

Alcohol Use Disorder

Alcohol floods the brain's reward center with dopamine (the 'feel-good' messenger) and cranks up GABA (the 'calm-down' messenger) early, then the brain fights back by turning down its own calming signals and turning up its stress signals—so over time you need alcohol just to feel normal (dependence) and more of it to feel good (tolerance).

THE ONE-LINE TRUTH

Alcohol Use Disorder (AUD) is diagnosed when someone shows 2 or more of 11 behaviors within 12 months—like needing more alcohol to get the same effect (tolerance), feeling sick when stopping (withdrawal), or continuing to drink despite harm to health, work, or relationships.

The chain — how it unfolds

1. Alcohol enhances GABA (the brain's main inhibitory neurotransmitter, which calms neurons) by binding to GABA-A receptors and making them more responsive, and it inhibits glutamate (the brain's main excitatory neurotransmitter, which activates neurons) by blocking NMDA receptors. This produces immediate anxiolysis (relief from anxiety) and euphoria (intense pleasure and relaxation). — why: The ventral tegmental area (VTA—a cluster of dopamine-making neurons deep in the midbrain) responds to alcohol by firing rapidly and sending a surge of dopamine to the nucleus accumbens (the brain's reward hub, sitting just above the brainstem). The nucleus accumbens tags alcohol as a powerful positive experience and signals the prefrontal cortex: 'Remember this—do it again.' This dopamine surge is the biological basis of reward and reinforcement, driving repeated drinking behavior.

2. Repeated alcohol exposure triggers neuroadaptation: GABA-A receptors down-regulate (the brain reduces their number and sensitivity) and NMDA glutamate receptors up-regulate (the brain increases their number and sensitivity), shifting baseline brain excitability upward. — why: The brain constantly seeks equilibrium (stable activity level). Because alcohol artificially boosts inhibition (via GABA) and suppresses excitation (via glutamate block), the brain compensates by reducing its own calming machinery and building more activating machinery. This is why tolerance develops—the same dose of alcohol now produces less calming effect, and the person needs more alcohol to feel relaxed or 'normal.' Tolerance is not safety; it's a sign the brain has chemically remodeled itself and is now dependent.
3. Without alcohol, the now-unopposed hyperglutamatergic state (excess excitatory tone with insufficient inhibitory tone) causes alcohol withdrawal syndrome: tremor (shaking, especially in the hands), a fast heart rate (tachycardia) (heart rate over 100), high blood pressure (hypertension) (systolic BP over 140), heavy sweating (diaphoresis) (heavy sweating), anxiety, insomnia, nausea, and overactive reflexes (hyperreflexia) (exaggerated reflexes). Severe withdrawal includes generalized tonic-clonic seizures (6–48 hours after last drink) and delirium tremens (DTs—48–96 hours out, with confusion, hallucinations, and autonomic instability). — why: The brain's compensatory up-regulation of excitatory circuits (more NMDA receptors, less GABA tone) is suddenly unmasked when alcohol—the sedative that was holding the system in check—is removed. Autonomic hyperactivity (overactive sympathetic nervous system—the fight-or-flight system) and CNS excitotoxicity (neuron injury from too much glutamate flooding the cells) produce the withdrawal syndrome. Untreated delirium tremens has a mortality rate of 5–15% due to cardiovascular collapse, hyperthermia (dangerously high body temperature), or seizure complications.
4. Chronic alcohol exposure damages the prefrontal cortex (the executive control center at the front of the brain, responsible for decision-making, impulse control, and planning) and the hippocampus (the memory center deep in the temporal lobe, responsible for forming and storing new memories). This impairs judgment, impulse control, working memory, and insight—making it nearly impossible to stop drinking despite mounting medical, financial, social, and legal consequences. — why: Gray matter atrophy (shrinkage of the neuron cell bodies) in the prefrontal cortex removes the brain's 'brakes' on impulsive behavior. The person knows intellectually that drinking is harmful—they can list the consequences—but they cannot override the craving, delay gratification, or plan effectively for long-term benefit over short-term relief. Hippocampal damage impairs memory consolidation, so the person may forget the severity of past consequences or fail to learn from repeated relapses. This is not a moral failure; it is structural brain damage that undermines the very capacities needed for behavior change.

5. Thiamine (vitamin B1) deficiency develops because alcohol impairs thiamine absorption in the small intestine (by damaging the gut lining and interfering with active transport) and increases thiamine consumption (the body uses more thiamine to metabolize alcohol). Thiamine is essential for glucose metabolism in neurons, so deficiency starves high-demand brain regions—the mammillary bodies (tiny memory relay stations at the base of the hypothalamus) and the thalamus (the sensory gateway in the center of the brain)—causing Wernicke encephalopathy and, if untreated, Korsakoff syndrome. — why: Neurons rely exclusively on glucose for energy, and thiamine is a required cofactor (helper molecule) for enzymes that break down glucose. Without thiamine, neurons cannot use glucose and begin to die. Wernicke encephalopathy presents acutely with the classic triad: confusion, ophthalmoplegia (weakness or paralysis of eye muscles—look for involuntary eye jerking (nystagmus), or jerky eye movements, and inability to move eyes outward), and loss of coordination (ataxia) (wide-based, unsteady gait). If IV thiamine is not given immediately—before any glucose infusion, which can precipitate acute crisis—the damage becomes permanent: Korsakoff syndrome, marked by irreversible anterograde amnesia (cannot form new memories), retrograde amnesia (loss of old memories), apathy, and confabulation (unconsciously fabricating stories to fill memory gaps without intent to deceive).
6. Co-occurring mental health disorders—major depressive disorder (MDD), post-traumatic stress disorder (PTSD), generalized anxiety disorder (GAD), and bipolar disorder—are present in 50–70% of people with AUD and independently predict relapse, worse functional outcomes, and higher suicide risk. — why: The brain circuits that regulate stress, reward, and emotion overlap heavily. Chronic stress and untreated depression or trauma keep cortisol (the body's main stress hormone, released by the adrenal glands) elevated, which sensitizes (makes more reactive) the amygdala (the brain's alarm center) and dysregulates the hypothalamic-pituitary-adrenal (HPA) axis (the body's stress-response system). This drives continued drinking as self-medication: alcohol temporarily calms the hyperactive stress system and numbs emotional pain, but it worsens depression and anxiety over time. Treating AUD without addressing co-occurring psychiatric illness leads to high relapse rates because the underlying driver—untreated mental suffering—remains.
7. Social determinants of health—housing instability, unemployment, food insecurity, trauma history (especially childhood trauma), incarceration, and lack of social support—independently predict AUD severity, treatment dropout, and relapse. — why: Chronic stress from unstable housing, violence, or financial crisis keeps the HPA axis activated, which sensitizes the brain's reward and stress circuits and makes alcohol cues more powerful and harder to resist. Without stable housing, employment, or a supportive social network, the person returns to alcohol as the only available coping mechanism. Recovery requires addressing both the biology (medication-assisted treatment, therapy) and the social environment (stable housing, job training, trauma-informed care, peer support) simultaneously—fixing one without the other usually fails.

8. Long-term heavy drinking causes progressive liver damage: hepatic steatosis (fatty liver—fat droplets accumulate in hepatocytes), alcoholic hepatitis (acute inflammation with yellowing of the skin and eyes (jaundice), fever, and right upper quadrant pain), and cirrhosis (permanent scarring that blocks blood flow through the liver). Cirrhosis leads to portal high blood pressure (hypertension) (high pressure in the portal vein, which brings blood from the intestines to the liver), causing esophageal varices (swollen, fragile veins in the esophagus that can rupture and bleed massively), fluid buildup in the belly (ascites) (fluid accumulation in the abdomen), hepatic encephalopathy (confusion and altered mental status from ammonia buildup the liver can no longer clear), and hepatorenal syndrome (kidney failure triggered by severe liver failure). — why: The liver metabolizes alcohol via alcohol dehydrogenase into acetaldehyde (a highly toxic compound that damages DNA, proteins, and cell membranes) and then into acetate. Acetaldehyde triggers oxidative stress (floods cells with reactive oxygen species) and inflammation, directly injuring hepatocytes (liver cells). Over years, repeated injury causes fibrosis (scar tissue formation), which stiffens the liver and blocks blood flow. Once cirrhosis develops, the liver cannot synthesize clotting factors (leading to bleeding risk), albumin (leading to swelling (edema) and fluid buildup in the belly (ascites)), or detoxify ammonia (leading to encephalopathy). Portal high blood pressure (hypertension) shunts blood around the liver, causing varices that can rupture without warning and bleed fatally. Cirrhosis also dramatically increases the risk of hepatocellular carcinoma (liver cancer).

Spot it — what you see, and why

- Tolerance: The brain tries to balance out alcohol's calming effect by turning down its own 'slow-down' switches (GABA receptors—docking sites on nerve cells that respond to the brain's main calming messenger) and turning up its 'speed-up' switches (glutamate receptors—docking sites that respond to the brain's main exciting messenger). Over time, the same amount of alcohol does less, so a person needs to drink more and more to feel the same buzz.
- Withdrawal symptoms: When alcohol suddenly stops, all those 'speed-up' switches are still cranked high, but the braking effect of alcohol is gone. The brain races out of control, causing shaking hands (tremor), a pounding fast heart (tachycardia—heart beating over 100 times per minute), high blood pressure, heavy sweating, anxiety, trouble sleeping, and nausea. In severe cases, this overactive brain can trigger seizures (sudden electrical storms in the brain) or delirium tremens (DTs—dangerous confusion with hallucinations and unstable blood pressure and heart rate, usually starting 2 to 4 days after the last drink).

- Drinking more or longer than intended: Alcohol shrinks and weakens the front part of the brain (the prefrontal cortex—the area that controls impulses and plans ahead). At the same time, a deeper reward center (the nucleus accumbens—the brain's pleasure hub deep beneath the forehead) floods with dopamine (a brain messenger that says 'do that again!') every time the person drinks. Together, these changes make it almost impossible to stick to a plan like 'just one beer' once drinking starts.
- Persistent desire or unsuccessful efforts to cut down: The control circuits in the prefrontal cortex (the front of the brain that pumps the brakes on urges) are damaged, so willpower weakens. Meanwhile, the brain's stress and craving circuits (especially the amygdala, the brain's alarm center, and the anterior cingulate cortex, which flags conflicts between what you want and what you should do) become extra sensitive—they fire more easily, making every urge to drink feel overwhelming. Even when the person sees the harm and truly wants to quit, the brain's wiring works against them.
- Spending a lot of time obtaining, using, or recovering from alcohol: The brain's reward system (centered in the ventral tegmental area and nucleus accumbens—deep structures that drive motivation and pleasure) gets hijacked: it now treats alcohol as the top priority, above hobbies, friends, and work. Getting alcohol, drinking it, and then recovering from being drunk or withdrawing can eat up hours or days at a time.
- Cravings or strong urges to drink: Reminders of alcohol—seeing a bottle, smelling liquor, or feeling stressed—trigger a burst of dopamine (the brain's 'do that again' messenger) in the reward circuits, and that burst screams 'drink now!' The brain's glutamate system (the main excitatory messenger that controls excitement and learning) also goes into overdrive during stress or early withdrawal, making cravings feel impossible to ignore.

Red flags — act now

- Delirium tremens (DTs): severe confusion, seeing or feeling things that are not there (hallucinations), unstable vital signs (fever, fast heart over 120, high or swinging blood pressure), usually 2 to 4 days after the last drink—life-threatening and requires intensive care with IV benzodiazepines to calm the brain
- Seizures during withdrawal: full-body convulsions (generalized tonic-clonic or grand mal seizures), typically 6 to 48 hours after stopping alcohol—require emergency benzodiazepines and hospital admission to prevent status epilepticus (a seizure that will not stop) (seizures that do not stop)
- Wernicke encephalopathy: sudden confusion, paralyzed or wobbly eye movements (ophthalmoplegia), and unsteady walking (ataxia) from severe thiamine (vitamin B1) deficiency—give IV thiamine immediately before any glucose to prevent permanent memory damage (Korsakoff syndrome)

- Suicidal thoughts or suicide attempt: alcohol use disorder increases suicide risk tenfold—screen every visit, ask directly about plans to harm oneself, and arrange immediate safety (remove means, involve family, consider hospitalization)
- Mixing alcohol with opioids or benzodiazepines: both types of drugs slow breathing and brain activity; together they can stop breathing entirely (respiratory arrest) and cause death—always ask about all drugs and pills

Treat it — in this order

1. Screen all adults age 18 and older annually with AUDIT-C (men score 4 or higher, women 3 or higher equals positive) or single-question screen ('How many times in the past year have you had 5 or more drinks in a day for men, or 4 or more drinks in a day for women?'—one or more times equals positive). Then confirm diagnosis using DSM-5-TR criteria: 2 or more of 11 symptoms in a 12-month period equals alcohol use disorder. → Universal screening catches unhealthy drinking and alcohol use disorder before cirrhosis, pancreatitis, heart failure, or cancer develops. Detecting the problem early allows brief intervention—a 5 to 15 minute conversation by any clinician (doctor, nurse, pharmacist) using motivational interviewing techniques (asking open-ended questions, listening without judgment, and helping the person identify their own reasons to change). Brief intervention reduces drinking in 1 out of 4 people who screen positive but do not yet meet criteria for alcohol use disorder. For people with alcohol use disorder, screening opens the door to pharmacotherapy (medication treatment) and specialty referral. The USPSTF gives screening and brief intervention a Grade B recommendation, meaning there is high certainty of moderate benefit and it should be standard care for every adult every year, just like blood pressure screening.

2. Naltrexone 50 mg by mouth once daily or 380 mg intramuscular injection once monthly (blocks mu-opioid receptors in the mesolimbic reward pathway, reducing the euphoria and reinforcement from drinking) OR acamprosate 666 mg by mouth three times daily (modulates GABA and glutamate activity in the brain, reducing craving and the discomfort of early abstinence) → Both medications are FDA-approved for alcohol use disorder and recommended as first-line by APA, ASAM, and the VA/DoD (Veterans Affairs and Department of Defense). Meta-analyses (studies that combine results from many trials) show naltrexone reduces heavy drinking days by about 4 days per month and cuts the chance of relapse to heavy drinking by 36 percent. Acamprosate is equally effective and is the better choice if liver disease is present because it is not metabolized by the liver. Naltrexone works by blocking the endogenous opioid (the body's own morphine-like chemicals) release that normally happens when you drink, so alcohol feels less rewarding. Acamprosate restores the balance between GABA (the brain's main calming chemical) and glutamate (the brain's main activating chemical) that is disrupted by chronic alcohol exposure. Both medications work best when combined with counseling, but medication alone is more effective than counseling alone. These are not 'willpower pills'—they change brain chemistry to give the prefrontal cortex (the front of the brain that handles decision-making and self-control) a fighting chance against the hijacked reward circuit.
3. Benzodiazepine-based alcohol withdrawal protocol using CIWA-Ar (Clinical Institute Withdrawal Assessment for Alcohol, revised—a 10-item scale that scores tremor, sweating, agitation, headache, nausea, and hallucinations) with symptom-triggered dosing of lorazepam 1 to 2 mg or chlordiazepoxide 25 to 100 mg every 1 to 2 hours as needed until CIWA-Ar is below 8, plus thiamine 500 mg IV or IM three times daily for at least 3 days → Benzodiazepines are GABA-A receptor agonists, meaning they activate the same calming receptors that alcohol does. This prevents the uncontrolled excitatory rebound (the glutamate surge in the brain) that causes withdrawal seizures and delirium tremens. Symptom-triggered dosing—giving medication only when withdrawal symptoms appear rather than on a fixed schedule—uses 50 percent less total benzodiazepine and shortens hospital stay compared to fixed-schedule dosing, according to ASAM and APA guidelines. Withdrawal seizures occur in 5 to 15 percent of people who stop drinking abruptly after chronic heavy use; benzodiazepines reduce seizure risk to near zero. Thiamine prevents Wernicke encephalopathy (acute brain damage from thiamine deficiency). This is the only pharmacologic approach with strong evidence for managing acute alcohol withdrawal. The brain's GABA and glutamate systems recalibrate over 3 to 7 days, then benzodiazepines are tapered and stopped. Outpatient withdrawal management is safe for people with mild withdrawal (CIWA-Ar under 10), no history of seizures or DTs, and a supportive home environment. Inpatient management is needed for severe withdrawal, medical comorbidities (other diseases like heart failure or infection), or lack of social support.

4. Screen for and treat co-occurring major depressive disorder, generalized anxiety disorder, PTSD (post-traumatic stress disorder), or bipolar disorder with evidence-based psychotherapy (cognitive-behavioral therapy, trauma-focused therapy such as prolonged exposure or EMDR—eye movement desensitization and reprocessing) and/or antidepressants (SSRIs like sertraline or escitalopram, SNRIs like venlafaxine) → About half of people with alcohol use disorder also have a co-occurring mental health disorder. Depression and anxiety are not just complications of drinking—they often came first and increase relapse risk by 2 to 3 times because the person uses alcohol to self-medicate (to numb emotional pain or quiet intrusive thoughts). Untreated trauma reactivates the amygdala (the brain's alarm center that flags danger and stores emotional memories) and the hypothalamic-pituitary-adrenal axis (the body's stress hormone system), which increases craving and impulsive drinking. Integrated treatment—addressing both the substance use disorder and the mental health disorder at the same time by the same clinical team—improves outcomes for both. SSRIs and SNRIs restore serotonin and norepinephrine signaling in the brain, reducing depression and anxiety. Cognitive-behavioral therapy teaches skills to challenge distorted thoughts ('I am worthless,' 'nothing will ever get better') and to break the link between emotions and drinking. Trauma-focused therapy processes traumatic memories so they lose their emotional charge. Treating the mental health disorder reduces the neurobiological drive to drink and gives the person a reason to stay sober.
5. Address social determinants of health: connect to stable housing (transitional housing, sober living, Housing First programs), food assistance (SNAP—Supplemental Nutrition Assistance Program), income support (SSI/SSDI—Supplemental Security Income or Social Security Disability Insurance for people unable to work, TANF—Temporary Assistance for Needy Families), and job training or supported employment programs → Homelessness, food insecurity, and unemployment create chronic activation of the stress axis in the brain. The hypothalamus (a control center deep in the brain) releases CRH (corticotropin-releasing hormone), the pituitary gland (a small gland under the brain) releases ACTH (adrenocorticotrophic hormone), and the adrenal glands (glands on top of the kidneys) release cortisol (the body's main stress hormone). High cortisol strengthens the amygdala's emotional memory circuits and weakens the prefrontal cortex's executive control, which increases craving and impulsive relapse. Studies show that providing stable housing through Housing First programs (giving people an apartment with no requirement to be sober first) reduces heavy drinking by 40 to 50 percent and increases engagement in treatment by nearly 60 percent. A safe place to sleep, regular meals, and a daily routine allow the prefrontal cortex to recover from alcohol-induced atrophy (shrinkage). MRI studies show the prefrontal cortex begins to regrow within 6 to 12 months of abstinence—but only if the environment is stable. This is not just social work; it is neuroscience-informed care. Addressing social determinants is harm reduction and is as evidence-based as any medication.

Your top priorities at the bedside

1. Assess for withdrawal using the CIWA-Ar (Clinical Institute Withdrawal Assessment for Alcohol, revised) score every 1 to 4 hours depending on severity—check tremor, sweating, agitation, headache, nausea, hallucinations, anxiety, and orientation. A score of 8 or higher signals moderate withdrawal needing medication; 15 or higher means severe withdrawal. — why: Alcohol withdrawal progresses in stages: mild symptoms (6 to 12 hours—tremor, anxiety, nausea), seizures (12 to 48 hours—sudden brain overactivity when alcohol's calming effect is gone), then delirium tremens (48 to 96 hours—autonomic storm with fever, a fast heart rate (tachycardia) over 120, high blood pressure (hypertension), confusion). CIWA-Ar scores guide symptom-triggered benzodiazepine dosing to prevent progression and save lives.
2. Administer benzodiazepines (most often lorazepam 1 to 4 mg IV or PO, diazepam 10 to 20 mg IV or PO, or chlordiazepoxide 50 to 100 mg PO) according to CIWA-Ar score or fixed-schedule protocol. Give lorazepam or oxazepam if liver disease is present because they bypass liver metabolism. — why: Alcohol enhances GABA (the brain's calming neurotransmitter) and blocks glutamate (the brain's excitatory signal). When alcohol is removed, glutamate floods the brain causing hyperactivity—tremors, seizures, a fast heart rate (tachycardia), high blood pressure (hypertension). Benzodiazepines mimic alcohol's GABA effect, calming overactive neurons and preventing seizures and delirium tremens, which kill 5 to 15 percent of untreated patients.
3. Give thiamine 100 mg IV or IM before any IV dextrose (sugar water), then continue thiamine 100 mg daily by mouth for at least 3 to 5 days. Add folate 1 mg daily and a multivitamin. — why: Chronic alcohol blocks thiamine (vitamin B1) absorption in the gut and storage in the liver. Thiamine is essential for brain glucose metabolism. Deficiency causes Wernicke encephalopathy (confusion, abnormal eye movements called involuntary eye jerking (nystagmus), unsteady walking called loss of coordination (ataxia)) and Korsakoff syndrome (permanent short-term memory loss). Giving IV dextrose without thiamine first burns up the last thiamine stores and can trigger or worsen Wernicke encephalopathy, causing irreversible brain damage.