# RESEARCH REVIEW ON ALCOHOL MISUSE AFTER TRAUMATIC BRAIN INJURY

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## PURPOSE

The purpose of this Research Review is to summarize published, peer-reviewed scientific literature on alcohol use disorder (AUD) after traumatic brain injury (TBI) with a primary focus on the military population. Topics include the characteristics, risk factors, impact, pathophysiology, evaluation, and management of alcohol misuse and AUD.

**Information in this Research Review is current as of June 2024 and is subject to change given emerging research and evidence.**

## BACKGROUND

TBI frequently impacts active duty military service members and veterans, with blast exposure as a common mechanism of injury.[1-5] Based on the duration of neurological dysfunction resulting from head injury and the presence of clinical signs evaluated through the Glasgow Coma Scale (GCS), TBIs are currently classified as mild, moderate, or severe.[6] Mild TBI (mTBI) is most common in both the general population and the military[7] and is characterized by a GCS score of 13–15, confusion or disorientation lasting less than 24 hours, and loss of consciousness (LOC) for up to 30 minutes, which may be accompanied by memory loss lasting less than 24 hours.[6] TBI can initiate the progressive development of adverse health-related outcomes, and even mTBI can cause persistent symptoms, including somatic, cognitive, and emotional or behavioral problems.[8] Additionally, various pre- and post-injury factors (e.g., social and environmental factors, demographic factors, mental health disorders) may contribute to the development of addictive behaviors after TBI, including alcohol misuse and AUD.

AUD is considered a problematic pattern of alcohol use leading to clinically significant impairment or distress.[9] AUD was defined by the American Psychiatric Association in 2013 with the development of the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM–5) and encompasses both alcohol abuse and alcohol dependence.[10] Under the DSM–5, those meeting 2 of 11 criteria during a 12-month period are diagnosed with AUD, which can be further classified as mild, moderate, or severe depending on the number of criteria met (Table 1).[9,10] Of note, the Centers for Disease Control and Prevention defines one drink as 12 ounces of beer (5% alcohol by volume [ABV]), 8 ounces of malt liquor (7% ABV), 5 ounces of wine (12% ABV), or 1.5 ounces of distilled spirits (80-proof or 40% ABV).[11] Drinking patterns that do not meet the criteria for AUD but that also increase the risk of adverse health and social consequences have been defined by the National Institute on Alcohol Abuse and Alcoholism (NIAAA) and include alcohol misuse, heavy alcohol consumption, and binge drinking (Table 2).[12] However, these terms are not used consistently in the field. For consistency, this paper uses the term "alcohol misuse" to refer to all subclinical forms of problematic alcohol use when discussing the general trends among studies and defers to terminology used in articles when discussing findings on specific patterns of problematic alcohol use (e.g., heavy and binge drinking); however, these terms may not precisely match the authoritative standards for terms related to alcohol misuse.

Heavy and binge drinking are frequently observed in military personnel, and a history of deployment and combat exposure appears to be associated with heavier use.[13-18] Additionally, evidence from both military and civilian populations indicates that individuals with TBI have a

higher incidence of alcohol misuse and AUD and higher scores on alcohol use assessments than those with no TBI history.[19-22] Alcohol misuse is concerning as it is associated with cognitive impairment, including substantial effects on learning and memory, executive function, and processing speed, as well as vestibular dysfunction.[23-26] Alcohol consumption at the time of and after TBI also increases the risk of reinjury and posttraumatic seizures and challenges return to work and productivity.[27-32] Understanding the risk factors for excessive alcohol consumption post-TBI is vitally important for both service members and clinicians treating patients to promote prevention, a high quality of life, and mission readiness.

## THE RELATIONSHIP BETWEEN ALCOHOL MISUSE AND TBI

### Alcohol Intoxication, Pre-Injury Alcohol Misuse, and TBI

The relationship between alcohol intoxication and TBI has been well characterized.[33-35] Civilian studies demonstrate that 23–53% of individuals exhibit alcohol intoxication at the time of injury.[36-45] Additionally, several studies have shown that 28–79% of individuals with TBI have a pre-injury history of alcohol misuse or dependence.[37,46-48] Acute alcohol intoxication[49-51] as well as prolonged alcohol misuse or AUD[52-55] have been shown to increase the likelihood of incurring a TBI of any severity and the odds of TBI-related hospitalization. To more accurately characterize the trajectory of alcohol use across multiple timepoints before and after TBI, a recent study used insurance claims data from over 200,000 patients with TBI of any severity and 400,000 frequency-matched controls without TBI.[56] During the year before the index event, the rate of receiving a diagnosis of alcohol dependence was nearly 8 times higher in the TBI group than in the non-TBI group after adjusting for covariates,[56] strongly supporting the link between pre-injury alcohol misuse and TBI.

### Alcohol Misuse and AUD after TBI

While many studies clearly demonstrate an elevated risk of TBI following acute alcohol intoxication and preinjury alcohol misuse, the relationship between TBI and post-injury alcohol misuse is more complex. Generally, most studies that have investigated drinking habits 1–2 years after TBI report a pattern of reduced drinking and fewer new alcohol dependence diagnoses immediately after TBI, followed by increased alcohol consumption over time.[18,37,47,56-58] This pattern has been found across the spectrum of TBI severity, but individuals with mTBI often return to alcohol use faster than those with moderate to severe TBI.[18,47] The initial decline in alcohol consumption after TBI is likely due to several factors, including adherence to clinical guidance during the early post-injury period, lack of access to alcohol due to hospitalization or inpatient treatment, or the initiation of treatment for AUD after injury.[33]

However, findings from several large multicenter studies—including Transforming Research and Clinical Knowledge in TBI (TRACK-TBI), TBI Model Systems (TBIMS), Long-Term Impact of Military-Relevant Brain Injury Consortium Chronic Effects of Neurotrauma Consortium (LIMBIC-CENC), and Army Study to Assess Risk and Resilience in Servicemembers Pre/Post Deployment Study (STARRS PPDS)—suggest that TBI increases the likelihood of alcohol misuse and AUD over time.[59,60] First, civilian studies show that those who report a lifetime incidence of TBI of any severity engage in greater alcohol consumption,[21,61] and both military

personnel[19] and civilians[20] with TBI history have a higher incidence of alcohol misuse than those without TBI history. Additionally, there is evidence of a relationship between TBIs sustained during childhood and the later development of high-risk substance use, including alcohol misuse, during adolescence and adulthood.[62-66] In one civilian study, those who sustained an mTBI with LOC before age 20 were more likely to binge drink than those were older than 20 at the time of injury.[66] A birth cohort study reported that children who were hospitalized for mTBI before age 6 were more likely to exhibit alcohol misuse in adolescence than those with no mTBI and those with mTBI who did not require hospitalization.[67] Other birth cohort studies have similarly found that TBIs sustained during early childhood were associated with an increased prevalence of later alcohol misuse[68] and earlier initiation of heavy alcohol consumption.[69] Importantly, these findings were obtained after adjusting for covariates, such as age, sex, race, socioeconomic status, and family exposure to adverse events; however, the covariates that were evaluated differed among studies. Nevertheless, these findings collectively support the idea that TBI contributes to the later development of alcohol misuse.

Among military service members and veterans, deployment-related TBI has been associated with an increased risk for post-deployment alcohol misuse,[70] binge and heavy drinking,[71-73] and receiving an alcohol-related diagnosis.[74-76] One study of over 4,600 soldiers who participated in the Army STARRS PPDS found that self-reported lifetime TBI was associated with 1.3 to 1.6 times higher odds of binge drinking and heavy drinking at 3 months and 9 months post-deployment.[65] Notably, this result was obtained even after controlling for pre-deployment binge drinking and mental health disorders, deployment-related stressors, and sociodemographic factors.[65] In a recent study of service members enrolled in the Substance Use and Psychological Injury Combat Study, AUD diagnosis was found to be more prevalent among those with a lifetime history of TBI of any severity than among those without a history of TBI.[77] Collectively, these studies suggest the importance of routine screening for deployment-related and lifetime TBI to prevent alcohol misuse in the military population. Conversely, prioritizing treatment for alcohol misuse may be an effective approach to reduce TBI risk in this population.

Despite this advancement in knowledge on the relationship between alcohol misuse and TBI, confirming a causal relationship is difficult for several reasons. First, many studies that report a causal relationship between alcohol misuse and TBI demonstrate that a history of alcohol misuse preceded the TBI that led to inclusion in the study, but do not account for a prior history of TBIs sustained before this index injury; thus, it is possible that unreported TBIs sustained earlier in life contributed to the development of alcohol misuse.[59] Those studies that do screen individuals for a history of prior TBI often do so to exclude individuals with prior TBI from analyses.[63] Additionally, many studies evaluating the effect of TBI on alcohol misuse similarly do not control for baseline problematic alcohol use and other potentially confounding factors.[56] Another concern is that, among studies involving service members, it is possible that problematic patterns of alcohol use are underreported due to perceived occupational consequences. Finally, studies investigating lifetime TBI incidence cannot be used to determine the exact temporal onset of problematic alcohol use after TBI, and there are limitations to the use of retrospective methodologies that involve both self-reported TBI history and alcohol misuse. Future studies should aim to ensure all findings are adjusted for potential confounding factors when possible and to obtain an accurate assessment of TBI history prior to the study, and prospective longitudinal studies should be conducted to better establish the relationship between TBI and alcohol misuse.[78]

## IMPACT OF ALCOHOL CONSUMPTION AFTER TBI

There is considerable evidence from decades of clinical research associating pre- and post-injury alcohol misuse with a variety of adverse outcomes in individuals who sustain TBIs of all severities. These include poor recovery from TBI,[79-84] increased incidence of reinjury or subsequent TBI,[28,29] cognitive impairment,[23,81,83-86] reduced employment and productivity,[32] sleep problems[87], and lower life satisfaction at 1–10 years post injury.[80] Alcohol misuse is also associated with greater risk of suicide, suicidal ideation,[88,89] and neuropsychological disorders including posttraumatic stress disorder (PTSD), depression, and anxiety[86,90-93] after TBI in both military and civilian populations. Additionally, a TBIMS study of veterans and service members who received inpatient rehabilitation for TBI of any severity revealed that pre-TBI heavy alcohol use was a significant predictor of being arrested 10 years post injury; those who reported pre-TBI heavy alcohol use were threefold more likely to incur a post-TBI arrest than those who did not.[94] The physiological effects of alcohol misuse include increased risk of posttraumatic seizures[27,30,31] as well as prolonged bleeding time and elevated platelet count[95] after moderate to severe TBI. Together, these studies show that alcohol misuse has widespread functional, physiological, psychological, and social effects after TBI.

Among these effects, several studies have specifically investigated the connections among alcohol misuse, TBI, and dementia. Interestingly, several large studies have demonstrated that moderate alcohol intake (1–6 drinks per week) is associated with a lower risk of dementia than abstinence among older adults, but heavier consumption (14 or more drinks per week) has been shown to confer a higher dementia risk than abstinence in this population.[96-98] Similarly, a recently published longitudinal study including over 30,000 individuals reported that "major" TBIs (defined as those involving a diagnosis of intracranial hemorrhage and hospital length of stay of at least three days) were associated with an increased risk of dementia.[99] Among those who sustained major TBIs, light alcohol consumption (1–13 drinks per week for men or 1–6 drinks per week for women) and physical activity were the strongest factors associated with a reduced risk of dementia.[99]

However, many studies reporting an association between low to moderate alcohol consumption and reduced risk of dementia have important study design limitations as they often do not account for potential confounding effects. For example, one systematic review reported that when analyses were adjusted for abstainer biases and study characteristics, low-volume drinkers did not have significantly reduced mortality risk.[100] It is possible that other factors, such as lower use of medications that interact with alcohol and higher extroversion, levels of social engagement, and activity levels among healthy individuals may contribute to the findings observed in these studies. Similarly, healthier individuals may be more able to engage in low to moderate alcohol use than those with chronic health conditions. Furthermore, other studies suggest that excessive alcohol consumption may confer an increased risk of dementia and neurodegenerative disease after TBI. For example, in a recent LIMBIC-CENC study of individuals with a history of deployment-related mTBI, AUD was associated with signs of accelerated brain aging often observed in those with Alzheimer's disease,[101] which is consistent with several other studies.[102-104] Additional studies conducted using prospective longitudinal study designs that carefully control for confounders are needed to confirm the relationship between alcohol use and the development of neurodegenerative diseases following TBI.

## RISK FACTORS ASSOCIATED WITH ALCOHOL MISUSE AFTER TBI

### Social Determinants of Health: Demographic, Psychosocial, and Environmental Factors

Several factors, including pre-injury alcohol misuse and demographic characteristics, have been studied as potential risk factors for AUD and alcohol misuse after TBI. Among these factors, a pre-injury history of alcohol misuse is consistently found to be the strongest predictor of AUD and alcohol misuse after TBI.[13,37,47,65,93,105,106] Similarly, individuals suspected to be intoxicated at the time of TBI of any severity are more likely to exhibit AUD during the first year after head injury.[47] Preinjury alcohol use among TBI survivors has been found to be more common among men,[36,107] younger individuals (20–29 years),[108] and college students.[107] For example, in the military population, veterans with a history of early adolescent (<15 years) binge drinking who sustained military-related mTBIs have been shown to have higher odds of AUD than those with military-related mTBIs who started binge drinking later.[90] Accordingly, most studies report that problematic alcohol consumption and AUD after TBI are more common among men[21,52,93,105,109,110] and individuals younger than 65[19,21,47,93,110,111] across the spectrum of TBI severity. Some studies dispute these findings,[112,113] including one small study that found no significant differences in alcohol use after mTBI between male and female veterans, although there was a trend toward higher use in males.[113] Because pre-injury alcohol misuse is highly predictive of post-injury alcohol misuse, many researchers argue that premorbid personality traits such as thrill-seeking, negative urgency, maladaptive coping, and impulsivity may be important contributors to one's risk of post-injury alcohol misuse.[106,114]

Few studies have explored the role of social and environmental factors in alcohol abuse after TBI. Some have revealed that a history of foster care,[115] homelessness,[54] or incarceration[116,117] is associated with increased incidence of co-occurring TBI and alcohol misuse. Single individuals (as opposed to those in a relationship) have also been shown to have a higher risk of problematic alcohol use after any severity of TBI.[47,105] One large longitudinal study found that individuals who experienced multiple adverse childhood events, familial alcoholism, and physical abuse were more likely to sustain TBIs through events involving binge drinking,[118] but the impact of these factors on post-TBI drinking patterns was not reported and has generally been less studied. Regarding environmental factors, a recent TBIMS study compared alcohol use between individuals who were exposed to the coronavirus disease-2019 pandemic (those with follow up after 2020, when the pandemic began in the United States) and pandemic unexposed individuals (those with follow up before 2020, before the pandemic began in the United States). The study found that civilians exposed to the coronavirus disease-2019 pandemic who had moderate to severe TBI drank more during the second year post-injury than during the first, with Black and Hispanic subgroups showing the greatest increase in alcohol consumption during this time.[110] Further research in this area is warranted to achieve a more comprehensive understanding of how social and environmental risk factors may contribute to the risk of alcohol misuse after TBI.

Some studies have evaluated whether comorbid mental health conditions confer an increased risk of alcohol misuse after TBI, with many focusing specifically on PTSD among military service members and veterans. In one study of service members who sustained TBIs during deployment, more severe TBI and PTSD symptoms were associated with a lower odds of substance misuse, including alcohol misuse, 12 months after study enrollment.[111] However, another study on service members returning from Operation Enduring Freedom/Operation Iraqi Freedom

(OEF/OIF) reported twice as much binge drinking among those with a self-reported history of TBI of any severity and mental health issues (e.g., PTSD, depression, and harmful thoughts) than among those with neither condition.[72] In another study, among service members who sustained military-related mTBIs, there was a significantly higher burden of PTSD symptoms (as measured on the Clinician-Administered PTSD Scale) in those who started binge drinking earlier in life (<15 years) than in those who started binge drinking later.[90] Additionally, one study of veterans found that men with TBI and PTSD reported greater alcohol use than women,[109] and these studies suggest that factors such as preinjury drinking patterns and sex may be important mediators of the relationship between PTSD and alcohol misuse after TBI. The effect of treatment for comorbid mental health conditions on this relationship has not been investigated in depth; thus, more studies are needed to fully characterize the interaction of alcohol misuse and PTSD after TBI.

While much work has been done to identify social determinants of health associated with alcohol misuse after TBI, there have been relatively few studies in this area, and some knowledge gaps remain, particularly within the military population. It is unclear how participation in specific military occupational specialties (MOS) impacts drinking habits after TBI. Some studies have reported that Special Operations Forces (SOF) and explosive ordnance disposal (EOD) personnel have a lower prevalence of binge drinking and AUD prior to TBI than conventional forces and non-EOD personnel, but differences in post-TBI drinking patterns between these groups have not been reported.[119,120] Since traumatic combat experience has been associated with an increased likelihood of alcohol misuse in certain MOS, including SOF,[121] it is possible that TBI further exacerbates the risk of alcohol misuse in certain populations. Further research is needed to determine the extent to which specific occupations influence the risk of alcohol misuse, which may inform targeted education and treatments.

**Injury Characteristics**

In addition to demographic, psychosocial, and environmental factors, characteristics of the injury itself have been studied as potential risk factors for alcohol misuse after TBI, though findings are limited. Regarding mechanism of injury, one meta-analysis found no difference in the prevalence of alcohol misuse between individuals who sustained blast and non-blast TBIs.[122] Regarding TBI severity, some studies have shown that after injury, individuals with milder TBIs have lower rates of abstinence,[37] consume more alcohol,[18,47] and have a higher likelihood of alcohol misuse[21,111] than those with more severe injuries, which is consistent with their faster rate of recovery from TBI and ability to return to drinking more quickly. Additionally, one study found that TBI with LOC was associated with an increased odds of binge and heavy drinking,[21] and this risk further increased when the number of TBIs with LOC reached three or more. However, due to the limited research in this area, further investigation is warranted.

Some studies have investigated the effect of the context in which the TBI was sustained, such as through assaults or during deployment, on post-injury drinking patterns. One TBIMS study of civilians with moderate to severe TBI found that individuals who sustained TBIs through self-inflicted firearm injury reported a higher incidence of pre-injury heavy alcohol use than those who incurred firearm-related TBIs through assault; however, there were no differences in the incidence of post-injury heavy drinking between these groups at the 1-, 2-, and 5-year follow-ups.[123] In another study of over 1,300 Iraq and Afghanistan veterans who were deployed to a war

zone, those who sustained a deployment-related TBI and those who sustained nondeployment TBIs (i.e., any TBI that occurred during time of service, excluding deployment) were both more likely to meet criteria for AUD than those with no TBI history. However, when individuals with PTSD were excluded, there was no longer an association between deployment-related TBI and AUD.[124] This finding suggests that PTSD and traumatic experiences related to deployment are important contributors to AUD after TBI.

## PATHOPHYSIOLOGY OF ALCOHOL MISUSE AND AUD AFTER TBI

Chronic excessive alcohol consumption involves a complex combination of psychological, physiological, and biochemical mechanisms that drive alcohol use and challenge abstinence. Many studies have identified impaired decision-making as both a risk factor for and consequence of alcohol misuse.[125-128] Other studies have revealed the role of cognitive flexibility, which is an executive function underlying adaptive behavior that likely contributes to the inability to abstain from drinking alcohol.[127,129] Consistent with this idea, studies report impaired cognitive flexibility in clinical AUD and animal models of chronic alcohol exposure.[127,130,131] At the physiological level, dopaminergic dysfunction plays a key role in the cognitive processes that contribute to addictive behaviors. Alcohol consumption triggers a sharp increase in the levels of dopamine, a monoamine neurotransmitter involved in motivation, pleasure, and memory.[106,132] However, the brain adapts to this heightened stimulation over time, and higher amounts of alcohol are needed to produce an equivalent euphoric effect, which contributes to a phenomenon known as tolerance.[106,132] The result is increased craving, which motivates alcohol-seeking behavior despite decreased liking of alcohol.[106,132]

Evidence also suggests a relationship between chronic alcohol use and altered brain structure. Chronic alcohol misuse is associated with a significant decrease in hippocampal and cortical volume, reduced white matter volume and integrity, as well as accelerated brain aging.[101-104,126,133-135] These pathologies likely contribute to the cognitive and emotional impairments often observed in individuals with AUD. Due to the large number of cross-sectional studies in this area, it is unclear whether this finding means that alcohol misuse directly shrinks the brain, or that lower brain volume is a risk factor for alcohol misuse.[135] However, a large body of controlled preclinical studies support the former, showing impaired neurogenesis and hippocampal shrinking in alcohol-exposed animals.[136-139] Alterations in synaptic structure,[140,141] neurodegeneration,[136] gene expression changes,[142,143] microglial activation,[140,143,144] epigenetic changes,[145] proinflammatory cytokine release,[146] and astrocyte reactivity[136] are also implicated in the cognitive and neurologic impairment and accelerated brain aging associated with alcohol misuse.

In the context of TBI, there is some evidence that alcohol misuse can worsen or increase the risk of certain pathologies. For example, in one study, alcohol misuse was a risk factor for isolated subdural hematoma that required surgery in mTBI patients at a level I trauma center.[147] Animal and human studies also suggest that alcohol consumption can contribute to neuronal damage[148] and neuroinflammation[148-150] after TBI. Conversely, TBI may contribute to pathologies associated with alcohol misuse. The sheer stress produced by a TBI can damage dopaminergic neurons, including those within structures of the mesocorticolimbic pathway underlying alcohol use disorder.[106] However, one imaging study found no differences in brain reactivity to the presence of alcohol or functional connectivity in these regions between individuals with both

TBI and AUD and those with AUD alone,[151] suggesting more studies are needed to characterize the effect of TBI on pathologies associated with alcohol misuse to develop more specific treatments to prevent the effects of alcohol misuse in the TBI population.

## EVALUATION OF ALCOHOL MISUSE AND AUD

A variety of tools have been developed to screen for alcohol misuse and AUD in hospital and primary care settings, including the Michigan Alcoholism Screening Test (MAST), Alcohol Use Disorders Identification Test (AUDIT), and the Single Item Alcohol Screening Questionnaire (SASQ) (Table 3).[152] The CAGE questionnaire assesses perceived issues with controlling alcohol consumption (cutting down alcohol use, drinking upon eye opening), as well as negative emotions associated with drinking (annoyance and guilt), and has shown high sensitivity and specificity in TBI patients when compared with the DSM-IV criteria for AUD.[153,154] However, this questionnaire does not assess hazardous drinking habits, and some studies have reported its low sensitivity in specific populations (e.g., women and students).[155] The MAST similarly evaluates one's perceptions of current drinking and drinking consequences but has been found to be less sensitive and specific than the CAGE questionnaire in individuals with TBI.[152,154] The AUDIT was originally developed by the World Health Organization to distinguish those with AUD from those at risk for AUD.[152,156] The AUDIT has been validated in many populations and settings, including active duty service members and veterans, and has moderate-to high test-retest reliability and high accuracy with DSM criteria for AUD.[157-160]

In the Veterans Health Administration and the Department of Defense (DOD), the alcohol consumption questions provided on the AUDIT (AUDIT-C), as well as the SASQ, are used to screen for alcohol misuse within the past year.[19,73,161,162] The AUDIT-C has been validated as a shorter alternative to the AUDIT to record the frequency and quantity of typical drinking and the frequency of heavy episodic drinking; the AUDIT-C is less time-consuming than the AUDIT but is just as psychometrically valid and predictive of alcohol-related health outcomes.[163-165] The SASQ evaluates both the frequency and quantity of drinking using a single screening question and has been shown to accurately identify a current AUD.[166] The 2021 Department of Veterans Affairs (VA)/DOD Clinical Practice Guideline (CPG) for the Management of Substance Use Disorders recommends the use of these tools during routine screening for unhealthy alcohol use in all patients in both general medical and mental health care settings.[162] However, the CPG emphasizes that most individuals who screen positive should not be given an AUD diagnosis solely based on the screening results and should instead be recommended for brief alcohol counseling.[162]

Other tools that can be used to document problematic alcohol use in the military include the Post-Deployment Health Assessment (PDHA) and the Post-Deployment Health Reassessment (PDHRA). The PDHA is a mandatory self-report questionnaire completed within 30 days of return from deployment, while the PDHRA is completed six months later, and both assessments contain items related to alcohol misuse during and shortly after deployment.[167,168] While these and the abovementioned tools are useful for evaluating alcohol misuse and AUD in clinical settings, many large TBI studies that evaluate active duty or veteran populations, such as the TBIMS studies, often use specific questionnaires developed by the study investigators to evaluate specific aspects of alcohol misuse or the MINI International Neuropsychiatric Interview Substance Abuse Modules to obtain a DSM-5 diagnosis of AUD.[18,169]

## PREVENTION AND MANAGEMENT OF ALCOHOL MISUSE AFTER TBI

In the military, the *VA/DOD CPG for the Management and Rehabilitation of Post-Acute Mild Traumatic Brain Injury* advises that individuals diagnosed with an mTBI be screened for common comorbidities, including substance use disorders like AUD, and limit alcohol consumption during recovery.[162] Additionally, the Traumatic Brain Injury Center of Excellence *Clinical Recommendation on Cognitive Rehabilitation for Service Members and Veterans Following Mild to Moderate Traumatic Brain Injury* states that diagnosed substance abuse disorders, such as AUD, should be treated before initiating cognitive rehabilitation programs for TBI.[170] The *2021 VA/DOD CPG for the Management of Substance Use Disorders* further recommends that individuals who screen positive for unhealthy alcohol use be considered for enrollment in brief alcohol counseling as the initial treatment approach.[162] Branch-specific alcohol treatment programs are also offered through the DOD.[171] Pharmacotherapies or psychosocial interventions can then be considered for those who receive an AUD diagnosis depending on the severity of AUD.[162] The Psychological Health Center of Excellence (PHCoE) also provides many resources on current and emerging treatments for alcohol misuse and AUD (Table 4).[172,173]

### Nonpharmaceutical Management of Alcohol Misuse or AUD after TBI

Screening and brief intervention (SBI) programs provide motivational interviews and education for individuals with AUD and those at risk of developing AUD.[174] These programs have been widely implemented across trauma centers and have been shown to reduce alcohol use, health care utilization, and motor vehicle accidents in many medical settings by promoting self-efficacy and the idea that changing one's drinking habits is possible.[175] These programs have also been used specifically in TBI patients[19]; some studies have reported a reduction in the number of TBI patients with positive blood alcohol results and decreased alcohol consumption in TBI patients at 6 months and 2 years after implementation.[176,177] A recent randomized controlled trial also found that an adapted SBI program was more effective than a screening and education with an attention control condition (which involves receiving social attention, rather than an intervention) at reducing the number of individuals who resumed drinking 12 months after discharge.[178] However, one study found that SBI did not affect alcohol misuse in TBI patients,[179] and few other studies have evaluated the efficacy of SBI in the TBI population. The limited number of studies in this area is concerning as cognitive deficits among individuals with TBI may interfere with the potential benefits of SBI.[175] Additionally, some studies suggest that individuals with more severe TBIs are less likely to be screened for alcohol misuse, which is likely due to the level of disability in these individuals and the prioritization of returning these individuals to a stable condition.[175,180] Future health care utilization studies are needed to assess the benefits of SBI in individuals with TBI of different severities and determine whether accommodations should be provided to address the unique needs of TBI patients in these programs.

For individuals with a diagnosed AUD, the *2021 VA/DOD CPG for the Management of Substance Use Disorders* weakly recommends various psychosocial treatments, such as cognitive behavioral therapy, 12-step facilitation (e.g., Alcoholics Anonymous [AA]), and motivational enhancement therapy (MET).[162] AA is a particularly popular program that promotes active engagement in group meetings and activities (e.g., discussions about urges to drink, drinking behavior, and recovery-oriented activities) and homework assignments related to each

step.[162] MET is less intensive than AA and involves motivational interviewing to improve self-efficacy for reducing drinking, strengthen coping skills, and promote commitment to change.[162]

Studies suggest these treatments may modestly improve some aspects of alcohol consumption in individuals with AUD, but they are not superior to pharmacotherapies.[181-183] Other treatments that have been explored for reducing alcohol misuse include exercise therapy, with promising findings from randomized controlled trials and meta-analyses.[184-187] Novel treatments, such as virtual reality (VR) cognitive training, also show promise for treating AUD.[188-190] However, very few studies have directly investigated these interventions for alcohol misuse in TBI patients. A recent study investigated the effect of both exercise and VR executive function training (EFT) on cognition in 30 veterans with TBI seeking treatment for AUD.[191] Both exercise and VR-EFT improved cognitive outcomes, but only exercise significantly reduced drinking habits.[191] While these results are encouraging, there is a need to determine whether these and other nonpharmaceutical approaches can be effectively utilized in the TBI population.

**Pharmaceutical Management of Alcohol Misuse or AUD after TBI**

Pharmacotherapies for managing alcohol misuse are most appropriate for those with diagnosed AUD, and the *2021 VA/DOD CPG for the Management of Substance Use Disorders* strongly recommends the use of naltrexone or topiramate for those with moderate to severe AUD.[162] Of note, naltrexone has been approved by the United States Food and Drug Administration for the treatment of AUD, while topiramate has been FDA approved for other indications and is used as an off-label treatment for AUD.[192] Naltrexone is an opioid receptor antagonist that can be orally administered once per day or via monthly intramuscular injection and has shown efficacy in reducing alcohol consumption.[193] Topiramate is an anticonvulsant with multiple mechanisms of action, including inhibition of voltage-gated sodium ion channels, blockade of glutamate neurotransmission, and enhancement of gamma-aminobutyric acid (GABA)-mediated inhibition through receptor positive allosteric modulation.[194] Though the pathways mediating its pharmacological efficacy in AUD are currently a subject of active research, topiramate is theorized to reduce dopamine surges associated with addiction.[194-196] For the treatment of AUD, topiramate is orally administered once per day and promotes abstinence while reducing alcohol craving.[194,195] Large meta-analyses of clinical trials conclude that these drugs can effectively reduce alcohol consumption,[197,198] but they also should be used in conjunction with a psychosocial intervention.[162] Other drugs that have been investigated include disulfiram and acamprosate, though findings on their effectiveness for treating AUD are limited.[162,173] Alternative pharmacotherapeutic approaches, such as psychedelic-assisted therapies (PAT), were first investigated for the treatment of AUD in the late 1960s, and renewed interest in these therapies due to recent legislation has led to more studies in this area.[199-201] Collectively, PAT studies demonstrate the efficacy of psilocybin- and lysergic acid diethylamide-assisted therapies for reducing alcohol consumption and promoting remission, as well as good tolerance of these treatments.[199-201]

While these findings are promising, very few studies have examined the use of pharmacotherapies for treating alcohol misuse in the TBI population. One small study of veterans with AUD who were treated with naltrexone or valproate found that those with a history of moderate to severe TBI were more likely to relapse than those without TBI history.[202] No studies have investigated the use of PAT for treating AUD in TBI patients. However, since

Section 723 of the 2024 National Defense Authorization Act supports DOD funding for studies on the use of PAT in service members with TBI, it is possible that future studies may be conducted to address this gap.[203] To date, evidence suggests that pharmacotherapies may be most beneficial for treating more severe AUD in the TBI population, but additional research is needed to confirm the safety and efficacy of these strategies in individuals with TBI.

## CONCLUSION

Substantial clinical research has revealed the complex relationship between alcohol misuse and TBI, demonstrating that alcohol misuse increases the risk of TBI, while TBI may lead to alcohol misuse. The harmful effects of heavy drinking after TBI are multifaceted and may be intensified in certain vulnerable populations, including those with a preinjury history of alcohol misuse and those with other comorbid mental health disorders. However, alcohol misuse is a modifiable behavior that can be improved with evidence-based interventions tailored to meet the needs of the patient. While many treatment options exist for preventing and treating alcohol misuse and AUD, future studies should aim to evaluate their efficacy specifically in TBI survivors. Future studies should also determine whether specific accommodations are needed to increase the benefit of treatment in the TBI population as a whole, as well as in those with common TBI sequelae. In the military, these efforts will support the prevention of TBI-induced pathologies and promote force readiness.

## KEY POINTS

- Evidence suggests heavy alcohol consumption increases TBI risk and that TBI increases the incidence of alcohol misuse and AUD; however, a causal relationship between TBI and alcohol misuse is difficult to confirm.
- The risk of developing alcohol misuse after TBI is highest among those with a preinjury history of alcohol misuse, milder TBIs (as opposed to moderate or severe TBIs), and comorbid mental health disorders.
- Due to the bidirectional relationship between TBI and alcohol misuse, screening for deployment-related and lifetime TBI may help prevent alcohol misuse in the military population, and prioritizing treatment for alcohol misuse may help reduce TBI risk.
- Alcohol misuse after TBI is associated with cognitive impairment, including substantial effects on learning and memory, executive function, and processing speed, as well as vestibular dysfunction.
- Heavy alcohol misuse after TBI is linked to other adverse health effects, including poor recovery from TBI, posttraumatic seizures, difficulty returning to work and daily activity, and mental health concerns that are prevalent in the military population, such as PTSD and suicide.
- AUD involves the complex interplay of a variety of neurological and psychological processes that promote its characteristic behaviors, such as craving and tolerance.
- Alcohol misuse and AUD are evaluated using various questionnaires, and treatments are recommended based on the severity of symptoms.
- Both psychosocial interventions (e.g., cognitive behavioral therapy, Alcoholics Anonymous) and pharmacotherapies have been recommended for the treatment of

alcohol misuse and AUD, but additional studies are needed to assess how cognitive impairment following TBI affects their efficacy and to identify potential accommodations for increasing the benefit of these strategies.

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**Disclaimer**

## APPENDIX A

### Table 1: Criteria for AUD[9,10]

| CRITERIA |
|---|
| 1. Alcohol is often taken in larger amounts or over a longer period than was intended. |
| 2. There is a persistent desire or unsuccessful efforts to cut down or control alcohol use. |
| 3. A great deal of time is spent in activities necessary to obtain alcohol, use alcohol, or recover from its effects. |
| 4. Craving, or a strong desire or urge to use alcohol. |
| 5. Recurrent alcohol use resulting in a failure to fulfill major role obligations at work, school, or home. |
| 6. Continued alcohol use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of alcohol. |
| 7. Important social, occupational, or recreational activities are given up or reduced because of alcohol use. |
| 8. Recurrent alcohol use in situations in which it is physically hazardous. |
| 9. Alcohol use continues despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by alcohol. |
| 10. Tolerance, as defined by either of the following:<br>a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect.<br>b. A markedly diminished effect with continued use of the same amount of alcohol. |
| 11. Withdrawal, as manifested by either of the following:<br>a. The characteristic withdrawal syndrome for alcohol.<br>b. Consuming alcohol (or a closely related substance, such as a benzodiazepine) to relieve or avoid withdrawal symptoms. |

**Table 2: Patterns of Alcohol Use**

| CONDITION | DEFINITION |
|---|---|
| Low-Risk Drinking[12] | • The NIAAA defines low-risk drinking, also referred to as drinking in moderation, as consuming no more than 1 drink per day for women and 2 drinks per day for men. |
| Binge Drinking[12] | • The NIAAA defines binge drinking as a pattern of drinking alcohol resulting in blood alcohol concentrations of 0.08 percent, or 0.08 grams of alcohol per deciliter, or higher. For a typical adult, this pattern corresponds to consuming 5 or more drinks (men) or 4 or more drinks (women), in about 2 hours. |
| Heavy Alcohol Use[12] | • The NIAAA defines heavy drinking as consuming 5 or more drinks on any day or 15 or more per week for men and 4 or more drinks on any day or 8 or more drinks per week for women. |
| Alcohol Misuse[204] | • Alcohol misuse describes alcohol consumption that increases the risk for adverse health and social consequences.<br>• The NIAAA defines alcohol misuse as excessive daily consumption (more than 4 drinks per day for men or more than 3 drinks per day for women), or excessive total consumption (more than 14 drinks per week for men or more than 7 drinks per week for women), or both.<br>• The Centers for Disease Control and Prevention defines alcohol misuse as having more than 1 drink per day on average for women and having more than 2 drinks per day on average for men. |
| Alcohol use disorder (AUD)[9,10] | • The DSM-5 defines alcohol use disorder as a problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by at least 2 of 11 criteria occurring within a 12-month period.<br>• AUD is classified as mild (2-3 symptoms), moderate (4-5 symptoms), or severe (6 or more symptoms).<br>• Symptoms include, but are not limited to, consumption of large quantities of alcohol or long durations of drinking, difficulty controlling or reducing alcohol use, excessive time spent in activities necessary to obtain alcohol or recover from its effects, craving, drinking that interferes with major obligations, reduced involvement in social, occupational or recreational activities because of alcohol use, alcohol use in hazardous situations, continued alcohol use despite physical or psychological problems that are likely to be caused or exacerbated by alcohol, continued use despite recurrent social or interpersonal problems caused or exacerbated by alcohol use, tolerance, and withdrawal. |

**Table 3: Questionnaires Used to Evaluate Alcohol Misuse and Drinking Patterns**

| TOOL | DESCRIPTION |
|---|---|
| Alcohol Use Disorders Identification Test (AUDIT)[152] | • The AUDIT contains 10 questions that assess alcohol intake, dependence, and adverse consequences.<br>• The score is calculated by summing the scores in these subdomains for a total possible score of 40, and scores of 8 or higher indicate potential alcohol misuse. |
| *Alcohol Use Disorders Identification Test-Consumption (AUDIT-C)[162] | • The AUDIT-C has 3 questions that assess the frequency and amount of drinking and the amount of drinking in one sitting.<br>• Each question is scored on a scale from 0 to 4 such that the total score ranges from 0 to 12, with higher scores indicating greater severity.<br>• In the VA and DOD, scores of 5 or higher indicate unhealthy alcohol use. |
| CAGE Questionnaire[152] | • The CAGE questionnaire has 4 questions as follows:<br>  • C: Have you ever felt the need to cut down on your drinking?<br>  • A: Have you ever felt annoyed by criticism of your drinking?<br>  • G: Have you ever felt guilty about your drinking?<br>  • E: Have you ever taken a drink first thing in the morning (eye-opener)?<br>• Scores range from 0 to 4, and scores of 2 or higher indicate possible alcohol dependence. |
| *Single Item Alcohol Screening Questionnaire (SASQ)[162] | • Contains one screening item to evaluate whether an individual regularly drinks above the recommended guidelines for heavy use.<br>• A positive screen is indicated by any report of drinking above these guidelines on an occasion in the past year. |

* indicates questionnaires recommended for assessing alcohol misuse in the 2021 VA/DOD Clinical Practice Guideline for Managing Substance Use Disorders.

**Table 4: Resources on Managing Alcohol Misuse and AUD**

| RESOURCE | DESCRIPTION | LINK |
|---|---|---|
| VA/DOD CPG for the Management and Rehabilitation of Post-Acute Mild Traumatic Brain Injury (2021) | • Provides an overview of evidence-based recommendations for the assessment and treatment of TBI patients.<br>• Recommends that individuals with mTBI limit alcohol consumption during recovery.<br>• Recommends that individuals with mTBI are screened for common comorbidities, including substance use disorders like AUD. | https://www.healthquality.va.gov/guidelines/rehab/mtbi/ |
| VA/DOD CPG for the Management of Substance Abuse Disorders (2021) | • Provides guidelines on screening individuals for unhealthy alcohol use and AUD.<br>• Provides evidence-based recommendations for pharmaceutical and psychosocial interventions for substance use disorders, including AUD. | https://www.healthquality.va.gov/guidelines/MH/sud/VADODSUDCPG.pdf |
| TBICoE Clinical Recommendation: Cognitive Rehabilitation for Service Members and Veterans Following Mild to Moderate Traumatic Brain Injury | • Provides recommendations for initiating cognitive rehabilitation after TBI.<br>• Recommends that individuals receive treatment for active substance abuse disorder, including AUD, before initiating cognitive rehabilitation programs. | health.mil/CogRehab-mTBI-CR-Full |
| PHCoE Evidence Briefs on Alcohol Use Disorder | • Expert-reviewed reports on existing and potential treatments for alcohol use disorder.<br>• Provide summaries of available scientific evidence and clinical guidance for providers, patients, and other individuals with questions about the effectiveness of these treatments.<br>• Topics include various pharmacotherapies and psychosocial interventions. | https://health.mil/Military-Health-Topics/Centers-of-Excellence/Psychological-Health-Center-of-Excellence/PHCoE-Research-and-Analytics/Psych-Health-Evidence-Briefs/Alcohol-Use-Disorder |

| RESOURCE | DESCRIPTION | LINK |
|---|---|---|
| PHCoE Clinician Resources for Screening for Alcohol Misuse | • Describes screening tools used in the DOD to assess alcohol misuse and AUD. | https://health.mil/Military-Health-Topics/Centers-of-Excellence/Psychological-Health-Center-of-Excellence/PHCoE-Clinician-Resources/Alcohol-Misuse/Screening-for-Alcohol-Misuse |
| PHCoE Clinician Resources for Treating Alcohol Misuse | • Describes current and emerging treatments for alcohol misuse. | https://health.mil/Military-Health-Topics/Centers-of-Excellence/Psychological-Health-Center-of-Excellence/PHCoE-Clinician-Resources/Alcohol-Misuse/Treatment-for-Alcohol-Misuse |
| PHCoE Clinician Resources on DOD Policy Guidance on Substance Misuse | • Provides links to specific DOD policies on managing substance abuse and branch-specific treatment programs for alcohol and substance abuse. | https://www.health.mil/Military-Health-Topics/Centers-of-Excellence/Psychological-Health-Center-of-Excellence/PHCoE-Clinician-Resources/Alcohol-Misuse/DOD-Policy-Guidance-on-Substance-Misuse |
| Alcoholics Anonymous (AA) | • A type of 12-step facilitation therapy aiming to promote active engagement in group meetings and activities (e.g., discussions about urges to use, drinking behavior, and recovery-oriented activities) and homework assignments related to each step. | https://www.aa.org/ |

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