Received: 10 September 2025 | Accepted: 12 December 2025

DOI: 10.1111/acer.70230

ALCOHOL CLINICAL & EXPERIMENTAL RESEARCH ISBRA

RESEARCH ARTICLE

# Alcohol use disorder is a chronic disease

**Nicholas W. Gilpin**[1,2,3,4] | **Patricia E. Molina**[1,2]

[1]Department of Physiology, LSU Health Sciences Center, New Orleans, Louisiana, USA

[2]Alcohol & Drug Abuse Center of Excellence, LSU Health Sciences Center, New Orleans, Louisiana, USA

[3]Neuroscience Center of Excellence, LSU Health Sciences Center, New Orleans, Louisiana, USA

[4]Southeast Louisiana VA Healthcare System (SLVHCS), New Orleans, Louisiana, USA

**Correspondence**
Nicholas W. Gilpin, Department of Physiology, LSU Health Sciences Center, 533 Bolivar Street Room 609, New Orleans, LA 70112, USA.
Email: ngilpi@lsuhsc.edu

## Abstract

Alcohol use disorder (AUD) is a chronic, relapsing brain disease with profound health, societal, and economic consequences. Alcohol misuse not only leads to AUD, but it is also a driver of multimorbidity, exacerbating a wide range of chronic comorbidities, including cancer. Despite being formally recognized over six decades ago as a medical condition, AUD remains one of the most prevalent and costly public health issues in the United States. Alcohol misuse contributes to more than 90,000 deaths annually in the United States, with hundreds of billions of dollars lost annually due to healthcare costs, lost productivity, and criminal justice expenditures. Beyond its economic burden, alcohol adversely affects nearly every organ system. Chronic heavy alcohol use changes brain structure and impairs brain function, drives neuroinflammation and neurodegeneration, and contributes to neurological and psychiatric comorbidities as well as cognitive decline. Alcohol-associated liver disease is a leading cause of cirrhosis and hepatocellular carcinoma. In addition, chronic alcohol misuse leads to cardiomyopathy, hypertension, and arrhythmia, and increased risk for pulmonary disease. Through alterations in endocrine signaling, alcohol leads to reproductive dysfunction, osteoporosis, and metabolic derangements including diabetes and obesity. Alcohol compromises musculoskeletal integrity, impairs immune responses, alters gut microbiota and increases cancer risk. Particularly concerning is the rising prevalence of alcohol misuse in women and older adults, populations with increased physiological vulnerability. There are three FDA-approved treatments for AUD, but they are underutilized, and patient response rates are variable, highlighting the need for continued investment in translational alcohol research. This paper summarizes the widespread and systemic impact of alcohol misuse on the health of US citizens and US society. Given the substantial burden of disease, disability, and death associated with alcohol, and the clear benefits yielded by alcohol research to date, sustained and enhanced support for alcohol-related biomedical research remains a public health imperative.

KEYWORDS
brain, gut, heart, liver, muscle

  

## INTRODUCTION

The goal of this review and commentary is to provide a high-level summary of the many negative health consequences associated with chronic alcohol use and/or diagnosis with alcohol use disorder (AUD). It has long been understood, even among the lay public, that chronic alcohol use negatively affects the brain and the liver. In recent years, we have gained new knowledge with respect to the effects of chronic alcohol use on several other organs, and emerging literature describes many adverse effects of alcohol on specific health outcomes beyond liver and brain. Here, we provide a snapshot of what is currently known about the myriad health consequences of alcohol use and to make the argument that this area of research is vital for improving human health and ensuring healthy aging. We discuss these health consequences both in terms of direct alcohol effects on the brain and body and in terms of worsening outcomes related to other comorbid conditions.

## ALCOHOL USE DISORDER

In 1956, the American Medical Association (AMA) designated alcoholism as a "major medical problem" (Henry, 2019). In their 1968 ruling on Powell vs. State of Texas, the US Supreme Court acknowledged this designation for the first time and provided that the AMA urged that alcoholics, a term considered to be undesired when speaking of people with an AUD, be admitted to general hospitals for care (Marshall & Supreme Court of the United States, 1967). Since that time, arguments have continuously been advanced that "addiction is a brain disease" (Heilig et al., 2021; Leshner, 1997).

Although addiction was mentioned in earlier editions of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM), the third edition (DSM-III) listed substance abuse and substance dependence (including alcohol as well as other illicit drugs) as separate diagnoses for the first time (Nathan et al., 2016). In the fifth edition of the DSM (DSM-5), addictive disorders were reclassified as substance use disorders (Nathan et al., 2016). There are some important differences in the diagnostic schemes presented across versions of the DSM, but in general, diagnosis with a disorder related to excessive alcohol use has relied on physiological and behavioral symptoms for the better part of five decades. To this end, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), one of the more than two dozen National Institutes of Health (NIH) institutes and centers, was established on December 31, 1970. The NIAAA website currently states that "alcohol use disorder (AUD) is a medical condition characterized by an impaired ability to stop or control alcohol use despite adverse social, occupational, or health consequences" and that "considered a brain disorder, AUD can be mild, moderate, or severe" (National Institute on Alcohol Abuse and Alcoholism [NIAAA], 2025d).

Recent federal guidance has emphasized that, going forward, the NIH should focus its efforts on understanding and treating chronic disease. The CDC defines chronic conditions as those which "last 1 year or more and require ongoing medical attention or limit activities of daily living or both." Executive Order 14212 states that "six in 10 Americans have at least one chronic disease, and four in 10 have two or more chronic diseases" and it further states that "to fully address the growing health crisis in America, we must re-direct our national focus, in the public and private sectors, toward understanding and drastically lowering chronic disease rates" (Trump, 2025).

Here, we emphasize that AUD is a chronic disease, that AUD is highly comorbid with many other chronic diseases, that the national burden of AUD in terms of economic loss and human disability is so high as to be almost incalculable, and that research understanding and combatting the causes and consequences of AUD is critical for the health and health care of Americans.

## ALCOHOL MISUSE: ECONOMIC AND HEALTH IMPACT IN THE UNITED STATES

### Alcohol misuse has a negative economic impact in the United States

In 2010, alcohol misuse cost the United States $249 billion (Sacks et al., 2015). Alcohol misuse is defined by the National Institute on Alcohol Abuse and Alcoholism (NIAAA, 2025c) as "drinking in a manner, situation, amount, or frequency that could cause harm to the person who drinks or to those around them." Alcohol misuse is a catch-all term that "includes binge drinking and heavy alcohol use," and chronic alcohol misuse can lead to an AUD diagnosis. Types of alcohol misuse include heavy drinking, defined by NIAAA as more than 4 or 5 drinks on any one day, or more than 8 or 15 drinks per week, for women and men, respectively, and binge drinking, defined by NIAAA as 4 or 5 drinks (or more) in a two-hour period, in women and men, respectively (US Department of Health and Human Services).

Alcohol misuse negatively impacts the economies of all 50 states in the United States (US Centers for Disease Control and Prevention, 2024). Some major sources of economic loss associated with alcohol misuse include healthcare costs, insurance costs, criminal justice costs associated with alcohol-related crimes, lost productivity, and early mortality. At a social level, alcohol misuse can lead to strained family relationships and child neglect. In fiscal year 2024, the US Congress appropriated $595.3 million to NIAAA (2024b), which amounts to <1% of the economic impact of alcohol misuse in the United States. NIAAA uses this budget to fulfill its mission by supporting alcohol-related research, collaborating with other institutes and programs on alcohol-related issues, and translating and disseminating research findings to healthcare providers, researchers,

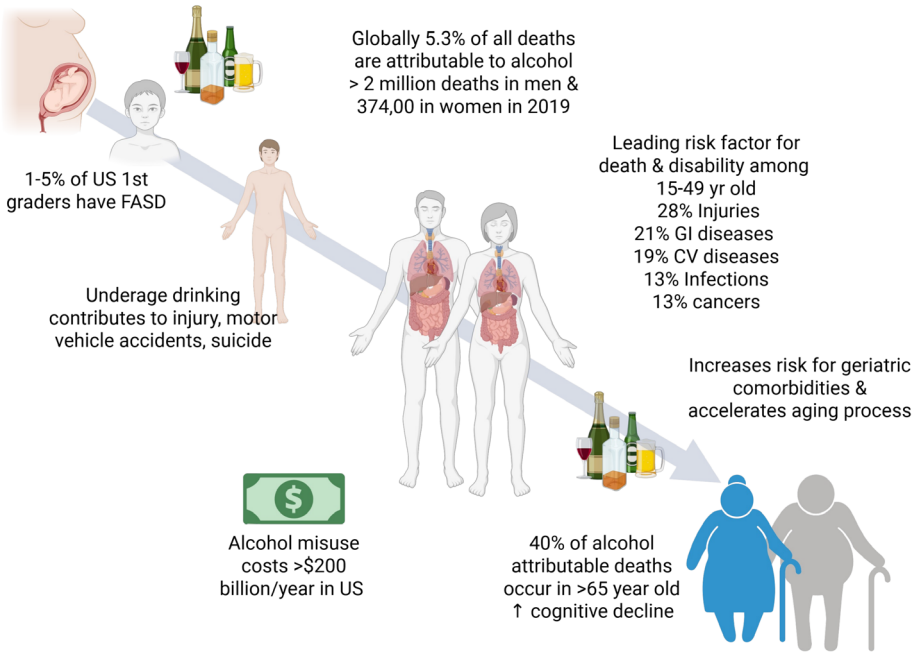


**FIGURE 1** Alcohol misuse negatively impacts health across the lifespan and the economy. AUD diagnoses contribute to increased risk of comorbidities, death, and disability. This is especially true in older individuals, and the US population is rapidly aging. The estimated annual financial cost of alcohol misuse in the United States is significant. Investment in research to prevent, treat, and rehabilitate individuals is a priority. Each dollar invested in NIH research returns more than $2.50 to the US economy.

policymakers, and the public (NIAAA, 2025b). Based on the economic cost of alcohol misuse to the United States, one could easily argue that research into the causes and consequences of alcohol misuse deserves an increase in attention and resources going forward (see Figure 1).

## Alcohol misuse has negative health impacts on Americans

Globally, 5.3% of all deaths are attributable to alcohol, rising to 13.5% among individuals aged 20–39 years. Despite recent (deserved) increases in attention to the opioid misuse crisis, alcohol misuse is by far the costliest form of substance use. According to the CDC, during the years 2011 to 2015, excessive drinking was responsible for an average of 93,296 deaths and 2.7 million years of potential life lost per year in the United States (Esser et al., 2020). Similarly, heavy alcohol consumption and binge drinking are associated with shorter lifespans (Nyberg et al., 2022). Alcohol ranks among the leading causes of global burden of disease, along with tobacco use, high blood pressure, being underweight during childhood, and unsafe sex. While some of these factors have a larger negative impact in developing regions, alcohol misuse has a major negative impact on disability adjusted life years (DALYs) in developed regions, including the United States (Ezzati et al., 2002). Between 2015 and 2019, the leading causes of alcohol-attributable deaths due to chronic conditions in the United States were liver disease (e.g., cirrhosis), cardiovascular disease, and cancer (NIAAA, 2024a). Other alcohol-related causes of death include severe alcohol withdrawal syndrome (Steel et al., 2021), traumatic injuries (e.g., due to alcohol-impaired driving and other risky behaviors), and suicide associated with alcohol misuse (NIAAA, 2024a). Chronic heavy alcohol use is associated with diabetes, gastrointestinal diseases, and fetal alcohol syndrome, which carry their own death tolls (see Figure 2).

## Alcohol misuse is comorbid with other serious health conditions

Alcohol use disorder is highly comorbid with chronic pain (Egli et al., 2012), traumatic stress disorders (Gilpin & Weiner, 2017), anxiety disorders (Castillo-Carniglia et al., 2019), major depressive disorder (Castillo-Carniglia et al., 2019), and schizophrenia (Castillo-Carniglia et al., 2019). AUD is also highly comorbid with diseases that affect organ systems other than the brain; for example, nonalcoholic steatohepatitis (NASH) liver disease (van Kleef et al., 2023) and infectious diseases such as HIV (Duko et al., 2019). Further complicating matters, individuals diagnosed with one substance use disorder (including alcohol) are more likely to exhibit misuse of or dependence on other substances (including alcohol) (Crummy et al., 2020).

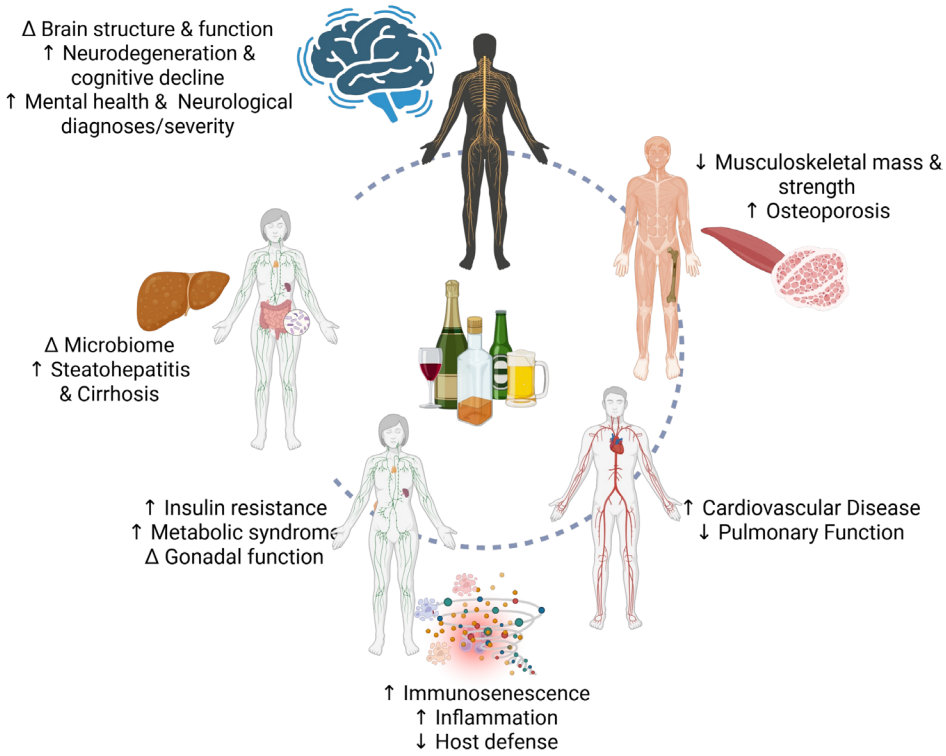


**FIGURE 2** Alcohol misuse is a major contributing factor to global health burden through its impact on multiple organ systems and diseases. Alcohol use increases the risk for many comorbid conditions, making alcohol the third leading lifestyle-related cause of mortality in Western civilization. The organ systems affected by alcohol include the liver, central nervous system, gastrointestinal tract, cardiovascular system, and musculoskeletal system.

### Alcohol misuse remains highly prevalent

Despite these economic and health burdens, treatment prevalence for AUD remains low (NIAAA, 2025a), probably due at least in part to ongoing stigma and inadequate healthcare provider training in the recognition and management of alcohol misuse. Alcohol misuse is linked to over 60 acute and chronic diseases (Im et al., 2023), with higher incidence observed in men. Approximately 18% of adults globally report heavy episodic drinking in the past month (World Health Organization, 2018); in the United States, 6.4% of males and 3.7% of females ages 12 and older report past-month heavy alcohol use (Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality, 2025a, 2025b).

Alcohol misuse in older adults has also increased, with age-related vulnerabilities that include multimorbidity, polypharmacy, reduced metabolic clearance, and cognitive decline heightening susceptibility to alcohol-related complications. Alcohol can interact with medications, disrupt sleep, and increase fall and injury risk in this population. Therefore, for adults over 65, recommended limits are no more than three drinks per day and seven drinks per week (Kuerbis et al., 2014; Meier & Seitz, 2008).

Alcohol misuse among women has risen significantly in recent years (NIAAA, 2025e). Women are more susceptible to alcohol-related harms and develop these conditions more rapidly and at lower intake levels than men. Biological differences, including lower average body weight and water content, reduce alcohol distribution volume in women. Additionally, women have lower concentrations of gastric alcohol dehydrogenase, resulting in reduced first-pass metabolism and higher blood alcohol concentrations for equivalent alcohol consumption, thereby increasing their risk of harm (Frezza et al., 1990).

## ALCOHOL MISUSE NEGATIVELY IMPACTS THE BRAIN

### Alcohol misuse leads to neurodegeneration and neuroinflammation

Chronic heavy alcohol use can lead to structural changes in the brain, including ventricular enlargement, cortical and subcortical gray matter volume loss, and white matter volume loss (Jernigan et al., 1991; Pfefferbaum et al., 1992), and these effects are modified by age (Pfefferbaum et al., 1992) and sex (Pfefferbaum et al., 2001). Thiamine deficiency associated with heavy alcohol use can lead to neurotoxicity and neuronal death, eventually leading to Wernicke–Korsakoff Syndrome, which is characterized by brain damage and cognitive impairment (Nutt et al., 2021). More recently, excessive alcohol use has received attention as a risk factor

ALCOHOL CLINICAL & EXPERIMENTAL RESEARCH ISBRA



for Alzheimer's disease and other dementias (Anton et al., 2025), an issue of rapidly escalating concern in an aging population (Urban Institute, 2024). Alcohol promotes brain inflammation, and heavy alcohol use during adolescence can have lasting effects on the brain (into adulthood) via increases in transcription of proinflammatory factors (Crews et al., 2024). Finally, chronic heavy alcohol use damages small and large peripheral nerves, culminating in what is termed "alcoholic neuropathy," which results from both direct toxic effects of alcohol and vitamin deficiency, and manifests clinically as sensorimotor deficits (Hammoud & Jimenez-Shahed, 2019; Noble & Weimer, 2014).

### Alcohol misuse alters brain function

Alcohol easily permeates the blood–brain barrier, and it is likely that no brain region, no brain cell type, and no brain circuit is spared from the effects of ingested alcohol (Gilpin, 2022; Gilpin & Koob, 2008). Acute alcohol intoxication leads to impairment of sensorimotor (Lovinger, 2025) and cognitive function (Garrisson et al., 2021) that eventually recovers once alcohol is metabolized and excreted, but chronic heavy alcohol use can lead to lasting or even permanent sensorimotor (Lovinger, 2025) and cognitive impairments (Sullivan & Pfefferbaum, 2019). Acute alcohol has rewarding effects during intoxication that promote continued and escalated use (Gilpin & Koob, 2008), but chronic heavy alcohol use leads to reward deficits (i.e., anhedonia) during abstinence, which promotes subsequent alcohol use (Koob & Vendruscolo, 2023). Similarly, acute alcohol reduces stress, anxiety, and pain, likely explaining its misuse in specific subsets of individuals, including those with pre-existing conditions (i.e., using alcohol as self-medication) (Egli et al., 2012; Koob & Vendruscolo, 2023), but chronic heavy alcohol use leads to higher stress, anxiety, and pain during periods without alcohol. Collectively, this leads to a vicious cycle in which the user experiences desirable effects during consumption, followed by aversive effects during withdrawal that promote subsequent continued intake (Koob & Le Moal, 2001). This progressively worsening cycle is defined by drug tolerance over time (i.e., the same alcohol dose has less effect after chronic use, leading to higher dose intake), and worsening of withdrawal symptoms over time due to higher doses that are consumed in more advanced stages of the disease. Decades of work have uncovered nuanced roles for specific brain regions, cells, and circuits in mediating specific effects of acute and chronic alcohol. This neuroscience research has led to the development of two of the three medications currently approved by the FDA for use in people with AUD: naltrexone and acamprosate both target the brain, whereas disulfiram targets alcohol metabolism. While naltrexone and acamprosate work well for some people diagnosed with AUD, they do not work for many others diagnosed with AUD, highlighting the critical importance of continued work in this area.

## ALCOHOL MISUSE NEGATIVELY IMPACTS MULTIPLE ORGAN SYSTEMS

### Alcohol misuse negatively impacts the liver

Alcohol-associated liver disease (ALD) is one of the primary comorbidities associated with AUD, and the morbidity and mortality associated with advanced forms of disease outpaces that of any other steatotic liver diseases. ALD-associated cirrhosis is a leading cause for both liver transplants and hepatocellular carcinoma in the United States. The complex pathophysiology of this disease, frequent confounding factors and comorbidities, as well as challenging diagnostic criteria are among reasons why effective therapies for ALD are lacking. The underlying pathology of ALD ranges from steatosis to cirrhosis-related liver failure (Aslam & Kwo, 2023). Progression beyond steatosis involves inflammation, immune infiltration, and ECM remodeling, termed alcohol-associated hepatitis (AH) with or without fibrosis (Mullish & Thursz, 2024). The most severe stage of ALD is cirrhosis, defined by nodular formation and significant replacement of hepatic parenchyma by fibrous septae, which impede intrahepatic blood flow and contribute to portosystemic shunting (Hernandez-Evole et al., 2024).

The rising incidence of obesity and metabolic syndrome has unveiled the overlap between metabolic stress and alcohol-associated liver injury (Diaz et al., 2023). The multiple shared mechanistic pathways leading to steatosis and inflammation synergize to increase the risk for steatotic liver disease. Epidemiological evidence indicates that individuals with alcohol misuse frequently have at least one cardiometabolic risk factor and develop more severe liver injury than individuals with similar cardiovascular risk factors that do not consume alcohol (Seitz & Neuman, 2021). These observations emphasize the greater comorbidity risk in persons with AUD and the need for better educational and preventive measures among individuals that misuse alcohol and in the population at large.

### Alcohol misuse negatively impacts cardiovascular function

Until recently, moderate and light alcohol drinking had long been considered cardioprotective. However, more rigorous examination of data reflecting a J-shaped curve—where low-to-moderate drinking is cardioprotective and heavy drinking increases cardiovascular risk—has raised concerns due to those studies reflecting limited populations or having low sample sizes (Israelsen et al., 2024). Lack of randomized controlled trials to confirm the benefits of alcohol on cardiovascular health is notable. While low levels of alcohol consumption may exert some cardioprotective benefits, significant evidence indicates that chronic heavy consumption of alcohol has detrimental effects on the cardiovascular system (Guzzo-Merello et al., 2014; Mirijello et al., 2017). Alcohol misuse is a significant risk factor for a range of cardiovascular diseases, including heart

failure (HF), hypertension, and arrhythmias (Ettinger et al., 1978; Klatsky, 2004). Pathophysiological mechanisms of alcohol-induced cardiovascular risk include cardiac hypertrophy, oxidative stress, mitochondrial damage, apoptosis, altered protein turnover, and development of cardiac fibrosis (Piano & Phillips, 2014). Alcohol-associated cardiac myopathy (ACM), characterized by left-ventricular hypertrophy, dilation of the heart chambers, and reduced ejection fraction, impairs cardiac function (Figueredo & Patel, 2023). In the United States, ACM is a leading cause of non-ischemic dilated cardiomyopathy, with approximately 21% to 32% of cases attributed to long-term alcohol use.

Alcohol also produces indirect cardiovascular effects through increased sympathetic nervous system (SNS) activity and activation of the renin–angiotensin–aldosterone system (RAAS), which increase blood pressure and cardiac afterload (Bigalke et al., 2024; Gardner & Mouton, 2015; Kawano, 2010; van de Borne et al., 1997). Persistent RAAS activation contributes to SNS stimulation and myocardial stress, promoting adverse ventricular remodeling and hypertrophy (Vacca et al., 2023). Alcohol is further linked to increased endothelin-1 production and reduced nitric oxide (NO) bioavailability, resulting in vasoconstriction, impaired coronary microcirculation, and exacerbated myocardial dysfunction. Epidemiological, clinical, and preclinical studies indicate that heavy alcohol consumption increases the risk of hypertension (Husain et al., 2014). In recent years, cardiovascular disease (CVD) deaths related to substance use have significantly increased, with alcohol being the most common psychoactive substance associated with CVD mortality. While abstinence can result in partial or full cardiac recovery, chronic alcohol misuse leads to irreversible myocardial damage and end-stage heart failure.

## Alcohol misuse negatively impacts pulmonary function

Among the respiratory complications arising from chronic alcohol use are pneumonia, aspiration, and acute respiratory distress syndrome (ARDS) (Moss & Burnham, 2003; Nielsen et al., 2024). Alcohol increases the risk of ARDS by priming the lung for exaggerated inflammatory responses during sepsis (Nelson & Kolls, 2002), trauma, or pneumonia, leading to increased requirements for mechanical ventilation and higher ICU mortality rates (Mehta & Guidot, 2017). Individuals with chronic alcohol use who smoke are at a higher risk of lung cancer (Guidot & Hart, 2005). Alcohol impairs pulmonary function by altering central respiratory control, damaging the alveolar-capillary barrier, and impairing respiratory muscle performance, and many of these changes are only unmasked by secondary insults such as infection, surgery, or trauma.

## Alcohol misuse negatively impacts endocrine function

Alcohol can disrupt endocrine function through its effects on neurotransmitter production, hormone levels, and substrate concentrations (Rachdaoui & Sarkar, 2017), manifesting in conditions such as hypothyroidism, stress intolerance, impaired reproductive function, osteoporosis, and growth retardation.

Alcohol reduces nocturnal plasma levels of growth hormone (GH), the principal driver of longitudinal growth, and diminishes tissue responsiveness to GH and insulin-like growth factor-1 (IGF-1) (De Marinis et al., 1993; McCullar et al., 2024). Suppression of the GH/IGF-1 axis is particularly detrimental during adolescence, a period of high-risk alcohol use, and during disease states. Chronic alcohol use also elevates circulating prolactin levels (hyperprolactinemia) in both men and women (Rachdaoui & Sarkar, 2017), which suppresses gonadotropin-releasing hormone (GnRH) release, leading to amenorrhea and galactorrhea in women, and decreased libido, reduced spermatogenesis, and gynecomastia in men. Additionally, chronic alcohol consumption lowers circulating antidiuretic hormone (ADH) levels and impairs the hypovolemia-induced ADH response, compromising homeostatic mechanisms essential for restoring blood volume following hemorrhage (Linkola et al., 1978; Taivainen et al., 1995).

Dysfunction of the hypothalamic–pituitary–thyroid (HPT) axis, commonly observed in individuals with AUD, contributes to behavioral manifestations associated with alcohol misuse, including depression (Sagaram et al., 2022). Alcohol-associated HPT disruption is characterized by decreased circulating thyroid hormone levels, decreased thyroid volume, increased fibrosis, and altered peripheral thyroid hormone metabolism (Baumgartner et al., 1994; Heinz et al., 1996; Majumdar et al., 1981).

Alcohol misuse is also linked to altered bone metabolism, reduced bone mineral density and mass, and an increased risk of fractures—even in the absence of liver disease (Gaddini et al., 2016; Ke et al., 2023; Zhang et al., 2015). The prevalence of osteoporosis among individuals with AUD exceeds 40%, partly due to attenuation of the hypothalamic–pituitary–gonadal (HPG) axis and associated reductions in circulating testosterone levels (Emanuele & Emanuele, 2001). Alcohol-related myopathy, decreased bone mineral content, and balance impairments resulting from alcohol intoxication further compound the risk of osteoporotic fractures and delayed fracture healing in aging individuals.

Heavy and chronic alcohol consumption is a major contributing factor to the development of pancreatitis (Samokhvalov et al., 2015). Alcohol intake exceeding 40 g/day is particularly detrimental, producing direct toxic effects on acinar cells, with pancreatic stellate cells implicated in the development of fibrosis. Although alcohol consumption alone rarely initiates pancreatitis, it sensitizes the pancreas to additional insults such as smoking, bacterial toxins, viral infections, and binge drinking (Setiawan et al., 2017) and contributes to the risk for pancreatic cancer.

Alcohol misuse is also an independent risk factor for type 2 diabetes mellitus (T2DM) (Cook et al., 2025; Rachdaoui & Sarkar, 2017; Wang et al., 2025) and reduced insulin secretion in response to a glucose load. Alcohol use is reported to increase beta cell apoptosis, decrease GABA receptor expression, elevate oxidative stress, reduce expression of insulin-secretion genes, and increase ghrelin secretion (Bansal et al., 2011; Dembele et al., 2009; Ford Jr. et al., 2016).

ALCOHOL CLINICAL & EXPERIMENTAL RESEARCH ISBRA



Alcohol use is associated with reduced glucagon-like peptide 1 (GLP-1) levels, an intestinal incretin that promotes insulin secretion (Farokhnia et al., 2022; Molina-Castro et al., 2024). Emerging evidence indicates that GLP-1 receptor agonists reduce alcohol consumption behaviors in animal models and may prevent alcohol-related adverse events in clinical populations (Leggio et al., 2023; Wium-Andersen et al., 2022). GLP-1-based therapies represent a promising strategy for treating AUD, potentially offering protection against alcohol-induced beta cell dysfunction.

Alcohol consumption disrupts stress-response pathways and the hypothalamic–pituitary–adrenal (HPA) axis, with alcohol's effects varying based on duration of use (Richardson et al., 2008). Acute alcohol exposure activates the HPA axis, increasing corticotropin-releasing factor (CRF), adrenocorticotropic hormone (ACTH), and glucocorticoid levels in a dose-dependent manner. In contrast, chronic alcohol use suppresses basal ACTH and glucocorticoid levels, decreases CRF mRNA expression, and attenuates pituitary responsiveness to CRF. Overall, chronic alcohol use blunts HPA axis responsiveness during baseline conditions and in response to stress, diminishes diurnal cortisol rhythms, and impairs glucocorticoid receptor sensitivity (Richardson et al., 2008). These neuroendocrine adaptations contribute to dysregulated stress responses, which are central to the pathophysiology of alcohol use disorder (AUD), mood disorders, and relapse vulnerability. Dysregulation of the HPA contributes to the pathophysiology of addiction, dependence, and relapse in AUD (King et al., 2006).

Circulating aldosterone levels positively correlate with alcohol consumption, craving, and anxiety in both preclinical models and humans (Leggio et al., 2008). Aldosterone levels rise during acute alcohol withdrawal and decline with abstinence. Additionally, actively drinking males exhibit a blunted angiotensin II-mediated aldosterone response, suggesting that dysregulation of the aldosterone–mineralocorticoid receptor (MR) pathway contributes to AUD, supporting MR antagonism as a promising therapeutic target (Aoun et al., 2018).

Chronic alcohol use also disrupts the hypothalamic–pituitary–gonadal (HPG) axis, resulting in reduced gonadotropin release, abnormal menstrual cycles, infertility, impotence, and decreased oocyte numbers (Li et al., 2013; Mendelson & Mello, 1988). In premenopausal women, heavy alcohol consumption is associated with elevated estrogen levels. In men, alcohol impairs reproductive function by reducing testosterone levels, semen volume, sperm count, and motility.

While alcohol's effects on some endocrine systems are better understood, many mechanisms underlying endocrine dysfunction in acute and chronic alcohol use remain unclear. Promising therapeutic approaches targeting the HPA axis, GLP-1 signaling, and MR pathways highlight the critical need for continued research in this area.

### Alcohol misuse negatively impacts the gut and microbiome

Acute and chronic alcohol consumption profoundly affects the gastrointestinal (GI) tract, increasing risk for gastritis, liver disease, portal hypertension, esophageal varices, pancreatitis, malabsorption, and nutritional deficiencies. Chronic use also increases risk for esophageal, gastric, and colorectal cancers (Rehm & Shield, 2020). Alcohol is classified as a Group 1 carcinogen by the International Agency for Research on Cancer (IARC), and in the United States, it is the third leading preventable cause of cancer after tobacco and obesity, contributing to approximately 100,000 cases and 20,000 deaths annually. Alcohol increases cancer risk via oxidative stress, inflammation, and interference with the uptake and metabolism of carcinogens.

Studies increasingly show that chronic alcohol use alters gut microbiome composition, leading to overgrowth of pathobionts and reduction in beneficial commensal bacteria (Day & Kumamoto, 2022). This dysbiosis contributes to intestinal inflammation and permeability, enabling translocation of toxins and microbial products that affect the liver and other organs (Hartmann et al., 2015; Leclercq et al., 2019). Overgrowth of pathogenic bacteria and reduction in Lactobacillus species are frequently observed in individuals with AUD.

### Alcohol misuse negatively impacts the musculoskeletal system

An often underrecognized consequence of chronic alcohol use is its detrimental effect on skeletal muscle (SKM), resulting in myopathy affecting up to 60% of individuals with AUD (Preedy et al., 1988; Simon et al., 2017), characterized by progressive muscle weakness, particularly in the proximal muscles, selective atrophy of type II glycolytic fibers, and reductions in both SKM mass and strength (Steiner & Lang, 2015). Alcohol-associated myopathy may occur independently of alcohol-associated nutritional and micronutrient deficiencies, is a frequent complication in patients with alcohol-related liver disease (ALD), and is further exacerbated by metabolic imbalances, nutritional deficiencies, and compounded by subclinical inflammation (Molina et al., 2014). In individuals with alcohol-associated cirrhosis, SKM loss is accelerated and is linked to increased mortality, particularly in females (Thapaliya et al., 2014), and aggravated by sedentary lifestyles.

## ALCOHOL RESEARCH IS CRITICAL FOR IMPROVING THE HEALTH OF AMERICANS

Alcohol use disorder is a chronic disease. AUD is highly prevalent with other chronic diseases, and AUD worsens outcomes associated with other chronic diseases. Chronic excessive alcohol use costs the US hundreds of billions of dollars, dwarfing the economic impact of most other drugs. Research in the field has definitively established AUD as a chronic disease impacting the brain, liver, and multiple organ systems contributing to the risk for and severity of several conditions including cardiovascular disease, pulmonary disease, musculoskeletal deficits, and impaired gastrointestinal

and endocrine function. Chronic excessive alcohol use worsens the health of Americans and accounts for tens of thousands of American deaths annually. Alcohol research funded by NIH has led to many successes over the past several decades, including the development of three FDA-approved medications for AUD, establishment of clinical guidelines regarding alcohol consumption during pregnancy, and increases in our understanding of chronic alcohol effects on multiple organ systems and various comorbid conditions. Each of these scientific advances has had major positive impacts on the health of Americans. In one way or another, it is likely that no US citizen is untouched by the consequences of AUD, and it is therefore likely that all US citizens benefit from biomedical alcohol research.

## ACKNOWLEDGMENTS

NWG thanks the D'Angelo family for their continuous support of alcohol & drug research activities through an endowed professorship at LSU Health New Orleans.

## CONFLICT OF INTEREST STATEMENT

NWG owns shares in Glauser Life Sciences, Inc., a company with interest in developing therapeutics for mental health disorders. The remaining authors declare no competing financial interests.

## DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

## ORCID

*Nicholas W. Gilpin* https://orcid.org/0000-0001-8901-8917
*Patricia E. Molina* https://orcid.org/0000-0002-3598-384X

## REFERENCES

Anton, P.E., Maphis, N.M., Linsenbardt, D.N. & Coleman, L.G., Jr. (2025) Excessive alcohol use as a risk factor for Alzheimer's disease: epidemiological and preclinical evidence. *Advances in Experimental Medicine and Biology*, 1473, 211–242.

Aoun, E.G., Jimenez, V.A., Vendruscolo, L.F., Walter, N.A.R., Barbier, E., Ferrulli, A. et al. (2018) A relationship between the aldosterone-mineralocorticoid receptor pathway and alcohol drinking: preliminary translational findings across rats, monkeys and humans. *Molecular Psychiatry*, 23, 1466–1473.

Aslam, A. & Kwo, P.Y. (2023) Epidemiology and disease burden of alcohol associated liver disease. *Journal of Clinical and Experimental Hepatology*, 13, 88–102.

Bansal, P., Wang, S., Liu, S., Xiang, Y.Y., Lu, W.Y. & Wang, Q. (2011) GABA coordinates with insulin in regulating secretory function in pancreatic INS-1 beta-cells. *PLoS One*, 6, e26225.

Baumgartner, A., Rommelspacher, H., Otto, M., Schmidt, L.G., Kurten, I., Graf, K.J. et al. (1994) Hypothalamic-pituitary-thyroid (HPT) axis in chronic alcoholism. I. HPT axis in chronic alcoholics during withdrawal and after 3 weeks of abstinence. *Alcoholism, Clinical and Experimental Research*, 18, 284–294.

Bigalke, J.A., Greenlund, I.M., Solis-Montenegro, T.X., Durocher, J.J., Joyner, M.J. & Carter, J.R. (2024) Binge alcohol consumption elevates sympathetic transduction to blood pressure: a randomized controlled trial. *Hypertension*, 81, 2140–2151.

Castillo-Carniglia, A., Keyes, K.M., Hasin, D.S. & Cerda, M. (2019) Psychiatric comorbidities in alcohol use disorder. *Lancet Psychiatry*, 6, 1068–1080.

Cook, S., Saxena, S., Mathur, R., Beaney, T., Gnani, S., Neves, A.L. et al. (2025) Diabetes complications in people with alcohol use disorder and type 2 diabetes. *BJGP Open*, 9, BJGPO.2024.0133.

Crews, F.T., Coleman, L.G., Jr., Macht, V.A. & Vetreno, R.P. (2024) Alcohol, HMGB1, and innate immune signaling in the brain. *Alcohol Research: Current Reviews*, 44, 4.

Crummy, E.A., O'Neal, T.J., Baskin, B.M. & Ferguson, S.M. (2020) One is not enough: understanding and modeling polysubstance use. *Frontiers in Neuroscience*, 14, 569.

Day, A.W. & Kumamoto, C.A. (2022) Gut microbiome dysbiosis in alcoholism: consequences for health and recovery. *Frontiers in Cellular and Infection Microbiology*, 12, 840164.

De Marinis, L., Mancini, A., Fiumara, C., Conte, G., Iacona, T., Ianiri, L. et al. (1993) Growth hormone response to growth hormone-releasing hormone in early abstinent alcoholic patients. *Psychoneuroendocrinology*, 18, 475–483.

Dembele, K., Nguyen, K.H., Hernandez, T.A. & Nyomba, B.L. (2009) Effects of ethanol on pancreatic beta-cell death: interaction with glucose and fatty acids. *Cell Biology and Toxicology*, 25, 141–152.

Diaz, L.A., Arab, J.P., Louvet, A., Bataller, R. & Arrese, M. (2023) The intersection between alcohol-related liver disease and nonalcoholic fatty liver disease. *Nature Reviews. Gastroenterology & Hepatology*, 20, 764–783.

Duko, B., Ayalew, M. & Ayano, G. (2019) The prevalence of alcohol use disorders among people living with HIV/AIDS: a systematic review and meta-analysis. *Substance Abuse Treatment, Prevention, and Policy*, 14, 52.

Egli, M., Koob, G.F. & Edwards, S. (2012) Alcohol dependence as a chronic pain disorder. *Neuroscience and Biobehavioral Reviews*, 36, 2179–2192.

Emanuele, M.A. & Emanuele, N. (2001) Alcohol and the male reproductive system. *Alcohol Research & Health*, 25, 282–287.

Esser, M.B., Sherk, A., Liu, Y., Naimi, T.S., Stockwell, T., Stahre, M. et al. (2020) Deaths and years of potential life lost from excessive alcohol use — United States, 2011–2015. *Morbidity and Mortality Weekly Report*, 69, 981–987.

Ettinger, P.O., Wu, C.F., Cruz, C.D.L., Weisse, A.B., Sultan Ahmed, S. & Regan, T.J. (1978) Arrhythmias and the "holiday heart": Alcoholassociated cardiac rhythm disorders. *American Heart Journal*, 95, 555–562.

Ezzati, M., Lopez, A.D., Rodgers, A., Vander Hoorn, S., Murray, C.J. & Comparative Risk Assessment Collaborating, G. (2002) Selected major risk factors and global and regional burden of disease. *Lancet*, 360, 1347–1360.

Farokhnia, M., Fede, S.J., Grodin, E.N., Browning, B.D., Crozier, M.E., Schwandt, M.L. et al. (2022) Differential association between the GLP1R gene variants and brain functional connectivity according to the severity of alcohol use. *Scientific Reports*, 12, 13027.

Figueredo, V.M. & Patel, A. (2023) Detrimental effects of alcohol on the heart: hypertension and cardiomyopathy. *Reviews in Cardiovascular Medicine*, 24, 292.

Ford, S.M., Jr., Simon, L., Vande Stouwe, C., Allerton, T., Mercante, D.E., Byerley, L.O. et al. (2016) Chronic binge alcohol administration impairs glucose-insulin dynamics and decreases adiponectin in asymptomatic simian immunodeficiency virus-infected macaques. *American Journal of Physiology. Regulatory, Integrative and Comparative Physiology*, 311, R888–R897.

Frezza, M., Padova, C., Pozzato, G., Terpin, M., Baraona, E. & Lieber, C.S. (1990) High blood alcohol levels in women. *New England Journal of Medicine*, 322, 95–99.

Gaddini, G.W., Turner, R.T., Grant, K.A. & Iwaniec, U.T. (2016) Alcohol: a simple nutrient with complex actions on bone in the adult skeleton. *Alcoholism, Clinical and Experimental Research*, 40, 657–671.

Gardner, J.D. & Mouton, A.J. (2015) Alcohol effects on cardiac function. *Comprehensive Physiology*, 5, 791–802.

Garrisson, H., Scholey, A., Ogden, E. & Benson, S. (2021) The effects of alcohol intoxication on cognitive functions critical for driving: a systematic review. *Accident; Analysis and Prevention*, 154, 106052.

Gilpin, N.W. (2022) *Neurocircuitry of addiction*, 1st edition. London, UK: Elsevier.

Gilpin, N.W. & Koob, G.F. (2008) Neurobiology of alcohol dependence: focus on motivational mechanisms. *Alcohol Research & Health*, 31, 185–195.

Gilpin, N.W. & Weiner, J.L. (2017) Neurobiology of comorbid post-traumatic stress disorder and alcohol-use disorder. *Genes, Brain, and Behavior*, 16, 15–43.

Guidot, D.M. & Hart, C.M. (2005) Alcohol abuse and acute lung injury: epidemiology and pathophysiology of a recently recognized association. *Journal of Investigative Medicine*, 53, 235–245.

Guzzo-Merello, G., Cobo-Marcos, M., Gallego-Delgado, M. & Garcia-Pavia, P. (2014) Alcoholic cardiomyopathy. *World Journal of Cardiology*, 6, 771–781.

Hammoud, N. & Jimenez-Shahed, J. (2019) Chronic neurologic effects of alcohol. *Clinics in Liver Disease*, 23, 141–155.

Hartmann, P., Seebauer, C.T. & Schnabl, B. (2015) Alcoholic liver disease: the gut microbiome and liver cross talk. *Alcoholism, Clinical and Experimental Research*, 39, 763–775.

Heilig, M., MacKillop, J., Martinez, D., Rehm, J., Leggio, L. & Vanderschuren, L. (2021) Addiction as a brain disease revised: why it still matters, and the need for consilience. *Neuropsychopharmacology*, 46, 1715–1723.

Heinz, A., Bauer, M., Kuhn, S., Kruger, F., Graf, K.J., Rommelspacher, H. et al. (1996) Long-term observation of the hypothalamic-pituitary-thyroid (HPT) axis in alcohol-dependent patients. *Acta Psychiatrica Scandinavica*, 93, 470–476.

Henry, T.A. (2019) *Court listened to AMA on defining alcoholism as a disease, not a crime*. American Medical Association.

Hernandez-Evole, H., Jimenez-Esquivel, N., Pose, E. & Bataller, R. (2024) Alcohol-associated liver disease: epidemiology and management. *Annals of Hepatology*, 29, 101162.

Husain, K., Ansari, R.A. & Ferder, L. (2014) Alcohol-induced hypertension: mechanism and prevention. *World Journal of Cardiology*, 6, 245–252.

Im, P.K., Wright, N., Yang, L., Chan, K.H., Chen, Y., Guo, Y. et al. (2023) Alcohol consumption and risks of more than 200 diseases in Chinese men. *Nature Medicine*, 29, 1476–1486.

Israelsen, M., Torp, N., Johansen, S., Hansen, C.D., Hansen, E.D., Thorhauge, K. et al. (2024) Validation of the new nomenclature of steatotic liver disease in patients with a history of excessive alcohol intake: an analysis of data from a prospective cohort study. *The Lancet Gastroenterology & Hepatology*, 9, 218–228.

Jernigan, T.L., Butters, N., DiTraglia, G., Schafer, K., Smith, T., Irwin, M. et al. (1991) Reduced cerebral grey matter observed in alcoholics using magnetic resonance imaging. *Alcoholism, Clinical and Experimental Research*, 15, 418–427.

Kawano, Y. (2010) Physio-pathological effects of alcohol on the cardiovascular system: its role in hypertension and cardiovascular disease. *Hypertension Research*, 33, 181–191.

Ke, Y., Hu, H., Zhang, J., Yuan, L., Li, T., Feng, Y. et al. (2023) Alcohol consumption and risk of fractures: a systematic review and dose-response meta-analysis of prospective cohort studies. *Advances in Nutrition*, 14, 599–611.

King, A., Munisamy, G., de Wit, H. & Lin, S. (2006) Attenuated cortisol response to alcohol in heavy social drinkers. *International Journal of Psychophysiology*, 59, 203–209.

Klatsky, A.L. (2004) Alcohol-associated hypertension. *Hypertension*, 44, 805–806.

Koob, G.F. & Le Moal, M. (2001) Drug addiction, dysregulation of reward, and allostasis. *Neuropsychopharmacology*, 24, 97–129.

Koob, G.F. & Vendruscolo, L. (2023) Theoretical frameworks and mechanistic aspects of alcohol addiction: alcohol addiction as a reward deficit/stress surfeit disorder. *Current Topics in Behavioral Neurosciences*, 71, 17–77.

Kuerbis, A., Sacco, P., Blazer, D.G. & Moore, A.A. (2014) Substance abuse among older adults. *Clinics in Geriatric Medicine*, 30, 629–654.

Leclercq, S., Starkel, P., Delzenne, N.M. & de Timary, P. (2019) The gut microbiota: a new target in the management of alcohol dependence? *Alcohol*, 74, 105–111.

Leggio, L., Ferrulli, A., Cardone, S., Miceli, A., Kenna, G.A., Gasbarrini, G. et al. (2008) Renin and aldosterone but not the natriuretic peptide correlate with obsessive craving in medium-term abstinent alcohol-dependent patients: a longitudinal study. *Alcohol*, 42, 375–381.

Leggio, L., Hendershot, C.S., Farokhnia, M., Fink-Jensen, A., Klausen, M.K., Schacht, J.P. et al. (2023) GLP-1 receptor agonists are promising but unproven treatments for alcohol and substance use disorders. *Nature Medicine*, 29, 2993–2995.

Leshner, A.I. (1997) Addiction is a brain disease, and it matters. *Science*, 278, 45–47.

Li, N., Fu, S., Zhu, F., Deng, X. & Shi, X. (2013) Alcohol intake induces diminished ovarian reserve in childbearing age women. *The Journal of Obstetrics and Gynaecology Research*, 39, 516–521.

Linkola, J., Ylikahri, R., Fyhquist, F. & Wallenius, M. (1978) Plasma vasopressin in ethanol intoxication and hangover. *Acta Physiologica Scandinavica*, 104, 180–187.

Lovinger, D.M. (2025) Alcohol effects on associative and sensorimotor cortico-thalamo-basal ganglia circuits alter decision making and alcohol intake. *Alcohol*, 127, 21–46.

Majumdar, S.K., Shaw, G.K., O'Gorman, P., Aps, E.J. & Thomson, A.D. (1981) Thyroid status in patients with alcoholic liver disease. *Drug and Alcohol Dependence*, 7, 389–391.

Marshall, T. & Supreme Court of the United States. (1967) *U.S. Reports: Powell v. Texas, 392 U.S. 514, in Series U.S. Reports: Powell v. Texas, 392 U.S. 514*.

McCullar, K.S., Barker, D.H., McGeary, J.E., Saletin, J.M., Gredvig-Ardito, C., Swift, R.M. et al. (2024) Altered sleep architecture following consecutive nights of presleep alcohol. *Sleep*, 47, zsae003.

Mehta, A.J. & Guidot, D.M. (2017) Alcohol and the lung. *Alcohol Research: Current Reviews*, 38, 243–254.

Meier, P. & Seitz, H.K. (2008) Age, alcohol metabolism and liver disease. *Current Opinion in Clinical Nutrition and Metabolic Care*, 11, 21–26.

Mendelson, J.H. & Mello, N.K. (1988) Chronic alcohol effects on anterior pituitary and ovarian hormones in healthy women. *The Journal of Pharmacology and Experimental Therapeutics*, 245, 407–412.

Mirijello, A., Tarli, C., Vassallo, G.A., Sestito, L., Antonelli, M., d'Angelo, C. et al. (2017) Alcoholic cardiomyopathy: what is known and what is not known. *European Journal of Internal Medicine*, 43, 1–5.

Molina, P.E., Gardner, J.D., Souza-Smith, F.M. & Whitaker, A.M. (2014) Alcohol abuse: critical pathophysiological processes and contribution to disease burden. *Physiology (Bethesda)*, 29, 203–215.

Molina-Castro, M., Seyedsadjadi, N., Nieto, D., Leggio, L., Rowitz, B. & Pepino, M.Y. (2024) The glucagon-like peptide-1 and other endocrine responses to alcohol ingestion in women with versus without metabolic surgery. *Addiction Biology*, 29, e13441.

Moss, M. & Burnham, E.L. (2003) Chronic alcohol abuse, acute respiratory distress syndrome, and multiple organ dysfunction. *Critical Care Medicine*, 31, S207–S212.

Mullish, B.H. & Thursz, M.R. (2024) Alcohol-associated liver disease: emerging therapeutic strategies. *Hepatology*, 80, 1372–1389.

Nathan, P.E., Conrad, M. & Skinstad, A.H. (2016) History of the concept of addiction. *Annual Review of Clinical Psychology*, 12, 29–51.

National Institute on Alcohol Abuse and Alcoholism. (2024a) *Alcohol-related emergencies and deaths in the United States*, in Series Alcohol-Related Emergencies and Deaths in the United States, NIAAA. https://www.niaaa.nih.gov/alcohols-effects-health/alcohol-topics-z/alcohol-facts-and-statistics/alcohol-related-emergencies-and-deaths-united-states

National Institute on Alcohol Abuse and Alcoholism. (2024b) *FY 2024 financial management plan*, in Series FY 2024 Financial Management Plan, NIAAA.

National Institute on Alcohol Abuse and Alcoholism. (2025a) *Alcohol treatment in the United States*, in Series Alcohol Treatment in the United States, NIAAA. https://www.niaaa.nih.gov/alcohols-effects-health/alcohol-topics-z/alcohol-facts-and-statistics/alcohol-treatment-united-states

National Institute on Alcohol Abuse and Alcoholism. (2025b) *National Institute on Alcohol Abuse and Alcoholism (NIAAA)*, in Series National Institute on Alcohol Abuse and Alcoholism (NIAAA), NIAAA. https://www.niaaa.nih.gov/our-work/mission-statement

National Institute on Alcohol Abuse and Alcoholism. (2025c) *Understanding alcohol drinking patterns*, in Series Understanding Alcohol Drinking Patterns, NIAAA. https://www.niaaa.nih.gov/alcohols-effects-health/alcohol-drinking-patterns

National Institute on Alcohol Abuse and Alcoholism. (2025d) *Understanding alcohol use disorder*, in Series Understanding Alcohol Use Disorder, NIAAA. https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/understanding-alcohol-use-disorder

National Institute on Alcohol Abuse and Alcoholism. (2025e) *Women and alcohol*, in Series Women and Alcohol, NIAAA. https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/women-and-alcohol

Nelson, S. & Kolls, J.K. (2002) Alcohol, host defence and society. *Nature Reviews. Immunology*, 2, 205–209.

Nielsen, L.B., Johansen, M.O., Riddersholm, S.J. & Weinreich, U.M. (2024) The association between alcohol consumption and pulmonary function: a scoping review. *European Respiratory Review*, 33, 230233.

Noble, J.M. & Weimer, L.H. (2014) Neurologic complications of alcoholism. *Continuum (Minneapolis, Minn.)*, 20, 624–641.

Nutt, D., Hayes, A., Fonville, L., Zafar, R., Palmer, E.O.C., Paterson, L. et al. (2021) Alcohol and the brain. *Nutrients*, 13, 3938.

Nyberg, S.T., Batty, G.D., Pentti, J., Madsen, I.E.H., Alfredsson, L., Bjorner, J.B. et al. (2022) Association of alcohol use with years lived without major chronic diseases: a multicohort study from the IPD-work consortium and UK biobank. *The Lancet Regional Health - Europe*, 19, 100417.

Pfefferbaum, A., Lim, K.O., Zipursky, R.B., Mathalon, D.H., Rosenbloom, M.J., Lane, B. et al. (1992) Brain gray and white matter volume loss accelerates with aging in chronic alcoholics: a quantitative MRI study. *Alcoholism, Clinical and Experimental Research*, 16, 1078–1089.

Pfefferbaum, A., Rosenbloom, M., Deshmukh, A. & Sullivan, E. (2001) Sex differences in the effects of alcohol on brain structure. *American Journal of Psychiatry*, 158, 188–197.

Piano, M.R. & Phillips, S.A. (2014) Alcoholic cardiomyopathy: pathophysiologic insights. *Cardiovascular Toxicology*, 14, 291–308.

Preedy, V.R., Duane, P. & Peters, T.J. (1988) Comparison of the acute effects of ethanol on liver and skeletal muscle protein synthesis in the rat. *Alcohol and Alcoholism*, 23, 155–162.

Rachdaoui, N. & Sarkar, D.K. (2017) Pathophysiology of the effects of alcohol abuse on the endocrine system. *Alcohol Research: Current Reviews*, 38, 255–276.

Rehm, J. & Shield, K. (2020) Alcohol use and cancers of the gastrointestinal tract. Epidemiology and preventive implications. *Frontiers in Oncology*, 10, 403.

Richardson, H.N., Lee, S.Y., O'Dell, L.E., Koob, G.F. & Rivier, C.L. (2008) Alcohol self-administration acutely stimulates the hypothalamic-pituitary-adrenal axis, but alcohol dependence leads to a dampened neuroendocrine state. *European Journal of Neuroscience*, 28, 1641–1653.

Sacks, J.J., Gonzales, K.R., Bouchery, E.E., Tomedi, L.E. & Brewer, R.D. (2015) 2010 national and state costs of excessive alcohol consumption. *American Journal of Preventive Medicine*, 49, e73–e79.

Sagaram, M., Royer, A.J., Hu, H., Rajhans, A., Parthasarathy, R., Krishnasamy, S.S. et al. (2022) Illustration of gut-thyroid axis in alcohol use disorder: interplay of gut dysfunction, pro-inflammatory responses, and thyroid function. *Cells*, 11, 3100.

Samokhvalov, A.V., Rehm, J. & Roerecke, M. (2015) Alcohol consumption as a risk factor for acute and chronic pancreatitis: a systematic review and a series of meta-analyses. *eBioMedicine*, 2, 1996–2002.

Seitz, H.K. & Neuman, M.G. (2021) The history of alcoholic liver disease: from an unrecognized disease to one of the most frequent diseases in hepatology. *Journal of Clinical Medicine*, 10, 858.

Setiawan, V.W., Monroe, K., Lugea, A., Yadav, D. & Pandol, S. (2017) Uniting epidemiology and experimental disease models for alcohol-related pancreatic disease. *Alcohol Research: Current Reviews*, 38, 173–182.

Simon, L., Jolley, S.E. & Molina, P.E. (2017) Alcoholic myopathy: pathophysiologic mechanisms and clinical implications. *Alcohol Research: Current Reviews*, 38, 207–217.

Steel, T.L., Afshar, M., Edwards, S., Jolley, S.E., Timko, C., Clark, B.J. et al. (2021) Research needs for inpatient Management of Severe Alcohol Withdrawal Syndrome: an official American Thoracic Society research statement. *American Journal of Respiratory and Critical Care Medicine*, 204, e61–e87.

Steiner, J.L. & Lang, C.H. (2015) Dysregulation of skeletal muscle protein metabolism by alcohol. *American Journal of Physiology. Endocrinology and Metabolism*, 308, E699–E712.

Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. (2025a) *2024 National Survey on Drug Use and Health. Table 2.29A-Heavy alcohol use in past month: among people aged 12 or older; by age group and demographic characteristics, numbers in thousands, 2023 and 2024, in Series 2024 National Survey on Drug Use and Health. Table 2.29A-Heavy alcohol use in past month: among people aged 12 or older; by age group and demographic characteristics, numbers in thousands, 2023 and 2024*, Substance Abuse and Mental Health Services Administration, Rockville, MD.

Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. (2025b) *2024 National Survey on Drug Use and Health. Table 2.29B-Heavy alcohol use in past month: among people aged 12 or older; by age group and demographic characteristics, percentages, 2023 and 2024, in Series 2024 National Survey on Drug Use and Health. Table 2.29B-Heavy alcohol use in past month: among people aged 12 or older; by age group and demographic characteristics, percentages, 2023 and 2024*, Substance Abuse and Mental Health Services Administration, Rockville, MD.

Sullivan, E.V. & Pfefferbaum, A. (2019) Brain-behavior relations and effects of aging and common comorbidities in alcohol use disorder: a review. *Neuropsychology*, 33, 760–780.

Taivainen, H., Laitinen, K., Tahtela, R., Kilanmaa, K. & Valimaki, M.J. (1995) Role of plasma vasopressin in changes of water balance accompanying acute alcohol intoxication. *Alcoholism, Clinical and Experimental Research*, 19, 759–762.

Thapaliya, S., Runkana, A., McMullen, M.R., Nagy, L.E., McDonald, C., Naga Prasad, S.V. et al. (2014) Alcohol-induced autophagy contributes to loss in skeletal muscle mass. *Autophagy*, 10, 677–690.

Trump, D.J. (2025) *Executive Order 14212 - Establishing the President's Make America Healthy Again Commission*, in Series Executive Order 14212 - Establishing the President's Make America Healthy Again

Commission, Office of the Federal Register, National Archives and Records Administration.

U.S. Centers for Disease Control and Prevention. (2024) *Addressing Excessive Alcohol Use: State Fact Sheets*, in Series addressing excessive alcohol use: state fact sheets, Centers for Disease Control and Prevention, Atlanta, GA.

Urban Institute. (2024) *The US population is aging*, in Series The US Population is Aging, Urban Institute.

Vacca, A., Bulfone, L., Cicco, S., Brosolo, G., Da Porto, A., Soardo, G. et al. (2023) Alcohol intake and arterial hypertension: retelling of a multifaceted story. *Nutrients*, 15, 958.

van de Borne, P., Mark, A.L., Montano, N., Mion, D. & Somers, V.K. (1997) Effects of alcohol on sympathetic activity, hemodynamics, and chemoreflex sensitivity. *Hypertension*, 29, 1278–1283.

van Kleef, L.A., de Knegt, R.J. & Brouwer, W.P. (2023) Metabolic dysfunction-associated fatty liver disease and excessive alcohol consumption are both independent risk factors for mortality. *Hepatology*, 77, 942–948.

Wang, J.J., Peng, Q., Kang, H.L., Jiang, Y., Zhang, H.W., Zhang, D.D. et al. (2025) Exploring the effects of effective parts of Schisandra sphenanthera on the gut-brain Axis of type 2 diabetes mellitus rats based on metabolomic and proteomic approaches. *Chemistry & Biodiversity*, 22, e00682.

Wium-Andersen, I.K., Wium-Andersen, M.K., Fink-Jensen, A., Rungby, J., Jorgensen, M.B. & Osler, M. (2022) Use of GLP-1 receptor agonists and subsequent risk of alcohol-related events. A nationwide register-based cohort and self-controlled case series study. *Basic & Clinical Pharmacology & Toxicology*, 131, 372–379.

World Health Organization. (2018) *Global status report on alcohol and health 2018*, in series global status report on alcohol and health 2018, World Health Organization, Geneva.

Zhang, X., Lin, J., Yang, X., Fei, Q., Wang, B., Yang, Y. et al. (2015) Investigation of osteoporosis prevalence and osteoporosis-related clinical risk factors among healthy elderly male. *Zhonghua Yi Xue Za Zhi*, 95, 3366–3369.

**How to cite this article:** Gilpin, N.W. & Molina, P.E. (2026) Alcohol use disorder is a chronic disease. *Alcohol: Clinical and Experimental Research*, 50, 1–11. Available from: https://doi.org/10.1111/acer.70230