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In the Clinic®

Alcohol Use

Unhealthy alcohol use—the consumption of alcohol at a level that has caused or has the potential to cause adverse physical, psychological, or social consequences—is common, underrecognized, and undertreated. For example, data from the 2020 National Survey on Drug Use and Health indicate that 7.0% of adults reported heavy alcohol use in the previous month, and only 4.2% of adults with alcohol use disorder received treatment. Primary care is an important setting for optimizing screening and treatment of unhealthy alcohol use to promote individual and public health.

CME/MOC activity available at Annals.org.

Physician Writers
Joseph H. Donroe, MD, MPH, MHS
E. Jennifer Edelman, MD, MHS
Yale Program in Addiction Medicine, Department of Internal Medicine, Yale School of Medicine, New Haven, Connecticut (J.H.D.)
Yale Program in Addiction Medicine, Department of Internal Medicine, Yale School of Medicine, and Yale Center for Interdisciplinary Research on AIDS, Yale School of Public Health, New Haven, Connecticut (E.J.E.)

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Alcohol consumption is common, with 54% of U.S. adults (approximately 136.5 million) reporting use in the previous month in 2020, although use may have increased during the COVID-19 pandemic (1). At least 7% of U.S. adults (approximately 17.6 million) met criteria for heavy alcohol use during the same period (1). Variable terminology is used to define different levels of alcohol use (**Figure**) (1–8). For this review, we use the following terms and definitions. *Lower-risk alcohol use* is consumption of alcohol below a level believed to cause physical or psychosocial harm (2). *Unhealthy alcohol use* is an umbrella term that captures any drinking that has caused or has the potential to cause physical, psychological, or social consequences (2). It includes *at-risk use* (drinking at a level with potential health consequences [see the **Figure** for various thresholds by which this is defined]), which includes *heavy episodic drinking* (≥4 drinks [women] or ≥5 drinks [men] on a single occasion) and *alcohol use disorder* (AUD). AUD is a pattern of alcohol consumption characterized by alcohol craving, use despite consequences, loss of control over intake, and physiologic dependence (7).

Health Benefits and Harms

Does alcohol use have positive health effects?

Observational studies have reported benefits of lower-risk alcohol consumption compared with abstinence or unhealthy use, particularly as it relates to cardiovascular health (9). Recent studies suggest a benefit of lower-risk drinking for diabetes, ischemic heart disease, dementia, depression, and overall mortality (10–15). Although not well understood, it is hypothesized that the health benefits of alcohol may be mediated by its influence on inflammation, platelet activation, lipid profile, fibrinogen, neurotransmitters, and social opportunities mitigating social isolation (10, 12, 14, 16).

The validity of the evidence of health benefits of lower-risk alcohol consumption has been questioned due to potential confounding by other lifestyle, socioeconomic, and behavioral factors that may be associated with lower-risk drinking and are not robustly measured in epidemiologic studies (14, 17). Data from randomized controlled trials are lacking, thus limiting inferences about causality between lower-risk alcohol consumption and health benefits. Reevaluation of the existing observational literature using techniques to limit confounding associated with epidemiologic studies is ongoing (17). A study using Mendelian randomization identified increased cardiovascular risk at all levels of alcohol consumption (18).

In a cohort study with 371 463 participants, the modest cardioprotective effect of moderate alcohol intake was attenuated after adjustment for smoking rates, body mass index (BMI), physical activity, red meat consumption, vegetable intake, and self-reported health. Genetic evidence using Mendelian randomization identified that, even in persons who reported light alcohol use, a 1-drink-per-day increase in the allele score was significantly associated with increased risk for hypertension (odds ratio [OR], 1.3 [95% CI, 1.1 to 1.5]) and coronary artery disease (OR, 1.7 [CI, 1.2 to 2.4]) (18).

Furthermore, there is growing literature indicating that any alcohol use may be harmful to health. The Global Burden of Disease Study 2016 found that lower alcohol consumption resulted in lower risk for most health outcomes associated with alcohol intake and that the overall risk for disease increased linearly with the number of standard drinks consumed (15, 19).

Which medical conditions are associated with or worsened by alcohol use?

Unhealthy alcohol use leads to and exacerbates myriad acute and chronic medical, psychiatric, and behavior-related

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Figure. **Terminology for alcohol use.**

Review Term	Similar Terms	Source	Definition
Lower-risk alcohol use			Consumption below an amount believed to cause physical or psychological harm
	Drinking in moderation	USDA*	Adults consuming ≤2 (men) or ≤1 (women) drinks per day†
Unhealthy alcohol use			Consumption above an amount that has caused or has the potential to cause physical or psychosocial harm. It covers the spectrum from at-risk use to alcohol use disorder.
At-risk alcohol use			Use that increases risk for health consequences
	Excessive alcohol use	CDC‡	Includes the following patterns of alcohol use: 1) binge drinking; 2) heavy drinking; 3) any drinking by pregnant women or persons aged <21 years
	Risky alcohol use	ASAM§	Use that increases risk for health consequences
	Heavy alcohol use	NIAAA‖	≥4 drinks in a day or ≥8 in a week (women); ≥5 drinks in a day or ≥15 in a week (men)
		SAMHSA¶	≥4 drinks (women) or ≥5 drinks (men) on the same occasion on each of ≥5 days in the previous 30 days
		CDC§, ASAM**	≥8 drinks (women) or ≥15 drinks (men) per week
	Hazardous alcohol use	ICD-11††	A pattern of alcohol use that appreciably increases risk for harmful physical or mental health consequences to the user or to others
Heavy episodic drinking			≥4 drinks† (women) or ≥5 drinks† (men) on a single occasion
	Binge drinking	SAMHSA¶, CDC§, ASAM¶	≥4 drinks (women) or ≥5 drinks (men) on a single occasion
		NIAAA‖	Pattern of consumption that raises the blood alcohol concentration to ≥0.08% (≥0.08 g/dL)
	Episode of harmful drinking	ICD-11††	An episode of alcohol use that has caused damage to a person's physical or mental health or has resulted in behavior leading to harm to the health of others
Alcohol use disorder			A pattern of consumption meeting at least 2–3 (mild), 4–5 (moderate), or ≥6 (severe) of 11 criteria that broadly include alcohol craving, loss of control over use, continued consumption despite consequences, and physiologic dependence*
	Alcohol dependence	ICD-11††	Disorder of regulation of alcohol use arising from repeated or continuous use of alcohol and characterized by impaired control over alcohol use, prioritization of alcohol use, and physiologic adaptions (withdrawal and tolerance) to alcohol use
	Pattern of harmful alcohol use	ICD-11††	A pattern of alcohol use that has caused damage to a person's physical or mental health or has resulted in behavior leading to harm to the health of others

ASAM = American Society of Addiction Medicine; CDC = Centers for Disease Control and Prevention; ICD-11 = International Classification of Diseases, 11th revision; NIAAA = National Institute on Alcohol Abuse and Alcoholism; SAMHSA = Substance Abuse and Mental Health Services Administration; USDA = U.S. Department of Agriculture.
* Reference 8.
† "Drinks" refers to standard drinks (14 g of alcohol in the United States).
‡ Reference 4.
§ Reference 2.
‖ Reference 5.
¶ Reference 1.
** Reference 3.
†† Reference 6.

complications (see the Box: Conditions Associated With or Worsened by Alcohol Use), particularly with higher cumulative and heavy episodic drinking patterns of consumption (20). In 2016, alcohol use was the seventh leading cause of death and disability-adjusted life-years globally (15). In addition to its direct effect on health, alcohol can worsen co-occurring disorders through its effect on mental health and cognition, nutrition, engagement in care, and medication adherence (20, 21).

What sociodemographic factors increase risk for unhealthy alcohol use and related harms?

Susceptibility to the consequences of alcohol use, including development of AUD and other medical consequences, is influenced by genetic and environmental factors. Specific risk factors include age, gender, and sociodemographic factors. Earlier age at drinking onset is correlated with heavier alcohol consumption later in life and increased risk for alcohol-related injuries (22). Older patients

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Conditions Associated With or Worsened by Alcohol Use

Injuries and interpersonal violence
Infectious diseases (tuberculosis, HIV, lower respiratory tract infections, viral hepatitis, COVID-19)
Cancer (oral cavity, larynx, esophagus, intestinal tract, liver, biliary tract, breast)
Cardiovascular disease (arrhythmias, cardiomyopathy, ischemic heart disease, hypertension, hemorrhagic stroke)
Digestive disease (acute and chronic pancreatitis, esophagitis, reflux, gastritis, chronic liver disease)
Neurologic and psychiatric disease (epilepsy, cognitive impairment, depression, suicidal thoughts, Wernicke encephalopathy, Korsakoff syndrome)
Respiratory disease (obstructive sleep apnea)
Endocrine conditions (hypogonadism, menstrual irregularities, osteoporosis)
Pregnancy-related conditions (fetal alcohol syndrome, miscarriage)

with unhealthy alcohol use are more likely to be harmed through alcohol's effect on cognition and interaction with co-occurring illness and polypharmacy. Although unhealthy alcohol use and associated harms are more prevalent in men, prevalence in women is increasing. Women are also more vulnerable to harms associated with alcohol, including more rapid progression to AUD and alcohol-associated liver disease (23). Finally, although per capita consumption rates tend to be higher in persons from higher socioeconomic strata, most harms associated with alcohol use are higher among those from lower socioeconomic groups (22). This effect seems to be mediated through various factors, including consumption patterns, access to care, prevalence of alcohol-attributable diseases in different regions of the world, and clustering of other risk factors (smoking, obesity, physical inactivity) (22). People from groups that have historically been marginalized on the basis of race, ethnicity, and sexuality may experience more alcohol-associated harms (24–26) and greater barriers to receipt of indicated alcohol-related care. In addition, availability of treatment services varies considerably on the basis of geography, with the greatest gaps in care in rural settings.

Health Benefits and Harms... Unhealthy alcohol use is associated with clear harms, and lower-risk consumption is associated with unclear benefits; thus, alcohol consumption should not be recommended to promote health. People who choose to drink alcohol should be educated about the potential harms of even limited consumption and encouraged to keep drinking below levels associated with at-risk use. Special caution with alcohol use is appropriate among young adults, older adults, women, persons with historically marginalized identities, and underserved populations, as well as those with certain medical conditions.

CLINICAL BOTTOM LINE

Prevention and Screening

When should clinicians screen for unhealthy alcohol use?

Although patients with unhealthy alcohol use commonly interact with the medical system, they often do not receive the recommended screening, preventive measures, and care for this condition. Increasing use of preventive services

for unhealthy alcohol use is one of the most effective means toward improving population health. To improve individual and public health by preventing and mitigating the harms of unhealthy alcohol use, clinicians providing care in diverse medical settings (such as primary care or inpatient settings) should be prepared to screen for unhealthy alcohol use and deliver effective treatments, including counseling and medications. The U.S. Preventive Services Task Force (USPSTF) and the Centers for Disease Control and Prevention (CDC) recommend routine screening of adults in the primary care setting, including all pregnant women, for unhealthy alcohol use and provision of brief counseling for those with at-risk alcohol use (27). Despite this recommendation, rates of screening for unhealthy alcohol use remain low and variable across health systems and populations (28).

What methods are effective for screening for unhealthy alcohol use in clinical settings?

The ideal screening tool for unhealthy alcohol use balances sensitivity and specificity for the intended population with feasibility of performing the screening in a busy practice environment. The Alcohol Use Disorders Identification Test–Consumption (AUDIT-C) and the Single Alcohol Screening Question (SASQ) have substantial evidence to support their use across a broad population (27) (**Appendix Figure 1**, available at Annals.org). The USAUDIT-C is an adaptation of the AUDIT-C to U.S. consumption standards and is recommended by the CDC (29, 30). The AUDIT-C, USAUDIT-C, and SASQ can be administered in less than 2 minutes (27). For detection of unhealthy alcohol use, the SASQ has sensitivity of 0.73 to 0.88 and specificity of 0.74 to 1.0 in adults (31); the AUDIT-C has sensitivity of 0.73 to 0.97 and specificity of 0.28 to 0.91 in adult females (using a cutoff score of ≥3) and sensitivity of 0.75 to 1.0 and specificity of 0.34 to 0.89 in adult males (using a cutoff score of ≥4) (31).

Integration of screening with the electronic health record (EHR), use of automated reminders, screening patients at any primary care visit rather than only at annual preventive visits, using the instrument as intended (verbatim language), and having patient-administered tools may lead to increased screening rates and more accurate detection of unhealthy alcohol use (32, 33).

A quality improvement study investigating the use of EHR-integrated screening to improve screening rates for alcohol and drug use in 6 primary care clinics found that the intervention led to high rates of screening (71.8% of eligible patients) and that rates were highest when screening was performed at any primary care visit (vs. targeted at annual visits). Self-administered (vs. staff-administered) screening resulted in higher detection of unhealthy alcohol use (32).

Unhealthy alcohol use can coexist with other substance use. Evidence-based tools to screen for both alcohol and other substance use disorders include the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST); the Tobacco, Alcohol, Prescription medication, and other Substance use (TAPS) tool (33); and the Drug Abuse Screening Test (DAST-10) (32). Patients should be screened in a nonjudgmental manner that optimizes comfort, helps them understand the relevance of alcohol use to their health, and occurs in the context of inquiry about other health-related behaviors (such as exercise, nutrition, or tobacco use).

Prevention and Screening... Standardized processes and approaches involving validated instruments, such as the AUDIT-C and the SASQ, should be incorporated into practices to facilitate routine screening of all patients for unhealthy alcohol use. Integrating screening with the EHR, screening at any health visit rather than limiting it to annual visits, and encouraging patient administration of screening tools can lead to process improvement.

CLINICAL BOTTOM LINE

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Diagnosis and Evaluation

What are the next diagnostic steps after screening patients for unhealthy alcohol use?

Patients with a negative screening result should be informed that health benefits of alcohol consumption are unlikely and counseled about guidelines for continued lower-risk drinking or abstinence. In the United States, for men up to age 65 years, lower-risk alcohol use is 4 or fewer drinks on any single day and 14 or fewer per week. For women (who tend to have lower volumes of distribution) and for men older than 65 years, lower-risk alcohol use is 3 or fewer drinks on any single day and 7 or fewer per week (16). However, these lower weekly risk limits for men (196 g of alcohol) may in fact be above the threshold for causing health consequences (34).

In an analysis of 599 912 persons with current alcohol use, increasing alcohol consumption above 100 g/wk was linearly related to higher risk for stroke (hazard ratio [HR], 1.14 [CI, 1.1 to 1.17]), coronary artery disease excluding myocardial infarction (HR, 1.06 [CI, 1.0 to 1.11]), heart failure (HR, 1.09 [CI, 1.03 to 1.15]), fatal hypertensive disease (HR, 1.24 [CI, 1.15 to 1.33]), and fatal aortic aneurysm (HR, 1.15 [CI, 1.03 to 1.28]). Compared with persons drinking less than 100 g/wk, those consuming more than 100 g/wk had a shorter life expectancy at age 40 years (34).

Patients with a positive screening result for unhealthy alcohol use need further assessment to stratify risk level (for example, at-risk use, heavy episodic drinking), including the presence of AUD. As defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5), AUD is present if a person meets at least 2 of the 11 criteria (**Box:** DSM-5 Alcohol Use Disorder Diagnostic Criteria) (7). Determining severity is important because patients with moderate or severe AUD (meeting ≥4 criteria) benefit from more intensive treatment. The Alcohol Symptom Checklist, which operationalizes the DSM-5 criteria, can be readily integrated into routine primary care to facilitate reliable diagnosis (35, 36) (**Appendix Figure 2**, available at Annals.org).

In a test–retest reliability study of 454 patients who screened positive for unhealthy alcohol use, the Alcohol Symptom Checklist showed high reliability for measuring DSM-5 AUD criteria in both primary care (intraclass correlation coefficient, 0.82 [CI, 0.77 to 0.85]) and mental health (intraclass correlation coefficient, 0.74 [CI, 0.62 to 0.83]) settings (35).

All patients diagnosed with unhealthy alcohol use should also be evaluated for co-occurring medical disorders, nonalcohol substance use (for example, nicotine, cannabis, and nonmedical use of prescription medications), and psychiatric disorders. As appropriate, treatment history, family history of substance use disorders and mental illness, and alcohol-related consequences should be assessed.

What is the role of the physical examination and laboratory testing in the evaluation of patients with unhealthy alcohol use?

In conjunction with the history, the physical examination and laboratory testing may be helpful in identifying and evaluating patients with unhealthy alcohol use. For example, alcohol withdrawal may manifest with abnormal vital signs (such as elevated heart rate, blood pressure, or temperature), autonomic hyperactivity, and central nervous system effects (**Appendix Table**, available at Annals.org) (37). Findings consistent with liver, cardiac, or neurocognitive disease may signal consequences of alcohol use (**Box:** Conditions Associated With or Worsened by Alcohol Use). For example, alcohol may be a contributing factor for hypertension that is

DSM–5 Alcohol Use Disorder Diagnostic Criteria*

A problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by ≥2 of the following occurring within a 12-month period:

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 is continued 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:
    a. A need for markedly increased amounts of alcohol to achieve intoxication or desired effect
    b. A markedly diminished effect with continued use of the same amount of alcohol
11. Withdrawal, as manifested by either of the following:
    a. The characteristic withdrawal syndrome for alcohol
    b. Alcohol (or a closely related substance, such as a benzodiazepine) is taken to relieve or avoid withdrawal symptoms

Mild: Presence of 2–3 symptoms; Moderate: Presence of 4–5 symptoms; Severe: Presence of ≥6 symptoms.

* *From reference 7.*

difficult to manage. Deliberately connecting these findings to the patient's alcohol use may be helpful for people who are contemplating reducing their alcohol consumption.

Laboratory assessment is not part of routine screening for unhealthy alcohol use. However, elevated results on some commonly performed laboratory tests may raise concern about unhealthy alcohol use (38). These include increased mean corpuscular volume of erythrocytes, elevated γ-glutamyl transferase, and increased aspartate–to–alanine aminotransferase ratio suggesting alcohol toxicity affecting hematopoiesis and causing liver injury, respectively (38). Discussion of these markers of bone marrow toxicity and liver injury coupled with guidance on reducing alcohol consumption may lead to more effective reductions in consumption in persons with unhealthy alcohol use (39). Markers related to ethanol metabolism, such as phosphatidylethanol (PEth) and carbohydrate-deficient transferrin, may be more useful for monitoring consumption in patients treated for AUD or when more objective measures of alcohol use are needed (38). When appropriate, these alcohol biomarkers should be used as a complement to self-report, in a patient-centered manner (akin to hemoglobin A_{1c}) and interpreted in the context of patient characteristics that may affect results. For example, patterns of alcohol use, elevated hemoglobin, liver fibrosis, BMI, and HIV status may affect the sensitivity of the PEth results (40).

What language is recommended to decrease the stigma associated with unhealthy alcohol use?

AUD remains a highly stigmatized condition, and imprecise, outdated, and stigmatizing language should be avoided. For instance, "problem drinking" has various

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definitions, making its use unsuitable. "Binge drinking" also has various definitions; the preferred terminology is "heavy episodic drinking." "Alcohol abuse" refers to an outdated DSM diagnosis and is often used in a generic sense to refer to unhealthy alcohol use or AUD (41). To avoid stigma and facilitate appropriate treatment, clinicians should use people-first language (for example, "a person with AUD"), focus on the medical aspects of unhealthy alcohol use and its treatment, and avoid use of slang and idioms. Thus, such terms as "alcoholic" and "alcohol abuser" should be avoided (2, 41). The term "relapse" is also associated with stigma; the preferred terminology is "return to use." When considering and discussing unhealthy alcohol use, it can be helpful to compare it with another chronic medical condition, such as diabetes, where the cause is also based on a combination of genetic and behavioral factors and treatment requires a comprehensive approach.

Diagnosis and Evaluation... Patients with negative screening results for unhealthy alcohol use should be counseled on maintaining lower-risk alcohol use or, for the greatest health benefits, abstinence. Those with positive results should be evaluated for AUD and alcohol-related consequences through a careful history, physical examination, and laboratory evaluation. Person-first, nonjudgmental, and nonstigmatizing language is essential when engaging with patients on their alcohol use.

CLINICAL BOTTOM LINE

Treatment

Despite a range of treatment options for unhealthy alcohol use, treatment of AUD is underused. The 2020 National Survey on Drug Use and Health found that only 4.2% of U.S. adults with AUD received treatment and 1.1% received medications for AUD (MAUD) in the previous year (1). The approach to caring for patients with unhealthy alcohol use is guided by the patient's risk level. Brief interventions advising less or no alcohol consumption are appropriate for those with at-risk alcohol use or mild AUD (42). For those with moderate to severe AUD, treatment options include medications and psychosocial interventions. Treatment of withdrawal symptoms, co-occurring substance use disorders, health consequences of alcohol use, and other mental health disorders should be part of the overall treatment plan.

What should clinicians do if they identify patients with at-risk alcohol use?

The goal for patients with at-risk alcohol use is to cease consumption or decrease it to lower-risk levels to prevent alcohol-related harms. Brief interventions (5 to 20 minutes) are feasible and effective in primary care settings (31). These interventions are designed to elicit the patient's perception of their alcohol use and its associated risks and should include clear advice with a specific recommendation regarding alcohol use, personalized and normative feedback about the effects of alcohol on the patient's health and their alcohol use relative to norms, and empathy with promotion of the patient's self-efficacy. Patients who express an interest in change should be provided a menu of options, situations that are likely to trigger excessive alcohol use should be discussed, and a drinking agreement and follow-up should be arranged. Those who are not ready to change should be given specific advice about recommended alcohol use, should be asked what it would take to motivate change (that is, increase readiness to change on a scale of 1 to 10), and should have a definitive plan for follow-up (43).

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A systematic review in patients with unhealthy alcohol use found that a brief intervention reduced intake by 1.6 drinks per week more than in those without a brief intervention at 6 to 12 months. Thus, a brief intervention with 7.2 (CI, 6.2 to 11.5) persons would reduce 1 patient's alcohol consumption to below the recommended limits (31).

What are treatment options for patients with AUD?

Options for AUD treatment include psychosocial interventions and, for patients with moderate to severe AUD, medications (44).

Patient preference for treatment options is an important consideration for AUD (45). Treatment goals should be collaboratively discussed with patients and may include reduction in drinking or abstinence. These goals should be reassessed regularly and updated on the basis of the patient's response to treatment. Any reduction in alcohol consumption is associated with favorable changes in mortality, although those who achieve abstinence have the lowest mortality risk (46).

What psychosocial interventions and other interventions are most effective for patients with AUD?

For patients with AUD and for those with at-risk alcohol use who are unable to meet treatment goals, psychosocial interventions are a mainstay of treatment. Cognitive behavioral therapy (CBT), motivational enhancement therapy, and mutual support groups are common treatments and have similar efficacy (47). CBT has 2 main components. First, patients are guided to identify the thoughts, feelings, and circumstances that occur before and after alcohol use. The goals are to help them understand why they consume alcohol, identify coping difficulties, and determine triggers for a return to use. Then, through skills-based training, patients develop new behaviors and techniques for coping with these triggers.

A meta-analysis of 30 randomized clinical trials on the combined role of CBT plus medication in patients with primarily AUD (50%) but also other substance use disorders (cocaine, 23%; opioids, 20%) found that the combination of CBT with medications was superior to medications plus usual care. No specific benefit was found with CBT over other psychotherapeutic interventions (motivational enhancement therapy, contingency management) plus medications. Rather, the addition of evidence-based therapy to medications improved outcomes over usual clinical management (44).

Motivational enhancement therapy, which is grounded in stages of change theory, can help motivate patients to change their alcohol use. Mutual help groups, including Alcoholics Anonymous (AA) and SMART Recovery, are an additional treatment option for patients with AUD. Twelve-step facilitation is a formal process of facilitating a patient's engagement in AA, as opposed to a simple referral. Other psychosocial interventions, such as mindfulness-based therapies, community reinforcement, contingency management, and behavioral couples therapy, are also supported by the literature (47). Recent literature supports the notion that mutual help groups are effective and likely produce substantial health care cost savings compared with other psychosocial interventions (48).

A Cochrane review that included 27 studies and 10 565 participants found that manualized AA/12-step facilitation improved rates of continuous abstinence at 12 months compared with other clinical interventions (risk ratio, 1.21 [CI, 1.03 to 1.42]). Manualized and nonmanualized AA/12-step facilitation may perform as well as other clinical interventions for percentage of days abstinent, longest period of abstinence, drinking intensity, and alcohol-related consequences (48).

Because mutual help groups are free and widely accessible, patients should be routinely referred and encouraged to attend at least 1 meeting.

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What evidence-based medication treatments are available for patients with AUD?

Medications should be recommended as part of evidence-based treatment for all patients with moderate to severe AUD (45). There are 3 U.S. Food and Drug Administration–approved medications that should be considered for patients with moderate to severe AUD: naltrexone in oral and intramuscular formulations, acamprosate, and disulfiram (**Table**) (16).

Naltrexone is an opioid receptor antagonist that reduces the rewarding effects of alcohol consumption. Its primary effect is reducing the return to heavy drinking, although data support its use to maintain abstinence (49).

A recent network meta-analysis found that naltrexone improved total abstinence (intramuscular: rate ratio, 1.64 [CI, 1.02 to 2.64]; oral: rate ratio, 1.19 [CI, 1.04 to 1.36]) and reduced heavy drinking (oral: rate ratio, 0.81 [CI, 0.73 to 0.89]) compared with placebo (50).

The formulation may be determined by patient preference, although intramuscular is preferred for patients at risk for poor adherence to a daily medication. It is contraindicated in patients who are opioid-dependent at the time of initiation and should be used with caution in patients with underlying liver disease.

The effect of acamprosate on alcohol use is believed to be mediated primarily through modulation of glutamate transmission and thus the neuronal hyperexcitability that can trigger a return to use during periods of abstinence. Its primary role is in the maintenance of abstinence (rate ratio, 1.33 [CI, 1.16 to 1.54] compared with placebo), although research also supports a benefit in reducing heavy drinking compared with placebo (rate ratio, 0.78 [CI, 0.71 to 0.85]) (49, 50). Acamprosate is dosed 3 times daily, requires dose reduction for mild to moderate renal impairment, and should be avoided in patients with creatinine clearance less than 30 mL/min and those with hypercalcemia.

Disulfiram inhibits aldehyde dehydrogenase, which leads to acetaldehyde accumulation, resulting in nausea, vomiting, flushing, and headache with alcohol consumption. Thus, disulfiram affects alcohol use through negative reinforcement and is ideal for patients who are motivated to abstain (rate ratio, 1.77 [CI, 1.38 to 2.27] compared with placebo) (50). Adherence is essential for it to be effective, so collaborative administration is the most effective strategy (51). Patients must be counseled to avoid all sources of alcohol, including food, medications, and mouthwash. Disulfiram should be used with caution or avoided in patients with cardiovascular disease, liver disease, psychosis, or any co-occurring condition that may be exacerbated by a disulfiram reaction.

Several medications that are currently used off label for AUD treatment in the United States should be considered in patients who are not achieving treatment goals with first-line modalities and those who have other indications for these medications. Topiramate, which has been shown to reduce heavy drinking and support abstinence (50, 52), is primarily an anticonvulsant and a medication for migraine prophylaxis, and it is also used off label to treat eating disorders and other substance use disorders. Initiation requires titration, monitoring for adverse effects (which can be frequent and a common reason for stopping the medication) (50), and dose adjustment in renal disease. Baclofen is primarily used to treat spasticity and has shown mixed results for abstinence and heavy drinking (50, 53). Because it has only limited hepatic metabolism, the American Association for the Study of Liver Diseases recommends consideration of baclofen and acamprosate to treat AUD in patients with alcohol-associated liver disease (54). Baclofen should be avoided in patients with hepatic encephalopathy. Gabapentin is indicated for postherpetic neuralgia and seizure disorders and may reduce heavy drinking and support

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Table. **Medications for Patients With an Alcohol Use Disorder**

*Medication**	*Typical Dosage*	*Mechanism*	*Adverse Effects*	*Notes*
FDA-approved				
Naltrexone	Oral: 50–100 mg/d Intramuscular: 380 mg/mo	Opioid antagonist that may reduce the subjective reward associated with alcohol use	Nausea, indigestion, headache, fatigue, depressive symptoms Rarely, medication-associated hepatitis Potential for precipitated opioid withdrawal if opioid use is present	Contraindicated if opioid use is present Avoid if decompensated cirrhosis is present; use with caution with hepatitis, compensated cirrhosis
Acamprosate	666 mg 3 times daily	May antagonize glutamate-mediated neuronal hyperexcitability and reduce prolonged (but not acute) withdrawal symptoms	Diarrhea, nausea/vomiting, myalgia, rash, dizziness, palpitations Rarely associated with renal impairment	Reduced dosage with renal insufficiency May be used with naltrexone Adherence may be challenging
Disulfiram	250–500 mg/d	Aldehyde dehydrogenase inhibition results in acetaldehyde accumulation with alcohol use, leading to unpleasant symptoms (i.e., alcohol-disulfiram reaction)	Drowsiness, rash Rarely, medication-associated severe hepatotoxicity, optic neuritis, peripheral neuropathy	Potential for many drug–drug interactions Patient must be abstinent for ≥12 hours before administration Avoid in patients with hepatic impairment or cardiovascular disease Most appropriate for patients with strong motivation to abstain and with support to promote adherence
Off-label use				
Topiramate	25–150 mg twice daily	Modulates GABA and antagonizes glutamate receptors	Dizziness; drowsiness; fatigue; anorexia; cognitive dysfunction, including memory impairment, impaired attention, decreased processing speed and verbal fluency; anxiety; depression; paresthesia; non–anion gap metabolic acidosis; nephrolithiasis	Titrate to initiate; taper to discontinue Requires dose adjustment for kidney impairment Caution advised with liver impairment Consider when co-occurring diagnosis present, including chronic migraine, seizure disorder, posttraumatic stress disorder
Baclofen	10–20 mg 3 times daily	GABA-B receptor agonist	Dizziness, drowsiness, nausea, confusion, weakness, constipation	Titrate to initiate; taper to discontinue Requires dose adjustment for kidney impairment Consider in patients with alcohol-associated liver disease
Gabapentin	600 mg 3 times daily	Modulates GABA activity	Dizziness; drowsiness; withdrawal if abruptly discontinued	Titrate to initiate; taper to discontinue Requires dose adjustment for kidney impairment Consider use when co-occurring diagnosis is present, including anxiety, chronic pain, seizure disorder Potential for extramedical use

FDA = U.S. Food and Drug Administration; GABA = γ-aminobutyric acid.
** The American Psychiatric Association practice guideline recommends against use of naltrexone, disulfiram, and acamprosate in pregnant women with alcohol use disorder. Benzodiazepines are recommended for management of alcohol withdrawal syndrome during pregnancy (45).*

abstinence, particularly at higher doses (55, 56). However, these effects were not observed in a recent network meta-analysis (50). Gabapentin can be titrated quickly in patients with AUD, should be dose-adjusted in renal disease, and has been associated with extramedical use (57). Treatment of AUD with nalmefene (approved for AUD in Europe), varenicline, ondansetron, prazosin, and other medications (47, 49) is being actively investigated.

What barriers exist to providing MAUD to patients?

MAUD is underused and unequally prescribed among different socioeconomic and demographic groups (26, 58). Primary care providers are less likely than psychiatrists to prescribe MAUD (58). Differences in prescribing practice among primary care physicians may be explained by time since graduation from residency, lack of training specific to prescribing of MAUD, lack of confidence in the efficacy of medications, misperceived low patient demand for medication treatment, and stigma (59). Patient barriers may include lack of problem awareness, fear of stigmatization, a desire to treat oneself, and low access to medications (59).

How can clinicians individualize their approach to MAUD?

Few data are available to inform the appropriate duration of treatment, so decisions about stopping or changing treatment strategies should be individualized until more data are available to guide such care. For patients not meeting treatment goals, it is reasonable to consider new medications and explore new psychosocial interventions.

In addition to considering patient preference, goals for reduced consumption or abstinence, and co-occurring conditions, the role of specific genotypes and phenotypes in predicting the response to MAUD is being actively investigated. One proposed strategy categorizes patients with AUD as phenotypically "reward drinkers" (those who drink primarily for the positive or euphoric reinforcing effect) or phenotypically "relief drinkers" (those who drink to avoid the negative reinforcing effects that may arise from withdrawal symptoms). Studies have shown larger treatment effects with naltrexone in persons who drink for reward and with acamprosate in those who drink for relief (60, 61). Although not yet clinically applicable, personalizing medications for patients with AUD is an area of active research.

Which populations are at increased risk for unhealthy alcohol use and merit additional treatment considerations?

AUD commonly co-occurs with other substance use and with other substance use disorders. One analysis found that approximately 29% of persons with AUD reported past-year drug use, and 13% met criteria for a specific drug use disorder (62). Rates of tobacco use are also higher in patients with AUD (63). In 2017, alcohol co-involvement was implicated in 14.7% of opioid overdoses in the United States (64). Injection drug use is the most common risk factor for hepatitis C virus (HCV) transmission, and alcohol use accelerates progression of viral liver disease and is an important barrier to HCV treatment uptake (65). Effective treatments for opioid use disorder (OUD), tobacco use disorder, and HCV infection exist and should be prioritized in this population. Collaborative care models have been shown to be effective (66).

A recurrent-event, case–control study of patients with OUD found that those prescribed medications for OUD had fewer emergency department and inpatient hospitalizations for alcohol-related events. Methadone was associated with a 66% reduction (OR, 0.34 [CI, 0.26 to 0.45]), buprenorphine was associated with a 43% reduction (OR, 0.57 [CI, 0.52 to 0.61]), oral naltrexone was associated with a 37% reduction (OR, 0.63 [CI, 0.52 to 0.76]), and extended-release naltrexone was associated with a 16% reduction (OR, 0.84 [CI, 0.76 to 0.93]) (67).

Unhealthy alcohol use is also common in patients with other psychiatric disorders, including mood disorders, anxiety disorders, posttraumatic stress disorder, and personality disorders. In 2020, almost 56% of adult patients with an underlying mental health disorder reported alcohol use and almost 9% reported heavy alcohol use in the previous month (1). Prevalence of unhealthy alcohol use is high in veterans, and co-occurring posttraumatic stress disorder, mood disorder, and traumatic brain injury are common (68). Addressing both unhealthy alcohol use and underlying psychiatric disorders is critical and may require an intensified treatment approach. Antidepressants, anxiolytics, antipsychotics, and mood stabilizers are not effective standalone treatments for AUD; however, they should be considered in patients with AUD who have co-occurring disorders in which antidepressants or anxiolytics are otherwise indicated (45).

Unhealthy alcohol use is associated with increased risk for sexually transmitted infections, including HIV, and worse adherence to antiretroviral treatment. A stepped-care model delivered in HIV clinics can improve treatment outcomes for HIV and alcohol use compared with usual treatment (69) and may be adaptable for primary care and other general medical settings.

Unhealthy alcohol use is also common in people experiencing

Indications for Referral for Inpatient Detoxification

Reasons for immediate referral

- Moderate to severe withdrawal
- History of seizures or delirium tremens
- Unable to adhere to daily follow-up
- Comorbid psychiatric or medical complications requiring hospitalization
- Unable to take oral medication
- Unsuccessful outpatient detoxification
- Pregnancy

Reasons to strongly consider inpatient detoxification

- Coexisting benzodiazepine use
- High risk for severe alcohol withdrawal, including older age, heavy drinking for an extended period, consumption of >100 g of ethanol daily, random blood alcohol level >200 mg/dL, or signs and symptoms of alcohol withdrawal when not drinking

homelessness. Models of care using long-acting naltrexone and harm reduction services may improve outcomes compared with usual care (70).

What additional care should primary care practitioners consider for patients with unhealthy alcohol use?

In addition to standard vaccinations recommended for healthy adults (such as for influenza and COVID-19), vaccination against hepatitis A and hepatitis B virus should be considered among those with established liver disease (www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf). Pneumococcal polysaccharide and zoster vaccination are recommended for those with AUD. Alcohol can interact with many commonly prescribed and over-the-counter medications (for a detailed list, see www.niaaa.nih.gov/sites/default/files/publications/NIAAA_Harmful_Interactions_English.pdf) (71). Given the prevalence of alcohol use, additional risks with opioids and sedatives should be discussed before they are prescribed. Alcohol use is associated with increased HIV risk behaviors, such as nonuse of condoms, and HIV acquisition; accordingly, HIV testing and HIV prevention with preexposure prophylaxis should be considered and recommended per CDC guidelines.

When should primary care physicians refer patients with unhealthy alcohol use for more specialized treatment?

Most patients with unhealthy alcohol use should be treated in a primary care setting. Visits should be frequent enough to monitor treatment goals and any associated medical, psychiatric, and behavioral adverse effects. Disease severity, response to treatment, need for medication monitoring, and other comorbidities should be considered when determining frequency of visits. Similar to the treatment of other complex chronic conditions, patients who are early in treatment, those with more severe disease, and those who are not achieving treatment goals should be seen more frequently and may need more support from other care team members (such as social workers), whereas visits for clinically stable patients can be less frequent. Referral to specialty care is appropriate for patients not meeting treatment goals despite evidence-based care and patients with severe co-occurring medical disorders, such as advanced liver disease. In addition, although some patients can safely be managed in the outpatient setting with close follow-up, primary care physicians should have a low threshold for referring patients with alcohol withdrawal syndrome to a supervised setting (see the **Box**: Indications for Referral for Inpatient Detoxification).

Although a discussion of outpatient management of alcohol withdrawal syndrome is outside the scope of this review, treatment for the underlying AUD should always be considered and started concurrently with or soon after management of the alcohol withdrawal syndrome (3).

Treatment... Primary care is the ideal setting for the care of patients with unhealthy alcohol use. For patients with at-risk and mild AUD, brief interventions can be effective for decreasing alcohol use. For patients with moderate to severe AUD, psychosocial interventions (CBT, motivational enhancement therapy, mutual support groups) in conjunction with medication are recommended. First- and second-line MAUD are safe, can be prescribed by general internists, and should be offered when indicated (even if psychosocial services are unavailable). Referral to specialty services, including addiction specialists, should be considered for any patient who does not respond to treatment and for those with significant comorbidity. Given the increased prevalence of comorbidities among patients with unhealthy alcohol use (such as substance use, mental illness, and chronic pain), screening for and addressing these conditions in addition to risky sexual behavior should be part of routine care.

CLINICAL BOTTOM LINE

Practice Improvement

What factors do U.S. stakeholders use to evaluate the quality of care for patients with unhealthy alcohol use?

Identification and treatment of unhealthy alcohol use consistently rank high as public health priorities (72). Guidelines addressing screening and brief intervention are available from the USPSTF (27). AUD treatment guidelines are available from the American Psychiatric Association, and guidelines for management of alcohol withdrawal syndrome are available from the American Society of Addiction Medicine (3, 45). Despite this, rates of screening and treatment for unhealthy alcohol use remain low compared with other recommended preventive health practices (72). Primary care practitioners, provider organizations and delivery systems, payers, and health plans can work together to improve practitioner knowledge, incentivize screening and treatment, improve reimbursement models for remote health visits, streamline access to medications and psychosocial services, improve access to specialist treatment for patients with more severe disease, leverage technology to improve screening practices and treatment provision (for example, clinical decision support), and use performance measures for practice improvement (73). Multifaceted interventions that target multiple organizational levels and stakeholders are most effective (74).

In the Clinic
Tool Kit

Alcohol Use

Patient Information

https://medlineplus.gov/alcoholusedisorderaud.html
https://medlineplus.gov/languages/alcoholusedisorderaud.html
Information and handouts in English and other languages from the National Institutes of Health's MedlinePlus.

www.niaaa.nih.gov/publications/brochures-and-fact-sheets
Brochures and fact sheets on alcohol's effects on health from the National Institute on Alcohol Abuse and Alcoholism.

www.cdc.gov/alcohol/index.htm
Information on alcohol and public health from the Centers for Disease Control and Prevention.

Information for Health Professionals

www.niaaa.nih.gov/health-professionals-communities
Resources for health professionals from the National Institute on Alcohol Abuse and Alcoholism.

https://journals.lww.com/journaladdictionmedicine/Fulltext/2020/06001/The_ASAM_Clinical_Practice_Guideline_on_Alcohol.1.aspx
Clinical practice guideline on alcohol withdrawal management from the American Society of Addiction Medicine.

https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9781615371969
Practice guideline for pharmacologic treatment of patients with alcohol use disorder from the American Psychiatric Association.

WHAT YOU SHOULD KNOW ABOUT ALCOHOL USE

What Is Unhealthy Alcohol Use?

Unhealthy alcohol use refers to drinking that causes or may cause physical, psychological, or social harm. Alcohol use is the seventh leading cause of death globally and is often underrecognized and undertreated. There are various levels of alcohol use, including:

- Lower-risk use (drinking below a level believed to cause physical or psychosocial harm)
- At-risk use (drinking at a level that may be harmful to your health [≥4 drinks/day or ≥8 drinks/week for women and ≥5 drinks/day or ≥15 drinks/week for men])
- Heavy episodic drinking (≥4 drinks [for women] or ≥5 drinks [for men] on a single occasion)
- Alcohol use disorder (a pattern characterized by craving and dependence, use despite negative consequences, and loss of control)

What Medical Conditions Are Associated With or Worsened by Alcohol Use?

Alcohol use has no clear benefits. Unhealthy alcohol use has negative effects on health and is associated with worsening of existing health conditions. Unhealthy alcohol use may impair mental health and cognition, nutrition, engagement in care, and medication adherence.

Medical conditions that are associated with or worsened by alcohol use include:

- Injuries and interpersonal violence
- Infectious diseases
- Cancer
- Cardiovascular disease
- Digestive disease
- Neurologic and psychiatric disease
- Respiratory disease
- Endocrine disease
- Pregnancy-related conditions (fetal alcohol syndrome, miscarriage)

What Are the Risk Factors?

Genetic and environmental risk factors are associated with unhealthy alcohol use. Starting to drink at an earlier age can lead to heavier alcohol use later in life and increased risk for alcohol-related injuries. Older patients with unhealthy alcohol use are more likely to be harmed by alcohol's effect on cognition and interaction with other existing health issues or medications. Although alcohol use is more common in men, women are more vulnerable to harms. Lower socioeconomic groups are at risk for greater harms associated with alcohol use. Groups that are marginalized on the basis of race, ethnicity, or sexuality may also experience more harm from alcohol use.

How Is Unhealthy Alcohol Use Diagnosed?

You will complete a questionnaire or your doctor will ask you a short series of questions about how much alcohol you drink and how often. These questions will help determine your level of risk. If you are diagnosed with unhealthy alcohol use, your doctor will ask you more questions about your medical history, which might include questions about family history of mental illness, substance use disorders, and other substance use (nicotine, cannabis, prescription and over-the-counter drugs). Along with these screening questions, a physical examination and laboratory testing can also help with diagnosis and understanding the severity of unhealthy alcohol use.

How Is Unhealthy Alcohol Use Treated?

If you are diagnosed with unhealthy alcohol use, your treatment will depend on the level of severity and health risks. In general, your doctor will speak with you about your specific risk levels and advise you about drinking less or stopping altogether. Any reduction in alcohol use is associated with improved survival, with the best effects achieved with abstinence. Treatment options for those diagnosed with moderate to severe alcohol use disorder should include medications combined with counseling and/or support groups. Treatment of withdrawal symptoms, other substance use disorders, and mental health disorders may require inpatient or more specialized care.

Questions for My Doctor

- How do I know if I am drinking too much or too often?
- What are the signs and symptoms of alcohol withdrawal?
- How often should I see you to discuss treatment for unhealthy alcohol use?
- Should I be on medication to help treat alcohol use disorder?
- Does alcohol interact with any of my medications?
- What vaccinations should I get to protect me from infections?
- Are there additional resources to help me with unhealthy alcohol use?

For More Information

ACP℠
American College of Physicians
Leading Internal Medicine, Improving Lives

Centers for Disease Control and Prevention
www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm

Substance Abuse and Mental Health Services Administration
www.samhsa.gov/sites/default/files/alcohol-use-facts-resources-fact-sheet.pdf

Patient Information

Appendix Figure 1. **Recommended screening and assessment instruments for general medical settings: the NIAAA Single Alcohol Screening Question and the AUDIT-C.**

NIAAA Single Alcohol Screening Question
Question: How many times in the past year have you had *x* or more drinks in a day? (where *x* is 5 for men and 4 for women)
Scoring: ≥1 episode is considered a positive screening result, which should be followed by administration of the AUDIT-C or another measure to categorize level of risk

AUDIT-C*					
Questions	Points				
	0	1	2	3	4
1. How often did you have a drink containing alcohol in the past year?	Never	Monthly or less	2–4 times a month	2–3 times a week	≥4 times a week
2. How many drinks did you have on a typical day when you were drinking in the past year?	0–2	3–4	5–6	7–9	≥10
3. How often did you have ≥6 drinks on 1 occasion in the past year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
Scoring: Points for each of the 3 items are summed. Total score of ≥4 for men and ≥3 for women is considered positive for unhealthy alcohol use. Cutoffs may vary depending on purpose and population of interest. For the USAUDIT-C, the response scale, the drinking threshold in question 3, and the scoring cutoffs differ from those in the AUDIT-C.					

AUDIT-C = Alcohol Use Disorders Identification Test–Consumption; NIAAA = National Institute on Alcohol Abuse and Alcoholism.
* The USAUDIT-C (30) has the same questions as the AUDIT-C but uses a 6-point scale rather than a 4-point scale to account for standard drink size in the United States. Scores >7 for women and for men aged >65 years and >8 for men aged ≤65 years are considered positive for unhealthy alcohol use.

Appendix Figure 2. **Alcohol Symptom Checklist for assessment of alcohol use disorder.**

In the past 12 months...

1. Did you find that drinking the same amount of alcohol has less effect than it used to or did you have to drink more alcohol to get intoxicated?	No	Yes
2. When you cut down or stop drinking did you get sweaty, nervous, have upset stomach or shaky hands? Did you drink alcohol or take other substances to avoid these symptoms?	No	Yes
3. When you drank, did you drink more or for longer than you planned to?	No	Yes
4. Have you wanted to or tried to cut back or stop drinking alcohol, but been unable to do so?	No	Yes
5. Did you spend a lot of time obtaining alcohol, drinking alcohol, or recovering from drinking?	No	Yes
6. Have you continued to drink even though you knew or suspected it creates or worsens mental or physical problems?	No	Yes
7. Has drinking interfered with your responsibilities at work, school, or home?	No	Yes
8. Have you been intoxicated more than once in situations where it was dangerous, such as driving a car or operating machinery?	No	Yes
9. Did you drink alcohol even though you knew or suspected it causes problems with your family or other people?	No	Yes
10. Did you experience strong desires or craving to drink alcohol?	No	Yes
11. Did you spend less time working, enjoying hobbies, or being with others because of your drinking?	No	Yes

From Sayre M, Lapham GT, Lee AK, et al. Routine assessment of symptoms of substance use disorders in primary care: prevalence and severity of reported symptoms. J Gen Intern Med. 2020;35:1111-9. [PMID: 31974903] doi:10.1007/s11606-020-05650-3

Appendix Table. **Signs and Symptoms of Alcohol Withdrawal**

Sign or Symptom	*Notes*
Minor symptoms	Diaphoresis, nystagmus, tachycardia, hyperreflexia, hypertension, nausea or vomiting, low-grade fever, diarrhea, mild agitation
Hallucinations (auditory, visual, tactile)	May occur while intoxicated; sensorium otherwise clear unless progression to delirium tremens
Withdrawal seizures	Grand mal; peak occurrence 12–48 hours after last drink
Delirium tremens	Agitated, delirious state with tremulousness, hallucinations, and autonomic overactivity