: 86.0-88.4), respectively, post-surgery.

The AUDIT-C score with the highest combined sensitivity and specificity for identifying alcohol-related problems and its subcomponents was a score of ≥3, among women both pre- and post-RYGB (Table 6.7). Both before and after RYGB, the combined sensitivity and specificity of an elevated AUDIT-C score was higher than the combined sensitivity and specificity for frequency of alcohol use and average quantity of drinks per drinking day, respectively.

The AUROC, which reflects the sensitivity and specificity, for identifying alcohol-related problems and its subcomponents, was similar across all thresholds of frequency of alcohol use,

quantity of drinks per drinking day, and AUDIT-C score (Table 6.7). Thresholds for identifying symptoms of alcohol dependence and alcohol-related harm are in Table 6.8.

6.5 DISCUSSION

Results from this large, prospective cohort study, which assessed past-year alcohol use and related problems annually for up to seven years following bariatric surgery, indicate that frequency of alcohol use, average quantity of drinks per drinking day, and AUDIT-C score have low sensitivity and specificity for identifying alcohol-related problems both pre- and post-RYGB. Not surprisingly, an elevated AUDIT-C score, which takes both frequency and quantity of alcohol into account, has better combined sensitivity (i.e., ability to correctly identify those with alcohol-related problems) and specificity (i.e., ability to correctly identify those without alcohol-related problems) for identifying alcohol-related problems among women pre- or post-RYGB than either frequency of alcohol use or average quantity of drinks per drinking day alone. However, contrary to expectation, the established AUDIT-C threshold of ≥3 for women[206] performed better than alternative thresholds both prior to and following RYGB. Furthermore, the frequency and quantity thresholds with the highest combined sensitivity and specificity did not differ pre- versus post-RYGB.

The AUDIT-C did not perform as well in this sample of female RYGB patients as in other samples. Both the pre-surgery sensitivity (67%) and specificity (84%), and the post-surgery sensitivity (76%) and specificity (82%), in this study were lower than those reported for identifying AUD in a US primary care sample of 927 women (sensitivity, 87%; specificity, 85%),[211] and in the general US population of women (sensitivity, 87%; specificity, 69%).[210] It is

unclear why the AUDIT-C did not perform as well in our sample of RYGB patients. One reason may be that our measure of alcohol-related problems likely identified some cases that would not meet the criteria for AUD based on the Diagnostic and Statistical Manual of Mental Disorders (DSM). Another potential explanation is that one of the questions from the AUDIT-C assesses frequency of occasions consuming 6 or more drinks. Research has shown that, following RYGB, peak BAC is approximately two times higher than in a pre-surgery group of individuals suggesting that the effect of consuming 6 drinks on one occasion post-RYGB is similar to that of a non-RYGB patient consuming 12 drinks; an event that is likely rare. However, this explanation only applies to the post-surgery period. It is interesting to note that, although the optimal thresholds for identifying alcohol-related problems were the same following (versus prior to) RYGB, the sensitivity for the optimal frequency threshold (drinking ≥2 times per month) was higher (85% versus 69%, respectively), and the specificity lower (61% versus 71%, respectively) indicating that the same threshold is better at correctly identifying individuals with alcohol-related problems following RYGB than prior to. The specificity for the optimal threshold for average quantity of drinks per drinking day was higher following RYGB versus prior to (87% versus 79%, respectively) while the sensitivity of average quantity of drinks per drinking day and sensitivity and specificity of AUDIT-C score were similar pre- and post-surgery.

While the AUDIT-C performed best of the three alcohol use measures we examined, the relatively low sensitivity indicates that it will still fail to correctly identify many patients with alcohol-related problems both before and after surgery. Optimal screening thresholds should be chosen based on a variety of factors unique to the population and condition being screened for.[212] A threshold with equal weight given to sensitivity and specificity tries to balance the cost of high sensitivity (i.e., time required for documenting screening results and further testing of patients

with false-positive screening results) with the cost of high specificity (i.e., missing the opportunity to identify patients who may benefit from referral for treatment of AUD).[212] Only one alcohol use threshold, an AUDIT-C score ≥2, had a sensitivity above 80%, a commonly used sensitivity threshold either pre- or post-RYGB. However, at each timepoint, most women who drank alcohol had an AUDIT-C score ≥2, indicating that a screening test that assesses symptoms of alcohol-related problems may be more cost-effective than performing the AUDIT-C prior to a screening tool that assesses symptoms.

Consistent with prior research among the general population,[88] we found that the risk of alcohol-related problems was higher at higher frequencies of alcohol use, average quantities of drinks per drinking day, and AUDIT-C scores at all time points. However, these findings are concerning when taken together with our findings that frequency of alcohol use and average quantity of drinks per drinking day significantly increased over 7 years following RYGB. The finding that average quantity of drinks per drinking day continues to increase up to 7 years following RYGB has not been previously shown. To our knowledge, this is the first study to examine change in alcohol use among adults who have undergone SG. While we found no difference over time in either alcohol measure, this may be due to the relatively small sample size of this group. Our findings are consistent with those from a study of adolescents who had undergone bariatric surgery that showed that frequency of alcohol use and average quantity of drinks per drinking day may have increased 1-2 years following SG.[213] However, the sample size in that study was equally small (N=42) and no statistical comparisons of alcohol use by time point were performed.

The findings of this study are subject to the following limitations. First, we did not assess AUD using the Structured Clinical Interview for DSM-5, which is the gold-standard.[214] Second,

frequency of alcohol use and average quantity of drinks per drinking day were rare at higher frequencies and quantities, so categories had to be collapsed for modeling alcohol intake over time. Third, because SG, now the most popular bariatric procedure,[48] was rare at the time of LABS-2 recruitment, analysis was limited in this group. Moreover, the AUDIT's frequency of alcohol use and average quantity of drinks per drinking day categories contain large ranges, such that we were unable to evaluate all potential thresholds of alcohol intake (e.g., ≥1 drink/week). Future studies using continuous measures of frequency and quantity may be warranted.

This paper has many notable strengths. First, we present results from a large and geographically diverse sample of adults who underwent bariatric surgery and were followed for up to 7 years post-surgery with relatively high retention,[41] whereas most published studies of alcohol use in US bariatric surgery patients have small samples, short follow-up and poor retention.[115,116,135] Additionally, this study used the AUDIT and AUDIT-C, validated measurement tools for identifying alcohol-related problems,[205] to assess three different alcohol endpoints.

6.6 CONCLUSIONS

These findings suggest that frequency of alcohol use and average quantity of drinks per drinking day increased 7 years following RYGB but not SG. The AUDIT-C had a better combination of sensitivity and specificity for identifying alcohol-related problems pre- and post-surgery than only frequency of alcohol use or only average quantity of drinks per drinking day. Current recommendations suggest that clinicians screen for AUD both before and after bariatric surgery but offer no further guidance.[201] These findings indicate that clinicians should first ask patients

about alcohol consumption, including assessment of both frequency and quantity. However, clinicians should be aware that even the AUDIT-C will fail to correctly identify many patients with alcohol-related problems both before and after surgery, so additional screening for alcohol-related problems such as the full AUDIT or other screening tools that assess symptoms of alcohol-related problems, should be conducted in this population.

6.7 TABLES AND FIGURES

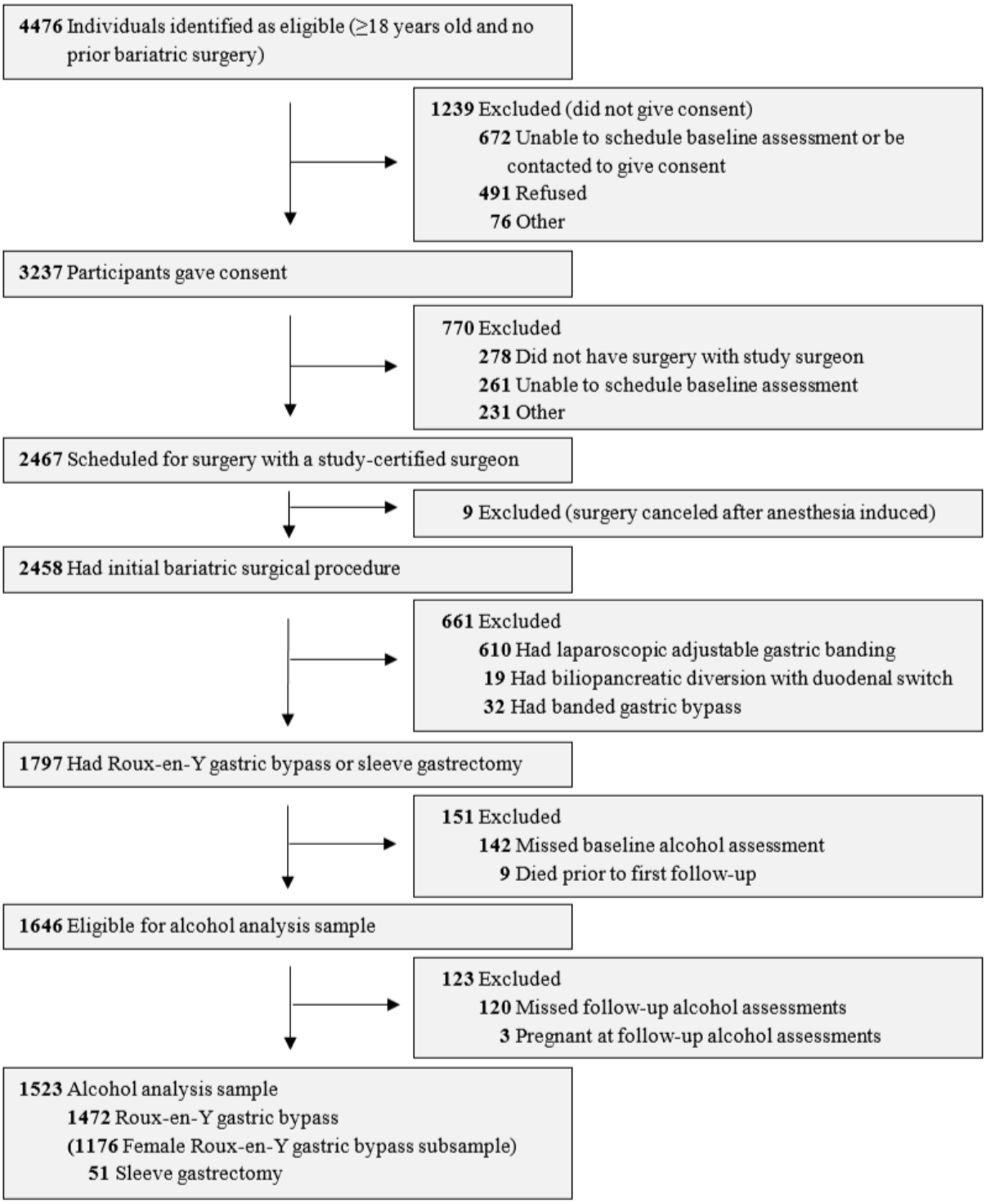


Figure 6.1. Flow of participants through recruitment, enrollment and alcohol measurements

Table 6.1. Baseline demographic and clinical characteristics of participants included in and excluded from the analysis sample due to missing data

	Analysis sample (n=1523)		Excluded (n=274)		*P*
	n	(%)[a]	n	(%)[a]	
Female	1211	(79.5)	217	(79.2)	0.90
Age (years), median (IQR)	46	(37-54)	42	(35-50)	<.001
Race					0.01
White	1295	(86.1)	215	(79.1)	
Black	159	(10.6)	45	(16.5)	
Other	51	(3.4)	12	(4.4)	
Hispanic ethnicity, n/total n (%)	71/1451	(4.7)	20/254	(7.3)	0.07
Relationship status	n=151		n=141		0.71
Never married	259	(17.1)	28	(19.9)	
Divorced, separated, or widowed	320	(21.1)	84	(59.6)	
Married or living as married	936	(61.8)	29	(20.6)	
Education	n=1517		n=141		0.56
≤ High school	360	(23.7)	31	(22.0)	
Some college	642	(42.3)	70	(49.7)	
≥ College degree	515	(34.0)	40	(28.4)	
Employed, n/total n (%)	1035/1509	(68.6)	101/140	(72.1)	0.38
Household income, U.S. $	n=1476		n=136		0.40
<25,000	304	(20.6)	23	(16.9)	
25,000-49,999	408	(27.6)	42	(30.9)	
50,000-74,999	337	(22.8)	42	(30.9)	
75,000-99,999	225	(15.2)	19	(14.0)	
≥100,000	202	(13.7)	10	(7.3)	
Body mass index, median (IQR)	45.8	(41.8-51.3)	47.5	(42.5-53.9)	0.11
Past-year psychiatric counseling, n/total n (%)	359/1509	(23.8)	35/137	(25.6)	0.64
Lifetime history of psychiatric hospitalization, n/total n (%)	165/1512	(10.9)	12/136	(8.8)	0.45
Smoking, n/total n (%)	202/1520	(13.9)	58/273	(21.3)	<.001
Frequency of alcohol use	n=1523		n=129		0.06
Never	656	(43.1)	61	(47.3)	
Monthly or less	560	(36.8)	47	(36.4)	
2-4 times/month	211	(13.9)	21	(16.3)	
2-3 times/week	68	(4.5)	0	(0.0)	
≥4 times/week	28	(1.8)	0	(0.0)	
Average quantity of drinks per drinking day	n=1512		n=129		0.90
0 drinks	656	(43.4)	61	(47.3)	
1-2 drinks	629	(41.6)	48	(37.2)	
3-4 drinks	163	(10.8)	14	(10.9)	
5-6 drinks	48	(3.2)	2	(1.6)	
≥7 drinks	16	(1.0)	4	(3.1)	
AUDIT-C score, median (IQR)	1	(0-2)	1	(0-2)	0.23
Elevated AUDIT-C score[b], n/total n(%)	169/1512	(11.2)	8/130	(6.2)	0.08
Alcohol-related problems[c], n/total n(%)	100/1518	(6.6)	6/132	(4.6)	0.42
Symptoms of alcohol dependence[d], n/total n(%)	52/1518	(3.4)	4/132	(3.0)	0.81
Alcohol-related harm[e], n/total n(%)	76/1521	(5.0)	6/132	(4.6)	0.82

AUDIT-C, Alcohol Use Disorder Identification Test-Consumption; IQR, interquartile range.
[a]Unless otherwise specified. [b]AUDIT-C score at least 3 among females and at least 4 among males. [c]Symptoms of alcohol dependence and/or alcohol-related harm. [d]Not being able to stop drinking once started, failing to meet normal expectations because of drinking, or needing a drink in the morning to get going at least once in the past 12 months. [e]Feeling guilt or remorse, being unable to remember, injuring someone, or eliciting concern due to drinking at least once in the past 12 months.

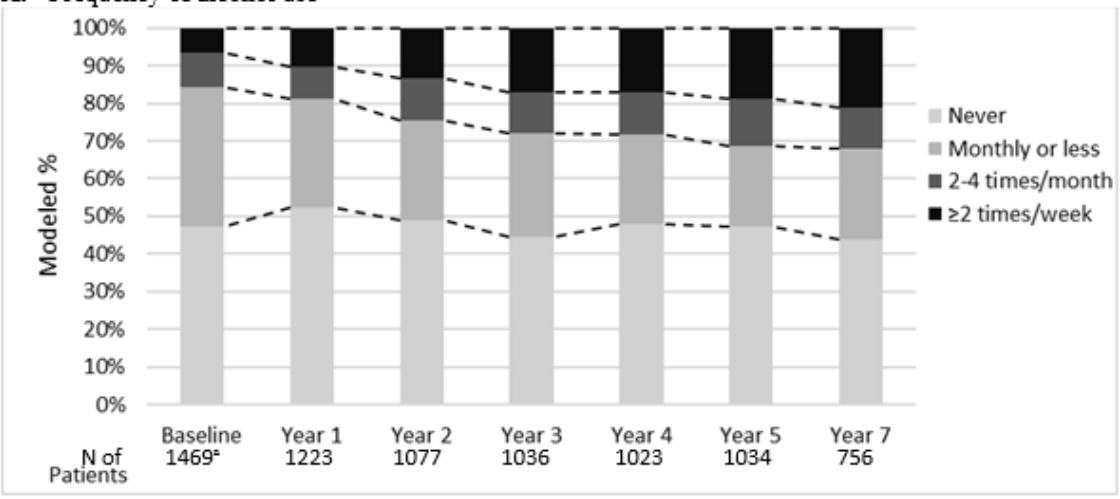
Table 6.2. Characteristic of adults before bariatric surgery, by surgical procedure, and for the female RYGB subsample

	RYGB (n=1472)	SG (n=51)		RYGB women (n=1176)
	n(%) [a]	n(%) [a]	*P*	n(%)[a]
Female	1176(79.9)	35(68.6)	0.051	
Age (years), median (IQR)	46(37-54)	50(35-56)	0.36	45(37-53)
Race	n=1455	n=50	0.69	n=1162
White	1254(86.2)	41(82.0)		988(85.0)
Black	152(10.5)	7(14.0)		131(11.3)
Other	49(3.4)	2(4.0)		43(3.7)
Hispanic ethnicity, n/total n (%)	67/1471(4.6)	4/51(7.8)	0.27	54/1176(4.6)
Relationship status	n=1464	n=51	0.02	n=1169
Never married	244(16.7)	15(29.4)		198(16.9)
Divorced, separated, or widowed	307(21.0)	13(25.5)		707(60.5)
Married or living as married	913(62.4)	23(45.1)		264(22.6)
Education	n=1466	n=51	0.36	n=1171
≤ High school	350(23.9)	10(19.6)		285(24.3)
Some college	621(42.4)	21(41.2)		498(42.5)
≥ College degree	495(33.8)	20(39.2)		388(33.1)
Employed	1002/1458(68.7)	33/51(64.7)	0.54	367/1166(31.5)
Household income, U.S. $	n=1426	n=50	0.92	n=1137
< 25,000	288(20.2)	16(32.0)		238(20.9)
25,000-49,999	398(27.9)	10(20.0)		327(28.8)
50,000-74,999	331(23.2)	6(12.0)		265(23.3)
75,000-99,999	217(15.2)	8(16.0)		175(15.4)
≥ 100,000	192(13.5)	10(20.0)		132(11.6)
Body mass index, median (IQR)	46.4(42.4-51.6)	58.2(46.8-64.8)	<.001	46.2(42.1-51.3)
Past-year psychiatric counseling, n/total n (%)	338/1459(23.2)	21/50(42.0)	0.002	287/1165(24.6)
Lifetime history of psychiatric hospitalization, n/total n (%)	156/1461(10.7)	9/51(17.7)	0.12	126/1166(10.8)
Smoking, n/total n (%)	194/1469(13.2)	8/51(15.7)	0.61	166/1174(14.1)
Frequency of alcohol use	n=1472	n=51	0.49	n=1176
Never	634(43.1)	22(43.1)		511(43.7)
Monthly or less	542(36.8)	18(35.3)		488(41.8)
2-4 times/month	206(14.0)	5(9.8)		123(10.5)
2-3 times/week	64(4.4)	4(7.8)		36(3.1)
≥ 4 times/week	26(1.8)	2(3.9)		11(0.9)
Average quantity of drinks per drinking day	n=1462	n=50	0.79	n=1169
0 drinks	634(43.4)	22(44.0)		511(43.7)
1-2 drinks	610(41.7)	19(38.0)		488(41.8)
3-4 drinks	156(10.7)	7(14.0)		123(10.5)
5-6 drinks	47(3.2)	1(2.0)		36(3.1)
≥ 7 drinks	15(1.0)	1(2.0)		11(0.9)
AUDIT-C score, median (IQR)	1(0-2)	1(0-2)	0.36	1(0-2)
Elevated AUDIT-C score[b], n/total n(%)	163/1462(11.1)	6/50(12.0)	0.88	140/1176(11.9)
Alcohol-related problems[c], n/total n(%)	93/1467(6.3)	3/51(5.9)	0.90	72/1173(6.1)
Symptoms of alcohol dependence[d], n/total n(%)	49/1467(3.3)	3/51(5.9)	0.33	40/1173(3.4)
Alcohol-related harm[e], n/total n(%)	74/1470(5.0)	2/51(3.9)	0.72	58/1175(4.9)

AUDIT-C, Alcohol Use Disorder Identification Test-Consumption; IQR, interquartile range; RYGB, Roux-en-Y gastric bypass SG, sleeve gastrectomy.

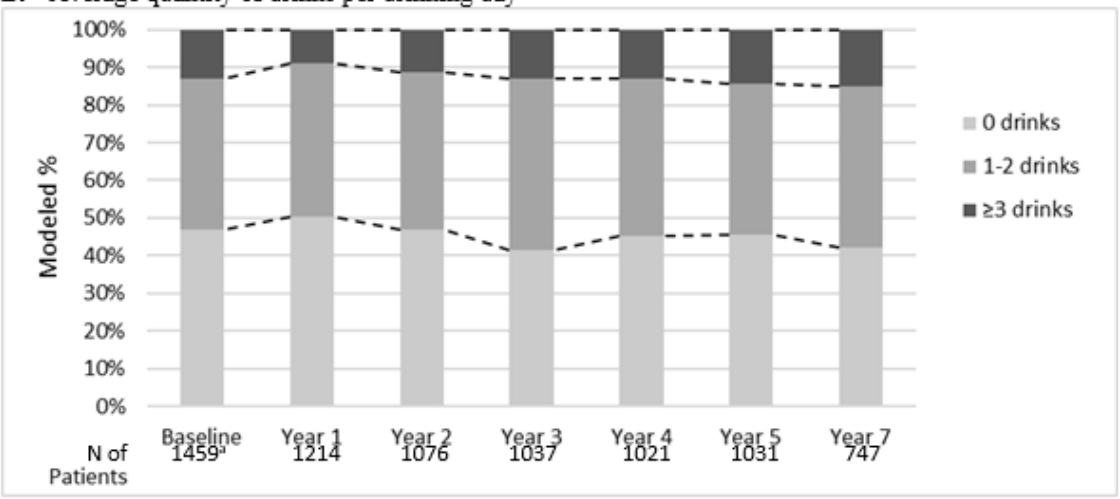
[a]Unless otherwise specified. [b]AUDIT-C score at least 3 among females and at least 4 among males. [c]Symptoms of alcohol dependence and/or alcohol-related harm. [d]Not being able to stop drinking once started, failing to meet normal expectations because of drinking, or needing a drink in the morning to get going at least once in the past 12 months. [e]Feeling guilt or remorse, being unable to remember, injuring someone, or eliciting concern due to drinking at least once in the past 12 months.

A. Frequency of alcohol use



Year 7 vs. baseline $P<.001$; Quadratic trend years 1-7 $P<0.001$

B. Average quantity of drinks per drinking day

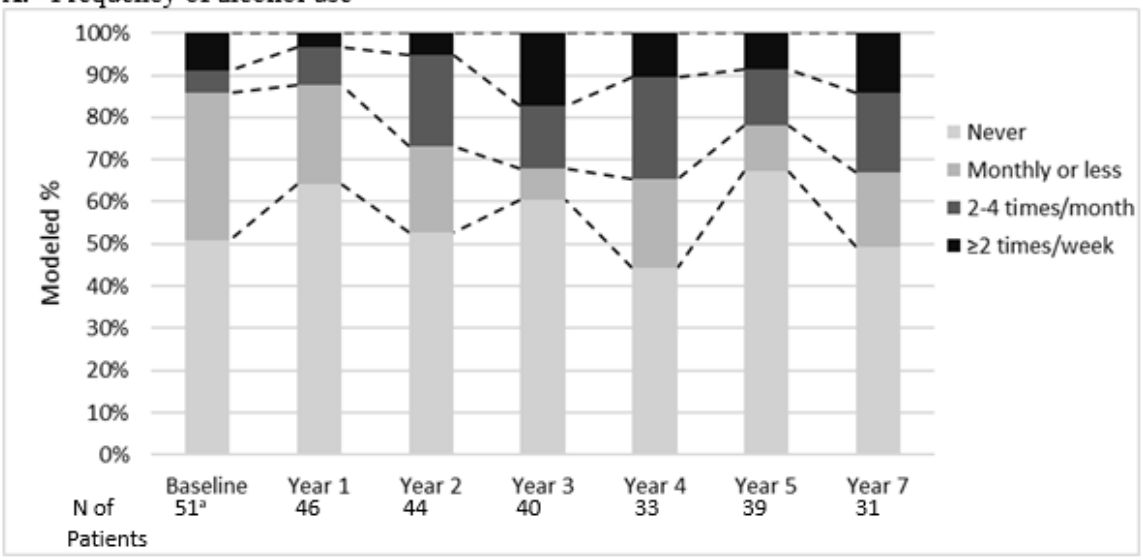


Year 7 vs. baseline $P=0.04$; Quadratic trend years 1-7 $P<.001$

[a]Sample size of model. Modeled data, adjusted for factors related to missing follow-up data (site, baseline age and smoking status), are shown. Modeled data with 95% CI and observed data are reported in Table 6.3.

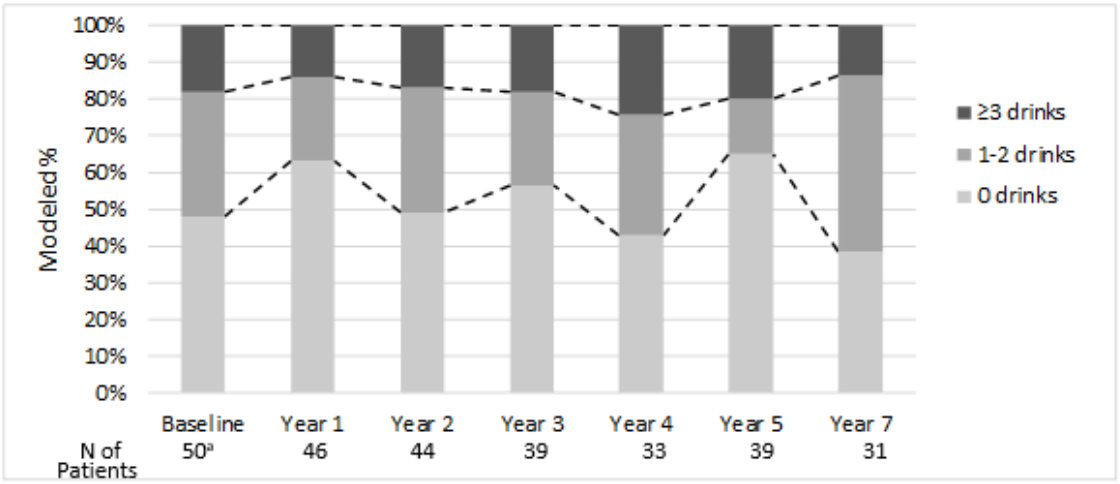
Figure 6.2. Frequency of alcohol use and average quantity of drinks per drinking day by time in relation to Roux-en-Y gastric bypass

A. Frequency of alcohol use



Time point *P*=0.29

B. Average quantity of drinks per drinking day



Time point *P*=0.74

[a]Sample size of model. Modeled data, adjusted for factors related to missing follow-up data (site, baseline age and smoking status), are shown. Modeled data with 95% CI and observed data are reported in Table 6.4.

Figure 6.3. Frequency of alcohol use and average quantity of drinks per drinking day by time in relation to sleeve gastrectomy

Table 6.3. Frequency of alcohol use and average quantity of drinks per drinking day, by time point in relation to Roux-en-Y gastric bypass

	Baseline	Year 1	Year 2	Year 3	Year 4	Year 5	Year 7
Frequency of alcohol use	Model-based estimates, % (95% confidence interval)[a,b]						
Never	47.1 (46.9-47.4)	52.2 (52.0-52.5)	49.0 (48.7-49.3)	44.5 (44.2-44.8)	48.0 (47.7-48.2)	47.2 (46.9-47.4)	43.8 (43.4-44.1)
Monthly or less	37.2 (36.9-37.6)	29.1 (28.7-29.4)	26.4 (26.0-26.8)	27.4 (27.0-27.8)	23.8 (23.4-24.2)	21.4 (21.0-21.8)	24.3 (23.8-24.8)
2-4 times/month	9.0 (8.7-9.4)	8.4 (8.0-8.8)	11.1 (10.6-11.6)	11.0 (10.5-11.4)	11.1 (10.6-11.6)	12.6 (12.2-13.1)	10.8 (10.2-11.3)
≥2 times/week	6.6 (6.4-6.8)	10.3 (10.0-10.6)	13.5 (13.2-13.8)	17.1 (16.8-17.5)	17.2 (16.8-17.5)	18.8 (18.4-19.1)	21.2 (20.7-21.6)
	Observed, n (%)						
	n=1472	n=1226	n=1080	n=1037	n=1024	n=1035	n=757
Never	634 (43.1)	564 (46.0)	465 (43.1)	401 (38.7)	427 (41.7)	422 (40.8)	290 (38.3)
Monthly or less	542 (36.8)	382 (31.2)	316 (29.3)	314 (30.3)	283 (27.6)	265 (25.6)	214 (28.3)
2-4 times/month	206 (14.0)	167 (13.6)	169 (15.7)	166 (16.0)	159 (15.5)	179 (17.3)	112 (14.8)
2-3 times/week	64 (4.4)	77 (6.3)	70 (6.5)	82 (7.9)	86 (8.4)	98 (9.5)	80 (10.6)
≥4 times/week	26 (1.8)	36 (2.9)	60 (5.6)	74 (7.1)	69 (6.7)	71 (6.9)	61 (8.1)
Average quantity of drinks per drinking day	Model-based estimates, % (95% confidence interval)[a,c]						
0 drinks	46.9 (46.6-47.1)	50.2 (49.9-50.4)	46.7 (46.4-47.0)	41.6 (41.3-42.0)	45.3 (44.9-45.6)	45.7 (45.3-46.0)	42.3 (41.9-42.7)
1-2 drinks	40.1 (39.8-40.5)	40.8 (40.4-41.1)	41.8 (41.5-42.2)	45.3 (44.9-45.7)	41.9 (41.5-42.3)	39.9 (39.5-40.3)	42.8 (42.3-43.2)
≥3 drinks	13.0 (12.7-13.4)	9.1 (8.7-9.5)	11.4 (11.0-11.9)	13.1 (12.6-13.5)	12.9 (12.4-13.3)	14.4 (14.0-14.9)	15.0 (14.5-15.5)
	Observed, n (%)						
	n=1462	n=1217	n=1079	n=1038	n=1022	n=1032	n=748
0 drinks	634 (43.4)	567 (46.7)	469 (43.5)	404 (38.9)	427 (41.8)	425 (41.2)	291 (38.9)
1-2 drinks	610 (41.7)	517 (42.5)	465 (43.1)	479 (46.2)	444 (43.4)	441 (42.7)	331 (44.3)
3-4 drinks	156 (10.7)	100 (8.2)	109 (10.1)	110 (10.6)	111 (10.9)	125 (12.1)	91 (12.2)
5-6 drinks	47 (3.2)	23 (1.9)	24 (2.2)	34 (3.3)	22 (2.2)	28 (2.7)	22 (2.9)
≥7 drinks	15 (1.0)	10 (0.8)	12 (1.1)	11 (1.1)	18 (1.8)	13 (1.3)	13 (1.7)

[a]Models adjusted for factors related to missing follow-up data (site, baseline age and smoking status). [b]N=1,469; p-value for year 7 vs baseline:<.001; p-value for quadratic trend between year 7 and year 1:<.001. [c] N=1,459; P-value for year 7 vs baseline:0.04; p-value for quadratic trend between year 7 and year 1:<.001.

Table 6.4. Frequency of alcohol use and average quantity of drinks per drinking day, by time point in relation to sleeve gastrectomy

	Baseline	Year 1	Year 2	Year 3	Year 4	Year 5	Year 7
Frequency of alcohol use	Model-based estimates, % (95% confidence interval)[a,b]						
Never	50.7 (45.4-55.9)	64.2 (58.9-69.5)	52.5 (46.5-58.5)	60.4 (54.6-66.3)	44.3 (35.9-52.8)	67.4 (61.8-72.9)	49.2 (40.6-57.8)
Monthly or less	35.1 (27.4-42.8)	23.4 (13.8-33.0)	20.7 (10.0-31.4)	7.6 (0.0-19.7)	21.2 (3.2-39.2)	10.8 (0.0-23.5)	17.8 (1.6-33.9)
2-4 times/month	5.2 (0.0-10.6)	9.1 (3.3-14.9)	21.5 (12.1-30.9)	14.8 (4.6-24.9)	24.1 (12.7-35.5)	13.3 (3.8-22.7)	18.9 (5.5-32.2)
≥2 times/week	9.0 (0.0-19.9)	3.3 (0.0-54.5)	5.2 (0.0-32.9)	17.2 (7.4-27.0)	10.4 (0.0-27.9)	8.6 (0.0-23.6)	14.1 (0.1-28.2)
	Observed, n (%)						
	n=51	n=46	n=44	n=40	n=33	n=39	n=31
Never	22 (43.1)	24 (52.2)	19 (43.2)	18 (45.0)	12 (36.4)	21 (53.9)	11 (35.5)
Monthly or less	18 (35.3)	13 (28.3)	11 (25.0)	6 (15.0)	8 (24.2)	6 (15.4)	7 (22.6)
2-4 times/month	5 (9.8)	7 (15.2)	11 (25.0)	9 (22.5)	9 (27.3)	8 (20.5)	8 (25.8)
2-3 times/week	4 (7.8)	1 (2.2)	0 (0.0)	4 (10.0)	2 (6.1)	1 (2.6)	3 (9.7)
≥4 times/week	2 (3.9)	1 (2.2)	3 (6.8)	3 (7.5)	2 (6.1)	3 (7.7)	2 (6.5)
Average quantity of drinks per drinking day	Model-based estimates, % (95% confidence interval)[a,c]						
0 drinks	47.9 (42.1-53.7)	63.0 (57.8-68.2)	49.1 (42.7-55.5)	56.7 (50.4-63.0)	42.9 (34.1-51.7)	64.9 (60.0-69.8)	38.4 (28.1-48.8)
1-2 drinks	34.0 (26.0-42.0)	23.2 (15.9-30.5)	33.8 (25.2-42.5)	25.4 (17.1-33.7)	32.9 (22.5-43.3)	15.3 (8.2-22.5)	48.0 (36.4-59.6)
≥3 drinks	18.0 (9.6-26.5)	13.8 (2.8-24.8)	17.0 (8.2-25.9)	18.0 (8.5-27.4)	24.2 (12.6-35.7)	19.7 (10.3-29.2)	13.6 (0.0-31.1)
	Observed, n (%)						
	n=50	n=46	n=44	n=39	n=33	n=39	n=31
0 drinks	22 (44.0)	24 (52.2)	19 (43.2)	18 (46.2)	12 (36.4)	21 (53.9)	11 (35.5)
1-2 drinks	19 (38.0)	16 (34.8)	18 (40.9)	15 (38.5)	14 (42.4)	11 (28.2)	16 (51.6)
3-4 drinks	7 (14.0)	5 (10.9)	4 (9.1)	3 (7.7)	6 (18.2)	6 (15.4)	3 (9.7)
5-6 drinks	1 (2.0)	1 (2.2)	1 (2.3)	2 (5.1)	0 (0.0)	1 (2.6)	1 (3.2)
≥7 drinks	1 (2.0)	0 (0.0)	2 (4.6)	1 (2.6)	1 (3.0)	0 (0.0)	0 (0.0)

[a]Models adjusted for factors related to missing follow-up data (site, baseline age and smoking status). [b]N=51; Overall p-value for time point: 0.29. [c]N=50; Overall p-value for time point: 0.74.

Table 6.5. Prevalence of alcohol-related problems among female current drinkers by frequency of alcohol use, average quantity of drinks per drinking day, and AUDIT-C score, by time point in relation to Roux-en-Y gastric bypass

	Baseline	Year 1	Year 2	Year 3	Year 4	Year 5	Year 7
	Observed, n/total n (%)						
Frequency of alcohol use							
Monthly or less	22/443 (5.0)	14/308 (4.6)	11/259 (4.3)	18/258 (7.0)	18/243 (7.4)	11/228 (4.8)	10/184 (5.4)
2-4 times/month	26/152 (17.1)	29/126 (23.0)	34/135 (25.2)	26/132 (19.7)	27/122 (22.1)	20/139 (14.4)	22/92 (23.9)
2-3 times/week	16/49 (32.7)	19/55 (34.6)	20/55 (36.4)	25/65 (38.5)	30/69 (43.5)	37/77 (48.1)	27/61 (44.3)
≥4 times/week	8/18 (44.4)	11/17 (64.7)	26/36 (72.2)	34/47 (72.3)	30/47 (63.8)	39/46 (84.8)	32/43 (74.4)
Average quantity of drinks per drinking day							
1-2 drinks	25/487 (5.1)	34/405 (8.4)	26/365 (7.1)	39/384 (10.2)	37/359 (10.3)	32/355 (9.0)	32/279 (11.5)
3-4 drinks	27/123 (22.0)	24/70 (34.3)	47/89 (52.8)	40/85 (47.1)	45/87 (51.7)	56/103 (54.4)	42/74 (56.8)
5-6 drinks	13/36 (36.1)	10/15 (66.7)	11/16 (68.8)	19/23 (82.6)	13/17 (76.5)	14/19 (73.7)	9/14 (64.3)
≥7 drinks	7/11 (63.6)	5/5 (100.0)	5/5 (100.0)	5/5 (100.0)	10/11 (90.9)	5/6 (83.3)	7/8 (87.5)
AUDIT-C score							
1	7/355 (2.0)	9/285 (3.2)	6/238 (2.5)	8/236 (3.4)	6/215 (2.8)	6/213 (2.8)	3/158 (1.9)
2	17/167 (10.2)	16/106 (15.1)	14/121 (11.6)	19/115 (16.5)	17/101 (16.8)	11/113 (9.7)	15/86 (17.4)
3[a]	20/88 (22.7)	19/72 (26.4)	24/60 (40.0)	21/69 (30.4)	27/75 (36.0)	18/71 (25.4)	16/56 (28.6)
4	16/35 (45.7)	13/25 (52.0)	20/36 (55.6)	14/35 (40.0)	25/53 (47.2)	30/48 (62.5)	20/39 (51.3)
5	9/12 (75.0)	8/10 (80.0)	13/15 (86.7)	16/22 (72.7)	13/18 (72.2)	18/21 (85.7)	18/20 (90.0)
6	2/3 (66.7)	7/7 (100.0)	5/6 (83.3)	16/16 (100.0)	5/7 (71.4)	10/10 (100.0)	4/6 (66.7)
7 or 8	1/2 (50.0)	1/1 (100.0)	9/9 (100.0)	9/9 (100.0)	12/12 (100.0)	14/14 (100.0)	15/15 (100.0)

AUDIT-C, Alcohol Use Disorder Identification Test-Consumption.
[a]Elevated AUDIT-C score.

Table 6.6. Associations of frequency of alcohol use, average quantity of drinks per drinking day, and AUDIT-C score with alcohol-related problems in female Roux-en-Y gastric bypass patients prior to and following surgery

	RR	(95% CI)	*P*[a]
Frequency of alcohol use (ref.=monthly or less)			<.001
2-4 times/month	2.62	(2.13-3.34)	
2-3 times/week	4.33	(3.41-5.51)	
≥4 times/week	7.66	(5.92-9.90)	
Average quantity of drinks per drinking day (ref.=1-2 drinks)			<.001
3-4 drinks	3.10	(2.50-3.85)	
5-6 drinks	4.36	(3.35-5.67)	
≥7 drinks	5.09	(3.69-7.02)	
AUDIT-C score (per 1 point higher)	1.50	(1.44-1.56)	<.001
Elevated AUDIT-C score[b] (ref.=no)	4.60	(3.77-5.61)	<.001

AUDIT-C, Alcohol Use Disorder Identification Test-Consumption; CI, confidence interval; RR, relative risk. All four models adjusted for factors related to missing follow-up (site, baseline age and smoking status).
[a]There was not a significant interaction between time point and frequency (P=0.99) or quantity (P=0.65) of alcohol in relation to alcohol-related problems. Although there was a statistically significant interaction between time and AUDIT-C score (P<.001), estimates at each time point were similar (range, 1.39-1.85) and thus are not reported by time. [b]AUDIT-C score of at least 3.

Table 6.7. Sensitivity, specificity, and area under the receiver operating characteristic curve of frequency of alcohol use, average quantity of drinks per drinking day, and AUDIT-C score, for identifying alcohol-related problems among female current drinkers before and after Roux-en-Y gastric bypass

	Sensitivity[a] (95% CI)	Specificity (95% CI)	AUROC (95% CI)
Pre-surgery			
Frequency of alcohol use			
≥ 2 times/month	69.4(58.8-80.1)	71.4(67.7-75.0)	0.911(0.881-0.942)
≥ 2 times/week	33.3(22.4-44.2)	92.7(90.6-94.8)	0.931(0.907-0.955)
≥ 4 times/week	11.1(3.9-18.4)	98.3(97.3-99.4)	0.943(0.918-0.968)
Average quantity of drinks per drinking day			
≥ 3 drinks	65.3(54.3-76.3)	79.0(75.7-82.3)	0.923(0.896-0.949)
≥ 5 drinks	27.8(17.4-38.1)	95.4(93.7-97.1)	0.956(0.939-0.973)
≥ 7 drinks	9.7(2.9-16.6)	99.3(98.7-99.9)	0.965(0.947-0.983)
AUDIT-C score			
≥ 2	90.3(83.4-97.1)	59.0(55.0-63.0)	0.945(0.916-0.975)
≥ 3[b]	66.7(55.8-77.6)	84.4(81.5-87.3)	0.931(0.908-0.954)
≥ 4	38.9(27.6-50.2)	95.9(94.3-97.5)	0.945(0.926-0.964)
Post-surgery			
Frequency of alcohol use			
≥ 2 times/month	85.3(82.6-88.0)	61.4(59.6-63.1)	0.916(0.903-0.928)
≥ 2 times/week	56.6(52.8-60.4)	87.3(86.0-88.5)	0.918(0.906-0.930)
≥ 4 times/week	29.2(25.7-32.7)	97.2(96.5-97.8)	0.936(0.926-0.947)
Average quantity of drinks per drinking day			
≥ 3 drinks	64.2(60.5-67.9)	87.2(86.0-88.4)	0.935(0.925-0.944)
≥ 5 drinks	20.0(16.9-23.1)	98.6(98.2-99.0)	0.951(0.943-0.960)
≥ 7 drinks	6.5(4.6-8.4)	99.9(99.7-100.0)	0.949(0.940-0.958)
AUDIT-C score			
≥ 2	92.9(91.0-94.9)	57.3(55.5-59.2)	0.931(0.920-0.942)
≥ 3[b]	76.4(73.2-79.7)	81.6(80.2-83.0)	0.921(0.909-0.933)
≥ 4	54.1(50.3-58.0)	93.8(92.9-94.7)	0.934(0.924-0.944)

AUDIT-C, Alcohol Use Disorder Identification Test-Consumption; AUROC, area under the receiver operating characteristic curve; CI, confidence interval; RYGB, Roux-en-Y gastric bypass.

Highlighted areas represent the highest combined levels of sensitivity and specificity for each alcohol use variable. When multiple areas are highlighted for a given alcohol use variable, the combined sensitivity and specificity values vary <1.0%.

[a]For identifying alcohol-related problems (i.e., not being able to stop drinking once started, failing to meet normal expectations because of drinking, needing a drink in the morning to get going at least once in the past 12 months, feeling guilt or remorse, being unable to remember, injuring someone, or eliciting concern due to drinking at least once in the past 12 months. [b]Elevated AUDIT-C score.

Table 6.8. Sensitivity, specificity, and area under the receiver operating characteristic curve of frequency of alcohol use, average quantity of drinks per drinking day, and AUDIT-C score, for identifying symptoms of alcohol dependence and alcohol-related harm, respectively, among female current drinkers prior to and following Roux-en-Y gastric bypass

	Prior to Roux-en-Y gastric bypass			Following Roux-en-Y gastric bypass		
	Sensitivity (95% CI)	**Specificity (95% CI)**	**AUROC (95% CI)**	**Sensitivity (95% CI)**	**Specificity (95% CI)**	**AUROC (95% CI)**
Symptoms of alcohol dependence[a]						
Frequency of alcohol use						
≥ 2 times/month	65.0(50.2-79.8)	69.0(65.3-72.6)	0.909(0.867-0.951)	88.4(85.3-91.5)	58.0(56.3-59.8)	0.926(0.912-0.940)
≥ 2 times/week	30.0(15.8-44.2)	91.2(88.9-93.4)	0.917(0.885-0.950)	62.1(57.4-66.8)	84.4(83.1-85.7)	0.924(0.911-0.937)
≥ 4 times/week	7.5(0.0-15.7)	97.6(96.4-98.8)	0.920(0.875-0.966)	32.8(28.2-37.4)	95.5(94.8-96.2)	0.935(0.923-0.947)
Average quantity of drinks per drinking day						
≥ 3 drinks	67.5(53.0-82.0)	76.8(73.5-80.2)	0.905(0.856-0.954)	73.7(69.4-77.9)	84.3(83.0-85.6)	0.938(0.928-0.949)
≥ 5 drinks	32.5(18.0-47.0)	94.5(92.7-96.3)	0.928(0.884-0.971)	26.2(21.9-30.5)	98.1(97.6-98.6)	0.949(0.939-0.959)
≥ 7 drinks	10.0(7.0-19.3)	98.9(98.0-99.7)	0.926(0.881-0.972)	9.2(6.4-12.0)	99.8(99.6-99.9)	0.944(0.933-0.955)
AUDIT-C score						
≥ 2	97.5(92.7-100.0)	56.9(53.0-60.8)	0.949(0.918-0.979)	96.6(94.9-98.4)	53.8(52.1-55.6)	0.910(0.879-0.941)
≥ 3[b]	70.0(55.8-84.2)	82.0(79.0-85.0)	0.919(0.884-0.955)	85.8(82.4-89.2)	77.9(76.4-79.4)	0.901(0.875-0.926)
≥ 4	35.0(20.2-49.8)	93.9(92.0-95.8)	0.926(0.898-0.953)	62.4(57.7-67.1)	91.0(90.0-92.0)	0.904(0.878-0.930)
Symptoms of alcohol-related harm[c]						
Frequency of alcohol use						
≥ 2 times/month	67.2(55.2-79.3)	70.3(66.7-73.9)	0.906(0.870-0.941)	86.3(83.4-89.1)	60.4(58.7-62.2)	0.916(0.902-0.929)
≥ 2 times/week	34.5(22.3-46.7)	92.2(90.1-94.4)	0.925(0.897-0.952)	65.7(61.8-69.6)	86.7(85.5-87.9)	0.915(0.903-0.928)
≥ 4 times/week	10.3(2.5-18.2)	98.0(96.9-99.1)	0.933(0.904-0.962)	31.6(27.8-35.4)	97.0(96.4-97.6)	0.933(0.922-0.944)
Average quantity of drinks per drinking day						
≥ 3 drinks	65.5(53.3-77.8)	78.0(74.7-81.3)	0.914(0.882-0.946)	64.5(60.6-68.5)	86.0(84.7-87.2)	0.931(0.920-0.941)
≥ 5 drinks	32.8(20.7-44.8)	95.3(93.7-97.0)	0.945(0.926-0.964)	20.2(16.9-23.5)	98.2(97.7-98.7)	0.950(0.941-0.959)
≥ 7 drinks	10.3(2.5-18.2)	99.2(98.4-99.9)	0.949(0.928-0.971)	6.8(4.7-8.9)	99.8(99.6-99.9)	0.949(0.940-0.958)
AUDIT-C score						
≥ 2	87.9(80.0-96.3)	57.6(53.7-61.5)	0.926(0.889-0.964)	92.6(90.5-94.8)	56.0(54.2-57.8)	0.910(0.928-0.953)
≥ 3[b]	65.5(53.3-77.8)	83.2(80.2-86.2)	0.919(0.891-0.948)	77.5(74.1-81.0)	80.4(78.9-81.8)	0.929(0.917-0.942)
≥ 4	41.4(28.7-54.1)	95.4(93.7-97.1)	0.937(0.914-0.960)	56.8(52.7-60.9)	93.2(92.3-94.1)	0.936(0.924-0.947)

AUDIT-C, Alcohol Use Disorder Identification Test-Consumption; AUROC, area under the receiver operating characteristic curve; CI, confidence interval. Highlighted areas represent the highest combined levels of sensitivity and specificity for each alcohol use variable. When multiple areas are highlighted for a given alcohol use variable, the combined sensitivity and specificity values vary <1.0%. [a]Not being able to stop drinking once started, failing to meet normal expectations because of drinking, or needing a drink in the morning to get going at least once in the past 12 months. [b]Elevated score. [c]Feeling guilt or remorse, being unable to remember, injuring someone, or eliciting concern due to drinking at least once in the past 12 months.

7.0 PUBLIC HEALTH SIGNIFICANCE

Understanding the associations between alcohol use, AUD, and weight status is critical to developing more effective prevention and treatment strategies for both diseases,[215] which are of particular public health significance since alcohol use, AUD, and obesity are increasing in prevalence and leading contributors to preventable death in the United States.[16,27,77] Specifically, understanding the relationship between alcohol use patterns and weight may lead to better weight-related alcohol recommendations. Moreover, results from these studies inform education and clinical practice guidelines for screening for alcohol-related problems in adults with varying weight status, including among adults who have undergone bariatric surgery.

We found, that among current drinkers, higher frequency of days with alcohol use is associated with lower odds of obesity, while higher continued volume is associated with higher odds of obesity. We were the first to demonstrate that the magnitude of the inverse association between frequency of alcohol use and odds of overweight-obesity is larger with each level of higher weight status (through class 3 obesity). While clinical guidelines recommend that individuals limit alcohol use for weight control, we found no associations between past-year attempt to lose weight and alcohol use, indicating adults may not change their alcohol intake when trying to lose weight. However, a longitudinal study is needed to confirm this interpretation. Furthermore, we were not able to assess whether individuals were unaware of the

alcohol-related weight loss recommendations or whether they were aware but did not follow them. When we examined whether alcohol use was related to weight loss among adults who had tried to lose weight in the past year, we found no associations among males or females. Because even modest weight loss can have profound health benefits at the population level, future research should determine the appropriateness of clinical guidelines suggesting individuals limit alcohol use for weight control.

We found that the relationship between alcohol use and AUD differs by weight status and that the interplay between weight status and alcohol use in relation to AUD differs by sex. Screening and advice for AUD delivered in the primary care setting results in substantial improvements in individual health, as well as decreases in the population burden of AUD.[193] Clinicians who screen for AUD should be aware that the relationships between levels and patterns of alcohol use and AUD differ by both sex and weight status. In particular, comprehensive AUD screening, which includes assessment of symptoms, may be warranted at lower levels of alcohol use among males with class 3 obesity. Among females, frequent use of any alcohol may be more concerning among lower weight status groups. These results can aid health care providers in screening patients with different weight status for AUD, hopefully leading to improved individual and public health.

Understanding how alcohol use changes after surgery is important for long-term clinical care because alcohol use is associated with higher total caloric intake,[110,202] vitamin deficiencies,[113] accidents and self-harm,[114,199] and AUD. Our findings suggest that both the frequency of alcohol use and the average quantity of drinks per drinking day increase throughout seven years following RYGB, one of the most common bariatric surgeries performed in the

United States.[37] This finding suggests the need for ongoing discussions regarding alcohol use and its potential impacts throughout long-term clinical care of adults who have undergone RYGB.

Screening guidelines for AUD in primary care, which usually rely on alcohol frequency and quantity as a first-level screen, are well established.[83,84] Evidence suggests that RYGB and SG alter alcohol pharmacokinetics,[113,128,132-134] and at least RYGB may increase the risk of developing AUD.[115] While current recommendations suggest that clinicians screen for AUD both before and after bariatric surgery, no further guidance is provided.[201] This study was the first to assess the sensitivity and specificity of screening tools for identifying alcohol-related problems in individuals who undergo RYGB. We found that, among women who underwent RYGB, the standard threshold for the AUDIT-C score, a common screening tool for AUD, had better combined sensitivity and specificity for identifying pre- and post-surgery alcohol-related problems than alternative AUDIT-C score thresholds or thresholds based on frequency of alcohol use or average quantity of drinks per drinking day alone. These findings indicate that clinicians should first ask patients about both frequency and quantity of alcohol use. Furthermore, because the AUDIT-C and questions on frequency or quantity of alcohol use alone fail to identify many RYGB patients with alcohol-related problems, additional screening for alcohol-related problems such as the full AUDIT or other screening tools that assess symptoms of alcohol-related problems, should be conducted in bariatric surgery patients.

With the increased understanding of the relationships between alcohol use, alcohol use disorder, and weight status gained by this research, opportunities to improve the health and well-being of individuals who may drink alcohol (i.e., better alcohol education, better AUD screening) are abundant. The addition of weight-specific AUD screening thresholds to already existing sex-specific AUD screening thresholds will enable clinicians to better target AUD

education and referral. Such changes have potential to make a profound impact on individual and public health.

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