REVIEW ARTICLE

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Identification and Treatment of Alcohol Use Disorder

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CME

Alcohol use disorder is a chronic relapsing and remitting syndrome in which excessive drinking of alcohol persists despite causing health and social problems.[1] The disorder is a leading contributor to illness and death[2] but is frequently not diagnosed or treated in clinical settings, and as a result, the burden of disease remains high. In the United States, an estimated 29 million persons are affected by the disorder, leading to approximately 178,000 deaths in 2021, a health burden that is approximately double that associated with the use of opioids.[3] Unhealthy alcohol use by a patient is suggested by history, biologic markers, and coexisting conditions such as liver disease. Treatment for alcohol use problems has been shown to improve outcomes in most cases. This review discusses ways of identifying the disorder, associated biomarkers, and psychosocial and pharmacologic treatments, with emphasis on their use in general medical settings.

Pathogenesis and Neurobiologic Characteristics

The enduring myth that alcohol use disorder results from a moral failure continues to influence public and professional views of the condition.[4] However, an estimated 50% of the risk of alcohol use disorder is thought to be inherited.[5] Furthermore, mental health disorders are associated with a doubled risk of alcohol use disorders.[6] Adverse early life experiences[7] and trauma in adult life (e.g., sexual assault or trauma during military service) have been reported to increase risk. Ready availability of alcohol at low cost and widespread outlets are considered additional important risk factors. The World Health Organization (WHO) global action plan to reduce consumption and harms from alcohol recommends increasing alcohol taxes, setting a minimum age for purchasing alcohol, and limiting hours for the sale of alcohol, among other actions.[8]

Consumption of alcohol activates the reward regions of the brain,[9] increasing the release of dopamine, with additional involvement of endogenous opioids, γ-aminobutyric acid (GABA), endocannabinoids, and other neurotransmitters. The reward system projects to the orbitofrontal cortex and provides a pathway for alcohol to influence decision making, including reduced inhibitory control. With repeated exposure, neurotransmitter responses are blunted in the most severe forms of the disorder. As a result, increasing doses of alcohol are needed to produce the same effect (alcohol tolerance), and alcohol withdrawal syndrome emerges when high levels of consumption are reduced or ceased. Pharmacotherapies for the disorder seek to target these neurobiologic changes (Fig. 1).

KEY POINTS

IDENTIFICATION AND TREATMENT OF ALCOHOL USE DISORDER

- A quantitative alcohol history should be recorded for all patients, because alcohol use contributes to many physical and mental disorders.
- A person-centered, nonjudgmental approach should be adopted.
- Brief interventions can be delivered effectively by most health care professionals.
- Pharmacologic treatment is effective and underused.
- Specialist services offer comprehensive care, including psychosocial interventions.
- Follow-up is recommended owing to the relapsing and remitting nature of alcohol use disorder.

CLINICAL ASSESSMENT

DEFINING ALCOHOL USE DISORDER

The *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5), defines alcohol use disorder as the presence of at least 2 of 11 symptoms (Table 1).[1] These symptoms relate to drinking behavior and its consequences and not directly to the amount consumed. Moderate drinking is defined by the Department of Health and Human Services as up to one drink per day for women and two for men, with each standard drink containing 14 g of alcohol.[10] Alcohol use disorders are commonly overlooked in clinical practice.[11] When appropriate, a quantitative alcohol history should be recorded by health care personnel because the risk of medical complications such as cancer and liver injury are related to the average daily consumption of alcohol. A history of alcohol withdrawal (see below) or intoxication should be sought. Common associated physical signs include overweight, hypertension, and stigmata of liver disease.

Systematic use of screening instruments reportedly increases detection of alcohol use disorder. The WHO has endorsed the Alcohol Use Disorders Identification Test (AUDIT), which is sensitive and has been implemented in various settings.[12] There is a version for use in an interview and another for patient self-reporting; both versions score 10 questions on a scale of 0 to 4, with higher scores indicating greater use or problems from use. Scores of 8 or greater are considered to be indicative of hazardous alcohol use. Short versions (AUDIT-C and AUDIT-3) have been devised to rapidly screen for quantity of use but not for its consequences.[12] The four-question CAGE (Cut Down Drinking, Annoyed by Criticism, Guilty Feelings, and Eye-Opener) screening is a brief instrument in which two or more affirmative answers suggest the presence of an alcohol use disorder; however, CAGE is insensitive for detection of mild problems with alcohol use.

Occasionally, patients do not accurately report their alcohol use (or deny more than minimal use) despite careful efforts at history taking, a factor that leads to considerable clinical uncertainty about the degree of alcohol use.[13] Adverse consequences of reporting alcohol use, such as stigmatization by family and clinicians or possible denial of access to treatment such as transplantation, may inhibit patient self-reporting.[14] Collateral history obtained from patient contacts or past medical records may be helpful.[15] A diagnosis of occult alcohol use may also be revealed by periodic reevaluation or observation in an alcohol-free hospital environment.

BIOLOGIC MARKERS OF ALCOHOL USE

Biologic markers have begun to play an important role in the detection of recent alcohol consumption and in monitoring ongoing alcohol use during treatment.[11] Tests of liver-enzyme concentrations are widely available but have limited sensitivity and specificity for detection of alcohol use. Among routinely performed tests, mean corpuscular volume and the levels of liver enzymes (γ-glutamyl transpeptidase, alanine aminotransferase [ALT], and aspartate aminotransferase [AST]) can be useful biomarkers of chronic alcohol use that are available without additional cost or consent issues.[16] Of the tests discussed here, the most sensitive and specific is γ-glutamyl transpeptidase, but levels of this enzyme are elevated in only approximately half of men with an alcohol use disorder and in even fewer women or younger people. Elevation of γ-glutamyl transpeptidase levels may result from non–alcohol-related liver disease, overweight, diabetes, heart failure, hyperthyroidism, and some medications, which makes the test nonspecific. Nevertheless, when elevated, serial γ-glutamyl transpeptidase levels

Table 1. Diagnostic Criteria for Alcohol Use Disorder.*

Broad Domain	DSM-5 Diagnostic Criteria
Impaired control	Drinking larger amounts or over longer periods than intended. Desire or unsuccessful attempts to cut down or control alcohol use. Great deal of time spent obtaining or using alcohol or recovering from alcohol use. Craving or a strong desire or urge to use alcohol.
Social dysfunction and physical risk	Failure to fulfill major role obligations as a result of alcohol use. Continued drinking despite social or interpersonal problems. Diminished social, occupational, or recreational activities due to drinking. Recurrent alcohol use in physically hazardous situations. Continued drinking despite physical or psychological problems.
Physiological dependence	Tolerance, as evidenced by a markedly diminished effect of alcohol use. Withdrawal syndrome or drinking to prevent withdrawal.

* Diagnostic criteria are from the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5). The diagnostic threshold is the presence of 2 of the 11 criteria during a 12-month period. The severity of the disorder is determined on the basis of the number of criteria met — mild (2 or 3 criteria), moderate (4 or 5 criteria), or severe (6 to 11 criteria). Previous versions of the DSM distinguished alcohol abuse from alcohol dependence, but there was no substantial difference in outcomes, and these two diagnoses were merged.

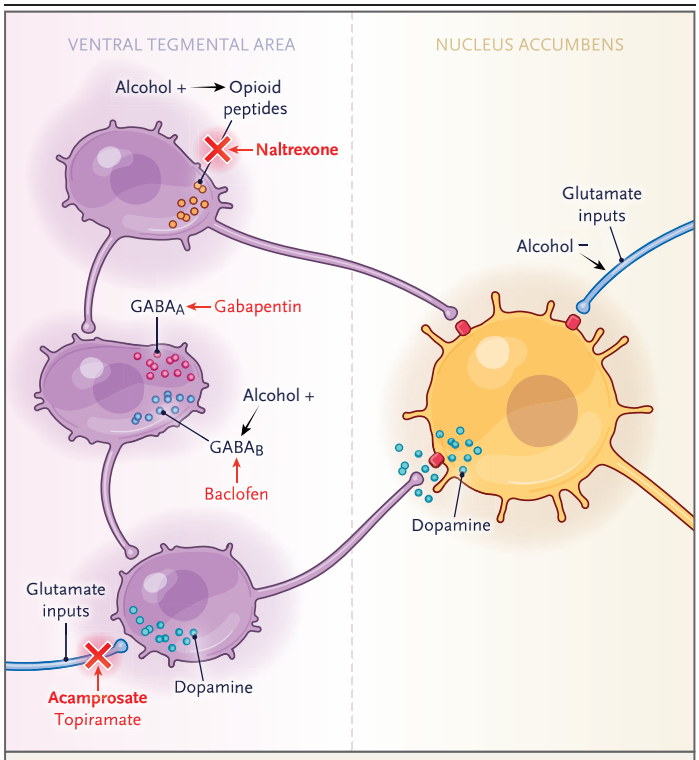

Figure 1. Overview of Presumed Actions of Pharmacotherapies for Alcohol Use Disorder.

Depicted are the hypothesized mechanisms of action of pharmacotherapies used in the treatment of alcohol use disorder. Acamprosate and naltrexone are approved in the United States for the treatment of alcohol use disorder; baclofen and topiramate are not specifically approved for this use. GABA denotes γ-aminobutyric acid.

have been used to monitor ongoing alcohol use, and with abstinence the serum concentration falls, with a half-life of approximately 2 to 3 weeks. ALT and AST levels and mean corpuscular volume are less informative with regard to chronic or heavy alcohol use.[16] Detection of ethanol itself in blood, breath, or urine reflects recent exposure but is positive for only a limited number of hours after drinking. However, the test can be particularly useful in the emergency department and other settings to confirm recent alcohol use.

Nonoxidative alcohol metabolites are emerging as clinically useful biomarkers of alcohol consumption. Phosphatidylethanol is a conjugate of phosphatidylcholine and ethanol that is present in red cells for several weeks after drinking. The half-life is approximately 10 days, yielding a detection window for alcohol use of 3 to 5 weeks depending on the baseline level. A negative phosphatidylethanol test (below the laboratory threshold for reporting) may help confirm abstinence in the context of conditions such as chronic liver disease[17] and in assessment for liver transplantation,[18] and liver centers increasingly rely on this test. Levels of phosphatidylethanol broadly correlate with the amount of alcohol consumed,[19] so this test can be used to assess recent alcohol use in patients who are receiving treatment for alcohol use disorder in primary care and those with metabolic-associated steatotic liver disease, described below. In the primary care setting, patients accepted this test when offered in a

clinically respectful context.[20] Ethyl glucuronide, another conjugated ethanol metabolite, is detectable in urine for approximately 48 hours after consumption of alcohol, but urine levels correlate poorly with the amount of consumption.

Carbohydrate-deficient transferrin (expressed as a percentage) refers to isoforms of transferrin with a reduced number of sialic acid residues. The sensitivity and specificity of this test is lower than those for the above discussed alcohol metabolites, but it still may be useful.[21] In current practice, longer-term alcohol use is assessed by γ-glutamyl transpeptidase level, carbohydrate-deficient transferrin percentage, or phosphatidylethanol level, whereas recent use is detected by ethyl glucuronide or blood ethanol level. Hair testing for alcohol metabolites can provide a measure of alcohol use over a period of several months but has been generally limited to forensic settings. Any positive biomarker result discordant with patient self-reporting is clinically challenging but can prompt clinical review, sensitive discussion, and engagement with regard to appropriate treatment.

COEXISTING CONDITIONS

The presence of coexisting conditions with alcohol use disorder is the rule rather than the exception and may entail other substance use disorders, mental health disorders, or physical health disorders. The most common coexisting condition is another substance use disorder, particularly smoking, which contributes to morbidity in this population. Coexisting mental health conditions occur in many, if not most, patients with alcohol use disorder, particularly those with severe alcohol use, and are more common in women than men.[22] Anxiety and depression and so-called externalizing disorders (antisocial personality disorder, attention deficit disorder, and hyperactivity) are particularly common in patients with alcohol use disorder. The risk of suicide is increased, particularly in the first 5 years after diagnosis of alcohol use disorder.[23] It is advisable to screen patients with this disorder for suicide risk and symptoms of other mental health conditions (ideally with the use of a validated instrument such as the nine-item Patient Health Questionnaire), include mental health care in the management plan, and if appropriate, engage specialist mental health services. Social problems commonly associated with alcohol use disorder are lack of employment, occupational safety risks (including driving), problems with housing and personal relationships, and legal issues. These issues may resolve with reduction of alcohol use, but aid from social service and other referrals may help.

MEDICAL COMPLICATIONS

The most common physical conditions that may be associated with alcohol use include overweight, systemic hypertension, and liver disease. Multiple medical complications often coexist. Problems with maintaining adequate nutrition relate in part to the "empty calories" of alcohol and include deficiency of micronutrients, particularly thiamine and zinc, as well as electrolyte disorders, protein deficiency, and weight gain.[24] Among neurologic disorders, cognitive impairment ranges in severity from clinically inapparent to severe and disabling and can arise from multiple causes such as head trauma, drugs of abuse, Wernicke–Korsakoff syndrome, subdural hematomas, and other conditions. Cognitive status should generally be reevaluated after resolution of withdrawal and any sedative effects, and the extent of any impairment should be considered during management planning. Osteopenia is another frequently overlooked problem associated with alcohol use, particularly in women.

Alcohol-related liver disease is now the most common underlying indication for liver transplantation[25] and has become an even greater challenge since the coronavirus disease 2019 pandemic (accounting for 41% of liver transplantations in 2022).[26] Patients with alcohol-related liver disease often first present to the hospital with life-threatening complications of cirrhosis. Alcohol-related liver disease may coexist with other liver diseases, such as chronic viral hepatitis. Alcohol use with coexisting metabolic-associated steatotic liver disease is recognized by the new classification of metabolic- and alcohol-related liver disease.[27] In the ambulatory care setting, the severity of liver disease may be assessed by means of routine blood tests; measures derived from these tests, such as the AST-to-platelet ratio index, calculated as (AST ÷ the upper limit of the normal range) × 100 ÷ the platelet count, and the Fibrosis-4 index, calculated as (age × AST) ÷ (platelet count × √ALT); the MELD (model for end-stage

liver disease) score; or newer hepatic fibrosis markers such as ELF (enhanced liver fibrosis), a proprietary score that is calculated from blood levels of tissue inhibitor of matrix metalloproteinase 1, N-terminal peptide of procollagen III, and hyaluronic acid.[28] The cutoffs for these scores vary with the desired sensitivity and specificity, for which reason several scores are often used in combination. Transient elastography is a noninvasive measure of liver fibrosis that may be offered at the point of care and can be tested serially to monitor the progress of fibrosis. Scores rise with recent alcohol use, so the test is ideally performed after at least a month of abstinence.[29]

MANAGEMENT

Treatment of alcohol use disorder is generally effective, but most affected persons do not receive treatment.[22] Persons with this disorder may be stigmatized by others, including clinicians, and self-reproach is common. Ambivalence about cessation of drinking and engagement in treatment are common challenges. Adoption of a person-centered and nonjudgmental approach that supports recovery is useful.[30] In addition, negotiation of a treatment plan in collaboration with the patient is advisable, particularly because there is limited evidence favoring any one specific approach. Culturally and racially relevant recovery support can be offered where available; however, access to certain treatments may be limited by cost or local availability. These practical considerations are particularly important for the ambivalent patient who may be, for example, more likely to engage in a local or less costly treatment option. Recovery may occur without engagement in health services or support services and has been described as "natural" recovery.[31]

Patients with multiple coexisting conditions may be overwhelmed by referral to multiple specialists. Integration of care offers advantages to the patient and health care systems. For example, integrated substance-abuse and liver-disease treatment programs have been relatively effective for patients with advanced alcohol-related liver disease[32] and in the context of liver transplantation,[33] but this model is not widely available.

Successful abstinence from alcohol may be associated with marked medical and social recovery. For example, abstinence improves survival in patients hospitalized for alcohol-related cirrhosis,[34] alcoholic hepatitis,[35] and alcohol-related pancreatitis[36] and reduces hospital admissions for recurrent attacks of pancreatitis,[37] which makes long-term abstinence from alcohol the foundation of treatment for persons with these disorders. Persons with less severe alcohol use disorder and without life-threatening harms may improve or recover with substantial reduction of alcohol use.[38] A period of abstinence may provide stabilization of the patient's condition and allow subsequent moderate consumption of alcohol within the limits recommended by the Department of Health and Human Services.[10] However, alcohol consumption may escalate and lead to further intervention. Accordingly, follow-up is recommended, as discussed below.

MANAGEMENT OF ALCOHOL WITHDRAWAL

Planning for elective withdrawal from alcohol use includes the selection of an appropriate setting.[39] Ambulatory care is suitable for most uncomplicated cases. For similar cases in which the patient does not have a safe home environment, a clinically supported nonhospital withdrawal-management unit may be appropriate. Hospital care is typically recommended for patients in whom complications of withdrawal are likely, including those who have had previous withdrawal seizures or who have concurrent medical or psychiatric illness or GABAergic drug dependence.[39,40] The diagnosis of alcohol withdrawal syndrome is made clinically. The main features are widely appreciated and include tremor, agitation, tachycardia, hypertension, low-grade fever, and in severe instances, agitated delirium with visual hallucinations (delirium tremens). Symptom rating scales, such as the Clinical Institute Withdrawal Assessment for Alcohol–Revised, are useful to monitor the progress of withdrawal but are not validated as diagnostic instruments, particularly in the presence of coexisting medical conditions.

Withdrawal is managed with benzodiazepines and, in the hospital setting, intravenous fluids to maintain hydration and nutritional support.[39] Long-acting benzodiazepines with active metabolites, such as diazepam and chlordiazepoxide, are effective but are subject to misuse and risk precipitation of encephalopathy in patients with advanced liver disease. Oxazepam and lorazepam

have shorter half-lives, lack active metabolites, and have been preferred for the treatment of patients with liver disease. Symptom-triggered medication as compared with fixed-schedule medication reduces the dose and duration of benzodiazepine treatment and has been recommended in settings where frequent monitoring of clinical status can be provided.[39]

In the intensive care setting, warranted in severe cases of withdrawal, intravenous administration of midazolam, phenobarbital, or dexmedetomidine has been effective for ameliorating withdrawal symptoms. For prevention of Wernicke's encephalopathy, high-dose thiamine is administered parenterally to hospitalized patients and continued in case of suspected Wernicke's syndrome. In the ambulatory setting, the usual prophylactic thiamine dose is 100 mg administered orally for 3 to 5 days.[39] Sleep disturbance may persist for weeks; it often predicts alcohol use relapse and may respond to behavioral treatment. Limited evidence suggests a role for the use of GABAergic agents[41]; however, dependence on benzodiazepines should be avoided.

Table 2. FLAGS Approach to Brief Intervention for Unhealthy Alcohol Use.

Feedback — Give feedback about the personal risks and consequences associated with drinking.
Listen — Listen to the patient's response. Discuss any false beliefs regarding the patient's alcohol consumption level in relation to guidelines.
Advice — Provide specific advice about the importance of changing current drinking using a nonjudgemental tone. Describe probable benefits of reduced drinking.
Goals — Discuss safe drinking limits and assist the patient to set goals for changing drinking patterns. Instill optimism in the patient that the chosen goal can be achieved. Motivation-enhancing techniques can be used to encourage patients to develop, implement, and commit to plans to stop drinking.
Strategies — Negotiate practical strategies to reach the agreed goal.

PSYCHOSOCIAL TREATMENT

Brief intervention refers to structured and time-limited advice regarding alcohol, typically one to three sessions, 5 to 20 minutes each, and is effective in a range of clinical contexts.[42] It allows the provider to give personalized feedback regarding the patient's alcohol use and its effects as well as advice on safe levels of consumption and encourages change with the use of a motivational interviewing approach (Table 2). Brief intervention is designed to be delivered by professionals who are not specialists in addiction treatment and may also be effectively delivered by means of telephone or online approaches.[42] Follow-up is important, and the intervention may be repeated as indicated.[43] Brief intervention may also motivate patients to begin pharmacotherapy or specialized treatment.

Peer-supported recovery is available in diverse forms. Support from Alcoholics Anonymous (AA; aa.org) is still the most widely used and effective intervention.[44] In one study, 23% of persons attended AA for more than 6 months, and of these, 72% were abstinent from alcohol at 16 years of follow-up.[45] Participation in AA may be encouraged for persons whose goal is abstinence and who are willing to participate. The SMART (Self Management and Recovery Training) method (smartrecovery.org) uses a harm-reduction approach to peer support led by trained clinicians, for which there is evidence of benefit.[46] Both programs offer in-person and online participation.

Effective psychosocial treatments include cognitive behavioral therapy, with 15 to 26% of participants having better outcomes than controls.[47] Among these treatments finding a place in clinical practice are motivational enhancement therapy, 12-step facilitation, and newer, so-called third-wave psychotherapies, including acceptance and commitment therapy,[48] mindfulness,[49] and dialectical behavior therapy.[50] In brief, motivational enhancement helps patients change behavior by emphasizing the capacity to make changes and its benefits. Twelve-step facilitation is an individualized intervention to actively encourage engagement with a 12-step fellowship. In acceptance and commitment therapy, the participant acknowledges adverse feelings or behaviors while emphasizing the need to address problematic behavior. Mindfulness encourages the person to observe their substance cravings and gain the capacity to dismiss them. Dialectical behavior therapy directs the participant to identify their emotions and increase their capacity to regulate the resulting behavior. A range of Web-based and electronic modes of delivery allow these therapeutic approaches to be presented in a manner that is increasingly available at low cost to many patients.[51] Physical exercise may be integrated with other approaches as appropriate general advice, particularly for patients with metabolic disorders, but a beneficial effect of physical activity on alcohol use has not been clearly established.[52]

Table 3. Medications for Alcohol Use Disorder.*

Medication	Mode of Action	Typical Dose	Use in Liver Disease
Approved for the treatment of alcohol use disorder			
Disulfiram	Acetaldehyde dehydrogenase inhibitor	200 mg per day	Contraindicated
Naltrexone	Mu opioid receptor antagonist	50 mg per day 380 mg monthly intramuscular injection	Risk of hepatotoxic effects precludes use in advanced liver disease May consider in early liver disease
Acamprosate	NMDA agonist† Calcium load†	666 mg three times daily (reduce if body weight is <65 kg)	Precaution in Child–Pugh class C cirrhosis‡
Not approved in the United States for the treatment of alcohol use disorder			
Baclofen	GABA B receptor agonist	10–25 mg three times daily	Acceptable side-effect profile in patients with liver disease Minimal hepatic metabolism
Topiramate	GABA A receptor agonist AMPA–kainite glutamate receptor blocker Calcium- and sodium-channel blocker	Up to 100 mg twice daily	Risk of encephalopathy precludes use in advanced liver disease May consider in compensated liver disease
Gabapentin	GABA A receptor agonist	Up to 900 mg twice daily	Uncertain
Varenicline	Nicotinic acetylcholine receptor partial agonist	2 mg per day	Uncertain

* AMPA denotes α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid, GABA A γ-aminobutyric acid type A, GABA B γ-aminobutyric acid type B, and NMDA *N*-methyl-D-aspartate.
† The mechanism of action is uncertain.
‡ The Child–Pugh score grades severity of liver disease: class A indicates well-compensated disease, class B decompensated disease, and class C advanced decompensated disease.

PHARMACOTHERAPY

Several pharmacotherapies are approved for alcohol use disorder (Fig. 1 and Table 3).[53] These can be prescribed in primary care, by internists, or by specialists, but the use of these treatments has been low. Naltrexone is a long-acting orally active opioid receptor antagonist that reduces craving and consumption of alcohol, with its effectiveness established in trials and confirmed in a meta-analysis.[54] Once-daily dose administration makes naltrexone a convenient first-line agent. Another agent, acamprosate, modulates glutamatergic neurotransmission, and its effectiveness has also been reported by meta-analysis. It has a favorable safety profile and is safe for use in patients with liver disease, but it requires administration in three daily doses. These drugs are only modestly effective, with a relative risk of heavy drinking reduced to 0.81 for naltrexone and the relative risk of any drinking reduced to 0.88 for acamprosate.[54] Disulfiram may be the most effective of the current pharmacotherapies in accomplishing abstinence in a motivated patient in whom administration is supervised.[55] Liver tests should be monitored early in treatment, and disulfiram is contraindicated in advanced liver disease owing to a risk of life-threatening hepatotoxic effects.[56] If alcohol is consumed, disulfiram precipitates an adverse reaction comprising flushing, nausea, tachycardia, and hypotension. The risk of this aversive reaction discourages further alcohol use. Polymorphisms that predict response to medications in alcohol use disorder have been evaluated but not prospectively validated, so their use has not been recommended.[53]

Other medications may be effective but are not approved in the United States for the treatment of alcohol use disorder.[53] Topiramate potentiates GABA type A activity, inhibits glutamate activity, and was at least as effective as naltrexone in a comparative trial.[57] Slow dose adjustment minimizes the side effects of topiramate (i.e., metabolic alkalosis, paresthesias, and mental clouding) to a generally acceptable level. Gabapentin has

been shown to be effective and to have a satisfactory safety profile, but it is associated with a substantial risk of abuse.[58] Baclofen is approved in France for the treatment of alcohol use disorder and has been widely used there. It was effective in several trials, but other studies have shown limited efficacy. This drug is sedating, carries a risk of abuse, and is dangerous in overdose, and therefore it has not been considered to be a first-line agent. Nalmefene is a second-generation orally active opiate receptor antagonist that has been approved for use in Europe and elsewhere (including Japan) but is not approved in the United States because the evidence for effectiveness is uncertain. New agents as well as repurposing of existing registered medications are under investigation for treatment of alcohol use disorder, including appetite-suppressing agents such as glucagon-like peptide 1, cannabinoids, and psychedelic agents such as psilocybin and 3,4-methylenedioxymethamphetamine, but evidence of the effectiveness of these drugs is still emerging.[59]

Alcohol consumption can alter cytochrome P450 drug metabolism, particularly metabolism of anticonvulsants and anticoagulants, and may affect medication adherence, so all medications should be prescribed with caution to patients with alcohol use disorder. Antidepressants may be prescribed for coexisting mood disorder but are not indicated for alcohol use disorder per se.[60] The prescribing of benzodiazepines should be limited to short-term treatment of withdrawal owing to a lack of long-term efficacy, sedative interaction with alcohol, and risk of abuse.

SUMMARY

Alcohol use disorder is a relapsing and remitting medical and psychological disorder that influences physical health, mental health, and social functioning, and continuing care is recommended. Alcohol use is assessed by patient self-reporting with assistance from laboratory biomarkers. Generalist clinicians can provide brief interventions, encourage treatment adherence, reinforce goals, monitor recovery related to coexisting conditions, and engage specialist services when appropriate.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

REFERENCES

1. Diagnostic and statistical manual of mental disorders, 5th ed. Washington, DC: American Psychiatric Association, 2013.
2. GBD 2016 Alcohol and Drug Use Collaborators. The global burden of disease attributable to alcohol and drug use in 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Psychiatry 2018;5:987-1012.
3. National Institute on Alcohol Abuse and Alcoholism. Alcohol-related emergencies and deaths in the United States. November 2024 (https://www.niaaa.nih.gov/alcohols-effects-health/alcohol-topics/alcohol-facts-and-statistics/alcohol-related-emergencies-and-deaths-united-states#:~:text=The%20Alcohol%2DRelated%20Disease%20Impact,States%2C%20behind%20tobacco%2C%20poor%20diet).
4. Cazalis A, Lambert L, Auriacombe M. Stigmatization of people with addiction by health professionals: current knowledge: a scoping review. Drug Alcohol Depend Rep 2023;9:100196.
5. Verhulst B, Neale MC, Kendler KS. The heritability of alcohol use disorders: a meta-analysis of twin and adoption studies. Psychol Med 2015;45:1061-72.
6. Puddephatt JA, Irizar P, Jones A, Gage SH, Goodwin L. Associations of common mental disorder with alcohol use in the adult general population: a systematic review and meta-analysis. Addiction 2022;117:1543-72.
7. Brady KT, Back SE. Childhood trauma, posttraumatic stress disorder, and alcohol dependence. Alcohol Res 2012;34:408-13.
8. World Health Organization. Global alcohol action plan 2022-2030. June 20, 2024 (https://www.who.int/publications/i/item/9789240090101).
9. Volkow ND, Koob GF, McLellan AT. Neurobiologic advances from the brain disease model of addiction. N Engl J Med 2016;374:363-71.
10. Department of Health and Human Services, Department of Agriculture. 2015–2020 Dietary guidelines for Americans. 8th ed. December 2015 (https://odphp.health.gov/our-work/nutrition-physical-activity/dietary-guidelines/previous-dietary-guidelines/2015).
11. Singal AK, Bataller R, Ahn J, Kamath PS, Shah VH. ACG clinical guideline: alcoholic liver disease. Am J Gastroenterol 2018;113:175-94.
12. Reinert DF, Allen JP. The alcohol use disorders identification test: an update of research findings. Alcohol Clin Exp Res 2007;31:185-99.
13. Kip MJ, Spies CD, Neumann T, et al. The usefulness of direct ethanol metabolites in assessing alcohol intake in non-intoxicated male patients in an emergency room setting. Alcohol Clin Exp Res 2008;32:1284-91.
14. Weinrieb RM, Van Horn DH, McLellan AT, Lucey MR. Interpreting the significance of drinking by alcohol-dependent liver transplant patients: fostering candor is the key to recovery. Liver Transpl 2000;6:769-76.
15. Yates WR, Labrecque DR, Pfab D. The reliability of alcoholism history in patients with alcohol-related cirrhosis. Alcohol Alcohol 1998;33:488-94.
16. Gough G, Heathers L, Puckett D, et al. The utility of commonly used laboratory tests to screen for excessive alcohol use in clinical practice. Alcohol Clin Exp Res 2015;39:1493-500.
17. Stewart SH, Koch DG, Willner IR, Anton RF, Reuben A. Validation of blood phosphatidylethanol as an alcohol consumption biomarker in patients with chronic liver disease. Alcohol Clin Exp Res 2014;38:1706-11.
18. Andresen-Streichert H, Beres Y, Weinmann W, et al. Improved detection of alcohol consumption using the novel marker phosphatidylethanol in the transplant setting: results of a prospective study. Transpl Int 2017;30:611-20.
19. Wurst FM, Thon N, Yegles M, Schrück A, Preuss UW, Weinmann W. Ethanol metabolites: their role in the assessment of

alcohol intake. Alcohol Clin Exp Res 2015;39:2060-72.
20. Thurfjell Å, Sandlund C, Adami J, Hasselström J, Hagströmer M, Lundh L. GPs' experiences of phosphatidylethanol in treatment of hypertension: a qualitative study. BJGP Open 2023;7:1-13.
21. Jones AW. Brief history of the alcohol biomarkers CDT, EtG, EtS, 5-HTOL, and PEth. Drug Test Anal 2024;16:570-87.
22. Grant BF, Goldstein RB, Saha TD, et al. Epidemiology of DSM-5 alcohol use disorder: results from the national epidemiologic survey on alcohol and related conditions III. JAMA Psychiatry 2015;72:757-66.
23. Edwards AC, Ohlsson H, Sundquist J, Sundquist K, Kendler KS. Alcohol use disorder and risk of suicide in a Swedish population-based cohort. Am J Psychiatry 2020;177:627-34.
24. Jophlin L, Liu T-Y, McClain CJ. Nutritional deficiencies in alcohol use disorder/alcohol-associated liver disease. Curr Opin Gastroenterol 2024;40:112-7.
25. Younossi ZM, Stepanova M, Al Shabeeb R, et al. The changing epidemiology of adult liver transplantation in the United States in 2013–2022: the dominance of metabolic dysfunction-associated steatotic liver disease and alcohol-associated liver disease. Hepatol Commun 2024;8.
26. Kwong AJ, Kim WR, Lake JR, et al. OPTN/SRTR 2022 annual data report: liver. Health Resources and Services Administration (https://srtr.transplant.hrsa.gov/ADR/Chapter?name=Liver&year=2022#fig:LItx-counts-diag).
27. Rinella ME, Lazarus JV, Ratziu V, et al. A multisociety Delphi consensus statement on new fatty liver disease nomenclature. Hepatology 2023;78:1966-86.
28. Moreno C, Mueller S, Szabo G. Noninvasive diagnosis and biomarkers in alcohol-related liver disease. J Hepatol 2019;70:273-83.
29. Gianni E, Forte P, Galli V, Razzolini G, Bardazzi G, Annese V. Prospective evaluation of liver stiffness using transient elastography in alcoholic patients following abstinence. Alcohol Alcohol 2017;52:42-7.
30. Bradley KA, Kivlahan DR. Bringing patient-centered care to patients with alcohol use disorders. JAMA 2014;311:1861-2.
31. Kelly JF, Bergman B, Hoeppner BB, Vilsaint C, White WL. Prevalence and pathways of recovery from drug and alcohol problems in the United States population: implications for practice, research, and policy. Drug Alcohol Depend 2017;181:162-9.
32. Arab JP, Addolorato G, Mathurin P, Thursz MR. Alcohol-associated liver disease: integrated management with alcohol use disorder. Clin Gastroenterol Hepatol 2023;21:2124-34.
33. Addolorato G, Mirijello A, Leggio L, et al. Liver transplantation in alcoholic patients: impact of an alcohol addiction unit within a liver transplant center. Alcohol Clin Exp Res 2013;37:1601-8.
34. Alexander JF, Lischner MW, Galambos JT. Natural history of alcoholic hepatitis. II. The long-term prognosis. Am J Gastroenterol 1971;56:515-25.
35. Chedid A, Mendenhall CL, Gartside P, French SW, Chen T, Rabin L. Prognostic factors in alcoholic liver disease. Am J Gastroenterol 1991;86:210-6.
36. Murruste M, Kirsimägi Ü, Kase K, Saar S, Talving P. Long-term survival, risk factors and causes of mortality in surgically treated chronic pancreatitis. Pancreatology 2021;21:714-23.
37. Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. Gastroenterology 2013;144:1252-61.
38. Witkiewitz K, Heather N, Falk DE, et al. World Health Organization risk drinking level reductions are associated with improved functioning and are sustained among patients with mild, moderate and severe alcohol dependence in clinical trials in the United States and United Kingdom. Addiction 2020;115:1668-80.
39. The ASAM clinical practice guideline on alcohol withdrawal management. J Addict Med 2020;14:Suppl 1:1-72.
40. Goodson CM, Clark BJ, Douglas IS. Predictors of severe alcohol withdrawal syndrome: a systematic review and meta-analysis. Alcohol Clin Exp Res 2014;38:2664-77.
41. Gallus S, Lugo A, Borroni E, et al. Symptoms of protracted alcohol withdrawal in patients with alcohol use disorder: a comprehensive systematic review. Curr Neuropharmacol 2023;21:409-16.
42. Haber PS, Riordan BC, Winter DT, et al. New Australian guidelines for the treatment of alcohol problems: an overview of recommendations. Med J Aust 2021;215:Suppl 7:S3-S32.
43. Lieber CS, Weiss DG, Groszmann R, Paronetto F, Schenker S, Veterans Affairs Cooperative Study 391 Group. I. Veterans Affairs Cooperative Study of polyenylphosphatidylcholine in alcoholic liver disease: effects on drinking behavior by nurse/physician teams. Alcohol Clin Exp Res 2003;27:1757-64.
44. Kelly JF. Is Alcoholics Anonymous religious, spiritual, neither? Findings from 25 years of mechanisms of behavior change research. Addiction 2017;112:929-36.
45. Moos RH, Moos BS. Participation in treatment and Alcoholics Anonymous: a 16-year follow-up of initially untreated individuals. J Clin Psychol 2006;62:735-50.
46. Beck AK, Forbes E, Baker AL, et al. Systematic review of SMART Recovery: outcomes, process variables, and implications for research. Psychol Addict Behav 2017;31:1-20.
47. Magill M, Ray L, Kiluk B, et al. A meta-analysis of cognitive-behavioral therapy for alcohol or other drug use disorders: treatment efficacy by contrast condition. J Consult Clin Psychol 2019;87:1093-105.
48. Thekiso TB, Murphy P, Milnes J, Lambe K, Curtin A, Farren CK. Acceptance and commitment therapy in the treatment of alcohol use disorder and comorbid affective disorder: a pilot matched control trial. Behav Ther 2015;46:717-28.
49. Garland EL, Gaylord SA, Boettiger CA, Howard MO. Mindfulness training modifies cognitive, affective, and physiological mechanisms implicated in alcohol dependence: results of a randomized controlled pilot trial. J Psychoactive Drugs 2010;42:177-92.
50. Maffei C, Cavicchioli M, Movalli M, Cavallaro R, Fossati A. Dialectical behavior therapy skills training in alcohol dependence treatment: findings based on an open trial. Subst Use Misuse 2018;53:2368-85.
51. Rogers MA, Lemmen K, Kramer R, Mann J, Chopra V. Internet-delivered health interventions that work: systematic review of meta-analyses and evaluation of website availability. J Med Internet Res 2017;19(3):e90.
52. Stoutenberg M, Rethorst CD, Lawson O, Read JP. Exercise training — a beneficial intervention in the treatment of alcohol use disorders? Drug Alcohol Depend 2016;160:2-11.
53. Kranzler HR, Soyka M. Diagnosis and pharmacotherapy of alcohol use disorder: a review. JAMA 2018;320:815-24.
54. McPheeters M, O'Connor EA, Riley S, et al. Pharmacotherapy for alcohol use disorder: a systematic review and meta-analysis. JAMA 2023;330:1653-65.
55. Skinner MD, Lahmek P, Pham H, Aubin HJ. Disulfiram efficacy in the treatment of alcohol dependence: a meta-analysis. PLoS One 2014;9(2):e87366.
56. Berlin RG. Disulfiram hepatotoxicity: a consideration of its mechanism and clinical spectrum. Alcohol Alcohol 1989;24:241-6.
57. Morley KC, Kranzler HR, Luquin N, et al. Topiramate versus naltrexone for alcohol use disorder: a genotype-stratified double-blind randomized controlled trial. Am J Psychiatry 2024;181:403-11.
58. Mersfelder TL, Nichols WH. Gabapentin: abuse, dependence, and withdrawal. Ann Pharmacother 2016;50:229-33.
59. Morley KC, Perry CJ, Watt J, et al. New approved and emerging pharmacological approaches to alcohol use disorder: a review of clinical studies. Expert Opin Pharmacother 2021;22:1291-303.
60. Pettinati HM. Antidepressant treatment of co-occurring depression and alcohol dependence. Biol Psychiatry 2004;56:785-92.